

A CASE OF RECURRENT FEVER OBSERVED IN HAVANA.

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The important role played by the spirochetes as etiological factors in many human diseases, give true worth and opportunity to the description of the following case of recurrent fever, which we have recently observed in Havana. Its appearance in this city compels us to make certain hygienic considerations before the American Public Health Association.

The clinical picture of this disease, formerly called "bilious typhoid fever," has a characteristic feature, a constant symptomatic identity. In regard to the temperature curve, due to the paroxysms it is really a cut difficult to be confounded with that of other diseases, provided we have before us the *complete curve*. But the diagnosis may lead to mistakes if we only examine the febrile paroxysms, without making an hematological examination.

Besides, the spirochete discovered by Obermeier, in 1873, in the blood of patients suffering from recurrent fever, is still considered as the only indisputable pathogenic organism of this disease.

While it is true that so far as the clinical aspect and the etiology of recurrent fever, it has not changed any, yet the place which belongs to the *Spirochete Obermeieri* among the organic beings is a subject of important discussion since Schaudinn showed that certain spirochetes were only evolutionary forms of animal parasites (leucytozoons, trypanosomes).

The clinical history of the case is as follows:

Henry Mason, a mulatto, 34 years of age, native of Chicago, U. S. A. Entered "Las Animas" Hospital on February 22d, 1906, sent by the sanitary authorities of the port of Havana. The case was sent because the patient was not an immune to yellow fever, had fever, and came from an infected port.

On admission he tells us "he had never been in Cuba except for a few hours; that he comes from Colon (Panama) where he remained three weeks; that he embarked on the steamer "Miramar" on February 7th and arrived at Havana on the 22d of the same month (the day he was admitted to the hospital)."

First paroxysm —

On the 18th and 19th he fell sick, with pains all over his body, but he was able to work; he believes he had fever; that on the afternoon of the 20th he had a chill.

His temperature on admission was 38.6° C., and his pulse 100 per minute. Severe headache, and epigastric pain radiating toward the left hypochondrium.

Examination of the blood showed: Sp. Gr. 1050. Hæmoglobin (Talquist's Scale) 80%. No malarial parasites. *Obermeier's Spirochetes* present.

The diagnosis is, of course, settled,—*recurrent fever*.

The typical temperature curve became evident in the course of a few days, as can be seen in the chart herein shown.

Feb. 23d. Was awake all night. During the day-time he vomited — greenish fluid. Urine examination: slight traces of albumen, Erlich's diazo-reaction, negative.

Feb. 24th. Had a fairly good night. At 9:15 A. M. perspires freely; at 11:30 A. M. perspiration continues very freely. Coincidentally with the profuse sweating the temperature fell below normal. Blood examined at 3:00 P. M., that is, during the descent of the temperature (37.1° C.) revealed no spirochetes. General condition is improved. Urine has albumen in quantity sufficient to precipitate.

Feb. 25th, 26th, 27th, 28th and March 1st (5 days). Feels well and afebrile except a degree for half an hour on the 25th.

Second paroxysm —

March 2d. Previous night had slight malaise. Examination of the blood in the morning shows the *reappearance* of the spirochetes. 12 M., rise of temperature: 5 P. M., severe headache. 6 P. M., refuses to drink milk. No albumen. Erlich-reaction negative.

