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DES MOINES

FOREWORD

Hardly a year passes without a rabies "scare" somewhere in Iowa. In such areas the cry of "mad dog" is usually amplified far out of proportion to the actual danger.

Rabies, of course, is a killing disease, but control of it will never be successful so long as panic reigns when the disease occurs. Control must be calm, deliberate, level-headed and not impeded by wild rumor.

There are several simple things to do when rabies is suspected, and in this bulletin I. H. Borts, M.D., associate director of the State Hygienic Laboratory of the Iowa State Department of Health, tells what they are. His discussion also shows the extent of rabies in Iowa and explains the nature of the disease.

The recognition and advisory control of this disease by the State Hygienic Laboratory constitutes one of the most valuable public services rendered to the people of Iowa.

Walter L. Bierring

Commissioner of Health

IOWA PUBLIC HEALTH BULLETIN

PUBLISHED QUARTERLY BY THE IOWA STATE DEPARTMENT OF HEALTH

WALTER L. BIERRING, M.D., Commissioner.....Editor
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RABIES

IRVING H. BORTS, M.D.,
Associate Director, State Hygienic Laboratory,
Iowa City, Iowa

Rabies or hydrophobia is an acute contagious and almost without exception a fatal disease caused by a specific virus. It is transmitted to man and susceptible animals through the saliva by the bites of rabid animals, most frequently the dog.

There are few diseases more dreaded by man than rabies. In comparison with tuberculosis and infantile paralysis, rabies has played a very small part in the death of human beings. When an individual is bitten by a questionable animal it is always best to confirm or disprove the presence of the disease. If absent, this fact should be carefully impressed upon the patient as otherwise the dread of infection may weigh heavily upon his mind, leading to distressing, nervous symptoms, "Lyssophobia" or fear of rabies.

Rabies in animals has been known since the time of Aristotle, 384 B.C. Celsus in the first Century gave the earliest detailed description of rabies in man following the bite of a rabid dog and recommended that the wounds be bathed and burned with hot irons.

Negri in 1903 was the first to describe specific bodies in the brain of rabid animals. These bodies are called "Negri bodies" and remain to this day the basis for the microscopic diagnosis of rabies.

Little Excuse for Rabies

There is little excuse for the continuation of this horrible disease for it can be controlled and completely eradicated, if the necessary eradication measures are strictly enforced.

Thousands of dollars worth of farm stock and a number of human lives are lost each year in the United States due to this disease. Since the dog is the chief agent responsible for the spread of the disease to man and domestic animals, control measures are centered around this animal. Compulsory muzzling of all dogs and quarantining of all imported dogs has led to complete eradication of rabies in England, North Germany, Ireland, Sweden, Norway, Denmark, Switzerland, Hawaii, Australia, Panama, and the Canal Zone.

That carriers of rabies exist is well exemplified by the vampire bat in Trinidad and Brazil whose bite leads to fatal rabies in man and cattle although the bats themselves show little or no effects of the disease. Locally the skunk is to be suspected as being a carrier of rabies or at least it appears to serve as an endemic focus of infection. During the past winter six skunks, one weasel, one mink and one oppossum were trapped.

Their brains were examined microscopically and by mouse inoculation for evidence of rabies with negative findings. On the other hand of eighteen skunks submitted as rabies suspects during the last thirty months all were found to be infected.

Contracted Through Bites

Rabies is invariably contracted through bites, skin abrasions or contamination of the mucous membranes such as those of the eye, with saliva of the infected animals. The virus, having special affinity for the central nervous system, travels from the point of bite or exposure by way of the nerve sheaths to the brain. The infectious agent is apparently contained in the saliva of the infected animal at irregular intervals. It may be present in the saliva a few days before the onset of rabies symptoms and survives in the brain tissue many days after the death of the animal. Milk from rabid animals does not contain the infecting agent. The virus is readily destroyed by drying, disinfectants such as cresol, boiling, burning and by exposure to sunlight.

It is generally agreed that the removing of heads or the skinning of suspicious animals should be carried out by a veterinarian or one specially familiar with the nature of the disease. It has been adequately demonstrated that all rabid animals do not constantly excrete the infectious agent in the saliva. This may help explain why only about 20 percent of human beings who have been exposed to rabid saliva but who failed to undergo the Pasteur treatment contract rabies. So uncertain is this situation, however, that all persons exposed should receive the treatment.

Minor abrasions and scratches are sufficient for the entrance of the

virus although large, deep and ragged wounds are of a more serious nature. The virus does not penetrate the unbroken skin. Bites about the head and neck are always very serious, hence no time should be lost in taking intensive treatment as the virus has a very short distance to travel to the brain. If treatment is delayed a fatal condition may develop. Bites through the clothing are less dangerous than those on the bare skin as the saliva may be absorved by the cloth.

Death Rates

According to the League of Nations Health Bulletin, among 635,142 persons bitten by rabid animals 0.38 percent died of rabies in spite of treatment. Among 1,715 persons bitten by wolves the death rate was 8.59 percent, indicating that deep puncture wounds are very serious. The death rates for deep and superficial bites were 0.73 percent and 0.18 percent respectively. Where the bare skin was exposed the death rate was 0.40 percent in these treated cases, whereas bites through the clothing caused a reduced death rate of 0.11 percent. In relation to position of the bite, while 2.2 percent died where the bite was about the head, bites about the arm, trunk and leg caused rates of 0.26 percent, 0.11 percent, and 0.18 percent respectively. Delay in starting treatment is shown to be responsible for an increased number of deaths. With delay of treatment up to 4 days 0.25 percent died, 5 to 7 days 0.27 percent, 8 to 14 days 0.23 percent and 14 days or more 0.83 percent died. The hazards of treatment are so small that one should not hesitate to take the treatment when indicated. Among 635,142 cases treated, paralytic accidents occurred in 37 or 1 in 17,221 cases. (.0058 percent).

INCUBATION PERIOD

The incubation period, the time intervening between exposure and the beginning of symptoms of rabies, varies widely and is dependent upon many factors, such as the location of the bite, severity of the wound or wounds, the amount of virus absorbed, the virulence of the virus, and the age, size and nutritional status of the persons or animals involved. There also appears to be a variation in susceptibility of different animals to different doses and races of virus. The incubation period in man may be as short as ten days where the bites are about the head or as long as four months where the exposure is on the trunk, arms or legs. The average period is about 45 days. In animals the period varies from 14 to 90 days depending on the above factors.

PREVALENCE OF RABIES

Rabies in man is rare compared to its wide prevalence among dogs

and other animals, both wild and domestic. Two thirds of the human cases occur in persons under 20 years of age. More cases occur among males than females. The death rate, averages about 0.075 per 100,000 population and is higher for the southern than for the northern half of the United States.

Dogs Responsible

Dogs, especially strays, are responsible for the greater number of rabies cases. This is due chiefly to the freedom with which they can contact animals and persons. Although horses, wolves and foxes sometimes inflict severe biting injuries this percentage is small in comparison with severe bites inflicted by dogs.

Table I indicates the number of rabies specimens received at the State Hygienic Laboratory during the interval January 1, 1938 to July 1, 1941. It also shows the type of animal and the number found positive and negative. The Iowa map shows the distribution over the state by counties.

TABLE I

Rabies Specimens Received at the State Hygienic Laboratory, January 1, 1938 to July 1, 1941

Animal	Positive	Negative	Total
Dog	28	82	110
Cat	17	29	46
Cow	27	11	38
Squirrel	6	20	26
Skunk	18	6*	24
Horse	10	2	12
Hog	6	4	10
Fox	4	0	4
Goat	1	0	1
Monkey (pet)	1	0	1
Sheep	1	0	1
Wolf	1	0	1
Gopher	0	1*	1
Mink	0	1	1
Mouse (field)	0	1	1
Oppossum	0	1*	1
Rabbit (domestic)	0	4	4
Rat	0	9	9
Weasel	0	1*	1
	120	172	292

* Apparently normal animals caught during the trapping season.

Positive Rabies Specimens January 1, 1938—July 1, 1941

SEASONAL INCIDENCE

Contrary to old beliefs, rabies is not more prevalent during the so-called "Dog Days" of July and August. Iowa's largest out-breaks of rabies occurred in the late winter and spring months of 1925 and 1931.

Table II indicates the monthly percentage of rabid animals diagnosed at the State Hygienic Laboratory during the year 1916-40 inclusive. A summary of 25 years indicates that in Iowa rabies has been somewhat more common in June and that the incidence is slightly less frequent for the last six months than for the first six months of the year.

TABLE II—RABIES IN IOWA BY MONTHS

Percentage distribution of 1,042 positive animals 1916 to 1940 inclusive.

	Percent of Total
January	9.1
February	8.3
March	8.4
April	9.0
May	10.7
June	11.8
July	8.0
August	8.0
September	6.5
October	7.4
November	5.9
December	6.9

BEHAVIOR OF RABID ANIMALS

Rabies Simulates other Diseases

Rabies in animals at times may simulate other disease conditions so that the final diagnosis requires the service of expert laboratory workers.

This disease may manifest itself either in the "furious" or "dumb" type of which both are dangerous.

In the furious type three stages may be observed. In the first stage the animal appears dull and melancholy and does not respond in the usual manner. In the second stage, the animal suddenly shows fits of excitement, foams at the mouth (excess salivation), bites everything that comes its way and has difficulty in swallowing. There is frequently a peculiar hoarseness to the voice. In this restless stage dogs leave home, travel many miles and bite dogs, animals, or persons that come in their path. The animal may die in this stage but frequently passes into the paralytic stage characterized by "biind staggers", weakness of the hind legs, paralysis of the hind quarters and death. While the entire period of the disease usually involves five to seven days death may not occur for as long as ten days.

Dog Owners Exposed

In the dumb type rarely are furious symptoms manifest. From the onset, weakness of the legs, and paralysis of the jaw, tongue, and throat are prominent. At this time the dog's behavior suggests that he may have a bone lodged in his throat. Owners of these animals are frequently exposed to rabies while attempting to inspect the throat to dislodge any obstructive object present. This reaction is due to paralysis of the throat muscles simulating an obstruction. The animal bites only if disturbed. Being too weak to run he seeks a dark hiding place and dies there in a few days following a progressive type of paralysis.

WHAT TO DO WITH THE SUSPECTED ANIMALS

Do not kill the animal. If it is killed early in the disease the Negri bodies may be so widely scattered or be so small as to be overlooked on microscopic examination. Thus it is always advisable to keep the suspected animal alive at least long enough to permit full development of symptoms. Put it in a secure pen, with plenty of food and water, or, preferably, place it in the hands of your veterinarian who is skilled in the diagnosis of rabies and other allied animal diseases. If the animal has rabies it will show progressive symptoms and die usually with-

in 3 to five days. If it is alive and well at the end of 14 days one can be fairly certain that rabies does not exist.

Use Rubber Gloves

If it is necessary to kill the animal do not shoot it in the head as the intact brain is essential for adequate laboratory examination. Rubber gloves should be used in severing the head of the animal which should then be placed in a tin container, such as a 10 to 25 pound lard pail. This pail, with its lid securely attached, should then be placed in a 50 pound lard can containing equal parts of ice and sawdust and taken to the State Hygienic Laboratory where the examinations are made free of charge. If this is not feasible, the specimen may be sent by Prepaid Express. The container should be marked "Rush—Rabies Suspect". Whenever possible the specimen should be taken to the laboratory as in hot weather icing is frequently inadequate and a reliable examination may not be possible due to putrefaction.

At the laboratory the microscopic examination of the brain can usually be accomplished in one or two hours. Realizing that this examination is not perfect, all negative microscopic specimens are inoculated into young mice for confirmation. Of 273 specimens received at the laboratory from January 1, 1938 to July 1, 1941, 18 (10 percent) found negative on microscopic examination were shown by mouse inoculation to be positive. This figure is somewhat lower than those reported by Koch and by Leach who found approximately 12 percent of the negative microscopic speciments positive by mouse inoculation. (See Table III) Mice so inoculated usually show evidence of rabies in 7 to 14 days but in a very few instances a longer period is required. Mice four to six weeks of age are essential for consistent results. Inoculated white mice develop only the dumb type of rabies, whereas, other experimental animals such as rabbits and guinea pigs usually develop the furious type.

TABLE III

Comparison of the Direct Microscopic Brain Examination for Negri Bodies and Mouse Inoculation. January 1, 1938—July 1, 1941
State Hygienic Laboratory, Iowa City, Iowa.

Positive	microscopic	examination	and	positive	mouse inoculation	95
Negative	"	"	"	positive	" "	18
Negative	"	"	"	negative	" "	161
Doubtful	"	"	"	positive	" "	3
Doubtful	"	"	"	negative	" "	8
Unsatisfactory	"	"	"	positive	" "	3
Unsatisfactory	"	"	"	negative	" "	6
						294

WHAT TO DO WITH THE PERSON EXPOSED

In general it is desirable that the Pasteur treatment be given promptly whenever one is bitten or the abraided skin exposed to the saliva of a suspicious animal.

A. **Consult your family physician at once** for cauterization of the wound with fuming nitric acid.

B. **Start Pasteur treatment immediately:—**
   1. Where the wounds or salivary exposure are about the head and neck.
   2. Where the wounds are deep and extensive on any part of the body, arms, or legs.
   3. Where the biting animal has escaped.

C. **Delay the Pasteur treatment for observation of the animal and for laboratory examination:—**
   1. Where the wounds are of a minor nature, such as scratches or abrasions not located in the region of the head.
   2. Where the apparently unbroken skin is contaminated with saliva.

Should the microscopic examination of the brain be reported positive, doubtful, or unsatisfactory, **start Pasteur treatment without further delay.** If the microscopic examination is negative and the animal appeared clinically rabid it is **desirable to take treatment** as it must be remembered that about 12 percent of brain specimens microscopically negative prove positive on mouse inoculation.

PREVENTION

As shown by countries that have controlled rabies, the procedures that must be followed are:—

1. Yearly vaccination of all dogs.
2. Muzzling of all dogs not penned or held on a leash.
3. Quarantine of all imported dogs for six months.
4. Disposal of all stray dogs.
5. Prompt destruction of all dogs and cats bitten by rabid animals. Valuable animals may be vaccinated and quarantined.

HOW TO OBTAIN ANTI-RABIC (PASTEUR) TREATMENT

Anti-rabic treatment may be secured at all hours at the State Department of Health, Des Moines, Iowa. Arrangements can be made by personal application or for delivery by mail or bus according to the emergency.

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RABIES

Virginia State Department of Health
Richmond, Virginia
1943

Rabies

Rabies primarily is a disease of dogs but is communicable to man, hogs, horses, cattle and other animals. The virus or germ is contained in the saliva of the infected animal and is chiefly conveyed by a bite or contact with the infective saliva.

It is commonly thought that rabies is a summer disease. This idea is without foundation. Rabies is just as prevalent in winter as it is in summer. Dogs are more irritable in hot weather and more likely to snap; but laboratory examinations of dogs' heads have, for years, indicated more rabies in the months of October, November and December than in the months of July, August and September.

Types and Symptoms

There are two types of rabies, dumb and vicious. Animals affected with the dumb type do not usually attack or wander from home. They usually stop eating when the disease appears; then as paralysis sets in the jaw gapes and swallowing becomes painful or impossible. The name *hydrophobia,* means fear of water. Saliva is increased and drips from the mouth. All through the stages of the disease there is a tendency on the part of the animal to chew hard objects such as chips of wood or rocks. Persons are infected from this type in their attempt to treat the sick dog, believing it sick from some other disease. This type occurs when the seat of the infection is in the spinal cord.

Dogs affected with the vicious type differ in symptoms in that in the early stages they wander, are nervous and excitable, and will run away or shy at the slightest noise. At certain times they will attack any man or animal that happens to cross their paths. With this type of disease the dog may travel many miles and attack many animals in his wanderings. In the latter stages the symptoms are the same as those of the dumb type.

What To Do With The Dog

When a dog is suspected of having rabies, *do not kill it.* The surest way of determining whether the dog has this disease is by observing the dog. Evidence of rabies usually can be found by examining the dog's brain, but the living dog gives the best evidence that it did not have rabies. If a dog has rabies it will always die from this disease within a few days; if a dog lives for fourteen days after biting anyone, this is positive proof that the dog did not have rabies at the time he bit the person. If circumstances are such that the dog cannot be shut up, then kill the dog, taking care not to injure the brain.

Remember that the safest course when a dog bites a person or even livestock is to confine the animal for two weeks to determine whether or not symptoms of rabies develop. If suspicious symptoms do develop, the dog should be killed and the head shipped to the nearest state laboratory.

Shipping Directions

Ship promptly by express prepaid. Since it virtually is impossible to make an accurate examination of a decomposed head, care should be exercised to prevent decomposition. Probably the best method is to place the head in a metal container and then to put this container in a large bucket filled with ice—a wooden outside bucket is preferable to a metal one. If it is impossible to get ice, sawdust may be used; but, especially in warm weather, it is far better to use ice.

Mark the bucket "PERISHABLE" and address the package carefully and plainly. Tack onto the outside bucket containing the head a note telling why the dog was killed or whether it died a natural death, whether it had been acting strangely, showed curious symptoms or had bitten any person or any animal. This information also should be forwarded in a letter to the Department. If these particulars are received the Department will be able to give advice.

The Laboratory Report

The results of the laboratory examination, when positive, are reported by telegram, collect, unless otherwise requested, and are confirmed by mail.

A report of POSITIVE means that the animal had rabies.

A report of NEGATIVE does *not* necessarily mean that the animal did not have rabies. In the early stages of the disease, microscopic examination of the brain may not show the disease. That is why the Department advises not to kill the dog if it can be avoided, but to confine it.

The Bite

Bites about the head and face are much more dangerous than those on the arms and legs, because the nerve supply in these regions is more abundant and in closer proximity to the brain. Rabies virus travels along the nerve fibers to the brain or central nervous system. The closer the bite is to the brain, the more quickly the disease will develop.

The slightest scratch from the tooth of a rabid dog is dangerous.

Cauterization alone should never be depended upon to prevent the development of rabies. Rabies vaccine should be administered in all cases where persons have been bitten by an animal known or suspected to be rabid.

Anti-Rabic Treatment

Anti-rabic treatment is a vaccine against the disease and not a cure for it. To be effective, this treatment should be used promptly after exposure. In case of a bite on the face, head, arms or hands, treatment should be started immediately. When the bite is on the body or the legs, it is safe to wait a few days until it has been determined whether the dog had rabies.

When used promptly, rabies vaccine almost invariably prevents the disease. That is why prompt treatment is advised. The treatment is relatively harmless and can be given by any physician.

Keep in mind that—*when rabies once develops there is no known remedy for it.* It is better, therefore, to be safe than sorry. The only money involved in taking the treatment is the risk of the county's or city's refusing to pay for the service when it can not be proved that the dog was rabid. As time is an important factor, the vaccine always should be ordered by telegram.

Anti-Rabic Treatment for Dogs

The State Department of Health does not advise the use of canine vaccine. While it may, and probably does, confer immunity in a relatively small proportion of cases, the Department believes that it gives an undue confidence which is not justified by any scientific study.

Nor does the Department recommend the regular rabies vaccine for dogs that have been bitten by a rabid animal. The treatment frequently is successful; but when a dog is bitten by a rabid animal and the vaccine is given it is not safe to let the dog go at large for at least three months. The only safe procedure when a dog has been bitten by an animal known to be rabid is to *kill the dog.* Furthermore, the law requires that this be done.

D/b

RABIES

BY

DR. HARALD N. JOHNSON

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CHAPTER XXVI

RABIES

By HARALD N. JOHNSON

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Definition

Rabies is an acute specific infection of the central nervous system caused by a filterable virus, transmitted to man by infected domestic or wild animals, usually the dog, by means of a bite or scratch and the contamination of resulting wounds or abrasions with infected saliva.

The average incubation period is 42 days with a possible range of

from 10 days to one year. The disease is characterized by great excitability, spasmodic reflex contractions of the muscles of respiration and deglutition, convulsive seizures and progressive sensory and motor paralysis. The disease invariably is fatal in man.

The histopathological changes produced by the virus are practically confined to the nervous system and salivary glands. The affected cells are destroyed with little or no secondary inflammatory cell infiltration. The occurrence of specific intracytoplasmic inclusion bodies in certain nerve cells of the brain is diagnostic, but these are not always present, especially where the disease was of short duration.

Epidemiology

Distribution

Rabies is a disease which has been known since ancient times. The aggressive and vicious character of animals afflicted with furious rabies caused the people of ancient Rome, Greece and Egypt to believe that such animals were inhabited by demons. Stone murals from this age depict mad dogs, and Greek mythology has references to the disease and mentions certain gods as having the ability both to make animals mad and to heal them.

Democritus in the fifth century B.C. probably was the first physician to write about the disease. He described it as an inflammation of the nerves, resembling tetanus in so far as it was accompanied by spasmodic contractions of certain muscles. Aristotle, 322 B.C., gave an account of the disease in dogs and other domestic animals. Celsus, 100 A.D., gave a detailed account of the disease in man and practised cautery of wounds resulting from the bite of rabid animals. It is apparent from these accounts that the disease as we know it today is much the same as it was in ancient times.

Europe. — Rabies is reported to have been prevalent in France in 1271 and in Spain during 1500. Abelinius in 1634 described an epizootic of canine rabies in the German provinces of Rhineland and Saxony.

The disease spread over most of Europe during the early part of the 18th century, beginning in Italy in 1708, invading Germany and France in 1719 and England in 1734. The majority of human rabies cases during this period were from exposure to rabid wolves, and the survival and spread of the disease seemed largely dependent on this animal.

There was subsequently a period of low incidence until 1800, when rabies became epizootic in Germany. In Prussia alone there were from

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There was subsequently a period of low incidence until 1800, when rabies became epizootic in Germany. In Prussia alone there were from

200 to 260 human rabies deaths annually between 1800 and 1810. The incidence then increased until 1819, when 356 human rabies fatalities were reported. Rigid dog control measures then were introduced, and canine rabies became relatively rare. The disease was, however, continued in the fox species, and from 1803 to 1828 there were repeated epizootics of fox rabies in Southern Germany and in Switzerland.

In 1815 rabies appeared for the first time in Denmark and Norway. In 1824 the disease was introduced into Sweden. Rabies was quickly eliminated from these three countries by sanitary measures, and they have remained free of the disease to the present time. Rabies was reported in Russia during 1810 and subsequently became highly prevalent among the wolves which were abundant in that country.

Beginning in 1852 there were repeated epizootics of canine rabies in Austria, Germany and France. From 1852 to 1853 the disease was highly prevalent in Prussia and Hamburg, and from 1861 to 1865 in France, the Rhineland, Würtemberg, Saxony and Austria. The disease reached a maximum incidence in Bavaria and Prussia during 1871.

