

RELAPSING FEVER IN PANAMA

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RELAPSING fever in Panama and the Panama Canal Zone has an extremely low incidence if local hospital records can be taken as a fair index of its presence. Prior to 1904 there were almost no institutions on the isthmus where routine examinations of blood films were made. It is our opinion that more cases of relapsing fever occur in rural native children than hospital records indicate. They usually have 1 or 2 paroxysms which then subside spontaneously. We believe that it is very infrequent that an adult rural native acquires a severe, acute attack of long duration. This is based on the fact that during the last 11 years of our experience in rural villages where malaria surveys were conducted monthly on the same individuals, using the thick-blood-film method, we found extremely few of these natives showing even light infections of the disease. They complained of no serious illness and simply considered that they were having a mild attack of malaria. In fact 3 of the 4 cases recently found in the hospitals near us were admitted for entirely other reasons and only the routine blood film examination disclosed the fact that relapsing fever was also present. The native rural population does not respond to the disease in the same active manner as the foreign white resident does. A tolerance to the disease is apparently gained during the very early years of life.

Darling (1908) states that relapsing fever had been reported from time to time in the Canal Zone since the American occupation in 1904, but that the first case in which the diagnosis was established by a microscopic examination of the blood was found in Colon Hospital in 1905. Annual Health Reports of the Panama Canal Zone did not begin their appearance in detail until 1906. Most of the early cases reported

were from Colon Hospital. Hirsch (1883) stated that nothing was known of the disease in Central and South America before 1881, although it may have been present and recorded at that time as typhus or malaria. Since that date he lists reports from Cuba, Peru, Chile, Bolivia, Colombia and Venezuela. No doubt it is present in all of the countries of Central and South America. In Darling's time on the Isthmus of Panama, the number of white to Negro employees was about 2 to 7, yet the cases of relapsing fever selected the white employees at a rate of 7 to 1. Darling believed that the relapsing fever of Panama was distinct from the analogous fever of Africa, Europe and Asia, but that it belonged to the same general class of disease.

No further local records were made on the disease until Connor (1917) reported on the treatment of some cases in Ancon Hospital, the Pacific side of the isthmus. He collected the hospital cases from January, 1909, to August, 1917. A series of 17 cases were found and all of them were in males. Eight of them were American soldiers. They were distributed over the Canal Zone according to their local residence as follows: Eight from the Atlantic Division; 5 from the Central Division; and 4 from the Pacific Division.

Relapses occurred from 1 to 4 times. The sources of infection were believed to be related to visits made in Colombia, Ecuador and the interior of Panama.

Four years after Connor's report, Bates, Dunn and St. John (1921) recorded their work on *Ornithodoros talaje* as the local vector of the disease. Their opportunity to secure cases and ticks came as a result of 2 trips to the interior by white American boys whose homes were in the Canal Zone. Nine boys ranging in age from 11 to 20 years spent several nights in the native

town of Arraijan which is located just beyond the western boundary of the Canal Zone and in a line about opposite Balboa, C. Z. The first party of 5 boys made their visit to Arraijan on March 15, 1921. They occupied the hut of a Chinese at night. This hut was of the usual thatched roof type with cane walls and a dirt floor, and contained a bed constructed of bamboo that was wide enough for 3 people. Three of the boys slept on it while 2 used hammocks. The boys who occupied the bamboo bed were so badly bitten by bugs during the night that they spent the second and third nights sleeping in the bush. On the fourth night they all slept in the hut again with the other 2 boys who had used the hammocks. They returned to Balboa March 19, 1921. Between March 25 and 27, 4 of the 5 boys were admitted to Ancon Hospital with relapsing fever. All of them showed many insect bites. They all agreed that they had been bitten by small reddish bugs full of blood when found.

The second party of 4 white American boys from Pedro Miguel, C. Z., also visited the same town and hut on March 21, 1921. The first night was spent in the bush but the following 3 nights 3 of the boys slept in the Chinaman's hut. One of them spent every night outside the hut. This boy did not acquire the disease but all of the others did. All made complete recoveries after one dose of neocarsphenamine (0.2-0.9 gm.). A visit to the Chinaman's house showed that the bamboo bed was heavily infested with ticks, *O. talaje*. A collection of 250 adults and nymphs and 75 unfed larvae were brought back to the laboratory. These ticks are somewhat similar in their habits to the well-known bedbug and a layman might easily mistake them for bedbugs.

