Since October 1943, an epidemic of relapsing fever has prevailed in French North Africa. This epidemic gradually worked its way up from the southern borders of Tunisia, first through Tunisia and then into Algeria and Morocco. A number of cases were also imported into Dakar by soldiers evacuated from Morocco to French West Africa. Many persons were affected, and a large number of deaths ensued; and the spread of a disease of this nature, which in former years had made grave inroads upon the people of Europe also, might well constitute a grave international danger.

On these grounds, UNRRA suggested that a special mission be sent to carry out a comprehensive investigation of the epidemic, its origins, its geographical and biological development, its clinical manifestations, the methods of treatment applied, and the prophylactic measures taken. This mission was of a purely informative kind, and the Governments concerned were themselves fully responsible for the initiation and execution of all the measures required within their territories.

With this end in view, an UNRRA Mission, with the agreement of the French Foreign Ministry and the two Departments concerned — Public Health and the Interior — proceeded to French North Africa in November 1945. This mission consisted of Dr. Gaud, Delegate to the Permanent Committee of the Office International d'Hygiène Publique and Dr. Morgan, Chairman of the Committee. The survey that follows was written with the aid of documents collected, and on the basis of the UNRRA Mission's observations during its stay in French North Africa.
Relapsing fever, called by other authors louse-borne relapsing fever or epidemic cosmopolitan louse-borne type, is a disease well known in the epidemiological history of North Africa. It is prevalent in an area ranging from Egypt in the east to Morocco in the west and, in a southerly direction, it seems confined within a line running from the coastal region of French West Africa to the Sudan. The last great epidemic outbreak occurred in North Africa between 1912 and 1915, and in French West Africa between 1922 and 1925.

Since that time, there had been practically no louse-borne relapsing fever in those areas. Specialists in this disease, like Georges BLANC, who studied it with NICOLLE during the last North-African epidemic, could find no trace of it in Morocco, and their research merely showed that small foci of tick relapsing fever existed, but had never spread.

After more than twenty-five years' quiescence, foci of epidemic relapsing fever have again been active in Tunisia since October 1943. They grew rapidly into an epidemic of vast proportions which spread beyond the frontiers, from east to west, like a wave, swamping first Algeria and then Morocco.

In the light of the numerous observations made in those countries concerning the course of the disease, its clinical forms and the means employed to combat it, it would seem of interest to lay down, in an epidemiological, clinical and therapeutic study, the data we have been able to establish to date.

I. EPIDEMIOLOGICAL STUDY

1. Origin of the Epidemic.—The focus in the Fezzan region.

In October 1943, the first focus of the epidemic appeared at Sfax, in Tunisia, but it was soon established that the first cases were natives or soldiers returned from the south. For a moment it was thought that there might have been contamination by the Axis troops, but this hypothesis was dropped; and, mindful of the 1922 epidemic in French West Africa, it was believed that the contagion had been brought by General Leclerc's troops from the Upper Volta, Niger and Chad regions. Actually, while cases of relapsing fever were certainly observed among troops coming from the south, it is now known that they became infected with it during their
crossing of the Fezzan region, a vast area south of Tripolitania which, according to available information, would appear to be the source of the epidemic. It is interesting to note, moreover, that, during the 1912 epidemic, Ch. NICOLLE thought that the reservoir of the virus was renewed in Fezzan.

A very thorough investigation made by Médecin-Capitaine GRAS, the Head of the Fezzan Medical Service, states the case with great precision. After much patient research and innumerable cross-checkings, he finally concluded that the first cases of this disease (which is very well known among the Arabs in the district, who refer to it as "relapse disease") made their appearance during the last quarter of 1942 among the nomad tribe of Megarha, who wander through the region between Djebel Sôda and the Chiati Valley. The first cases were not diagnosed by the Italians who then occupied the country but remained confined to their fortresses. In April 1943, the villages of the Chiati Valley were attacked by the disease and, in May, cases were reported at Sebha and Onbari. Thence, the relapsing fever spread to Mourzouk; and at the same time caravans leaving Chiati spread the disease to Ghadamès, Derj and Sinaoun. Between May and July, the disease strengthened its hold, reached its peak in August and then almost completely disappeared in September. But in February 1944, it reappeared and attacked all the villages which had hitherto escaped. It raged throughout these in March, April and May, and then finally disappeared from the country.

Dr. GRAS, who personally and with great accuracy followed the development of the epidemic in the village of Gorda, in the district of Sebha, gives that village as a typical example.

In that small village of 750 inhabitants, the following cases were observed:

<table>
<thead>
<tr>
<th>Month</th>
<th>Cases</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>July 1943</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>August</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>September</td>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td>October</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>February 1944</td>
<td>50 with 5 deaths</td>
<td></td>
</tr>
<tr>
<td>March</td>
<td>49</td>
<td>1</td>
</tr>
<tr>
<td>April</td>
<td>19</td>
<td>1</td>
</tr>
<tr>
<td>May</td>
<td>20</td>
<td>3</td>
</tr>
</tbody>
</table>

This represents a total of 224 cases, all verified by blood tests. Dr. GRAS concludes with the opinion that about half the population of the Fezzan district—i.e. about 15,000 persons—suffered from the disease, with a death rate varying between 8 and 10 per cent.
2. The Course of the Epidemic.