From 1875 to 1914 the general incidence of rabies was low over most of Europe. Epizootic canine rabies occurred in Hungary from 1888 to 1893, in Austria from 1891 to 1900, in Germany in 1898 and again in 1903–1904 and in France in 1899–1900. It was noted that the epizootic in Hungary began along the Russian and Rumanian frontiers, where wolves were abundant and were known to be infected with rabies.

Prior to the World War I rabies was quite prevalent in Poland, Rumania, Serbia, Bulgaria and Russia. During this war there was a general increase in incidence in all the warring countries. The disease became especially common in France, near Paris, in 1919, in Germany in 1923–1924 and in Poland and Russia in 1924–1925. In more recent years the incidence of rabies has been relatively low in Western Europe but has remained high in Poland and the Balkan countries.

Great Britain. — Rabies was first reported in England in 1734. During 1757 large numbers of horned cattle died of rabies in England. The disease was first reported in Ireland in 1807. From 1853 to 1885 there was a gradual increase in the incidence of rabies both in man and animal. During 1885 27 human rabies deaths were reported in London, but in 1886 dog control regulations were enforced rigorously in that city, and no human cases developed. The emergency sanitary measures then were relaxed, and canine rabies increased until 1889, when there were 10 human cases in London out of a total of 30 for all of England and Wales. The dog control regulations then were generally enforced with a sharp drop in the incidence of the disease. The regulations again were relaxed, and

rabies gradually became more prevalent until 1895, during which year there were 20 human and 672 dog rabies cases reported in England and Wales. The dog control measures again were intensified and enforced throughout Great Britain and in 1897 made even more rigid, so that from 1899 to 1902 there were only isolated cases of dog rabies with no human cases reported, and by 1903 the disease was completely eradicated. Although rabies was again introduced in 1918 by a dog carried over from the continent by plane, by 1921 England was free of rabies and has remained so to the present time.

Rabies in England was propagated almost entirely by dogs. The only wild animals affected appeared to be deer, and two interesting epizootics occurred in that species. In 1886–1887 rabies became epizootic in the protected herd of deer in Richmond Park, and in 1887 a total of 257 of these animals died of the disease. A similar epizootic occurred in the deer herd at Suffolk in 1888. The latter outbreak was traced to a rabid dog which had bitten one or more of the deer, and 500 of the 650 animals in this herd died of rabies.

Africa and Asia. — Rabies has been prevalent in parts of these continents since ancient times and seems to have been constantly present in Egypt and Arabia. Although rabies has been reported in Algeria, Tunisia, Anglo-Egyptian Sudan and India, there are no satisfactory records of its progressive geographical distribution. The disease has been especially common in India. The first authentic case of rabies in South Africa occurred in 1893.

It is probable that rabies has been present in China since ancient times. It was present in Indo-China and the Dutch East Indies before 1900. Rabies first appeared in the Philippine Islands in 1900 and in Japan in 1901. Australia and the Hawaiian Islands have remained free of the disease.

North America. — The earliest account of rabies in North America was in 1768, when the disease first appeared in the vicinity of Boston. During 1770–1771 it increased in prevalence in this area and spread to the fox species. The disease soon appeared in Pennsylvania, Maryland and North Carolina and was especially prevalent in and about Philadelphia. By 1785 the disease was enzootic throughout New England and had appeared in the plantation areas of the South. By 1860 it had invaded most of the states east of the Mississippi and had been reported as far west as New Mexico. By 1899 the disease had invaded California and since then has remained enzootic over most of the United States.

Several major outbreaks of rabies in wild animals have been reported in North America. In 1875 the disease appeared in the small spotted

skunk species in Kansas, and from 1907 to 1910 skunk rabies was prevalent in Arizona. Epizootic fox rabies occurred in Massachusetts in 1812, in Alabama in 1890, in Alaska in 1915 and in Georgia in 1940–1941. The extensive epizootic of rabies in coyotes of Nevada, Oregon and California during 1915–1916 is a good example of the rapid spread of the disease in an abundant species of wild animals.

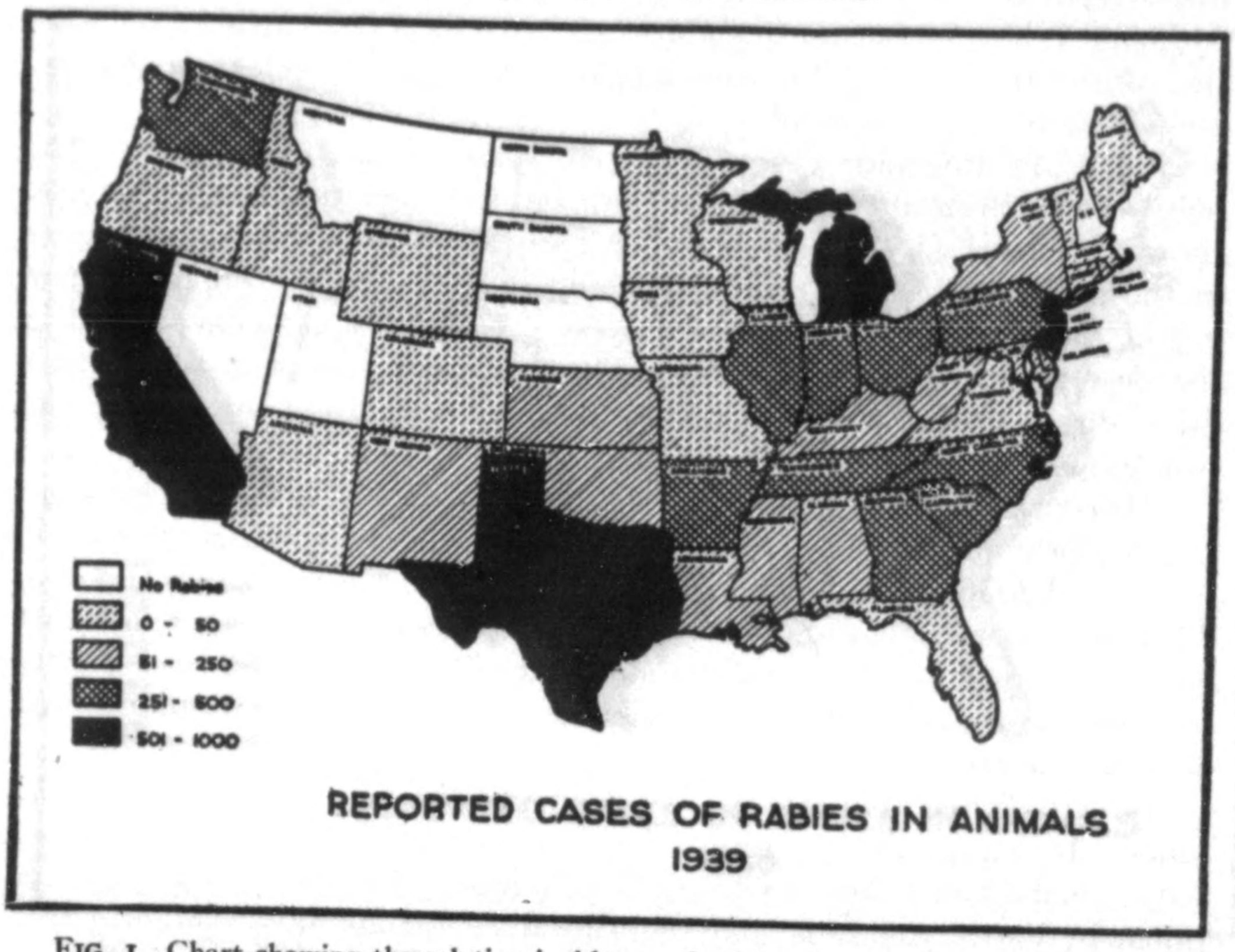


FIG. 1. Chart showing the relative incidence of rabies in animals during 1939 based on the reports of the Committee on Rabies of the U. S. Livestock Sanitary Association.

From 1923 to 1938 the number of human rabies cases reported annually in the United States varied from 53 to 103. During this period 44 of the 48 states reported one or more cases of human rabies.

Rabies was reported in Greenland in 1859. Expeditions visiting the island in 1866–1867 and in 1875–1876 noted that the Eskimo dogs occasionally developed the disease. Rabies was prevalent among the arctic wolves of the Barren Lands in 1897. Rabies has occurred in most parts of Canada, but in recent years, due to vigorously enforced quarantine restrictions, the disease has decreased in incidence almost to extinction. Rabies was epizootic in the coyotes of Northern Mexico in 1892. The disease has remained enzootic in Mexico since that time.

West Indies and South America. — Rabies was introduced into the West Indies in 1873. South America appears to have been free of the disease until the latter part of the nineteenth century. In recent years canine rabies has been uncommon in the northern part of the continent, but a new vector, the vampire bat, has become a dangerous source of the disease in Brazil and Venezuela.

Influence of Climate and Season

Rabies has been reported from the arctic to the highly tropical regions. Climate seems to have no effect on the character or incidence of the disease. There is an old superstition that rabies is most apt to occur in the fall. It has, however, been found from repeated analysis that the peak of incidence falls in the late winter and spring period. This may well be due to the fact that the stray dog, wolf and fox are the principal vectors and during these months will travel about in search of food and mate. Epizootics of rabies may and do occur at any time of the year.

Relation to Human Population

Rabies is rare in sparsely settled areas unless it becomes established in an abundant species of wild animal. In thickly settled areas the disease, once established, occurs in proportion to the number of stray dogs. Periods of rapid geographical distribution of the disease usually are associated with wars or migrations of civilians.

Influence of Race, Sex and Age

There is no satisfactory evidence to indicate differences in susceptibility of the white, yellow or black races. Males and females appear equally susceptible, although incidence is higher in males. The majority of cases of human rabies occur in children, but this cannot be considered as proof of a greater susceptibility on their part. They are more liable to exposure due to their fondness for playing with animals and lack of defense if attacked.

Cyclical Character

Major epizootics of rabies develop from time to time, but the cycle is not regular. Epizootics are short lived in any one place, rarely lasting more than one year. After the epizootic subsides, sporadic cases continue

to occur from year to year unless rigid control measures are adopted and enforced. It appears that the virus, at times, naturally tends to assume the characteristics of "fixed" virus, i.e., increased neurotropism and a corresponding decrease in the ability to invade the salivary glands. Natural propagation in one species of animal may increase or decrease the pathogenicity of the virus for other species.

Natural Vectors

The early history of rabies shows that the wolf and related wild canine species have played a major rôle in the perpetuation of the disease. In more recent times the dog, especially the stray and semi-wild variety, has been responsible for the continuation of the disease in the thickly inhabited sections of the world. The feline species apparently are only secondary vectors, except for the related meercat and mongoose species in South Africa and India. The vampire bat acts as a true carrier and is able to perpetuate the disease. It is possibie that a symptomless carrier state may develop occasionally in the canine species. There is no evidence to suggest that insects or rodents play any part in the propagation of the disease.

Source of Human Infection

Infection from the dog or domestic cat accounts for all but one to two per cent. of human infections. Infection from rabid wild animals rarely occurs in the United States. In South America the vampire bat may infect man. In South Africa and India human infections have been reported from the bite of the meercat, mongoose, jackal and monkey. Human infections have been reported in rare instances following exposure to rabid domestic animals such as the cow. There is apparently little danger in handling objects contaminated with the virus, such as carcasses, hides, rope and bedding. Infection from drinking the milk of rabid cows or eating the meat of animals infected with the disease is extremely unlikely. While exceedingly rare, infection from man to man is possible either by bite or by exposure of fresh skin abrasions to saliva from such cases. As maniacal and murderous activity is uncommon in human rabies, and heavy sedation is given routinely, there is little danger of infection from man. Laboratory infections are uncommon and have occurred only when the person was bitten by an experimentally infected animal or by accidental injury when performing autopsies.

Human Mortality and Attack Rate

The mortality statistics are diverse. Bouley under the auspices of the French Committee of Hygiene collected 383 cases of exposure to rabid dogs from records covering 1862 to 1872 with 180 deaths (47 per cent.). Renault reported that of 254 persons bitten by rabid wolves, 164 (65 per cent.) died of rabies. These are in sharp contrast to other mortality statistics. Faber reported that only 36 (6 per cent.) of 597 persons bitten by rabid animals developed rabies. Kirchner of Prussia recorded 38 deaths (3 per cent.) among 1,453 persons bitten by rabid dogs. Schuder noted only 1,325 deaths in a group of 14,959 persons bitten by rabid animals (9 per cent.). Von Frisch called attention to the factor of septic infection as a cause of death among persons bitten by rabid animals, especially wolves. Tetanus may occur as the result of puncture wounds produced by rabid animals.

It is interesting to note that Youatt of England published a report of 400 persons, bitten by supposedly rabid dogs and given only local treatment, with no deaths from rabies. Ekstrom in 1830 reported that of 106 persons bitten by rabid animals during the rabies epizootic in and about Stockholm during 1824 and treated by incision and cautery of the wounds none succumbed to rabies. There were only 5 cases of human rabies during the entire epizootic. One of 11 people bitten by one rabid dog did not allow local treatment and developed rabies.

There are no satisfactory data available concerning the attack rate for rabies in man following exposure by the bite of a rabid dog. It has been the practice to give the antirabic vaccine treatment to all persons exposed since the preventive treatment was first introduced in 1885.

The location of the bite is an important factor in the susceptibility to rabies. Dobert noted 12 cases of rabies among 118 persons bitten on the head (10 per cent.) compared with 24 cases among 1,251 persons bitten on the arms (2 per cent.), one out of 564 bitten on the legs (0.2 per cent.) and no deaths among 72 bitten on the trunk.

Another factor, which reduces the attack rate, is the occasional absence of the virus in the saliva of vicious rabid animals. The death rate may be lower in modern times due to more adequate cleansing of wounds. It is probable that the bite of rabid wild animals is more infectious than that of rabid domesticated dogs.

Review of Investigative Work

The causative agent of rabies was shown to be present in the saliva of rabid dogs by Zinke (1804), and this was confirmed by Gruner and

Salm (1813). Magendie and Bouchet (1813) were able to infect dogs with saliva obtained from a human case of rabies and so proved that hydrophobia in man and rabies in the dog were synonymous. In 1771 Van Swieten described the occurrence of paralytic rabies in man. Galtier of Lyons (1879) demonstrated that rabbits were susceptible to rabies.

The modern concept of rabies and virus diseases in general was developed by Pasteur. He first became interested in the disease in 1880 when he saw a young girl dying of rabies at the Saint Eugene Hospital in Paris. He immediately began an intensive study of the disease in collaboration with Chamberland and Roux. The discovery that the virus was always present in the brain of man or animals dying of rabies and the development of a trephine technique, whereby rabbits could be consistently infected with suspensions of infected brain material, formed the basis for the epoch making studies of Pasteur. He was soon able to show that the causative agent was invisible in microscopical preparations and would not grow in culture media in the manner of bacteria. He therefore called the infective agent, "virus", from the Latin word meaning poison. Serial intracerebral passage of the virus in rabbits gradually decreased the incubation period, but finally this reached a fixed interval. This he called "fixed" virus. Because dogs sometimes developed rabies following subcutaneous inoculation with the fixed virus, he attempted further to alter the virus by drying. The method employed was to suspend the spinal cord of a rabbit, killed when prostrate with fixed virus rabies, in a sterile jar containing sticks of potassium hydroxide. The virulence of cords so treated gradually diminished, so that after 7 to 10 days' exposure they were no longer infectious. A series of about 100 dogs were immunized by the daily administration of suspensions of dried cord, beginning with those dried 14 days and each subsequent day using cord dried for a shorter period until fresh cord was given. The dogs so treated did not contract rabies from the treatment and subsequently were immune to experimental inoculation with virus obtained from naturally infected dogs, which Pasteur called "street" virus. The French Academy of Science became interested in this method of immunization and appointed a committee to investigate the work of Pasteur. It was recognized subsequently as an extremely important discovery.

Pasteur then began a series of studies in which the same type of treatment was given to dogs following exposure to rabies. The results of these studies are not clear from the published data, but Pasteur evidently obtained results which convinced him that the disease could be prevented by such a course of treatment. Before these studies had been confirmed

by other investigators, the preventive treatment was tried in a human exposed to rabies. In July 1885 Joseph Meister, a peasant boy who had been severely bitten by a rabid dog, was brought to Pasteur, and in view of the serious nature of the exposure and due to the plea that something be done the treatment used for the experimental studies on dogs was given to the boy. The treatment appeared to be without ill effects, and the boy remained well. This was hailed as a remarkable feat, and soon other exposed individuals came to Pasteur for the treatment. Though the majority of the treated persons did not contract rabies, an occasional case did come down with the disease despite the treatment, and therefore, a more intensive scheme was devised, beginning with more than one injection daily for the first 5 days and continuing the injections for 15 to 21 days, depending on the severity of the exposure. Because so few of the exposed individuals developed rabies following the improved treatment, no further experimentation was carried out with dogs, and it was felt that the worth of the procedure had been proved.

Besides developing a method of vaccination, Pasteur made numerous other contributions regarding the nature of rabies virus. He noted that guinea pigs, fowl, monkeys, sheep and other warm blooded animals were susceptible, that dumb and furious rabies was the same disease, and that the virus was present in the nerves and salivary glands.

The studies of Pasteur stimulated widespread interest in rabies research. Subsequent reports on prophylactic and post-exposure vaccine treatment experiments in animals were conflicting.

As the Pasteur vaccine treatment occasionally failed to prevent the development of rabies in exposed persons, modifications of the dried cord method and new methods of vaccine production were introduced. The only significant modifications of the dried cord method were the introduction of glycerin preservation by Calmette for storing the dried cord used in treatment and intensification of the treatment by beginning with cord material dried only 5 to 8 days. The subcutaneous injection of live fixed virus appeared to be without ill effects in man, so the tendency was to increase the dosage of virus. Ferran of Barcelona in 1888 introduced the use of fresh fixed virus. His plan of treatment was based on the assumption that drying only killed some of the virus, and the amount of active virus could be reduced similarly by dilution. He used a 1 to 100 suspension of fresh rabbit fixed virus cord material and gave 3 injections daily for 5 days. Borregi began using this method in his clinic in 1889. Over a short period of time 5 patients died of vaccine rabies, and the clinic was closed by order of the Italian government. This temporarily discouraged the use of fresh fixed virus. Höyges in 1897

again advocated the dilution method for human vaccination. He began the treatment with highly diluted noninfectious suspensions of fresh infected rabbit cord material, increasing the concentration in graded doses and finishing the course with a 1 to 100 suspension.

Fermi in 1908 was the first to use a chemical inactivating agent for preparing human rabies vaccine. He introduced a phenol-inactivated fixed virus vaccine, which, after modification by Semple in 1911, has largely supplanted other vaccines. Formalin-inactivated vaccines have been recommended by Cumming and van Stockum and ether-treated vaccines by Remlinger, Alvisatos and Hempt. The heat inactivated vaccine of Babes and the serum virus vaccines of Fermi and Marie have been used also on a considerable scale. The chloroform-treated vaccine of Kelser has not been extensively used for the treatment of man.

Harris and Sellers are among the later advocates of live virus vaccines. There are no clear-cut experimental studies proving the superiority of any one type of vaccine; consequently most of the vaccines mentioned above are in use at one place or another.

Though Virchow, Golgi, Babes and other early pathologists presented accurate histological studies of the pathology of rabies, except for the description of the rather characteristic but nonspecific perivascular and perineuronal cellular infiltration, no practical microscopical method for the diagnosis of rabies was found. In 1903 Adelchi Negri described the occurrence of specific intracytoplasmic inclusion bodies in the nerve cells of man and animals which had died of rabies. Despite his failure to recognize the rôle of these structures, the discovery of Negri proved to be very important, as it made possible the rapid microscopical diagnosis of rabies.

Hoyt and Jungeblut (1934) made an important contribution to the knowledge of rabies when they demonstrated that intracerebral inoculation of mice with rabies virus consistently produced infection with a short and relatively constant incubation period. Webster and Dawson subsequently demonstrated the practicality of using the mouse for diagnostic animal inoculation and serum neutralization tests.

Kanazawa and Webster and Clow were the first workers to cultivate rabies virus in vitro. Rabies virus grown in tissue culture has not as yet proved to be a practical source for making vaccine. Untreated tissue culture virus has not been used for immunization because of its high pathogenicity for experimental animals when inoculated intracerebrally. Neither has it been possible to prepare a chemically or physically inactivated vaccine from tissue culture virus that compares in potency with vaccines made from infected animal brain.

ETIOLOGY

Nature of the Virus

The causative agent of rabies is an ultramicroscopic filterable virus. The size of the individual infectious unit has been estimated at 100 to 150 millimicrons (Elford). This figure was obtained by filtration of rabies fixed virus through graded collodion membranes. Rabies virus is not readily filterable. The virus passes the V grade Berkefeld filter fairly well, but the finer N and W type filters withhold the virus, the former allowing partial filtration and the latter, little or none. It is seldom possible to obtain any virus in the filtrate where the Seitz number I serum-sterilizing filter is used, even with cell-free suspensions of high titre. The difficulty in filtration may be due in part to adsorption of the virus in the filter.

Resistance of Virus to Physical and Chemical Agents

The virulence of infected brain tissue, if exposed to air, is rapidly lost. The original Pasteur rabies vaccine treatment depended on a gradual decrease in the virulence of spinal cords of infected rabbits, dried for varying periods of time at room temperature.

The loss of virulence due to exposure to air must be largely due to hydrolysis and oxidation, as with modern methods of quick freezing and drying at sub-freezing temperature under vacuum a completely dry preparation of high virulence is obtainable. When the sealed ampoules are stored at −25° C., there is no significant alteration in titre over a period of several months.

Rabies virus is very sensitive to sunlight or artificially produced ultraviolet light. Sunlight will inactivate virus suspensions in a few hours. Ultraviolet light irradiation will inactivate concentrated virus suspensions in 10 to 30 minutes.

Water suspensions of rabies virus are destroyed readily by heat. Suspensions of fixed virus usually are inactivated in 4 to 5 days at 37° C. A temperature of 45° C. will inactivate concentrated fixed virus suspensions in 24 hours, 50° C. in one hour, 52 to 58° C. in thirty minutes, 60° C. in five minutes and 100° C. in two minutes.

Distilled water is the best diluent for rabies virus, as normal saline or other isotonic chemical solutions exert a deleterious action on the virus. If 10 per cent. serum is added to the distilled water, the virus survives still longer.

One of the peculiarities of rabies virus is its resistance to the action of phenol. Saline suspensions of infected rabbit brain containing 0.5 per cent. phenol remain infectious for periods up to two months when stored in an ordinary refrigerator. Pure glycerin has little harmful effect on the virus but does inactivate bacteria, which makes it an excellent medium for preserving infected brain material. If stored in pure glycerin, animal brains infected with rabies virus remain virulent for several weeks at room temperature. Similar material stored in an ordinary refrigerator will be virulent for at least one year.

