

THE EPIDEMIOLOGY OF RELAPSING FEVER IN THE ANGLO-EGYPTIAN
SUDAN, INCLUDING AN EXPERIMENTAL STUDY OF THE ABYSSINIAN
LOUSE-BORNE STRAIN.

ROBERT KIRK.

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I N T R O D U C T I O N

The observations recorded in this paper were originally undertaken with a strictly practical end in view. The grave epidemic of relapsing fever which decimated the population of Darfur in 1926-1927 was for the Sudan a calamity still well within the memory of most of the present inhabitants. When the disease reappeared in 1936, and in 1937 seemed to be springing up all over the country the possibility of another major epidemic was regarded with more than a little apprehension. It became a matter of urgency to obtain all possible information about the infection so that preventive measures might be instituted along the most efficient lines. It had to be explained why the disease was appearing simultaneously in different parts of the country: whether it had a single origin or many. At the same time it was of prime importance to make certain that the vector was as in previous years, the louse, although it was decided at the outset to regard the disease as louse-borne, pending investigations.

At a comparatively early stage of the present investigation, it was possible to incriminate the louse as the vector, and it soon became evident that the origin of the disease was from Eritrea and Abyssinia. Relatively little is known of the medical conditions existing in these regions. Although louse-borne relapsing fever has been reported from these areas during the last few years, it is only with reference to a tick-borne strain that scanty experimental records, which are in addition confusing, can be found in the literature. WENYON (1926) for instance, states that

Ornithodoros savignyi is the vector of relapsing fever in Abyssinia, while BRUMPT (1936a) points out that this tick, although easily infected in the laboratory, has never been found naturally infected in any country.

Owing to such uncertainty, the possibility had to be considered that in this Abyssinian relapsing fever one might be dealing with a strain of spirochaete differing from any of those which had already been studied. To determine whether or not this was the case a laboratory study of the virulence and other features of the strain was undertaken. For reasons which are later given fully, particular attention was paid to the possibility of transmission of the fever by ticks as well as by lice.

The possibility of tick-borne infections in the Sudan was one which had interested the writer for some time. But the complete absence of cases had restricted his activities during the previous three years to the study and collection of the ticks themselves. This was not however without advantage. When the clinical cases did occur, one already had from one's own observations, a fairly comprehensive knowledge of the distribution and habits of the ticks of the Northern Sudan. This enabled one at the outset to define, within fairly narrow limits, the possibilities of tick transmission. From the practical point of view also it gave one the advantage of knowing where to obtain ticks for experimental purposes, almost at any moment.

From the conclusions of these experiments as well as from other information which was brought to light during this investigation, it became apparent that the history of

relapsing fever in the Sudan provided an epidemiological study of unique interest, which had reference, moreover, to a very large area of the African continent. The Sudan is surrounded by countries from which it is separated physiographically, and in which relapsing fever is endemic. With the opening up of communications during the last fifty years, it has been invaded by the fever, at different times from the North, from the South, and from the West (see Fig.2). Although devastating epidemics have resulted, all the evidence suggests that the disease has never become established in endemic form in the Sudan. In how far this is due to the energetic preventive measures which have been undertaken is difficult to estimate. With the recent military upheavals in East Africa the Sudan has again been invaded by relapsing fever, this time from the East. The future is likely to see a further increase of communication across Africa from East to West, and whether or not it will be possible to prevent the disease becoming established in endemic form in the Sudan remains to be seen.

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to his colleagues in charge of hospitals in the affected areas, who readily afforded him access to the cases under their care: to the Medical Officer of Health, Khartoum, for co-operation in several instances and to Mr. N. Macdonald, of the Stack Laboratories, who carried out daily examinations of the blood of one of the experimental animals for some time after the writer had gone on leave.

TABLE OF CONTENTS

(A) INTRODUCTION

- (1) GEOGRAPHICAL AND ETHNOLOGICAL DATA.
- (2) CLIMATIC FACTORS.
- (3) THE GEZIRA.
- (4) THE POPULATION.
- (5) MOVEMENTS OF THE WESTERN PEOPLES.

(B) HISTORICAL SURVEY.

(C) RE-INFECTION OF THE SUDAN FROM ABYSSINIA.

- (1) RECRUDESCENCE OF THE DISEASE IN 1936 and 1937.
- (2) RELAPSING FEVER IN ABYSSINIA.
- (3) FACTORS LEADING TO THE INFECTION OF THE SUDAN.

(D) LABORATORY STUDIES.

- (1) MORPHOLOGY AND MOVEMENTS OF THE ABYSSINIAN RELAPSING FEVER SPIROCHAETES.
- (2) APPEARANCES IN FROZEN BLOOD.
- (3) CULTURE:-

Yuan Po's Egg Medium: Citrated Human Blood;
Diluted Human Serum: Diluted Horse Serum;
Modified Noguchi's Medium.

- (4) ANIMAL INOCULATION:-

Various Rodents: White Mice:
Gerbilles: Monkeys.

- (5) IMMUNITY:-

Evidence of Immunity: Erratic Nature
of the Immunity: Presence of
Several Antigenic Strains.

- (6) THE EFFECT OF SPLENECTOMY IN MICE AND MONKEYS.
- (7) RESIDUAL AND LATENT INFECTIONS.

APPENDIX. CASE HISTORIES OF THE MONKEYS.

(E) TRANSMISSION OF INFECTION

- (1) TRANSMISSION BY THE LOUSE:-

Spirochaetes found in lice:
No infected nits found:
Transmission to a monkey.

- (2) TRANSMISSION EXPERIMENTS WITH TICKS.
- (3) DISTRIBUTION AND HABITS OF ORNITHODORUS SAVIGNYI
IN THE SUDAN.
- (4) METHODS.
- (5) RESULTS:-

EXPERIMENTS WITH ARGAS AND PEDICINUS.
GENERAL CONCLUSIONS.

(F) OBSERVATIONS ON THE HUMAN DISEASE.

- (1) EPIDEMIOLOGY.
Incidence:- Sex: Age: Race: Season.
- (2) RELATION TO MALARIA, TYPHUS AND PLAGUE.
- (3) CLINICAL FEATURES AND COURSE OF THE DISEASE.
- (4) PATHOLOGY.
- (5) PREVENTION.

(G) SUMMARY.

(H) BIBLIOGRAPHY.

(K) ILLUSTRATIONS.

(A) INTRODUCTION

GEOGRAPHICAL AND ETHNOLOGICAL DATA

The Anglo-Egyptian Sudan lies between 23° and 3° North latitudes. It is of vast extent, and infinite in variety, so that a brief reference to certain of its more salient features is necessary in order to orientate some of the observations which follow.

The Sudan is bounded on the North by Egypt, on the East by the Red Sea, Eritrea, and Abyssinia, on the South by Kenya, Uganda, and the Belgian Congo, and on the West by French Equatorial Africa. Physiographically five main provinces can be recognised:-

- (1) The desert in the North, extending from the Egyptian border nearly as far South as Khartoum.
- (2) The Red Sea Hills, which extend between the Egyptian and Eritrean borders and mark the Eastern flank of the Great Rift Valley in this part of Africa.
- (3) The red sand regions lie South of Khartoum, and extend Westwards through Kordofan, Darfur, and beyond. The vegetation of this region is enough to fix the soil, and comprises short grass and trees, including the gum Arabic acacia. There is good grazing, and excellent crops are raised over large areas.
- (4) South of the sand belt, the plains of dark soil extend from the Southern parts of the Red Sea Hills Westwards across the Southern Sudan to Southern Darfur. They extend to almost 6° North. The surface is covered with grass or savanna forest. Wide tracts are cultivated, and it affords wide areas of grazing. The contour of the plains is broken occasionally by groups of hills which rise like islands in a sea. Permanent water supplies are associated with these hill groups, and the well drained slopes afford favourable sites for villages.

- (5) In the Anglo-Egyptian Sudan the dark soil in the South merges into the red soil of the humid tropics. The transition is gradual, and no fixed limits can be drawn. In the Western Sudan, Nigeria, etc., there is no belt of dark soil, and the red sand merges directly into the red soil of the humid tropics. Bordering the Sudan on the East are the highlands of Abyssinia, where different conditions prevail. Consequently, the types of country of the Sudan plains are practically limited by the boundary.

CLIMATIC FACTORS.

Rainfall is the dominating factor. It will be seen from Fig.3 that the rain belt in the Sudan may be divided into two portions. The more Northerly belt stretches roughly from the 20th parallel to the 13th parallel, and has an annual rainfall of from 25 mm. in the North to 400 mm. in the South. The Southern belt stretches from the 13th parallel to the Southern boundary of the Sudan, its rainfall ranging from 600 mm. to 1,200 mm. per annum. Khartoum is at the Northern border of rain cultivation, where results are uncertain, while Singa is in the heart of it, where good crops can always be relied on.

Temperature in the desert reaches extremes (30° - 126° F.), while in the more humid South the range is less.

Relative Humidity of the Northern and Central Sudan is extremely low. Figures as low as 5 per cent. are occasionally recorded even as far South as Khartoum.

The Sequence of Weather may be followed in the belt containing Kassala, Medani, El Obeid, and Fasher, to which our observations more especially apply. The general march of the seasons may be regarded as beginning with the

rains. The NNE. trade winds give place to Southerly winds in April, and there may be small showers of rain. May is usually fairly dry, but the weather is unsettled by dust storms, or 'huboobs'. In June there may be heavy showers, but the rains can only be regarded as commencing in earnest in July, when 'huboobs' cease. Rainy conditions, with cloudy skies and humid atmosphere continue throughout July, August and September. An occasional shower may fall in October, but this month marks the period known to the people as the 'durat', -- a few weeks of hot, rather humid weather between the rains and the onset of the trade wind in November. This wind (NNE) is very dry, and with the increase in the declination and failing power of the sun, brings the dry days and cool nights of the winter months. The annual vegetation soon dries up, crops ripen and are harvested. There is much variation in the years and it has been said that in the Sudan there is seldom a normal season.

The Nile flood is mainly derived from rains that fall on the Abyssinian plateau. This is remote enough for there to be little relation between it and the Sudan plains. It does not follow that because there are favourable rains and good crops in the Sudan there is necessarily a high flood in the Nile.

THE GEZIRA

The Gezira is a flat bare plain, which lies in the triangle formed by the Blue and White Niles before they join at Khartoum. It contains about 5,000,000 acres,

of which some 505,000 acres are irrigated with Nile waters from Sennar dam. On this ground some of the finest cotton crops in the world are produced. This is the true economic centre of the Sudan. From its share of cotton profits the Sudan Government derives directly a large part of the revenues from which the various social services of the country are maintained: accordingly economic conditions in the Gezira are to a large extent reflected by those in the country as a whole.

THE POPULATION

From the point of view of its inhabitants, the Sudan may be divided into two distinct entities, the Northern Sudan and the Southern Sudan. The line of division follows approximately the 400 mm. line on the rainfall map.

The Northern Sudan might almost be regarded culturally as part of Asia. Its original peoples seem to have been of mixed Caucasian-negro stock, but from the seventh century onwards Arab invasion introduced a large measure of Asiatic blood and culture. A common basis of Arabic race, language, and religion exist throughout the whole Northern Sudan. The negro is a familiar enough type, but he is Arabicised and Islamicised.

The Southern Sudan, on the other hand, is true negroid Africa. In place of the white robes of the North we find the elaborate coiffure of the Shilluk, or the ash-smearred Dinka. Although the races of the South appear bewildering in their variety, they are essentially all negroid: not the Islamicised negroid of the North, but the

negroid comparatively untouched, naked and unashamed, living in his own natural conditions, so primitive in some cases that in him we can visualise the early ancestors of mankind. It is of practical importance to note that in their nakedness these people have an efficient protection against louse infestation, and the diseases that follow in its train. Consequently the spread Southwards of louse-borne relapsing fever is to a large extent limited by the habits of these peoples.

MOVEMENTS OF THE WESTERN PEOPLES.

The extreme West of the Northern Sudan is inhabited by races of negroid origin. Although they have adopted Islam these peoples remain comparatively untouched by the influence of Arabic language and culture, and their indigenous dialects and folk beliefs still survive. Racially they are more akin to the peoples of French West Africa than to the inhabitants of the Northern Sudan proper. With the people of French West Africa they are often collectively grouped under the term 'Westerners', and conform to a common physical type, which can be readily distinguished from the other racial types of the Northern Sudan.

The epidemiology of relapsing fever in the Sudan during the last twelve years has been very largely determined by the habits and movements of these peoples.

In former years they were regularly raided by the Arab slave-traders, to whom they constituted an important source of wealth and man-power. Now they travel long distances across the African continent in search of

paid work, which will enable them to accumulate enough money to buy cattle and a wife when they settle down in their own districts.

Every year there is a large influx of these Westerners into the Gezira for the cotton harvest in November and December. Here, lacking the sophistication of the Arab, they make better labourers, and earn good wages. After the cotton picking is over they may return to their own country, if they have accumulated enough money. A few settle in various parts of the Sudan. Others drift further Eastwards in search of work, their movements from place to place being affected by the demand for casual labour. Large numbers of them continue their Eastward journey on the pilgrimage to Mecca.

The pilgrimage is probably as big an incentive to the Westerners to leave their homes as the economic urge. Their Mohammedan religion is curiously mixed up with the innumerable African superstitions on to which it has only recently been grafted, and is consequently of a credulous and fanatical type. Most of those who leave their homes do so with the hope of ultimately reaching Mecca and later returning.

The pilgrimage is long for one who must find a livelihood by the way. It may be a quest of years, or even of a lifetime, with perhaps death en route. Some pilgrims settle either permanently, or for long periods, in the countries through which they pass. Others, gaining money quickly, return to buy a wife, leaving the pilgrimage for a future occasion.

The result is a slow, irregular, almost imperceptible, yet continuous infiltrating migration of Westerners Eastwards across the Sudan, and a smaller Westward returning movement. The magnitude of this migration is difficult to estimate, but it is probably quite considerable. It may be temporarily deflected, accelerated, or delayed by irregular changes in the labour markets, or by other political or economic events.

(B) HISTORICAL SURVEY.

HISTORICAL SURVEY.

According to all accounts conditions in the Sudan before the British occupation were eminently suitable for relapsing fever - the old 'famine fever' of Europe, which appeared typically in times of unrest and depression. From 1864 when the Mahdi drove out the Turco-Egyptian exploiters of the country, to the defeat of the Khalifa Abdullahi at Omdurman in 1898, there stretch fourteen years of massacre, famine, and pestilence. But these were only the culmination of a remoter and longer period, as foul as its consequence. From 1821, when Mahommed Ali the Great subjugated for his overlord the Sultan the peoples he called the Sudan - 'the country of the blacks' - the conquerors ran the land purely as an enormous slave farm. What the Turco-Egyptian regime meant to the population can be roughly estimated by the result - in sixty years it dwindled from thirteen millions to a plague stricken, starved, and inconceivably miserable three millions (KEUN, 1930).

From old descriptions, the best of which are those given by BRUCE (1810), and BURCKHARDT (1822), the principal diseases which ravaged the population seem to have been malaria, the dysenteries, cerebro-spinal meningitis, and smallpox. Possibly relapsing fever may have been present in this period, but the original descriptions are indefinite. BURCKHARDT (1822), relates how the Mamelukes, after their flight from Egypt to Dongola 'died of a putrid fever which regularly prevails in Dongola during the hot weather'. PONCET (1709) describes the depopulation of Dongola by plague so that he found

'towns and villages without inhabitants, and large provinces, at other times very fertile, quite laid waste and entirely abandoned'. It is interesting to note that plague has never been found in the Sudan, while according to CRAGG (1922) plague is the disease which is most commonly confused with epidemic relapsing fever. These descriptions may possibly refer to old epidemics of relapsing fever, especially as at the time the country was in the throes of wars between the Fung kings of Sennar and the Shaikiya, but this can only be a speculation.

Dr. Hassan Zaki who served with the Egyptian Medical Corps in the Sudan during the time of Gordon, and as a captive was the Mahdi's physician in Omdurman, still lives in Khartoum. He tells me that the disease was not recognised during that period.

Apparently the first cases of relapsing fever recorded from the Sudan were seen by CUMMINS (1910) in El Obeid in 1908. These were two Egyptian soldiers, who had just returned from leave in Egypt, where the disease had already been fully described clinically by SANDWITH (1905), and studied experimentally by GRAHAM-SMITH (1909) and DREYER (1910). According to RUSSELL (1932) the presence of relapsing fever in Egypt had been suspected as long ago as 1857 by GRESSINGER, on clinical grounds.

During the next two years BOUSEFIELD (1911) reported six cases seen in Khartoum - also Egyptian soldiers recently arrived from Egypt. Writing with a knowledge of the medical conditions in the country at the time BOUSEFIELD makes the interesting remark that 'human spirochaetosis is probably not endemic in the Northern

Sudan, otherwise it seems scarcely possible that it would have missed recognition'. BALFOUR (1911) carried out some experimental work with the spirochaetes obtained from these cases, but was unable to identify the vector, although he attempted to infect ticks, lice, and bed-bugs.

In 1913 one case was found at Wadi Halfa on the Egyptian border, and one in Khartoum. In 1916 there was a small outbreak at Halfa - 112 cases in all - but the origin of this infection was once more traced to Egypt. For the years 1917 to 1924 the records are scanty, but some fifty cases were observed during this period, in and around Atbara. BOUSEFIELD had pointed out the danger of Egyptian immigrants being able to introduce the disease into the Sudan, and so permanently infecting a district apparently free from human spirochaetosis. The distribution of the cases from 1908 to 1924 certainly suggested that the disease had a tendency to spread along the lines of communication between Egypt and the Sudan.

During 1925, however, there were no further cases in the Northern Sudan, but six cases were found in Mongalla, on the Uganda frontier. Tick-borne relapsing fever is prevalent in Uganda, and Ornithodoros moubata was found in some of the rest-houses which had been occupied by these cases. So it may be presumed that on this occasion the disease was tick-borne.

It is probable, therefore, that until 1926 relapsing fever had not established itself in the Sudan, nor had it, at any rate under British administration, assumed epidemic form.

In 1926 louse-borne relapsing fever invaded Darfur from the West in epidemic form.

RIDING and MACDOWELL (1927) suggest that this disease originated from an endemic focus in the Marra mountains. According to ATKEY (1929) the infection was introduced into the Sudan by immigrant labourers from the French Sudan. There seems more support for this argument. Louse-borne relapsing fever first appeared in French West Africa in 1921, where, according to KERREST, GAMBIER, and BOURON (1922), it was introduced by repatriated Senegalese troops from Syria. Other observers, notably RIGOLETT (1925) and NOGUE (1925) maintain that this epidemic originated from some unknown endemic focus in West Africa, and produce considerable evidence in support of their views.

However it may have arisen, this was undoubtedly one of the greatest historical epidemics of relapsing fever. It spread unchecked over British and French West Africa into the Tchad region (LASNET, 1930), and finally appeared in Wadai (LE GAC, 1931).

The mortality in these areas is unknown. 128,750 deaths were estimated in Kano alone, (McCULLOCH, 1925), and in other districts the mortality is said to have been higher still.

In September 1926 the disease reached Darfur, the most Westerly province of the Sudan. Here it spread from village to village with amazing rapidity, and in the space of six months had killed over 10,000 people. It commonly swept through a village and infected half or a third of the population, with a case mortality of

70 per cent. after which its virulence abated (MAURICE, 1932).

