

ON RELAPSING FEVER

A Thesis

submitted for the

M.D. Degree

by

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RELAPSING FEVER.

INTRODUCTION.

Relapsing Fever may be defined as an acute specific infection characterised by a period of pyrexia lasting four or five days, following which the temperature falls by crisis to normal where it remains for seven days, only to be succeeded by a further period of Pyrexia similar in character to the first. In some cases one or more further relapses take place. The condition has been referred to in Medical Literature under various names such as Chronic Fever, Recurrent Fever, Seven Day Fever and Tick Fever.

These synonyms are of course self explanatory, Chronic, Recurrent, and Seven Day Fever referring to the type of Pyrexia. Famine Fever to its close association with conditions of privation, and Tick Fever to one of the means of the transmission of the Fever. It is probably also identical with Carpata disease in the Zambesi described by Livingstone, and also with Miana Disease in Persia. The etiology of this disease may now be considered to be on a sound basis.

As a result of modern work, the causal organism and the different modes of transmission have been brought to light, and further as the result of the discovery of the Arylarsonates we have at our disposal a definite specific for the treatment of this disease.

The importance of such discoveries both from the prophylactic and curative point of view is obvious.

During the time I was in Military Service in charge of the Infectious Diseases Hospital in Salonika I had the opportunity of observing and treating a number of cases of this condition. Most of the cases which came under my care were natives of Macedonia belonging to the Macedonian Labour Corps attached to the British Army. These men were engaged in building and repairing the military road from Salonika to The British Front Line near the town of Seres.

While Relapsing Fever has been stamped out in Great Britain and Western Europe generally, it is still endemic in semi-tropical and tropical countries and particularly so along the Mediterranean Littoral and in the Balkans. When one considers the widespread geographical distribution, and the large incidence of the disease amongst native populations it must prove to be a factor of great economic importance.

In this respect Relapsing Fever is probably second only to Malaria.

In this Thesis I propose to give a resumé of our present knowledge of the disease, and to incorporate in it the result of my own experience in the observation and treatment of seventy-seven cases.

PART II.

HISTORICAL.

Relapsing Fever was known to Hippocrates and he describes an epidemic in the island of Thasos.

There is no mention of the disease from that time until the year 1770, when there was an outbreak in Dublin. This epidemic was described by Ritty in "The Chronological History of the Prevailing Diseases in Dublin". He writes "It terminates sometimes in four , for the most part in five or six days, sometimes in nine and commonly in a critical sweat: the crisis however was very imperfect for they were subject to relapse, even sometimes to a third time."

There were further epidemics in Ireland in 1800, 1817-1819 and 1826-1827 and again in 1847-48 and 1868-1873. In Scotland in the County of Fife, there was an outbreak in 1841 and in the next two years it spread to the large towns including Edinburgh, Glasgow, Aberdeen and Dundee.

It is interesting to note that it was from this epidemic that we got our first reliable account of the disease. There were further outbreaks in Glasgow and Edinburgh as late as 1869.

The first account of the disease in England was of an outbreak in London and North Shields in 1868, but it appears to have been confined to the lower quarter of the towns occupied for the most part by Irish and Jews.

In the same year it appears to have become general throughout the large towns, involving Liverpool, Leeds, Manchester and Newcastle-on-Tyne. This epidemic persisted in London and Newcastle-on-Tyne until 1873.

While it is probable that Relapsing Fever was prevalent on the Continent of Europe, we first hear of it when it attacked The Grand Army in the retreat from Moscow. It also occurred in the Allied Armies in the Crimea.

There was a large and widespread epidemic in 1863 starting at Odessa and involving St. Petersburg, Novgorod and Moscow, and spreading in the following year to Finland, Siberia and Poland. This disease was also recognised and reported on in Germany where it became widespread in 1868, showing itself simultaneously in Pomerania, Upper Silesia, East and West Prussia and in Posen, Breslau, and Stettin, and was imported into Berlin and Magdeburg.

The last outbreak of the Disease in Germany was in 1879.

There was a series of small outbreaks in Austria from 1847-1877 but it did not appear to assume epidemic proportions until 1877-78.

It is interesting to note that the disease was quite unknown in France, Switzerland, Italy and the Iberian Peninsula.

As early as 1820-1830 Naval Surgeons described a disease along the Mediterranean Littoral and in Malta and The Aegean Archipelago, which they recognised as similar to Irish "Typhus."

This/

This disease, undoubtedly Relapsing Fever, was later referred to as Cyprus Fever, Levant Fever and Smyrna Fever.

The first mention of the disease in India was an account of an epidemic in Patna by Sutherland in the Indian Annals of Medical Science (1859). From there it spread over a large part of Lower Bengal. There was also an outbreak in the same year in the North-west Provinces and over the territories of Behar and Benares where it assumed epidemic forms in prisons.

There were further outbreaks in 1863-1866 in the Punjab spreading to the Europeans.