Bichloride of mercury, formalin and strong acids rapidly destroy the virus. Nitric acid is used widely in the treatment of wounds inflicted by rabid animals because of its rapid destruction of the virus. Bile, pancreatic lipase and 1 per cent. hydrochloric acid inactivate the virus. Trypsin and diastase are less effective in destroying the virus.

Cultural Characteristics of Virus

It has not been possible to cultivate the virus on ordinary bacteriological media. Multiplication takes place only in the presence of living cells. Continued growth is possible in tissue culture with a medium of Tyrode's, glucosol or saline solution containing 5 to 10 per cent. human or monkey serum and a small amount of finely minced mouse embryo brain. The virus may be maintained indefinitely in this manner. To date it has not been possible to obtain a high yield of virus in tissue culture, nor has there been a report of any significant decrease in the pathogenicity of the culture virus either for man or for the canine species.

The virus does not multiply in the chorioallantoic membrane of the developing chick embryo, but serial passage in chick embryo is possible when the virus is inoculated into the embryo brain.

Toxic Products of Virus

No soluble toxin has been isolated from tissue virus suspensions or tissue culture material.

Pathogenicity of Virus

Rabies virus is pathogenic for all warm blooded animals. Infection does not take place through the intact skin or by ingestion, but the dog and mouse often will develop the disease if the virus is instilled into the nose. It is difficult to infect animals by subcutaneous or intraperitoneal inoculation, but injection into the skin, muscle or nervous tissue in that

order is increasingly efficacious in producing the disease. Intracerebral inoculation of concentrated virus suspensions is practically always fatal.

Ducks, geese, doves and chickens are susceptible but relatively refractory. Young birds in general are susceptible to intracerebral inoculation, but the incubation period is prolonged. Recovery from rabies is relatively frequent in adult chickens. Buzzards are more susceptible than chickens and may be infected by intranasal inoculation. Cold blooded animals are very refractory.

Mode of Transmission of Virus

Transmission of the disease depends on the ability of the virus to reach and to multiply in the salivary glands of a rabid animal. The virus then is excreted with the saliva. Generally it is necessary for the animal to become vicious and bite so that the virus will be implanted in a fresh wound in order to transmit the disease. The exceptions are found in the vampire bat, which inflicts a wound in order to feed, and in cases in which persons are exposed by attempting to treat animals ill with paralytic rabies.

The question arises whether the saliva is infectious before the onset of symptoms. Some writers report finding the virus in the saliva several days before the onset of symptoms. It is probable that they refer to the classical stage of the disease. It is unlikely that the virus is present in the saliva before the development of prodromal symptoms. At this stage, however, the animal may appear quite normal.

The saliva probably functions in a two-fold manner; (1) to preserve the virus by the protective action of the mucus and (2) to act on the exposed tissue, possibly by some digestive action, to assist the entry of the virus into the nerves.

There is still some doubt as to whether the virus reaches the central nervous system by way of the axons or the perineural lymphatics, but the former route appears more likely. The symptomatology and pathology indicate that the virus travels predominantly by way of the sensory nerves. The ability to infect animals by means of a slight scratch on the cornea or skin supports this theory. The blood stream and lymphatics do not appear to play any significant part in the invasion or propagation of the virus.

Distribution of the Virus in the Body

The virus is almost always demonstrable in the central nervous system of man and animals dying of rabies. The possible exception is found when

the disease is prolonged. The concentration of the virus varies in the different parts of the brain, but usually it is high in the thalamus and medulla. The virus content of the cerebral cortex is subject to great variation in naturally infected animals. This may account for the variable clinical pattern of the disease. The maximum concentration of virus occurs during the early acute phase of the disease, then decreases gradually in amount. There is no satisfactory evidence to prove that the virus enters the blood stream during the incubation period or at any time during the course of the disease. The spinal fluid rarely contains any virus.

Rabies virus is not strictly neurotropic. The submaxillary glands are the best source of virus aside from the central nervous system, and the concentration of the virus in this gland is often as high as that in the brain. The histopathological changes in these glands indicate that the virus has an especial affinity for the mucus-secreting cells. In a series of dogs experimentally infected by injection of street virus in the masseter muscles, the submaxillary gland was positive for virus in 39 of 67 animals, 58 per cent. The percentage of positive glands varied with different strains of test virus. The parotid gland was positive in 4 of 47 dogs, 9 per cent., and the lacrimal gland in 12 of 33 dogs, 33 per cent. The adrenal glands often contained the virus. The pancreas and kidney were invaded in rare instances by the virus. In one of four lactating dogs the virus was found in the breast tissue. Numerous tests of whole blood and bone marrow, spleen, liver, lymph nodes, ovary, testes, prostate, rectal glands and the mucosa of the appendix and of the small and large intestines have been consistently negative.

Virus Strains

There is no satisfactory evidence to indicate that there are antigenically different strains of rabies virus. Variation in street virus strains has received much attention since first advanced by Putoni. The major difference in virus strains concerns the alteration of the virus by intracerebral passage in animals.

Fixed Virus. — This term is applied to virus strains that have been propagated by serial intracerebral passage in some experimental animal, usually the rabbit, and the incubation period has reached a minimum, "fixed" interval. Fixed virus rabies is characterized by a short incubation period, usually 4 to 6 days after intracerebral inoculation, absence of typical inclusion bodies, wide dissemination in the central nervous system with consequent high titre and by the uniformly rapid and paralytic

disease course produced. Such virus strains have largely lost their tropism for organs other than the brain.

Street Virus. — There are a number of reports in the literature of unusual strains of rabies street virus. Most of these accounts concern virus strains isolated from human or animal rabies, cases in which the recovered virus has certain characteristics of "fixed" virus. The species specificity of rabies street virus may be altered by passage through certain animal hosts. This probably accounts for the atypical character of the "oulou fato" rabies of French West Africa and the "vampire bat" rabies of South America. Street virus rabies ordinarily is characterized by a long and extremely variable incubation period and the rather constant production of inclusion bodies in the brain. By intracerebral inoculation the incubation period in rabbits usually is from 12 to 15 days with a range of from 10 to 90 days. Street virus rabies often results in a prolonged excitement stage with irritability and viciousness. In a variable but high percentage of cases the virus is able to reach the salivary glands and be excreted in the saliva.

Natural Resistance to Rabies Virus

Man appears to have some natural resistance to infection with rabies virus. The pathogenicity of the virus for man is altered by passage in certain animals such as the rabbit. The resistance to infection seems to increase with age. There is no satisfactory explanation for the occasional occurrence in the blood of man or animals of a high concentration of virus-neutralizing substance not preceded by vaccination or known exposure to the virus.

Acquired Immunity to Rabies

Pasteur demonstrated that, if fixed virus is inoculated subcutaneously into dogs, infection is rarely produced, and that, if repeated injections are given, the animals subsequently become highly resistant to experimental infection. Early investigators also found that the intraperitoneal injection of large amounts of virus produced a high degree of immunity. There appears to be a quantitative relationship between the amount of virus given and the degree of immunity produced. The blood serum of animals so treated has a uniformly high content of virus neutralizing substance. Immunity may be produced also by the injection of vaccines prepared from infected brain tissue treated by certain chemical agents so as to render the virus inactive. The duration of immunity acquired by vaccination has not been determined.

Immunological Tests

It is necessary sometimes to resort to special tests in order to identify atypical strains of rabies virus, especially those modified by intracerebral passage. This may be accomplished either by determining whether the virus is neutralized by a known immune serum or by vaccinating animals with a known strain of rabies virus and testing them with the virus in question in parallel with an equal number of control animals.

Canine Rabies

Rabies is primarily a disease of the canine species, i.e., the dog, wolf, coyote and jackal. The disease is perpetuated easily in such hosts because of the instinctive fighting and biting nature of such animals. With the development of rabies they often become extremely aggressive against their own kind as well as against any living thing they meet. The potentially long incubation period allows survival of the virus from year to year through the medium of only a few animals. In an area, in which any one of these species becomes unduly abundant, rabies may become epizootic, but for the most part the disease maintains a low incidence. The general disease picture of canine rabies is best illustrated by the course of the disease in dogs.

The incubation period for naturally-infected dogs is rarely under 10 or over 90 days. In most instances the disease will develop between the twenty-first and sixtieth day after exposure. Latent periods of over 200 days have, in rare instances, been noted in this country, and European writers have reported incubation periods of over one year.

The early symptoms include congestion of the mucous membranes of the eyes and nose. The temperature of the body generally is elevated one to two degrees above normal. The animal exhibits either depression or excitation depending on the manner in which the body reacts to the infection. When the depressive phase is predominant, the animal is morose and seeks seclusion. Where the excitation phase is predominant, the dog will be unusually active, playful and friendly. There will be a tendency to fawning and licking. The ears tend to point, producing an alert appearance. A certain degree of restlessness and irritability is present so that slight provocation may cause the animal to bite. The normal tendency to chase cats and chickens is increased. At this period of the disease the animal is very dangerous to children, as they are apt to pick up and fondle the apparently affectionate dog.

Two general types of canine rabies are described; the one is called "furious", and the other "dumb" or paralytic rabies. In the latter the paralytic phase develops early and is associated with depression and apathy. The majority of cases show some manifestation of both types of the disease, i.e., a short excitation phase characterized by restlessness and nervousness, rapidly followed by depression and paralysis. Sudden death without appreciable premonitory symptoms may occur. The incidence of furious versus dumb rabies is not constant but depends on the virulence of the virus and the species of animal affected.

Furious Rabies

This is the type where the classical "mad dog" symptoms appear. Dogs so affected become increasingly restless and are easily startled. There is usually some weakness of the vocal cords which produces a characteristic voice change. A hoarse, howl-like bark is followed by a succession of baying barks of lower pitch. The maximum pitch is attained in the middle of the bark rather than at the beginning. The appetite is perverted, and there is a desire for undigestible material such as sticks, straw, dirt, etc. Priapism and sexual excitation are common. The eyes present a peculiar appearance because of the congestion of the conjunctivæ, dilation of the pupils and difficulty in closing the eyes. The cornea become dry and glazed due to infrequent blinking. The animal becomes increasingly apprehensive.

If caged, the dog will make every effort to escape, even breaking off the teeth in an effort to chew its way out. If free, the animal often will leave home to wander for miles and seems impelled to attack any living thing that it sees. There seems to be little desire to kill, and if several animals are present, the dog will attack first one and then another. A dog so affected may travel a long distance before succumbing to paralysis and exhaustion. More often the animal returns home after one or two days' absence, emaciated, wounded and almost unable to walk because of incoördination and beginning paralysis. Salivation of some degree generally is present, but in the terminal stage the mouth often becomes dry and parched.

The dog with furious rabies may have some weakness of the jaw but usually can close the mouth and drink and eat. In some instances the dog will die suddenly, perhaps in a convulsion. More often the animal will develop paralysis. The legs become gradually weaker, the jaw droops, and death occurs after the development of coma. Dogs with this type of the disease usually live 4 to 7 days but may live as long as 10 days after the onset of symptoms.

Dumb or Paralytic Rabies

In this type of the disease the excitation phase is short or absent, and the animal rarely will attempt to bite even if provoked to do so. The early symptoms of depression and apathy soon are followed by paralysis of the jaw and muscles of deglutition. Salivation usually is profuse, thick, stringy saliva drooling from the open mouth. The difficulty in swallowing causes choking, gagging and retching. The dog is unable to bark, hence the name "dumb" rabies. Paralysis of the extremities develops rapidly and is associated with marked incoördination due to the spastic character of the paralysis. The dog soon is prostrated and comatose, lying on its side, the legs moving rhythmically back and forth. The eyes are wide open, and the corneæ soon become glazed and opaque. Respirations are slow and irregular. Death usually occurs in 1 to 3 days, rarely over 5 days, after the onset of symptoms.

All dogs with rabies are relatively insensible to pain. They do not fear blows or threats. Dogs with furious rabies may mutilate themselves, biting out large pieces of skin and muscle without apparent pain. An early symptom referable to sensory paralysis is the loss of the corneal reflex. The excitation of muscles causes tic-like contractions, tremor and occasionally, general convulsive seizures. The muscular reflexes are increased. Trismus of the jaw may occur. There is no definite pattern of muscular paralysis. The weakness may begin in one or both of the front or hind extremities and progressively involve other muscles. There is no fear of water such as occurs in human rabies. The body temperature usually is subnormal during the greater part of the disease. A high terminal temperature may occur. The disease is practically always fatal to the dog.

Rabid wolves and foxes lose their normal fear of human beings and human habitation and will fearlessly invade farm premises and attack man and domestic animals. Wild animals with paralytic rabies are found rarely. Animals so affected probably die in seclusion, avoiding even their own species.

Possible Carrier State

There are numerous reports in the literature of persons dying of rabies following the bite of a dog that did not appear abnormal or later die of rabies. This is suggestive of a possible *carrier state.* It is probable that the history in such cases was incomplete and more than one in-

stance of exposure to rabid animals had occurred, or the identity of the biting dog was not definitely established.

The only proved instance of recovery from rabies in dogs is the case described by Remlinger. He observed an experimentally infected dog that presented symptoms of rabies for a period of three weeks and subsequently recovered. The virus was recovered from the saliva of the animal during the symptomatic stage and up to five days after the cessation of symptoms.

The author has observed several hundred dogs experimentally inoculated with rabies virus. In rare instances a dog would exhibit transient excitation, apathy, incoördination or muscular weakness at some time during the three month period of observation. In no instance was it possible to demonstrate rabies virus in the saliva of these animals. When such animals were killed three months after the virus inoculation, the salivary glands were tested for rabies virus by intracerebral inoculation of mice with a suspension of the gland material. These tests were consistently negative. There was no instance of a dog developing characteristic symptoms of "furious" rabies followed by recovery.

It is the author's opinion that dogs in rare instances may develop an abortive type of rabies and recover. It is extremely unlikely that the animals so affected will have the virus in the salivary glands. There is at present no evidence to indicate that the dog can act as a symptomless carrier of rabies such as may occur in vampire bats.

Vampire Bat Rabies

The vampire bat was not recognized as a vector of rabies until 1916, when Rehaag succeeded in infecting laboratory animals with brain material from a bat captured while feeding on a cow. An unidentified paralytic disease had caused great loss of livestock in Brazil as early as 1906. In 1911 Carini demonstrated inclusion bodies in the brains of cattle dying of ascending paralysis in the Sao Paulo district of Brazil. He concluded that the disease was rabies, but quarantine and destruction of dogs and cats did not affect the spread of the disease. In 1921 Haupt and Rehaag proved that the atypical livestock disease was rabies and came to the conclusion that the vampire bat was the principal source of the infection. A severe epizootic of rabies in cattle began in 1931 in the states of Matto Grosso and Santa Catarina, Brazil. Torres and de Queiroz Lima captured several vampire bats in an area, where the disease was prevalent, and several of these bats proved to be carriers of rabies. These men later proved that bats could harbor the virus in the salivary

glands for as long as 110 days and still remain symptomless. Experimentally infected bats sometimes developed paralytic symptoms and died after long periods of infectiousness. The incubation period following experimental inoculation varied from 7 to 171 days. Some bats failed to develop the disease.

Torres and de Queiroz Lima sometimes found that captured bats had the virus in the salivary glands but not in the brain. De Vertueil and Urich later reported that one experimentally infected bat remained a carrier for 5 months. The species specificity of the virus appears to have been altered by passage through bats. Dogs were found to be only slightly susceptible to this strain of virus. Though rabbits and guinea pigs were susceptible to infection, rats had a low susceptibility, even though inoculated intracerebrally.

The vampire bat is a normal inhabitant of a large part of Central and South America. The animal is relatively small, having a body length of four inches and a wing spread of thirteen inches. It subsists entirely on fresh blood, which it laps up after inflicting a superficial, crater-like wound with its sharp incisor teeth. Its saliva contains an anticoagulant which causes prolonged and profuse bleeding from relatively minor wounds. These animals live in caves or hollow trees and normally feed only at night. Their favorite hosts are cattle, horses and chickens, but, where the livestock is protected at night, they will enter homes and feed on man. Their ability to bite and feed without awakening the victim is legendary.

The fruit-eating bats form an additional reservoir of rabies, for although they do not transmit the disease to man and animal, they can perpetuate the disease in the bat species.

In 1929 a severe epizootic of cattle rabies began in Trinidad, British West Indies. Hurst and Pawan showed that the disease was introduced and transmitted by vampire bats. From 1929 to 1935 there were 55 cases of human rabies in Trinidad as the result of infection from bats.

The disease in man was paralytic in type, and the classical hydrophobia symptom was encountered rarely. The duration of the disease was relatively longer than usual for human rabies. One patient lived for 30 days after the onset of symptoms. The first symptom usually was some abnormal sensation about the site of infection. This was followed by gradual ascending paralysis.

Iturbe and Gallo reported the presence of vampire bat rabies in Venezuela. It has been reported also in Paraguay, Argentina and British Guinea.

Rabies in Man

Incubation Period

The incubation period averages 42 days. Rabies may develop as early as 10 days after exposure. Incubation periods of over 90 days are relatively rare. Högyes in 1886 reviewed the histories of 210 cases of human rabies. Of these 88 per cent. had an incubation period of less than 90 days, with 65 per cent. under 60 days. He included one case with a latent period of 646 days. The records of 137 cases of human rabies have been collected by the author. The average incubation period was 42 days with a range of from 12 to 210 days.

There is no good evidence to support the hypothesis that the incubation period depends on the distance the virus has to travel from the point of infection to reach the brain. In the author's series two patients bitten on the face had incubation periods of 63 and 146 days respectively. The average incubation period was 30 days for the 44 persons bitten on the head, 50 days for the 56 persons bitten on the upper extremities and 44 days for the 12 people bitten on the leg. Experimental studies show that the amount of virus introduced and the type of tissue exposed influence the duration of the latent period. In all experimental animals the inoculation of a concentrated virus suspension results in a shorter average incubation than when dilute virus is given. Long latent periods are frequent when street virus is introduced into the skin of the face, and incubation periods up to 90 days are noted occasionally in dogs inoculated in the masseter muscle or in the brain. It is, therefore, evident that the incubation period is largely dependent on a temporary arrest of virus multiplication, either at the site of infection or at some place in the nervous system.

The relatively high morbidity and short average incubation period of rabies following face exposure may be accounted for by the frequent severe laceration in such exposures, the superficial aspect of the muscle tissue and the abundant sensory innervation of the face. Then, too, there is a tendency not to use nitric acid for cauterizing face wounds for fear of disfigurement.

There is no satisfactory proof that the average incubation period is shortened or lengthened by the rabies vaccine treatment.

Other factors said to influence the incubation period include the virulence of the virus, the species of biting animal and the age of the exposed individual. The average incubation period for children developing rabies is shorter than that of adults.

Prodromal Symptoms

Prodomata last 2 to 4 days. General symptoms, such as headache, anorexia, nausea and sore throat, often are present. Lacrimation and a watery nasal discharge may occur early in the disease. Headache, when it occurs, most often is localized in the occipital region or over the vertex. Vomiting may be protracted or even projectile in character. The patient often complains of fever, but this symptom is out of proportion to the degree of elevation of the body temperature, which may be normal or elevated one to three degrees. Respirations may be shallow with an occasional deep inspiration. The patient, while speaking, may be interrupted by a sighing inspiration. The pulse rate usually is increased and is more rapid than would be expected in proportion to the degree of fever. The patient may complain of a dry throat and extreme thirst but will drink very little at a time or not at all.

Nervousness, irritability, anxiety, melancholia, apathy and depression are common manifestations. Insomnia or interrupted sleep gives evidence of the stimulation of the central nervous system. The patient may wake up suddenly as if suffering from bad dreams.

The most diagnostic early symptom of rabies is some abnormal sensation about the site of infection. This will occur in about 80 per cent. of the cases and, when present, is substantial evidence for a diagnosis of rabies. There may be pain, burning, sensation of cold, pruritus, tingling or formication about the old wound. The pain may be local or radiating. Pain along the affected nerves may be dull and constant or intermittent and stabbing in character. Referred pain in the neck, back, chest or abdomen has been noted occasionally. Local numbness of the skin about the old wound is often present. It is probable that the inflammation of the old wound, so often described in rabies, is secondary to scratching or rubbing due to the abnormal cutaneous sensations. It is also possible that some sort of urticarial or angioneurotic-like skin reaction may occur.

In general, the early symptoms can be ascribed to the stimulative action of the virus on various groups of brain cells, predominantly affecting the sensory system. In addition to symptoms of this nature already mentioned, there may be general hyperesthesia of the skin and sensitivity to drafts and bed clothes.

Acute Phase of Rabies in Man

The symptoms noted in the prodromal stage become more prominent. For the most part the excitation phase is predominant up to death. The

patient is extremely nervous, apprehensive and extraordinarily sensitive to all types of physical stimuli. Often he will be able to be up, wandering aimlessly about and speaking in disconnected sentences, and may suffer from intermittent spells of delirium. Maniacal seizures may occur, but vicious and murderous action, such as biting and fighting, is infrequent. In general the patient is well oriented and will answer questions in an intelligent fashion.

A sense of impending death is frequent. The eyes are bright and starry and seldom fix on any object. Despite the great fear and anxiety there are no tears. There is usually an accumulation of thick, tenacious mucus in the throat and mouth, and in an effort to expel it the patient emits a harsh coughing sound which sometimes has been interpreted as a bark.

The outstanding clinical symptom is related to the act of swallowing. On attempting to drink, when the fluid comes in contact with the fauces, it is expelled with considerable violence, and painful contractions of the muscles of deglutition and of the accessory muscles of respiration are produced. This is so classical when present that the disease has been called hydrophobia, the fear of water. The fear of swallowing is not related to water alone but to any fluid, food or medicine. Choking, when attempting to swallow saliva or fluids, may occur, and convulsive seizures often are precipitated under this stimulus. The choking may result in such spasm of the respiratory muscles that prolonged apnea occurs with concomitant cyanosis and gasping attempts at respiration. Due to the inability to take fluids there is excessive thirst and progressive dehydration. The voice is apt to be hoarse. There is excessive reaction to external physical stimuli, such as noise, drafts, bed coverings and bright light.

The entire muscular system is activated, and tic-like vermiform and fibrillar muscular contraction and general tremors may occur. Convulsive seizures are common and may be so extreme as to produce opisthotonos. The convulsive seizures usually are of short duration and are apt to recur in a cyclical rhythm. There is usually some ataxia.

In the majority of instances the patient will die in the early acute phase of the disease during a convulsive seizure. Therefore, the paralytic phase due to degeneration of motor nerve cells is usually not very evident. However, weakness of muscle groups related to the site of exposure is present in about 25 per cent. of human rabies cases. Ocular palsies leading to strabismus and incoördination of ocular muscles may occur. Weakness of the masseter and facial muscles may be present in some of the patients.

Paralytic Phase

When the acute phase of the disease is prolonged more than three days, paralysis of various muscle groups is the rule. There is then increasing paralysis of the muscle group related to the site of exposure, if previously affected, and subsequent development of weakness in the contralateral musculature. This extends until death occurs from respiratory paralysis or cardiac arrest.