From Fezzan, where the epidemic was rampant from the end of 1942 until the summer of 1944—i.e., a period of 19 months—it spread in a westerly direction towards Southern Algeria, and also to the north, gradually invading Tunisia, then Algeria and Morocco.

The spread of the disease to the west has been described by Médecin-Lieutenant TEDDE, Head of the Medical Service of the annex of El-Oued. "The epidemic of relapsing fever", he states, "which began in December 1944, reached its peak in April 1945. The number of cases then gradually decreased until the end of July, and in August the disease completely disappeared. The epidemic came from Fezzan. It first attacked the east and south and spread northwards and westwards, and after that extended to the neighbouring regions of Touggourt and Biskra. 2,750 cases in all were observed, with 136 deaths, representing a case fatality-rate of about 5 per cent. But there is every reason to think that a far greater number of persons caught the disease. Very often, indeed, a native suffering from a febrile condition sits back resignedly and waits for the condition to clear up. Many hide, for fear of the quarantine station or of isolation measures, which are irksome, but are enforced during a period of epidemic." Dr. TEDDE considers that the number of cases registered represents only about one-tenth of the real number.

But this westward spread, towards the desert, is only an insignificant episode when compared with the ravages caused by the epidemic on its way north.

Tunisia. — As we have already observed, the first focus of the epidemic was found at Sfax in October 1943. During the winter of 1943/44, the epidemic spread progressively through various areas of Tunisia, but did not really gain in scope. Only in April 1944 did the monthly total of cases begin to rise gradually from 400 to 2,000 in July. There was a slight pause during August and September; and then the epidemic reached really explosive proportions. The peak was reached in March 1945, with more than 6,000 cases. From then onwards, the decrease was rapid and in September 1945 there were only some 200 cases.

Of course, here again the number of cases recorded was not the real total, and the Directorate of Public Health in Tunisia considers that, in order to obtain a more or less accurate estimate of the total number of cases, the number of cases notified and treated should be
multiplied by 8. Some 50,000 cases were treated; so it would seem that some 400,000 persons caught the disease—in other words, about 20 per cent. of the population of Tunisia.

In the military forces, where a close watch is kept, where all cases are reported and treated, where hygienic conditions are very much better than those in the native quarters, and where prophylactic measures are applied more successfully and thoroughly, the curve of the epidemic ran exactly parallel to that of the disease in the civilian population. The total number of cases amounted to 1,448, which represents 6.5 per cent., out of 22,000 men of the Tunisian Division.

*Algeria.* — While in Tunisia the infection, during the first eight months, did not spread in a spectacular way, and no epidemic outbreak occurred until a sufficient reservoir of virus had accumulated, in Algeria the disease spread immediately and with full force.

In November 1944, thirteen months after relapsing fever had made its first appearance in Tunisia, the first cases occurred in the Department of Constantine, which borders upon Tunisia. Then, very rapidly, the disease began to make inroads on the whole department, spreading to the Department of Algiers in December and, one month later, to that of Oran.
In all three departments of Algeria, the number of cases rose very sharply and reached its height in April with about 1,000 cases for Constantine; in March came the peak for Algiers, with 1,700 cases, and in July for Oran, with 900 cases. From that moment, the numbers decreased; and by October 1945 the curve had reverted to the level of the early months of the epidemic.

The official total of cases diagnosed reached 16,119; but, as in Tunisia, this appears to be a good deal too low. Dr. GRENOILLEAU, the Director of the Algerian Public Health Service, considers that this number should be multiplied by 10 to represent anything like the real figure, which would thus be one of about 160,000 cases. For a population of 8 millions, it represents a degree of morbidity much lower than that in Tunisia.

The truth is that even the figure of 160,000 seems still too low, when compared with the number of cases that occurred among the troops. Out of 100,000 men stationed in Algeria, a total of 5,419 contracted the disease — i.e., 5.4 per cent. of the total man-power there. If we presume that the percentage of civilians suffering from the disease was not higher, it would mean 432,000 cases for Algeria. We may accept this latter as a minimum though the actual figure was very likely higher.

**Morocco.** — As the epidemic gained a firmer hold, it also began to spread more rapidly. While a full year elapsed between the first cases in Fezzan and those in Tunisia, and another year went by between the appearance in the latter and the first cases in Algeria, there was a time-lag of only three months between the first cases in Algeria and those in Morocco. As Dr. BONJEAN, Director of the Public Health Service in Morocco, observes in his Report to the Committee for Epidemiology in North Africa, this highly infectious disease found an excellent breeding-ground among the Moroccan population, a large proportion of which is infested, lives huddled together in towns, and was at that time underfed owing to the drought and the failure of the crops.

"Relapsing fever", writes Dr. BONJEAN, "first appeared in January 1945, when 5 cases were reported, 1 at Oudjda (a male nurse at the native hospital), 1 in the suburban district of Meknès, 2 at Rabat (one of the patients being a miner at Sidi-Bou-Becker, south of Oudjda), and 1 at Casablanca, where 1 case had already
been notified in December (the patient being a European from Tunis). These were only sporadic cases, and the disease did not reach epidemic proportions until February."