A summary of the study made on these ticks follows:

Typical spirochetes were found in the naturally infected ticks.

Two white rats were infected by inoculating them with a suspension of macerated naturally infected ticks, *O. talaje*.

One monkey, *Macacrus rhesus*, was infected by feeding a number of larvae (*O.*

talaje) on an infected white rat and 22 days later allowing the same ticks, as first stage nymphs, to feed on the monkey.

Three human volunteers were infected as follows:

Subcutaneous injection of an infected white rat's blood.

Subcutaneous injection of a suspension of macerated naturally infected ticks.

Biting by naturally infected ticks.

Briefly summarizing the experiments, these workers proved conclusively that in this particular series of cases *O. talaje* was the vector of relapsing fever.

St. John and Bates (1922) made a lengthy laboratory study of this spirochete and came to the conclusion that the spirochete of relapsing fever in Panama is a distinct species and that it is serologically unrelated to *Sp. obermeieri*, *Sp. novyi*, *Sp. kochi* and *Sp. duttoni*.

A little later, Bates and St. John (1922) published a note suggesting the name of *Spirochaeta neotropicalis* as the name for the spirochete of relapsing fever in this part of the world. The neotropical region, from the viewpoint of the zoologist, includes all of Central and South America. These authors believe that our form of relapsing fever is common to Latin America.

Dunn (1923) reported on the tropical bedbug in relation to the transmission of relapsing fever in Panama. His report was first read by title before the December, 1921, meeting of the Medical Association of the Isthmian Canal Zone. His work indicates that bedbugs that had fed on man and on rats infected with relapsing fever did not transmit the disease to uninfected animals by feeding on them at subsequent intervals. Bedbugs did cause relapsing fever when macerated and inoculated into a white mouse as late as 32 days after they had fed on an infected animal. Spirochetes were found in the coelomic fluid of bedbugs 15 days after feeding on infected blood. This would indicate that the spirochetes survive and apparently multiply in the bugs for a while at least. If such a bug were crushed on skin containing an abra-

sion, the disease no doubt could be transmitted.

Dunn (1923-1924) made a survey in Colombia to determine the prevalence of *O. venezuelensis* and to gain information regarding the relative number and the distribution of these ticks that were infected with relapsing fever spirochetes. Approximately 4,880 specimens were collected from 68 houses located in 20 villages, towns and cities. A total of 2,483 of these ticks, representing collections from 61 houses, survived to be later tested in lots for relapsing fever spirochetes by being macerated and injected into white mice and white rats. Positive results were obtained from 17 of the lots tested, indicating that ticks infected with relapsing fever were present in 17, or 27.9 per cent of the houses in which collections were made. These 17 houses represented 7 different villages, towns or cities.

A second species of *Ornithodoros*, *O. talaje* and a transmitter of relapsing fever is also present in Colombia. Adult specimens of this species were taken in houses in the Barranquilla district and larval forms were found on a gray rat, *Mus norvegicus*, captured in the district. It seems probable that this second species accepts man mainly as a host of necessity and usually confines its attacks to rodents and larger animals and possibly plays an important role in the spread of relapsing fever among these mammalian hosts. It appears to be the larval stage, only, of *O. talaje* that is found on animals. This is due to the larvae remaining attached to the host for several days while becoming replete. The nymphal and adult stages secure their blood meals in less than an hour and do not remain attached to the hosts.

Dunn (1931) reports a house in the Canal Zone in which *O. talaje* was found and some evidence that they attacked man. However, he is of the opinion that rats were responsible for bringing *O. talaje* into the house. A rat campaign had recently cleared the house of rodents and he believes that the tick was then forced to feed on man.

Dunn's (1933) observations on *O. talaje* in Panama have shown that this tick may select human, mammalian, avian, and reptilian hosts. His experience in Panama led him to believe that *O. talaje* acts as an important agent in transmitting the spirochete of relapsing fever from animal to animal, but that *O. venezuelensis* must be considered as the vector of the organism from animal to man and from man to man.

A little later Dunn (1933) definitely arrived at the conclusion that the Argasine tick, *O. venezuelensis* Brumpt, is the principal transmitting agent of relapsing fever of man in tropical America.