In rare instances the paralytic type of the disease takes on the ascending pattern such as occurs in Landry's syndrome, and beginning with the muscles of the legs, a progressive ascending paralysis occurs with no relation to the site of exposure. Patients so affected may have no difficulty in swallowing until the terminal phase of the disease.

The affection of the general visceral, efferent, nervous system leads to a variety of symptoms. The eyes may exhibit a variety of signs due to overstimulation of one or the other types of innervation. The salivation often noted does not necessarily mean increased secretion but rather, inability to swallow saliva, leading to drooling. The mucous membranes in general are dry owing to decreased secretion, so that the eyes become glassy, and the throat and nasal passages become dry and irritated. There is often abnormal stimulation of the innervation of the sex organs with resultant priapism and increased libido. The bladder and rectum are affected so that retention and constipation are the rule, though incontinence may occur, especially if the disease is prolonged.

Objective Symptomatology

Due to dehydration and marked apprehension the facies present a wild, fearful and gaunt appearance. The eyes are sunken, and the corneæ are glazed and reflect the light. The circumocular muscles may be weak, so the patient cannot completely close the eyes. The skin is increased in turgor, and the normal elasticity is diminished. The conjunctival and mucous membranes elsewhere are dry and congested.

Though there may be stiffness of the neck, Kernig's and Brudzinski's signs usually are not elicited. Tenderness over the spine may be present. The corneal reflex is decreased or absent. The pupils usually are widely dilated but may be constricted or unequal. Hippus, nystagmus, diplopia or strabismus may occur. The retina is usually normal in appearance, but partial blindness is not uncommon.

The respirations are shallow and irregular with occasional forced inspiration or sighing expiration. Cheyne-Stokes type of respiration is noted often. The pulse rate usually is rapid and the volume shallow. Bradycardia may be encountered in rare instances.

The chest and abdomen usually are normal to palpation and auscultation. Local involuntary muscle activity may be noted. The superficial reflexes of the abdominal musculature may be absent, normal or increased. The tendon reflexes are increased during the early stages and disappear where the disease is prolonged. The muscular paralysis usually is flaccid in type.

Though the skin in general is hyperesthetic, local sensation to pin prick, heat and cold is diminished. The body temperature may be normal, subnormal or slightly increased. There is rarely high fever except in occasional instances in the terminal stage of the disease.

Clinical Pathology

Blood. — The red blood cell count is not altered in rabies except where excessive dehydration occurs and the blood is concentrated. The white blood cell count generally is increased and may reach 20,000 to 30,000. Blood smears are apt to show a relative increase in the percentage of polymorphonuclear and large mononuclear cell types.

Urine. — A slight albuminuria frequently is present, and hyaline casts may be seen in the urine sediment. A reaction for glucose is noted often.

Spinal Fluid. — There is no marked increase in the spinal fluid pressure, but the level usually will be above normal. The fluid is consistently clear. Protein tests may show a slight positive reaction. The cell count usually is normal. Cell counts of from 25 to 150 are encountered in rare instances. Where the cell count is increased, the cells are predominantly of the mononuclear type. The spinal fluid rarely contains any virus.

Differential Clinical Diagnosis

If the patient is known to have been bitten by a rabid animal and the symptomatology is characteristic, there is no difficulty in making a correct clinical diagnosis. However, in some instances it is impossible to obtain a history of exposure to a rabid animal. In such cases, should the clinical course be atypical, the differential diagnosis may prove difficult.

Treatment Paralysis. — This may be one of the most difficult diseases

to distinguish from rabies. The course may be clinically very similar to the paralytic type of rabies. It is important to ascertain whether the patient had any systemic reaction to the vaccine treatment. The excitation phase so characteristic of rabies is absent. The spinal fluid cell count is of little aid in the diagnosis, as it is only slightly increased, but xanthochromia usually is present in treatment paralysis cases.

Hysteria. — This diagnosis should be considered always as it is encountered frequently. The nature of the convulsive-like seizures should make the diagnosis evident. The patient often will try to emulate a mad dog.

Poliomyelitis. — Both the bulbar and spinal type of this disease may be confused with rabies. The spinal fluid cell count in poliomyelitis usually is higher than that in rabies, and the relative absence of polymorphonuclear cells in the latter disease may help to differentiate the two.

Tetanus. — The incubation period of tetanus is shorter than that of rabies, usually 6 to 14 days, and the psyche is normal. Trismus of the jaw, though a very constant symptom of tetanus, is rarely present in rabies. The muscular spasticity in tetanus is constant and general, while in rabies it is intermittent and chiefly restricted to the muscles of the throat.

Prognosis and Treatment

There are a few reports in the literature of rabies in man followed by recovery, but these are questionable, as the virus in no instance was isolated. Rabies in man, as far as known, is invariably fatal.

A variety of chemicals have been used in an attempt to cure rabies. At the present time there is no medicinal known which will alter the course of the disease. The use of hyperimmune serum has been recommended, but here again there has been no evidence that it has had any curative effect. Though intravenous administration of fluids might prolong the disease and will relieve the dehydration, it has not resulted in recovery. The main treatment has consisted of the administration of strong sedatives to relieve the anxiety and the administration of anesthetic drugs to stop the convulsions.

Though morphine is the choice of drugs for relieving the symptoms of rabies, the marked resistance to the drug exhibited by persons so afflicted requires that large doses be given. Even gr. 1 (60 mgm.) of morphine, given subcutaneously, often fails to quiet the patient. Phenobarbital sodium given subcutaneously or intravenously also is an excellent sedative.

PATHOLOGY

Gross Pathology

There are no gross abnormalities which can be regarded as diagnostic of rabies. The macroscopical changes produced by the virus of rabies are similar to those resulting from a variety of bacterial, rickettsial and virus infections and from toxic or allergic reactions. Rabies produces rapid dehydration, and at death the body presents a cachectic appearance.

The meninges are normal except for vascular congestion, and the spinal fluid is clear and colorless. The surface of the brain and cord usually exhibits a pink or red discoloration due to marked engorgement of the blood vessels. There is slight to moderate cerebral edema as shown by flattening of the cerebral convolutions and partial obliteration of the sulci. On section the cut surface of the brain and cord has a pink cast due to vascular congestion. Usually this is most marked in the thalamus, medulla and cervical spinal cord. Perivascular hemorrhage is rarely evident on gross examination. When the site of exposure was located on one of the extremities, the cut surface of the cord sometimes will show unilateral, pinkish-gray discoloration and obliteration of the normal markings. This lesion, when present, is most marked in the posterior horn area.

The lungs usually show some pulmonary edema and focal atelectasis, and the mucosa of the trachea and bronchi is congested. The thymus gland may be edematous and congested. The small intestine sometimes presents the picture of paralytic ileus. The mucous membrane of the gastrointestinal tract is congested. Local digestion of the gastric mucosa with perforation of the stomach and diaphragm and the presence of stomach contents in the pleural cavities is a frequent finding. The viscera otherwise are quite normal in appearance.

Microscopical Pathology

Central Nervous System. — The meninges usually are normal. A variable degree of hyperemia and slight perivascular infiltration with mononuclear cells may be seen. The cerebral and cerebellar cortex and adjacent white matter show no significant alteration other than hyperemia and acute neuronal degeneration. In the midbrain, basal ganglia and pons the neuronal degeneration generally is severe and is associated with marked hyperemia. Small perivascular hemorrhages are seen frequently. These are most noticeable in the thalamus and subependymal neuroglial tissue. Neuronal degeneration is especially severe in the thalamus, hypo-

thalamus, substantia nigra and the cranial nerve nuclei. These areas show a slight perivascular and perineuronal mononuclear cell infiltration. The medulla uniformly presents the maximum pathological alteration. The cranial nerve nuclei exhibit marked neuronophagia, and the inflammatory cellular infiltration is proportionally greater than elsewhere.

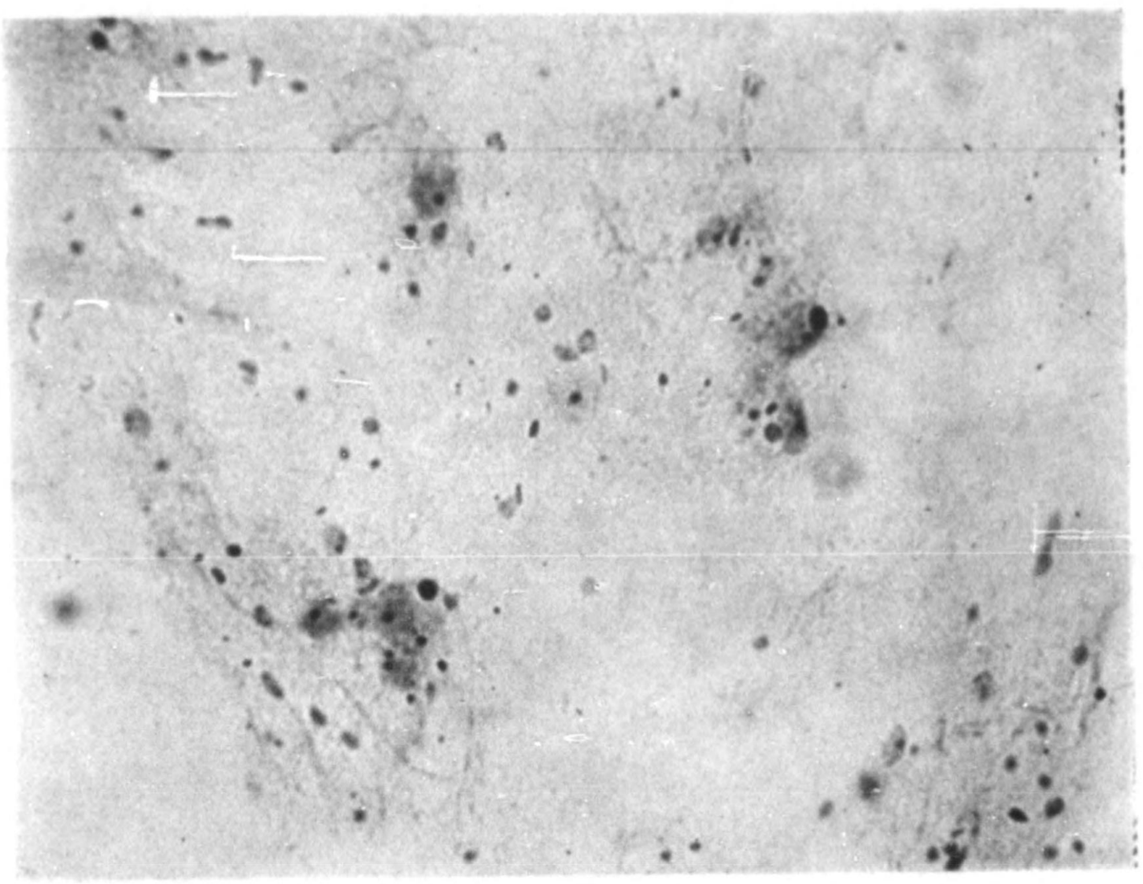
The spinal cord shows hyperemia and perivascular cellular infiltration. These findings are especially marked in the cervical portion at the decussation of the motor tracts. Neuronal degeneration is general, but the posterior horns of the gray matter are affected especially severely. When the site of exposure is located on one of the extremities, the corresponding posterior horn area is apt to show marked hyperemia and cellular infiltration. Small hemorrhages may be present. The tracts of Goll and Burdach and the posterior funiculus may show marked degeneration of axons and myelin sheaths.

In general the leucocytic infiltration is largely perivascular, but clusters of mononuclear cells are found about degenerating neurons, especially in the cranial nerve nuclei. The infiltrating cells are, for the most part, of the small and large lymphocyte type. There is usually a slight diffuse mononuclear cell infiltration of the interstitial tissue of the pons, medulla and cervical spinal cord, varying in proportion to the degree of neuronophagia. Relatively few polymorphonuclear cells are seen. A few mast cells usually are found in the medulla. Cellular infiltration is more marked when the disease has been of longer duration.

The neuroglial cells of the substantia gelatinosa about the central canal show a variable degree of proliferation. This is especially evident in the spinal cord. The neuroglia about degenerating neurons becomes more prominent than is normal. This is probably in part a functional increase in size, but where the degeneration is heavy, there appears to be some actual proliferation. The oligodendroglia throughout the brain show swelling, which is evidently a manifestation of the moderate cerebral edema which is regularly present.

The major proportion of the neurons of the central nervous system shows some pathological alteration. The main change consists of pyknosis of the nucleus and ballooning of the cytoplasm. The Nissl substance is decreased in amount, and the cytoplasm exhibits variable vacuolization and granular and flatty degeneration. Some neurons show condensation of the cytoplasm, presenting a coagulative type of necrosis. Other neurons exhibit fragmentation of the cytoplasm and general loss of cell detail.

Inclusion Bodies. — The inclusion bodies, which frequently occur in the neurons of both man and animals dying of rabies, generally are referred to as "Negri bodies" (Figs. 2 and 3). These structures usually



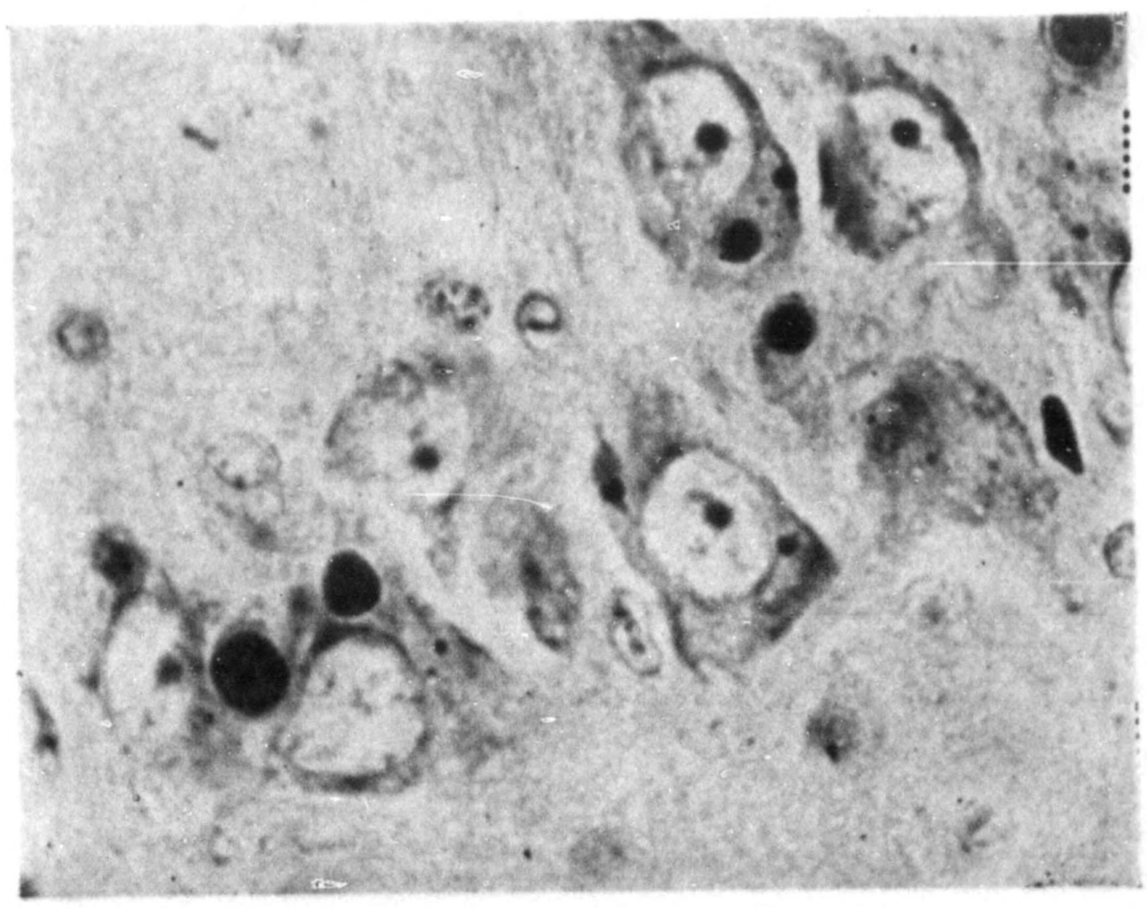


FIG. 2. (top) Routine diagnostic impression preparation of the Ammon's horn of a dog dying of furious rabies; Sellers stain; magnification 250; photograph by J. B. Haulenbeck.

FIG. 3. Paraffin section of the Ammon's horn of a dog experimentally infected with rabies; modified eosin methylene blue stain; magnification 1,000; photograph by J. B. Haulenbeck.

are very characteristic, and if they are demonstrable, it is possible to make a definite diagnosis of rabies. The inclusion bodies are found in the cytoplasm of large neurons which present the ballooning type of degeneration. They consist of sharply defined, spherical, oval or elongated, eosinophilic staining bodies, varying from 1 to 30 micra in diameter. There may be several of various sizes in one neuron. They are most frequent in the cytoplasm between the nucleus and the dendridic prolongations of the neuron. They often occur in the first part of the dendride and in such instances are elongated. The characteristic inclusion body contains an inner structure of basophilic staining granules. These granules vary from 0.2 to 0.5 micra in diameter and are surrounded by a clear zone in most stained preparations. The larger inclusions have a central granule and one or more layers of these inner bodies, separated by a finely granular ground substance or matrix. Though the matrix is basically eosinophilic as to staining reaction, it tends to take on a composite stain, bluish pink in preparations stained with eosin methylene blue, and mauve in carbolfuchsin methylene blue preparations. Small inclusion bodies are more abundant than the larger forms, and these are less characteristic in appearance. Some contain a central blue granule, but most of them are uniformly acidophilic.

The characteristic inclusion bodies are more typical and abundant in the Ammon's horn of the hippocampus than in any other part of the central nervous system. In this area they are especially numerous in the large neurons about the granule cell layer. Typical inclusion bodies generally are demonstrable in the pyramidal cells of the cortex, the Purkinje's cells of the cerebellum and the larger neurons of the basal ganglia and cranial nerve nuclei. The scarcity of typical inclusion bodies in the pons and medulla is probably explained by the rapid destruction of the neurons. When the disease has been of short duration, inclusion bodies are either absent or predominantly small, with only occasional large forms. When the disease has been of long duration, inclusion bodies are more numerous, less scattered in distribution, and there are relatively more large forms. The neurons of the ganglionic layer of the retina may contain inclusion bodies.

When Negri discovered the inclusion bodies of rabies, he believed they represented a form in the development of a protozoan-like parasite. Subsequent studies of the inclusion bodies of rabies, as well as of other diseases, indicate that although they may contain the elementary bodies of the virus, their structure is made up largely of a matrix derived from the cell protoplasm. The matrix of the inclusion body of rabies appears to be largely composed of saturated fatty acids and sterols as shown by

their staining reaction. There does not seem to be any definite relation between the occurrence of inclusion bodies and the concentration of virus as determined by titration in animals.

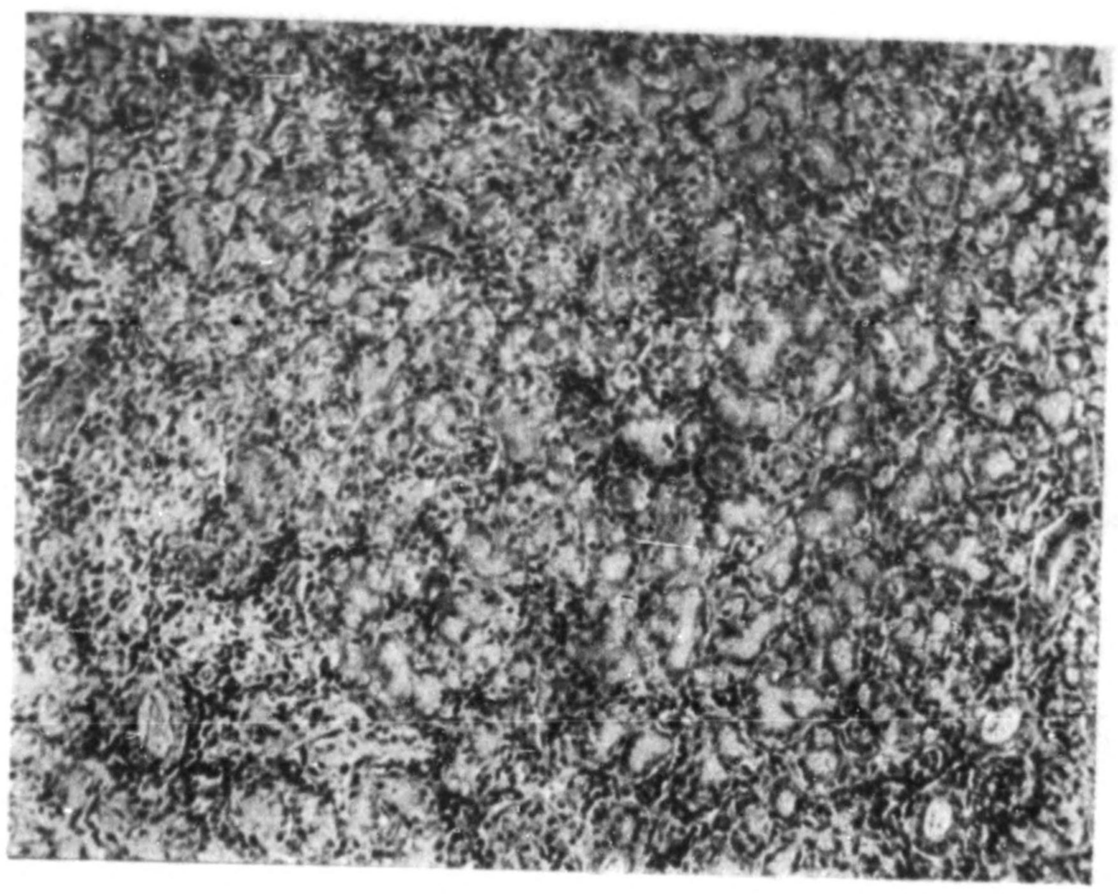
The studies of Goodpasture suggest that the inclusion bodies may be derived in part from the neurofibrillar and mitochondrial apparatus. The occurrence of small eosinophilic and basophilic granules in the cytoplasm of degenerating neurons is noted often. There is no satisfactory evidence to indicate that these represent the elementary bodies of the virus.

Ganglia. — Before the discovery of the specific inclusion bodies of rabies the examination of histological sections from the superior cervical sympathetic ganglia formed the principal method for the microscopical diagnosis of rabies. The nerve cells here show acute degeneration and are surrounded by large mononuclear cells in a rosette-like arrangement (Fig. 4). It is believed that the Schwann sheath cells hypertrophy to form the first layer of large cuboidal cells which have a distinctive appearance. The interstitial tissue of the ganglia often is heavily infiltrated by mononuclear cells. The neurons show degenerative changes similar to those described in the brain. Vacuolization of the cytoplasm is, however, more pronounced in the neurons of the ganglia.