During that month, the Oudjda region reported a further 123 cases, out of a total of 165 for the entire region. From that moment, the incidence of the disease rapidly increased throughout the region until May (343 cases in March, 746 in April, 1,221 in May). During the two months that followed, it remained practically stationary (1,213 cases in June, 1,124 in July). In September, there was a definite decrease (267 cases). The epidemic began in the town and spread to the south and the north-west, then to the west: two other foci appeared almost simultaneously at Martimprey and Bou-Arfa.

In the other regions, the situation remained fairly quiet during February and March; and, on the whole, the cases continued relatively few in number. The Fez region, with 63 cases, came second after Oudjda, its neighbouring region. The first cases were traceable to Algeria.

Gradually, during April, a limited advance of the disease was noted in the Fez region (73 cases), Meknès (28 cases), where several of the patients were pilgrims to the Moussem of the Aissaouas, Rabat (42 cases), and Casablanca (90 cases), while the Marrakesh region also reported its first cases, to a total of 35.

May brought a sudden increase in the cases in the Fez, Meknès, Rabat and Casablanca regions; but the general trend of the curve showed a rise much less steep than had been the case at Oudjda, two months earlier.

In June and July, the Marrakesh region was gravely affected (283 cases in June and 741 in July). Here the disease curve showed the sudden steep rise which had characterized its progress at Oudjda three months previously, while at Meknès and Casablanca only a moderate increase was observed in July.

In August and September, there was a marked decrease in the number of cases in the Oudjda region (267 cases in September and 563 in August, compared with 1,213 in July); the curve displayed a certain stability in the Fez district (around 400 cases), Casablanca (around 450 cases) and Rabat (between 150 and 250 cases). On the other hand, there was an increase at Meknès (935 cases in September) and at Marrakesh (849 cases).
In October, the curve generally showed a downward tendency (2,794 as against 3,333 in September). But the number of cases reported in the Rabat and Fez areas was on the increase compared with the previous month. In Eastern Morocco, however, there had been a continuous and noticeable decrease since July.

In this way, throughout the territory, the epidemic relapsing fever, which had made its first appearance in January, rapidly spread over a considerable area—in fact, from the Oudjda region, it spread all over the country. In July, it gained its maximum hold with 3,438 cases, after which there was a slackening-off which continued until the end of October.

Between January and October 1945, a total of 18,369 cases was reported, which, if multiplied by 10, as the health authorities admit that it should be, means a total of 180,000. This is considerably higher than that for Algeria, which has a substantially similar population figure. We must also take into account the fact that the epidemic is not yet at an end, and that with the winter weather there may be a serious recrudescence.

A complete parallel between the incidence curves among the military (about 100,000 men) and among civilians is to be seen from the very beginning of the epidemic.

<table>
<thead>
<tr>
<th></th>
<th>1945</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Military</td>
<td>Civilians</td>
</tr>
<tr>
<td>January</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>February</td>
<td>10</td>
<td>165</td>
</tr>
<tr>
<td>March</td>
<td>17</td>
<td>484</td>
</tr>
<tr>
<td>April</td>
<td>32</td>
<td>1,014</td>
</tr>
<tr>
<td>May</td>
<td>87</td>
<td>1,868</td>
</tr>
<tr>
<td>June</td>
<td>117</td>
<td>2,327</td>
</tr>
<tr>
<td>July</td>
<td>297</td>
<td>3,438</td>
</tr>
<tr>
<td>August</td>
<td>258</td>
<td>2,941</td>
</tr>
<tr>
<td>September</td>
<td>232</td>
<td>3,333</td>
</tr>
<tr>
<td>October</td>
<td>237</td>
<td>2,794</td>
</tr>
<tr>
<td></td>
<td>1,287</td>
<td>18,369</td>
</tr>
</tbody>
</table>

The racial distribution of cases among the troops was as follows:

- North-African natives: 1,066
- Senegalese: 157
- Europeans: 64
RELAPSING FEVER IN NORTH AFRICA (1943-1945)

Tangier and Spanish Morocco. — It would have been of peculiar interest to know the health situation in Spanish Morocco, a thin strip of territory along the Mediterranean, whose southern border, however, is contiguous with the infected regions in northern French Morocco, from the Algerian frontier to the Ocean—i.e. over a stretch of more than 370 miles. Any observations made there would have been all the more useful as the coastal towns of Spanish Morocco are in constant and easy contact with the ports of southern Spain. In this way, the disease might easily reach Europe. It has unfortunately been impossible to obtain exact information on this matter with which we were much concerned; but it is only logical to assume that Spanish Morocco, like French Morocco, has become infected with the disease.

The example of Tangier would appear to confirm this hypothesis. The small international zone and the town of Tangier form a part of north-western Spanish Morocco. They remained unscathed for a long time; but, since the beginning of November 1945, several cases of relapsing fever have made their appearance in the town, and the number is rapidly increasing. Fifty-three cases were reported during the first fortnight of November.


