

Epidemiological Studies on Relapsing Fever in California*

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RELAPSING fever is an acute infectious disease characterized by attacks of fever followed by remissions during which the patient feels quite well, only to be seized again by relapses. The onset is generally acute, with chills, high fever, intense frontal headache, and excruciating pains in the back, limbs, and joints. Nausea and vomiting may occur and prostration is marked. The attack lasts from 2 to 4 days and is usually terminated by crisis, the temperature falling rapidly to normal with profuse sweating, and within a few hours there is an apparent restoration to health. The afebrile periods last from 3 to 12 days. Without specific treatment there are generally 2 to 4 attacks, occasionally as many as 8, each of decreasing severity. One injection of neoarsphenamine is considered sufficient to effect a complete cure. In California the disease may be confused with influenza and malaria. However, there is a leucocytosis in relapsing fever and quinine has no effect on the course of the disease.

Relapsing fever is caused by *Treponema recurrentis*. This organism is a long slender flexible spiral filament, tapering at both ends. It is 10-20 microns long and usually has about 8

undulations, occasionally as many as 10 or 12. Long chains are sometimes observed, being arranged end to end. It is actively motile. The laboratory diagnosis of relapsing fever is either by blood smears or animal inoculation. The blood smears may be stained by the methods of Wright, Giemsa, or gentian violet. These methods are satisfactory during the febrile period when the organisms are usually found in abundance, but during remissions or at other times when they cannot be demonstrated by stains it is necessary to resort to animal inoculation. The patient's blood may be immediately inoculated into white mice or may be shipped as clotted blood to the laboratory. Our observations show that the spirochetes remain viable un-iced for as long as 6 days.

In the California group of cases there have been no serious complications or sequelae and no deaths. This is in contrast to the epidemic louse-borne type seen in the Old World where the mortality may be as high as 50 per cent or more.

While the disease is very common in various parts of the world and often reaches epidemic proportions, there have been relatively few cases in the United States. In 1844¹ the first cases were reported in Philadelphia, and for a number of years the disease appeared in Eastern United States, where the last epidemic was reported in 1869.

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TABLE I
RELAPSING FEVER IN CALIFORNIA
CASES BY YEARS

Year	Number of Cases
1921	2
1923	1
1925	1
1927	2
1928	1
1930	4
1931	12
1932	16
1933	19
1934 (to Aug. 18)	11
Total	69

In 1875, Dr. P. B. M. Miller gave an account in the *Pacific Medical and Surgical Journal*² of an epidemic of relapsing fever among Chinese laborers at Oroville, Calif. This prevailed during the months of August, September, and October, 1874, and it was estimated that there were several hundred cases. No further mention is made in the literature of this disease in California until 1906, when 2 deaths were recorded

in the *19th Biennial Report* of the State Board of Health³ and in 1907, 1 death was reported in the *20th Biennial Report*.⁴ There is no comment on these deaths as to the geographic distribution or laboratory diagnosis.

The first proved cases were described by Dr. LeRoy Briggs⁵ of San Francisco, in 1921. These patients were infected at Polaris, near Lake Tahoe. They were proved positive by blood smear examination. Reports of one or two cases yearly are on record in the files up to 1930, when 4 were brought to the notice of the California State Department of Public Health. In July, 1931, the State Board of Health, recognizing the public health importance of the disease, passed a resolution making it reportable and to date (August 18, 1934), 69 cases have been recorded.

In Table I the group of cases shows twice as many males as females, which is comparable to the incidence in the Old World. There, the variation is attributed to differences in chances of ex-

