



RELAPSING FEVER IN PANAMA¹

THE HUMAN TICK, *ORNITHODOROS TALAJE*, DEMONSTRATED
TO BE THE TRANSMITTING AGENT OF RELAPSING FEVER
IN PANAMA BY HUMAN EXPERIMENTATION.

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There were six cases of relapsing fever in Ancon Hospital during the last week of March and the first week of April of this year (1921). All six patients were white American boys between eleven and twenty years of age. All had spent several nights in the native town of Arraiján within the two weeks previous to their admission to the hospital. Four of these boys were from a party of five who went to Arraiján hunting on March 15, 1921, and two were from a party of four who went there on March 21, 1921.

First party. The boys of this party all lived in Balboa, Canal Zone. They left Balboa for Arraiján on March 15, 1921, and arrived there a few hours later the same day. Arraiján is a native village of about 600 population outside the Canal Zone, approximately 8 miles from Balboa. As the trade winds of the dry season sometimes become sufficiently cool at night to cause sleeping outside to be rather unpleasant, the first night was spent in a hut belonging to a Chinaman, who keeps a store in this village. This Chinaman with his wife, who is a native Panamanian, and three children, had been living in the hut but upon the arrival of the American boys, moved into the store to live while the boys occupied the hut. All five boys slept in the hut the first night, three of them sleeping on a wide bamboo bed, the other two occupying hammocks. They were so badly bitten by insects during the night that three of them spent the

bark being used to bind the bamboo poles to the cross pieces of the frame and the latter to the crotched sticks. This bed was nearly square and occupied one side of the small room where it was located. The room being without windows was very dark even at midday, therefore the bed was taken apart and moved out of doors into the sunlight for examination. There it was found that human ticks, *Ornithodoros talaje*, were present in large numbers. They were found in the small crevices of the black palm frame and in the ends of the bamboo poles near the first exposed joint. They evidently go into hollow joints of the ends of the bamboo poles to deposit their eggs and molt. About 250 adults and nymphs and 75 unfed larvae were collected from the bed, nearly every joint being infested. Many of the villagers watched the work with much interest and some of them volunteered the information that nearly all of the houses in Arraiján were infested with "Chinche mamones," as they are called by the natives. A few of them modified this statement by saying that all of the older houses in the village were badly infested but that the newer ones were free from them. Our stay in the village was too short to permit investigation of other huts, however most of the huts in the village were of the same type as the one we visited.

The human ticks are somewhat similar in habits to the bedbug, remaining secreted in the cracks and crevices of the beds and walls by day and coming out at night to feed on the occupants. After becoming engorged with blood they again return to a place of secretion. Therefore one of these huts provides an ideal place of abode for them as hiding places are innumerable.

ANIMAL INOCULATIONS WITH TICKS

Naturally infected ticks injected into rats

On April 7, 1921, 22 ticks, 16 adults and 6 nymphs, that had been collected from the bed in the Chinaman's hut at Arraiján on April 1 and kept in an incubator at 37° C. for five days, were macerated in 2.5 cc. of normal saline solution and this divided into equal parts and injected into two white rats, no. 2 and no. 3.

TABLE 2

Result of blood film examination rat 2

DATE	RESULT	NUMBER OF FIELDS EXAMINED
April 8, 1921	Negative for spirochaetes	600
April 9, 1921	Negative for spirochaetes	600
April 10, 1921	Negative for spirochaetes	600
April 11, 1921	Negative for spirochaetes	600
April 12, 1921	Negative for spirochaetes	600
April 13, 1921	<i>Positive for spirochaetes</i>	

The first spirochaete was found in 120 fields; the second in 3 fields; the third in 40 fields; the fourth in 10 fields and the fifth in 3 fields. This rat was killed while blood was being taken from it to inject into another rat. The rat was autopsied (Animal Autopsy No. 1959) by Dr. H. C. Clark, who found many spirochaetes in smears of crushed heart muscle.

TABLE 3

Result of blood film examination rat 3

DATE	RESULT	NUMBER OF FIELDS EXAMINED
April 8, 1921	Negative for spirochaetes	600
April 9, 1921	Negative for spirochaetes	600
April 10, 1921	Negative for spirochaetes	600
April 11, 1921	Negative for spirochaetes	600
April 12, 1921	Negative for spirochaetes	600
April 13, 1921	<i>Positive for spirochaetes</i>	1 in 140
April 14, 1921	Negative for spirochaetes	600
April 15, 1921	Negative for spirochaetes	600
April 16, 1921	<i>Positive for spirochaetes</i>	1 in 315
April 17, 1921	Negative for spirochaetes	600
April 18, 1921	Negative for spirochaetes	600
April 19, 1921	<i>Positive for spirochaetes</i>	*2 in 251
April 20, 1921	Negative for spirochaetes	600
April 21, 1921	Negative for spirochaetes	600
April 22, 1921	Negative for spirochaetes	600
April 23, 1921	Negative for spirochaetes	600
April 24, 1921	Negative for spirochaetes	600
April 25, 1921	Negative for spirochaetes	600

* These had their ends close together as though they might have divided by transverse fissure a short time previous. Two more were found in 6 fields later.

Each rat received part of the fluid intraperitoneally and part subcutaneously. Dark field examinations and stained smears of this fluid failed to show the presence of spirochaetes.

TRANSMISSION EXPERIMENT

Spirochaete infection carried from rat to monkey by tick bites

April 15, 1921, a number of larvae were fed on infected rat no. 309. After molting and developing into first stage nymphs, 24 of these were placed on monkey no. 68 to feed on May 7. All

TABLE 4

Result of blood film examination monkey 68

DATE	TIME	TEMPERATURE	RESULT	NUMBER OF FIELDS EXAMINED
		°F.		
May 8, 1921	10 a.m.	102.6	Negative for spirochaetes	1000
May 9, 1921	10 a.m.	100.8	Negative for spirochaetes	1000
May 10, 1921	10 a.m.	101.8	Negative for spirochaetes	1000
May 11, 1921	10 a.m.	102.0	Negative for spirochaetes	1000
May 12, 1921	10 a.m.	101.4	Negative for spirochaetes	1000
May 13, 1921	10 a.m.	102.4	Negative for spirochaetes	1000
May 14, 1921	10 a.m.	102.8	Negative for spirochaetes	1000
May 15, 1921	10 a.m.	102.6	Negative for spirochaetes	1000
May 16, 1921	10 a.m.	103.2	<i>Positive for spirochaetes*</i>	
May 17, 1921	10 a.m.	106.2	<i>Positive for spirochaetes</i>	Average 2 per field

No further examinations made.