(a) Environment. Throughout North Africa, doctors are agreed that the general condition of the population has done much to further the spread of the epidemic. All the countries in North Africa, indeed, are in the midst of a grave economic crisis. While 1944 was fairly dry and yielded very mediocre harvests, 1945 was a year of extraordinary drought, and the crops were practically nil, especially in Algeria and Morocco. As a result, the inhabitants have lived through a period of under-feeding, amounting to famine in certain regions, especially in the south. Also, as always happens in periods of extreme poverty, parasites, lice and bugs increased considerably; and this increase is aggravated by the almost complete lack of linen and soap among the North-African natives. It must be pointed out, however, that among the military, who receive a normal diet and where the standard of personal cleanliness is very much higher than that of the civil population, the number of cases was still fairly high.
(b) *Seasonal Influence.* It is generally claimed that the seasonal curve of relapsing fever closely resembles that of typhus. According to the classical conception, it is a winter disease, beginning in October or November, and reaching its height in March-April, after which it shows a rapid decrease and disappears completely during the summer.

In the Fezzan focus, the first cases appeared during the last quarter of 1942, but the epidemic continued to increase until August 1943. Then it disappeared in September to re-emerge in February 1944. In May 1945, it finally came to an end.

In Tunisia, the epidemic began in October 1944, grew in intensity very gradually until April, and then continued to do so at an accelerated pace from April to July, when the peak of the curve was reached. After a slight decrease in August and September, the epidemic suddenly returned in full force in October 1944 and reached its peak in March 1945. This was the epidemic year. From March onwards, the epidemic rapidly waned until, in September, there were 200 cases as against 6,000 in March.

In Algeria, the first cases occurred in November, with a sudden increase in January and February. The peak was reached in March, after which there was a steady decrease.
In Morocco, the epidemic made its appearance in January, developed regularly and rapidly during the hot season and remained stationary until the autumn.

Considering the superimposed curves of the epidemic's course in the three principal countries of North Africa in all of which the epidemic wrought enormous havoc, it would appear, allowing for the shifting of the curves, that, contrary to the classical notion that relapsing fever develops chiefly during the winter, epidemics always develop rapidly, irrespective of the season of their inception. Dr. ROUTHIER, in his report on the trend of the epidemic at Marrakesh, specifies that, "unlike the other louse-borne disease, typhus fever, the epidemic appearance of relapsing fever has been definitely a summer phenomenon. While typhus had practically disappeared from the region since June-July, as is normally the case, relapsing fever appeared in June and raged throughout the hot season." It would seem, then, that the seasonal trend in relapsing fever is much less regular than that in typhus.

(c) Epidemic Expansion and Manner of Propagation. The evolution curves of typhus and relapsing fever are not parallel, partly because the spread of the two diseases does not proceed in the same fashion. The upward rise of the typhus curve is slow and regular, while that of relapsing fever is much more sudden and violent. This fact has struck all observers in North Africa. It would seem that, from the moment when the human reservoir of virus has reached a certain level, the rate of infection increases very quickly and that the progress of the epidemic suddenly gains speed.

These differential elements—a variable seasonal incidence, and sudden and rapid extension—have led some observers to question, once more, whether there were not another germ-carrier. It would appear, indeed, that if relapsing fever, like typhus, were transmitted only by the louse, these differences should not—other things being equal—stand out so sharply. Georges BLANC, having eliminated various categories of insect carrier, has reverted to investigating the possibility of infection by bugs. This hypothesis has been put forward many times before; and it would agree fairly well with the observations made to date. Bugs, indeed, are very plentiful and extremely aggressive in North Africa; cases of relapsing fever are, if anything, more frequent in urban than in rural districts, where the bugs do not find such favourable living-conditions; finally, certain
patients suffering from the disease declared that they had never had lice, but had been bitten by bugs. Georges BLANC has undertaken a biological study of this highly complex problem at the Casablanca Pasteur Institute. So far, he has been able to report that bugs, after being hatched out, can infect themselves by biting a person suffering from relapsing fever and that, after the first slough, the infection remains; in fact, when crushed and injected, it is found that they transmit the infection. At the present, Georges BLANC draws no conclusions from this fact, but deems that further research along these lines should be pursued.

Apart from the role which may be played by insects other than the louse (though this is not proven), there is no valid explanation for the epidemiological peculiarities of relapsing fever as compared to typhus. Yet, there is one fact that should influence the way in which the disease spreads: the fact that the infective element remains active in man for a very long period.

The spirochete may not be found in a patient's blood in its normal form, except during actual fever attacks, but it is known that, during the periods between attacks, the blood remains infectious, probably owing to the presence of elements of an evolutive nature which we cannot detect.

Now, between the first invasion and the end of the recurrent attacks, a very long time-lag of weeks, or possibly even months, may occur. It has been observed, indeed, that patients, after three, four, or five months, appeared, clinically speaking, to develop a second attack of typical relapsing fever. Is this a case of re-infection? It may be so, but it is unlikely, and it would appear rather that it is a distant recurrence of the original disease. However this may be, it nevertheless remains true that, while in cases of typhus man is only very temporarily a virus reservoir, the patient suffering from relapsing fever remains infectious for a very long time, even when from the point of view of actual illness he is able to resume a normal communal life. It is certain that, when a fairly considerable number of persons have been contaminated, the "walking" reservoir of virus, as it were, becomes considerable and this greatly increases the possibilities of the rapid spread of the epidemic.