THE ANIMAL RESERVOIR

Darling (1922) directed attention to the probable role of the rat as a disseminating agent of relapsing fever in Panama and other countries of tropical America. His presumptions were based mainly on the susceptibility of the rat to the disease, the infestation of rats with *O. talaje* and the fact that both the tick and rat may be found in human habitations. We have not yet found a rat with a naturally acquired infection but, on the other hand, we have not yet been fortunate enough to collect rats from a house or village in which relapsing fever was known to exist. For many years we have been making studies of the blood stream parasites of domestic and wild animals. A number of mammals have been under observation in our animal house. A routine examination of the blood of every animal obtained alive has been made daily for a period of from 1 to 14 days after their admission. In the course of these studies naturally acquired spirochetal infections that compare favorably with the species causing human relapsing fever have been found. A report was made by this laboratory in 1933 and some findings have been made since that date. The report follows:

Monkeys. We have found 3 specimens of *Leontocebus geoffroyi* (Pucheran), the local marmoset or squirrel monkey, carrying this spirochete. The infection kills these monkeys in about one month's time. It is the most sensitive laboratory animal

we have for this disease. Two specimens of *Cebus capucinus capucinus* (Linnaeus), the Colombian white face or white throated capuchin, have also been found with the infection. Both of these monkeys are open to the added possibility of acquiring the disease by the ingestion of infected ticks since they are great bug eaters.

Opossums. In 1931 and 1932 a total of 61 of these animals, *Didelphis marsupialis etensis* Allen, were examined and 6, or 9.8 per cent, were found to be positive for spirochetes. These animals are great prowlers in and around houses and are hosts for *O. talaje*.

Armadillos. Thirty-two of the nine-banded armadillos, *Dasypus novemcinctus fenestratus* Peters, were examined and 2 of them, or 6.2 per cent, were positive for spirochetes. These animals are also hosts for *O. talaje* and like to burrow under native rural houses for their dens.

Grison. This animal is commonly spoken of as the bridled weasel of the tropics and is listed by Goldman in his Mammals of Panama, 1920, as *Grison canaster* Nelson. We have only received 3 of these animals but one of them had a natural infection with spirochetes. It also is a host for *O. talaje*. This animal was not included in our report of 1933.

Otter. We have had 4 of these tropical otters in our cages. Goldman lists it as *Lutra repanda* Goldman. One of them had a spirochetal infection but it was caged with the positive grison and its infection was found so long after being in captivity that we suspect it acquired it from the grison. No ticks have been found on it.

Cattle. During the very large and frequent surveys of herds of cattle we have from time to time found one with a natural infection. Six calves, 3 cows, 1 steer and 1 bull have been found with natural infections. The calves have the best opportunity to acquire the disease because for several days after birth they are apt to be kept tied to bush fences surrounding houses and corals. The dead bark on these fence posts form a fine refuge for *O. talaje* which have been found on calves.

Horses and mules. Many large herds have repeatedly been surveyed in the past 12 years for trypanosomiasis and in the course of these surveys we have found 3 horses with natural spirochetal infections. It is interesting to note that the infected horses were all saddle or draft animals kept in corals near farm house headquarters. None were found in unbroken animals ranging over unfenced plantations.

In spite of the strong circumstances that indicate rats as animal reservoirs we have yet to find one that is positive. However, when we find another infected house or hut we shall make further efforts to survey this animal. It would appear that any animal can be a temporary carrier of the disease.

LABORATORY EXPERIMENTAL ANIMALS

White mice, white rats and the marmoset monkey are the best animals for laboratory use. The marmoset is extremely sensitive and is of great importance in those human cases where it is difficult to find a spirochete. The opossum can also be used but is not as satisfactory as the other animals named.