* The first spirochaete was found in 40 fields; the second in 49 fields; the third in 101 fields; the fourth in 4 fields and the fifth in 18 fields.

of them attacked, 21 becoming engorged, the other 3 although attacking and taking some blood did not become engorged. With but one exception they all remained attached for about three and a half hours and it was then necessary to remove them as none detached themselves although fully engorged. The one exception after becoming engorged detached in two hours and fifteen minutes. This was the only one observed to secrete any (coxal?) fluid while attached. One of the three that attached but did not engorge was dissected and examined and spirochaetes were demonstrated in the coelomic fluid.

SMEARS FROM TICKS

The most of the ticks brought from Arraján were saved for animal and human inoculation. However a few were set aside for direct examination. These were kept in an incubator with a temperature of 35° C. for six days, then kept at room temperature (21° to 28° C.) for two days and then smears were made from fluid which exuded after pulling off a leg and from gut contents. These smears were stained with a polychrome stain (Hasting's) and examined. Smears were made from males, females and nymphs. Spirochaetes with both the morphology and staining characteristics of the relapsing fever spirochaete were found in coelomic fluid smears and also in gut content smears (possibly contaminated with coelomic fluid) of the seventeenth tick examined, which was a deplete female.

INOCULATION OF THE HUMAN SUBJECT

The evidence to incriminate the tick as the transmitting agent of relapsing fever in Panama now seemed as complete as could be obtained without experimental human inoculation and permission to do this was requested and granted.

Three soldiers, Otto F. Lueckhert, Kenneth K. Glover and Lewellyn N. Jourden of Company A., Military Police, Quarry Heights, Canal Zone, who volunteered to be inoculated, were admitted to Ancon Hospital on April 19, 1921, and the work undertaken. This research work or investigation would have been impossible had it not been for the active coöperation of Col. H. C. Fisher, Chief Health Officer of the Panama Canal, General C. W. Kennedy, Commanding General of the Panama Canal Department of the United States Army, Col. H. A. Webber, Department Surgeon and Col. L. T. Hess, Superintendent of Ancon Hospital.

As it was possible that only a small number of the ticks brought from Arraján might be infected it was decided to inoculate one man with blood from the infected white rat to prove that the spirochaete recovered in its blood was the spirochaete of relapsing fever, to inoculate a second man with a suspension

of ticks brought from the bamboo bed in Arraiján, above referred to, and to allow ticks from this bed to bite a third man.

We felt confident that the first man would have relapsing fever, concerning the other two we felt doubtful, but considered that in the event that they did contract the disease this additional proof would incriminate the tick as the transmitting agent of relapsing fever in Panama beyond all question of a doubt.

Case I. Human subject inoculated with rat blood containing relapsing fever (?) spirochaetes. (Rat infected by ticks, O. talaje, from bed where the original relapsing fever cases presumably had been infected.)

O. F. L., Ancon Hospital No. 237516 (Army Serial No. R105716). White American, age thirty years, was admitted to Ancon Hospital on April 19, 1921, for this investigation. His family history was negative. He had had the common diseases of childhood but otherwise had always been healthy. On the day of admission he stated that he had never felt better in his life. A complete and careful physical examination showed him to be in excellent physical condition. For two months previous to his admission he had not been away from the sanitized areas of the Canal Zone nor in any place where he might have been exposed to either malaria or relapsing fever infection.

April 19, 1921. O. F. L. was injected with 1.5 cc. of blood taken directly from white rat No 311, which rat's blood film at the time showed one spirochaete in 600 fields. Equal parts of this blood were injected subcutaneously on each side of the median line of the abdomen. One-half cubic centimeter of blood from this same rat was also diluted with an equal quantity of citrate solution and injected into his right arm.

April 4, 1921. Rat 2 was inoculated with one-half of 2.5 cc. of normal saline solution in which twenty-two (22) ticks from Arraiján had been macerated. For details see paragraph "Animal inoculations with ticks."

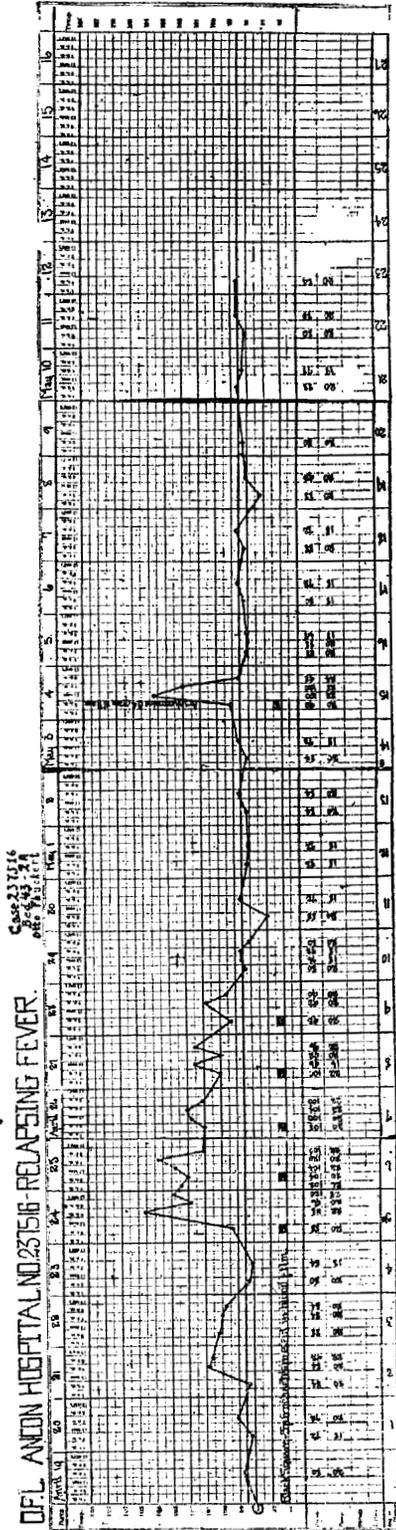
April 13, 1921. Rat 310 was inoculated from rat 2.