There was a further outbreak in India in 1868. On this occasion it was attributed to mule drivers returning home from Abyssinia and landing at Bombay.

In 1879 Carter described an outbreak of this disease in India and it was during this outbreak that it was first demonstrated that the disease was transferable to monkeys.

There are accounts of epidemics also in New York and Philadelphia in 1844, 1847 and 1869, the disease being introduced into America by immigrants from Liverpool.

Apart from the accounts of the disease brought home by naval surgeons in 1830 from the Mediterranean Coast, there have been outbreaks in Egypt, Algeria and the Soudan.

Corapata disease described by Dr. Livingstone as endemic in the Zambesi Valley is now recognised as "Tick" Fever and more/

more recently the disease has been recognised in Uganda, the Congo Free State and in East Africa.

From the above Historical and Geographical Data it is clear that during the eighteenth and nineteenth centuries Relapsing Fever was endemic throughout a large part of the world and that every few years it assumed epidemic proportions. It is interesting to note that this disease has largely been eradicated in countries which have adopted general public health measures and that in Great Britain its decline closely coincided with the passing of the first Public Health Act (1875).

PART III.

MOLOGY AND PATHOGENESIS.

At a comparatively early date, viz. 1873, a highly characteristic organism was discovered by Obermeier in the blood of patients suffering from Relapsing Fever.

This organism is generally known as the Spirochaete Obermeieri, or the spirillum of Relapsing Fever.

He also observed that this organism was present in the blood during the fever, that it disappeared during the afebrile period of the disease, and that it reappeared during a relapse.

Since that time these observations have been fully confirmed, as have also his views as to its causal relationship to the disease.

The organism, as seen in the blood during the fever, is a delicate spiral filament of from seven to nine " μ " in length and 0.25 u. in breadth. The body of the organism is composed of three, four, or six turns, the number varying according to the length of the organism, and the extremities are pointed. They are actively motile, due to a long terminal flagellum (5-7 μ) and can be seen moving across the field of the microscope with a peculiar corkscrew movement, pushing aside the corpuscles by their passage. Abnormally long forms occur and are due to the end-to-end union of two or more parasites.

The/

The organisms are stained readily by the Romanowsky's Stains and the flagellum may be stained by Loeffler's whip-stain.

They take up the stain evenly with the exception of the extremities where the tint is rather lighter.

They lose the stain by Gram's method.

There has been considerable difference of opinion amongst authorities as to whether the organism is a bacterium or a protozoon.

While the matter has not definitely been settled, the bulk of the evidence seems to favour the latter view.

Normally the spirochaetes live in the liquor sanguinis but they are occasionally seen coiled up in the red blood corpuscles. Balfour, experimenting on spirillosis in chicks, noticed that during the crisis, whether artificially produced by a dose of Karsivan or occurring naturally in the disease, the spirochaetes underwent a remarkable change. He observed, working with a dark ground illumination, that the spirochaetes developed a large number of "Refractive Granules," under their periplastic sheaths. The spirochaete then, by a series of shaking movements, which he compares to a dog shaking itself, succeeds in ex-
~~tending~~^{ruding} them. The body of the spirochaete shrivels up until nothing is left but the periplastic sheath. He further states that/

that the "Refractive Granules" enter the red blood corpuscles and there complete a cycle of schizogony.

Should such a phenomenon occur in the human subject it would furnish an explanation of the disappearance of the spirochaetes as such from the blood stream at the crisis, and their reappearance at the time of the relapse. Since the original discovery of the spirochaete by Obermeier this disease has been studied in various parts of the world and several different varieties of spirochaetes have been discovered.

Thus, Dutton and Todd, while studying Tick Fever in Africa, discovered that this disease was due to a spirochaete to which they gave the name of Sp. Duttoni. Relapsing Fever in America, is attributed to a spirochaete also named after its discoverer - Novyi.

Carter working in India demonstrated a further variety which is now known as Sp. Carteri.

That type of the disease which occurs in Egypt and North Africa is caused by the Sp. Berbera, while the European type of disease is attributed to the original Sp. Recumbentis of Obermeier.

These various strains of spirochaetes, while undoubtedly closely allied to the original organism, described by Obermeier, present definite differences. They show differences in/

in morphological character, serological reactions, and also in the type of fever which they evoke in man. (See table below).

It is not justifiable, however, to conclude on those grounds that they are specifically distinct. It has been proved that in some strains the usual transmitters are interchangeable.

It is possible that the passage of hundreds of generations of the parasite through a certain transmitter may have modified its morphological character and its pathogenic qualities.

PALESTINE

INDIA

AMERICA

AFRICA

EUROPE

ALGIERS

EGYPT

S. BERBERA ? S. BERBERA S. RECURRENT S. DUTTONI S. NOVYI S. CARTERI

MINIMAL

13.5 u. 12 u. 12 u. 13 u. 7 - 9 u. 12 u.

SHAPE Irregular open flex-ures. Irregular open flex-ures. Spiral ures. Open flex-ures. Regular Spiral ures. Tend to enter figure of eight and circular forms.