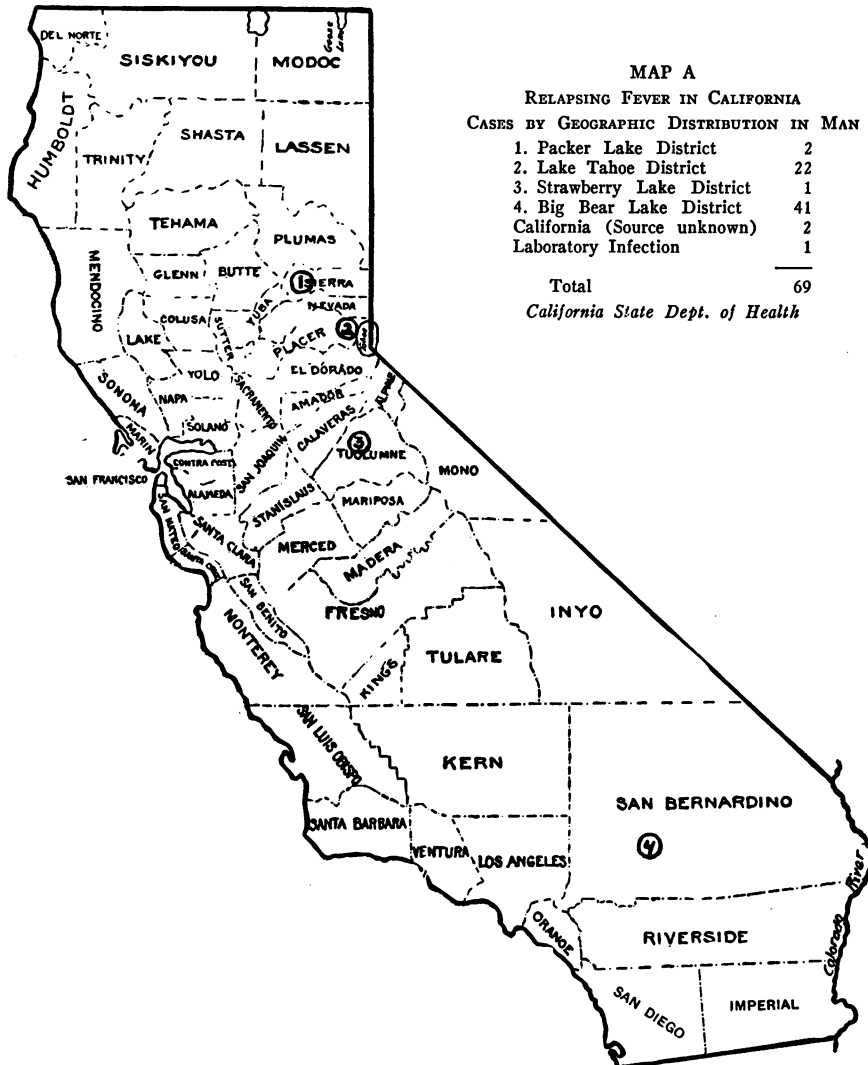
TABLE II
RELAPSING FEVER IN CALIFORNIA
CASES BY MONTHS OF ONSET

Month	Year											Total
	1921	1923	1925	1927	1928	1930	1931	1932	1933	1934		
January
February	1*	1†	2
March
April	1‡	1
May	1	..	1
June	2	1	1	..	1	3	6	2	..	16
July	3	9	5	6	6	..	29
August	2	5	6	2	..	15
September	1	1	1	..	1	4
October
November
December
Unknown	1	1
Total	2	1	1	2	1	4	12	16	19	11	..	69

* Owner of fox farm. Pelting done in February

† No laboratory confirmation

‡ Laboratory infection



posure but in our series of cases no such explanation is plausible. All ages from 4 years to above 55 are represented.

According to dates of onset the majority of cases occur in June, July, and August. This is also true in Texas, as contrasted with the epidemic louse-borne form which is more prevalent in the winter months. The occurrence of cases runs practically parallel with the appearance and disappearance of rodents. Table II shows the cases by years and months of onset. Two cases

are recorded in February. One of these patients owned a fox farm. The animals are pelted in February and during the process the operator receives many scratches and cuts. It is possible the infection was passed by direct transmission from these foxes. This was not proved, as blood was not obtained from these animals at the time of pelting. The second case reported in February was not confirmed by laboratory methods and is open to question. The April case was contracted through a

laboratory accident. One case had its onset in May, 1934, but this year the season was far more advanced than normal which may account for this.