April 16, 1921. Rat 311 was inoculated from rat 310.

April 19, 1921. Patient O. F. L. was inoculated from rat 311.

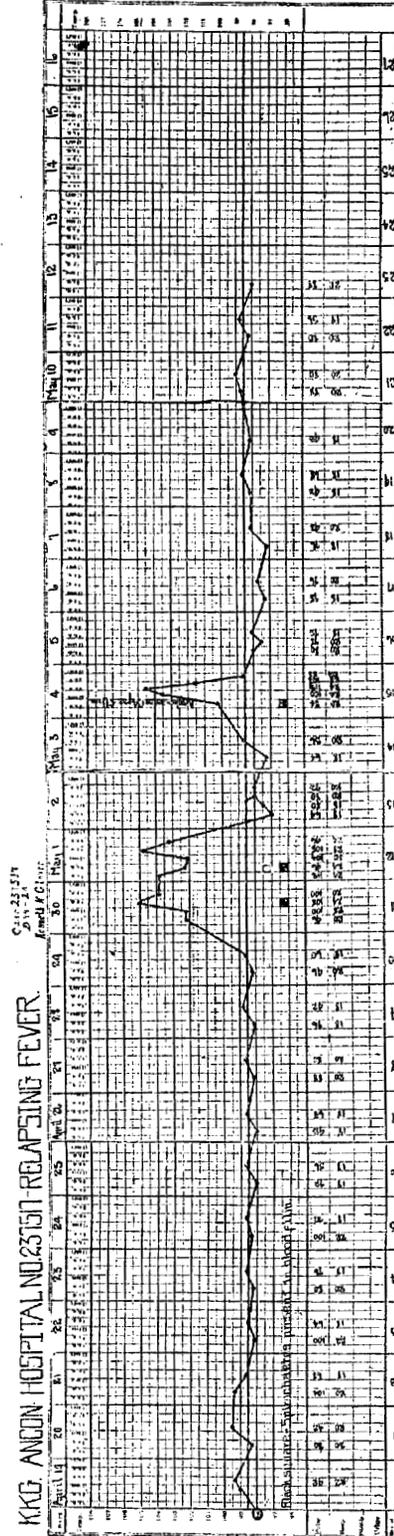
April 21 and 22, 1921. Although during these two days he had fever varying from 100° to 100.8° F. he did not feel sick and no spirochaetes could be found in his blood.

April 24, 1921. During the night of April 23-24, 1921, he had a severe frontal headache and slept scarcely any. At 8 a.m. his temperature was 99.4° F. and a blood film made at 9 a.m. contained spirochaetes, averaging one in 200 fields.



CASE I. RELAPSING FEVER CAUSED BY INJECTING THE VOLUNTEER PATIENT WITH WHITE-RAT BLOOD

The rat had been infected with a strain of spirochaetes obtained by injecting rats with naturally infected ticks.



CASE II. RELAPSING FEVER CAUSED BY INJECTING THE VOLUNTEER PATIENT WITH NATURALLY INFECTED TICKS

April 25, 26, 27, 29, 1921. During these four days he had headache except when it was relieved with phenacetin and codiene, slept very poorly at night, had no appetite and vomited several times. His fever, which was 104.5° F. on April 24, gradually fell by lysis during these four days, reaching normal on April 29, 1921. Spirochaetes were found in blood films made on each of these days.

May 4, 1921. On this date he had a relapse with symptoms similar to those of the first attack. Spirochaetes were again present in a blood film. A 0.4 gram dose of arsphenamine given at 11 a.m. cut the attack short and he made an uneventful recovery. He was kept under observation in the hospital for seven days after his temperature reached normal and for seven days more as an outpatient.

Case II. Human subject inoculated with suspension of macerated ticks. (O. talaje from bed where the original relapsing fever cases presumably had been infected.)

K. K. G. Ancon Hospital No 237517 (Army Serial No. 6414102). White American, age nineteen years, was admitted to Ancon Hospital on April 19, 1921, for this investigation. His family history was negative. He had had the common diseases of childhood. A complete and careful physical examination showed him to be in excellent physical condition. For two months previous to his admission he had not been away from the sanitized areas of the Canal Zone nor in any place where he might have been exposed to either malaria or relapsing fever infection.

April 19, 1921, 11 a.m. He was given a subcutaneous inoculation in the left arm of 1.5 cc. of sterile water containing a suspension of 31 adult ticks and 7 larvae ticks, all *Ornithodoros talaje* which had been collected from the bed in Arraiján on April 1, 1921. These ticks were ground in a mortar under aseptic precautions. At 5.30 p.m. the arm around the site of inoculation was red and warm, the reaction appearing very much like that seen after an injection of typhoid prophylactic. However the arm was not tender and there was no general reaction. At this time 5000 units of tetanus antitoxin were given (this as a precautionary measure).

April 20, 1921. The redness had extended the entire length of the upper arm but the arm was not tender and there was no general reaction. After this date the local reaction rapidly disappeared, except for a hard lump at the site of inoculation about the size of a filbert, which lasted for about two weeks.

TABLE 5
Result of blood film examination O. F. L.

DATE	TIME	RESULTS	NUMBER OF FIELDS EXAMINED
April 19, 1921	(Before inoculation)	Negative for spirochaetes	600
April 20, 1921	9 a.m.	Negative for spirochaetes	600
April 21, 1921	9 a.m.	Negative for spirochaetes	600
	5 p.m.	Negative for spirochaetes	600
	8 p.m.	Negative for spirochaetes	800
April 22, 1921	9 a.m.	Negative for spirochaetes	800
April 23, 1921	9 a.m.	Negative for spirochaetes	700
April 24, 1921	9 a.m.	Positive for spirochaetes	2 in 400
April 25, 1921	9 a.m.	Positive for spirochaetes	1 in 54
April 26, 1921	9 a.m.	Positive for spirochaetes	3 in 70
April 27, 1921	9 a.m.	Positive for spirochaetes	1 in 400
April 28, 1921	9 a.m.	Positive for spirochaetes	2 in 200
April 29, 1921	9 a.m.	Negative for spirochaetes	600
April 30, 1921	9 a.m.	Negative for spirochaetes	600
May 1, 1921	9 a.m.	Negative for spirochaetes	600
May 2, 1921	9 a.m.	Negative for spirochaetes	600
May 3, 1921	9 a.m.	Negative for spirochaetes	600
May 4, 1921	9 a.m.	Positive for spirochaetes	1 in 51
May 5, 1921	9 a.m.	Negative for spirochaetes	600

TABLE 6
Result of blood film examination K. K. G.