Although the hypothesis of contamination by the crushing of the infected louse, or the fracture of one of its joints, is not altogether satisfactory, it has been impossible to find any fact or even any indication pointing towards another way of transmitting
the disease. There have been cases of direct contamination between human beings, like that of the Fez midwife who became infected from having attended in childbirth a woman in the throes of an attack of relapsing fever, but that is a case of what practically amounts to an inoculation with infectious blood, through a crack in the skin or the mucous membranes, or again by inoculation of the conjunctiva. Cases of that nature seem to come under the same heading as laboratory infections.

4. Prophylactic Measures.

As always in sound prophylaxis, the control of relapsing fever includes the tracing of cases, their compulsory notification, the isolation and immediate treatment of patients in order to sterilize the virus reservoir, disinfestation of patients, suspects and contacts, restriction of traffic in infected areas, etc.

All these classical measures are excellent in the early stages of an epidemic; but it must be admitted that they are practically useless when the epidemic is in full swing and threatens to overrun the country like a tidal wave. The overworked doctors can neither visit nor diagnose the cases, treatment cannot be given to patients at their homes, where they dig themselves in, nor can they be admitted into medical institutions, which soon become quite inadequate to cope with the influx of cases. De-lousing and disinfection by old-fashioned methods were of use only in limited groups and not for an entire population. As for measures to restrict traffic, long experience has shown that these are entirely theoretical, for the native has a talent for slipping through the meshes of any restrictive sanitary network as water does through a sieve.

But for the recent introduction of dichloro-diphenyl-trichlorethane (DDT), we should have been defenceless and forced to confine ourselves to advising a certain section of the public to avoid all doubtful contacts. The use of DDT powder has revolutionized the methods of control of relapsing fever at least as much as the use of sulphonamides and penicillin has revolutionized therapeutics.

The systematic use of the insecticide has proved to be perfectly efficacious. In closed communities like the Barberousse Prison at Algiers, or the Moslem Orphanage at Casablanca, etc., or in groups with freer outside contacts, like the dockers of the ports of Algiers or Casablanca, the results achieved have been remarkable and the
Relapsing fever presents an extremely varied clinical picture. Its various symptoms demonstrate to what extent every organic system is affected. There is no need here to recapitulate a complete clinical study of the disease. In the light of the very numerous indications collected during the epidemic, we shall merely describe the average form which was most frequently observed, together with the most frequent complications. We shall then consider the differential diagnosis and the death rate during the illness.

1. *Customary Form.*

The onset of relapsing fever is always sudden. After a period of very quiet incubation, the duration of which it is not easy to establish, for it is seldom possible to fix the exact date of contamin-
ation, though, according to the various observers, it may be estimated at a period varying between 9 and 14 days, the patient develops a temperature between 103° F. and 104° F., with rigors. Headache is always extremely violent, with very marked pains, especially in the neck, the lumbar region and the root of the limbs. Bilious vomiting and painful joints often accompany these early symptoms. Immediately after comes the period of acme. The temperature remains stationary at about 104° F., the tongue is coated and thick but rarely dry and scorched as in typhus. There is very marked debility, and frequent epistaxis. The face is ashen, as in anaemia with sub-icterus.

The liver is hypertrophied and sensitive and the spleen is palpable. Urine is scanty and dark; constipation, which is always present in the early stages, is often followed by diarrhoea. This clinical picture, which resembles that of all major infections, generally persists for five or seven days. After this, the temperature drops suddenly, and this drop is accompanied by profuse sweating.

After about a week's apyrexia, during which the patient is depressed and weak, the first relapse generally takes place. The temperature rises suddenly and remains high for a variable period which, however, is generally a good deal shorter than during the period of invasion. Often only one relapse takes place, but not infrequently two, three, four and even five have been observed. It appears that the gravity of the disease increases with the number of relapses.

2. Complications.

The complications are as numerous as they are frequent and varied, so that observers, according to temperament and tendencies, have described the following specific forms of the disease: pseudo-typhic, pseudo-influenzal, pseudo-meningeal, rheumatoid, tetanic, renal, pulmonary, etc., or else various syndromes: icteric, hæmorrhagic, neuro-sensorial, obstetrical, etc.\(^1\)

The most frequent complications are hepato-nephritis and hæmorrhagic syndromes.

Hepato-nephritis is characterized by this symptomatic triad:


strong and rapidly-developing icterus, acute nephritis, often of a hæmorrhagic character, rapidly developing into anuria and a considerable degree of azotæmia (3 to 6 g. per 1000). This very serious complication may assume a hyper-acute form which is fatal within 48 hours.

The hæmorrhagic syndromes may appear anywhere and assume any given form: epistaxis, sub-conjunctival hæmorrhages, hæmaturia, rectal hæmorrhages, purpura, etc.