The superior cervical sympathetic and gasserian ganglia present the most characteristic lesion, but the same changes occur to a variable degree in the other sympathetic and dorsal root ganglia. Similar pathological changes have been reported in diseases other than rabies. Furthermore, the lesion is not likely to be very definite where the disease has been of short duration.

Nerves. — The nerves supplying the region of exposure in human cases of rabies rarely have been studied. Dogs experimentally infected with rabies by inoculation of street virus into a peripheral nerve serve to illustrate the pathology of affected nerves. Sections central to the point of inoculation show coalescence of the neurofibrillæ and fragmentation of axis cylinders, vacuolization of the myelin sheath and a variable degree of chronic inflammatory reaction in the lymphatics of the nerve sheath.

Other Organs. — The mucosa of the conjunctiva and upper respiratory tract often exhibits an acute inflammatory reaction. The mucous glands of the submucosa may show acute degeneration of the acinar cells. The salivary and lacrimal glands may be normal in appearance. In some cases there is marked acute degeneration of the acinar cells, especially those of the mucous type, and the interstitial tissue is infiltrated by mononuclear cells (Fig. 5). Glands so affected generally contain a high concentration of virus. Although various types of granules and vacuoles are apparent, there is no satisfactory evidence that specific inclusion bodies are formed.



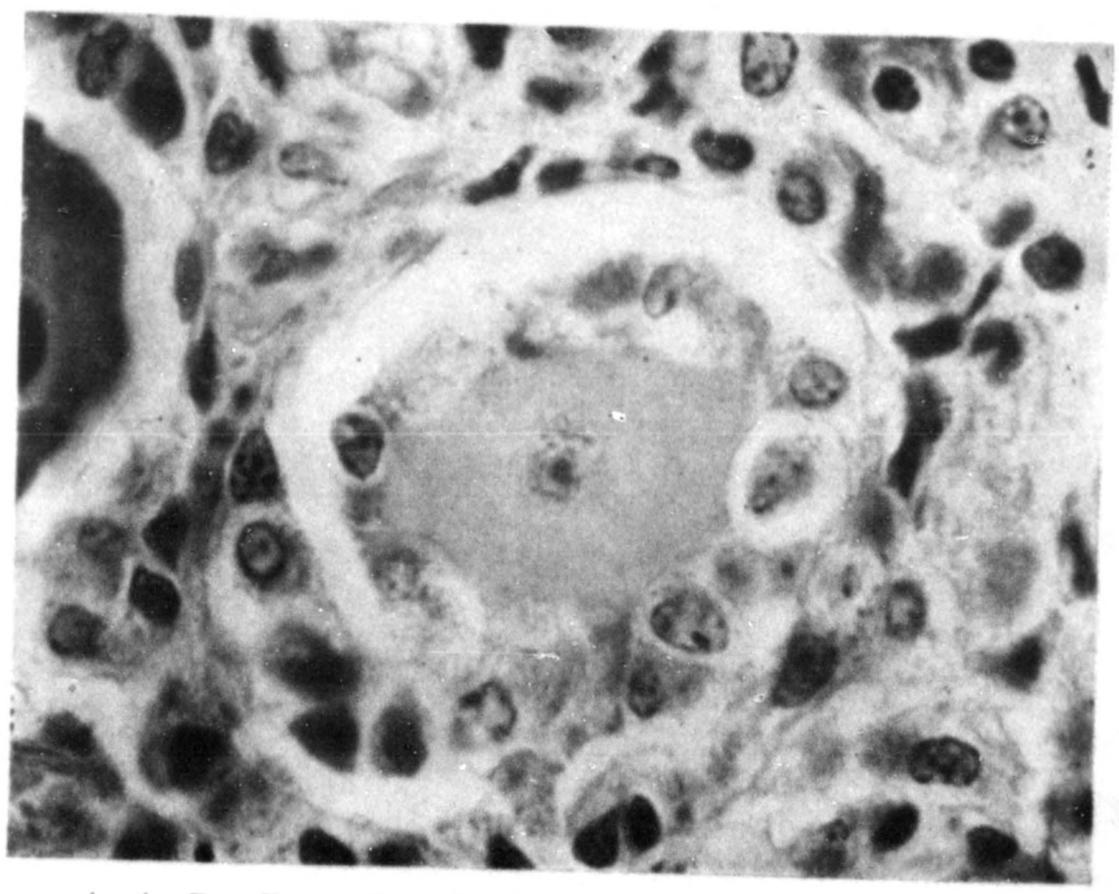


FIG. 4. (top) Paraffin section of the submaxillary gland of a dog experimentally infected with rabies; gland positive for virus; modified eosinmethylene blue stain; magnification 100; photograph by J. B. Haulenbeck.

FIG. 5. Paraffin section of the superior cervical sympathetic ganglion of a dog experimentally infected with rabies, illustrating the neuronal degeneration; modified eosinmethylene blue stain; magnification 1,000; photograph by J. B. Haulenbeck.

The ducts are normal but may be markedly distended with inspissated material which appears to be largely made up of mucus. The medullary cells of the adrenal gland often show acute degeneration associated with mononuclear cell infiltration of the medulla. The adrenal cortex is not appreciably altered in appearance. The tubule cells of the kidney may show acute degeneration, but inflammatory cellular infiltration of the interstitial tissue is seen rarely. The gastrointestinal tract shows no significant alteration other than congestion and edema of the mucosa. The neurons of the sympathetic plexuses may show changes similar to those described in the ganglia. The other abdominal organs show no characteristic pathology.

The secreting cells of the sweat glands of the axilla may show acute degeneration. The acinar cells of the breast tissue may exhibit a similar change. The eyes are not remarkable except for degeneration of the neurons of the ganglionic layer of the retina. The internal ear apparently is not affected except for neuronal degeneration.

The pathological changes in the central nervous system of persons dying of rabies are similar to those found in some other diseases, notably typhus fever, poliomyelitis and rabies treatment paralysis. When specific inclusion bodies are not demonstrable, sometimes it is impossible to make a pathological diagnosis of rabies. The diagnosis then depends on animal inoculation and isolation of the infecting agent.

Laboratory Diagnosis of Rabies

Microscopical Examination of Animal Brains

For microscopical diagnosis it is necessary to use a procedure that can be completed quickly and one which produces uniform results. It has been found that the inclusion bodies of rabies, when present, are readily demonstrated in smears or impressions of the Ammon's horn of the brain, stained by the method of Sellers (Fig. 2). This staining procedure is most practical because the preparation is fixed and stained at the same time, and the preparation of the stain is simple and inexpensive. The impression method is good because there is little distortion and rupture of cells; however, some prefer the smear method because more tissue will be obtained on one preparation.

To make an impression preparation it is best to cut a 1 to 2 mm. cross section from the middle of the Ammon's horn and place this on a piece of blotting paper. Using a clean glass slide, several impressions are obtained by pressing the slide down on the cut surface of the section.

While still wet, layer over with Sellers' stain for about ten seconds, rinse under the tap, blot and dry. The preparation then is ready for examination. The impression may be covered with a cover slip mounted in balsam or examined directly under oil.

Sellers' Stain

Stock Solution:

a) Saturated solution of basic fuchsin in methyl alcohol

b) Saturated solution of methylene blue in methyl alcohol

Staining Solution:

Stock basic fuchsin	3.5 c.c.
Stock methylene blue	15.0 c.c.
Methyl alcohol	25.0 c.c.

The staining solution can be kept in a dropper bottle, and if stored in a refrigerator when not in use, it will be good for several months.

The inclusion bodies of rabies, when stained by Sellers' method, appear mauve to pink-red in color, and the basophilic-staining inner bodies are well demonstrated. The cell cytoplasm, nuclei and nucleoli stain blue, and the interstitial tissue and fibrillæ stain pink (Fig. 2).

There are a variety of staining procedures that may be used for impression and smear preparations. Most of these require special fixation prior to staining. Fixation in methyl alcohol, with or without picric acid, generally is used for smears and impressions. For paraffin work acetic-Zenker's solution seems to be the best fixative. The preparations then may be stained with Mallory's or Mann's eosin methylene blue or Giemsa's or van Gieson's stains. There are a variety of modifications of these procedures.

If the eosin methylene blue technique is employed, the most satisfactory results are obtained when the alcohol-soluble ethyl eosin is used (Fig. 3). This is made up in a concentration of 1 per cent. in 95 per cent. ethyl alcohol. This solution should be adjusted to a pH of 3.5 to 4.5 with acetic acid as recommended by Stovall. The slides should be kept in this stain for about 30 minutes. The methylene blue counter stain should be alkaline, and the method of Unna is preferable. Five minutes is sufficient time for the counter stain. The sections then are differentiated in absolute alcohol containing a small amount of rosin. This technique is applicable also to smear and impression preparations. Goodpasture's method with carbolfuchsin methylene blue is excellent for demonstrating the inclusion bodies, but the nucleoli tend to take the red stain, which may be confusing. Wolbach's modification of Giemsa's

While still wet, layer over with Sellers' stain for about ten seconds, rinse under the tap, blot and dry. The preparation then is ready for examination. The impression may be covered with a cover slip mounted in balsam or examined directly under oil.

Sellers' Stain

Stock Solution:

a) Saturated solution of basic fuchsin in methyl alcohol

b) Saturated solution of methylene blue in methyl alcohol

Staining Solution:

Stock basic fuchsin	3.5 c.c.
Stock methylene blue	15.0 c.c.
Methyl alcohol	25.0 c.c.

The staining solution can be kept in a dropper bottle, and if stored in a refrigerator when not in use, it will be good for several months.

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stain readily demonstrates the inclusion bodies. However, unless the worker is experienced in the use of this method, the results are not likely to be uniform. Hematoxylin and eosin with formalin-fixed tissue occasionally gives fairly good results, but this more often is entirely unsatisfactory. The water-soluble eosin-yellow stain, if used according to the method of Mallory and where the pH of the stain is not adjusted to the acid side, is likely to give similar results.

When the microscopical preparations are from human material, there is little chance of making a mistake by confusing the inclusion bodies of rabies with those which occur in other diseases. In dog brains, however, inclusion bodies sometimes are encountered which, though similar to those occurring in rabies, are caused by other conditions, notably canine distemper. A trained observer will recognize these inclusions, as they are pale red and more refractile than those due to rabies and have no inner structure. They also tend to irregularity in outline and occur more frequently in the thalamus and lentiform nuclei than in the Ammon's horn.

Atypical intracytoplasmic inclusion bodies may be found in the brains of mice which do not have rabies. These in all probability are due to a natural virus disease of mice. These inclusions are pink to bright red in color, very refractile, uniformly round and do not have any inner structure. They show usually a blue staining margin.

Animal Inoculation

It is a well known fact that Negri bodies cannot be found always in men and animals dying of rabies. Therefore, if the microscopical examination of a brain specimen is negative, it is necessary to resort to animal inoculation in order to establish the diagnosis. In the past the guinea pig and rabbit have been considered the most suitable test animals for this purpose. Since the demonstration that the intracerebral injection of rabies virus into white mice produces a typical and constant infection, the white mouse has become increasingly popular as a test animal. The chief advantages of the mouse as the test animal are the low cost, making it possible to use several animals for one specimen, the relatively short incubation period, 6 to 10 days for street virus, and the consistency of production of inclusion bodies in mice inoculated intracerebrally with street virus.

A positive microscopical diagnosis is sufficient proof for the diagnosis of rabies. When the microscopical examination proves negative or questionable, a pool of the medulla, basal ganglia and cerebral cortex should

be ground in a mortar, using some abrasive such as sterile sand or alundum, and diluted with distilled water to make a 10 per cent. suspension. This is centrifuged and the supernatant fluid saved for animal inoculation. For diagnostic mouse inoculation 0.03 c.c. should be injected intracerebrally into each of 4 to 6 mice using a $\frac{1}{4}$ inch, 27 gauge needle and a $\frac{1}{4}$ c.c. tuberculin syringe. No antiseptic is necessary over the surface of the head, as bacterial infection of the brain rarely develops unless the material used for injection is contaminated. When bacteria are seen in the microscopical preparation, small portions of the brain should be placed in pure glycerin for a period of one week, or if it is necessary to avoid delay, the supernatant fluid from the brain suspension may be treated with 0.5 per cent. phenol for 6 hours, which rarely destroys enough virus to alter the results. Treatment with 1:5,000 merthiolate solution may be used also.

Any of the various strains of white mice are equally suitable as test animals. The injected mice should be held for 30 days. When 4 mice are inoculated with each specimen, except in rare instances one or more will develop rabies by the seventh to eighth day, if the specimen is positive. Mice developing symptoms are to be killed, and impression preparations, made from a cross section of the brain through the Ammon's horn area, are to be stained with Sellers' stain. This is necessary as other virus diseases may produce symptoms similar to rabies. The inclusion bodies of rabies usually are demonstrable in mice 2 days before the development of symptoms following intracerebral inoculation with street virus.

In the series of human rabies case records collected by the author 42 had reports of the microscopical examination of the brain. Of these 12 or 29 per cent. were negative for inclusion bodies. The demonstration of inclusion bodies in the brains of rabid animals, who have bitten human beings, is of importance in order to determine whether the person bitten was really exposed to rabies. In 1913 Negri and Luzzani reported the results of a study of 4,961 brain specimens by both microscopical examination and animal inoculation. No inclusion bodies were demonstrable in 6.7 per cent. of the specimens proved positive for rabies by animal inoculation. J. Koch and G. Jahn published a similar survey of the specimens received at the Robert Koch Institute at Berlin from 1913 to 1929. A total of 4,682 specimens were found positive for rabies by animal inoculation, and of these 11.8 per cent. were negative for inclusion bodies. In a series of routine brain specimens obtained from the Georgia State Health Department during 1937, 771 were positive for rabies by mouse inoculation. Of these 81 or 10.5 per cent. were negative for inclusion bodies.

The presence or absence of inclusion bodies in rabid animals depends to a considerable extent on the duration of the disease before the animal is killed or dies of rabies. For that reason it is advisable to hold biting dogs in quarantine rather than to kill them immediately and send the brain to a laboratory for diagnosis. There is a double reason for this. First, it will allow observation for symptoms of rabies in the animal, and as the mortality is to all intents 100 per cent., if the animal has rabies, it will die. Secondly, the longer the animal is allowed to live, the better the chance of obtaining a positive microscopical diagnosis. This is substantiated by the author's observations of experimentally infected dogs. Of 188 dogs infected with rabies by intramuscular inoculation of street virus and allowed to die, 87 per cent. of the animals that lived over 3 days were positive for inclusion bodies. Only 48 per cent. of the dogs developing paralytic rabies were positive by microscopic examination.

Biting dogs, i.e., those with furious rabies, are apt to live three or more days after the onset of symptoms, and a positive microscopical diagnosis probably can be made in about 90 per cent. of animals so affected.

Prevention of Rabies after Exposure

Local Treatment

It is imperative that lacerations, abrasions or scratches occurring as a result of exposure to rabid animals be given prompt local treatment. The experimental work of Galtier, Remlinger and Rosenau and the author's own observations have shown that infection can be produced readily in animals by rubbing the virus into the scarified skin. Wounds in areas heavily supplied with sensory organs, such as the face and hands, are especially dangerous. Wounds penetrating the muscle tissue probably are even more serious.

The experimental work of Follen Cabot and Rosenau form the basis for the use of nitric acid for the treatment of dog bite wounds to prevent rabies. They showed that cauterizing with nitric acid was highly effective in preventing the disease in guinea pigs exposed by intramuscular injection of rabies virus even when performed twenty-four hours after inoculation. Partial protection was obtained in those treated forty-eight hours after inoculation. More recently Shaughnessy and Zichis have compared the effectiveness of nitric acid, 20 per cent. green soap solution and tincture of iodine for the treatment of wounds in experimentally infected guinea pigs. They found that the green soap solution was as effective as nitric acid where the treatment was carried out within two hours after exposure. Tincture of iodine was less effective.

The first and most important step in treating wounds produced by rabid or suspected rabid animals is thorough cleansing with warm water and soap. In this way the saliva can be removed and bleeding encouraged before cautery is applied. Cleansing of deep lacerations can be carried out effectively with a syringe. For the present, in the opinion of the author, all patients should receive local treatment with nitric acid. Because of its diffusibility and penetration it remains the surest method of destroying the virus in puncture wounds and especially of penetrating the tissue and killing the virus, if local treatment is delayed. The wound should be sponged dry and the nitric acid applied with a capillary pipette or wooden applicator. Especial care should be taken not to miss small superficial abrasions, and the margins of the torn skin of larger wounds should receive particular attention. Where the wounds are severe, the cauterization should be performed under anesthesia. Following cauterization with nitric acid the wounds should be treated with a solution of sodium bicarbonate.

There are occasions where children are so badly lacerated about the face that thorough cauterization with nitric acid is not feasible. In such instances the author recommends thorough cleansing of the wounds with green soap solution followed by nitric acid cauterization of superficial abrasions, puncture wounds and the margins of the lacerated skin.

As has been noted previously, there are records of large series of cases of exposure to rabid animal bite treated only by incision and actual cautery or other local treatment with a very low mortality rate. In view of this too much reliance should not be placed on the post-exposure vaccine treatment.

Vaccine Treatment

Rabies vaccine of one type or another is recommended by public health authorities throughout the world for the treatment of exposed persons. The remarkably low mortality in treated persons has been considered adequate proof for its use despite the absence of satisfactory data as to the susceptibility of man to rabies and the effect of local treatment alone.

There are a variety of vaccines available for the treatment of persons exposed to rabies. There is no clear-cut evidence that any one is superior in preventing the disease.

Treatment Failure Rate. — McKendrick has presented several analytical reviews of the reports of Pasteur Institutes on human rabies vaccination. In his eighth review he included 705,855 completed treatments with

2,676 treatment failures, a mortality rate of 0.38 per cent. It must be noted that the Pasteur Institutes do not consider as treatment failures those cases that develop symptoms within two weeks after the completion of treatment. There were 5,943 persons bitten on the face, and the treatment failure rate for this group was 1.83 per cent. Kraus, Gerlach and Schweinburg analyzed 3,646 case records of persons bitten on the head and given the vaccine treatment. A total of 211 of these died of rabies, or 5.51 per cent. Discarding those cases, which occurred prior to two weeks after completion of treatment, they listed a reduced treatment failure rate of 1.89 per cent.

Despite the marked differences in the preparation of various human rabies vaccines there does not seem to be any significant statistical difference in the results obtained by the various methods.

Criteria for Treatment. — Several factors are to be considered before advising rabies vaccine treatment for persons bitten or scratched by dogs, cats or other domestic and wild animals. First, it should be ascertained whether there has been any rabies reported in areas where the patient had resided during the previous year; next, whether the animal was apprehended or killed. If the animal was captured, it should be turned over to a veterinarian, and he should be consulted as to whether there are any clinical signs of rabies. If the animal is clinically normal, it should be quarantined for 14 days. The attending physician should be notified immediately, if the animal subsequently shows clinical signs of rabies. If the animal was killed or dies while in quarantine, the brain should be submitted to a diagnostic laboratory for microscopical examination. When the laboratory is located at some distance, the animal head should be dispatched in a water-tight container packed in ice. Unfortunately, persons are often bitten by a stray dog which is not apprehended or which has been killed immediately. In such cases an attempt should be made to ascertain the behavior of the animal before the person was bitten, and an attempt should be made to locate the animal if it ran away. Taking these factors into consideration, the following procedure is recommended: Rabies vaccine treatment is to be started immediately when a person has been bitten or scratched under the following conditions:

1. The animal was apprehended and presented clinical signs of rabies.
2. The animal was killed and the brain found positive for rabies by microscopical examination.
3. The animal was killed, and although the brain was negative, the animal was suspected of being rabid.
4. The person was exposed by a stray animal which escaped and where rabies was known to be present in the community.

The vaccine treatment is recommended also for persons who have handled animals diagnosed as rabid by clinical or laboratory means, and when fresh abrasions of the skin were contaminated by the saliva of the infected animal.

It must be emphasized that, when an animal is apprehended after attacking a person and rabies is suspected, it should not be killed but should be confined under supervision of a veterinarian. If the animal has rabies, usually it will die within 2 to 3 days. This is important, as the immediate laboratory diagnosis of rabies depends on the demonstration of specific inclusion bodies in the brain of the animal, and these often are absent in the early stages of the disease.

It is apparent then that treatment should be begun, if the biting animal, though apparently normal at the time of biting, later develops clinical signs of rabies while in quarantine. Treatment may be discontinued, if the biting dog, held in quarantine, remains well for 10 days.

The mouse inoculation test for the diagnosis of rabies in animals has a limited value as regards the question of rabies vaccine treatment. However, when an animal is killed immediately after biting a person, and the brain is examined and found negative by microscopical examination, a confirmatory mouse inoculation test should be performed. If the test is negative, it reassures the patient, who might otherwise live in fear of developing the disease.

Vaccines Containing No Live Virus

Semple Vaccine. — A number of state health departments in this country prepare and dispense this vaccine free of charge. It is also available commercially. The vaccine is prepared from the brains of rabbits killed when prostrate with fixed virus rabies. An 8 per cent. suspension of finely ground brain material is made up in normal saline containing one per cent. phenol. This is incubated for 24 hours at 37° C. It is then diluted with an equal volume of normal saline to make a 4 per cent. brain emulsion in normal saline containing 0.5 per cent. phenol. The vaccine then is stored in a refrigerator. The dose is 2 c.c., and the usual scheme consists of 14 daily subcutaneous injections.

Cumming Vaccine. — This vaccine is used by the Michigan State Health Department. It is also available commercially. There have been some modifications of Cumming's original method, but in general they are similar in that a 1 or 2 per cent. suspension of rabbit brain fixed virus in distilled water is treated with 0.1 or 0.2 per cent. formaldehyde solution. The formaldehyde then is dialyzed out through collodion tubes immersed

in running distilled water. A small amount of tricresol then is added as a preservative. The vaccine is dispensed in 2 c.c. amounts which constitutes the final dosage. Fourteen to 21 daily doses are recommended.

Kelser Vaccine. — This is available commercially but as yet has had only a limited clinical trial. The virus is completely inactivated by exposure to one per cent. chloroform at refrigerator temperature. The human vaccine contains 25 per cent. brain and cord tissue in normal saline. The treatment consists of 14 daily injections of 0.5 c.c. vaccine.

Live Virus Vaccines

Pasteur Vaccine. — The dried cord vaccine is no longer recommended by health officials in the United States and is not available on a commercial basis. A number of Pasteur Institutes in other countries still use this method. The treatment usually is begun with a five day cord and ended with a one day cord. The dosage is 2 c.c. of a 5 per cent. tissue suspension in normal saline. The treatment takes 14 to 21 days depending on the severity of exposure.