DATE	TIME	RESULT	NUMBER OF FIELDS EXAMINED
April 19, 1921	(Before inoculation)	Negative for spirochaetes	600
April 20, 1921	9 a.m.	Negative for spirochaetes	600
April 21, 1921	9 a.m.	Negative for spirochaetes	600
April 22, 1921	9 a.m.	Negative for spirochaetes	600
April 23, 1921	9 a.m.	Negative for spirochaetes	600
April 24, 1921	9 a.m.	Negative for spirochaetes	600
April 25, 1921	9 a.m.	Negative for spirochaetes	600
April 26, 1921	9 a.m.	Negative for spirochaetes	600
April 27, 1921	9 a.m.	Negative for spirochaetes	600
April 28, 1921	9 a.m.	Negative for spirochaetes	600
April 29, 1921	9 a.m.	Negative for spirochaetes	600
April 30, 1921	9 a.m.	Negative for spirochaetes	3000
	12 noon	Positive for spirochaetes	Average 1 in 600
		Positive for spirochaetes	Average 1 in 100
May 1, 1921	9 a.m.	Negative for spirochaetes	600
May 2, 1921	9 a.m.	Negative for spirochaetes	600
May 3, 1921	9 a.m.	Negative for spirochaetes	600
May 4, 1921	9 a.m.	Positive for spirochaetes	Average 1 in 270
May 5, 1921	9 a.m.	Negative for spirochaetes	600

His temperature was taken twice daily, morning and afternoon, a white blood count was made every morning, a urinalysis was made every morning, and blood films were stained and examined every morning. The routine procedure was to examine 600 fields of each film.

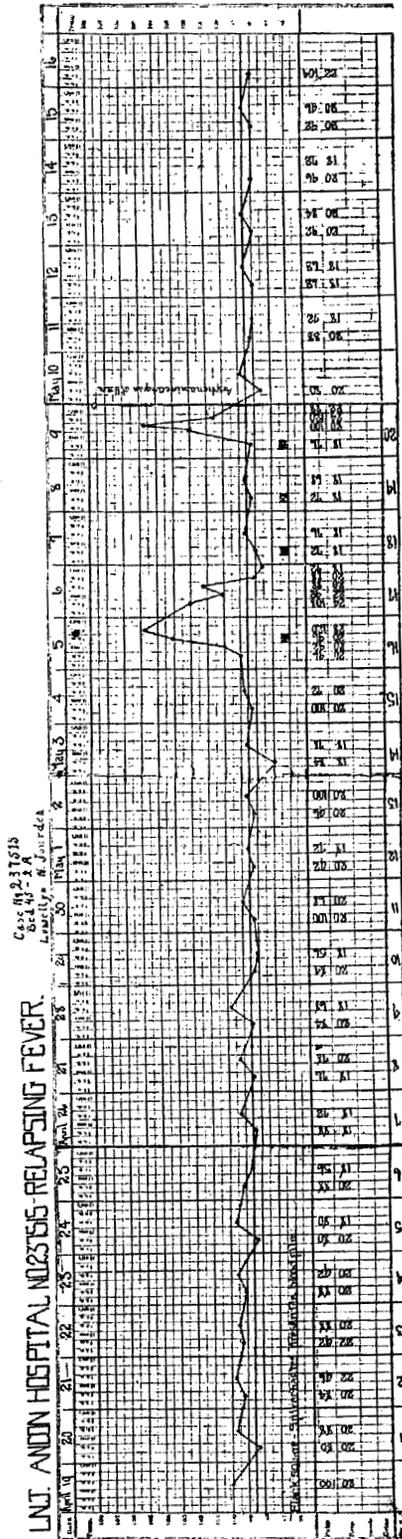
April 30, 1921, eleven days after inoculation, his temperature rose to 102.2° F. at 8 a.m. and to 105° F. at 4 p.m. Blood films made at 9 a.m. were negative for spirochaetes (3000 fields examined); films made at 12 noon, at which time his temperature was still 102.2° F., contained 1 spirochaete in 600 fields.

April 30, 1921, and May 1, 1921. During these two days he had fever, a severe headache and complained of aching all over his body. He slept but one or two hours during either night. Five grains of phenacetin and one-quarter grain of codiene were given in capsule every four hours as needed for the headache and made him fairly comfortable. He had no appetite and showed considerable prostration. He had no true chill but did have chilly sensations from time to time and desired to be constantly covered with a blanket. His spleen was not enlarged to palpation or percussion and there was no jaundice.

May 4, 1921. He suffered an attack similar to that on April 30 and May 1. His temperature was 100.2° F. at 8 a.m. and spirochaetes were present in a blood film made at 9 a.m., averaging one in 280 fields. A 0.4 gram dose of arsphenamine was given at 11 a.m. and following this he made an uneventful recovery. He was kept under observation in the hospital for seven days after his temperature reached normal and for seven days more as an outpatient.

Case III. Human subjects bitten by ticks. (O. talaje from bed where the relapsing original fever cases presumably had been infected.)

L. N. J. Ancon Hospital No. 237515 (Army Serial No. R280766). White American, age twenty years, was admitted to Ancon Hospital on April 19, 1921, for this investigation. His family history was negative. He did not remember having had the common diseases of childhood. About eight years ago he had a severe attack of scarlet fever. In 1913 he had three attacks of appendicitis. On admission he was found by complete and careful examination, to be in excellent physical condition. He left the United States on October 20, 1921, and arrived here in November. He was stationed in Colon from the time of his arrival until about one and one-half months ago, since then he has been stationed at Pier 18, Balboa, Canal Zone. For two months previous to his admission he had not been away from the sanitized areas of the Canal Zone nor in any place where he might have been exposed to either malaria or relapsing fever infection.