For four years the Eastward spread of the disease into the Central Sudan was prevented by a vigorous campaign, including the establishment of quarantine posts, the destruction of lice, and the treatment of the sick (BEVERIDGE, 1928). Had this virulent disease invaded the Gezira, the work in the cotton fields would have been seriously disorganised, and the whole Sudan might have been faced with an economic disaster of the first magnitude.

During these four years the virulence and infectivity of the disease appeared to diminish. The widespread epidemics which had decimated the population of Darfur died down, and gave place to smaller, localised epidemics, of lesser virulence and infectivity. This decrease in virulence was accompanied by the appearance of mild subacute, or ambulatory cases (ATKEY, 1932), extremely difficult to detect at the quarantines. It was inevitable that sooner or later some of those cases would slip through, and pass in the stream of immigrant labour into the irrigated areas of the Gezira.

This happened in 1930. From April till August of that year sporadic cases occurred in various parts of the Gezira, and on August 30th six cases were reported in one locality. From that time onwards fresh cases continued to occur, in spite of vigorous control measures, until June 1931, when the incidence fell abruptly. A small recrudescence took place in the autumn of 1932, but was readily stamped out. During the next three years the Northern Sudan was free from relapsing fever, although

in 1934 one isolated case was found at Malakal, in the Southern Sudan. No definite evidence exists as to whether this infection was tick-borne or louse-borne as no investigations were made.

(C) RE-INFECTION OF THE SUDAN FROM ABYSSINIA.

- (1) RECRUDESCENCE OF THE DISEASE IN 1936-1937.
- (2) RELAPSING FEVER IN ABYSSINIA.
- (3) FACTORS LEADING TO THE INFECTION OF THE SUDAN.

RECRUDESCENCE OF THE DISEASE IN 1936 and 1937.

In 1936 relapsing fever appeared once again in the Sudan. On the 22nd August of that year one case was reported from Singa, in the Fung district, and blood slides were sent to the Laboratories for confirmation of the diagnosis.

During the remainder of the year, a few cases occurred in the same district, the monthly incidence being as follows:-

August.....	7
September.....	15
October.....	0
November.....	1
December.....	1

Enquiries about their movements revealed that the patients had recently come from Abyssinia. The cases and their contacts were promptly isolated and disinfested. By the end of the year it appeared that the situation was well in hand, and that any tendency to epidemic spread had been scotched.

This, unfortunately, was not so. Odd cases continued to occur during the early part of 1937, and by the end of March, 1937, the total in the whole Sudan for the year was 39. Infections were reported from places as far apart as Kassala (8 cases) and Fasher (2 cases). One case was found in Nahud, and the remainder were distributed between the Fung and Gezira districts of the Central Sudan. CRAGG (1922) describes how epidemic relapsing fever in the United Provinces of India frequently appears to take origin simultaneously from multiple foci in different parts of the country, and it looked as if the same thing were about to happen in the Sudan.

In August the incidence rose abruptly. It was everywhere noticed that the disease, as in former years, was almost wholly confined to natives of the Western Sudan and French West Africa. The possibility of another major epidemic was disquieting. In October 1937 the writer was commissioned by the Director of the Sudan Medical Service to make a tour of investigation, and report on the origin, spread, and any other features relative to prevention of the disease.

During this investigation, which was carried out partly in Khartoum and partly in the affected districts, the 'laboratory saloon' proved invaluable. This is a railway coach (Fig.22), the interior of which is equipped as an up-to-date laboratory. It can be readily transported to any station on the railway line, thus bringing the facilities of a well equipped laboratory within easy reach of some of the more outlying districts. Without this mobile laboratory it would have been impossible to carry out the necessary investigations with any degree of expedition.

RELAPSING FEVER IN ABYSSINIA

In spite of the almost complete restriction of the disease to natives of the Western Sudan and French West Africa one of the first things to become apparent was that the source of the infection was this time from an entirely new quarter, viz, Abyssinia and the other countries East of the Sudan.

The existence of relapsing fever in Abyssinia has been known for many years. The infection was first

reported by DOREAU (1908), and in the same year BRUMPT (1908) reported that he had successfully infected a monkey in Paris by means of Ornithodoros moubata sent to him by a missionary from Harrar, thus establishing the existence of a tick-borne strain. MESNIL (1908) in a review, called the spirochaete Sp. Abyssin, BERGSMA (1928) gave an account of some clinical cases and noted the prevalence of Ornithodoros moubata and Ornithodoros savignyi.

Louse-borne relapsing fever has been reported from Addis Abbaba by SIBILIA (1937). This author claims to be the first to report the louse-borne disease, but NAGELSBACH (1934), three years earlier, had noted that in the highlands of Abyssinia, where ticks were not found, lice and relapsing fever were both common, and concluded that the lice must be the vectors.

It is interesting to note that de PAOLI (1930) describing an epidemic of relapsing fever in Asmara in 1929, in which ticks were not found but lice were plentiful, states that the disease was imported into Eritrea from Abyssinia. Corroboration of his views is given by BRUNS (1937) who records a very fatal epidemic of louse-borne relapsing fever in the Djig district of Abyssinia in 1929. According to CACCIAPUOTTI (1936) the disease is now endemic in many towns and villages in Eritrea.

According to BRUNS (1937) relapsing fever is endemic in many districts of Abyssinia, but apt to break out in epidemic form during the rainy season. The louse, Ornithodoros moubata and Ornithodoros savignyi are all

cited as vectors by this author.

It may be noted that with the exception of BRUMPT (1908), these authors rely largely on epidemiological data for their views on transmission, and do not substantiate them by experimental transmission of the disease by the alleged vector.

A similar state of affairs obtains in the adjoining countries, British and Italian Somaliland, where Ornithodoros savignyi, DRAKE-BROCKMAN (1913), CLARKE (1936) Ornithodoros moubata (DONALDSON, 1925) and the louse (MODUGNO, 1937) have at different times been cited as the principal vectors. Here again, the evidence is largely epidemiological, and there is a notable absence of laboratory confirmation.

FACTORS LEADING TO THE INFECTION OF THE SUDAN

The factors leading to the infection of the Sudan may in a general sense, be described as part of the aftermath of the Italo-Abyssinian war. But it may definitely be stated that the introduction of the disease into the Sudan was not the result of an influx of Abyssinian refugees. It has already been noted that the victims of the disease were not Abyssinians or local natives, but natives of the Western Sudan and French West Africa, and an analysis of the factors which led up to this state of affairs is of some interest.

After the military occupation of Abyssinia by the Italians there still remains the longer process of pacification and development, requiring money and labour.

Attention has already been directed to the migratory movements of the Westerners across Africa, and to the way in which the demands of the labour market influence these movements. Being good labourers, suited to African conditions, they were the obvious immigrants to encourage in the face of a task such as confronted the Italians in Abyssinia. Consequently large numbers of Westerners made their way into Abyssinia and Eritrea during the last three years, in the reasonable expectation that there they would find a market where labour would command a high price.

Extracts from a Report by me to the Director, Sudan Medical Service, indicate briefly the fortune encountered in the Italian territories and its bearing on the introduction of relapsing fever into the Sudan:

(14) "98 per cent. of the Kassala and Blue Nile cases have been in males over 15 years of age, and over 90 per cent. are Westerners or natives of the Sudan returning from Eritrea and Abyssinia"

(15) 'Condition of the Immigrants'

"Generally speaking the cases are individuals who have trekked across Africa to Eritrea and Abyssinia, attracted by promises of ample work and good pay. 15 piastres a day, all found was what they were led to expect. Many have been 12 - 18 months on their Eastward trekk, and for most the journey has been arduous enough"

(16) "Once in the Italian territories, however, they found conditions disappointing. Those who were lucky got 7 - 8 piastres a day: many got less. Often there was no money available, and they had to accept instead carpets and other goods of Italian origin. Those who were lucky enough to obtain money found that its export was prohibited by the authorities. Their food they had to pay for and they were unable to obtain it except from appointed canteens, where the price was high and the quality poor. The work (mostly road making) was hard and the conditions

(16) exacting. Those who fell sick by the way had to look after themselves. No medical attention was provided for minor or major ailments. According to their reports numerous minor Abyssinian insurrections added to the general stress of living, and they say that in the interior many persons are dying of smallpox and fever"

(17) "The result is that those immigrants are now leaving the Italian territories as rapidly as they can, and pouring back into the Sudan in large numbers, hoping either to find work here, or to return to their homes"

(18) "Physically they are under-nourished, verminous, and weary with long journeying. Their spare bodies and dry skins are evidence of their devitalised condition"

"In addition to the epidemic diseases, relapsing fever and smallpox, which they are bringing in, attention may be drawn here to the large number of chronic septic conditions and sloughing ulcers which are crowding out the hospitals on the Sudan border. All these cases are recent arrivals from Italian territory"

(19) "In short, we have here a classical picture of relapsing fever with all the associated circumstances which have been recognised since the days of Hippocrates - unrest and misery, war, fatigue, overcrowding, malnutrition, verminousness, and the spread of the disease among communities along the main lines of travel"

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(21) "From recent Italian medical literature (CACCIAPUOTI, 1937) it is evident that louse-borne relapsing fever has been present in epidemic form in Eritrea for the last two years at least. The possibility of infected persons, either incubating the disease or in an apyrexial period, having passed through into the Sudan at various times cannot be ignored. This may be the explanation of the sporadic cases which occurred in different parts of the country during 1936 and the earlier part of 1937"

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(23) "Since then the situation has become one of considerable urgency. For some time now each Westbound train passing Sennar has brought in some 400 - 500 persons coming from the heavily infected countries on the Eastern border of the Sudan. A certain small number are probably also travelling through Atbara. For the reasons given in paragraphs 11 and 12, numbers of these infections may pass undetected till the persons concerned have proceeded further on their Westward journey, or infiltrated the Gezira in their search for work, thus starting new epidemic foci in these parts of the country"

Fig 4 shows the routes by which the infection was invading the Sudan. Particularly noticeable is the part played by the Kassala-Sennar railway in shortening the time of travel and enabling people to proceed long distances from the source of infection during the incubation period or in the apyrexial interval.

The popularity of the railway line was not without advantage from the public health point of view. It was apparent that as long as the vast majority of immigrants chose the railway line some measure of sanitary control was possible, especially as the main routes from the border to the railway converged on Kassala, where the main quarantine station was established. No pains were spared to avoid irksome or stringent control measures on the railway which might divert the stream of immigrants into channels less easily controlled from the public health point of view. Even as it was, a smaller number of immigrants were finding their way from the border into the Blue Nile without travelling by rail. Most of those were stragglers across the Abyssinian border whose route took them down to the railway line somewhere near Gedaref. In this district there was a brisk demand for labourers

in connection with the durra and simsim fields. Persons travelling by this route journeyed slowly, taking advantage of a few day's employment here and there as it offered. On this account it was much more difficult to keep any trace of them.

(1) MORPHOLOGY AND HABITATS OF THE
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(D) LABORATORY STUDIES

- (1) MORPHOLOGY AND MOVEMENTS OF THE ABYSSINIAN RELAPSING FEVER SPIROCHAETES.
- (2) APPEARANCES SEEN IN FROZEN BLOOD.
- (3) CULTURE.
- (4) ANIMAL INOCULATION:-
 - (a) RODENTS
 - (b) MONKEYS
- (5) IMMUNITY.
- (6) THE EFFECT OF SPLENECTOMY.
- (7) RESIDUAL AND LATENT INFECTIONS.

Relapsing fever of Abyssinian origin has not previously been encountered in the Sudan. The uncertainty which exists in the literature about the transmission and other features of this strain has already been noted. As a matter of interest, therefore, as well as from the practical point of view, it seemed desirable to take the opportunity of carrying out a laboratory study of this strain of relapsing fever.

MORPHOLOGY AND MOVEMENTS OF THE SPIROCHAETE.

Typical spirochaetes (Borrelia) were found in the blood during the pyrexial stages of the disease. In the ordinary thin blood films, stained by Leishman's or Giemsa's methods, the organisms were extremely polymorphous. Among many hundreds, hardly one was seen which presented the characteristic corkscrew arrangement. They had either lost this close spiral structure and appeared as undulating or worm-like forms, or they were twisted into figures of eight, concentrically wound hoops, and other coiled and distorted forms (Fig.6). Sometimes dividing forms were seen in which the two daughters were intertwined and still attached by a thin portion in the centre, but this appearance was not seen in living films.

Occasionally, clear areas could be seen along part of a spirochaete's length, giving it a beaded appearance. In one lucky slide, taken at the time of the crisis, the spirochaetes were seen to have clumped together and to be undergoing a process of disintegration by breaking up into granules along their length.

Under dark-ground illumination, examination of the living organisms produces an entirely different picture. The spirochaetes appear as long, closely coiled, usually rigid spirals, tapering slightly at both ends, and actively motile. Three types of movement could be clearly made out:-

(1) An extremely rapid wave-like movement, passing down the spiral turns, which might take place without the organism altering its position in space.

(2) A movement of translation by which the organisms swam rapidly across the field: it was always accompanied by the wave-like movement in the spiral.

(3) Various contortionist movements, recalling the forms seen in the stained films. Spirochaetes would frequently bend to one side or the other, coil themselves up into hoops or figures of eight, from which they would uncoil again with almost explosive violence. Sometimes a spirochaete would suddenly cease all movements and lie absolutely still for a few seconds, in a remarkably regular corkscrew spiral and then as rapidly start moving again.

APPEARANCES NOTED IN FROZEN BLOOD

Variations in length and in the number of turns in the spiral were considerable. It was found that by freezing citrated blood containing spirochaetes, keeping it for a few days in the ice-chest, and thereafter making films, beautiful preparations could be obtained in which the regular spiral structure of the organisms was preserved (Fig.12).

These films were ideal for measurements. The average length of 200 consecutive spirochaetes seen in such a film was found to be 18 μ the extremes being 10 μ and 40 μ . Wider extremes were observed in other films.

In these films of frozen blood, irregular globose swellings were frequently seen in the spirochaetes, sometimes terminal, sometimes situated at various distances along the length of the spirochaete. They probably correspond to the swellings seen by BUTLER (1908) in Sp.duttoni which had been kept for some time outside the human body. In all probability they were due to degenerative changes.

In those films of frozen blood, too, various structures could be seen inside the red blood corpuscles. Some of them recalled the appearances figured by BALFOUR (1911) in the development of the intra-corpuscular granules of Treponema anserinum (Spirochaeta granulosa penetrans). Indeed all the appearances seen by CARTER (1908) could readily be identified in the corpuscles of these films. CARTER regarded them as stages in the life cycle of the spirochaete, but the appearances seen in the frozen blood were almost certainly artefacts, because

- (1) They were only seen in frozen blood, never in fresh films.
- (2) The spirochaetes showing these peculiarities were always motionless in the dark-field and therefore, presumably dead.
- (3) Other and obvious artefacts were observed in the same films.

CULTURE.

It was found impossible to grow the spirochaetes in the new egg medium described by YUAN-PO (1933, 1936). At the outset much time was lost by confining one's attempts at culture to this medium and refusing to accept repeated failures, largely owing to the glowing reports of YUAN-PO who claimed to have obtained 100 per cent. success with Sp. recurrentis in this medium.

Spirochaetes could be found in the cultures for periods up to ten and even twenty days after inoculation. From the seventh day onwards their movements under the dark-field became very feeble. Finally they stopped and the spirochaetes disappeared, though it was not possible to determine the manner of their going. Short, immobile forms of only two or three turns were observed, and probably resulted from the disintegration of dead or dying spirochaetes.

Batches of medium were made up according to the original recipe (YUAN-PO, 1933) and also according to the modified simple method (YUAN-PO, 1936), but there was no difference in the result. No evidence of multiplication could be adduced in either medium. The instructions of the author were followed to the letter in both cases, and the resulting pH was found to be identical with that obtained by him, so there is no reason to believe that the media differed in any way from those used by YUAN-PO.

After many attempts this medium was finally discarded, and other methods were tried.

Citrated human blood, kept either at room temperatures 37°C, was not found successful. The

spirochaetes died rapidly as estimated by their movements under dark ground illumination. They were always completely immobile in three days, and there was no evidence of multiplication. It was found that as the corpuscles sedimented, the spirochaetes tended to settle in the layer just above the corpuscles, and a false impression of multiplication might be obtained if fluid from this layer were selected for examination. In some cases a tendency to auto-agglutination was observed. The blood used was of human origin, taken from the infected patients and contained spirochaetes at the time of withdrawal.

Diluted human serum, far from being a successful culture fluid, appeared to have a lethal action on the organisms which were all motionless in twenty four hours.

Diluted horse serum was similarly found to be useless as a culture medium. Although six tubes were inoculated from two different strains, it should be admitted that the serum was all obtained from one horse. HOELTZER and ZABBLOTZKAJA (1926) have stated that sera from different horses often vary considerably, one giving a good growth while another appears to have an inhibitory effect.

Excellent cultures were finally obtained in a modified Noguchi's medium, prepared as follows -

Under aseptic precautions $\frac{1}{2}$ inch of egg albumen was pipetted into the bottom of test tubes, and then coagulated by placing the tubes in hot water at approximately 80°C. Thereafter the tubes were filled to within an inch and a half from the top with freshly drawn ascitic fluid.

The tubes were inoculated by introducing 3 - 5 drops of blood containing spirochaetes, and incubated

at 37°C.

Within 48 hours there was an obvious increase in the ease with which spirochaetes could be found in the dark-field, and the high proportion of long and dividing forms was evidence of active multiplication. On the third day after inoculation, each dark-field from the fluid lying just above the coagulated egg-white contained twenty to thirty actively motile spirochaetes, with a high proportion of dividing forms. Enormously long filamentous forms were sometimes encountered. In one of these, appearance of thinned parts along its length suggested that it was in the process of dividing transversely into four daughters.

This medium never failed to grow the spirochaetes. The impression was gained that growth was improved by the addition of 5 - 10 drops of sterile 50 per cent. glucose, but it was difficult to be certain. The addition of the glucose was certainly not necessary in order to obtain a good growth.

The addition of a layer of liquid paraffin on the top of the ascitic fluid was found to have no influence on the growth. Culture tubes without the paraffin on the top are indeed preferable as the oil tends to adhere to the pipette with which samples are withdrawn for examination, and refractile oily globules appear in the dark-field. As compared with YUAN-PO's medium, which is full of granular debris, the ascitic fluid gives beautifully clear dark-fields against which the spirochaetes stand out distinctly.

Subcultures were readily made by introducing 3 - 4 drops from a culture showing plentiful spirochaetes

into a fresh culture tube by means of a capillary pipette, adding at the same time 3 - 4 drops of citrated or freshly-drawn rabbit's blood. One strain was passed through twelve successive subcultures at 3 - 5 day intervals without any apparent loss of vitality, and the process was only given up because of my departure on leave. After nine subcultures the inoculation of $\frac{1}{2}$ c.c. of the culture fluid into the peritoneum of a mouse resulted in the appearance of spirochaetes in the peripheral blood in twenty-four hours. The course of this infection was not followed out.

Attempts were made with these cultures to utilise the "adhesion test" as a method of differentiating the strains. The technique described for leptospira (BROWN and DAVIS, 1927) was followed, but instead of B. coli an emulsion of a salmonella organism isolated from a case of food poisoning was used. The results were unsatisfactory. While the writer was on leave in June, 1938, he discussed the findings with MAJOR H.C. BROWN, who stated that he himself had recently been obtaining similarly unsatisfactory results, and that the further investigation of the matter had led him to the discovery of a hitherto unrecognised property of red blood cells and bacteria, as a result of which some were suitable indicators for adhesion and others were not.