Nervous complications, too, are frequent, especially pseudomeningeal conditions with headache, vomiting, constipation, stiffness of the neck with Kernig's sign and exaggerated reflexes. Psychic forms are also found, with delirium during the fever attacks, auditory and sensory hallucinations, and persistent agitation, for which reason the patient has to be isolated.

Professor TOULANT, of Algiers, has published an excellent work dealing with the ophthalmic complications found in relapsing fever. In his hospital at Algiers he collected 61 histories of ophthalmic complications, including 52 of spirochætal infection of the uveal tract and 9 cases in which the optic nerve was affected. The lesions connected with uveitis—iritis, cyclitis, choroiditis—are always late in appearing: they develop between the 32nd and 90th days of illness. They develop without pyrexia and blood tests have always remained negative. Lesions of the optical nerve are grave. They are always bilateral, and blindness has ensued in 7 cases out of 9. Three of these 9 patients developed a triple complication: deafness due to affection of the acoustic nerve, blindness, and paraplegia due to myelitis. Neuritis developed precociously in the midst of the febrile period, along with the other nerve complications. It should, however, be observed that 4 cases out of the total of 9 had been treated with acetylarsan; and in view of the dangers inherent in this method of treatment, there is some reason for doubt as to the purely spirillar origin of these cases of neuritis.

Finally, two categories of complications have appeared so frequently that they might almost be considered as a normal corollary. As Professor BENHAMOU states, they are: (1) the obstetrical syndrome and (2) the de-nutritional syndrome. All observers have noted, in virtually every case, the premature termination of preg-

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nancy and the debility of the infants which almost invariably led to their death.

While most practitioners blame retro-placental hæmorrhages for abortion or premature childbirth, Professor BENHAMOU attributes these phenomena rather to the enormous drop in plasmatic proteins. This explains both the dehydration and the cachexia of patients; also, the death of the ovum before the placenta lets through the *Spirochaeta recurrentis* (obermeieri) and lastly accounts for the death or the lack of viability in the infants, whether or not they be carriers of spirochoætes. Be this as it may, these facts are of the greatest importance from a social point of view. For, besides the number of fatal cases of the disease, we get a considerable decrease in the birth rate, due to the very large number of abortions and premature births. Moreover the natives' capacity for work during their convalescence is greatly reduced and remains so for a long time, owing to their poor general condition. This inability to work may last from several weeks to two months. Dr. ROUTHIER further points out that relapsing fever favours the subsequent development of tuberculosis; and he has observed several cases of post-relapsing-fever pleurisy at Marrakesh Hospital.


It is natural that so polymorphous a disease should, clinically speaking, present considerable difficulties from a diagnostic point of view. Unless the epidemic character of the disease is recognized and in the absence of the result of laboratory tests, patients suffering from relapsing fever are frequently mistaken for malarial patients. At the beginning of an epidemic, hospital admissions are made under the most diverse diagnoses: typhus, typhoid, influenza, rheumatic fever, meningitis, pulmonary congestion, infectious jaundice, suppurating parotitis, etc.; and it must be admitted that, in view of the intensity and predominance of certain symptoms, these errors are excusable. It would therefore be useless to attempt systematically to establish a clinical differential diagnosis between relapsing fever and the various diseases mentioned above. In practice, recognition of the epidemic character of the disease is one factor which should guide the diagnosis; a second confirms it and is the only valid one: the finding of *Spirochaeta recurrentis* in the patient's blood.
And this takes us back to the routine blood-test which, in North Africa, should be made compulsory for all patients suffering from intense fever. The thick drop which is first examined makes it, to all intents and purposes, possible to confirm or eliminate malaria and relapsing fever. On the eighth day, the Weil-Felix test and the blood culture indicate the possibilities of typhus or typhoid infections. A blood count should compulsorily round off these blood tests, which are within the reach of practically every medical officer and of practising physicians in North Africa. If this simple rule were methodically applied, three-quarters of the errors in diagnosis could be avoided and the prophylactic measures and treatment properly directed.

In the diagnosis of relapsing fever, however, there remains an element of doubt owing to what certain observers have described as "associated forms". ¹

It is, in reality, a question not of association but of the overlapping of diseases. You may find relapsing fever in a malarial patient during an attack, or in a tubercular patient during an active stage of the disease, or in patients undergoing anti-rabies treatment. Cases have been seen of patients suffering simultaneously from diphtheria and relapsing fever, or even from typhoid and relapsing fever. This obviously leads to discordant positive symptoms which make diagnosis difficult, but these cases are exceptions and need not be taken into account in current practice.


It is impossible to give an accurate assessment of the mortality rate during an epidemic, when neither the real number of cases nor the total number of deaths are known. It is impossible to obtain accurate information, except from hospitals which have records of the exact number of cases treated, or from closed circles like the Army. But the information in both cases deals with treated cases—i.e., those among whom the death rate is lowest. The patient's condition prior to his illness is also of importance in assessing the death rate. We find an excellent example of this among the Casablanca records. The case-fatality figure was 3.6 per cent. at the Jules-Marrau Hospital, where patients in easy circumstances were

¹ GÉRARD, S. "Note clinique sur 857 cas de fièvre récurrente mondiale". _Maroc méd._, 1945, 24, 138.
treated; but in the Ain-Chok Infirmary, to which patients found in the streets are admitted, in a state of complete physical poverty and misery, it went up to 8.7 per cent.