The animal strains found in our surveys were tested against white mice and rats as a routine measure, except for the original marmoset monkey strain. This was experimented with by the use of mice, rats, marmosets and the human being. Clark, Dunn and Benavides (1931) reported this experiment. This marmoset came from Arraijan, R. de P., the same region from which Bates *et al.* got their human cases and ticks for their experiment. Two men were given direct blood inoculations from squirrel monkeys infected with the disease. One of them received a combined intradermal and subcutaneous inoculation while the other received a deep muscular injection. Both men developed the disease and recovered after the administration of a proper course of treatment. It was passed from one man to a clean squirrel monkey and from the other man to 3 other persons, one of whom failed to show spirochetes in his blood films but recovered from a severe

attack when treated with neoarsphenamine. The spirochetosis was also transferred by the bite of 31 nymphal and adult ticks, *O. venezuelensis* to man. One paroxysm developed but the blood films failed to show spirochetes. A clean squirrel monkey inoculated with this man's blood on the day of his paroxysm did develop the disease and show spirochetes. The marmoset died at the end of a month's course. A total of 60 larval ticks, *O. venezuelensis*, reared from eggs deposited by females which had fed on a squirrel monkey with the disease were permitted to feed on a human volunteer, but the disease, in this experiment, was not transmitted. F. M. Johns (1931) of New Orleans tried to use our monkey strain in the treatment of paresis. The course of the attacks did not appear to modify the mental state in any way. Dr. Johns made a parallel study of a Texas human strain with our monkey strain. He considers them identical but stated definitely that neither was satisfactory in the treatment of paresis.

We were never able to grow the spirochete in culture media. It is quite possible that mammals may prove to be a more abundant and natural source of origin for many cases of relapsing fever than the human carrier of the disease. We believe that relapsing fever and Chagas' disease in our region belong more to animal life than to the human being. The field is open for more extensive investigations in our hemisphere. Mammals that live in tree holes and in ground burrows together with their ectoparasites deserve study. The vampire bat can naturally acquire the spirochetal infection as well as Chagas' disease, but thus far it has not been able to transmit either of these diseases in our experiments. The reduvid bugs also deserve further attention.

The hospital records on morbidity and mortality have been saved for the end of this report in order to leave with the reader the striking impression of its low incidence in our region.

RELAPSING FEVER RECORDS

	Number cases of relapsing fever	Deaths due to relapsing fever	Total number of discharges from all causes
Panama Canal Zone, 1906-1940	103	3	565,235
Hospital Santo Tomás, 1922-1940	17	0	255,133
Panama Hospital, Herrick Clinic, 1929-1940	8	0	20,539
*United Fruit Company Tropical Hospitals (10), 1922-1940	1	0	499,117
Totals	129	3	1,340,024

* 2 hospitals in Cuba; 2 in Spanish Honduras; 2 in Panama; 1 in Guatemala; 1 in Costa Rica; 1 in Colombia; and 1 in Jamaica.

129 cases with 3 deaths, or a death rate of 2.3 per cent.

SUMMARY

1. Relapsing fever in Panama has an extremely low incidence. Only 129 cases are listed among 1,340,024 hospital discharges. The disease is of academic interest but is not of very great economic importance.

2. The new style of canvas cot that has almost entirely taken the place of the old immovable board or bamboo bed has done much to deprive the tick of its refuge and breeding places in rural huts.

3. Non-immune foreign white people who visit remote rural places and must temporarily use old native huts for sleeping quarters until their camps are constructed take the greatest risk of acquiring the disease. Mobile military units, prospectors, archeologists, explorers, are the class of people that should be warned of the danger.

4. Our local vectors are *O. talaje* and *O. venezuelensis*. The former may select human, mammalian, avian and reptilian hosts. The latter is the vector from animal to man

and from man to man. The bedbug can become a reservoir for the disease but cannot transmit it by feeding on man. It is, however, open to the same possibility of transferring the disease as the louse in the eastern hemisphere if it is killed by crushing it against the skin while in the act of biting. The vampire bat and triatoma bugs have not experimentally transmitted the disease although they can acquire it.

5. Relapsing fever of Panama is apparently more prevalent in animal life than in people and this reservoir probably perpetuates the disease in our region more than the human carrier. The white rat and white mouse and the marmoset monkey are the best laboratory animals for a study of the disease.

6. The native people, except for young children, show a high degree of tolerance that has probably been naturally acquired in childhood. The foreign white non-immune will develop severe acute attacks and in some instances have a long course unless the diagnosis is established and satisfactory treatment is given. Rural native people seldom seek treatment.

7. The name *Spirochaeta neotropicalis* has now been recorded for the spirochete of relapsing fever in Central and South America.

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