Epidemiologic Study of Human Tularemia Reported in Missouri, 1949-65

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TULAREMIA is a disease of rabbits, ticks, human beings, and other animals caused by *Pasteurella tularensis*. McCoy and Chapin reported the first isolation and described the causative organism more than 50 years ago (*1*). The infection was first noticed in squirrels in Tulare County, Calif. (*2*).

Tularemia is perpetuated in nature mainly by a mammalian cycle (fig 1). Man is infected by contamination of his hands, mouth, or conjunctiva with infected tissue or fluids of rabbits and other lower animals, bites of an infected bloodsucking arthropod, or contaminated drinking water.

Tularemia is maintained in the rabbit population primarily by ticks. Once infected, ticks remain infected for their entire lives (*3*). Tularemia is transovarially transmitted in the tick

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(*4*), a phenomenon of great importance in maintaining the infection in the animal population. Tularemia is not usually transmitted directly from man to man (*5*).

There are few published reports about tularemia in Missouri, but all point to a greater incidence of tularemia in southern rural Missouri than in the rest of the State. Bost and associates (*6*) studied 54 cases of tularemia from the Ozark region of Missouri and Arkansas. Their findings indicated that the majority of the cases were contracted during the summer, and 63 percent were transmitted by ticks. Callaway and associates (*7*) reported that in a small general hospital in southwest Missouri, tularemia accounted for 1 percent of the admissions, and tick bites were the cause of 69 percent of the 78 cases of tularemia. They warned that tularemia, then a rural problem, might become a nonrural problem as urban persons increasingly used the countryside for camping and recreation. This trend may lead to new reservoirs of the infection in urban rodents and pets. Ossman (*8*) called attention to the remarkable response of patients with tularemia to streptomycin.

Tularemia is widely reported in Arkansas, with 66 cases in human beings recorded for the year 1965 alone (*9*). Of the 66 cases, the tick was reported as vector in 50 (75.8 percent), the rabbit as reservoir in 5 (7.6 percent), and the source of infection as unknown in 11 (16.6 percent).

It has been commonly accepted that the cottontail rabbits are the major known reservoir of tularemia in North America (*10*). It has been speculated that tularemia may exist in a chronic form among smaller rodents, and wild rabbits may be victims of a variety of circumstances which contribute to an increased incidence of the disease in other animals (*11*). The purpose of this study is to compile and analyze recorded information on cases of tularemia in Missouri. It is hoped that the data obtained on the epidemiologic pattern of reported tularemia in Missouri will assist physicians and veterinarians in recognizing the disease as a significant local public health problem.

Sources of Data

The data were obtained from the Missouri Division of Health, Jefferson City, to which 536 cases of tularemia were reported during 1949–65. Not all cases of tularemia are reported, so these data probably do not reflect the true incidence of the disease. However, certain trends

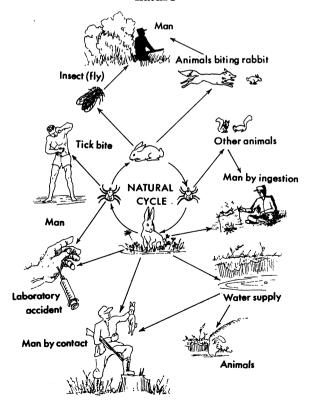## Figure 1. Maintenance of tularemia in nature

Table 1. Reported cases of tularemia in human beings in Missouri, 1949–65

Year of reporting	Number of cases	Number of deaths	Case fatality rate (percent)
1949	81	3	3. 7
1950	52	0	----------
1951	34	2	5. 8
1952	23	0	----------
1953	20	2	10. 0
1954	15	0	----------
1955	26	1	3. 8
1956	17	0	----------
1957	47	0	----------
1958	36	0	----------
1959	20	0	----------
1960	31	0	----------
1961	27	1	3. 7
1962	26	0	----------
1963	28	0	----------
1964	32	0	----------
1965	21	0	----------
Total	536	9	1. 7

noted in these cases are of value to the physician in recognizing and treating human beings infected with tularemia.

The 536 cases were studied for all epidemiologic parameters on which information was available. These parameters were source of contact, time distribution in year and month of onset, case fatality rate, geographic distribution, and age and sex distribution.

This information was not available for all reported cases, and the analysis on each parameter is based on the total number of cases for which applicable data were available. The validity of these cases when reported was checked before recording for positive agglutination test and case history from the reporting physician.

Results

The total number of cases reported annually varied from 15 in 1954 to 81 in 1949 (table 1). Although the number of cases reported remained fairly constant, there was a decrease in the case fatality rate, particularly between the periods 1949–55 and 1956–65 from 3.2 percent to 0.35 percent. This modest but significant reduction in the case fatality rate may be attributed to the increased use of antibiotics. Unfortunately, no data for the period prior to 1949 are

available, and this suspicion cannot be confirmed. The fatality rates for tularemia are from 4.0 percent to 7.4 percent for all clinical types (12).