ANIMAL INOCULATION

RODENTS. Of laboratory animals, white rats, rabbits and guinea-pigs proved insusceptible. So also

did ordinary brown and black rats (Rattus rattus and Rattus norvegicus) caught locally by the Khartoum Sanitary Service.

This at the outset suggests a louse-borne infection. RIDING and MACDOWELL (1927) found that field rats, the only animals they had available, were insusceptible to the louse-borne strain in Darfur in 1927, although it is notable that MATHIS and GUILLET (1925) working in Senegal with what was in all probability the same strain, found the local grey mouse could be readily infected. The West African strain on the Gold Coast has been successfully inoculated into white and black rats by SELWYN CLARKE, LE FAUN and INGRAM (1923). Perusal of their records, however, show that infection was scanty, transient and uncertain, and only resulted when relatively enormous doses of infected blood were inoculated.

Probably more significance can be attached to the results of guinea-pig inoculation. NICOLLE (1932) recommends guinea-pig inoculation as the most ready method of differentiating between louse-borne and tick-borne strains in Northern Africa, and suggests that if this procedure were resorted to more frequently, many infections in Egypt, Algeria and Lybia at present regarded as louse-borne, would prove by their virulence to guinea-pigs to be in reality due to tick-borne strains.

White mice obtained originally from the Wellcome Bureau of Scientific Research, London, were found to be susceptible. The infection in these animals was observed to run a very constant course. As a general rule the intraperitoneal route was used for inoculating the

spirochaetes. The treponemes were invariably found in the peripheral blood in 12 - 24 hours after inoculation. They were always present 48 hours after inoculation, but usually disappeared during the following twelve hours. The infection ran an exceedingly mild course in these white mice. It was apparently symptomless, and daily examination of the blood for 20 days after the disappearance of the spirochaetes failed in every case to show any evidence of relapse. Subinoculations from mouse to mouse were not successful, even when a large inoculum of infected material was given. This was effected by bleeding a mouse to death into sterile citrate solution thirty hours after inoculation, when the blood, as shown by films taken immediately before bleeding, contained numerous spirochaetes. About three-quarters of a c.c. of blood was obtained in this way and inoculated immediately into the peritoneum of two fresh mice, but no infection resulted. Negative results were likewise obtained when the organisms were inoculated subcutaneously instead of intraperitoneally, and also by the percutaneous method, which TOMOIKA (1924) had found to give rise to a much more severe infection with the European strain in mice than intraperitoneal inoculation.

According to the tables drawn up by BALFOUR (1911) and MANSON-BAHR (1935), passage through monkeys increases the virulence of the European strain of T. recurrentis for small rodents. This was not found to be the case with the Abyssinian strain. Rats, rabbits and guinea-pigs were still refractory after passage of the spirochaetes through monkeys and the virulence of the organisms for white mice was, if anything, diminished. Twenty-four hours after inoculation the spirochaetes were present in the peripheral blood of the

mouse, but at forty-eight hours they were exceedingly scanty and difficult to find. After this they disappeared and no relapse took place. Sub-inoculations from mouse to mouse were still unsuccessful.

It is interesting to note that the course of the infection in these mice inoculated from monkeys did not vary with the severity of the disease in the monkeys. Nor did it seem to signify whether the original monkey was splenectomised or not, or whether it was originally infected by the inoculation of blood from a case, or by experimental transmission from an infected mouse. It will be seen later that these variations made a considerable difference in the severity of the infection in the monkey.

The gerbille or desert rat of the Northern Sudan, was also susceptible and in this animal the course of the infection was similar to that in mice, but the parasites sometimes persisted in the blood for three or even four days. Sub-inoculations from gerbille to gerbille sometimes resulted in a transitory appearance of scanty spirochaetes about 48 hours after inoculation. The gerbille seems undoubtedly to be the most susceptible of the rodents at one's disposal.

An interesting observation made in these rodent infections was that in a small percentage of white mice the spirochaetal infection was accompanied by, or more commonly followed by, a low grade septicaemia in which a mixture of organisms were concerned, principally diphtheroids, cocci and bacilli. This always persisted for some time after the spirochaetes had disappeared from the blood and generally seemed not to upset the health of the animals, although in

two mice the number of organisms observed in the blood films steadily increased, and the animals became ill, and finally succumbed. Post-mortem revealed no peritonitis or abscess formation, and clinical examination of other affected mice showed no evidence of peritonitis or local reaction at the site of inoculation.

At the time not much attention was paid to these organisms which were seen in the blood films, except to exclude the possibility of their being due to faulty technique when the blood films were taken. It is difficult to understand why the intraperitoneal inoculation of spirochaetes withdrawn directly from a human vein should cause a septicaemia without local reaction unless the organisms were of extreme virulence, in which case the septicaemia might reasonably be expected to be rapidly fatal.

It is possible that the condition may have been due to an increase in the invasive powers of commensal organisms, brought about by the spirochaetal infection. SARANELLI (1927) maintains that the spirochaetal infection is harmless in itself, but in some way is able to increase the invasive powers of other organisms and these are responsible for the disturbance which takes place. KULESCHA and TITOWA (1923), cited by RUSSELL (1932) made out that many of the relapsing fever fatalities in the Russian epidemic of 1920 - 1921 were due to secondary infection, and point out that from the literature it is apparent that many of the past European epidemics have been complicated by a pyaemia in the same way.

Monkeys. The common grey monkey of the Sudan (Cercopithecus sebaeus) was found to be susceptible and

in these animals the infection is similar to the human disease. The spirochaetes commonly appear in the peripheral blood after an incubation period of 2 - 4 days, persist from 2 - 5 days, and then, after a lapse of some 10 days, reappear for 1 - 3 days after which there is no further relapse. Some variation between individual monkeys was encountered. Thus, one monkey had no relapse, and another was found which appeared to be quite immune: attempts to infect it with two different strains were quite unsuccessful.

It was found that one monkey could be readily infected by the inoculation of blood containing spirochaetes from another monkey. A strain obtained from infected human blood was passed through two monkeys in this way, and one obtained directly from a louse was passed through three successive monkeys. No attempt was made to find out how many passages could be effected in this way without the strain losing its virulence. It may be recalled that SARGENT and FOLEY (1910) were unable to pass the Algerian strain even to a second monkey.

Enlargement of the liver and spleen were readily detected in all the infected monkeys, but no attempt was made to follow out the clinical course of the disease in these animals. Except for very obvious illness, attention was confined to the examination of the blood for organisms.

In general terms, the virulence of the strain for laboratory animals may be summarised as follows. Rodents, with the exception of white mice and gerbilles, were insusceptible. In these two latter the infection

runs an exceedingly mild course, ending in recovery. There is no relapse, and the strain cannot be maintained in these animals. In monkeys, the infection runs a mild clinical course with one relapse, and tends to recovery. Passage through at least three monkeys is possible.

These results conform in the main with those which have been found fairly universally with the louse-borne strains of relapsing fever and especially the North African group.

IMMUNITY

Evidence of Immunity. On 24/1/38 blood containing numerous spirochaetes was inoculated from a human case in Khartoum North directly into two mice which had previously been infected on two occasions, and at the same time, into two fresh mice. In twenty-four hours the latter developed a typical two days' infection, while spirochaetes never appeared in the blood of the two previously inoculated mice. A similar result was obtained on 26/2/38 when blood was inoculated from an infected monkey into two fresh mice and two previously inoculated mice.

Monkey R. (1) proved resistant the second time an attempt was made to infect it. Monkey R. (2) which had been twice infected previously was insusceptible when a third attempt was made on 5/3/38. On both these occasions it was possible to infect other monkeys by inoculation of the same blood which failed to infect monkeys R. (1) and R. (2) respectively, showing that the absence of infection was not due to loss of virulence of the spirochaetes.

Evidence exists therefore that a state of immunity to further infection can be brought about by a previous infection.

Erratic Nature of the Immunity. The evidence of this immunity, however, is inconstant and erratic. Other and more numerous experiments can be cited in which previous infection failed to protect against further infection.

Thus, two mice infected on 13/11/37 were found to be susceptible again on 16/11/37, and two mice

infected on 16/11/37 were as readily susceptible again on 25/11/37. In both cases the second infection was similar to the first in its intensity and duration.

The case with monkeys was similar. Monkey R.(1)⁽¹⁾ was susceptible on one occasion and thereafter resistant, while monkeys R.(2) and R.(3) were readily infected on a second occasion.

PRESENCE OF SEVERAL ANTIGENIC STRAINS

These discrepancies are probably due to antigenic differences in the various strains studied. BALTHAZARD (1936) and other workers have found that no two strains of relapsing fever are the same, and that infection with one strain results in the development of immunity against that strain only and no other.

CUNNINGHAM (1925) has postulated the alternation of two serological variants with successive relapses. Some of our experimental results at least suggest that the "relapse strain" is different from that of the first paroxysm.

On 24/1/38 two monkeys and two mice were inoculated with blood containing numerous spirochaetes from a case in Khartoum North. Of those four animals one of the monkeys, R.(2), was the only one to show spirochaetes in its blood afterwards, although they had all been previously infected with one strain. On this previous occasion, however, one of the monkeys, R.(1),

(1) p. 56.....

relapsed, while the other did not, R.(2). The mice were both inoculated from monkey R.(1) during the first paroxysm, and again during the relapse. In both instances they were susceptible. The fact that both mice were resistant on the third inoculation, as well as monkey R.(1), suggests that the difference between the two monkeys was this time due to other factors than individual variations in natural resistance.

It is reasonable to assume that the resistance of the one monkey and the two mice was due to acquired immunity brought about by previous experience of an antigenically similar strain. That the immunity was not due to the strain causing the first paroxysm is shown by the successful infection of the other monkey, R.(2), which also had a first paroxysm in the previous infection. Presumably, therefore, the immunity in monkey R.(1) and the two mice was due to the relapse which never appeared in monkey R.(2). If this be so, the original and "relapse strains" were probably different from each other.

The effect of the Khartoum strain on mice infected previously with the "relapse strain" only would have given valuable information in this instance. Had one been able to foresee the possibility of these two strains being related antigenically in this way, the experiments might have been planned accordingly, but as it was, the correlation only became suggestive afterwards, when the results of the experiments were being reviewed.

Another monkey, R.(3), had a relapse during its first infection, and thus probably experienced two

different variants. This did not prevent it being successfully infected two months later by the inoculation of infected blood from another monkey. It is probable, therefore, that more than two antigenic variants were present among the strains.

There is possibly also a factor in the immunity which is not specific to the strains. Two infections seemed always to make our animals immune to further infection. It may be noted, too, that the relapse is usually of much shorter duration than the original attack. It may be observed further, although the number of our experiments on this point is small, that when previously infected monkeys are splenectomised, and then inoculated with a strain to which they are susceptible, the effect of the splenectomy on the infection is different from that which results when splenectomy is done before the first infection.

EFFECT OF SPLENECTOMY

According to MELENEY (1927), KRITSCHESKI and RUBINSTEIN (1927), and KALAJEW (1931), the increased susceptibility of experimental animals to relapsing fever which results from splenectomy is evidenced by a much heavier infection of the blood with spirochaetes, and an increase in the death rate of inoculated animals. On the other hand BRITTL and KINGHORN (1906) found that splenectomy had no effect whatever on the course of African relapsing fever, and VELU, BALOZET and ZOTTNER (1931) have reached a similar conclusion with regard to

T. hispanicum infections. RUSSELL (1931) found with the West African strain that splenectomy might result in a slightly higher death rate but otherwise had no effect on the infection.

In experimental work with organisms of relatively low virulence such as this Abyssinian strain, anything which will increase the susceptibility of the hosts and make the infections a little more definite, is a practical advantage. Presumably it was for this reason that FENG and CHUNG (1937) used splenectomised squirrels in their transmission experiments with the Chinese strain. A few experiments carried out by the writer under this heading were undertaken primarily to determine whether any advantage would be gained by the use of splenectomised rather than normal animals for transmission experiments, although in point of fact the experiments had already been undertaken with splenectomised animals.

Mice. Two mice, splenectomised five days previously were inoculated intraperitoneally with approximately 0.2 c.c. of infected blood withdrawn from a monkey on 26/1/38. Two normal mice were inoculated at the same time, as controls. In all four animals the disease pursued a similar course, spirochaetes being found in the blood during the first two days following inoculation, after which they disappeared and did not return.

Six days after the disappearance of the spirochaetes the two control mice were splenectomised, but this did not result in the reappearance of the spirochaetes.

Two of these four mice were infected on a second occasion on 5/3/38 and the infection ran a typical course, exactly similar to that in two fresh mice inoculated at the same time. A third attempt to infect them some days later was not successful.

The effect of splenectomy on the course of the infection in mice appears to be negligible, although it is readily admitted that the number of these experiments is too small to allow of anything more than tentative conclusions being made.

Monkeys. In monkeys the results were different. The number of observations we were able to make was restricted, but even these few indicated that splenectomy does modify the course of the disease in these animals and does increase their susceptibility to the infection.

On 5/3/38 two splenectomised and one normal monkey were inoculated with blood containing abundant spirochaetes. In the normal monkey, R.(8), the infection ran a fairly typical course. In the splenectomised monkeys, R.(7) and R.(6), no striking departure from the normal was noticed in the first paroxysm, but the relapses appeared earlier, lasted longer, and showed a much heavier infection of the blood with spirochaetes - almost comparable in this respect to the fatal infection of monkey R.(4) which was infected directly from a louse (see later, p.64). In one of the splenectomised monkeys a second relapse was observed. The other subsequently died. Owing to my departure on leave it was not possible to follow out these infections fully, so there may have been further relapses which were not observed.

It is hardly permissible to include in this comparison the monkey which was found immune, nor one which was infected directly from a louse, but their inclusion in the series gives a very striking picture of the effect of splenectomy, thus -

Character of Disease	Five Normal Monkeys	Four Splenectomised Monkeys
Immune	1	-
No relapse	1	-
1 relapse	3	1
2 relapses	-	1
Death rate	Nil	50 per cent.

Note:- One splenectomised monkey died during the first paroxysm, and another, which ultimately died, probably had more than one relapse.

Splenectomy had not the same effect on previously infected animals, whether undertaken before or during the course of the second infection. Thus, the course of the second infection was no more severe in monkey R.(3) than in monkeys R.(1) and R.(2), which had been splenectomised. Even more striking evidence of this was obtained on 5/3/38 when one splenectomised monkey which had been infected twice previously was inoculated with the same blood as a normal monkey which had been infected once. The latter was found susceptible, the former immune. KRITSCHIEWSKI and RUBINSTEIN (1931) found that while

splenectomy had no effect on acquired immunity it might cause the reappearance of the spirochaetes in the blood. This was not found in our animals.

A possible explanation why the effects of splenectomy were more apparent in monkeys than in mice is suggested by an experiment of RUBINSTEIN (1930). This author found that when splenectomised rabbits were inoculated with the ordinary doses of the infective material the death rate was the same as in control rabbits given the same doses. When a much larger dose was used, however, the death rate of the splenectomised as compared with the normal animals was strikingly increased. The effect of the splenectomy was apparent only in an infection which was likely to run a severe course in the normal animal: with very mild infections the reserves of the reticulo-endothelial system are sufficient to mask any effects of the splenectomy. In the case of our mice the course of the infection was very mild. The more severe infection in the monkey presumably entailed a greater tax on the reticulo-endothelial system, which was then less able to withstand removal of a large part of its substance.

RUBINSTEIN and GOLOBEWA (1930) have shown that in Trypanosoma equiperdum infections the effect of splenectomy is inversely proportional to the length of time which elapses between the splenectomy and subsequent infection. In this connection it is interesting to observe that the only one of our monkeys in which the inoculation of infected blood resulted in a fatal issue was one which had been recently splenectomised. The others had undergone the operation several months previously and

in the meantime had received numerous inoculations of foreign material, a process which might reasonably be expected to induce some degree of compensatory hypertrophy in the remainder of the reticulo-endothelial system.

LATENT INFECTIONS.

WENYON (1926) and ANZAR (1926) have recorded that when mice, previously inoculated with spirochaetes, were infected with trypanosomes several months after the apparent disappearance of the spirochaetes from the blood, this resulted in the reappearance of the spirochaetes in the blood stream. BUSCHKE and KROO (1923) and other workers have shown that the spirochaetes, after their disappearance from the blood, settle in the tissues of the central nervous system, where they may remain viable for long periods.

The importance of these observations from the point of view of the human infection is that they suggest the possibility of spirochaetes lying dormant in the tissues of recovered patients and invading the blood stream as a result of some debilitating infection, malaria, for example. This might lead to infection of lice and start a new outbreak.

On 13/1/38 three mice which had been infected with spirochaetes at different periods during the previous two months were inoculated with Trypanosoma evansi. For this I am indebted to Dr. S.C.J. BENNETT, Senior Veterinary Research Officer of the Sudan Government. After an incubation period of six days the trypanosomes appeared

in the blood stream. They persisted for four days only. In examinations of the blood carried out for the following twenty days neither trypanosomes nor spirochaetes were seen.

On another occasion 12 white mice, which had been infected on one or more occasions at periods varying from two to eight weeks previously, were killed. Emulsions were made of their brains and inoculated subcutaneously into six gerbilles, each gerbille receiving material from two mouse brains. During the course of the following 12 days none of the gerbilles developed an infection, after which their blood was not examined.

Gerbilles were chosen as they had shown themselves to be the most susceptible of the small rodents to the infection, but the experiment was not hopefully undertaken. If passages were not successful when blood rich in spirochaetes was inoculated, they were hardly likely to succeed with brain emulsions containing possibly a few organisms. Negative results in this instance can have no significance.

Probably the only successful way to investigate this aspect of the Abyssinian strain would have been to use monkeys only. The important point is not so much the proof of latent infection, but to estimate the tendency of the strain to cause such infection, as shown by the proportion of ordinary infections which are followed by latent infection. Unfortunately any satisfactory work along these lines would have required more monkeys than were at disposal.

CASE HISTORIES OF THE EXPERIMENTAL MONKEYS

These case histories are presented as chronological tabulations of events, with the view that the facts are more readily appreciable in this form.

MONKEY T.O.

- 16/11/37. At Sennar, inoculated intraperitoneally with 1 c.c. blood from a human case, showing abundant spirochaetes in the blood.
- 17/11/37. Blood negative.
- 18/11/37. Blood negative.
- 19/11/37. Blood negative.
- 20/11/37. Blood negative.
- 21/11/37. Blood negative.
- 22/11/37. Blood negative.
- 23/11/37. Blood negative.
- 24/11/37. Blood negative.
- 25/11/37. Blood negative.
- At Kassala. Inoculated intraperitoneally with 1 c.c. blood from a human case, showing abundant spirochaetes.
- 26/11/37. Blood negative.
- 27/11/37. Blood negative.
- 28/11/37. Blood negative.
- 29/11/37. Blood negative.
- 30/11/37. Blood negative.
- 1/12/37. Blood negative.
- 2/12/37. Blood negative.
- 3/12/37. Blood negative.
- 4/12/37. Blood negative.
- 5/12/37. Blood negative.
- 6/12/37. Blood negative.
- 7/12/37. Blood negative.