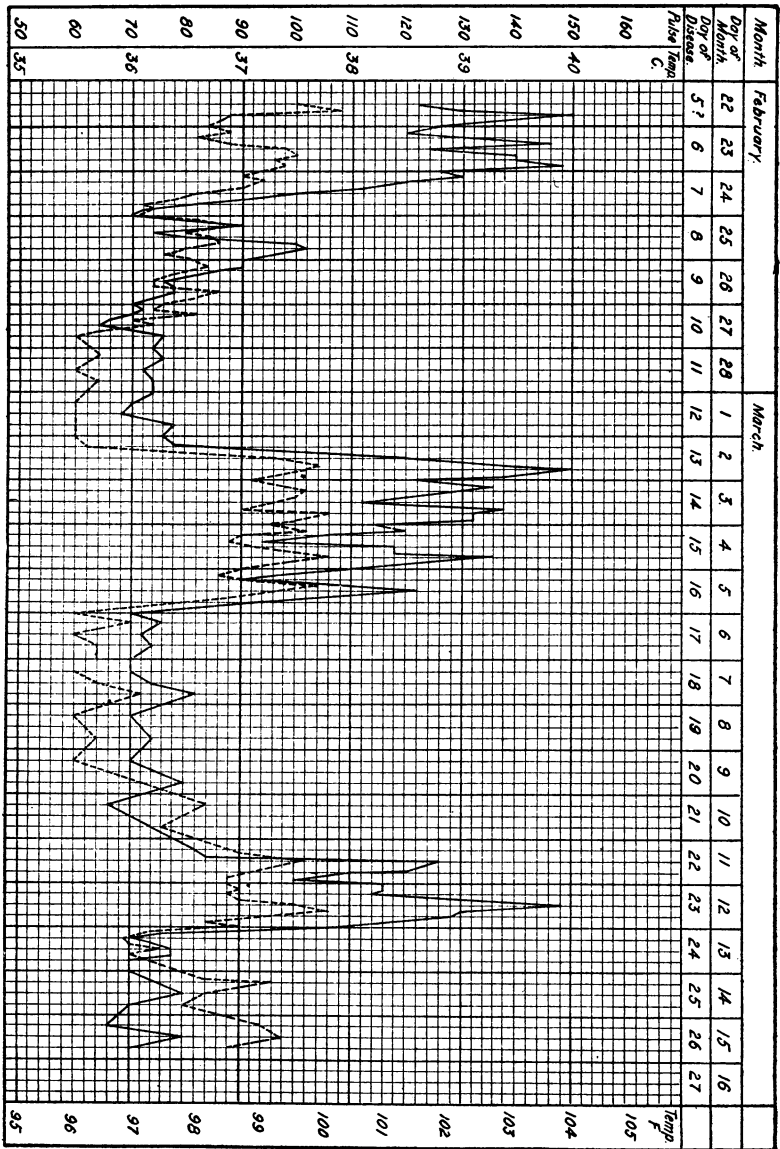
March 3d. Vomited large quantity of greenish fluid at 6 and at 8:30 P. M.

March 4th. He refuses to take milk during the night. At 8 A. M., has a bad headache and besides, pains in both limbs from the knees down and in the right shoulder. Feels bad, worse than ever, and has great tendency to vomit, and therefore refuses the nourishment. Marked icterus in the sclerotic coat. The examination of the blood still shows *Obermeier's spirochetes*. 10 P. M., vomited a large quantity of white fluid. 10:30 P. M., perspires freely.

March 5th. Interesting point; the temperature reaches the normal at 6 A. M., but again rises immediately, recording at 9 A. M., severe chill. 12 M., an examination of the blood does not show the spirochetes (temperature being 38.6° C.) 9 P. M., profuse perspiration. Apyrexia.

March 6th, 7th, 8th, 9th and 10th (5 days). Feels well and without fever.

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Third paroxysm—

- March 11. Sleeps well. 8. A. M., slight headache and chill. The pulse begins to rise, although the temperature is 36.7° C. Painful sensation in the splenic region. The examination of the blood shows again the spirochetes.
- March 12th. Chills. Feels very bad. 3 P. M., vomited greenish fluid.
- March 13th. Since midnight the fever descends, and at 3 A. M. there is no fever. The spirochetes disappear from the blood, and the patient is free from his troublesome symptoms.

From that date on, the febrile paroxysms cease and the patient convalesces rapidly.

Studying and grouping the most prominent symptoms of this clinical history, we can make the following summary which shows, after comparing one paroxysm with another, that there exists an interesting symptomatic uniformity, except in regard to the duration of each individual paroxysm, because each succeeding one was shorter than the previous one.

The length of the sickness, from the first paroxysm (February 17th) to the last fall of the temperature (March 12th) was twenty-three days

The length of each individual paroxysm, was as follows:

| | |
|--------------------|----------|
| 1st paroxysm | 6½ days. |
| 2d paroxysm | 4 days. |
| 3d paroxysm | 2 days. |

The length of each afebrile period, was as follows:

| | |
|--------------------------------------|---------|
| from the 1st to the 2d paroxysm..... | 5 days. |
| from the 2d to the 3d paroxysm..... | 5 days. |

The headache and slight chills, always preceded the elevation in the temperature of each paroxysm.

The appearance in the blood of the spirochetes also preceded by a few hours, the elevation of the temperature.

Vomiting never appeared in the first day of the fever, but always on the second, coinciding with the pains and the general malaise.

The disappearance of the spirochetes in all three paroxysms occurred always before the complete defervescence.

The defervescence was always accompanied in each paroxysm by a prolonged and profuse perspiration.

The general condition of the patient during the febrile periods was relatively excellent.

PARASITOLOGICAL STUDY.

The parasite observed by us in this case was unquestionably the *Spirochete Obermeieri*.

We studied it only in *stained* preparations. Its appearance was thread-like, serpentine, rather wavy more than spirally.

The dimensions were very variable, depending on the larger or smaller inflection of the spirals or undulations; these apparent diversities in the forms of the organism, from the spiral form, to the undulating and the slightly straight ones, are perhaps due to the technic employed in preparing the smear of blood, or to the method of fixation.

Generally we notice two sizes of spirochetes, one rather small, the other a large one. The length of the longer was usually twice the size of the small one, and some times in exceptional instances was thrice as long.

The small spirochetes averages..... 7.5 μ

The large spirochetes averages..... 16.5 μ

We have failed to find the maximum sizes described by Kolle and Heltsch,¹ who claim for the spirochets 10, 20 and 30 μ in length.

Most of the larger specimens have in the middle of each a sort of thinning process which refuses to stain, and so simulate two small organisms joined together end to end. (This corresponds probably to some advanced stage of transverse division.)

Again, in other long varieties we have been able to observe a true cut across the thickest portion of the spirochetes; this cut is sharply defined because the two opposing surfaces of the two fragments of the divided spirochetes are plainly seen. (This probably corresponds to a somewhat recent stage of transverse division.)

The stains usually employed were Giemsa's and a ten per cent saturated aqueous solution of gentian violet. The latter preparation is especially useful in the smears where few spirochetes are present, because a thick smear may be obtained and decolorizing the red cells with an acetic acid solution, the spirochetes will show to advantage. Stain for five or ten minutes, warming the flooded preparation from time to time, but never to boiling. Wash and examine.

None of the staining methods revealed to us any undulating membrane, nor evidences of longitudinal division, nuclei, nor spores in the spirochetes.

¹ Kollé and Dr. H. Heltsch.

Unsuccessful attempts were made to cultivate the organism in medium made up of agar-agar and defibrinated rabbit's blood; in the preparation of the agar, Liebig's meat extract was employed. The cultures were made on the condensation fluid.

Negative results were also obtained with the common bed-bug in experiments similar to those of Tictin.² We could not coax the bugs to suck blood from the patient in spite of the fact that we chose for the experiment those that were completely free of nourishment.

Until very recently it was believed, that experimentally Obermeier's spirochetes could only be inoculated successfully to apes and men, and that all other animals were fully resistant against the disease.

It has been conclusively shown that man acquires recurrent fever by direct inoculation of blood containing the spirochetes. An investigator experimenting with monkeys infected with spirochetes from a recurrent fever case of Dr. R. J. Carlisle,³ inoculated himself accidentally. The monkey during a febrile period, during which there was an abundance of spirochetes in the blood, was bleeding from the gums, and biting the investigator really made a direct inoculation of spirochetes.

The same result is obtained in the monkey by the simple subcutaneous injection, — a classical experiment — personally known to us, because in this hospital a monkey was successfully inoculated with blood from a case of recurrent fever (Dr. Biada's case⁴) which came to Havana in 1902.

What really is an event worthy of notice, is the fact shown by Norris, Pappenheimer and Flournoy,⁵ that white mice and rats may be inoculated successfully with blood containing Obermeier's spirochetes, employing for that purpose from a few drops up to 1.5 c. c. with the addition of sodium citrate. They observed that the spirochetes multiplied themselves while in the animal's body, demonstrating their presence in the peripheral circulation during two or three days. By subsequent passages from animal to animal, they succeeded in having the spirochetes alive for months.

Inoculated men and monkeys suffer evident disturbances in their general state of health, they apparently become ill and may even die, but inoculated mice and rats do not seem to suffer in the least. Does the above facts prove that the spirochetes of Obermeier are only

² J. Tictin. — *Centralblatt für Bakt.* 1897, 21.

³ R. J. Carlisle, *Journ. of Inf. Diseases*, Chicago, 1906.

⁴ Dr. Biada M., *Un case de fièvre seurecute*, *Revista de Medicina y Cirujia de la Habana*, 1902.

⁵ Norris Pappenheimer and Flournoy, *Journ. of Inf. Diseases*, Chicago, 1906.

pathogenic for men and monkeys, and that in white mice's blood they only find an appropriate medium in which to thrive and multiply temporarily? — No. — This erroneous conclusion can be upset by an irrefutable proof, to wit: that the spirochetes cause intimate biochemical modifications in the white mouse, for the latter acquires an immunity equally as great as man and monkey, against a new attack of the disease.

How long the immunity lasts has not been definitely settled as yet.

UNITY OR DUALITY OF HUMAN RECURRENT FEVER.

In East Africa there is a disease which has great clinical and parasitic similarity to the European recurrent fever.

That is today one of the most important questions for investigation, — whether we are dealing with one, or two diseases.

African recurrens or tick fever has for its pathogenic organism, a spirochete.

Koch,⁶ who has had the opportunity to study numberless cases of *African recurrens*, in the German Protectorate of East Africa, gives the following two important clinical differences:

1st. Short duration (two days at the utmost) of each febrile paroxysm; total number of paroxysms, four.

2nd. Scanty number of spirochetes in the blood of patients, even during the period of highest elevation of temperature.

In spite of these differences, Koch thinks that as the complications and sequelae in both fevers (European and African) are so similar, it is not worth while to consider *African recurrens* a new disease, but he grants that it may be thought of as an *African variety of recurrent fever*.

Dutton and Todd, investigators of human tick fever in the eastern part of the Congo Free State are equally inclined.

Searching for further proofs in order to know if they are one or two diseases, the comparative study of the spirochetes has been resorted to, testing the virulence and infectiousness of each in various animals.

Breinl and Kinghorn⁷ succeeded in infecting intraperitoneally, with blood containing *tick fever's* spirochetes, a monkey, a horse, a dog, rabbits, guinea-pigs, rats and mice. The disease produced in each of those animals was of a grave nature, and the rabbits, rats, mice and some of the guinea-pigs succumbed to the infection.

⁶ Robert Koch, Berliner klinische Wochenschrift, 1906, No. 7.

⁷ The Lancet, March 10, 1906.

It is evident that there exists a great difference for various animals, judging from the above experimental proof, between the virulence of the European and the African spirochetes. — Norris, Pappenheimer and Flournoy, besides successfully inoculating monkeys and white mice, as has been mentioned before, also inoculated rabbits and guinea-pigs. Two of the inoculated rabbits manifested slight infection; the others escape; the guinea-pigs were absolutely resistant against the infection.

Undoubtedly, therefore, the *Sp. Obermeieri* has for man and monkey, slight virulence; the guinea-pig does not acquire the disease; nevertheless for all of them the spirochetes of tick fever has an extreme virulence.

The comparative morphological examination of both spirochetes according to Novy and Knapp,⁸ proves that there are two distinct organisms, evidently shown by structural details, position, undulations, and chiefly by the length, being greater in the *Sp.* of tick fever than in the European.

In short, there are two recurrent fevers, the African and the European and Indian fever, which, though having very slight clinical differences between them, yet are distinct. For each of them there is a separate spirochete: the European, due to *Sp. Obermeieri*, and the African, due to *Sp. Duttoni*, as has been proposed to call it, with all justice by Novy and Knapp in memoriam of the lamented Dutton, who died victim of that disease, in the Upper Congo (Africa), February 27, 1905.

Which is the propagating agent of recurrent fevers? — Unquestionably it must be some blood-sucking insect.

Dutton and Todd, and Koch, have shown in a most positive manner, how *African recurrens* is transmitted by means of a tick, — the *Ornithodoros moubata* (Mourray). They have proved furthermore, that infected *Ornithodoros* may transmit through the ova the infection to their offspring, and, therefore, the latter are born already infected and infectant.

Would the *Ornithodoros* be a good propagator for the *Sp. Obermeieri* Perhaps. If not, we must take for granted that there is some analogous specie of tick, or Argas or bed-bug (this insect has been experimented with poor success) as playing the role of propagating agents.

That in America must exist an insect, a host, similar to those mentioned, can not be doubted — as can be inferred from our own case and similar interesting ones already reported.

⁸ Novy and Knapp, Journal of Inf. Diseases, Chicago, May 1906.

IS THERE AN AMERICAN FOCUS OF RECURRENT FEVER?

The investigation as to the origin of the infection in our case has great importance.

It is a fact, that on the arrival of our patient at Havana, he was in the midst of the first febrile paroxysm. Hence, there can be no doubt that he acquired the disease either on board, during the voyage or else at Colon (Panama) the port of sailing.

Considering that he went on board at Colon on the 17th of February, and in the following day while on board the "Miramar" he had the first symptoms, we must set aside the possibility of an acquired infection in so few hours while on the vessel.

On the other hand, he had been at Colon (Panama) during three consecutive weeks, and therefore the inference may justly be drawn that it was there that he got the disease.

With a positive diagnosis and with the above conviction, the Cuban sanitary authorities deemed proper to notify the health officers at Panama that the case of recurrent fever, which had come to our port, had originated at Colon.

Indeed, Colonel Gorgas, chief sanitary officer of the Isthmian Canal Commission, in a letter replying to the despatch of the chief sanitary officer of Cuba, says, that during the summer of 1905, there had been two cases of recurrent fever at Colon.

It had also been brought out by data, obtained by Dr. Carlisle, that besides the two cases at Colon, there had been several others at Tuxpam (a sea port between Veracruz and Tampico) during April, 1905, and "that death occurred from this disease during every month throughout the year."

Besides, the same author has observed, in New York, a case of recurrent fever, which could only have had, as possible origin of the infection, New York, Galveston, or Key West.

Published reports show that the cases of recurrent fever which have presented themselves in the countries represented in the American Public Health Association, have been relatively numerous. It follows, therefore, that those cases must have originated from one or more American foci, probably situated in Central America.

We would like to especially call the attention of this Association to this matter, believing that in some locality of easy communication there may be a large number of cases of recurrent fever, which pass unnoticed, probably, with the diagnosis of malaria, because unfortunately the blood examination of every febrile individual is not made systematically and compulsory in order to make a rapid diagnosis; a

doubt is left, therefore, as to the nature of the disease, leading to mistakes in therapeutics, and causing serious risks to the public and international hygiene.

The recent reported cases in America, including our own, are undoubtedly cases of recurrent fevers due to *Spirochete Obermeieri*.

We believe that the first cases which originated the possible focus or foci in America came from Europe. In 1902, Dr. Biada observed in Havana another case of recurrent fever traceable to Liverpool, which place he considered as the infected origin.

In Central America the infection, by way of the Pacific, that is, through the Western coast, is possible, although difficult, but in this instance the introduction of *African recurrens* would be more feasible.

Everything connected with recurrent fever makes it a dreaded disease if it becomes endemic for the following reasons:

1st. Because it is easily carried to great distances, owing to the nature of the disease itself, which lasts at least twenty days; the first paroxysm being as infectant as the last.

2d. Because of the resistance of the parasite itself. — Karlinsky has found alive spirochetes in bed-bugs *thirty* days after the latter had sucked infected blood.

3d. Because of the great vitality of the propagating agent (bed-bugs or ticks.)

CONCLUSIONS.

We can make the following conclusions:

1st. Recommend to the Association that at the next meeting, "Recurrent fever" shall be one of the topics of special interest for discussion.

2d. That the attention of those who are in proper condition to investigate as to infected localities which may exist in Central America, be enlisted in this work.

3d. To emphasize the importance of investigations in regard to the identity or duality of European and African recurrent fevers.

4th. To investigate the possible propagating insect, which serves as host for the *Spirochete Obermeieri* in America.