Tularemia has been popularly called rabbit fever because of the association of this infection with the dressing of wild rabbits. Actually, the disease appeared to be transmitted more often by infected ticks (table 2).

The seasonal distribution of reported cases, by date of onset, was distinct (fig. 2). A bimodal distribution was noted, with peaks in the periods May–July and November–January. Though cases were reported as having onset in every month of the year, the months of May, June, and July accounted for 47.5 percent of the cases. The November–January period accounted for 28.5 percent of the reported cases. Thus, more than 75 percent of the reported cases occurred in these two seasonal periods.

However, there can be a great time lag between the date of onset and the date of reporting, so that it is difficult to draw conclusions about the disease from the dates of reporting. Only 233 of 421 cases (53 percent) in which the date of onset and reporting were both known were reported within 1 month of onset, and 198 of 421 (47 percent) were reported from 1 month to more than 1 year from the date of onset.

The source of infection had a very strong effect on the seasonal distribution of the disease (fig. 2). Those cases reported as contracted from ticks had a May–September distribution, whereas those cases reported as contracted from direct contact with rabbits had an equally sharp peak
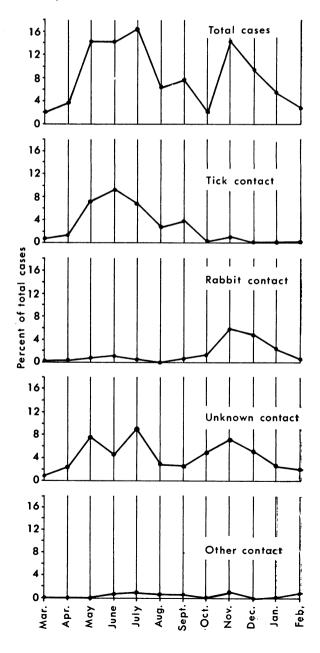
Table 2. Source of contact for reported cases of tularemia in human beings in Missouri, 1949–65

Source of contact	Reported cases	
	Number	Percent
Unknown	311	58. 1
Ticks	139	25. 9
Rabbits	72	13. 4
Other [1]	14	2. 6
Total	536	100. 0

[1] Includes cats, squirrels, dogs, and raccoons.

in the November–January period. As might be expected, the cases with an unknown source of contact had peaks in the summer and winter periods, while the "other contact" cases were too few from which to draw generalizations. Since the peak rabbit hunting season in Missouri occurs after the peak season by month of onset

Figure 2. Seasonal distribution of reported cases of tularemia in human beings in Missouri by date of onset and source of contact, 1949–65

for reported cases, the theory of the rabbit as chief reservoir is questionable.

The geographic distribution of reported cases of tularemia, by county of residence of the patients (fig. 3), shows that the southern half of Missouri was the area from which the greatest number of cases were reported. The counties in which the incidence was high (3.6–47.4 cases reported per 10,000 population) were in the southern portion of the State. This is the area of greatest tick population because of the fauna and rough, forested terrain. These areas which reported a large number of cases of tularemia include some of the counties most heavily populated with rabbits in the State. However, the majority of counties in areas reporting large numbers of cases had a small rabbit population. Northeastern Missouri, an area with a large rabbit population, reported few cases. (Source of data on the rabbit population is K. C. Sadler's Cottontail rabbit census data for 1947–63, a 1963 memorandum of the Missouri Conservation Commission.)

The rates of cases reported in various counties of Missouri are paralleled by the rates in Arkansas, bordering Missouri on the south, which reported significant numbers of cases (9), as well as those in Iowa, which borders Missouri on the north and did not report many cases (12).

Some counties in northern Missouri reported

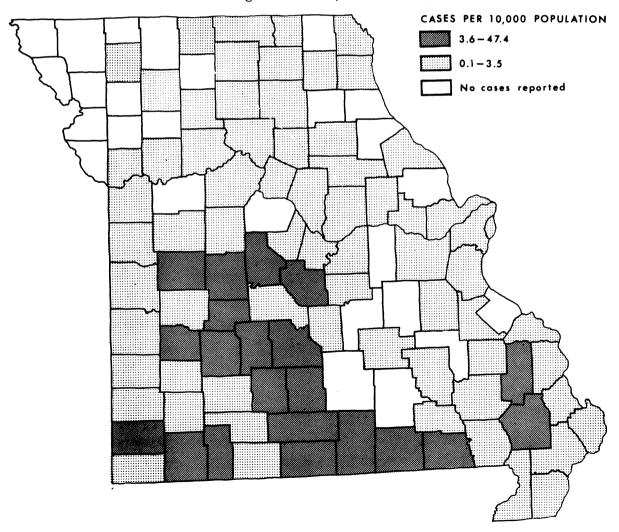**Figure 3. Geographic distribution per 10,000 population of cases of tularemia in human beings in Missouri, 1949–65**