FLAGELLA ? ? Peritrichous Peritri-chous. Terminal ? - -

ANIMALS SUSCEPTIBLE Gerbils Monkey (Cercopithecus) Rats and mice with difficulty Monkey (Macacus) Small ro-dents only after passage thro' Monkey. Small ro-dents and many animals susceptible. Small ro-dents very susceptible. Small ro-dents with difficulty

COURSE IN MAN. Fairly severe. attack 2-8 days. Relapses 2 or 3. Fairly severe. 1st attack 2-8 days. Relapses 2 or 3. Incubation 5-7 days. Relapses 2 or 3. Severe. Duration 5-7 days. Incubation 5-6. Apyrexia 7-10. Relapses 2 or 3. Mild. Incubation 5-7. Duration 5-6. Apyrexia 7-10. Relapses 1 or 2. Severe. Incubation 5-7. Duration 5-7. Apyrexia 5-7. Relapses 5-13. Relapses 1 or 2. Severe. Duration 1-2 Apyrexia 5-14 very irregular. Relapses 4 or 5.

PARASITES IN BLOOD. Variable Variable. Heavy infection. - - - Scanty.

(Continued on next page)

	EGYPT S. BERBERA ?	ALGIERS S. BERBERA	EUROPE S. RECURRENT	AFRICA S. DUTTONI	AMERICA S. NOVYI	INDIA S. CARTERI	PALESTINE
NATURAL TRANS- MITTERS	Lice.	Lice, Tick Argas Per- sicus.	Lice. Bed bug, Acan- this Lectu- laria.	Ticks. Ornithodo- rus Momba- ta.	Live (?) Ticks (Or- nithodo- nithod.	Lice. Bug? Civex RO- tundatus.	Ticks. (Argas Persicus)
SERUM RE- ACTIONS	?	Immune ser- um possibly without ef- fect on Sp. Recurrent.	Immune ser- um without effect on S. Novyi or S. Duttoni.	Immune ser- um without effect on S. Novyi or S. Re- current.	Im. serum without effect on S. Recurrent S. Duttoni S. Carteri	Im. serum without effect on S. Novyi.	?

The above table is taken from Manson's "Tropical Medicine," except column "8" which is compiled from an article in The Lancet, October 16th, 1920, by W. K. Caldwell.

TRANSMISSION.

It has been proved repeatedly that the disease may be transmitted from one human being to another by the direct inoculation of blood containing spirochaetes. In 1897 Tietin propounded the theory that the disease was conveyed by the bite of the bed bug.

He allowed bed bugs to feed on monkeys suffering from the disease and produced the disease in other monkeys by inoculating them with blood from the stomach of the bed bug.

This experiment has not been confirmed and other observers have obtained negative or only partially successful results.

In 1904 Philip Ross and Milne while working on Tick Fever in Uganda proved that the disease was conveyed by a tick viz. *Ornithodoros Moubata*. This was confirmed by Dutton and Todd in the Congo and they went further, in that they proved that not only was the adult tick, capable of conveying the disease, but that it laid eggs containing the spirochaete, and succeeded in demonstrating the presence of the spirochaete in the various stages of the development of the tick.

It is thus proved that an infected tick transmits the parasite to succeeding generations - a point of great practical importance.

The/

The spirochaete is not conveyed to the human host by the biting parts of the tick but is deposited upon the skin with the faeces.

The bite causes irritation and the scratching caused thereby produces an abrasion of the skin through which the victim is inoculated.

The form of Relapsing Fever which occurred in America due to the Spirochaete Novyi is supposed to be conveyed by another variety of tick, viz. Ornithodoros Talaji and in the type of the disease which occurs in Persia and Algiers the Argus Persicus is considered to be the means of transmission.

In an epidemic of Relapsing Fever which broke out amongst the British Troops in Palestine, Caldwell considered that the disease was conveyed by the Argus Persicus and this view was later confirmed by Nicholson in an article on Tick Fever in Palestine (B.M.J. Dec. 20th, 1919).

The Relapsing Fever which occurs in Europe, India and Egypt is not considered to be conveyed by ticks but by the body louse and also to a lesser extent by the clothes louse.

This view was first brought forward by Mackie in 1907 and was confirmed by Nicolle who also demonstrated that the offspring of infected lice was also infected. As in the case of ticks the infection is not transmitted by the biting parts of the insect but by the faeces.

It/

It is pointed out that both in the case of lice and tick, that they act merely as mechanical transmitters and that there is no biological connection between the parasite and its intermediate host as there is between the malarial parasite and the mosquito. It therefore follows that, while doubtless the disease is largely conveyed by lice and ticks, any biting insect should be capable of acting as transmitter. In the cases of Relapsing Fever which came under my observation in the Balkans I formed the conclusion that the disease was conveyed by means of lice. As I pointed out, the majority of the cases occurred amongst the members of Mediterranean Labour Corps. These men lived in Camps and in spite of periodical inspection were frequently found to be infested with lice. In no case were "ticks" found ⁱⁿ on them or their tents. The outbreak of the disease never reached epidemic proportions but was rather of the nature of a series of isolated cases (the seventy-seven cases being spread over a period of a year).