Among the troops, Tunisia reported a death rate of 0.7 per cent.; Algeria gives a similar figure; but in Morocco it was 1.7 per cent. The figures from Morocco are particularly interesting, for they give the number of deaths according to race:

<table>
<thead>
<tr>
<th>Race</th>
<th>Cases</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europeans</td>
<td>64</td>
<td>2</td>
</tr>
<tr>
<td>North-African natives</td>
<td>1,066</td>
<td>11</td>
</tr>
<tr>
<td>Senegalese</td>
<td>157</td>
<td>9</td>
</tr>
</tbody>
</table>

While the total death rate was 1.7 per cent. among the military, it was particularly high (5.7 per cent.) among the Senegalese troops; and this fact goes to confirm the gravity of relapsing fever for the coloured race, as had already been emphasized during the epidemic of 1922-1925 in the French Sudan.

As regards the situation in the hospitals, Dr. Gérard reports 8 deaths for 857 cases treated in the isolation wing of the Hospital Charles-Nicolle at Tunis. This represents a very low case fatality rate: 0.93 per cent.

At El-Kettar Isolation Hospital at Algiers, 2,028 patients were treated. There were 32 deaths, or 1.6 per cent.

Elsewhere we have given the percentage of deaths in the two isolation hospitals at Casablanca: 3.6 and 8.7 per cent. respectively. At Rabat Hospital, the death rate amounted to 2 per cent., at Marrakesh to 5.88 per cent., and at Fez to 8.9 per cent., in September.

Among the untreated population, observers agree that the figure must have varied between 5 and 10 per cent., according to regions.

In this way, we may conclude that relapsing fever is a disease liable to make severe inroads upon human life when the patients are in poor condition, or are not treated. On the other hand, except in the case of the coloured races, it is comparatively benign, provided that the diagnosis is established in time and the patients receive appropriate treatment. As Charles Nicolle wrote: “No one need die of relapsing fever provided that it is diagnosed in time.”

III. TREATMENT

In the matter of therapy, it is always difficult to achieve unanimity among practitioners, for they rarely agree: each one claims to have his own personal method. During this epidemic, which
continued over a long period of time, doctors were able to try every known spirochætidal method; and it appears useful now to draw conclusions from these with a view to laying down a standard treatment.

The remedies employed were, of course, the classical spirochætidal ones: arsenic, bismuth, mercury, antimony. In Tunisia, experiments were carried out with a new method: the use of convalescent serum.

Antimony was used methodically by the Tunisian Military Health Service. Five per cent. of the patients were treated by stibophen (fouadin) and 1 per cent. by anthiomaline. These remedies did not yield satisfactory results; and in every case it was necessary to substitute arsenic for antimony.

Bismuth salts, administered in Tunisia in the form of muthanol to 15 per cent. of cases among the troops, yielded no better results. Nevertheless, Dr. Mamou considers that bismuth, while it gives less brilliant results than arsenic alone, in the form of “bicarbol”, of “quiny” or of American bismuth salicylate, will be useful in the treatment of hepatic lesions with icterus.

Mercury salts were used in the form of mercury biniodide and of mercury cyanide. The former was injected intramuscularly; but its action is slow and it does not prevent relapses. As for mercury cyanide, injected intravenously, according to Dr. Mamou, when the patient is able to withstand it and it is administered in doses similar to those used in cases of syphilis, it is a valuable remedy and several patients suffering from moderately severe forms of relapsing fever were cured without relapse.

Arsenic. But arsenical salts were the remedy that was used most frequently and with the greatest measure of success.

Pentavalent arsenical compounds, like stovarsol, acetylarsan, and arsaminol, contain a very high proportion of arsenic.

Stovarsol, administered at a rate of 3 tablets of 0.25 cg. daily for five days, was, as Dr. Routhier, of Marrakesh Hospital, states, a fairly inefficacious remedy. This was also observed in Algeria, with regard to American stovarsol.

Acetylarsan and arsaminol, on the contrary, proved efficacious. They were administered in doses totalling three ampoules, injected every other day; and defervescence was often achieved immediately after the first or second injection.

But Dr. Routhier also points out that it is only with these
preparations that serious mishaps have occurred: two cases of bilateral optical neuritis leading to blindness and one serious case of polyneuritis. All observers agree on this point, and it may be concluded that, while pentavalent arsenical compounds are beneficial in the treatment of relapsing fever, they should nevertheless be rejected because of the serious complications of a neuritic type which they are liable to entail.

So the physicians directed their attention towards the less toxic trivalent arsenical compounds. This group included: neoarsphenamine, sulpharsphenamine, arsenomenyl, mapharsen.

Mapharsen in particular was tried out in Algeria, at El-Kettar Hospital, where it gave excellent results in a dose of 0.06 g., injected intravenously. One injection was given at the onset of the febrile period, or two injections at an interval of one day. In the *Bulletin of Communicable Diseases*, Vol. 2, No. 12, published by UNRRA, a comparative experiment with American stovarsol, arsphenamide and mapharsen was analyzed. This last preparation has one limitation, pointed out by those who administered it, especially in Morocco: it produces considerable shock at the first injection. Also, the Army Medical Service observes that it has a less beneficial action on relapses than arsphenamine.