CASES PER 10,000 POPULATION

3.6 – 47.4

0.1 – 3.5

No cases reported

Table 3. Distribution of reported cases of tularemia in human beings by age, Missouri, 1949–65

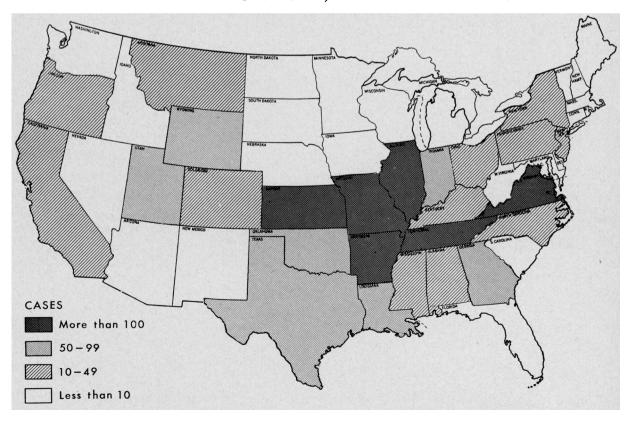| Age (years)	Cases	
	Number	Percent
Under 1–10	27	5. 0
11–20	64	11. 9
21–30	61	11. 4
31–40	97	18. 1
41–50	95	17. 7
51–60	90	16. 8
61–70	55	10. 3
71–80	26	4. 9
81–100	2	. 4
Unknown	19	3. 5
Total	536	100. 0

no cases, probably a reflection of a lack of reporting and recognition of the disease. Of 26 counties that did not report a single case of tularemia in the last 17 years, 17 are located north of the Missouri River, which bisects the

State. Only 55 of 536 cases (10.2 percent) were reported from counties north of the Missouri River. Three southern Missouri counties reported 176 of the 536 cases (32.8 percent), reflecting efficiency of reporting rather than accuracy of diagnosis.

Missouri reported the fourth highest number of cases in the nation, exceeded only by Arkansas, Illinois, and Tennessee for the period 1959–63. As shown in figure 4, the five-State region of Missouri and Arkansas, Kansas, Illinois, and Tennessee—States adjacent to Missouri—reported the greatest number of cases of tularemia (12).

The age distribution of tularemia is affected by the potential exposure to ticks and to direct contact with rabbits. Only 55 of the 517 patients whose age was known (10.3 percent) were in the age groups of under 1–10 years and 71–100 years (table 3). The remaining patients were distributed rather uniformly in the ages 11 through 70 years, with the peak at 31–60 years of age.

Figure 4. Geographic distribution of reported cases of tularemia in human beings in the United States, 1959–63

Of the 536 cases of tularemia reported, 365 (68 percent) were in males and 171 (32 percent) in females. The difference probably reflects different exposure potentials rather than difference in susceptibility. It is of interest to note that 70 percent of males and 58.3 percent of females contracted tularemia from ticks. Tabulation of age groups on a sex-specific basis revealed nothing significant.

The influence of race is undetermined. While only 14 (2.6 percent) of the cases were reported in nonwhites, the population of nonwhites in the areas with a high incidence of tularemia is very small.

Discussion

In a study that is based on reported cases the problem of underreporting and bias of reporting becomes obvious. Indeed, accuracy of reporting influences such a study as much, if not more, than actual incidence of disease. For example, Greene County reported only five cases of tularemia in the 1949-65 study period, while the literature (7) contains a discussion of 78 cases from this county during the period 1947-51. Of these cases, 29 occurred between 1949 and 1951, and obviously were not reported to the official health agency. Howell County has had 90 cases reported in the last 17 years. Of these, 55 were reported by one physician, who has reported 72 cases to the Division of Health of Missouri. Research should be conducted in the future to include other possible arthropod vectors and other mammalian reservoirs to assure that the true perspective of tularemia is known.

Summary

A total of 536 cases of tularemia have been reported to the Division of Health of Missouri during the period 1949-65. These cases form the basis for an epidemiologic analysis which reveals certain characteristics of the disease, influenced to unmeasurable extent by reporting bias.

Although tularemia is popularly associated with wild rabbits, the disease appears to be transmitted more often by infected ticks. Of 536 cases of illness reported in Missouri in the period 1949-65, 25.9 percent were known to be transmitted by contact with ticks, while only 13.4 percent were transmitted by contact with infected rabbits. More than 58 percent had an unknown source of contact.

The white male between the ages of 11 and 70 years, residing in the southern half of Missouri, seems most prone to infection (or the likelihood of his infection being reported is greatest). This person is at greatest risk when his activities expose him to ticks in the summer and rabbits in the winter. The probability of the patient dying from the disease is low especially if he receives appropriate therapy.

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