It was found that in most instances the infection could be attributed to visits to their homes or other native houses in the villages near their camps.

The opportunity of examining lice did not arise as the patients and their belongings were always effectually "de-loused" before they arrived at the hospital.

I had the opportunity on several occasions of examining bed/

bed bugs found on the patients, but always with negative results. Relapsing Fever has since the earliest times been associated with Overcrowding, Filth, Famine, War, etc. In view of what has now been proved regarding the Etiology of this disease, it is obvious that these factors can only play at most an indirect effect in the propagation of the disease, in that, they produce conditions suitable for the growth and multiplication of the transmitting agencies.

The reasons for the prevalence and endemicity of this disease in the Balkans are not far to seek. Anything more insanitary than the native villages would be difficult to imagine. The houses of the peasants are largely built of dried mud and contain numerous crevices suitable for the development of insects of all kinds. No method of sewage disposal exists and domestic refuse is merely shot into the village street.

Of even more importance are the personal habits of the native population. They are dirty to a degree and wear most bulky and voluminous garments which they are never known to remove either night or day. This latter characteristic doubtless being due to the predatory instincts of their neighbours.

It is a striking point that while the British Army, numbering some 200,000 men and living under precisely similar conditions/

conditions with regard to climate, food and accommodation, produced only eleven cases of this disease, while the Macedonian Labour Corps produced sixty-six out of a total of two or three thousand at most.

It has long been observed that conditions which produce Relapsing Fever and Typhus Fever are very similar and that epidemics of the two diseases frequently occur at the same time. Indeed in the earlier Medical literature there appears to have been considerable confusion between the conditions.

It is suggested that the two diseases may prove to have a common transmitting agency though of course nothing can be proved in this connection until the causal organism of typhus fever is discovered.

PART IV.

SYMPTOMATOLOGY AND DIAGNOSIS.

European Type.

Incubation Period is from five to ten days, seven days being commonest. It is occasionally as long as a fortnight.

In cases where the disease is produced artificially the incubation period is from two to six days.

The onset of the disease is sudden, with marked frontal headache, vertigo and pains in the back and limbs. Vomiting occurs occasionally but is not a prominent feature. Pain in the back of the neck about the level of the seventh cervical vertebra and radiating downwards and across the shoulders is a prominent feature in the earlier symptoms of the disease and occurs in practically all cases. The tongue is dirty and covered with whitish or light brown fur. However, it remains moist except in very severe cases.

Shivering and a feeling of chilliness is the rule but in the cases which came under my observation a definite rigor was uncommon.

The temperature rises rapidly and reaches 103° F. or 104° F. within twelve hours. It is occasionally higher and I have seen one case where it rose to 106° F.

The/

The pulse and respiration rates are also raised in accordance with the temperature.

A tinge of icterus is common and in some cases it is very marked (See case M. R. quoted in detail below.)

The bowels are as a rule constipated during the febrile period but in some cases the disease is ushered in by symptoms clinically indistinguishable from dysentery. There is usually a little tenderness over the gall bladder and in severe cases the liver may be felt to be enlarged. The spleen is also definitely enlarged and tender, but as most cases of Relapsing Fever now occur in malarious districts this sign is not one of any great diagnostic value.

The urine is scanty and rather high coloured with a specific gravity of about 1025. A trace of albumen is present and on centrifuging, the deposit contains hyaline, granular, and epithelial casts, a few leucocytes and red blood corpuscles. Spirochaetes can also be demonstrated in the urinary deposit.

Two of my series of cases developed definite nephritis, with, in both cases, a fatal result. The lungs are as a rule not implicated but occasionally a few scattered rales and rhonchi are to be heard at the bases.

During the febrile period of the disease, spirochaetes are readily demonstrable in films taken from the peripheral blood, frequently as many as five or six being seen in one field
of/

of the microscope under $\frac{1}{12}$ oil immersion lens.

A slight leucocytosis of from 13,000-15,000 occurs, the different types of leucocytes maintaining their normal numerical proportions. This being in contra-distinction to the African Tick Fever where a differential count shows a lymphocytosis. Evanescent rashes of the "rose spot" or reddish mottling type occur and some authors have even noted a petechial form.

In none of my cases did any rash occur. In untreated cases the temperature remains elevated with slight morning remissions, for four or five days.

It then falls by crisis to subnormal in the course of twelve hours. During the crisis the patient sweats profusely and there is usually slight diarrhoea. In old or otherwise debilitated subjects the sudden fall in the temperature is often accompanied by an alarming collapse.

In the majority of cases with the fall of the temperature the improvement in the general condition is remarkable. The patient looks, and feels, quite well, the appetite returns, and it is with difficulty he is persuaded to remain in bed.