The geographical distribution of human cases is of decided epidemiological interest (see Map A). Sixty-six of the cases recorded have occurred in 4 foci of the state: Lake Tahoe, Packer Lake, Strawberry Lake, and Big Bear Lake. These districts, as may be noted on the map, are in widely separated mountainous sections at elevations of 5,000 feet and over. The topography in all is similar. The mountains are heavily wooded and abound in animal life. The winters are rather severe with heavy snowfall usually lasting until late May or early June, while the summers are warm and pleasant, which makes these districts popular as resorts. Many wealthy people have summer homes around the lakes. The dates of onset of recorded cases correspond roughly to this seasonal change, to the return of animal and insect life, and to the sudden increase in population due to the influx of those on vacation. There is considerable evidence that the disease has long been established and is prevalent in these areas, as the natives speak of "squirrel fever" which is undoubtedly relapsing fever.

The possibility of an animal reservoir of *Treponema recurrentis* presented it-

self. Surveys were made in 3 of the foci: Big Bear Lake, Lake Tahoe, and Packer Lake in an attempt to determine the animal reservoir and the agent that may transmit the disease (Map B). The field work was started in the spring as soon as weather conditions permitted and the rodents were present in sufficient numbers. A mobile laboratory unit was used. Table III gives a summary of the rodents examined. Included under "other animals" were tree squirrels, Oregon fuzzi-tail squirrels, rabbits, rats, mice, fitch, fox, woodchuck, weazels, bats, and birds. A total of 905 animals were examined for the presence of *Treponema recurrentis* in the two surveys 1931 and 1932. In the 1932 survey, 13 strains of spirochetes were isolated from these rodents⁷; 2 strains from tamarack squirrels; and 11 from chipmunks. The same species of rodents were found to harbor spirochetes in the 3 foci investigated.

A comparative study was made of the rodent and human strains to determine if they were identical. Morphologically the organisms from both sources appear to be the same. The field incident in which there appeared to be direct transmission of spirochetes from a tamarack squirrel to a member of the survey crew offers further proof that the two strains, animal and human, are identical.^{6, 7} Mr. X accidentally contaminated an open

TABLE III
RELAPSING FEVER IN CALIFORNIA
RODENT SURVEY

Animal	Big Bear		Lake Tahoe		Packer Lake		Total
	1931	1932	1931	1932	1931	1932	
Chipmunk	44	134	66	151	17	21	433
Golden Mantled Ground Squirrel	29	17	51	109	1	10	217
Ground Squirrel	27	13	47	64	5	3	159
Tamarack Squirrel	9	8	10	6	33
Other Animals	3	32	15	3	2	8	63
Total	103	196	188	335	35	48	905

wound on his hand with blood from a squirrel recently shot, which later was proved positive for spirochetes. Seven days later he developed a clinical case of relapsing fever and similar spirochetes were demonstrated in his blood. Experimental work now in progress in this department, which will be reported later, seems to support the evidence that the spirochetes found in tamarack squirrels and chipmunks are identical with those found in patients associated with them, and that these rodents act

as a reservoir of infection for relapsing fever in California.

Nicolle and Anderson⁸ as a result of their extensive observations on relapsing fever in Tunis have developed the interesting hypothesis that blood spirochetes were originally parasites of small burrowing mammals and that rodents commonly serve as animal reservoirs of the disease. This is comparable to our observations, *i.e.*, positive findings in chipmunks and tamarack squirrels.⁷ The disease is transmitted



through the agency of ectoparasites such as various species of *Ornithodoros* according to the above authors. Clark, Dunn, and Benavides⁹ also suggest that relapsing fever is primarily a disease of animals and that man is only an accidental host—probably attacked by ticks as a matter of necessity.

In Texas, relapsing fever is transmitted by *Ornithodoros turicata*¹⁰ and in Panama by *O. talaje* and *O. venezuelensis*.¹¹ This means of transmission seems to be the most likely in California because of the following facts: (1) the endemicity of the disease, (2) seasonal distribution (3) class of people affected and their living conditions, (4) geographic distribution. The case histories were studied for reports of insect bites. Of the 69 patients 24 reported bites of some description caused by ticks, mosquitoes, fleas, and possibly bed bugs and other insects. In only a few instances could ticks be definitely incriminated. This may be because: (1) the larval and nymphal stages of these ticks are responsible for the transmission; (2) these forms are small in size, having been compared with the seeds of a strawberry; (3) ticks of species *Ornithodoros* do not remain attached after completing a blood meal; (4) after feeding, these ticks conceal themselves and hibernate, perhaps for months, therefore would be most difficult to find. A series of 5 cases reported in British Columbia¹² gave no history of insect bites, which might indicate that the problem there is similar to ours. As part of the epidemiological study in this state all the animals surveyed were examined for ectoparasites, with negative results except for fleas and lice. The burrows and nests of rodents were searched for ticks as were also the homes of patients. At Lake Tahoe nymphal forms of *O. turicata* were discovered in a cabin where a case had developed, and, associated with a number of cases, nymphal