CASE III. RELAPSING FEVER CAUSED BY ALLOWING NATURALLY INFECTED TICKS TO BITE VOLUNTEER PATIENT

April 19, 1921. Thirty-seven ticks, 29 adults, 1 nymph and 7 larvae, were placed on his left upper arm and forearm. Only 6 of these could be induced to attack and feed. Of these 6, 4 adults and 1 nymph became fully engorged and secreted a clear colorless fluid termed "coxal fluid" by various observers on ticks of the family Argasidae; the sixth took blood but detached before engorgement and apparently secreted no fluid. Blood oozed from each bite site and mixed with the clear fluid and this mixture upon drying formed a small scab. No excreta was noticed. The patient was instructed not to scratch the bitten areas. He stated that but one bite stung sharply, the others giving the sensation of a faint prick, like a mild mosquito bite. Four of these bites were on the upper arm 2 inches above the elbow on the anterior surface and 2 were about the same distance below the elbow.

April 22, 1921, p.m. Ticks were again placed on this man's left arm, 4 attacked. Three of these were adults, 1 a large female and the fourth a nymph. One of the adults became partially engorged and did not secrete any fluid. The other 3 each secreted fluid after drawing blood. This fluid usually covered the site of the bite. One, the large female, engorged in about fifteen minutes, detached itself and then quickly secreted a quantity of fluid on the bite. None of the 4 took more than thirty minutes to engorge.

April 23, 1921. p.m. Ticks were again fed on this man's left arm on the anterior surface. Eleven adults and 3 young larvae became engorged. Nine of the adults secreted (coxal?) fluid. The other 2 adults and the 3 larvae did not secrete any fluid.

April 25, 1921, p.m. One more tick was fed on this man's left forearm. This tick became nearly engorged but detached in about thirty minutes without secreting any fluid.

To summarize: Twenty-five ticks brought from the hut in Arraiján on April 1, 1921, fed on this man's arm sometime during the seven days between April 19 and April 25, both inclusive. This was their first feeding after collection. The bites remained in evidence and became more prominent on May 3, 4, and 5.

May 5, 1921. This patient remained well until noon of this date, when a severe headache developed. He did not mention this until his four o'clock temperature was taken, which was 103°F. Blood films made at this time contained spirochaetes. The first spirochaete was found after searching 60 fields, the second one after 437 fields, the third after 287 fields, the fourth after 212 fields and the fifth after 97 fields. He said that he ached all over, was chilly and could not eat.

He kept covered with a blanket. He stated that he slept very little during the night of May 5-6. His face was flushed and he was somewhat prostrated. No other sign or symptoms were noted.

May 6, 1921. He felt much better and at 8 p.m. and his temperature was again normal.

TABLE 7

Result of blood film examination L. N. J.

DATE	TIME	RESULT	NUMBER OF FIELDS EXAMINED
April 19, 1921	(Before inoculation)	Negative for spirochaetes	1000
April 20, 1921	9 a.m.	Negative for spirochaetes	1000
April 21, 1921	9 a.m.	Negative for spirochaetes	1000
April 22, 1921	9 a.m.	Negative for spirochaetes	1000
April 23, 1921	9 a.m.	Negative for spirochaetes	1000
April 24, 1921	9 a.m.	Negative for spirochaetes	1000
April 25, 1921	9 a.m.	Negative for spirochaetes	1000
April 26, 1921	9 a.m.	Negative for spirochaetes	1000
April 27, 1921	9 a.m.	Negative for spirochaetes	1000
April 28, 1921	9 a.m.	Negative for spirochaetes	1000
April 29, 1921	9 a.m.	Negative for spirochaetes	1000
April 30, 1921	9 a.m.	Negative for spirochaetes	1000
May 1, 1921	9 a.m.	Negative for spirochaetes	1000
May 2, 1921	9 a.m.	Negative for spirochaetes	1000
May 3, 1921	9 a.m.	Negative for spirochaetes	1000
May 4, 1921	9 a.m.	Negative for spirochaetes	1000
May 5, 1921	9 a.m.	Negative for spirochaetes	1000
May 5, 1921	4 p.m.	<i>Positive for spirochaetes</i>	Maximum 1 in 97 Minimum 1 in 604
May 6, 1921	9 a.m.	Negative for spirochaetes	1600
May 7, 1921	9 a.m.	<i>Positive for spirochaetes</i>	1 in 405
May 8, 1921	9 a.m.	<i>Positive for spirochaetes</i>	1 in 309
May 9, 1921	9 a.m.	<i>Positive for spirochaetes</i>	1 in 823
	4 p.m.	Negative for spirochaetes	1000
May 10, 1921	9 a.m.	Negative for spirochaetes	1000
May 11, 1921	9 a.m.	Negative for spirochaetes	1000
May 12, 1921	9 a.m.	Negative for spirochaetes	1000

May 8, 1921. He felt well on this date but search of blood films made at 9 a.m. revealed one spirochaete in 309 fields.

May 9, 1921. At 4 p.m. he suffered a relapse, his temperature rising to 102° F. A blood film made at this time showed one spirochaete in 823 fields. At 6 p.m. his temperature was 104.8° F.

May 10, 1921. At 8 a.m. his temperature was 97.6° F. and he felt much better. At 9 a.m. he was given a 0.4 gram dose of arsphenamine and following this he made an uneventful recovery. He was kept under observation in the hospital seven days after his temperature reached normal and for seven days more as an outpatient.

(See temperature charts at the end of this article.)

LITERATURE

A large amount of work by many investigators has been done upon the relapsing fevers of Asia, Europe, Africa and the Americas. It may be possible that the human transmission work detailed in this paper has been previously done, if so it is our desire to give credit where it belongs and to contribute this report as additional proof that relapsing fever is transmitted by the tick. However, in the literature at hand we were not able to find where this had been done and as our opportunity to carry out this investigation with naturally infected ticks was so exceptional we did not feel justified in waiting until we could make a still more exhaustive search of the literature. The Manual of Tropical Medicine by Castellani and Chalmers, third edition, 1919, gives a fairly comprehensive review of the literature and as a supplement to that we reviewed all the Tropical Diseases Bulletins which we have received during the past four years.