The relapse takes place on the seventh or eighth day after the completion of the first attack.

It is similar to the first attack but is generally shorter in duration and less severe in character.

Second/

Second relapses occasionally occur but are not common in the European Type of disease.

Complications.

Neuritis occurred in twenty cases out of a total of seventy-seven cases.

This condition manifested itself four or five days after the fever had subsided. In every case it was confined to the legs being usually more marked in one leg than in the other. There was definite and severe pain along the course of the anterior tibial nerve and extending on to the dorsum of the foot. The nerve was definitely and acutely tender on deep palpation. In many cases the condition was so severe that the patient was quite unable to walk. The neuritis was not associated with much wasting of the limb, at least not more than could be attributed to disease.

The condition gradually improved and was usually quite gone in three weeks though in one case it persisted as long as five.

In an account of an epidemic of Relapsing Fever in Egypt, three cases of post-pirochaetal neuritis with paralysis are recorded. In these cases the upper limbs only were affected.

In two of the cases, there was paralysis of the rhomboids and the scapulae magnus, with the production of winged scapulae/

scapulae, while in the third the deltoid was paralysed with accompanying inability to abduct the arm.

These conditions are attributable to a toxic neuritis of the fifth, six and seventh cervical nerves.

In these cases the paralysis was of a permanent nature.

In describing the symptomatology of my own cases I drew attention to what was a very constant early symptom, viz. pain about the level of the 7th cervical vertebra. When one considers the origin of the 5th, 6th and 7th cervical nerves this pain has a very definite significance suggesting that in practically every case these nerves are the seat of a toxic neuritis and that in severe cases it is liable to cause definite paralysis.

In an account of 56 cases occurring in Palestine two cases of facial paralysis are recorded.

Nephritis. Two cases of this complication occurred with a fatal result in both cases.

Case I. Patient was admitted to hospital with report that he had been ill for five days and that spirochaetes had been found in his blood. 0.3 gms. of galyl having been administered on the day prior to his admission. General condition on admission was very poor. Temperature 102° - pulse 100 and feeble. There was marked anasarca, patient "pitting" on pressure all over the body. There was a large quantity of free fluid in the/

the abdomen.

Heart sounds normal but rather muffled.

There was no dilation or hypertrophy.

Spleen enormously enlarged (due to chronic malaria).

Urine 1025. Reaction acid. Boiled solid. Deposit contained hyaline, waxy, granular and blood casts.

Patient died thirty-six hours after admission, treatment having no effect on his condition.

Post-mortem. There was general oedema, and free fluid in the abdomen, pleurae, and pericardium. Spleen enormously enlarged (5 lbs.) and hard in consistence due to chronic malaria.

Kidneys showed old standing renal disease. They were considerably enlarged and the capsule slightly thickened and adherent.

Heart was normal and did not show any compensatory hypertrophy.

Case II. Lab. D.B. aet.48.

Patient had been ill four days prior to admission.

Spirochaetes ++.

•3 gms galyl given before admission to hospital.

General condition on admission was very poor.

Temperature normal. Pulse 76 and very feeble.

Tongue dry and furred. There was slight jaundice with tenderness/

tenderness and rigidity over the gall bladder.

Spleen slightly enlarged and tender.

No urine passed.

2nd day.

No urine passed - bladder not distended.

Patient commenced to vomit.

3rd day.

Patient very restless with twitching of the limbs.

Headache severe and vomiting persistent.

XX $\frac{7}{8}$ urine passed. High coloured. Reaction - acid.

S.G. 1028 - loaded with albumen. Blood present.

Casts epithelial - granular - fatty and blood.

Patient became comatose and died on the third day.

In this case there was no oedema at any time during his illness.

No P.M. was made.

The only other complication met with was one case where the disease closely simulated dysentery. As this type of case is apparently uncommon, I quote in some detail.

M. R. aet. 35. R.F.C. Temperature and pulse normal.

Patient was admitted with diagnosis of dysentery. He had severe abdominal colic and frequent passage of stools containing blood and mucus. Straining was not a marked feature. There was marked jaundice and the liver was tender and enlarged/

Enlarged to two inches below the costal margin. There was marked rigidity of the right belly of the rectus muscle over the region of the gall bladder.

Spleen was slightly enlarged and tender.

Stools were examined for Flexner and Shigar bacilli and Amoebae with negative results.

He remained in this condition for five days in spite of the usual anti-dysenteric treatment. On the fifth day the temperature rose sharply to 103.5° F. and the case was considered to have probably developed malaria. A blood film was examined and showed no malarial parasites but spirochaetes.

.2gms. of Karsivan was given intravenously with immediate improvement in all his symptoms.

The temperature became normal within twelve hours and diarrhoea ceased.

The jaundice, liver enlargement, and abdominal rigidity subsided within a week and the patient made an uninterrupted recovery.

In an outbreak in Egypt of Relapsing Fever there were four cases of this type recorded - with one fatal result.