forms of *Ornithodoros* (identification not completed) were found at Big Bear Lake. *O. coriaceus* was also found at Lake Tahoe. These specimens, however, were so limited in number that very little experimental work could be accomplished, and definite proof that these ticks are infected in nature is lacking in this state.

The California situation seems to be directly opposed to the epidemiological findings in Texas and Tropical America, in both of which places ticks of the species *Ornithodoros* are very prevalent; the native huts in Panama often yielding large numbers (4,880 specimens from 68 huts)^{11, 13} and certain caves in Denton County, Tex.,¹⁰ have supplied ticks in abundance. In California, the ticks are found with great difficulty and never in large numbers. If ticks were as numerous in California as in Panama and Texas, more cases would undoubtedly be reported because of the high incidence of infection found among wild rodents (chipmunks and tamarack squirrels). All indications in California are that the ticks hibernate during the winter with these rodents and become infected from feeding on their hosts, and are disseminated in the spring at the time the rodents become active and leave their nests.

Altitude seems to play a very important part in California, as the cases have been confined to mountainous districts over 5,000 feet in elevation. There is apparently no such limitation to the incidence of the disease in Panama and Texas. The actual elevation, however, is of less significance than the climatic factors present in these particular locations. The wild rodents, chipmunks and tamarack squirrels, in which spirochetes resembling *Treponema recurrentis* have been found are limited to these higher altitudes also, which is strong evidence that they act as the animal reservoir of relapsing fever in this state. On the other hand, the

species of ticks incriminated is probably not limited to the high altitudes. So, in explanation of the peculiar distribution of endemic foci in our state the suggestion is offered that it is determined by the animal reservoir rather than by the transmitting agent.

SUMMARY

1. Relapsing fever has been reported in California since 1874.

2. It is endemic in this state, 69 definite cases having been reported from 1921 to August 18, 1934.

3. Seasonal distribution is marked—the majority of cases occurring in June, July, and August.

4. Sixty-six of the 69 cases have been reported from 4 foci; 2 of the remaining 3 were of unknown source and the third was a laboratory infection.

5. The 4 foci are all mountainous districts over 5,000 feet in elevation and popular as summer resorts.

6. The same wild rodents (chipmunks and tamarack squirrels) have been found to harbor spirochetes resembling *Treponema recurrentis* in 3 of these foci. They probably act as the reservoirs of infection.

7. No definite vector has been determined. Ticks of the species *Ornithodoros* have been obtained at Big Bear Lake and at Lake Tahoe associated with proved cases of relapsing fever.

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Test for Protective Power Against Yellow Fever

A METHOD of testing sera for protective power against yellow fever is described and designated as the intraperitoneal protection test in mice. The test consists essentially of the inoculation of mice intraperitoneally with yellow fever virus, fixed for mice, together with the serum to be tested, and the simultaneous injection of starch solution into the brain to localize the virus. If the serum lacks protective power the mice die of yellow fever encephalitis.

The test is highly sensitive. Consequently it is useful in epidemiological studies to determine whether individuals have ever had yellow fever and in tests to find whether vaccinated persons or

animals have in reality been immunized. When mice were given large intraperitoneal injections of yellow fever virus fixed for mice, the virus could be recovered from the blood for 4 days although encephalitis did not occur. If the brain was mildly injured at the time of the intraperitoneal injection, the symptoms of yellow fever encephalitis appeared 6 days later, but the virus was then absent from the blood. Strains of white mice vary greatly in their susceptibility to yellow fever. W. A. Sawyer and Wray Lloyd. *The Use of Mice in Tests of Immunity Against Yellow Fever. J. Exper. Med.*, 54:533 (Oct.), 1931. Abstract in *J. A. M. A.*, 104, 4:275 (Jan. 26), 1935.