In practice, neoarsphenamine was used most frequently and with the most consistent measure of success. In 75 per cent. of the cases, defervescence with profuse sweating was produced after the first injection. Practitioners differ as to the rate at which these injections should be given; but all are agreed that, in order to obtain really lasting results as to sterilization, small doses should not be given, and the treatment should be methodically pursued. In Tunisia, at the Charles-Nicolle Hospital, three injections are given of 0.30, 0.60 and 0.90 g. respectively, with a two-day interval between each; at Rabat Hospital, three injections are given, of 0.60 g. on the first day, 0.75 g. on the third and 0.75 g. on the sixth. At Marrakesh Hospital, the injections are given as follows: 0.30 g. the first day, 0.45 g. the second and 0.60 g. the fourth. It would seem that the latter produced the best results for the minimum of toxic preparation injected.

*Use of Convalescent Serum.* A new method of treatment was suggested to the North-African Committee for Epidemiology by Médecin-Colonel Cros, Director of the Army Medical Service in
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Tunisia. This is treatment with convalescent serum. This sero-
therapy, according to Colonel Cros, has been applied in military
hospitals since May 1945. It is based upon the lytic action of con-
valescent serum on the spirochète, confirmed in vitro and in vivo
at the laboratory of the Louis-Vaillard Military Hospital by Médecin-
Commandant STORA; it was stabilized according to the method
of the Transfusion Centre in Tunis, and used in 32 cases.

It was used in particular in cases where the hepatic or renal
condition (icterus, high degree of azotœmia, hæmorrhagic syndrome)
justified some hesitation in the use of arsenical compounds.

The results fully confirmed the experimental observations: in
80 per cent. of the cases, an intravenous injection of 20 cc. of serum
was sufficient to obtain, in 12 hours, definitive apyrexia without
relapse, and the rapid disappearance of the hepatorenal symptoms.

Twenty per cent. of patients suffered a relapse, and in one case,
the spirochætes were found active in the blood during the attack;
but a further injection of 20 cc. at the onset of the relapse brought
about the sudden and definitive cure of the patient under the same
conditions as mentioned above.

Finally, we must emphasize the remarkable hæmostatic action
of the "stabilized normal human serum". With its aid, it has
been possible rapidly to check grave epistaxes, hæmoptyases and
intestinal hæmorrhages, the appearance of which seemed to justify
a pessimistic prognosis.

* * *

To summarize, the UNRRA Mission in North Africa was able to
study the origin and development of an epidemic of relapsing fever
of exceptional proportions, which developed in the Fezzan district
in 1942, extended from east to west, covering 2,100 miles of territory,
claimed more than one million victims and caused, if we accept an
average case fatality rate of 5 per cent., at least 50,000 deaths.
Even now, the epidemic still rages in Morocco.

Our investigation in North Africa remains incomplete, for the
epidemic, according to information received, has now spread to
Egypt, where 14,000 cases have so far been notified, and where the
death rate is very much higher than that which we observed else-
where. Cases have also been imported into West Africa by Senegalese infantry evacuated from Morocco. Fortunately, thanks to the
energetic measures taken by the Directorate of Public Health in
French West Africa, the fever did not gain ground in West Africa as was the case in 1922, when relapsing fever was imported by native infantry landed at Conakry. The epidemic has also spread to Tangier, and probably to Spanish Morocco, whence it may easily spread to Spain.

The North-African health services made heroic efforts to check the spread of the epidemic; but the impetus of the epidemic was such that they were powerless to arrest its onrush. It is to be hoped that efficacious measures may be taken to deal with it in countries that are threatened but where it has not yet appeared. The following measures are essential:

1. Compulsory notification of cases, as recently laid down under French law;
2. Disinsectization with DDT powder to be widely and methodically applied;
3. Rapid and systematic treatment of patients to avoid the formation of a considerable reservoir of virus.

Too many treatments have been tried unsuccessfully or even with the gravest consequences for the patients; it therefore appears necessary to make provision for standard treatments.

The attention of public health services of the countries concerned should be directed towards these essential factors.

Apart from these practical conclusions, the study of this epidemic shows, once more, the close epidemiological relationship existing, from the Red Sea to the Atlantic Ocean, between all the North-African countries from Egypt to French West Africa. One of us has frequently emphasized this fact. The recent war has again served to show its truth and importance.

This immense region along the south coast of the Mediterranean is the real sanitary frontier of Europe. Beyond this frontier, all the major epidemic diseases are rampant—plague, typhus, smallpox, relapsing fever—as well as permanent endemic diseases, such as dysenteries, amoebiasis, malaria; and this sanitary frontier is one which is all the more easily crossed because the Mediterranean is "a sea which unites and not one which divides". Moreover, communications are becoming more and more frequent and rapid.

The UNRRA Mission would be happy to feel that its work had served to underline the importance for world epidemiology of the health problems besetting North Africa.