The most striking feature of this type of case is that for the first five days of the disease they present a picture which is clinically indistinguishable from dysentery. If the blood in the stools is examined at this stage spirochaetes can be/

be demonstrated, but they do not appear to be present in the peripheral blood stream until the temperature rises on the fifth day of the disease.

The post mortem report of a fatal case states;

"The pathological changes that were observed were slight inflammation of the mucous membrane of the large intestine and the presence of small areas of sub-mucous haemorrhages along the tract from the rectum to the caecum and extending to some extent into the beginning of the ilium. Among the haemorrhagic areas small bits of mucous and sub-mucous tissues were seen in a gangrenous condition, but no ulcerations were to be found. The spleen was enlarged to one and a half times its normal size and was in a state of congestion."

Other complications met with are Ophthalmia (Iritis) pneumonia, Herpes Labialis, parotitis and adenitis .

Iritis appears to be much more common in the African Tick Fever than in the European type. Pregnant women usually abort.

Types of Disease.

In the type of Relapsing Fever known as African Tick Fever the symptoms closely resemble those of the European type and need not be recapitulated. Certain differences however should be noted. The initial fever is generally shorter in duration and may terminate within three days. The apyretic intervals/

intervals vary greatly in length and tend to become longer later in the disease. Several Relapses take place, usually five or six, and occasionally as many as eleven have been noted.

Diarrhoea and dysenteric symptoms are common, as are also eye symptoms.

Occasionally the fever is of a low chronic type, lasting several weeks and accompanied by severe headache and vomiting.

Spirochaetes are as a rule scanty and a careful search is necessary to demonstrate their presence.

The blood shows a lymphocytosis.

"Tick Fever" is usually much more debilitating than the European variety and a common sequel is myocarditis associated with severe tachycardia. In natives the disease runs a much milder course. The initial fever lasts only a day or two and relapses are uncommon.

This mild type of fever in natives is no doubt accounted for by the fact that they have an active immunity developed in previous attacks.

The Mortality from the disease differs greatly in different epidemics, varying between 6% to 33%. It must to a large extent depend upon whether specific treatment is adopted or otherwise.

Since the introduction of treatment by the arylarsonates the mortality averages about two per cent. In my own series of/

of cases, all of which were treated by Karsivan, there were two deaths in seventy-seven cases, representing a mortality of 2.6 per cent.

Diagnosis.

The definite diagnosis of this disease, of course, depends on the demonstration of the spirochaete in the blood. In this connection it should be remembered, as has been pointed out above, that the spirochaete only appears in the peripheral blood during the febrile period of the disease - and also that in Tick Fever they are often very scanty.

A thin blood film is prepared on a slide in the usual way and stained by means of one of the Romanowsky stains. Leishman's modification is very satisfactory and convenient for this purpose. If a blood film taken during a febrile period of the disease is examined under 1/12 oil immersion lens, as many as four or five spirochaetes may be seen in one field. The parasites take up the stain uniformly but occasionally have a slightly granular appearance. They consist of longer slender filaments presenting five or six turns and have pointed extremities. They are usually about twice the length of a blood corpuscle.

Differential Diagnosis.

As Relapsing Fever usually occurs in malarial districts it is most frequently mistaken for malaria. In the onset with headache/

headache, rigor, temperature, and tenderness of the spleen, it closely simulates malaria and at this stage of the disease can only be differentiated with certainty by a blood examination. As the disease develops the different character of the fever will be observed. In the case of malaria the quotidian intermissions are in contrast to the pyrexia of Relapsing Fever which lasts four days or five days. The failure of Relapsing Fever to respond to quinine is also a point of difference.

Cerebro-Spinal Meningitis.

Some cases of Relapsing Fever, in the early stages, on account of the pains in the neck, back and limbs and the severe headache, have been mistaken for cerebro-spinal meningitis. While there is often pain and tenderness at the back of the neck, there is no definite rigidity, and Kernig's sign is absent. Negative evidence will also be obtained on lumbar puncture.

Dysentery.

As has been pointed out above, a few cases of Relapsing Fever closely resemble dysentery, and it is difficult to say how the error is to be avoided, particularly so during the first four or five days of the disease when the patient remains afebrile. A diagnosis can only be made on demonstrating the spirochaete in the blood of the stools and noting the absence of the usual organisms of dysentery.

When/

When the temperature rises on the fifth day, a blood examination will naturally suggest itself and the diagnosis will be obvious.

Sand Fly Fever:

Closely resembles relapsing fever in its sudden onset, with headache, vertigo and general prostration. It is generally not so severe and rigors as a rule do not occur. In Sand Fly Fever the face is usually very flushed and appears swollen and the fauces and palate are often congested.

In my opinion this condition cannot definitely be distinguished without a blood examination, where in addition to the absence of spirochaetes, a leukopenia will be noticed in the case of Sand Fly Fever.

Influenza:

is distinguished from Relapsing Fever principally by its associated catarrhal symptoms and pains on pressure over the eyeballs.