As this monkey seemed to be insusceptible, no further attempts were made to infect it. The animal died two months later, without apparent cause. Post-mortem findings were negative.

MONKEY R.(1).

- 23/12/37. At Sennar. Inoculated intraperitoneally with 1 c.c. blood from a human case showing abundant spirochaetes.
- 24/12/37. Blood negative.
- 25/12/37. Blood positive, infection of moderate severity. Heart puncture performed under ether anaesthesia and 5 c.c. blood withdrawn. One half c.c. inoculated directly into each of the following, into the peritoneum:-
- 2 white mice
 - 2 gerbilles
 - 2 white rats
 - 1 guinea pig
 - 1 rabbit
 - 1 monkey R.(3).
- 26/12/37. Blood positive.
- 27/12/37. Blood positive.
- 28/12/37. Blood negative. Remained negative until 4/1/38.
- 4/1/38. Blood positive. The two white mice inoculated on 25/12/37 were inoculated once again with blood from the ear, diluted with citrate.
- 5/1/38. Blood negative. After this date spirochaetes were never found again in the blood of this monkey.
- 20/1/38. Under ether anaesthesia, splenectomy was carried out. No spirochaetes were seen in smears made at once from the spleen, nor in paraffin sections of the spleen, stained by Levaditi's method. Splenectomy did not cause a reappearance of the spirochaetes in the blood during the next four days.
- 24/1/38. At Khartoum North. Inoculated intraperitoneally with 1 c.c. blood from a human case, showing abundant spirochaetes in the peripheral blood.
- 25/1/38. Blood negative, and remained negative during the next twelve days after which no further examinations were carried out. Monkey is still under observation from the point of view of Kala Azar.

It is interesting to note that in fresh spleen smears Leishman-Donovan bodies were discovered, though there was no history of attempted infection with Kala Azar, and no clinical symptoms of this disease. Up to date (23/5/38) this monkey is alive and well. It came originally from a Kala Azar area. There was no evidence of Kala Azar in the patient from whom the monkey was inoculated, and no Leishmania found in the spleen of the other monkey inoculated

from the same patient.

This is the first record of *Leishmania* occurring naturally in a monkey. Its presence would seem to have been subclinical, perhaps made obvious by only the debilitating effect of the spirochaetal infection. This observation has been more fully explored in a separate study.

MONKEY R.(2).

- 23/12/37. At Sennar. Inoculated intraperitoneally with 1 c.c. blood from the same case as monkey R.(1).
24/12/37. Blood negative.
25/12/37. Blood positive, infection of moderate severity.
26/12/37. Blood positive.
27/12/37. Blood negative. There was no relapse in this monkey. The blood remained consistently negative until
24/1/38. At Khartoum North. Inoculated intraperitoneally with 1 c.c. blood from the same case as monkey R.(1).
25/1/38. Blood negative.
26/1/38. Blood negative.
27/1/38. Blood positive, infection of moderate severity. Under ether anaesthesia splenectomy done and about 0.2 c.c. of blood inoculated directly into the peritoneum of:-
2 splenectomised mice (Typical infection).
28/1/38. Blood positive.
29/1/38. Blood positive.
30/1/38. Blood positive.
31/1/38. Crisis. Agglutinating and fragmenting forms only seen in the blood, and very scarce.
1/2/38. Blood negative. No relapse. Blood remained negative for the next fourteen days.
5/3/38. At Khartoum. Inoculated intraperitoneally with $\frac{1}{2}$ c.c. blood from monkey R.(4) at a time when spirochaetes were abundant in the blood.
6/3/38. Blood negative, and continued to be so for the next fourteen days.

MONKEY R.(3).

- 26/12/37. At Khartoum. Inoculated intraperitoneally with $\frac{1}{2}$ c.c. blood containing numerous spirochaetes from monkey R.(1).
- 27/12/37. Blood negative.
- 28/12/37. Blood positive, infection of moderate severity. Under ether anaesthesia blood withdrawn from the heart and about 0.2 c.c. inoculated into:-
1 mouse: 1 guinea pig: 1 rabbit.
- 29/12/37. Blood positive.
- 30/12/37. Blood positive.
- 31/12/37. Blood negative. Continued negative until 8/1/38.
- 8/1/38. Blood positive, infection of moderate severity.
- 9/1/38. Blood positive - scanty infection.
- 10/1/38. Blood negative.
- 11/1/38. Blood negative and continued negative for the following eighteen days.
- 5/3/38. Inoculated intraperitoneally with $\frac{1}{2}$ c.c. blood containing abundant spirochaetes from monkey R.(4).
- 6/3/38. Blood negative.
- 7/3/38. Blood positive, infection of moderate severity.
- 8/3/38. Blood positive.
- 9/3/38. Blood positive.
- 10/3/38. Blood negative. No further relapse during the following eighteen days.

MONKEY R.(4).

- 2/12/37. Splenectomy under ether anaesthesia.
- 3/12/37. Bitten by eight ticks, batches A. and B. and tick coxal fluid inoculated subcutaneously.
- 14/12/37. Bitten by five ticks, and coxal fluid inoculated subcutaneously.
- 20/12/37. Bitten by six ticks and the coxal fluid inoculated subcutaneously.
- 24/1/38. Inoculated percutaneously with an emulsion of eight lice taken from a case in Khartoum North. No infection resulted from this: lice negative for spirochaetes on microscopical examination.
- 26/2/38. Inoculated percutaneously with a portion of the haemocoel fluid of a louse taken from a case in Omdurman.
- 27/2/38. Blood negative.
- 28/2/38. Blood negative.
- 1/3/38. Blood negative.
- 2/3/38. Blood positive, heavy infection.
- 3/3/38. Blood positive.
- 4/3/38. Blood positive.
- 5/3/38. Blood positive, infection very heavy, almost as many spirochaetes as red blood cells.
- 6/3/38. Blood positive: monkey very dull, and ate no food today.

Monkey continued to have a heavy blood infection, lost flesh rapidly till on the morning of 10/3/38 it was unconscious and moribund. The animal died that evening.

MONKEY R.(5).

5/12/37. Splenectomy, under ether anaesthesia.
14/12/37. Inoculation subcutaneously of tick contents.
20/12/37)
26/12/37) Various attempts were made on these dates to
12/1/38) infect the monkey by subcutaneous inoculation
25/1/38) of material from ticks, but no infection
2/2/38) resulted.
8/2/38)
5/3/38. Inoculated intraperitoneally. $\frac{1}{2}$ c.c. blood
rich in spirochaetes from monkey R.(4).
7/3/38. Blood positive and continued to be positive until
10/3/38. Blood negative. Continued negative until 15/3/38.
15/3/38. Blood positive, heavy infection. Continued
positive until
21/3/38. Blood negative. Continued negative during the
next three days until
24/3/38. Blood positive, heavy infection.
25/3/38. Blood negative.
26/3/38. Blood negative.
27/3/38. Blood negative.
28/3/38. Blood negative.

It was not possible to follow out this infection any further. No further blood examinations were made.

MONKEY R.(6).

24/12/37. Splenectomy under ether anaesthesia.
26/12/37)
12/1/38)
25/1/38) Various attempts made on these dates to infect
30/1/38) the monkey by subcutaneous inoculation of
2/2/38) material from ticks but no infection resulted.
8/2/38)
20/2/38. Inoculated percutaneously with emulsion of
eight *Pedicinus* collected from monkey R.(2)
twenty days after the disappearance of the
spirochaetes from its blood. No infection
resulted.
20/3/38. Inoculated with about 0.2 c.c. blood from
monkey R.(7).
23/3/38. Blood positive.

This infection was not followed out. It proved, however, that the monkey was susceptible.

MONKEY R.(7).

- 1/3/38. Splenectomy under ether anaesthesia.
5/3/38. Inoculated intraperitoneally with $\frac{1}{2}$ c.c. blood rich in spirochaetes from monkey R.(4).
6/3/38. Blood negative.
7/3/38. Blood positive, infection of moderate severity. Continued positive for five days until
12/3/38. Blood negative.
13/3/38. Blood negative.
14/3/38. Blood negative.
15/3/38. Blood negative.
16/3/38. Blood positive, heavy infection. Continued positive, with a heavy infection for the following nine days until
25/3/38. Blood negative.
26/3/38. Blood negative.
27/3/38. Blood negative.
28/3/38. Blood negative.

It was not possible to follow out this infection any further. No further blood examinations were carried out.

MONKEY R.(8).

- 5/3/38. Inoculated intraperitoneally with $\frac{1}{2}$ c.c. blood rich in spirochaetes from monkey R.(4).
6/3/38. Blood negative.
7/3/38. Blood positive, infection of moderate severity.
8/3/38. Blood positive.
9/3/38. Blood positive.
10/3/38. Blood negative. Continued negative until
18/3/38. Blood positive, heavy infection.
19/3/38. Blood negative.

No further relapse was recorded. Blood was examined until 28/3/38 by me and for a further ten days by another.

(E) TRANSMISSION OF INFECTION

- I. TRANSMISSION BY THE LOUSE.
- II. TRANSMISSION EXPERIMENTS WITH TICKS.
- III. DISTRIBUTION AND HABITS OF ORNITHODORUS SAVIGNYI IN THE SUDAN.
- IV. METHODS.
- V. RESULTS:-

EXPERIMENTS WITH ARGAS AND PEDICINUS.

TRANSMISSION BY THE LOUSE.

Spirochaetes found in lice. It has been possible to demonstrate that the louse is the intermediate host of the relapsing fever under study. It may be said that 100 per cent. of the returning immigrants were lousy, and a minimum of eight lice could readily be obtained from any one of them.

Metacyclic forms of the spirochaete were found in the haemocoel fluid of lice from infected persons. Compared with the organisms found in the blood these forms are smaller, finer, and more regularly spiral in structure. Stained by Leishman's method they do not show the same tendency to twist themselves into figures of eight and other coiled or irregular forms. They were frequently found in enormous numbers, forming large tangled masses in the haemocoel of the louse (Fig.14).

The best method of demonstrating the spirochaetes in the louse was found to be that described by RIDING and MACDOWELL (1927). The louse was seized with fine forceps, and laid on its back in a small drop of distilled water on a clean slide. The abdomen was transfixed by a needle, lateral to the gut, and the haemocoel fluid allowed to escape from the puncture, the movements of the louse's legs assisting the mixing of the haemocoel fluid and the water on the slide. The fluid could then be examined by dark ground illumination or allowed to dry in the air and stained by Leishman. This method was infinitely superior to making smears of crushed lice, and gave admirable preparations, free from debris. The lice were kept in a test-tube for twenty-four hours between removal from the

patient and examination for spirochaetes.

The percentage of infected lice varied in different cases, presumably according to the duration of the disease, although it was not possible to verify this as histories were unreliable, and steps were taken to cut short the disease with treatment as soon as the diagnosis was verified under the microscope. Most commonly 15 - 20 per cent. of the lice were found infected. In 30 per cent. of cases no infected lice were found. In one case which was investigated in Kassala the infection rate was as high as 60 per cent. (six infected out of a total of ten lice obtained from the patient's clothing).

No infected nits found. Both male and female lice were found to be infected. No evidence of hereditary transmission in the louse was found, although large numbers of nits were examined, including a number actually deposited in captivity by infected lice. Microscopical examination alone was made: the nits were crushed on a slide and examined under the high power, stained by Leishman. No animal inoculation experiments were carried out, so that the possibility of hereditary infection by an invisible granule stage was not investigated.

Transmission of the disease to monkey from louse. The spirochaetes in the lice were motile under dark ground illumination, and they were able to reproduce the disease in monkeys. Only one successful transmission experiment was carried out, but this took place under somewhat dramatic circumstances.

A blood slide from a patient admitted to the Church Missionary Hospital in Omdurman on 24/2/1938 was

found to be positive for relapsing fever. The hospital was informed, and it was requested that the lice (if any) from this patient be collected and transmitted to me. Unfortunately, it transpired that the patient had already been washed and his clothes removed for disinfection.

The following day, however, owing to the vigilance of the Medical Officer of Health, Khartoum, a single louse was found on a pair of pants which must somehow have escaped the delousing process, although removed from the patient. This louse was given a feed from the writer's arm, and kept for another day at 37°C.

On 26/2/1938 this louse was transfixed on a slide and its haemocoel fluid was allowed to mix with distilled water in the manner described above. Some of this fluid was rubbed into a small scarified area on the shaved abdomen of a splenectomised monkey, and allowed to dry, as in a vaccination. The residue on the slide was stained by Leishman's method, and examined microscopically. It was found to contain spirochaetes.

After an incubation period of four days spirochaetes appeared in the monkey's blood. During the next eight days they became progressively more numerous, until there appeared to be as many organisms as red blood cells. The monkey became obviously ill on 6/3/1938 and died on 10/3/1938, eight days after the first appearance of the spirochaetes in the blood.

According to this observation the disease acquired from the louse is more virulent than that which results from the inoculation of blood containing spirochaetes. In no other experimental animals were the spirochaetes observed in the peripheral blood in such enormous numbers

as in this monkey, which was, moreover, the only animal to die in the first paroxysm of experimental relapsing fever. Although this is in accord with the experimental findings in tick-borne relapsing fever, LIPSTEIN (1936) working with S. novyi, found that the infection derived from lice was always benign, while that which followed the inoculation of infected blood was always fatal.

The writer did not develop relapsing fever, nor did he expect to do so. On two occasions it was necessary to feed infected lice on my own blood in order to keep them alive until such time as it was possible to examine them. I was well aware of NICOLLE, BLAIZOT and CONSEIL'S (1913) work on the mechanism of transmission, and was confident that the risk was negligible, provided care was taken not to crush or injure the lice.

A similar attempt had previously been made to infect this monkey by means of lice, thirty days earlier, but was unsuccessful. In this instance, however, examination of stained smears of the haemocoel fluid of the lice showed that the latter were not infected.

It was considered that these experiments, together with the results of animal inoculation, and the demonstration of infected lice in a large proportion of the human cases were sufficient to incriminate the louse as the vector, and no further experiments were carried out along these lines.

TRANSMISSION EXPERIMENTS WITH CERTAIN TICKS.

It was suggested many years ago by NICOLLE and ANDERSON (1926) that the epidemiology of louse-borne relapsing fever would ultimately be clarified by the discovery of some reservoir, most probably a tick, in which the virus was able to persist for long periods independently of the human host. This hypothesis would obviously be strengthened if it could be shown experimentally that the louse-borne strains were able to persist in ticks, and to be transmitted once more to susceptible animals through the medium of these arthropods. But the carefully devised experiments of NICOLLE, BLAIZOT, and CONSEIL (1913) to transmit the Tunisian louse-borne strain by means of Ornithodoros savignyi gave only negative results, and other workers have recorded similar failures.

SARGENT and FOLEY (1910) failed to transmit the Algerian strain by means of Argas persicus. BRUMPT (1908) also was unable to transmit either this strain or the American strain by Ornithodoros moubata. BALFOUR (1911) recorded negative attempts with the Egyptian strain, and Ornithodoros savignyi, and INGRAM (1924) was unable to transmit the Gold Coast strain by Ornithodoros moubata. More recently BRUMPT (1936a) and FENG and CHUNG (1937) failed independently to transmit the Chinese louse-borne strain by Ornithodoros moubata.

On the other hand the text-books all record that MANTEUFEL (1908), NEUMAN (1909), and SCHUBERG and MANTEUFEL (1909) succeeded in transmitting the Russian and American strains by means of Ornithodoros moubata. I have been unable to consult the original papers of these authors, but BRUMPT (1936a) criticising this work points out that nothing is

known of the conditions under which these experiments were carried out. The incubation periods in the rats infected by tick bites were apparently unduly long and, as the spirochaetes were shown to be readily transmissible by rat lice, BRUMPT suggests that the infection was transmitted in reality by these parasites, and not by the bites of the Ornithodoros ticks.

A further criticism may be made of the experiments of NEUMAN and MANTEUFEL in that there seems to be some doubt as to the origin of the strains used by these authors. The 'Russian strain' studied by them was in all probability the so-called 'Frankfurt strain' which has been maintained in Germany in rats since 1907, and the original history of which has been lost. More recently BRUMPT (1936b) concluded from an experimental study of this strain that it was not a true S. recurrentis, but a strain of S. duttoni which had become modified in various interesting ways by the continued passage through rats.

The confusion which may arise from the employment of laboratory strains the origin of which is in any way doubtful has been emphasized in a special paper by NICOLLE and ANDERSON (1929), who recommend that such doubtful strains should be discarded.

In spite of these failures to transmit the louse-borne strains by the intermediary of ticks the possibility still exists that in some country strains may be found having the special aptitude of surviving in ticks, just as there are some strains which are readily inoculable from man to other animals and some which are not.

As this Abyssinian strain had not to my knowledge, previously been studied, it seemed of interest to ascertain

whether it was able to persist in ticks or not. This appeared, moreover to be a matter of no small practical importance from the point of view of prevention, as it would enable one to estimate how far intensive measures directed against lice might hope to be successful in eradicating the disease from the Sudan.

Experiments were therefore carried out to determine whether this strain could persist in Ornithodoros savignyi. This particular tick was chosen for numerous reasons.

REASONS FOR SELECTING ORNITHODORUS SAVIGNYI.

In the first place this tick was readily available in sufficient numbers for experimental purposes. Some experiments with Ornithodoros moubata also would have been admittedly desirable, but this tick was quite unobtainable.

It has been shown by NICOLLE, ANDERSON and, COLAS-BELCOUR (1928), and BRUMPT (1908) that under experimental conditions Ornithodoros savignyi can transmit all the varieties of relapsing fever transmissible by Ornithodoros moubata. Thus if this Abyssinian ^{Strain} can survive in ticks there is no a priori reason to believe that experiments with Ornithodoros savignyi are less likely to be successful than those carried out with other ticks.

It will be seen from the map in Fig.5 that if any Ornithodoros tick plays a part in the epidemiology of relapsing fever in the Northern Sudan it is most likely to be O. savignyi.

Attention has already been drawn to the fact that the relapsing fever concerned is apparently being

introduced from the countries on the Eastern border of the Sudan. Ornithodoros savignyi has been cited as one of the principal vectors in at least two of those countries, Abyssinia (BRUNS, 1937) and Somaliland (DRAKE-BROCKMAN, 1915, CLARKE, 1936).

Certain further epidemiological features of the disease in the Sudan seemed to throw suspicion on this tick. These are, firstly, the well-marked seasonal incidence of the disease after the rain, at which period, our observations suggest, this tick is more prevalent and more active. CLARKE (1936) has drawn attention to the striking seasonal incidence of the Somaliland disease, which is rather an unusual feature in the tick-borne infection.

Even more suggestive is the fact that Ornithodoros savignyi is not a house tick, but occurs typically under trees and in other similar situations out of doors. The relapsing fever in the Sudan occurs almost exclusively in persons who do not live in houses viz, wandering negroids from the West, who take their mid-day rest and make their camping grounds for the night in just such places as are frequented by Ornithodoros savignyi.

DISTRIBUTION AND BIONOMICS OF ORNITHODORUS SAVIGNYI IN THE SUDAN.

DISTRIBUTION.