According to Castellani and Chalmers the relapsing fever of Europe, caused by the *Spiroschaudinnia recurrentis* or *S. obermeyeri*, is transmitted by the louse ("Most authorities consider lice to be the carriers," p. 443) and the relapsing fever of India, caused by *S. carteri*, "is spread by the louse in all probability." Concerning the relapsing fever of West Africa they state it is "an acute specific relapsing fever caused by *Spiroschaudinnia duttoni* Novy and Knapp, 1906, and spread by *Ornithodoros moubata* Murray." In the paragraph entitled History they further state:

Nabarro, in August, 1903, was the first to observe a spirochaete in human beings in Uganda, but as his publication, through no fault of his own, did not appear until much later, his discovery was forestalled by those of Ross and Milne in 1904, and Dutton and Todd, also in

1904, who found the cause of the tick fever to be a spirochaete, the latter observers also proving that it was introduced into the blood by the bite of a tick, *Ornithodoros moubata*.

Dutton and Todd (1) above referred to made a very careful study of relapsing fever in West Africa in 1904-1905. They were able to infect monkeys and a white rat with relapsing fever by allowing naturally infected ticks to feed on them; to transmit the spirochaete from animal to animal; and to transmit the spirillum by the bites of young ticks newly hatched in the laboratory from eggs laid by infected parents. In addition they collected a large amount of evidence pointing to the tick as the common transmitter of this disease. This work has been generally accepted as proof that relapsing fever may be transmitted by the tick *O. moubata*. However, they do not state that they transmitted the disease by allowing either naturally or artificially infected ticks to feed on the human subject.

Castellani and Chalmers make no reference to the possible transmitting agent of relapsing fever in North and Central America. Referring to the Relapsing Fever of South America they state "According to Robledo, this parasite is carried by *Ornithodoros turicatus*." Robledo (2) apparently bases his statement upon the frequency with which he has found his cases to have been bitten by ticks. The part of his article referring to the tick reads as follows:

Autant que j'ai pu l'observer, notre parasite a été toujours transmis aux malades par la piqure d'*Argas americanus* (*Ornithodoros chinche* P. Gervais, 1859). Cet acarien, très abondant dans les régions chaudes de Colombie, surtout dans les maisons abandonnées, où reste de l'herbe, de la paille, etc., s'attaque aux voyageurs avec une grande avidité. Sa piqure est suivie presque toujours d'une démangeaison très intense, et parfois de vésicules, surtout chez les individus à peau fine.

En dépit de mes efforts pour transmettre la fièvre récurrente à l'aide de *Pediculus capitis*, jamais je n'ai réussi. Mais, peut-être n'ai-je pas été placé dans de bonnes conditions et est-il possible que la maladie soit quelquefois transmise par cet insecte?

IDENTIFICATION OF THE SPIROCHAETE

The amount of work which we have done thus far does not permit us to apply a specific name to the spirochaete with which we have been working; however, we feel that that part of the work of identification which has been completed should be included in this paper and is therefore given. Relapsing fever spirochaetes are differentiated by agglutination reactions, immunity experiments and animal reactions. We have not yet secured cultures of the various types of spirochaetes or their respective agglutinating sera so therefore have not performed any agglutination tests. The following is a summary of the animal reactions to the different types of the spirochaete as given by Darling.³

Group A. The group causing a relapsing or recurring infection in man, monkeys, white mice and white rats, including *Sp. Duttoni* and the tick-fever of Africa.

Group B. The group causing the infection in man, monkeys and white mice, but with a single paroxysm in white rats. This group comprises the relapsing fever of Panama and the two cases studied by Carlisle.

Group C. The group causing a recurring infection in man and monkeys but failing to cause an infection in small rodents with blood direct from human sources, yet causing an infection in small rodents after a preliminary passage through the monkey. This group includes the relapsing fever of Europe, caused by *Sp. Obermeieri*.

Group D. The group causing a recurring infection in man and monkeys but only transient infections in white rats and white mice. This group includes the relapsing fever of Bombay caused by *Sp. Carteri*.

The results obtained by inoculation of our spirochaete into white rats, white mice, monkeys, guinea-pigs, rabbits and wild rats are given below.

White rats

Injection of infected material into the white rat, either by the subcutaneous or intraperitoneal method, is usually followed by a prompt appearance of spirochaetes in the blood stream in

from twenty-four to forty-eight hours. The initial appearance, however, may be delayed for one or two days longer.

The subsequent course of infection varies in different rats but it is usual to find spirochaetes in large numbers on the second and third days following their initial appearance and in small numbers at irregular intervals thereafter up to the thirteenth day. This statement is based on a series of eleven rats examined daily for eleven days or longer. There was a return of the spirochaetes in the blood stream after an apparent freedom, in seven but not in four. The return of the spirochaetes was characterized by the small number present, their irregular time of appearance and the short period of time in which they could be found in the blood stream.

Seven of those white rats may have had a continued spirochaetosis as described by Darling (4). He states

The infection in white rats is characterized by the rapid disappearance of spirochaetes from the blood stream. The disappearance is not complete but it is rarely possible to demonstrate the spirochaetes in the peripheral blood twenty-four hours after the height of the infection.

However if we accept the return of spirochaetes in the peripheral blood after an apparent absence of several days duration, although few in number, as evidence of a relapse in rodents we may conclude that some white rats but not all are subject to relapse.

In all tables given a Bausch and Lomb $\frac{1}{12}$ oil immersion objective and 5× eyepiece were used.

White mice

The reactions in white mice agree in the main with those obtained by Darling in 1907, as will be seen by reference to table given below showing results obtained in our series. Darling states

In the initial paroxysm there is a greater number of spirochaetes per field per day and the duration of the paroxysm is somewhat longer

than subsequent ones. The first paroxysm lasts about three days. The period between the first and second paroxysm is from four to five

TABLE 8

White rats inoculated with relapsing fever spirochaetes April and May, 1921

RAT NUMBER	DAYS EXAMINED																				
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Rat 293	0	2	600	0	1	0	1	1	3	3	0	0	0	0	0	0	0	0	0	0	0
Rat 306	0	30	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rat 308	1	50	200	0	0	0	1	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Rat 309	x	900	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rat 311	0	0	0	1	0	0	1	0	0	0	0	2	0	0	0	0	0	0	0	0	0
Rat 312	0	2	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
Rat 333	1	0	0	0	0	0	0	0	1	1	0	1	0	x	x	x	x	x	x	x	x
Rat 444	3	25	600	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	x	x
Rat 327	0	2	800	x	0	0	0	0	0	0	0	0	1	x	x	x	x	x	x	x	x
Rat 329	0	3	300	0	0	0	0	0	0	0	0	x	x	x	x	x	x	x	x	x	x
Rat 372	x	0	10	0	0	0	0	0	0	0	0	x	x	x	x	x	x	x	x	x	x
Summary.....	+	+	+	+	+	0	+	+	+	+	+	+	+	0	0	0	0	0	0	0	0

Numerals = Number of spirochaetes found in 300 fields.