Sellers Vaccine. — This vaccine is prepared and dispensed by the Georgia State Health Department. It is not available commercially. The treatment recommended depends on the severity of the exposure. The usual treatment consists of 21 daily injections of 2 c.c. of a 1:150 suspension of rabbit brain fixed virus made up in 20 per cent. glycerin saline containing 0.5 per cent. phenol. For severe exposures three injections are given daily, increasing the concentration of the brain suspension to 1:100 on the seventh day and 1:50 on the tenth day and finishing the course in 15 days.

Harris Vaccine. — Harris introduced the use of desiccated virus for human vaccine treatment. The dosage is calculated by the titre of the dried virus. In the original method the treatment was begun with 500 M.L.D. virus, followed by increasing concentrations of virus until the fifth, sixth or seventh days, when 3,000 M.L.D. were administered. A modified Harris vaccine is now dispensed commercially. The dosage is the same for each day. Each dose consists of a calculated dosage of rehydrated virus, and 14 daily injections are recommended.

Reactions to Rabies Vaccine Treatment

The administration of repeated injections of human rabies vaccine may be followed by a variety of local and general reactions. This is to

be expected in view of the amount of foreign protein introduced and the number of injections that are required. Since the introduction of this treatment, a number of reasons have been advanced to explain the neuritic and paralytic manifestations that sometimes occur. At first these reactions were attributed to the presence of live virus in the vaccine, but in view of the occurrence of such symptoms following the administration of vaccines containing no demonstrable virus, the present opinion seems to be that the reactions are on an allergic basis, that is, sensitization to the brain tissue in the vaccine.

The studies of Schwentker and Rivers support the theory that these reactions are due to sensitization to the brain protein. They found that brain tissue could function as a complete antigen, which was organ specific rather than species specific.

Acute General Reaction. — This occurs in persons who have been sensitized previously to rabbit brain protein. It is characterized by syncope or general urticaria or angioneurotic edema. This is an infrequent complication and is relieved quickly by adrenalin.

Delayed Local Reaction. — This is characterized by erythema and edema about the site of vaccination with accompanying pruritus, pain and tenderness. The wheal-like skin lesion may be 3 to 5 cm. in diameter. There may be slight malaise and a slight rise in the body temperature. This reaction is most likely to develop on the seventh to eighth day of treatment and tends to subside despite continued treatment. A second flare-up may occur again on the fifteenth to sixteenth day of treatment, when 21 injections are being given. This type of reaction is quite frequent and should cause no alarm.

Severe Delayed Reaction. — Here the delayed local reaction symptoms are accompanied by constitutional symptoms such as headache, fever, nausea, lymphadenopathy and general malaise. This type of reaction should warrant careful consideration before continuing treatment, as neuritic and paralytic manifestations are prone to develop, if the treatment is continued. An acute encephalitis may develop also. The severe delayed type of reaction is relatively uncommon. It is not apt to begin until after the seventh or eighth injection.

Peripheral Neuritis. — This develops most often during the latter part of the treatment course and may be accompanied by fever. The symptoms often are referable to the facial nerve. Neuritic symptoms involving the spine and lower extremities are next in frequency.

Dorsal-Lumbar Myelitis. — This is characterized by fever and gradual onset of weakness, numbness and tingling of the lower extremities. Patients thus affected usually recover. Treatment should be discontinued,

if not already completed. This complication may occur at any time from the tenth injection to one week after completion of treatment.

Paralysis of Landry's Type. — This symptom complex usually is ushered in by high fever, headache, nausea, vomiting, girdle pains, urinary retention and ascending paralysis of the lower extremities. It may come on after 5 to 10 injections or any time up to two weeks after the completion of treatment. The paralysis may progress to involve the bulbar nuclei, resulting in respiratory and cardiac arrest. Recovery may be rapid or gradual over a period of months. In rare instances there is permanent disability. The mortality rate appears to be about 30 per cent.

McKendrick, in his eighth analytical review of reports from Pasteur Institutes on the results of antirabic treatment, listed 112 paralytic accidents with 38 deaths from a series of 703,980 treatments. From reports of rabies treatment reactions in the United States it appears that about one in 3,000 persons treated will develop treatment paralysis. Treatment reactions are more common in persons who have had previous courses of treatment.

Author's Recommendations for Treatment with Vaccine

The author recommends the Semple vaccine for treatment of persons exposed to rabies. Fourteen daily injections of 2 c.c. of this vaccine are to be given beginning as soon as possible after exposure. The scheme of treatment for children is the same as that for adults. The vaccine should be given subcutaneously in the abdominal area using a different site for each injection. It should be made certain that the needle is not introduced into a vein. Adrenalin should always be at hand to treat an acute reaction, if that appears. There is no evidence to support the use of a more intensive scheme of treatment for persons severely bitten. During the course of treatment the patient should be permitted to lead a normal life.

The occurrence of local reaction to the injection of vaccine does not contraindicate the continuation of the treatment, but the development of general symptoms, either acute or delayed, especially neurological manifestations, warrant prompt discontinuation of the treatment.

It must be noted that, as a rule, the patients exhibit no discomfort of any kind from the treatment, and severe reactions are rarely encountered. Patients receiving a second course of treatment should be watched carefully as most of the severe reactions occur in such cases.

Control of Rabies

Due to the lack of concerted action in establishing rigid dog control legislation, rabies has continued to be prevalent in the United States. Vectors other than the dog have played but a minor part in the propagation of the disease in this country. Where rabies has become established in wild life species, it has been possible to control the disease by reduction of the species of wild life affected.

The best example of the effect of rigid dog control regulations on the incidence of rabies is the program which made possible the eradication of the disease from England. The procedures used were similar to those carried out in Sweden, Norway, Denmark, Prussia and Switzerland. The following sanitary procedures were enforced:

1. Imposition of a tax on all dogs.
2. Seizure and destruction of all ownerless and wandering dogs.
3. Destruction of all dogs with rabies or suspected of being or becoming rabid.
4. Requirement that all other dogs wear a properly constructed and well fitting muzzle, while rabies prevails and for a period of the longest latency after the last reported case.
5. Subjection of all imported dogs to a six months' quarantine period.

Taxation is a necessary factor in dog control legislation. It allows collection of data as to the number of dogs in a given area and shows the ownership of a dog by the attached license. It also secures some reduction in the total number of dogs. The ownership of dogs then is largely limited to those who will take good care of the animals and who assume responsibility for the same. It is generally agreed that unspayed female dogs should be subject to a higher tax than males and spayed animals. This is essential, because it will lessen the number of mongrel dogs that so often become strays. Then, too, the female dog in heat attracts large groups of dogs, which in fighting may cause the infection of numerous animals, should one be a carrier or in the early stages of the disease.

The ownerless and wandering dog is a menace where rabies is prevalent. All are agreed that these animals should be eliminated, but in order to do this funds and a suitable personnel must be available to collect such animals. This control measure, then, to a certain degree rests on taxation of dogs, as this makes the funds available to carry out such a program.

The question then arises: Who is to have the responsibility of enforcing dog control legislation? In England the Department of Agriculture

was responsible for the dog control program. The Livestock Sanitary Association, acting under the Federal Bureau of Animal Industry, is the best agency for carrying out such legislation in this country. To date the authorities have been handicapped by the failure to include the dog under livestock acts and regulations. In order to obviate antipathy on the part of the public to collecting dogs and to the enforcement of regulations on owned dogs, the local enforcement of the regulations should be in the hands of a competent veterinarian acting in accord with the State Health Department and the State Veterinarian. Rabies in animals should be a reportable disease, and these reports should be available to both the State Health Officer and State Veterinarian.

In districts, where rabies is present in the dog population, certain regulations are imperative. When a rabid dog is found, every effort should be made to locate the owner and find out where the dog has been seen and what animals were exposed. All animals bitten by the dog should be killed. The potential long incubation period and possible carrier state make this important. Where valuable animals have been exposed, they may be allowed to live, if kept in quarantine for six months. A quarantine for all dogs in the immediate territory should be imposed at once and kept in force until 90 days after the last reported case of rabies. All owned dogs are to be kept on the owner's premises or on leash, and any dogs running free should be impounded. The authority in charge of dog control regulations should notify transportation companies regarding the quarantine and also the inspectors in adjoining districts. No dog should be allowed to leave an area which is under quarantine.

The use of vaccination of dogs as a means of controlling rabies was not considered practical until Umeno and Doi in 1921 introduced a single injection method of immunization. They stated that one injection of a 25 per cent. phenolized fixed virus brain emulsion containing live virus would produce immunity to rabies. Vaccination of dogs subsequently was made compulsory in Japan. The sharp decline in the incidence of rabies for that country cannot be entirely attributed to vaccination, as other dog control regulations were enforced also. Eichhorn and Lyon in 1922 introduced the Umeno and Doi vaccine in the United States, and this method was used on a considerable scale until the U. S. Department of Agriculture passed a ruling that canine rabies vaccine must not contain live virus. This law was passed because occasional vaccinated dogs developed fixed virus rabies. Reichel and Schneider in 1923 and Schlingman in 1925 reported that a single injection of phenolized vaccine containing no live virus was effective for immunization of dogs. Their work was not substantiated by Schoening in 1930, Barnes, Metcalf, Martindale and

Lentz in 1934 or Webster in 1939. Kelser introduced a chloroform-inactivated canine rabies vaccine in 1930. Although experimental studies have produced some evidence that this, as well as other types of vaccines containing no active virus, will produce immunity in the dog, the lack of properly controlled experiments have led to conflicting reports as to the value of vaccination in controlling rabies.

It is difficult to determine the value of vaccination from the reports of its use in the field control of rabies. Other sanitary measures usually are included. Johnson and Leach have shown that one 5 c.c. subcutaneous injection of canine rabies vaccine containing no demonstrable live virus can produce a high resistance in the dog to intramuscular inoculation of street virus. In one test 50 dogs were given a single 5 c.c. dose of chloroform-inactivated canine rabies vaccine containing 33⅓ per cent. brain material and tested one month later by injection of street virus into the masseter muscles. Only 2 of these dogs died of rabies, 4 per cent., compared to 34 of 55 control dogs similarly inoculated, 62 per cent. A test of a phenol-inactivated vaccine of the same brain concentration produced a similar degree of protection. Four states in this country have adopted compulsory vaccination, but the law has been difficult to enforce, and although a reduction in the incidence of rabies has been attained, the disease has continued to occur.

Vaccination of dogs no doubt can be a useful adjunct to the dog control regulations previously mentioned and might be made compulsory in infected areas, but vaccinated dogs should not be allowed special privileges.

When rabies becomes established in wild animals, it is necessary to institute a vigorous trapping and hunting program to reduce drastically the number of animals. When rabies is found to be present in a wild animal species, the state and federal wild life agencies should be notified immediately, and they will supervise the control program. Vampire bat rabies apparently has been eradicated from Trinidad in British West Indies by a drastic reduction of the bat population. A similar program is under way in South American countries where the vampire bats are known to be infected. Large scale vaccination of domestic animals with phenolized live virus rabies vaccine has been used in Brazil and Venezuela with apparent success.

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March 1, 1943.

D16

Rabies

HOW IT IS CONTRACTED

Rabies, or hydrophobia, is caused by a disease agent called a "virus." This virus attacks the brain and spinal cord. It is spread mainly by the bite of infected dogs. Cats, cows, horses, coyotes, goats, hogs, sheep, skunks, wolves, squirrels, and other warm-blooded animals are also susceptible to the disease. An animal suffering from rabies is commonly said to be "rabid" or "mad."

Rabies virus is present in the saliva of a rabid animal. If a person is bitten by the animal, the saliva, loaded with virus, enters his body through the bite. Or saliva from a rabid animal may enter the body through any wound in the skin that is exposed to it. The virus reaches the brain by traveling along the nerves.

The Incubation Period of Rabies—The length of time it takes after infection for the virus to reach the brain and produce the symptoms of rabies is called the "incubation period." The average period of incubation in man is from 50 to 60 days and in dogs from 15 to 30 days, but in either the disease may develop in less than 10 days after a bite, or it may not develop for several months. The closer the wound is to the brain, the more quickly the virus will reach the brain. For example, rabies develops earlier after bites on the head and face than after bites on the hand and arm.

Not everyone develops rabies after a rabid animal bite or after wound contact with the saliva of a rabid animal. But no one who has once shown symptoms of rabies has ever recovered. THE DISEASE IS 100-PERCENT FATAL, BOTH FOR MAN AND BEAST.

How a Person Bitten by a Rabid Animal May Be Protected from Rabies—The fact that it usually takes a comparatively long time for rabies to develop makes possible the prevention of the disease *after* the virus has entered the body. The protective measure used is a series of inoculations with weakened rabies virus. This treatment, which is called the Pasteur treatment, prevents the development of the disease in the great majority of cases if it is started soon enough after infection and if continued long enough to give adequate protection. The treatment is of no value after the symptoms of rabies appear.

How Rabies in Animals May Be Detected—In dogs there are two types of rabies—the "furious" type and the "dumb," or paralytic, type. A dog suffering from the furious type alternates periods of excitement with periods of repose. As the disease progresses the dog becomes vicious and bites any person or animal in its way.

A dog suffering from the dumb, or paralytic, type appears only to be sick and shows little or no irritability. Someone not knowing what ails the dog may try to treat it or to pet it. If this person has any break in the skin, no matter how slight, it is possible that the dog's saliva may come in contact with the wound and cause infection. To guard against this danger, a sick dog should be handled with extreme care and kept under observation in a place by itself until a definite diagnosis can be made. The safest procedure is to have a sick animal treated by a veterinarian.

The last stage of both types of rabies is paralysis of the muscles. Usually the paralysis is noted first in the lower jaw, which hangs down. If this happens, saliva runs out of the mouth, and the dog is said to be "frothing at the mouth." Paralysis rapidly spreads to other parts of the body, and death follows in two or three days.

What to Do in Case of Animal Bite—In all cases of animal bite, wash the wound under *running water* to remove the animal's saliva. Then go to a physician as quickly as possible to have the wound thoroughly cleaned out and other needed treatment given. After the wound has been cared for, the next step is to determine whether the person bitten should be given the Pasteur treatment for the prevention of rabies. This depends primarily on whether the biting animal is rabid. It should not be killed immediately (except to protect others), since it may not have rabies, and a valuable animal may thus be saved. If a dog escapes after biting someone, no effort should be spared to capture it. It may wander a considerable distance, but may be traced by thorough and persistent inquiry.

To find out whether the biting animal is rabid, shut it up securely and watch it closely for symptoms of rabies. If the dog appears normal and remains so for from 10 to 14 days, the possibility of rabies may be dismissed. In this case there is no danger from the bite, except the danger of infection common to all wounds.

If it is clearly evident that the biting animal is rabid, or if it cannot be caught and observed, the victim should receive the Pasteur antirabic treatment as promptly as possible. The treatment should be started at once without waiting to find out whether the animal is rabid, if the bite is on the head or neck. If the dog is killed, or dies while under observation, its head should be packed in ice and sent immediately to the nearest health department laboratory for examination. If it is necessary to shoot an animal for the protection of others, it should not be shot through the head, since this may interfere with the laboratory examination of the brain. Treatment should not be delayed for the laboratory report if the animal's symptoms before death suggested rabies. In case the examination shows that the

animal had rabies, the person or persons bitten by it must be given the Pasteur treatment *without delay*. If you are unable to employ a private physician, go at once to the local health officer.

How to Prevent the Spread of Rabies—The way to prevent the spread of rabies is, of course, to keep human beings and animals from coming in contact with rabid animals. If a dog is found to have rabies, a search should be made for other domestic animals or persons who have been bitten, so that they can be controlled or given treatment promptly. Dog owners should be made aware of the danger of rabies; a license fee and a tag should be required for all dogs, and ownerless dogs should be eliminated.

Measures taken in various localities to stamp out rabies include the requirement that all dogs must be muzzled effectively or held on a leash while in the streets, the confinement of all dogs to leash or paddock during an epidemic of rabies, and the compulsory reporting to the health department of all cases or suspected cases.

If cases of rabies occur in your community, you will be asked to obey the rules or ordinances put into force by your local health authorities to control the outbreak. These rules are for the protection of your pets and farm animals, but, what is more important, they are for the protection of your family and neighbors. No one need die of rabies, but unless animal owners cooperate with the authorities it is almost certain that some deaths will occur.

Recently a preventive vaccine has been prepared which, when given to dogs, is believed to protect them from rabies for a limited period. Although the effectiveness of dog vaccination is in question, many health officers and veterinarians consider it to be a procedure that certainly is warranted, particularly where quarantine and other methods of control are ineffective or unavailable.

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D 16

Rabies

OTHER NAMES—HYDROPHOBIA. MAD DOG

General Information for Those Who Have to Deal with Persons Bitten by Animals

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Issued by the IOWA STATE DEPARTMENT OF HEALTH
Des Moines, Iowa

Question: What is Rabies?

Answer: Rabies is an acute infectious disease to which man and certain lower animals are susceptible, characterized by spasms of the larynx, pharynx, and other muscles, and is always fatal. The sick animal is usually said to be "mad".

Q. Is the disease more prevalent in summer than in winter?

A. Many Pasteur Institutes where most of the infected people are treated, report that there are more patients in the winter than in the summer. Laboratories where large numbers of specimens are examined report that while more specimens are examined in the summer months, specimens found rabid are about equally divided between summer and winter months. Season apparently has no effect upon rabies. This has been found true in Iowa.

Q. What animals are subject to rabies?

A. Man, dogs, skunks, cats, squirrels, horses, cows, hogs and other warm blooded animals have been found rabid.

Q. Would the bite of a dog "just mad with the heat" cause rabies?

A. Unless an animal has rabies its bite can not cause the disease. The irritability of a dog on a hot day is probably about the same as that of a person under similar circumstances.

Q. Does the hot weather make dogs have rabies?

A. No. The only way an animal can get rabies is to be bitten by another animal that has the disease.

Q. How do cattle, hogs, etc., get rabies?

A. Usually they are bitten by dogs or wild animals such as skunks in the early stages of rabies.

Q. Is the loss of stock from rabies important?

A. Yes. The loss is very great each year.

Q. What are the first symptoms of rabies?

A. Change of disposition. A dog that has always been playful and careful with the children or their master, will growl and snap at them. In the light of later happenings the owner frequently says that he noticed that the dog "didn't act just right", or that he thought the dog "behaved queerly" or, "acted as if he were sick". Any dog with changed behaviour should be suspected—it, no doubt, is ill or diseased.

Q. How does the dog act when the disease is fully developed?

A. Frequently for very little obvious reason, except that he is a sick animal, he will bite or "snap at" a former playmate or friend. He is probably having painful convulsions of the muscles of the throat. If suspicious, consult your veterinarian.

Q. How does the dog look at this time?

A. His eyes are glassy, his mouth usually hangs open and the saliva frequently drools from his mouth. He may act as if he had a bone lodged in the throat. In the later stages the dog is usually quite excited and runs about snapping at everything that might harm him. Occasionally this later stage is quite the opposite and the dog lies about quite dumb and sleepy, only biting at persons and things that disturb him. Many of these cases of so-called "dumb rabies" are not diagnosed because the terminal symptoms are so different from the usual type. If your dog acts suspiciously call your veterinarian.

Q. What can be done for a dog with rabies?

A. Make him comfortable in a secure place where he cannot bite any person or dog. He will die in less than fourteen days.

Q. Is this disease always fatal to human beings?

A. Yes, it is always fatal, if symptoms develop.

Q. Can the development of symptoms be prevented after a person is bitten by a rabid animal?

A. Yes. The Pasteur Treatment given promptly will prevent the development of symptoms. Persons who have been bitten on the face or hands or who received extensive lacerating bites should begin treatment immediately. In cases of ordinary bites about the extremities, especially if through clothing, treatment may be delayed until the dog dies and laboratory examination can be made.

Q. How can I be sure that the animal that bit my child is not rabid?

A. If the animal lives fourteen days, he was not rabid at the time of biting. If the animal head sent to the laboratory proved negative on microscopic and mouse inoculation, the animal was not rabid.

Q. If the child cannot identify the dog or the dog cannot be found, what should be done?

A. The only safe policy against rabies is to consider all biting dogs or other animals as rabid until it is conclusively proven that they are not rabid.

In Case of Dog Bite

WHAT TO DO WITH THE DOG:

1. Don't kill the dog unless this is necessary to effect capture.
2. Securely shut him up in a cage or stall.
3. Call a veterinarian.
4. Keep the dog in a comfortable place.
5. Treat the dog kindly, but take no chances of being bitten.
6. Give the dog plenty of food and drink.
7. MAKE SURE that the dog does not escape.
8. Keep children and inquisitive adults away.
9. If the dog is alive after fourteen days, HE WAS NOT RABID.
10. If the dog dies within fourteen days,
    (a) Cut off the whole head. Carefully disinfect axe or knife used.
    (b) Put the head in a tin pail with a cover, (for example, a 10 lb. lard pail).
    (c) Pack this pail in the middle of a 5-gallon lard pail, with ½ sawdust and ½ ice.
    (d) If at all possible take the specimen so packed to the laboratory, or ship at once by prepaid express to "State Hygienic Laboratories, Iowa City, Iowa." Tack letter on outside of pail—giving history of dog and state whether a person (give name and address) was bitten. Also give name and address of attending physician.

IF THE DOG MUST BE KILLED TO EFFECT CAPTURE:

1. Do not damage the head in any way.
2. Cut off the head, pack and ship it as described, at once.

WHAT TO DO FOR THE PERSON BITTEN:

1. Take the patient to a physician at once to have the wounds cauterized. This is of especial and urgent importance.

2. In bites above the shoulder, begin the Pasteur treatment **immediately**, without waiting to ascertain whether the animal is rabid. Every hour of delay is dangerous.

3. If the bites are on the body and extremities, and are extensive in character, have wounds cauterized and start Pasteur treatment at once.

4. In minor bites about the extremities, if there is doubt that the animal is rabid, it is permissible, after cauterization of the wounds, to postpone Pasteur treatment pending observation of the animal or reports from the laboratory, as stated above. At the laboratory, every properly preserved specimen of suspected rabies is examined both miscroscopically and by mouse inoculation for the presence of rabies. The mouse test detects approximately ten percent of rabies which cannot be detected by the microscopic test.

5. Important! The State Department of Health at Des Moines has anti-rabic vaccine ready to send on telegraphic request to physicians, for all persons bitten by dogs not known to be free from rabies. This treatment will be furnished to your physician at cost, and is obtainable at any hour of the day or night from the State Department of Health at Des Moines.

Note: Extra copies of this pamphlet may be obtained, free, by writing to

The Iowa State Department of Health,
Des Moines, Iowa.

D 16

The Commonwealth of Massachusetts

DEPARTMENT OF PUBLIC HEALTH

RABIES (Hydrophobia)

PUBLICATION OF THIS DOCUMENT APPROVED BY THE COMMISSION ON ADMINISTRATION AND FINANCE

25m—6-'34. No. 1716.

THE COMMONWEALTH OF MASSACHUSETTS

DEPARTMENT OF PUBLIC HEALTH

RABIES (*Hydrophobia*)

Rabies is a fatal disease affecting chiefly dogs but transmissible also to other animals and to man. When the disease develops there is no treatment, death occurring in a few days. Your only protection against rabies is to prevent its development.

How is rabies spread? Rabies is caused by what is known as a filterable virus. This virus is present in the saliva of a rabid animal, and may also be present for several days before it is known that the animal is sick. The virus enters the body through breaks in the skin such as may be caused by a bite. Cuts, scratches or other breaks in the skin, if they are exposed to the saliva of a rabid dog, may be the portal of infection.

After the virus enters the body, it grows along the nerves until it reaches the brain. It is for this reason that bites around the head and neck are especially dangerous, for the virus has a shorter distance to travel before it reaches the brain. Bites through clothing may be rather less dangerous than those on exposed parts of the body because the clothing may wipe some of the saliva from the dog's teeth. This should not, however, be relied upon for protection.

Rabies in dogs—There are two types of the disease, but there is no difference in danger between the types. In the one, "dumb" rabies, the animal becomes slowly paralyzed, and shows little or no excitement. Difficulty in swallowing has often led the owner to reach into the dog's throat in search of the supposed bone on which the dog is thought to be choking. The other and more common "rabid" type begins with a changed disposition, the dog being irritable. It later becomes excited and often runs many miles snapping at everything in its way. Paralysis follows as in the "dumb" type.

Rabies in dogs can be prevented. Annual injections of a single dose of especially prepared vaccine will protect most dogs against rabies. Although occasionally a dog so treated may develop rabies, if exposed, this is unusual. Vaccination of dogs has been used with great success in many places to control rabies. To be effective it must, however, be repeated every year. Similarly a dog bitten by

another dog known or suspected to be rabid may be protected against rabies though this requires a series of injections. A dog that is worth having is worth protecting.

Incubation period—By this is meant the time that elapses between the bite and the beginning of symptoms. In animals this varies from two or three weeks to six months. The same figures apply to man. The commonest period is about six weeks, with rarely the longer period of six months. This allows time to begin proper treatment.

Anti-rabic treatment—Before the work of Pasteur, rabies took a heavy toll of human lives because there was no effective means of prevention. Pasteur developed a method of inoculating persons against rabies. Since it usually takes weeks for the disease to develop after the bite, there is time to take these treatments and be protected by them. These may consist of either 14 or 21 injections, depending upon the type of bite and type of anti-rabic vaccine. If you have been bitten by a rabid or stray dog, this is your only reliable protection.

What to do if bitten by a dog—

(1) *Do not kill the dog.* If you are the owner, tie it up until your local animal inspector has pronounced it safe to release. He will keep it under observation for two weeks to make sure that it is not developing rabies. If the dog is owned by someone else, obtain the name of the owner and notify the board of health. They will notify the animal inspector who will keep the dog under observation. If the dog is a stray dog and its owner is unknown, notify the police so that they can catch it.

(2) After learning the identity of the dog, *go at once to your family physician.* He will cauterize the wound to help prevent the development of rabies in case the dog proves to be rabid. Cauterization helps but it cannot be relied upon. Mercurochrome or iodine do not cauterize.

(3) After the preliminary cauterization, *keep in touch with your physician* and let him know of any sickness on the part of the dog.

(4) *If it is impossible to locate the dog which did the biting,* you will never know whether or not it was rabid. In this case *the only safe course to follow is to take anti-rabic treatment.*

(5) If the dog is located, it must be kept under observation. Should it become sick, the animal inspector will arrange to have its head examined in the State Laboratory. It is possible to tell by such examination whether or not the dog had rabies, but if the dog

was killed immediately such examination often shows nothing for it may be too early in the disease for the characteristic changes, (by which the disease is recognized under the microscope) to have developed.

(6) *If laboratory examination shows the dog was rabid,* you will be notified by the State Department of Public Health. In such a case *get in touch at once with your physician and have him give you anti-rabic treatment.* It does not pay to take a chance for if rabies develops there is no treatment for it.

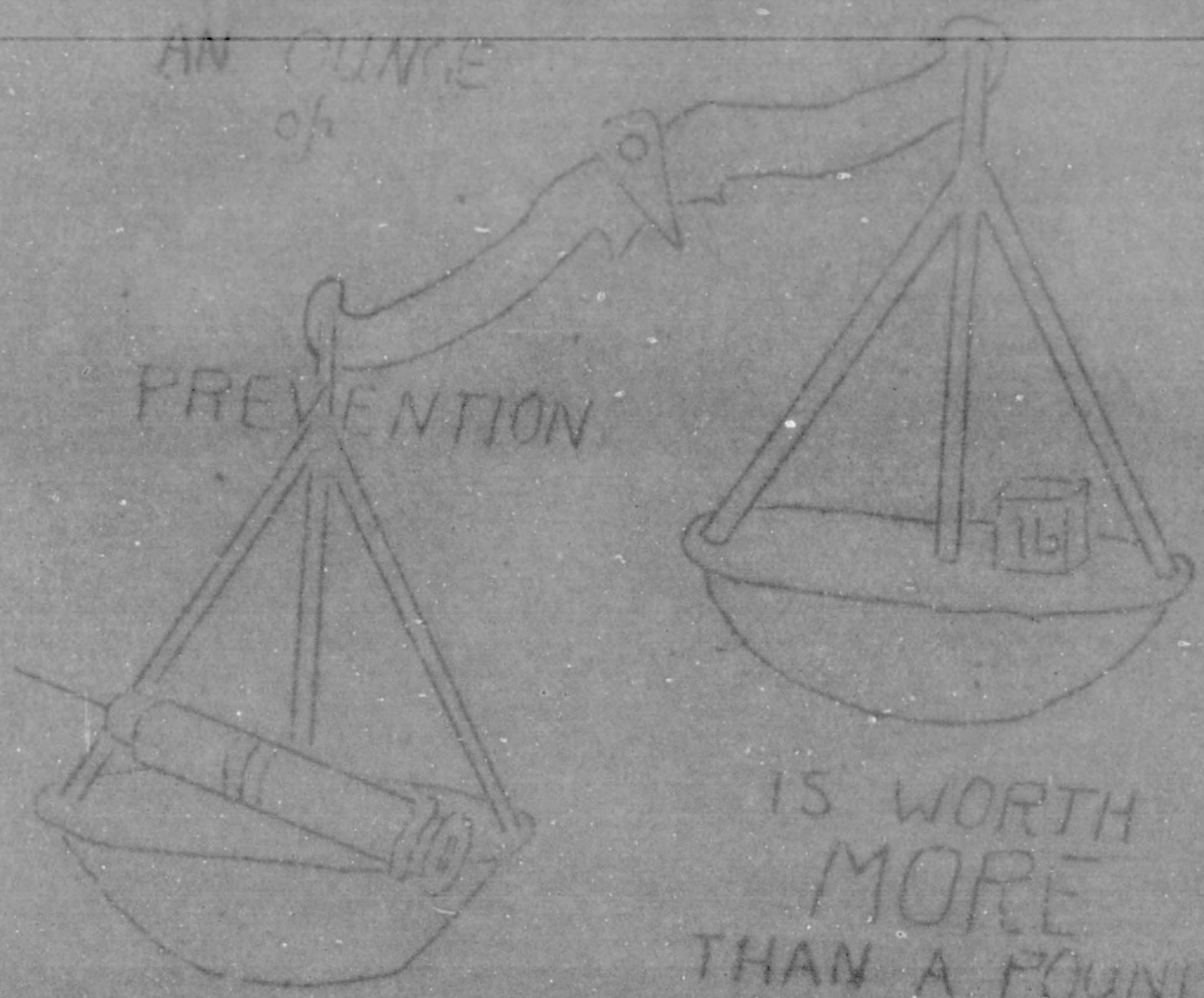
REMEMBER

(1) *Don't kill or permit another to kill a dog that has bitten someone; keep it under observation.*
(2) *Always consult your physician at once.*
(3) *Report all dog bites to your board of health.*
(4) *If the dog is rabid, anti-rabic treatment should be begun at once.*
(5) *Bites by stray dogs or those which cannot be located should be treated as though the dog were known to be rabid.*
(6) *If the dog is pronounced rabid by a veterinarian, don't wait for the laboratory report; begin treatment at once.*

D16

AN OUNCE
of

PREVENTION



IS WORTH
MORE
THAN A POUND
of
CURE

FOR THERE IS NO CURE
FOR
RABIES

WHAT IS RABIES?

Rabies is an acute disease spread from an infected animal to another animal or man, usually through a wound caused by a bite.

The unconfined rabid animal, usually a dog, may bite a person and through the open wound, the very tiny germ - a virus - travels to the brain, producing paralysis.

During the latter part of 1944 and the early part of 1945, there were 200 dogs in Chatham County diagnosed with rabies.

GEORGIA ANTI-RABIES LAW

Prior to July 1 of each year every dog owner is required to have his dog (three months of age or older) inoculated against rabies.

Licensed veterinarians or the local rabies inspectors are all qualified to immunize your dog.

After immunizing the dog, the owner is given a certificate and a dog tag; this tag must be attached to the collar or harness of the dog.

The inoculation fee is $1.00 including the cost of the tag.

The Rabies Inspector may fine any dog owner whose pet is not inoculated.

DO YOU KNOW

That the dog is the only animal wholly dependent on man?

That dogs can be inoculated against rabies?

That inoculation is a safeguard for dogs, and that this in turn is a protection to people, especially children?

That your dog is not safe from any rabid animal unless he is confined to his own yard?

That your private veterinarian and the rabies inspectors hope to protect every dog in this county by injecting antirabic vaccine at any one of the locations on the body as indicated by an x in this drawing?

PROTECT YOUR DOG NOW BY HAVING IT INOCULATED WITH ANTIRABIC VACCINE.

IF YOU ARE BITTEN -

1. Immediately report the case to the Health Department.

2. Administer first aid.

   Wash the wound with soap and water. Then apply tincture of iodine.

3. If severely bitten, or if bitten on or near the face - go to your Doctor.

IF A DOG IS SUSPECTED OF HAVING RABIES -

1. Call a Veterinarian.

2. Quarantine the dog.

3. Don't shoot the dog - he may not have rabies.

Savannah -
Chatham County
Health Department

Savannah, Georgia

March, 1946

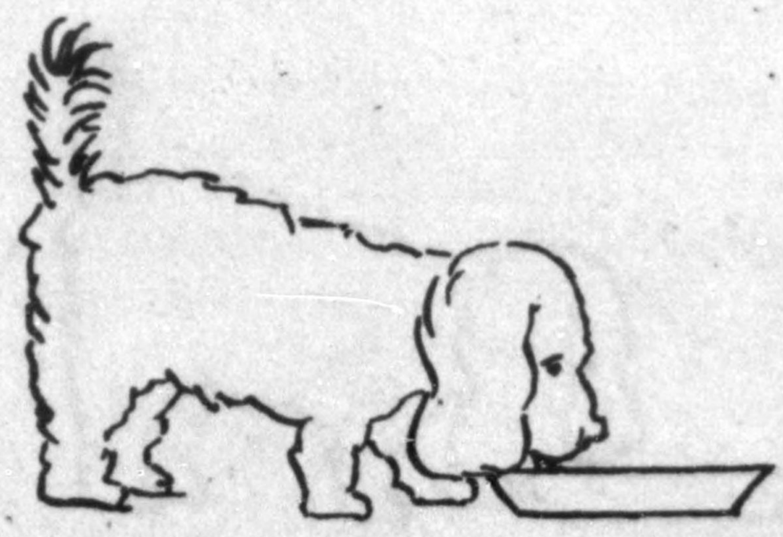
D16

BOBBY AND RAGS

Bobby ran all the way home from school. He had forgotten to do something that morning and he had been worrying about it all day.

When Bobby came in sight of his home Rags, his little dog, ran to meet him. Rags looked at Bobby as if he wanted to tell him something. Rags did not need to tell Bobby that he had not been fed. That was what Bobby had been worrying about all day.

Bobby and Rags raced to the house. They went straight to the pantry. Bobby put some food in Rags' plate. Rags began to eat, and Bobby went to tell his mother that he was at home.



B4

Mother was glad to see Bobby. She reminded him that this was the day for him to go to see Dr. Carson, his dentist. Bobby and Dr. Carson were good friends.

Rags and Dr. Carson were good friends too. In fact, Doctor Carson had given Rags to Bobby. Dr. Carson was sure that a boy who took such good care of his teeth would take good care of a dog. Bobby had taken good care of Rags and was proud of him.

Bobby and his mother both thought it would be nice to take Rags to see Dr. Carson. Rags seemed to think so too, for he wagged his tail when Bobby told him that he could go.

This was Rags' first visit to Dr. Carson's office. He saw many funny looking things. He wanted to investigate them but, being a well-behaved dog, he stood just where Bobby told him to stand.

Rags watched Dr. Carson and Bobby. First, Dr. Carson cleaned Bobby's teeth. Rags' teeth were already clean and white. Then, Dr. Carson examined each one of Bobby's teeth. Rags could see that Bobby was having a good time. When Dr. Carson said that Bobby's teeth were all right, Bobby smiled and Rags wagged his tail.

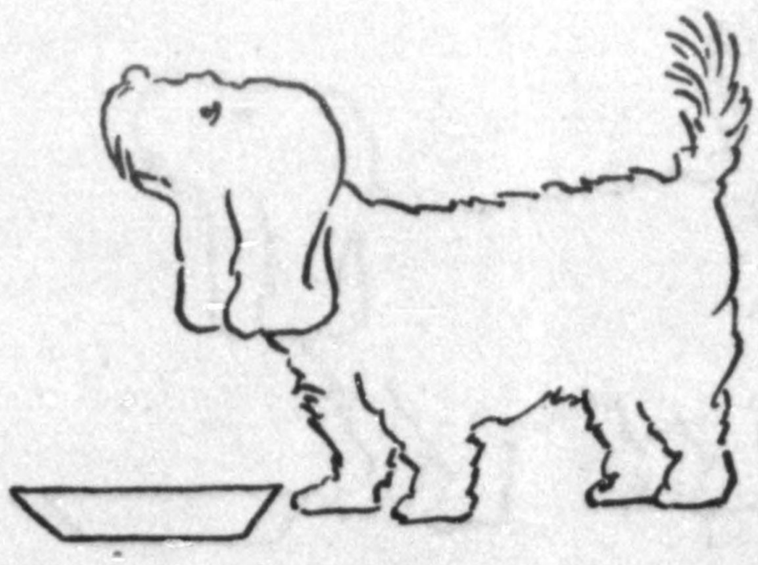
Dr. Carson patted Bobby on the back. He was glad that Bobby was still taking good care of his teeth and of Rags. Bobby did not tell Dr. Carson that he had forgotten to feed Rags that morning, and Rags did not tell on Bobby.

Instead of telling Dr. Carson that he had forgotten to feed Rags, Bobby told him that he remembered about taking care of his teeth. He told Dr. Carson four things that boys and girls must do to have good teeth. These are the four things:

1. Brush your teeth twice a day.
2. Eat the right foods.
3. Exercise your teeth.
4. Visit your dentist twice a year.

Dr. Carson asked Bobby to name some of the right foods. These are the foods that Bobby named: milk, fruits, vegetables, eggs, and whole grain breads and cereals.

Rags wanted to tell Dr. Carson about his food, but Bobby whistled for him to come and go home.



FILL THE BLANKS

Rags was _____ _____.

Dr. Carson was _____ _____.

Bobby forgot to _____ _____.

Bobby remembered to _____ _____

_____ _____ _____.

Brush your teeth _____ _____ _____.

Eat the _____ _____.

Visit your dentist at least _____ ___ _____.

Foods that are good for your teeth are:

_____ _____

_____ _____

_____.

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twice a year; Bobby's dog; right foods; milk, eggs, vegetables, fruits, whole grain breads and cereals; twice a day; take care of his teeth; Bobby's dentist; feed Rags.

N. C. State Board of Health
Division of Oral Hygiene

D16

Rabies and its Control

NATIONAL RESEARCH COUNCIL

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Rabies and Its Control

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The wide prevalence of rabies in the United States calls for concerted action for the control of this dreadful disease. The scientific facts necessary to that end are known.

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RABIES is an acute, specific infection of the central nervous system caused by a filterable virus. In a state of nature, the disease is propagated in dogs and related animals, such as the wolf, fox, and coyote. Man and all warm-blooded animals are susceptible.

The virus is often present in the saliva of rabid animals, and the disease therefore is most commonly transmitted by a bite. The virus cannot penetrate the normal skin but may enter the body if infected saliva gets into a fresh wound.

INCIDENCE OF RABIES

Rabies is a disease that has been known since ancient times. It is world wide in distribution and has been reported in the Arctic as well as in tropical regions. Only a few islands, such as Australia and Hawaii, have remained free of the disease. Though rabies has been present in Europe, Asia, and Africa for centuries, there is no evidence to indicate that the disease existed in North America prior to colonization. Historical archives of Virginia contain references to canine rabies as early as 1753 and those of North Carolina as early as 1762. The disease became prevalent in the vicinity of Boston in 1768. By 1785, it had been disseminated throughout New England. By 1860, it had invaded most of the states east of the Mississippi and had been reported as far west as New Mexico. In 1899, the disease appeared in California and since then has remained enzoötic over most of the United States.

Though rabies has been spread and maintained almost entirely in domestic dogs, there have been repeated outbreaks in wild animals. Epizoötic fox rabies was reported in Massachusetts in 1812, in Alabama in 1890, and in Alaska in 1915. During the past seven years, there have been repeated epizoötics of fox rabies in Alabama, Georgia, Louisiana, Mississippi, and North and South Carolina. Sporadic cases of fox rabies have been identified in Arkansas, California, Illinois, Iowa, Indiana, Kansas, Kentucky, Maryland, New York, Pennsylvania, Ohio, Tennessee, Texas, Virginia, West Virginia, and Wisconsin during this same period. Epizoötic skunk rabies was reported in Kansas in 1875, and in Arizona in 1907. Epizoötic coyote rabies was reported in northern Mexico in 1892, in Ne-

vada, Oregon, and California in 1915, and in New Mexico in 1943. Thus, although the large majority of rabies cases occurs among dogs, the presence of rabies in wildlife species complicates the control of the disease.

The statistics on rabies collected by the Bureau of Animal Industry of the United States Department of Agriculture have been made available to this committee through the courtesy of the chief of the Bureau, Dr. A. W. Miller. This information was obtained by means of a questionnaire sent annually to the directors of state public health and livestock sanitary departments. The reporting of animal rabies cases is limited almost entirely to those diagnosed by laboratory examination, and the true incidence is probably much higher.

Table 1 gives the number of cases of rabies in man and in animals for the years 1938-1944, inclusive. The cases listed under "other animals" consist largely of wild species such as foxes, coyotes, skunks, etc.

Table 2 gives the distribution of rabies by states for the period 1940-1944, inclusive. Table 3 gives the statistics on rabies for man and animals by states for the year 1944.

The information given in table 1 shows that the disease is on the increase, both among domestic and wild animals. Fox rabies is a particularly serious problem.

TABLE 1—Reported Cases of Rabies in the United States, 1938-1944

Year	Dogs	Cattle	Horses	Sheep	Swine	Cats	Goats	Other animals	Man	Total
1938	8,452	413	32	164	42	207	11	44	47	9,412
1939	7,386	358	36	17	38	269	10	172	30	8,314
1940	6,194	326	25	53	71	260	4	277	28	7,238
1941	6,648	418	39	68	159	294	9	212	30	7,877
1942	6,332	288	15	48	32	250	12	160	28	7,165
1943	8,515	349	35	45	60	316	19	310	41	9,690
1944	9,067	561	32	40	43	419	14	311	53	10,540

Seasonal Prevalence

Contrary to the popular opinion that the disease is practically limited to the "dog days" of autumn, rabies is most common in the late winter and spring. Outbreaks of rabies may develop at any season of the year and in any climate. The reason for the high prevalence of rabies in the spring is that stray dogs range the country at this time in search of food and mates.

Rabies in Dogs

A normal dog that is bitten by a rabid animal may develop rabies in as short a time as ten days, or it may show no symptoms until several months later. In most instances, rabies will develop from twenty-one to sixty days after exposure. The virus is not present in the saliva until the early symptoms of the disease appear.

Rabies in dogs is usually classified as furious or dumb, depending upon the symptoms shown by the animal.

Furious Rabies.—During the early stage of the disease, a dog may appear quite normal and be even more affectionate than usual. Despite its friendly actions the dog will be easily irritated, especially if restrained in any way. If picked up, it will immediately try to break away and, if not promptly freed, will bite savagely. This is usually the way children are bitten, because they will pick up a friendly looking dog and try to hold it when the animal attempts to get away. Restlessness and excitement are other early symptoms that will be shown by the dog. The dog will seldom be still for more than a moment and will snap at flies and chase chickens, cats, and domestic animals. It also will have a tendency to eat sticks, straw, earth, and other indigestible material. After a period of one to three days, the dog may become extremely vicious and will bite any living thing that gets in its way, including its master. The eyes will be glazed and constantly wide open. Often there will be a peculiar howl-like bark. During this stage, the dog will usually wander away from home, roam the countryside, and attack any person or animal it sees. Within a few days paralysis will develop, first shown by a wobbly or staggering gait. Paralysis will then extend until the animal cannot get up. Dogs with this type of the disease usually live several days and may live as long as 11 days after developing symptoms.

Dumb Rabies.—In this type of the disease, the early symptoms consist of sleepiness and melancholia; the dog will try to hide or to get away by itself. These symp-

toms are soon followed by paralysis of the jaw, throat, voice, and leg muscles. There will be no irritability or tendency to bite, but persons may be exposed to rabies by trying to look at the animal's throat or while giving medicine. Animals so affected seldom live more than three days after developing symptoms.

In most cases, rabid dogs show symptoms of both types of the disease, that is, a period of restlessness, excitement, and irritability, during which they appear friendly and unusually alert, followed by rapid progression to paralysis of the dumb-rabies type. Some animals affected with rabies die suddenly without showing any symptoms of illness. In other instances, the first symptom is a convulsive seizure during which the animal may die.

It is to be noted that dogs and other animals suffering from rabies are without fear. Rabid wild animals, such as foxes and skunks, will fearlessly invade farm premises and attack persons, dogs, and domestic animals in daytime. The disease makes them insensible to pain, and blows or gunshot will not frighten them.

Rabies In Other Animals

Both domestic and wild animals affected with rabies exhibit essentially the same types of symptoms as those described for

TABLE 2—Distribution of Rabies by States for the Period 1940-1944, Inclusive

State	1940	1941	1942	1943	1944	Totals
Alabama	202	170	222	137	249	980
Arizona	0	22	36	243	338	639
Arkansas	194	260	233	288	251	1,226
California	398	443	532	742	914	3,029
Colorado	8	69	43	11	1	132
Connecticut	0	3	0	0	0	3
Delaware	4	13	9	6	2	34
Dist. of Columbia	0	1	1	105	146	253
Florida	0	264	268	128	252	912
Georgia	601	545	554	564	619	2,883
Idaho	0	0	2	0	1	3
Illinois	327	1,101	462	582	363	2,835
Indiana	254	272	199	153	304	1,182
Iowa	34	49	51	41	88	263
Kansas	17	27	11	8	75	138
Kentucky	109	302	111	104	73	699
Louisiana	86	61	84	924	996	2,151
Maine	7	1	3	2	1	14
Maryland	2	1	9	114	288	414
Massachusetts	77	31	24	5	0	137
Michigan	715	442	166	294	416	2,033
Minnesota	56	16	1	0	2	75
Mississippi	151	143	217	205	262	978
Missouri	31	1	126	453	312	923
Montana	0	0	0	0	0	0
Nebraska	0	0	1	4	1	6
Nevada	0	0	0	0	0	0
New Hampshire	0	0	0	0	0	0
New Jersey	420	309	187	42	68	1,026
New Mexico	107	129	215	322	72	845
New York State[1]	102	109	64	189	314	778
New York City	118	32	49	14	36	249
North Carolina	389	436	191	252	293	1,561
North Dakota	0	0	0	0	0	0
Ohio	592	500	394	394	479	2,359
Oklahoma	255	259	196	218	337	1,265
Oregon	43	20	4	0	1	68
Pennsylvania	345	244	358	830	904	2,681
Rhode Island	67	8	1	1	1	78
South Carolina	165	251	233	215	172	1,036
South Dakota	0	0	0	2	0	2
Tennessee	486	522	567	534	505	2,614
Texas	392	351	1,109	1,143	950	3,945
Utah	5	0	0	5	16	26
Vermont	0	0	0	0	0	0
Virginia	87	49	55	246	316	753
Washington	74	64	6	0	1	145
West Virginia	156	315	163	168	116	918
Wisconsin	161	42	8	2	5	218
Wyoming	1	0	0	0	0	1
Totals	7,238	7,877	7,165	9,690	10,540	42,510

[1]Not including New York City.

dogs. Cattle and horses are less apt to bite and attack other animals but, due to the natural behavior of these animals, this is to be expected. In contradistinction, rabid domestic cats are apt to be more savage than dogs. This holds true also for wild animals, such as foxes, coyotes, wolves, and skunks.

Exotic Rabies

Though in most countries rabies is perpetuated by the natural canine host, in some places the disease has become established in unusual types of wildlife. In the Union of South Africa and in India, the meercat and mongoose have been shown to be important vectors of rabies. More unusual still is the vampire-bat rabies of Mexico, and Central and South America. The vampire bat is the only known host that can act as a true carrier of rabies over an extended period without exhibiting evident illness. The majority of vampire bats that contract rabies evidently die of the disease, following a short interval of infectivity, but some have been shown to be capable of infecting animals over a period of five months without showing symptoms of the disease. The vampire bat subsists entirely on fresh blood, which it laps up after inflicting a superficial, crater-like wound with its sharp incisor teeth. These animals live in caves or hollow trees and normally feed only at night. Their favorite hosts are cattle, horses, and chickens, but where livestock is protected at night, they will enter homes and feed on man. The presence of vampire bat rabies in Mexico, near the border of the United States, makes it necessary to consider this vector because, although this species of bat has not been identified in the United States, it may migrate into this country.

Laboratory Diagnosis of Rabies

It is a well-known fact that specific intracytoplasmic inclusion bodies or Negri bodies cannot be found always in brain cells of man and animals dying of rabies. In the absence of these bodies, it is not possible to make a definite diagnosis of rabies by microscopic examination, as the degenerative and inflammatory lesions produced by the virus are not sufficiently characteristic. Therefore, if the microscopic examination of a brain specimen is necessary to resort to animal inocluation in order to establish the diagnosis. In the past, the guinea pig and rabbit have been considered the most suitable test animals for this purpose. Since the demonstration that the intracerebral injection of rabies virus into white mice produces a typical and constant infection, the white mouse has become increasingly popular as a test animal. The chief advantages of the mouse for this purpose are the low cost, making it possible to use several animals for one specimen; the relatively short incubation period, ordinarily six to ten days, with street virus; and the consistency of production of inclusion bodies in the brains of mice infected by intracerebral injection with street virus.

A positive microscopic diagnosis is sufficient for the diagnosis of rabies. It has been found that the specific intracytoplasmic inclusion bodies of rabies, when present, are readily demonstrated in smears or impressions of the Ammon's horn of the brain, if stained with Sellers' carbol-fuchsin and methylene blue. This is the most practical of the various staining methods that have been developed, as the stains are dissolved in methyl alcohol and the brain tissue is fixed and stained at the same time. Large-scale animal-inoculation studies of dog brain specimens from animals suspected of having rabies have shown that only about 90 per cent of the proved rabid dogs will have Negri bodies in the brain. The presence or absence of these intracytoplasmic inclusion bodies in the brain of a rabid animal depends to a considerable extent on the duration of the disease before the animal is killed or dies of rabies. When the virus of rabies develops an enhanced virulence, as is the case with fixed virus, the brain cells are destroyed before a characteristic inclusion body can develop. Small inclusion bodies are found in the cytoplasm of brain cells in animals dying of fixed virus rabies, but these are not sufficiently characteristic to make it possible to differentiate them from those that occur in other virus infections. Similar atypical intracytoplasmic inclusion bodies are found often in animals killed during the early stages of street virus rabies. Dogs living less than three days after the onset of symptoms of rabies often are negative for rabies by microscopic examination of the brain. Experimental studies of rabies indicate that dogs with dumb rabies are apt to die be-

TABLE 3—Rabies in the United States by States During the Year 1944

State	Dogs	Cattle	Horses	Sheep	Swine	Cats	Goats	Miscel.		Man	Total
Ala.	175	19	3	0	0	18	0	Mule	1	0	249
								Rabbit	1		
								Fox	1		
Ariz.	246	52	3	0	5	16	1	Skunk	32		
								Coyotes	1		
								Antelope	3		
Ark.	181	11	1	0	0	11	0	Rabbits	1	1	338[1]
								Squirrel	8		
Calif.	854	19	0	0	0	28	4	Not stated	1		
								Rat	45	2	251
								Rabbit	1		
								Fox	1		
Colo.	1	0	0	0	0	0	0	Squirrel	1	3	914
Conn.	0	0	0	0	0	0	0	Coyote	1		
Del.	1	0	0	0	0	0	0	Opossum	1		
Dist. of Col.	131	0	0	0	0	1	0		0	0	1
Fla.	234	11	0	0	0	13	0		0	0	0
Ga.	480	22	1	0	1	5	0		0	0	2
Idaho	1	0	0	0	0	0	0	Fox	0	2	146
Ill.	314	6	3	0	4	32	0	Fox	1	0	252
Ind.	245	34	0	2	3	14	0	Bobcat	60		
Iowa	42	19	4	2	2	9	0	Fox	1	5	619
Kans.	47	11	1	0	2	10	0	Skunk	0	0	1
Ky.	66	1	0	0	0	4	0	Fox	1		
La.	875	60	6	0	0	10	0	Skunk	3	2	363
Maine	1	0	0	0	0	0	0	Fox	6		
Md.	240	6	0	0	14	10	0	Squirrel	2	3	304
Mass.	0	0	0	0	0	0	0	Civet cats	2	0	88
Mich.	368	35	3	4	1	4	0	Fox	2	2	75
Minn.	2	0	0	0	0	0	0	Skunk	1		
Miss.	215	15	2	0	0	18	2	Fox	1	0	73
Mo.	287[3]	10	0	0	0	9	0		40	5	996
Mont.	0	0	0	0	0	0	0	Squirrel	0	0	1
Nebr.	0	1	0	0	0	0	0	Fox	1		
Nev.	0	0	0	0	0	0	0		16	1	288
N. H.	0	0	0	0	0	0	0		0	0	0
N. J.	64	2	0	0	0	0	0		0	1	416
N. Mex.	50	8	0	0	0	1	0		0	0	2
N. Y. State[4]	233	47	3	0	2	3	1	Fox[2]	8	2	262[3]
N. Y. City	34	0	0	0	0	12	2	Skunk	1		
N. Car.	259	9	0	0	0	1	0	Rat	1	3	312[3]
N. Dak.	0	0	0	0	0	11	0	Squirrel	1		
Ohio	428	32	1	1	1	0	0		0	0	0
Okla.	305	12	0	0	0	11	0		0	0	0
Ore.	0	0	0	0	0	13	0		0	0	0
Penn.	792	51	0	26	3	1	0		0	1	68
R. I.	0	0	0	0	0	28	0	Racoon	8	0	72
S. Car.	152	4	0	0	0	1	0	Fox	1	1	314
									15		
								Fox	0	1	36
									13	1	293
								Not stated	0	0	0
								Wolf	5	0	479
								Civet cat	1		
								Monkey	1	3	337
									2		
								Not stated	0	0	1
									2	2	904
								Fox	0	0	1
									2	1	172

[1]Approximately 50 per cent reported on clinical grounds.
[2]Rabies in foxes in eight counties.
[3]Probably mostly dogs.
[4]Not including New York City.

fore the fourth day of the disease, and less than 50 per cent of the dogs with this type of the disease can be diagnosed by microscopic examination of the brain. Biting dogs, that is, those with furious rabies, are apt to live three or more days after the onset of symptoms, and a positive diagnosis can be made in about 90 per cent of such cases. Therefore, it is evident that it is advisable to hold biting dogs in quarantine rather than to kill them immediately and send the brain to a laboratory for diagnosis. There is a double reason for this. First, it will permit observation for symptoms of rabies that may allow a clinical diagnosis of the disease, and as the mortality is to all intents 100 per cent, if the animal has rabies it will die. Secondly, the longer the animal is allowed to live, the better the chance of obtaining a positive microscopic diagnosis.

Method of Obtaining a Laboratory Diagnosis of Rabies

Animals suspected of having rabies should be submitted for diagnosis whether or not there has been human exposure. This is essential in order to know the extent of the disease. The entire head should be removed by a veterinarian or someone familiar with the handling of rabies specimens. In order to preserve the brain during shipping, the head should be placed in a watertight container, which, in turn, should be packed in a larger receptacle containing an equal mixture of packing and ice. Specimens should be sent by Railway Express, labeled "rabies suspect, rush," and addressed to the nearest laboratory of the State Health Department. If the diagnostic laboratory is located nearby, the entire animal or the head may be taken directly to this place for examination. If delivery is delayed, the specimen should be kept under refrigeration.

The Human Rabies Problem

Though relatively few people die of rabies each year in the United States, it is still a major public health problem. It is necessary to give the rabies vaccine treatment to approximately 30,000 persons each year. The treatment is complicated by the necessity of giving daily treatments for two to three weeks, which is a time-consuming and expensive procedure. The horrible character of the disease in man and its invariably fatal outcome make it one of the most dreaded of human ailments.

Management of Dog Bite Cases.—Where rabies is present in the community, every biting dog must be suspected of having the disease. The wound produced by a dog bite or scratch should be cleansed thoroughly with soap and water. This will remove most of the saliva, which transmits the infection, if the dog has rabies. Immediately after this first cleansing of the wound a doctor should be consulted as to further local treatment and as to whether the vaccine treatment should be given.

Any dog that has bitten a person should be confined for a period of fourteen days. If the animal has rabies, it usually will die in a few days, and will assuredly succumb within a two-week period. If rabies is present in the community, a veterinarian should be consulted as to whether the biting dog has rabies. If the biting dog is a stray and has escaped capture, local authorities should be notified so that the dog can be caught and held for observation. Even if the dog appears to have rabies, it should not be killed unless this is absolutely necessary. During the early stages of the disease it is often impossible to make a diagnosis of rabies by examining the brain of the animal, but if the dog is allowed to die of the disease, microscopic examination of the brain will usually show quickly whether or not the animal had rabies.

Local and Vaccine Treatment for Persons Exposed to Rabies.—If a person is bitten by an animal and the veterinarian and the physician feel that the animal has, or probably has, rabies, the wound produced by the bite should be treated by a physician as soon as possible. The object of local treatment is to remove or inactivate any virus that may have been deposited in the wound. Shaughnessy and Zichis have shown that, as a local treatment, thorough irrigation with a 20 per cent soft soap solution is preferable to cauterization with fuming nitric acid.

Because local treatment cannot be fully depended upon, and as it usually takes several weeks for rabies to develop in man, it is advisable to resort to vaccination as an added safeguard. The usual treatment consists of 14 to 21 daily injections of vaccine. In rare instances the vaccine fails to prevent the disease.

For persons known or suspected to have been bitten or to have been scratched by the claws, vaccine treatment should be started immediately when (1) the animal is apprehended and presents clinical signs of rabies; (2) the animal is killed and the brain is found positive for rabies by microscopic examination (3) the animal is killed and, though the brain proves negative by microscopic examination, the animal is suspected of being rabid; (4) the person is exposed by a stray animal that escaped or one that can not be identified. The vaccine treatment is rarely indicated where there is no satisfactory evidence of the person having been bitten.

It must be emphasized that when an animal is apprehended after attacking a person and rabies is suspected, the animal should not be killed but should be confined under the supervision of a veterinarian. This is important as the immediate laboratory diagnosis of rabies depends on the demonstration of specific intracytoplasmic inclusion bodies in the brain of the animal, and these are often absent in the early stages of the disease.

Rabies Control Procedures

The actual measures necessary to control rabies are known. It is the manner of organization and the maintenance of the program that require attention. Rabies has gradually become more and more prevalent in the United States because of the lack of a uniform policy and concerted action in combating the disease.

Quarantine measures for dogs can control, and even eradicate, the disease, provided wild animals are not involved in its propagation. Actually, vectors other than the dog have played but a minor part in spreading the disease in this country. Where rabies has become established in wildlife species, it has been possible to control the disease by reduction of the species of wildlife affected.

The best example of the effect of rigid dog-control regulations on the incidence of rabies is the program that made possible the eradication of rabies in Great Britain. The following sanitary procedures were enforced: (1) imposition of a tax on all dogs; (2) seizure and destruction of all ownerless and wandering dogs; (3) destruction of all dogs with rabies or suspected of being or becoming rabid; (4) requirement that all dogs be confined while rabies prevailed and for a period of the longest latency after the last reported case; (5) subjection of all imported dogs to a six-month quarantine period.

This program was generally adopted in 1889 but was not satisfactorily enforced until 1897. The disease decreased gradually in prevalence and by 1903 disappeared completely. Rabies was again introduced into Great Britain in 1918 by a dog or dogs illegally imported. By 1922, Great Britain was again free of rabies and no further outbreaks have occurred.

There has been considerable criticism of the six-month quarantine provision. It is therefore of interest to note that 16 cases of rabies in quarantined dogs were found during the period 1919-1939 in Great Britain. Four of these animals developed rabies four to six months after entry, and 1 dog that was held for an additional period because of possible exposure developed rabies six months and twenty-four days after arriving on the Island.

Rabies has been eliminated repeatedly from many communities in the United States, only to be reintroduced. It is therefore necessary to develop a coördinated control program if we are to make any headway in eliminating the disease in this country. The rabies-control program in Great Britain was coördinated through the Ministry of Agriculture. This is true also for the Dominion of Canada, where rabies has ceased to be a problem although the disease has been reintroduced from time to time by entry of dogs from the United States. New cases of suspected rabies are reported promptly, and quarantine regulations are enforced immediately and continued for six months after the last reported case of rabies.

At present, rabies control on a state-wide basis is under three types of administrative setup: (1) under the jurisdiction of the State Department of Public Health; (2) under the jurisdiction of the State Department of Agriculture, Live Stock Sanitary Division; (3) administered as a joint project of the State Department of Public Health and the State Department of Agriculture.

For the most part, rabies-control work is conducted on a municipal or county basis under the authority of the city or county

board of health, and the work is maintained only as long as the emergency persists.

Most officials engaged in rabies-control work favor the development of a national program of rabies control by the United States Department of Agriculture, Bureau of Animal Industry. The disease is an interstate problem and the reporting of rabies cases and the work of rabies control must be coördinated through some national agency. Since it is maintained solely among animals, the disease is essentially a veterinary problem.

Rabies in animals should be reported to some central authority promptly. Past experience has shown that the disease is apt to be of epizoötic proportions in a given locality before the state authorities responsible for rabies control are aware of the outbreak.

No rabies-control program can succeed unless there is adequate provision for a constantly functioning dog pound and for veterinary personnel to investigate new cases of rabies, impound biting dogs, enforce destruction or prolonged quarantine of dogs exposed to rabies, and effect elimination of stray dogs.

Dog owners should be responsible for financing dog-pound work. They are the source of the problem, and it is very difficult to obtain funds for this work without taxation and licensing of dogs. Licensing of dogs allows collection of data as to the number of dogs in a given locality and shows the ownership of a dog by the attached license. It also secures some reduction of the total number of dogs, especially those that are apt to breed indiscriminately. It limits the ownership of dogs largely to those who will take care of the animals and assume responsibility for their actions.

It is necessary to have the coöperation of the public in any scheme of rabies control. This can be best obtained through an educational program. New cases of dog rabies should be publicized in the press so that the public will be cognizant of the disease. Informative articles on rabies and its control should be released to the press by enforcement authorities. Pamphlets on rabies, giving the basic information about the disease and its control, as well as pamphlets on the care of dogs and responsibilities of dog owners, might be distributed to dog owners at the time they receive the dog license or at vaccination clinics. These pamphlets should be available to practicing veterinarians and to civic organizations. Posters can also be used to advantage.

The traditional rabies-control program is one that requires strict quarantine for all dogs for a period of six months after the last reported case of rabies. It is difficult to enforce adequately such a provision in most parts of the United States. It is usually necessary to maintain the quarantine for an extended period. In most instances this has failed to eliminate the disease because the public has failed to coöperate.

In recent years, some communities have been able to eliminate rabies in a few months by a program of vaccination of all dogs, in conjunction with the collecting and impounding of stray dogs and the enforcement of a short quarantine period to facilitate this work. There has been criticism of the value of vaccination as a means of preventing rabies. Recent studies have shown that commercial, canine rabies vaccines are effective immunizing agents. The Bureau of Animal Industry of the United States Department of Agriculture now requires that all commercial rabies vaccines must pass a prescribed potency test. This has led to improvement in methods of manufacturing vaccine, and a superior and more uniform product is now available. Experimental studies have shown that a single subcutaneous injection of 5 cc. of vaccine will confer a high degree of immunity in dogs, and this immunity continues at a significant level for at least a year after vaccination. Three weekly injections produce a more solid immunity and should be recommended to dog owners, but this is not a practical method for mass immunization of dogs. It is evident that rabies cannot be maintained among a group of dogs vaccinated by the single-injection method. Field experience has shown that the disease can be eliminated from a community if all dogs are vaccinated by this method and if unvaccinated dogs found at large are impounded.

Given a situation where the state official responsible for rabies control is notified promptly of all new cases of rabies as soon as a positive laboratory diagnosis is made, this official can declare the existence of the disease in any given locality, and can apply control measures over an area sufficiently wide to be effective.

A thirty-day quarantine for all dogs, so as to facilitate the impounding of stray dogs and the vaccination of owned dogs, should be required. Owned dogs should not be allowed at large until thirty days after vaccination. Vaccination could be carried out on a voluntary basis, whereby vaccinated dogs may have their freedom after a designated period, but dogs, whose owners do not wish them vaccinated, must be kept confined until three to six months after the last reported case of rabies.

The control of rabies among wild animals depends upon an organized campaign to reduce the number of the affected species until the disease disappears. The United States Department of Interior, Division of Predatory Animal Control of the Fish and Wildlife Service, is now prepared to supervise any such program.

Recommendations for the Control of Rabies in the United States

Organization.—(1) In order to have an effective program of rabies control in the United States, such a program must be coördinated through some national agency. In view of the fact that the disease is maintained solely in animals, primarily the dog, control work is strictly a veterinary problem. It is therefore recommended that the United States Department of Agriculture, Bureau of Animal Industry, be given authority to coördinate and supervise rabies-control work. The actual control work would then be carried on in coöperation with each State Department of Agriculture, Live Stock Sanitary Division. The presence of rabies in wild animals in certain sections of the country requires the participation of the United States Fish and Wildlife Service of the Department of Interior and state wildlife agencies. The United States Public Health Service and state departments of public health have a direct interest in the rabies problem, and all of these agencies should participate in the planning and enforcement of the control program.

2) Rabies-control work on a state basis should be under the supervision of a full time veterinarian.

3) Rabies in animals should be made a reportable disease, new cases to be reported immediately to the veterinarian in charge of rabies control, and to be reported weekly through regular reporting channels to the United States Department of Agriculture, Bureau of Animal Industry. All diagnostic laboratories engaged in rabies diagnosis should report promptly all positive cases of rabies to the state veterinarian in charge of rabies control. The heads of all domestic and of all wild animals suspected of having rabies should be submitted for examination, regardless of whether or not there was human exposure to the disease.

4) Wherever rabies is found to exist in wildlife species, the state authority responsible for rabies control should notify the United States Fish and Wildlife Service and the State Wildlife Department, and with them arrange a coöperative control program.

5) The organization responsible for rabies control should promote an educational program so as to inform the public concerning the hazards of the disease and the measures necessary to its control.

Control Methods.—(1) Taxation and licensing of dogs is recommended as the most effective means for insuring enforcement of rabies-control regulations.

2) Vaccination of dogs, combined with other dog-control provisions, appears to be the most satisfactory method for securing prompt recession of the disease.

3) It is recommended that a strict quarantine of all dogs be enforced for a period of thirty days, as soon as rabies appears in a community.

4) Vaccination of all dogs, or confinement until the area is officially certified free of rabies, should be required. Vaccinated dogs, properly tagged, may be allowed at large thirty days after vaccination.

5) Vaccination should be done free of charge in order to obtain maximum coöperation. A single subcutaneous injection of 5 cc. of an approved vaccine should be required, but dog owners should be advised that a course of 3 weekly injections of vaccine will produce a more certain immunity to rabies.

6) Dogs under 6 months of age are particularly susceptible and not readily immunizable. These should be kept confined until the area is officially certified free of rabies.

7) Biting dogs and suspected rabid dogs should be impounded for a period of at least fourteen days. Dogs known to have

been exposed to rabies must be destroyed or kept confined for six months.

8) Adequate provision for enforcing the quarantine must be arranged so that unvaccinated dogs and stray dogs will be picked up promptly throughout the control program. Otherwise the methods of rabies control given above will not be successful.

9) The control program should be continued for at least ninety days after the last reported case of rabies. Investigation of each new case of rabies and contact cases is essential.

10) If rabies becomes established in wild animals, it is necessary to carry out a program of reduction of the number of the affected species until the disease disappears. It is evident that the heads of animals taken in this type of program should be examined for rabies so as to determine the incidence of the disease and when it has abated.

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