Ornithodoros savignyi resembles O.moubata very closely but differs from it by the possession of eyes and in certain other minor anatomical details. It is the most xerophilic of the Ornithodoros ticks. In Africa its geographical distribution overlaps to some extent that of

O. moubata. In the Sudan it is widely distributed throughout the arid North, but absent from the more humid South.

Ornithodoros moubata, on the other hand, does not occur in Northern Sudan, though it has been observed in Mongalla province, in the South. The distribution of Ornithodoros ticks in the Sudan is illustrated by the map in Fig.5, the names underlined being those of places where the writer has personally identified O. savignyi.

BIONOMICS.

O. moubata is exclusively a human tick, and is found typically in houses, rest houses and other dwellings. The hosts of O. savignyi, on the other hand, are various, including man and most of the domestic animals, such as sheep, camels, horses and dogs. One has occasionally found this tick in the compounds of native houses, particularly those of the more prosperous individuals, whose numerous stock animals are herded into the compounds at night. Most commonly, however, it is found in outdoor situations, where animals are frequently tied up or confined, or in the sand under the trees surrounding desert wells. Here the ticks conceal themselves under the sand, and there may be no indication of their presence until some unsuspecting host seeks rest in the shade of a nearby tree. By some unknown means the ticks become aware of the new arrival, and only a few minutes elapse until the first tick works its way out of the sand and proceeds towards its prospective host. A few moments later another appears and yet another, until, within half an hour or so, upwards of a hundred ticks may be advancing upon the host or actually in situ feeding. The way in which each tick on emerging from the sand starts

at once in the straightest line for its prospective host is almost uncanny. The bite is distinctly perceptible, and raises a wheal which may remain uncomfortable for days. We have seen a horse tied up under a tree where these ticks were abundant become literally frantic as a result of the numerous bites. In Kerdofan, camels tied barracked in compounds heavily infested with these ticks have been known to die within a few days as a result of the massed attack to which they are subjected.

The eggs of O. savignyi, few in number, are deposited in the sand, and hatch in about ten days. The six-legged larvae cannot be induced to feed, but after 3 - 4 days, moult, and become eight-legged nymphs which bite readily.

Apart from rare accidents it is difficult to know what the natural hazards of these ticks are. They can resist drought and starvation for many months, but in the laboratory we have never been able to keep them longer than one year without a feed. They are readily eaten by poultry, and perhaps also by other birds. We have observed fully gorged, but otherwise healthy ticks being subjected to a mass attack by ants, which rapidly demolish them, by eating a hole in the cuticle and then eating out the soft internal parts. Whether this is a frequent occurrence in nature or not it is impossible to say.

METHODS

The methods employed consisted essentially in allowing ticks to bite infected persons or animals. Thereafter, at varying periods, attempts were made to infect susceptible animals by the bites of these ticks, by the inoculation of the coxal fluid, and finally by the inoculation of the total contents of the ticks, emulsified in saline.

To avoid the many pitfalls which beset experiments of this nature, particular attention was paid to detail, the importance of which is emphasised by consideration of previous experiments recorded in the literature.

The common grey grivet monkey of the Sudan (Cercopithecus Sebacus) was chosen as the animal most likely to be infected from the ticks, because, of the animals at our disposal, it was undoubtedly the most susceptible to the disease. It was important that the specimens used should be as sensitive as possible to the infection, in order to obviate light infection, which might be missed, or latent infections of the type found by VELU, BALOZET, and ZOTTNER (1930) in rabbits. With this in view the monkeys were splenectomised, as our own results and those of several other workers had shown that the effect of this operation, if anything, was to increase the susceptibility to relapsing fever.

The monkeys were obtained with the help of local natives from the woods of the Sennar and Singa districts of the Sudan, and were all young animals. NICOLLE and ANDERSON (1927b) say that no wild animals should be used for experimental work with relapsing fever, as so many of

them may harbour latent natural spirochaetal infections. It was fully realised that these monkeys were in all probability the same species in which PLIMMER (1912) found spirochaetes in the London Zoo, and that RANKEN (1912) has recorded from the Southern Sudan a natural spirochaetal infection in the allied Cercopithecus ruber. Except for white mice, however, no laboratory animals were found susceptible. A few experiments with white mice were carried out, but it is doubtful if even these animals can be regarded as absolutely safe, since VINZENT (1927) has recorded the spontaneous appearance of a spirochaete in a 'Clean' laboratory-bred strain of mice after inoculation with trypanosomes. To exclude any which showed obvious spirochaetes, the blood of all our monkeys was examined before they were used for experiment but was invariably negative.

At an early stage of this work a monkey was found which appeared to be quite insusceptible to the spirochaetal infection. Because of this, the further precaution was taken of proving that the animals used for the transmission experiments were susceptible before negative results were accepted. This was done by inoculating them directly with blood containing spirochaetes, after the conclusion of the transmission experiments.

All the monkeys were found naturally infested with lice (Pedicinus sp.). Although attempts to transmit the spirochaetes experimentally by these lice were unsuccessful, precautions were taken to segregate monkeys which had been infected to exclude the possibility of any transference of ectoparasites from infected to healthy monkeys. It may be recalled that BRUMPT (1936b) has

discredited the experiments of NEUMAN and MANTEUFEL on the grounds that this precaution was probably omitted. The animal houses in Khartoum are mosquito proof, thus obviating the possibility of mechanical transmission by Stomoxys (SCHUBERG and KUHN, 1911) and tabanids, which are common enough in the vicinity.

As HINDLE (1911), SCHUBERG and MANTEUFEL (1910) and KLEINE and KRAUSE (1932) have shown that a certain proportion of Ornithodoros seem to be insusceptible to spirochaetal infection, care was taken to use a sufficient number of ticks to exclude fallacy arising from this cause.

NICOLLE, ANDERSON and COLAS-BELCOUR (1928) maintain that the nymphs of a vicarious vector can often be infected when the adults cannot, and stress the necessity for using nymphs as well as adults in transmission experiments. This is denied by KLEINE and KRAUSE (1932) and also by KRITSCHIEWSKI and DVOLAITSKAYA-BARISCHEWA (1931), but in order to ensure that the optimum possible conditions for the infection of the ticks were presented a certain proportion of nymphs was used in the transmission experiments.

As the experiments were designed to find out whether O. savignyi could act as a true vector and not whether mere mechanical transmission was possible, it was necessary to ensure that sufficient time elapsed between the infective feed and any attempt to transmit the spirochaete to a new host by means of the tick. HINDLE (1911) has shown that spirochaetes may persist up to four weeks in the alimentary canal of the tick after a feed. At least one month was allowed therefore, except in the case of the first two batches of ticks, when feeding experiments only

were carried out after a lapse of less than a month. Tissue emulsion from the ticks were not inoculated in any instance until at least a month had elapsed from the date of the infective feed.

BORREL and MARCHOUX (1905) and later MARCHOUX and COUVY (1913) have stated that Argas loses its power to transmit fowl spirochaetes if kept in the cold, but regains it after 2 - 3 days at 30° - 35°C. We therefore made a practice of keeping the ticks in the incubator (37°C) for about five days before trying to infect animals from them. Although BRUMPT (1936c), as a result of experiments and observations in ^{nature} natives disagrees with the findings of BORREL and MARCHOUX, HINDLE (1911) and other workers have shown that the procedure of 'warming' the ticks for a few days results in an active development and multiplication of the spirochaetes, thereby making them more readily visible in the secretions of the tick, or in its tissues during dissections.

In the earlier attempts of the writer to transmit the spirochaete by ticks, feeding experiments, examination of the coxal fluid, dissections and examinations of the tissues of the ticks were carried out. This is a tedious process, and sometimes it was difficult to induce the ticks to feed in the required numbers at a given time. It was found that the only satisfactory method entailed having the host animal spread-eagled on a board and firmly tied down. In an early experiment when attempts were being made to induce ticks to bite a mouse, the mouse bit and killed two of the ticks.

After a number of negative results these detailed methods were discarded and reliance was placed on simple inoculation of the total contents of the tick. This was obtained by opening the tick dorsally, and gouging out all the soft tissues. A saline emulsion of these soft tissues was made, Griffiths' tubes being found particularly suitable for this purpose. The emulsion was filtered through glass wool and inoculated into the animal.

For these inoculations the subcutaneous route was always used, as the material inoculated was certain to be contaminated with organisms of various sorts. No abscesses resulted, however, although by the time the experiments were concluded two of the monkeys had indurated areas in the subcutaneous tissues at sites where several inoculations had been given.

NICOLLE and ANDERSON (1927a) have pointed out that infection following inoculation of the tissues of a supposed vector cannot be regarded as evidence that this vector is capable of transmitting the disease in nature. This objection would have been of prime importance had our results been positive, but as they were consistently negative this method provided the most complete proof that the spirochaetes had disappeared entirely from the tissues of the ticks.

An ample supply of ticks was held in reserve to be used as controls in the event of a positive transmission being recorded, but were not required. Batches of ticks from Khartoum, El Obeid, and from Kassala were dissected, and smears made from their tissues, but no sign of spirochaetes was ever encountered.

The following is a brief record of the transmission experiments carried out with Ornithodoros savignyi:-

(I) FEEDING EXPERIMENTS

- Batch A. 13/11/37. Twelve ticks were fed on a case of relapsing fever in Sennar. Two ticks were found dead three days after the feed.
- Batch B. 13/11/37. Twelve ticks were fed on a second case in Sennar. One tick died three days after the feed.
- Batch C. 22/11/37. Twelve ticks were fed on a case in Kassala. One tick died.
- Batch D. 22/11/37. Twelve ticks were fed on a second case in Kassala.
- Batch E. 25/11/37. Twelve ticks were fed on a third case in Kassala. This case was a definite relapse. One tick was found dead four days after the feed.
- Batch F. 26/12/37. Eighteen ticks and thirty nymphs were fed on Monkey R.(2) during first attack of fever after inoculation from a case in Sennar. Two ticks died three days after the feed.
- Batch G. 27/12/37. Sixteen ticks and thirty nymphs were fed on Monkey R.(1), inoculated in Sennar from the same case as Monkey R.(2). One tick died.
- Batch H. Eight ticks. Four were fed on 27/11/37 on two mice inoculated from Monkey R.(1), the other four were fed on 28/12/37 from two mice inoculated from Monkey R.(3).
- Batch J. Eighteen ticks and twenty nymphs were fed on monkey R.(2) inoculated from a case in Sennar. The monkey relapsed, and the ticks of this batch were fed during the relapse.

(II) ATTEMPTED TRANSMISSIONS

- 1/12/37. Eight ticks, four from Batch A. and four from Batch B. were allowed to bite Monkey R.(4), and the coxal fluid exuded at the time of the bite was sucked up in a syringe and inoculated subcutaneously into the monkey.

- 4/12/37. Three ticks from Batch B. were induced to bite a white mouse, and the coxal fluid was inoculated into the mouse. Two ticks from Batch A. were lost by being killed by the mouse.
- 10/12/37. Four ticks from Batch A. were induced to bite two white mice, and the coxal fluid inoculated subcutaneously. The ticks were dissected, and smears made from the gut, malpighian tubes, and the haemocoel fluid. Fungal bodies only discovered: no spirochaetes.
- 14/12/37. Five ticks from Batches A. and B. were allowed to bite Monkey R.(4). Coxal fluid collected and inoculated subcutaneously. The ticks were dissected and smears from gut, haemocoel, and malpighian tubes proved negative, except for fungal organisms. Total contents of ticks inoculated into Monkey R.(5).
- 20/12/37. Six ticks from Batches A. and B. were allowed to bite Monkey R.(4). Coxal fluid was inoculated. Smears were made from gut, haemocoel and malpighian tubes of four ticks. Total contents of ten ticks were inoculated subcutaneously into Monkey R.(5).
- 26/1/38. Total contents of eleven ticks (Batch C) were inoculated into Monkeys R.(5) and R.(6).
- 12/1/38. Total contents of twelve ticks (Batch D) inoculated subcutaneously into Monkeys R.(5) and R.(6).
- 25/1/38. Total contents of nineteen ticks (Batches E. and H) were inoculated subcutaneously into Monkeys R.(5) and R.(6).
- 30/1/38. Total contents of sixteen ticks (Batch F) were inoculated into Monkeys R.(5) and R.(6). Smears from gut, haemocoel and malpighian tubes of two ticks from this batch were examined and found negative.
- 2/2/38. All the nymphs of Batches F. and G. were ground up in saline and inoculated into Monkeys R.(5) and R.(6).
- 8/2/38. Nymphs and contents of ticks (16) of Batch J. were emulsified in saline and inoculated into Monkeys R.(5) and R.(6).

RESULTS

The results of these experiments were entirely negative, although a variety of strains was used. Care was taken to include relapse strains as well as those from the original infection, and strains which had been passed through monkeys and mice as well as strains taken directly from human patients. The blood of the animals whose infection was attempted was examined daily during the course of the experiments, and for twenty days after the last attempt was made to infect them, but spirochaetes were never found, although the animals were later shown to be susceptible. Nor were spirochaetes ever found by dark-ground examination of the coxal fluid exuded by the ticks, nor in stained smears of the tissues of the ticks.

A curious organism was almost invariably found in the tissues of the ticks examined, more particularly in the malpighian tubes. Sometimes the organism appeared as bacillary forms, of various length: at other times it had a filiform septate appearance, and resembled the mycelium of a fungus more than anything else. This organism was found in ticks which had not fed on infected blood as well as in those used in the experiments. On two occasions attempts were made to remove a piece of malpighian tube under aseptic conditions, and grow the organism from it, in broth. In both instances a fungus appeared in pure culture in the broth. In its general features this fungus resembled so closely some of the ordinary air-borne fungi which are found everywhere in the tropics that it was difficult to be sure it was not a contamination without the opinion of a competent mycologist. Many years ago BALFOUR (1911b) observed what appears to have been the same organisms in these ticks, but I have found no other reference to it.

Possibly it is a symbiotic organism such as have been described in a great number of other haematophagus animals.

Another interesting fact noticed during these experiments was that a certain proportion of the ticks died some 2 to 3 days after a meal of infected blood. Smears always revealed spirochaetes in the gut of these ticks after death, similar in appearance to those found in the blood, and where dark-ground examination was done the spirochaetes were motile. No attempt was made to investigate the reason for these deaths among the ticks. The observation is merely recorded, and it is not possible to say at present whether the deaths were due to the spirochaetes, to the blood from an unusual host or to some other reason.

EXPERIMENTS WITH OTHER ARTHROPODS.

Argas persicus. One attempted transmission was carried out with Argas persicus, a tick which has been cited as the vector of relapsing fever in Persia (WRIGHT and HAROLD, 1920), in Quetto (BROWSE, 1912) and in Palestine (NICHOLSON, 1919), all on very questionable evidence. This tick is widely distributed throughout the Northern Sudan, where it can be found in any village infesting principally domestic poultry. Like other ticks it can live for long periods between meals - we have kept some for ten months without food or water, during which period they not only survived, but produced eggs, from which young emerged. These ticks can usually be found in the 'suk' or market where poultry are sold, and also in most native compounds, as the Sudanese commonly share their living accommodation with their domestic animals.

On 8/1/38, eight adult Argas were induced to feed on a monkey which had numerous spirochaetes in the peripheral blood. Six weeks later the soft tissues of these ticks were emulsified in saline and inoculated into two white mice, but no infection resulted.

SERGENT (1933) and SERGENT and LEVY (1935) have drawn attention to the possible role of the dog tick (Rhipicephalus sanguineus) as a vector of relapsing fever. It is perhaps to be regretted that no experiments were conducted with this tick for like Argas persicus it is widely distributed in the Sudan and readily obtainable. At the time I was unaware of SERGENT and LEVY'S work.

At the instigation of MAJOR H.C. BROWN, of the Wellcome Bureau of Scientific Research, attempts were made to obtain specimens of the bug Bragada picta which he had suspected of playing some part in the transmission in India, in order to find out if the spirochaetes could persist for any length of time in this arthropod. I was unable to obtain any specimens of this bug.

No experiments were carried out with the bed bug. This parasite has once again been brought under suspicion as a possible reservoir by the experiments of ROSENHOLZ quoted by HINDLE (1932). The bed bug is widely distributed throughout the Sudan, but as it is strictly a house-frequenter it is unlikely to play an important part in the epidemiology of the Sudan disease. In practice, it seemed reasonable to accept ROSENHOLZ'S work as defining sufficiently the possibility of this arthropod acting as a vicarious vector.

Some work was carried out with regard to the ability of the lice found naturally on the monkeys (Pedicinus) to transmit the disease. During the experiments with the

Ornithodoros it was stated that care was taken to prevent possible infection of one monkey from another by the agency of these lice, as MANTEUFEL and NEUMAN had found the European strain easily transmissible by the rat louse. FENG and CHUNG (1937) found likewise that the Chinese strain was transmissible by the squirrel louse from one squirrel to another. On 4/1/38 lice were collected from Monkey R.(1) which had spirochaetes in its blood on that day, and had had a three day attack some ten days previously. Twelve lice were collected, of which six were examined microscopically in crushed smear preparations, and six ground up in saline and inoculated into a gerbille, after a fast of 24 hours. The gerbille did not develop an infection. In the smears of the lice spirochaetes were found in fair numbers, but in their shape and disposition they resembled those seen in the blood, rather than the metacyclic forms, although they were relatively much more numerous than the red blood corpuscles, which had presumably largely been digested.

Sixteen days later, a further six lice were collected from this monkey, and another attempt made to infect the gerbille but it was unsuccessful. The lice were not examined on this occasion.

On 20/2/38 eight lice were collected from Monkey R.(2) which had had spirochaetes in its blood twenty days previously. These were ground up in saline and inoculated percutaneously into a splenectomised monkey but no infection resulted. On this occasion also the lice were not examined microscopically.

When Monkey R.(4) died after eight days of experimental relapsing fever, ten lice were collected from

its body and examined. Abundant spirochaetes were found in some of these lice, even when no blood corpuscles were observed. These spirochaetes, however, resembled the forms seen in human blood in being thicker and more irregular than the forms commonly seen in Pediculus. As far as one could make out they appeared to be restricted to the alimentary canal.

In the smears examined appearances were seen which suggested that the spirochaetes were actually boring their way into the cells of the gut, coiling up inside them, and breaking up into granules. It is impossible to say whether this represents invasion of the tissues by living organisms, or merely phagocytosis of the spirochaetes. The negative transmission experiments suggest the latter, but they are comparatively few in number, and it may be mentioned that it appears much more difficult to obtain positive transmission results with lice than with ticks. WENYON (1926) remarks on the scarcity of experimental transmissions from the louse. In the cells of Pedicinus bacteria were also constantly present. They were, however, easily recognisable as such, and not likely to be confused with disintegrating spirochaetes.

GENERAL CONCLUSIONS.

Working with spirochaetes from some of the Egyptian cases, BALFOUR (1911) concluded that the louse was the vector: he was unable, moreover, to infect ticks (Ornithodoros savignyi and Argas persicus) with these spirochaetes. RIDING and MACDOWELL (1927) showed that the Darfur epidemic was louse-borne, and INGRAM (1924) working

in West Africa with what was presumably the same strain of spirochaete, was unable to infect Ornithodoros moubata. The present writer has been able to show that the Abyssinian disease which invaded the Sudan during 1936 - 1937 was also louse-borne, and was unable to infect ticks (Ornithodoros savignyi and Argas persicus).

No experimental work was carried out in connection with the few cases which occurred in the Southern Sudan in 1925 and 1934, so that it is possible that these may have been due to tick-borne infections: those which occurred in Mongalla in 1925 almost certainly were. No views can be expressed as to the origin of the infection which was found by RANKEN (1912) in the monkey.

It has already been pointed out that the southward spread of louse-borne relapsing fever is likely to be limited by the freedom from louse-infestation which is enjoyed by the naked Southern races. It is unlikely also that tick-borne infections will become established in the Northern Sudan, owing to the absence of a suitable vector. It will be seen from map in Fig.5 that the distribution of Ornithodoros ticks in the Sudan appears to be limited to O. savignyi in the North and O. moubata in the South. Although the former tick has been regarded at different times as the probable vector of relapsing fever in Abyssinia (WENYON, 1926), in British Somaliland (DRAKE-BROCKMAN, 1915) and in Angola (WELLMAN, 1905), these conclusions are based on general considerations only, and have not been substantiated by laboratory findings. It is true that under experimental conditions Ornithodoros savignyi can transmit all the varieties of relapsing fever transmissible by Ornithodoros moubata. But the infection

is not passed on to the next generation in the case of Ornithodoros savignyi, and it is possibly for this reason, as BRUMPT (1936d) has suggested, that the latter tick has not been found naturally infected in any country. Batches of Ornithodoros savignyi from various parts of the Sudan have at different times been examined by ARCHIBALD (1910), BRUMPT (1936d) and by the present writer, but on no occasion has any evidence of spirochaetal infection been found.

The epidemiology of relapsing fever in the Northern Sudan can probably therefore be regarded as that of the louse-borne infection alone. Moreover, although the disease has been introduced at different times from three separate and distinct sources of infection, all attempts to infect ticks with the particular strain of spirochaetes concerned on each occasion have been unsuccessful. As far as the Northern Sudan is concerned, therefore, no evidence can be found that these arthropods have played any part whatsoever in the epidemiology of relapsing fever.

(F) OBSERVATIONS ON THE HUMAN DISEASE.

I. EPIDEMIOLOGY

(a) GENERAL REMARKS

(b) INCIDENCE

(c) RELATION TO OTHER DISEASES.

II. CLINICAL FEATURES AND TREATMENT.

III. PATHOLOGY.

IV. PREVENTION.

EPIDEMIOLOGY.

GENERAL REMARKS.

It is stated (SELWYN CLARKE, LE FAUN and INGRAM, 1923) that epidemics of relapsing fever begin slowly and increase in virulence and infectivity. In the Sudan the epidemic of 1926 began with explosive violence. By 1930 the virulent disease of 1926 had become a relatively benign infection with a mortality of 10 per cent. instead of 70 per cent., and the appearance of healthy carriers whose infection was entirely subclinical, although spirochaetes were readily found in their blood (ATKEY, 1932). It is suggested that this epidemic died out during its passage across the Sudan, as epidemics frequently do (CURRIE, 1929), by progressive enfeeblement of its contagium. There seems to be no evidence to connect this epidemic with the 1929 epidemic in the Djig region of Abyssinia (BRUNS, 1937), nor with the reappearance of the disease in the Sudan in 1936.

It is, of course, theoretically conceivable that the disease of 1936 might be merely a reactivation of the 1926 disease, which had meantime lain dormant in some reservoir, or in residual brain infections, which became active again as a result of malaria or some other disease. No evidence can be obtained to support these views.

The way in which unrecognised sporadic cases maintain the infection in Algeria during the periods between epidemics has been described by SERGENT and FOLEY (1922). The possibility of this happening in the Sudan is difficult to exclude, and incidentally may provide a public health problem for the future. Yet it seems clear from our

studies that this process, if it be assumed to occur, is at the present time of academic importance only, compared with the obvious heavy influx of infection across the Eastern frontier. Comparison of the routes taken by the immigrants (Fig.4) with the foci of apparent origin of the disease in the Sudan shows that no other factor need be invoked to explain the distribution and spread of the disease. Similarly, in the face of a major epidemic slowly spreading across Africa from the West, there seems no necessity, in the absence of concrete evidence, to assume the persistence of the old Egyptian disease in sporadic or endemic form to account for the epidemic of 1926.

It is suggested that the view expressed by BOUSEFIELD (1911), is probably true as far as the Northern Sudan is concerned. Human spirochaetosis is not endemic, but has at various times been introduced from adjoining countries. During 1908 - 1925 it was from Egypt, in 1926 from French West Africa and in 1936 from Abyssinia and Eritrea. The disease of 1925 may or may not have been an introduction from Uganda.

The classical epidemiological associations of relapsing fever - war, civil unrest, economic stress, etc. have been shown clearly at work in the propagation of the 1936 disease. Their influence is less clear in previous epidemics. It would be easy to invoke the world-wide economic depression of 1929 - 1930, which hit the Sudan badly, in explanation of the disease in the Gezira in 1930 but it is doubtful if this could be justified. The evidence all suggests that this epidemic was the tail end of the Eastward

spread from Darfur of the 1926 disease, which began in West Africa in 1921. Attempts to define the factors underlying the spread of this disease across Africa during these particular years lead into realms of pure speculation.

INCIDENCE.

SEX. As in India, West Africa and other countries in which relapsing fever is found, the majority of cases occur in males, the actual incidence in the Sudan being 98 per cent. males and 2 per cent. females. Except for the cases described in West Africa by SELWYN CLARKE, LE FAUN and INGRAM (1923) this is a much heavier percentage incidence in males than is generally observed.

This very large preponderance of males is not dependent on the degree of leuciness of the two sexes, for this infestation is shared in equal measure by both men and women. Indeed, women are often more heavily infected with head lice than men owing to the habit of shaving the scalp almost universal among the latter, while elaborate coiffures are favoured by the women. The true explanation lies in the fact that the infected males belong most exclusively to immigrant tribes from the West, who had come originally to Abyssinia and Eritrea in search of work and money. It is contrary to the traditions and habits of these people to bring their women-folk with them, especially if there is any question of proceeding further on the pilgrimage to Mecca.

AGE. As the majority of cases occur among immigrant males from the West, it follows that most of the

cases will be adults, since the journey across Africa to Eritrea and Abyssinia is not a thing to be undertaken lightly by other than healthy adults. The age varied from 15 - 55 years, but the greater proportion of cases observed fell into the 20 - 35 age group. Ages were assessed approximately on the physical appearance of the patients.

RACE. SELWYN CLARKE, LE FAUN and INGRAM (1923) recorded that 80 per cent. of their cases in West Africa were natives of one particular tribe, the Zabramah. A similar pronounced racial incidence is observed in the Sudan where over 90 per cent. of the infections occur in these races which are grouped together under the collective term of 'Westerners'. This may be described as the principal epidemiological feature of the disease in the Sudan, and has been so ever since the 1926 epidemic invaded Darfur. Various factors combine to produce this striking racial incidence in the present instance. To begin with, these people being immigrants from the infected countries, would naturally be the first to contract the disease. Once infected, their habits and traditions, together with the conditions under which they have been living, would ensure a ready spread of the disease.

Owing to the scarcity of water in their home districts except during the wet season, these people do not wash frequently. Their standard of personal cleanliness is much below that of the riverain peoples of the Sudan who have more frequent opportunities of washing and who are, on the whole, subject to a much less heavy louse infestation.

In respect to physical conditions the plight of these immigrants was little different from that of refugees,

They were dirty, tired and harassed. Their homes were in another land, and they possessed no house property or relatives with satisfactory living accommodation in the districts they passed through. For months they had probably had to live on a very inadequate diet: the most constant complaint against the conditions they had suffered was 'el akl wishan' - the food was filth.

SEASON. In the Sudan a definite tendency can be observed in the incidence of relapsing fever to rise abruptly in August and September, i.e. during the hot humid weather after the rains. A similar tendency to seasonal prevalence of relapsing fever has been observed in India (GILL, 1922, CRAGG, 1922) where it has been correlated with hot humid weather: in Algeria (SARGENT and FOLEY, 1922) where it has been correlated with the cold winter months: in Abyssinia (BRUNS, 1937) where it seems to depend on the rains: and in other countries. In China, (SHREMPTON, 1936) points out that the seasonal incidence is liable to be masked or disturbed by epidemics, and the same occurs in the Sudan. Fig.8 shows graphically the relation between relapsing fever and rainfall in the Blue Nile province of the Sudan where the most accurate figures are obtainable. It should be read in conjunction with Fig.9 which shows the relation to the incidence of malarial fever.

CRAGG (1922) has drawn attention to the effect of variations in temperature and humidity on lice, and it is probable that in India, and other places where the disease is endemic this may be one of the most important factors influencing its prevalence. In the Sudan, however, there is another factor to be considered as well as meteorological variations, viz, immigration. It is probably of at least equal importance.

It has already been described how the ripening of the cotton crop, bringing an annual demand for labourers will cause an immigration of Westerners. The actual harvest takes place in November and December, and the largest influx occurs then. During September and October, work begins on a smaller scale with various minor weeding, 'hishing' and cleaning operations, and at this time there is a smaller preliminary influx of Westerners. This close correlation between the seasonal movements of immigrant labourers and the seasonal incidence of relapsing fever, is, in our opinion, of more significance than any direct relation with meteorological variations.

RELATION TO OTHER DISEASES.

MALARIA. The diagram in Fig. 9 shows the seasonal incidence of relapsing fever compared with that of malaria in the Blue Nile province. It will be observed that there is a fairly close correspondence. It is practically axiomatic that the seasonal incidence of malaria in the Northern Sudan is determined by the distribution of the rains throughout the year.

TYPHUS. SERGENT and FOLEY (1922) have drawn attention to the close association between epidemics of louse-borne relapsing fever and louse-borne typhus in Algeria where the two diseases have the same seasonal prevalence, the same general course, and commonly follow each other or coincide.

No similar association occurs in the Sudan. It is often a matter of surprise that clinical typhus has never been reported in the Sudan, although from time to time various

suspicious cases of fever have been noted. There is no real clinical evidence that any of these have been Rickettsia infections, and the few sera which it has been possible to obtain from such cases have been negative. In order to determine whether this absence of typhus is real or merely apparent, and during 1937 a survey was carried out on a large number of human sera and also on the sera of wild rats.

Human sera were obtained from all parts of the Sudan. A few were from suspicious cases of fever, some were the routine sera for Kahn reaction, some were sera sent in for the Widal reaction which had been negative for the enteric group, others were specially collected in out of the way districts of the Sudan.

Rat sera (R. rattus, R. alexandrinus, R. norvegicus) were obtained through the collaboration of the Sanitary authorities from the larger centres of population in the Northern Sudan.

Three suspensions of Proteus were used OX19, OX2 and OXK, of which OX19 and OX2 were alcoholised agar cultures and OXK a formolised broth culture, as for some unknown reason all alcoholic suspensions of agar cultures prepared from this strain showed some spontaneous agglutination.

The results in 1,000 human sera, and 240 rat sera were as follows:-

Strain	OXK		OX2		OX19	
	Human	Rats	Human	Rats	Human	Rats
1 - 12.5	98	63	4	3	3	2
1 - 25	5	1	0	1	0	0
1 - 50	1	0	0	0	0	0
1 - 125	0	0	0	0	0	0
1 - 250	0	0	1	0	0	0
1 - 500	1	-	0	-	0	-

The results are clear cut and indicate the complete absence of agglutination (less than 1 - 12.5) in the majority of sera, while if the more usual dilution 1 - 25 is taken as the minimal titre only 0.8 per cent. of the human sera are positive. Only two of the sera showed any significant titres:— 1 - 250 OX2 and 1 - 500 OXK. The former case could not be traced: the latter serum was sent in for routine Kahn test and inquiries of the man's previous history failed to elicit anything. Of the rat sera none showed agglutination in any significant titre (1-50) and in dilutions of 1 - 25 or over only two were positive (0.8 per cent).

The serological results from both human and rat sera thus appear to confirm the experience of the clinicians with regard to the absence of typhus fever in the Sudan.

PLAGUE. Like typhus, this disease has never been reported clinically in the Sudan. CRAGG (1922) has pointed out the inverse seasonal prevalence of plague and relapsing fever in the United Provinces of India. From this inverse relationship he was able to deduce, in retrospect, that an abnormally high peak in the 'deaths from fever' curve was due to an unrecognised epidemic of relapsing fever. A glance at the monthly malaria incidence graph (Fig.9) will show the fallacy of drawing such conclusions in the Sudan.

NICOLLE and ANDERSON (1927) have suggested that the relapsing fevers originated as infections of small rodents. It is a very striking epidemiological coincidence, and one which has interested the writer for some time, that three of the principal infections of rodents transmissible to man are unknown in Northern Sudan. Reference has been made above

to plague and typhus, and the present writer (1938) has elsewhere drawn attention to the apparent absence of leptospirosis.

CLINICAL FEATURES AND COURSE OF THE DISEASE.

The following brief summary of the main clinical features of the disease, and their approximate frequency is based on 62 cases observed by the writer.

Fever was an invariable feature, usually of sudden onset, and frequently severe: temperatures of 105° and 106°F. were not uncommon. This fever was accompanied by severe headache in 83 per cent. of cases, but in a certain number of the remainder the patients seemed quite unaware of their fever.

Enlargement of the spleen, usually accompanied by pain in the left hypochondrium, was a very characteristic symptom and occurred in 83 per cent. of cases. The enlargement was of moderate degree (2 - 3 fingers' breadth below the costal margin) and frequently of fairly rapid origin. It usually subsided rapidly after the fever was controlled by novarsenobillon. Numbers of these immigrants had enlarged spleens due to causes other than relapsing fever - old malaria, bilharzia, etc. - but these enlargements were as a rule chronic and painless.

Enlargement of the liver was less frequent. It was observed in 60 per cent. of cases. The degree of enlargement was usually about two fingers' breadth beneath the costal margin and slight tenderness was the rule.

Jaundice was uncommon, being pronounced in only 10 per cent. of cases. As the patients were black-skinned,

the only visible evidence of the jaundice was yellowness of the eyeballs. Various degrees of subicteric discolouration were frequently met with, but it would be difficult to say how many of these were due to jaundice and how many were the result of mild degrees of xerophthalmia and other conditions, so only cases of well-marked jaundice are included in the figure given.

Even when jaundice was present the pulse was always rapid. Vomiting occurred in less than 10 per cent. of cases. The appetite and condition of the tongue varied considerably.

Epistaxis was a frequent symptom and occurred in 50 per cent. of cases. Albuminuria was rare, being only seen in five cases. Pain in the joints was occasionally complained of, and a slight generalised adenitis seemed to be present in most of the cases examined.

Skin rashes were never seen, neither were cases with meningeal symptoms. No eye complications were observed, but in a few cases which the writer did not see personally iritis is said to have occurred. This complication was frequent in the epidemic described by DRAKE-BROCKMANN (1913) in British Somaliland, and is said to have been transmitted by Ornithodoros savignyi.

The commonest and most typical picture of the disease as seen by the writer may be summed up in the three cardinal signs - fever, epistaxis and painful splenic enlargement.

The only certain diagnosis was made by finding the spirochaetes in the peripheral blood. The infection was of moderate severity, and, although several fields had sometimes to be examined before the spirochaetes were found, there was never any real difficulty. They were found only during the

pyrexial stages of the disease.

The apyrexial period, after the first relapse, varied from four up to fourteen days, during which time the patients felt remarkably fit, and spirochaetes were never found in the blood.

The occurrence of healthy carriers, harbouring the organisms in the blood, as in the Darfur epidemic of 1926, was not a feature of the 1937 disease. Particular attention was directed to this on account of its importance as a possible factor in the spread of the disease. With the co-operation of the Medical Officer of Health, Khartoum, it was possible to obtain blood slides from all contacts with cases observed in Khartoum during the time these were undergoing the process of delousing. Among over 300 contacts whose blood was examined the only positive was found in a boy, obviously jaundiced, and with a temperature of 101^oF. Smaller batches of contacts examined at Gedaref and Sennar were all negative.

No cases were seen which had more than one relapse. This cannot be taken as the normal course of the disease, as in no case was the disease allowed to run its natural course. The diagnosis of relapsing fever, confirmed under the microscope, was always an indication for treatment at the earliest possible moment.

The blood. The presence of a polymorphonuclear leucocytosis was a prominent feature in all the blood slides examined. Total blood counts were not carried out, but differential counts gave the following proportions as an average of thirty blood films:-

Polymorphs.....	70 per cent.
Lymphocytes.....	19 per cent.
Large mononuclears.....	6 per cent.
Eosinophils.....	5 per cent.

In the Sudan, as compared with temperate countries, a relative increase in the non-granular cells is the rule, even in apparently healthy individuals, and should be regarded as normal both in natives and in Europeans who have spent any length of time in the country. This conclusion has been reached as the result of considerable experience in the examination of blood in the Sudan, and no explanation is put forward to account for the alteration. In the present instance it signifies that the average differential count we have quoted represents a greater relative increase in the polymorphs than is apparent when it is compared with the standards generally accepted as normal in colder climates.

RIDING and MACDOWELL (1927) and other observers have stated that when the disease has been present for some time the granular cells become relatively less prominent and the polymorphonuclear leucocytosis is succeeded by a lymphocytosis. This was not seen in any case examined by the writer, probably because the infection was never allowed to persist long enough to reach this stage.

Fifteen cases with no history or clinical signs of syphilis had their sera tested by the Kahn reaction, which was positive in four only, so that relapsing fever is not always a fallacy for this test. Other observers record various findings with blood spirochaetosis and the serum tests for syphilis. FAIRLEY, cited by MANSON BAHR (1935), found that 25 per cent. of cases of relapsing fever gave a positive Wasserman reaction. ROAF (1922) found 11 positive Wassermans in 18 cases, and concluded that a transient positive reaction was the rule during the acute

stages, CHU, DEITRICK and CHUNG (1931) obtained negative Wassermans in 25 out of 26 cases. PAI (1937) found that Kahn always negative, although 5 out of 13 febrile non-luetic cases, and 1 out of 15 afebrile ones gave a positive Wasserman.

Treatment. Novarsenobillon, intravenously, was the only remedy used and was found effective, although in weakly or very toxic individuals the drug was undoubtedly dangerous. The larger doses used at first were later discarded in favour of smaller doses (0.3 - 0.45 gm.), with a view to diminishing the risk of toxic effects. These smaller doses appeared to be as effective therapeutically as the larger ones. One dose was usually sufficient to cause disappearance of the spirochaetes from the blood within 48 hours (as observed in four-hourly blood films), and to reduce the temperature to normal. But one dose did not always prevent relapse. It is stated in the text books that the administration of this drug should be avoided just before the crisis, as this often is followed by a relapse. Clinically it is by no means easy to tell when the crisis is imminent, and this may be the explanation in the few cases which did relapse. Careful attention to the diet is necessary, particularly in the period of recovery after specific treatment with novarsenobillon. The appetite is often extremely voracious and it may be difficult to prevent the patients grossly overtaxing their digestive powers.

It was our impression that the administration of novarsenobillon in debilitated, very toxic, or moribund patients frequently accelerates the fatal issue. But this is no indication to withhold the drug, as such persons will

certainly die if left without treatment. In these cases especially, the reduced doses of the drug are to be recommended, repeated if necessary, and accompanied by the administration of glucose and intravenous thiosulphate of soda (0.6 gm.).

It may be recalled that in the Gezira, during 1930 - 1931, Grey Oil, a mercurial preparation, was found effective in treatment (ATKEY, 1932) and in Tanganyika mercurochrome, intravenously, is recommended (MANSON-BAHR), (1935). Our experience was restricted to the arsenicals.

MORTALITY.

The mortality in the cases observed in Kassala and the Blue Nile provinces was 9 per cent. This compares with a mortality of 18 per cent. in 1930 - 1931 in the Gezira, and a mortality of 70 per cent. in 1926 - 1927 in Darfur. It is noteworthy that in a small outbreak of sixty cases which occurred in Kuttum in November, 1937 the mortality was 30 per cent. A similar discrepancy was noted in 1930 - 1931 between cases in Darfur, where the mortality was 40 per cent. and those in the Gezira.

It is difficult to explain this discrepancy on the grounds of racial or dietetic differences in the provinces concerned. It is the same races which are affected, and according to their own account the food they had to live on, at least in the Italian colonies, compared unfavourably with that in their own countries in the West.

It may be suggested that the difference in mortality is due to the way in which medical attention is hindered by transport difficulties in a rural area like

Darfur as compared with the highly organised Gezira and the places near the railway line.

Probably, therefore, the Darfur mortality is much nearer what the figure for the untreated disease would be, and suggests that in the absence of proper medical and sanitary measures this disease might very well repeat the havoc of previous years.

PATHOLOGY.

Among primitive peoples, such as we had to deal with, post-mortem examinations are violently resented. Mutilation of the dead is anathema to the Mohammedan, in any shape or form, as the mutilation goes with the dead man to paradise. On account of the fanatical religious beliefs of the peoples concerned, attempts to secure post-mortems were to be deprecated - principally because the trust and confidence of the people themselves were so essential to the success of any scheme to restrict the spread of the disease. The slightest suggestion of terror or black magic associated with the hospitals and quarantine posts would have aroused such fear and distrust in the minds of the people that these institutions would have been avoided altogether. Under these circumstances the task of collecting the immigrants together and inducing them to submit to delousing etc. would have been well nigh impossible.

Principally for these reasons pathological material was scanty. We were fortunate however in obtaining a complete post-mortem of one case, and sections from the liver and spleen of another.

The former died of lobar pneumonia, complicating the relapsing fever. This pneumonia was not of spirochaetal origin, but was associated with the pneumococcus in the alveoli in large numbers.

Apart from the lungs, the only other organ to show any departure from normal macroscopically was the spleen. This was enlarged and congested and numerous small infarctions could be seen on the outer surface as yellowish areas of irregular shape.

Paraffin sections of the liver in both cases showed a tissue that was substantially normal.

Sections of the kidneys showed extensive cloudy swelling and catarrhal changes in the tubule cells, amounting in places to actual necrosis of cells.

In the case of the spleen, RUSSELL (1932) has described a characteristic pathological lesion in relapsing fever - a peripheral necrosis affecting the outer layers of cells in the malpighian corpuscle, associated with the presence of spirochaetes in the cells. The illustrations in her paper depict this lesion very clearly. RUSSELL claims that this lesion is sufficiently characteristic of relapsing fever to enable a post-mortem diagnosis to be made from the histology of the spleen.

In the two spleens which we examined the principal changes were congestion and, in the region of the infarctions, necrosis. Clear-cut typical military lesions of the type pictured by RUSSELL were not seen. In the spleen sections from the case which died of pneumonia there could occasionally be made out a lesion of the type shown in Fig.19 in which the malpighian corpuscle was much reduced in size, and surrounded by a layer of necrosis and cellular

infiltration. There can be little doubt that these correspond with the military lesions of RUSSELL, but they were much less clearly defined, and in the sections we examined they were much less frequent than the figures of this author. It is doubtful if the discovery of such a lesion as that shown in the photograph in a spleen section, most of which resembled Fig.18 would warrant a pathological diagnosis of relapsing fever, especially as spirochaetes were not seen even when the sections were stained by Levaditi's method.

In the experimental animals singularly little change could be made out in the organs, although clinically enlargement of the liver and spleen below the costal margin could be detected. All the organs of Monkey R.(4) which died of experimental relapsing fever, and all the organs of a mouse which was bled to death at the height of the infection were examined microscopically by smears and sections. The only organ in which any appreciable histopathological changes could be seen was the liver of this mouse, which showed a mild degree of generalised fatty degeneration (Fig.21). This was of interest, because it indicated that, in spite of its mild course, the infection does cause tissue damage.

After splenectomy, the spleens of animals which had been infected were always examined for spirochaetes by fresh smears, and sections were made and stained by Giemsa, by haematoxylin and eosin, and by Levaditi's silver impregnation method. Although those spleens were removed during the febrile paroxysm, on the day following the crisis, and also several days after recovery, no evidence could be seen of phagocytosis or penetration of the cells by the

spirochaetes such as has been described by several authors. Nor could it be said that these spleens showed any very definite histopathological change. Fig.17 shows a microphotograph of a spleen removed the day after the crisis. The periphery of the malpighian corpuscles is somewhat more prominent than usual, but the section might well pass for that of a normal spleen.

PREVENTION.

All the evidence we have been able to obtain incriminates the louse, and the louse alone, as the vector of this disease. The indication for prevention is, therefore, destruction of lice.

This is easily enough accomplished in individual cases, but its application to a population which is subject to the effects of immigration and the movements of people in search of work is by no means so easy. A detailed discussion of the administrative and other difficulties which have to be overcome is outside the scope of this work. In general terms, however, there are two main principles to be followed.

The first is the prevention of further infection from without, by the establishment of quarantine stations along the routes of immigration, where immigrants can be disinfested before proceeding further into the Sudan, or detained if sick.

This alone will not be sufficient, as infected persons have passed into the central Sudan. They may still pass through even the most vigilant quarantine system in

small numbers and thus lead to the appearance of the disease in various parts of the Sudan. The prevention of its further spread will then depend on speedy recognition and the rapidity with which effective control measures can be applied in the affected districts. This is the second line of defence.

In proportion as the measures along the routes of immigration are made effective, so the number of cases likely to pass into the Sudan unnoticed will be diminished. So also the number of possible new epidemic foci to which these might give origin will be decreased, and the chances correspondingly reduced of the epidemic suddenly assuming uncontrollable proportions.

Experience in the Sudan has shown that louse-borne relapsing fever is controllable, if sufficient ^{effort} is made, and that the ultimate effort required is inversely proportional to the rapidity with which control measures can be made effective at the beginning of an epidemic. Under present conditions it is believed that the chances of any epidemic suddenly assuming major proportions throughout the country are remote: but a greater risk at the present time seems to be that the disease may become established in endemic form. With the further pacification and colonization of Abyssinia, the future is likely to see a further increase in traffic across the Sudan from infected countries in the West to infected countries in the East, and vice versa. Whether it will still be possible under these circumstances to prevent the disease becoming endemic among the population of the Sudan remains to be seen.

(G) SUMMARY

- (1) The history of relapsing fever in the Sudan is summarised and certain relevant physiographical, racial, and economic features of the country are noted.
- (2) Louse-borne relapsing fever was introduced into the Sudan during 1908 - 1924 from Egypt, in 1926 from French West Africa, and in 1936 from Italian East Africa.
- (3) The infection of the Sudan in 1936 and 1937 from Abyssinia was a consequence of the Italo-Abyssinian war, although it was not effected by Abyssinian refugees.
- (4) The morphology, movements, etc. of the Abyssinian strain of louse-borne relapsing fever are described. It was successfully cultured in an Egg-albumen ascitic fluid medium, but not in YUAN PO'S egg medium and other media.
- (5) Gerbilles, and white mice were the only rodents found to be susceptible. In these animals the disease runs a very mild course. There is no relapse, and the strain cannot be maintained in these animals, even after passage through monkeys.
- (6) Monkeys (Cercopithecus sebaeus) were susceptible, and in them the infection runs a course similar to the human disease. It appears possible to maintain the strain in these animals for at least three passages.
- (7) Evidence of immunity was found in infected animals, but several antigenic variants of the spirochaete are apparently present.
- (8) In monkeys splenectomy was found to influence the course of the first infection, but had no effect on acquired immunity. In mice, splenectomy had no effect at all. A possible explanation of these results is discussed.
- (9) No evidence of latent or residual infections was found in rodents after recovery.
- (10) The intermediate host is the louse. Virulent spirochaetes were found in lice from infected cases, which were able to reproduce the disease in a monkey.
- (11) In the monkey, the infection derived from the louse is more severe than that derived from the inoculation of infected blood.
- (12) The Abyssinian strain of louse-borne relapsing fever resembles in its general features the other members of the North African group of louse-borne strains.

- (13) It is not transmissible by Ornithodoros savignyi, and does not persist in that tick.
- (14) Consideration of the geographical distribution of Ornithodoros ticks in the Sudan shows that O. savignyi is the only one likely to play any part in the epidemiology of relapsing fever in Northern Sudan.
- (15) Attempts to transmit the spirochaete by means of the tick Argas persicus and the monkey louse (Pedicinus) were not successful.
- (16) Epidemiological considerations suggest that relapsing fever has not established itself in endemic form in the Northern Sudan, although it has been introduced on different occasions from the adjoining countries.
- (17) During the last 12 years the incidence of the disease has been confined almost entirely to adult male 'Westerners', i.e. negroid immigrants from the Western Sudan and French Equatorial Africa.
- (18) The disease shows a tendency to seasonal incidence during the hot humid weather after the rains, but this may be obscured by the presence of epidemics. This is correlated with seasonal movements of immigrant labourers rather than with meteorological variations.
- (19) Although a close association has been observed elsewhere between epidemics of louse-borne relapsing fever and louse-borne typhus, no such association exists in the Sudan, where epidemic typhus is apparently unknown.
- (20) Infections in the Southern Sudan may be tick-borne, but there is no evidence that these arthropods have played any part in the epidemiology of relapsing fever in the Northern Sudan.
- (21) The most characteristic clinical symptoms are fever, painful splenic enlargement and epistaxis.
- (22) Miliary lesions at the periphery of the malpighian corpuscles were seen in sections of the spleen in fatal cases, but these were obscured by other changes, and in the cases examined would not have been sufficient to warrant a diagnosis being made from post-mortem examination of spleen sections.

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(K) ILLUSTRATIONS

(A) MAPS

1. General map of the Anglo-Egyptian Sudan.
2. Diagram showing the origin of epidemic relapsing fever at various times.
3. Rainfall map of the Anglo-Egyptian Sudan.
4. Map of the Eastern Sudan showing the routes by which infection was spreading in 1936 and 1937.
5. Map showing Distribution of Ornithodoros ticks in the Sudan.

(B) DIAGRAMS

6. Polymorphous forms assumed by the spirochaetes in stained blood films.
7. Appearances seen in films of frozen blood.
8. Diagram showing the seasonal incidence of relapsing fever in the Gezira.
9. Diagram showing the relation between relapsing fever and malaria.
10. Diagram showing the behaviour of the spirochaetes in Pedicinus.

(C) PHOTOGRAPHS

11. Spirochaetes in blood film.
12. Spirochaetes in film of frozen blood.
13. Spirochaetes from the haemocoel of the louse.
14. Mass of spirochaetes from a louse.
15. Ornithodoros savignyi, natural size.
16. Human spleen, showing areas of infarction.
17. Spleen of monkey - photomicrograph.
18. Human spleen - photomicrograph.
19. Human spleen - miliary lesion in malipighian corpuscle - photomicrograph.
20. Human kidney in relapsing fever - photomicrograph.
21. Mouse liver in relapsing fever - photomicrograph.
22. The laboratory saloon.



I L L U S T R A T I O N S

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FIG. I. GENERAL MAP OF THE ANGLO-EGYPTIAN SUDAN.

Scale 1 : 15,000,000.

International boundaries —————

Province boundaries. - - - - -



FIG.2. RELAPSING FEVER: DIAGRAM SHOWING THE SOURCE OF INFECTION AT VARIOUS TIMES IN THE SUDAN.



FIG.3. RAINFALL MAP OF THE ANGLO-EGYPTIAN SUDAN, SHOWING THE DIVISION OF THE COUNTRY INTO NORTHERN SUDAN AND SOUTHERN SUDAN.



FIG. 4. SKETCH MAP OF THE EASTERN SUDAN, SHOWING THE ROUTE BY WHICH INFECTION WAS ENTERING DURING 1936-37. ROUTE OF INFECTION SHOWN IN RED.

International boundaries ~~-----~~ Railways -----
By tracing the previous movements of cases found in the Sudan, and finally by the establishment of quarantine posts along the route of infection, the latter could be defined with considerable accuracy.



FIG.5. SKETCH MAP SHOWING THE DISTRIBUTION OF ORNITHODORUS TICKS IN THE SUDAN.

Names underlined indicate places where the writer has personally identified Ornithodoros savignyi.




- Ornithodoros meubata, known distribution..... 
- Ornithodoros moubata, suspected distribution.. 
- Ornithodoros savignyi..... 



FIG. 6. POLYMORPHOUS FORMS ASSUMED BY THE SPIROCHAETES IN STAINED BLOOD FILMS.

Drawings made under the micro-projector. x2000, approx. A - E, shapes commonly assumed in

stained films. F, dividing form - daughters still attached by thin portion, and intertwined. G, a group of agglutinated and disintegrating spirochaetes seen in a bloodfilm taken near the crisis.

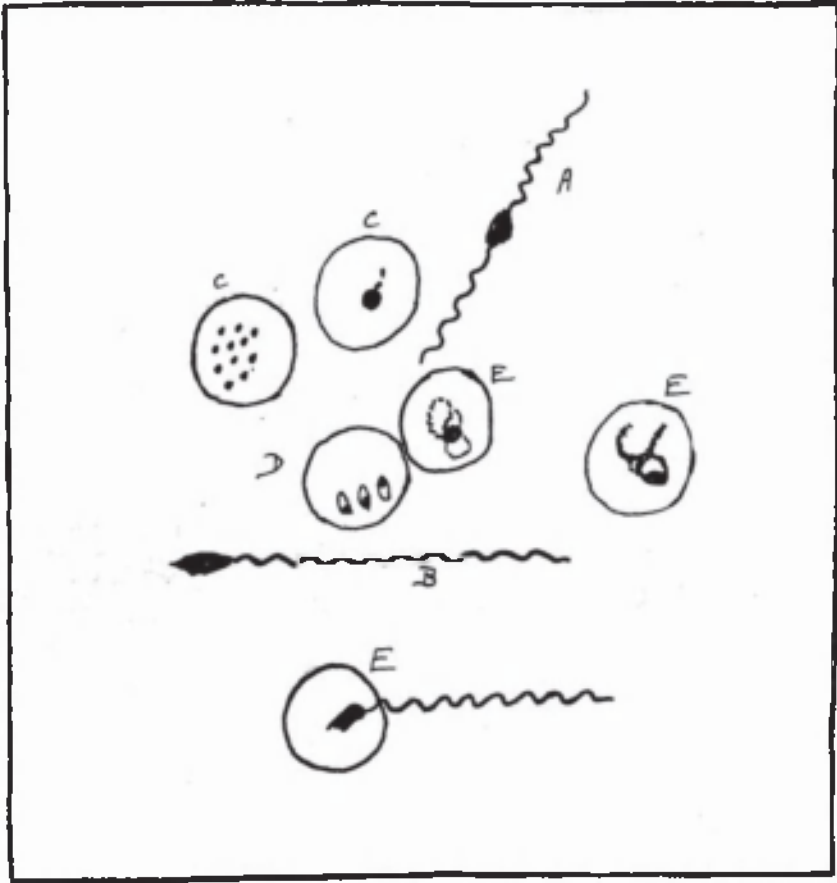


FIG.7. APPEARANCES SEEN IN FILMS OF FROZEN BLOOD.

Drawings made under the micro-projector. x2000, approx. A, swelling in middle of spirochaete. B, terminal swelling in spirochaete. C, granules in red blood cells. D, Babesia-like appearances in red blood cells. E, appearances suggesting penetration of red cells by spirochaetes, followed by disintegration of the spirochaetes.

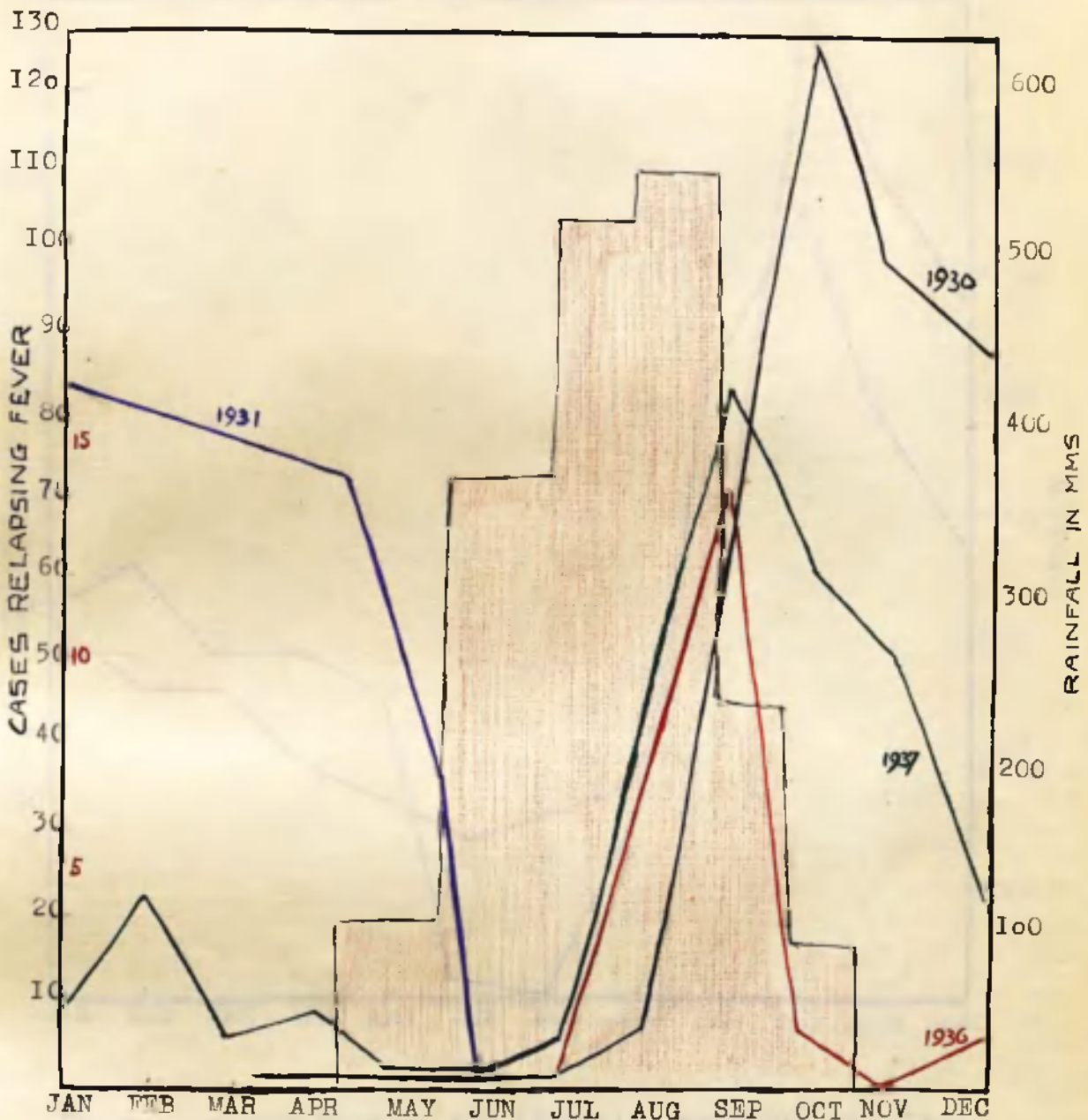


FIG.8. GRAPHS SHOWING THE SEASONAL INCIDENCE OF RELAPSING FEVER IN THE BLUE NILE PROVINCE (GEZIRA) WITH A HISTOGRAM SHOWING THE AVERAGE RAINFALL DURING THE YEARS CONCERNED.

The figures for 1936 are shown on a magnified scale, which is indicated by the red figures on the left side.

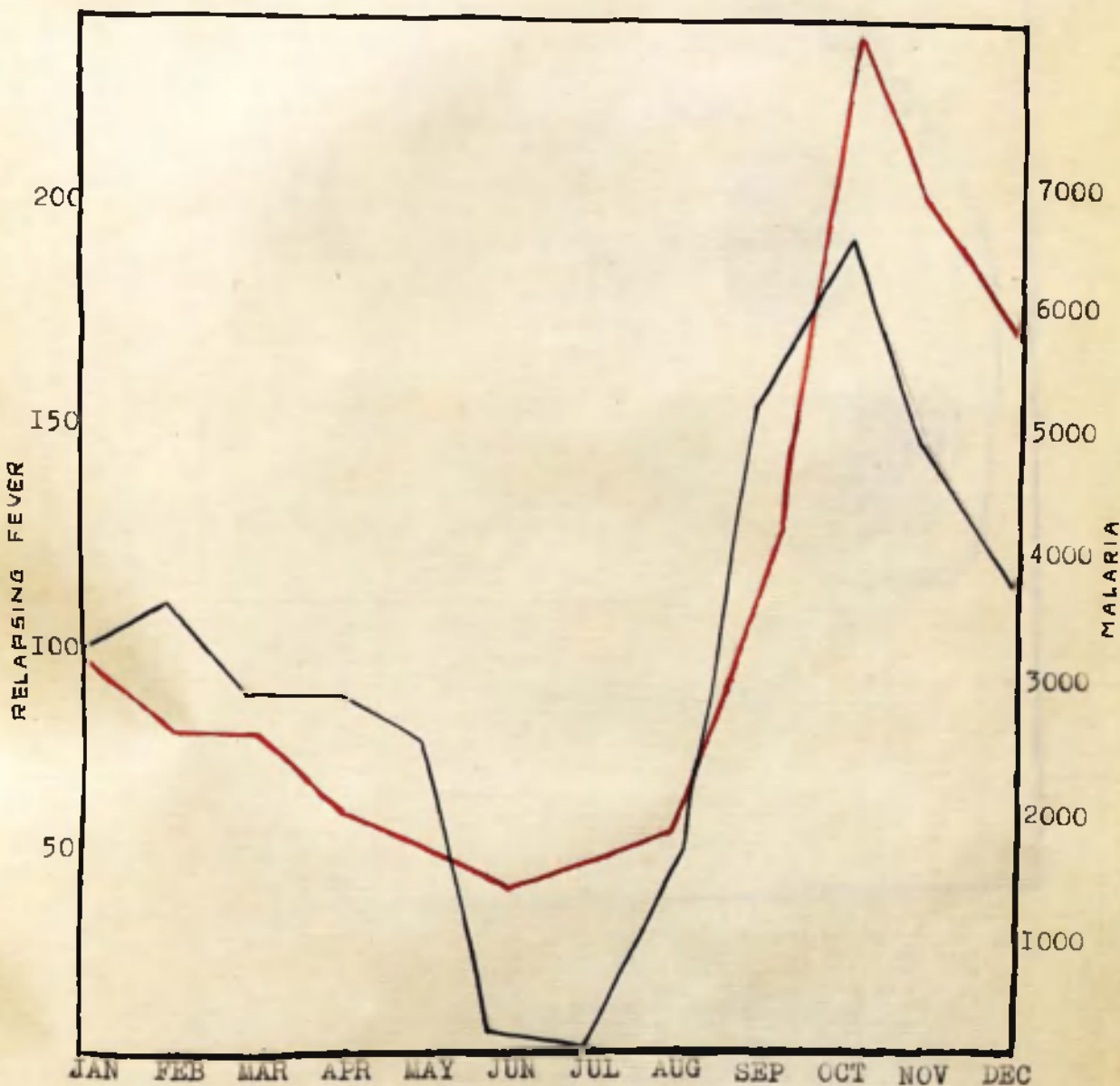


FIG.9. GRAPHS SHOWING THE SEASONAL INCIDENCE OF RELAPSING FEVER COMPARED WITH THAT OF MALARIA.

Malaria shown in red. The values for relapsing fever are the summation of each January, February, etc., during the period 1930-37, and the values for malaria are averages taken over the same period.



FIG.10. DRAWINGS MADE UNDER THE MICRO-PROJECTOR
TO SHOW THE FATE OF THE SPIROCHAETES IN
THE CELLS OF PEDICINUS. x2,500 approx.

Coiled up spirochaetes, and spirochaetes apparently
undergoing disintegration can be seen inside the cells.

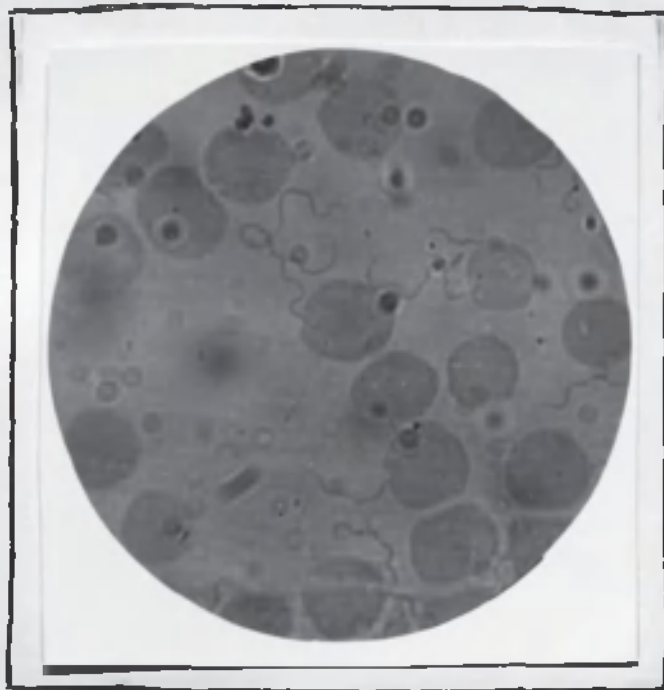


FIG.II. SPIROCHAETES IN BLOOD FILM.

Showing the polymorphous appearances commonly seen in routine blood films. (x 1,900)

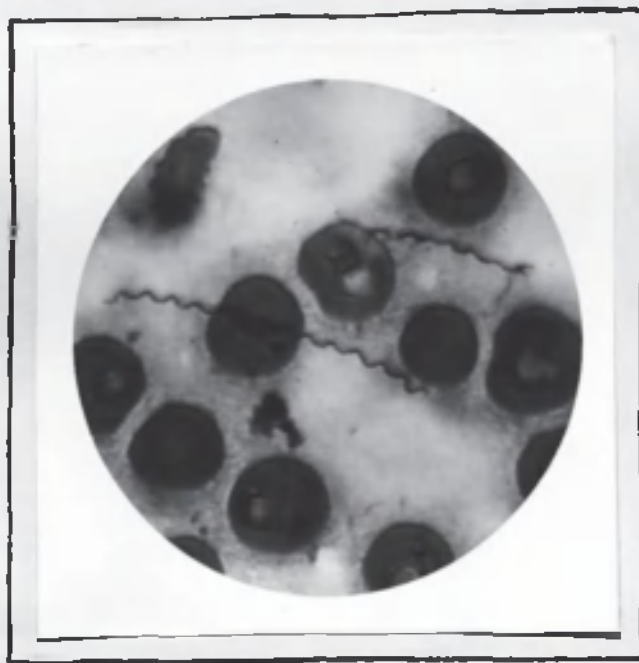


FIG.I2. SPIROCHAETES IN FILM OF FROZEN BLOOD.

The organisms in this film show the regular corkscrew arrangement, seen in the living state.

(x 1,900)

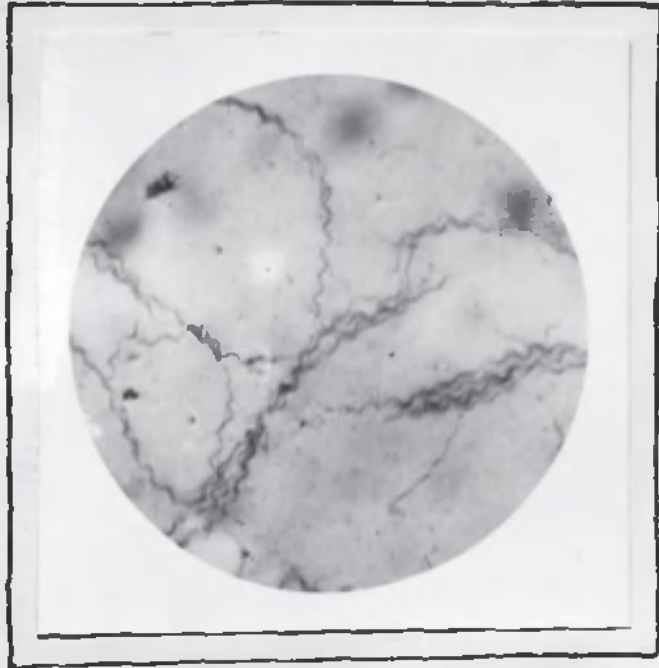


FIG.13. METACYCLIC SPIROCHAETES
FROM THE HAEMOCELE OF A
LOUSE. (x 1,900)

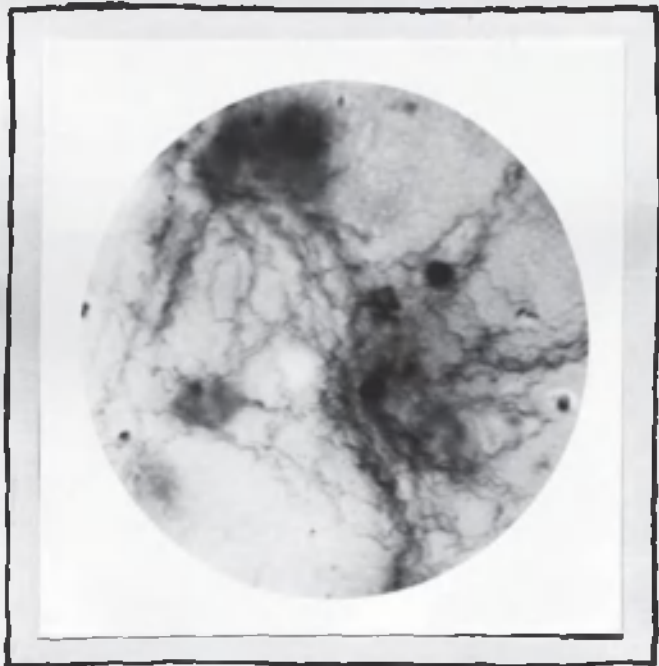


FIG.14. LARGE TANGLED MASS OF SPIROCHAETES
FROM THE HAEMOCELE OF A LOUSE.
(1,900).



FIG. 15. ORNITHODORUS SAVIGNYI
NATURAL SIZE.



FIG. 16. PORTION OF HUMAN SPLEEN IN RELAPSING
FEVER, SHOWING INFARCTION.

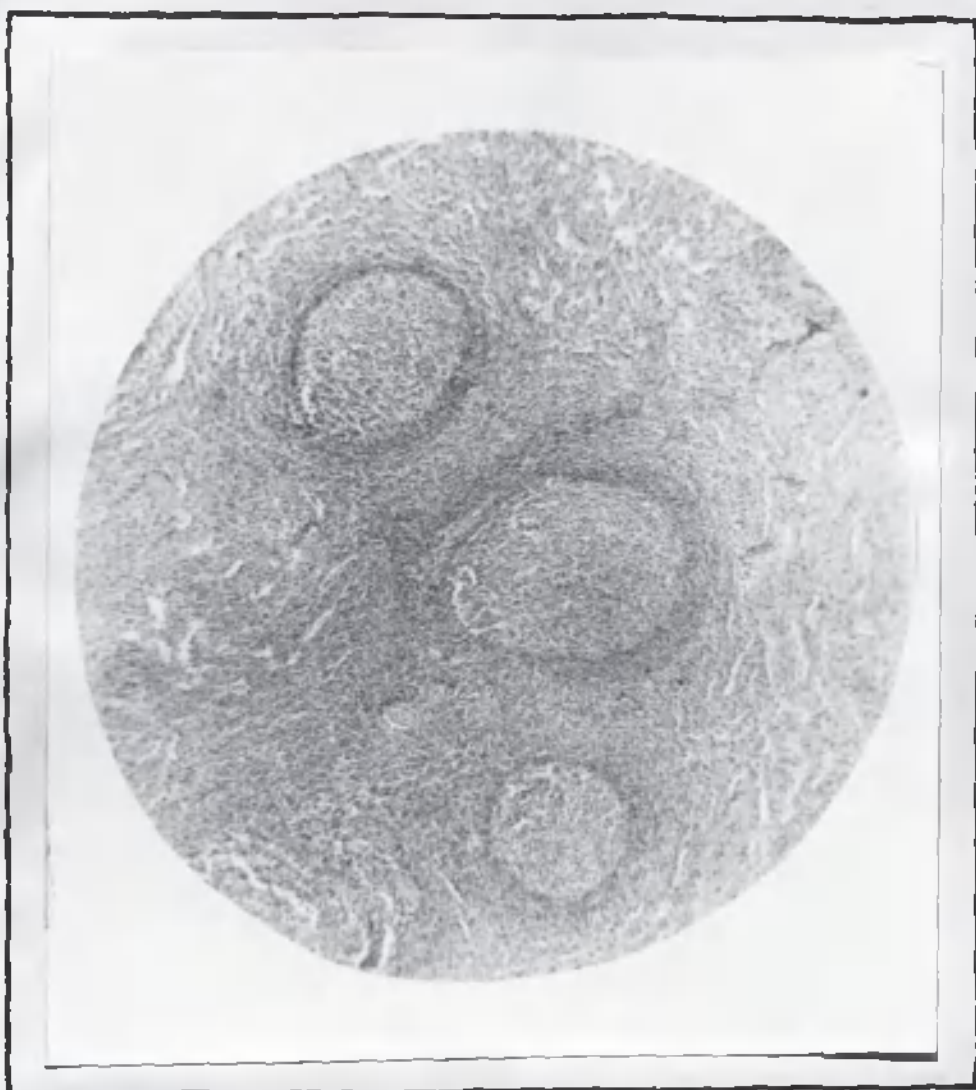


FIG.17. MICROPHOTOGRAPH OF MONKEY'S SPLEEN -
EXPERIMENTAL RELAPSING FEVER. x 75.

The appearances are substantially those of the
normal spleen.



FIG.18. MICROPHOTOGRAPH OF HUMAN SPLEEN IN
RELAPSING FEVER - AREA OF INFARCTION.
x 75.

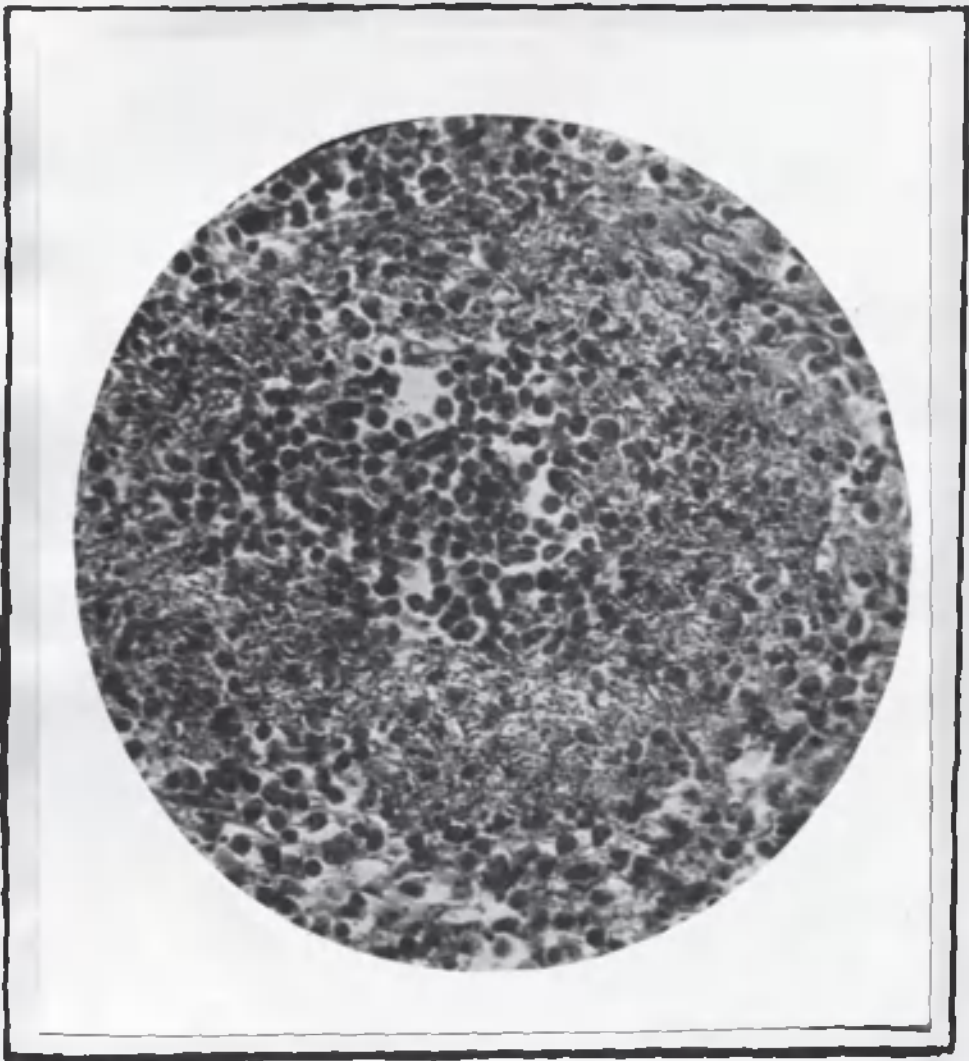


FIG.19. MICROPHOTOGRAPH OF HUMAN SPLEEN IN RELAPSING
FEVER, SHOWING MILIARY LESION IN MALPIGHIAN
CORPUSCLE. x480.

The malpighian corpuscle is relatively much smaller than normal, probably as the result of chronic malaria, or some similar condition. Surrounding it can be seen a poorly defined zone of necrosis, better seen if the plate is viewed at arm's length.



FIG.20. MICROPHOTOGRAPH OF HUMAN KIDNEY IN RELAPS-
ING FEVER. x480.

Shows catarrhal changes in the tubules, and cloudy
swelling of the tubule cells, amounting to actual
necrosis in places.



FIG.21. MICROPHOTOGRAPH OF MOUSE LIVER IN
EXPERIMENTAL RELAPSING FEVER. x 480.



FIG.22. THE LABORATORY SALOON.

This is a Railway coach, equipped as a travelling laboratory, by means of which it is possible to provide the necessary facilities for laboratory work at any station on the railway line. It was of immense value during the course of the work recorded in this paper.