0 = No spirochaetes found in 300 fields.

x = No examination made.

TABLE 9

White mice inoculated with relapsing fever spirochaetes April and May, 1921

MOUSE NUMBER	DAYS EXAMINED																				
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Mouse 326	0	15	90	0	0	0	0	0	0	0	0	x	0	0	0	0	0	0	0	0	0
Mouse 325	0	1	0	0	0	0	0	0	2	Died											
Mouse 323	6	18	0	0	0	0	0	2	Killed												
Mouse 363	36	3	0	0	0	0	0	0	6	0	0	0	0	1	0	0	0	0	0	0	0
Mouse 365	30	24	0	0	0	0	1	9	0	0	0	0	1	0	0	0	0	0	0	x	x
Mouse 366	24	9	0	0	0	0	0	24	0	0	6	0	0	0	0	0	0	0	0	0	0

Numerals = Number of spirochaetes found in 300 fields.

0 = No spirochaetes found in 300 fields.

x = No examination made.

days. The second paroxysm lasts from two to three days. This may be followed by an intermission of four or five days, and followed by a third relapse lasting two or three days.

Monkeys

The reaction in the *Macaccus rhesus* is comparable to that of man. One or more relapses occur and the animal during the attack is irritable and refuses to take his food. The temperature curve, while not reliable, usually shows a rise of one or two

TABLE 10

Monkeys inoculated with relapsing fever spirochaetes April and May, 1921

MACACCUS NUMBER 317			MACACCUS NUMBER 318		
DAYS	SPIROCHAETES SEEN IN 600 FIELDS	TEMPERATURE	DAYS	SPIROCHAETES SEEN IN 600 FIELDS	TEMPERATURE
		°F.			°F.
1	0	100.4	1	1	100.2
2	2	102.5	2	48	102.4
3	300	103.6	3	1200	102.8
4	900	105.4	4	1200	102.2
5	0	102.6	5	0	101.0
6	0	101.4	6	0	101.2
7	0	101.0	7	0	101.6
8	9	102.2	8	8	102.2
9	20	101.8	9	3600	104.2
10	600	103.6	10	0	101.8
11	24	102.4	11	0	102.0
12	0	100.4	12	0	101.0
13	0	101.4	13	0	102.0
14	0	101.6	14	0	100.4
15	0	101.4	15	10	101.4
16	0	101.4	16	150	101.8
17	0	101.8	17	0	101.4
18	0	103.8	18	0	101.8
19	0	103.0	19	0	102.6
20	0	102.4	20	0	103.2
21	0	103.4	21	0	102.4
			22	0	102.8
			23	0	103.0

degrees at the height of the infection. There is also an apparent loss of weight. It will be noted that two relapses occurred in monkey No. 318 while monkey No. 317 had but one. The spirochaetes, after their first appearance, showed a daily increase in number until the height of the infection was reached, after which they abruptly disappeared from the peripheral blood to reappear as a relapse in from three to five days.

Monkey 317 received, on April 27, 1921, 1.5 cc. of heart's blood (citrated) from rat 362. Rat 362 had 10 spirochaetes to 100 fields at the time the blood was withdrawn. This strain of spirochaetes was obtained from experimental human case O. F. L.

Monkey 318 received, on April 23, 1921, 2 cc. of heart's blood from rat 304. Rat 304 had 1 spirochaete in 100 fields at the time the blood was withdrawn. This strain of spirochaetes was obtained from (J. T. B.), a relapsing fever patient in Ancon Hospital and had been passed through three white rats and one wild (cotton) rat.

Guinea-pig and rabbit

An adult guinea-pig and adult rabbit resisted infection. Guinea-pig 331 and rabbit 330 each received on May 7, 1921, 0.75 cc. of heart's blood from rat 328. Rat 328 had 4 spirochaetes in 100 fields on the date of inoculation. Daily films were made for ten days succeeding inoculation and 300 fields examined daily but no spirochaetes were found.

Wild rats

The black rat (*Mus rattus*) and the cotton rat (*Sigmodon hispidus chiriquensis*) were found to be susceptible to infection with this spirochaete, reacting in a general way the same as the white rat.

TABLE 11

MICRONS	4-6	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Number of parasites.....	1	0	1	10	10	13	11	17	8	21	6	10	8	4	0	5	2	2	1

Films were made from man, rat and monkey and the spirochaetes were drawn as encountered. No appreciable difference existed in the length of the spirochaetes whether they were from man, monkey or rat. The day of the paroxysm (whether second, third or fourth) did not materially affect the average length of the spirochaete, although a slight increase in length occurred as the paroxysm advanced.