On account of the erythematous rashes which occasionally occur in Relapsing Fever, it may be necessary to make a diagnosis from scarlet Fever or measles. In Relapsing Fever the rashes are very transient in character and are not accompanied by the typical tongue and throat conditions of Scarlet Fever or the coryza of Measles.

In the African (or Tick) type of the disease, where the condition/

condition manifests itself as a low chronic fever, it is apt to be mistaken for Typhoid or Paratyphoid Fever. This is particularly so when, as is frequently the case, diarrhoetic symptoms are present. The differential diagnosis will ultimately depend on a blood examination, but it must be emphasized that in this type of Relapsing Fever spirochaetes are often difficult to find.

The Widal reaction will also be of assistance.

Another point of differentiation is that rigors do not occur during the course of enteric or paratyphoid fevers.

The African type of fever with its irregular form of pyrexia associated with rigors and sweating may also simulate septicaemia.

In septicaemia there is, usually, however, some obvious cause for the condition, such as a septic wound or an ulcerative endocarditis.

It is of the greatest importance to differentiate Relapsing Fever from Typhus. As has been frequently observed, the two diseases arise under precisely similar conditions and are conveyed by the same carrier. The characteristic rash of typhus does not appear until the ^{fourth or} fifth day of the disease and it is prior to its appearance that errors arise.

Where facilities for blood examination exist the diagnosis is easy, but in the absence of such assistance reliance must be placed/

placed on the facies of the patient. In typhus the features become bloated in appearance and the conjunctiva congested, bands of injection extending from either canthus to the cornea. There is also observed slight contraction of the pupil. Another early sign of diagnostic value in typhus is that the pulse-rate becomes rapid while the temperature remains normal.

On the second or third day of the disease, there is frequently observed in typhus a general reddening of the skin and what has been termed a watercourse appearance, red channels running here and there about the skin to form erythematous patches.

While I have enumerated various symptoms which may be of assistance in making a differential diagnosis between Relapsing Fever and other conditions, in my opinion there is nothing characteristic about the early symptoms of Relapsing Fever. It has been my experience that in the great majority of cases the diagnosis was made while examining blood films for malarial parasites.

PART V.

TREATMENT.

Prophylaxis.

It follows that as this disease is almost always associated with bad hygienic conditions, the most important factor in preventing its occurrence is the maintaining of good sanitary conditions in camps, settlements, etc.

As the louse and the tick have been proved to be the principal carriers of the disease, in addition to general hygienic measures, a special campaign must be waged against these pests. In the case of lice, as a routine measure all clothing, blankets, etc., should be disinfected (preferably by submitting them to a steam disinfecter) at regular intervals. Huts and tents should be sprayed with formalin. Of equal importance is to insist on habits of personal cleanliness amongst the inhabitants. The want of personal cleanliness amongst natives is, in my opinion, the main reason why the disease is endemic in certain parts of the world and in the absence of such precautions, more general sanitary measures are liable to fail.

Ticks being very widespread throughout the animal kingdom, any attempt at their total extermination would be futile. We must therefore concentrate our attention on preventing, as far as/

as possible, a close contact with them.

They are frequently to be found in the crevices in the walls of old native huts and rest-houses. Such places of course should be avoided and if possible destroyed.

As the *ornithodoros morbata* is nocturnal in habit, special precautions should be taken to avoid being bitten during sleep.

Sleeping on the ground should be avoided and bedsteads, if used, should be high and the legs smoothed to prevent ticks climbing up.

A mosquito curtain is also of use.

It is safest to sleep in a hammock.

A night-light should be used as it has a deterrent effect on ticks.

In the presence of an actual outbreak of the disease, patients should be removed to an isolation hospital and their personal belongings disinfected, as above. On arrival in hospital, the patient should be subjected to a thorough "de-lousing." The axillary and pubic hair should be shaved and the hair of the head treated with linamentum saponis and later with a mixture of vinegar and kerosene, the latter being allowed to act for half an hour. Thorough cleansing of the body should also be undertaken and for this purpose a soap jelly, made by dissolving one part of soap chips in four parts of water to which mixture/

mixture two parts of kerosene oil is added, is recommended. One part of the jelly is added to four parts of water. When one considers that spirochaetes are present in the urine and faeces of patients suffering from the disease, it is obvious that disinfection of the excreta should be undertaken, particularly so in camp hospitals where no water carriage system of sewage disposal exists. The faeces are best dealt with by mixing them with an equal quantity of sawdust and burning them in an incinerator. Urine should be boiled, and for this purpose any small boiler may be used.

It is important that patients should not be discharged from hospital until after the date when the first relapse is due has passed. Under specific treatment the majority of cases make a very rapid recovery and in two or three days are apparently quite fit. Such cases have been returned to their respective camps only to relapse in a day or two and so prove to be a further source of infection.

Prior to discharge the blood, urine, and if possible the faeces of patients should be examined to ensure the absence of spirochaetes.

Curative Treatment.

Prior to the introduction of Salvarsan and its allied preparations there was no specific treatment for Relapsing Fever.

Owing/

Owing to the success in the treatment of Syphilis, and the morphological resemblance between the causal organisms, these preparations suggested themselves as likely remedies in the treatment of Relapsing Fever.

All the cases which came under my care were treated by intravenous injections of arsivan.

The routine treatment was to administer 0.2 gms of this drug as soon after admission as practicable. The effect of the treatment was to cut short the febrile attack. The temperature occasionally showed a slight rise soon after the administration of the drug. This slight temporary exacerbation of the temperature being due either to the wholesale destruction of the spirochaetes and consequent liberation of a large amount of toxins, or a natural reaction to the drug. Following this temporary rise, the temperature fell by crisis to subnormal in the course of twelve hours. The crisis was accompanied by profuse sweats and occasionally a little diarrhoea. It was found that by the time the temperature had reached normal all the spirochaetes had disappeared from the peripheral blood stream.

All the symptoms subsided with the fall of the temperature and the great majority of cases were convalescent within twenty-four hours.

In debilitated subjects this crisis was associated with

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a severe collapse, which however responded readily to the usual stimulative measures. The first forty-eight cases which were admitted to hospital were treated by this single-dose method. It was found that of the cases thus treated eight relapsed.

It was further observed that of the eight cases which relapsed, in only two cases was the remedy administered during the febrile period of the disease. It is suggested that this is accounted for by the fact that in the febrile period of the disease the spirochaetes being present in the peripheral blood stream are more vulnerable to the effects of the drug. It follows that where cases come under specific treatment for the first time during an afebrile period of the disease, a larger dose of Karsivan should be administered, or what, in my opinion, is better, the "two-dose" method of treatment should be adopted. In this method of treatment .2 gms. of Karsivan were administered as soon as the case came under observation, and a further .2 gms. after an interval of seven days calculated from the termination of the first attack. The object of the second dose being to anticipate the development and secure the destruction of any spirochaetes as they appear in the peripheral blood stream. There was no relapse in twenty-nine cases treated by this method.

Cases of the dysenteric type should be treated by similar/

similar methods and the results appear to be equally satisfactory, the administration of the drug being followed by the disappearance of all dysenteric symptoms. In the two cases which developed nephritis, this remedy supported by the usual anti-nephritic treatment did not have any beneficial result and both cases had a fatal termination. In cases which develop neuritis of the legs, rest in bed is essential.

This should be supplemented by massage to prevent wasting, as soon as the inflammation in the nerve has subsided sufficiently to permit it. In cases which develop definite paralysis, no treatment appears to be of any avail, and the condition becomes permanent.

SUMMARY OF CASES.

Total number of Cases 77.

Cases treated by Kharsivan 77.

				<u>1st</u> <u>Relapse.</u>	<u>2nd</u> <u>Relapse.</u>
"	"	"	" (Single-dose method)	48	8
"	"	"	" (Two-Dose method)	29	nil.

Types of Cases.

Ordinary Febrile (European)	76
Dysenteric	1

Complications./

SUMMARY AND CONCLUSIONS.

It may now be held to be definitely established that Relapsing Fever is due to one or other of the various varieties of the Spirochaeta Recurrentia, all of which are closely allied to the original organism described by Obermeier. Two definitely different types of the disease occur, viz. European Relapsing Fever and African Tick Fever, the spirochaete being transmitted in the former principally by means of the body louse and in the latter by ticks. The main difference between the two varieties of the disease is in the type of the fever evoked. In European Relapsing Fever the fever is of a regular type and duration, terminating by crisis, whereas in African Tick Fever the fever follows an irregular course, is often intermittent in type, and tends to be considerably prolonged. There is nothing very characteristic about the symptoms of this disease and a definite diagnosis can only be made by demonstrating the causal organism in blood films. This is particularly so in the earlier stages of the disease.

The principal complications met with are nephritis, neuritis, paralysis, dysenteric symptoms, and iritis, the last two being for the most part associated with the African type of disease.

The/

The prognosis is good, even in untreated cases, though it varies considerably in different epidemics. It must also to a large extent depend upon whether specific treatment is adopted or otherwise. In any campaign which might be inaugurated with a view to stamping out this disease, a more prominent place must be given to ensuring habits of personal cleanliness, than to the more general hygienic measures.

In the Arylarsonates we appear to have a specific for this disease more particularly so in the European variety of the disease.

It is of importance that the remedy should be administered during the febrile period of the disease, as if given during the afebrile period it does not appear to be so efficacious and relapses occur.

Even when given in the febrile period of the disease, an occasional relapse occurs.

The most satisfactory method of treating this condition is to adopt the "two-dose" method of treatment detailed above, the second dose being administered at such a time as would anticipate any relapse which would otherwise occur.

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DISEASE

TYPICAL CHART of EUROPEAN RELAPSING FEVER.

19

DATES OF OBSERVATIONS