Morphology and division

Dark field preparations. The movements of the spirochaete whether in the fresh blood or in Noguchi's medium are charac-

terized by a rapid spring-like spiral movement which propels the organism for a distance of about twice its length. The systole is preceded by a short diastolic period during which the organism partially doubles on itself as though gathering itself together for its spring forward or backward as the case may be. Occasionally one extremity of a spirochaete becomes anchored to the cover slip and it lashes its body around this pivot. The attached extremity is circular in outline. At times when con-

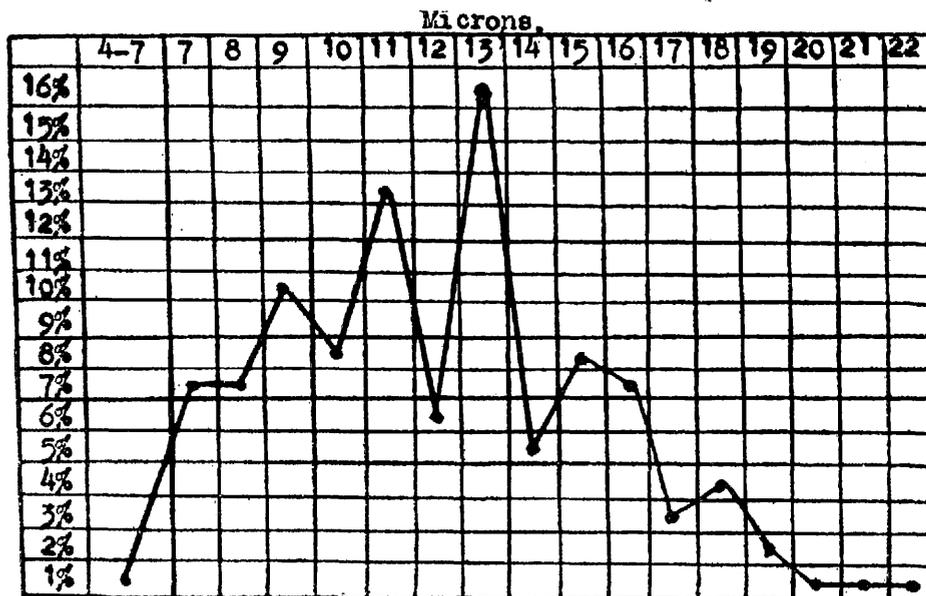


FIG. 1. MEASUREMENT OF SPIROCHAETES. LENGTH OF SPIROCHAETES.
(130 MEASURED)

Blood films dried and stained with Hasting's stain. Measured by the camera lucida method. Shortest form measured 4.6 microns in length. Longest form measured 22. microns in length.

ditions are unfavorable and just before motion ceases there is a distinct vibratory non-progressive movement. After all movement has stopped the spirochaetes are seen as refractile chains held together by a poorly refractile envelope.

In rats blood taken when the infection is at its height, both long and short forms are seen but the long forms predominate. If Noguchi's medium is then richly inoculated, with 1 cc. or more of blood, and examined six and twenty-four hours later the majority of the spirochaetes will be found to have increased

allowing the same ticks as first stage nymphs to feed on the monkey.

Three human beings, volunteer patients, have been infected with relapsing fever as follows:

1. The first by a subcutaneous injection of blood from a white rat which had been infected with relapsing fever by a combined subcutaneous and intraperitoneal injection of naturally infected ticks.

2. The second by a hypodermatic injection of a suspension of naturally infected ticks.

3. The third by being bitten by naturally infected ticks.

Tabulations of the results obtained by inoculating white rats, white mice and monkeys, *Macaccus rhesus*, with the spirochaetes of the relapsing fever in Panama are presented. Also a brief allusion is made to their measurements and appearance in cultures.

CONCLUSION

The human tick, *Ornithodoros talaje*, has been proven to be the transmitting agent of the relapsing fever in Panama by human experimentation.

SUMMARIO

Dos ratas blancas infectadas con la fiebre recurrente por medio de la inoculación de una suspensión macerada de garrapatas (*Ornithodoros talaje*) naturalmente infectadas.

En Panamá se han encontrado espiroquetas típicos en garrapatas naturalmente infectadas.

Después de haber conseguido que un número de larvas (*O. talaje*) se alimentaran sobre una rata blanca ya infectada, se consiguió la infección de un mono, *Macaccus rhesus*, veintidós días más tarde, permitiendo que las mismas garrapatas, en estado de ninfas de primer grado, se alimentaran sobre el cuerpo del mismo.

Tres seres humanos, pacientes voluntarios, fueron infectados con la fiebre recurrente, de la manera siguiente:

1. El primero, mediante una inyección sub-cutánea de sangre obtenida de una rata blanca que había sido ya infectada con la

fiebre recurrente por medio de una inyección combinada, cutánea é intra-peritoneal, de garrapatas naturalmente infectadas.

2. El segundo, mediante una inyección hipodérmica de una suspensión de garrapatas naturalmente infectadas.

3. El tercero, permitiéndosele que fuera picado por garrapatas naturalmente infectadas.

Se presentan cuadros demostrativos de los resultados obtenidos inoculando ratas y ratoncillos blancos y monos (*Macaccus rhesus*) con los espiroquetas de la fiebre recurrente de Panamá. Así mismo se hace una alusión de su tamaño y apariencia en cultivos.

CONCLUSION

Se demuestra, por experimentos humanos, que la garrapata humana (*Ornithodoros talaje*) es el agente transmisor de la fiebre recurrente de Panamá.

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HEADQUARTERS PANAMA CANAL DEPARTMENT,
Quarry Heights, Balboa Heights, C. Z.,
May 17, 1921.

GENERAL ORDERS, }
No. 26.

Recognition of Unusual Service

The following named enlisted men of Company A, Military Police, Panama Canal Department:

Private KENNETH K. GLOVER, 6414102,
Private OTTO F. LUECKERT, R-105716, and
Private LEWELLYN N. JOURDEN, R-280766,

entered Ancon Hospital on April 19, 1921, and each voluntarily allowed himself to be inoculated "with suspected relapsing fever material in order to deter-

mine the intermediate host" in the transmission of relapsing fever in Panama. Each suffered an acute attack of relapsing fever, but from which all happily have recovered.

By means of the coöperation and voluntary assistance of these men, it has been proven that the human tick *Ornithodoros talaje* (Guerin-Meneville) is the transmitting agent of relapsing fever in Panama.

These three men were selected from approximately thirty men of Company A, Military Police, who volunteered for this experiment. By their self-sacrifice they have aided in establishing a scientific fact which will aid in the control of disease and result in less sickness and loss of life among our troops operating in the field and on the Isthmus. The Department Commander desires to commend these soldiers for their devotion and self-sacrifice, and the other soldiers who, though not called upon to undergo this ordeal, showed their willingness to imperil their lives in the cause of humanity. A copy of this order will be filed with their service records.

(201.4)

By command of Brigadier General KENNEDY:

H. O. WILLIAMS,
Chief of Staff.

Official.

J. W. CRAIG,
Adjutant.

True Copy: