CHAPTER 10

RELAPSING FEVER

RELAPSING fever, though not a serious military problem, caused considerable temporary invalidity among the men it attacked in the forces in Palestine, Syria and the North African littoral of Libya and Cyrenaica. Fortunately the type encountered was the sporadic tick-borne disease and not the epidemic variety carried by lice. As is well known, the infective agent is a spirochaete, causing irregularly recurring bouts of fever and with a predilection for attacking the central nervous system. The febrile attacks in themselves were not very different from those of several other pyrexial diseases. The temperature was often high and a rigor was common, particularly in the first attack, in which the temperature frequently exceeded 103°F. The primary bouts of fever usually lasted one to three days. The accompanying symptoms included severe headache, pain and tenderness in the eyes, photophobia, dizziness, pains in the joints and limbs, nausea and vomiting. Similar symptoms were seen in the relapses but usually they were then less intense. The most significant symptom was headache, which was practically always present and was characteristically intense and severe. Prostration was often considerable. Enlargement of the spleen occurred in at least a third of the cases. Tenderness of the spleen was a feature of the disease in some areas, particularly in Tobruk. Enlargement of the liver was less frequent; jaundice was only occasionally seen, and then usually in the most severe cases. The cervical lymph glands were sometimes enlarged. In a few patients erythema or scattered petechiae were observed on the skin, and herpes of the lips was not uncommon, particularly in the recurring bouts of fever.

Tick bites were found in at least a third of the patients when first seen: a small papule was present at each site and sometimes reactivation of these occurred during successive attacks. These bites were at first not noticed by the patient, since the ticks introduced a substance at the time of biting which acted as a local anaesthetic. This produced immediate analgesia in the region of the bite, thus permitting the adult or larval tick to feed undisturbed for its required period of fifteen to thirty minutes. This analgesia lasted up to two days. Clinical symptoms did not appear till five to eight days had elapsed after the biting. Relapses were usually, but by no means invariably, less severe than primary attacks; they generally lasted a shorter time, sometimes a few hours only. Both the number and the intervals between attacks varied. In many cases seen in hospitals in Palestine there were five or six relapses, but only one or two occurred in others. Higher numbers have been reported. The interval between attacks was sometimes as short as a few days, but could extend to a month or six weeks. Periodicity, though unusual, was occasionally a striking feature: some patients missed a cycle, only to relapse again later. During these intervals some patients remained well, but others had persistent

headache, malaise and general asthenia. Continuing headache was a significant symptom and was associated with residual infection of the nervous system in many instances.

COMPLICATIONS

The nervous system bore the brunt of most of the complications. Rigidity of the neck during the febrile stage and a degree of meningismus were regarded as part of the clinical picture; some actual involvement of the meninges was common and in rare instances the meningeal reaction was intense. Cranial nerve affections were not uncommon; sometimes these were not seen till months after the original infection. The commonest was facial palsy, which was occasionally bilateral. As a rule it resolved, but some permanent residual paralysis has been observed. Lesions of the 3rd, 4th and 6th cranial nerves were occasionally seen, causing ptosis or affection of eye movements. The 5th and 8th have been affected too in some epidemics, but no such lesions seem to have been observed in Australian soldiers. The frequency of these complications varied considerably in different areas. Among 68 men treated for relapsing fever in Tobruk, Cooper saw 7 facial palsies, and in addition 13 instances of meningeal involvement. Adler found only 2 patients with neurological complications out of 45 seen in Palestine before the war, but Scott in experiences with the R.A.M.C., found 9 out of 41. One of his patients was an Australian soldier who had right abducens palsy with meningitis; this man later had an upper motor neuron lesion affecting his left leg, but some months later appeared to have made a complete recovery.

Involvement of the spinal nerve roots occurred rarely: in one instance the 7th cranial nerve, and the 5th and 6th cervical nerves were paralysed. Encephalitic signs of wide variety were sometimes seen. Ataxia of movement and speech with other cerebellar signs have been seen.

Iridocyclitis also occurred. Hamilton saw 4 cases among 28 men infected in the Western Desert, but none in 63 patients from Syria. The possible significance of this will be discussed presently. Iridocyclitis yielded to rest and mydriatics and left no sequel. Papillitis was seen in a few cases in association with encephalitic symptoms; it too resolved, and no optic atrophy was observed.

The predilection of the infecting spirochaete for the nervous system is shown by the observations on the cerebro-spinal fluid. Lumbar puncture during the febrile period frequently showed the fluid to be under increased pressure. A pleocytosis was observed in about half the cases, and was often associated with moderate increase in the protein content of the fluid. The cellular increase was due to lymphocytes, but in some instances a small number of polymorpho-nuclear cells was found too. On a few occasions the cell count of the fluid reached over 400 per millilitre. Such changes were more frequently seen in patients showing signs of involvement of the nervous system. Occasionally spirochaetes were demonstrated in the cerebro-spinal fluid. Blood counts commonly revealed a moderate neutro-

phile leucocytosis, up to 12 to 15 thousand cells during the pyrexial periods.

DIAGNOSIS

The diagnosis of a primary attack was often difficult. Even the intense and sometimes persisting headache was not at first helpful in diagnosis, for it was also a feature of malaria, particularly of the malignant tertian type, and to a less extent of sandfly fever. Casualties from the Syrian campaign might have been suffering from any of these diseases. Combinations were seen too; M.T. and relapsing fever co-existed in several patients, thus complicating diagnosis. It was obviously important to demonstrate the spirochaete in the blood. This was not always easy to do as these organisms were scanty in the peripheral blood, but the pathological diagnosis was usually satisfactorily established if persistent search was made for spirochaetes in thick blood films. Such a search frequently had to be pursued into the apyrexial period, when it was often possible to find spirochaetes that were elusive during florid fever. Incubation of the blood was not found particularly helpful, nor was examination of the white cell layer of centrifuged citrated blood. In Syria, G. B. Hall and E. Ford tried the method of centrifuging a large amount of blood without any resultant improvement in diagnosis. Animal inoculation was definitely helpful in making a diagnosis, obscure by other means, but guinea pigs were difficult to rear in Palestine and the Lebanon and consequently were scarce.

In the history-taking of men with suspicious forms of illness, enquiry into their movements was often helpful, to discover whether they had been resting in rocky places or in caves or dug-outs, which were the common habitat of ticks in known infected areas. Review of individual histories sometimes made the diagnosis simple. Recurring attacks of fever of the appropriate pattern established a clinical picture which became quite distinctive when the involvement of an eye or one of the cranial nerves was added to it. There is no question that some of the alleged multiple attacks of sandfly fever, sometimes self-diagnosed, from the first Libyan campaign were due to relapsing fever. The morphology of the spirochaete was consistent with the usual descriptions, and its recognition gave rise to no trouble once it was found.

EPIDEMIOLOGY

The epidemiology of the disease had some interesting features. It was important to be sure of the nature of the vector. There was really no doubt felt that this was the tick-borne type of disease, but the possibility of the louse-borne variety was discussed at one time during the winter campaign in the Western Desert. There was little possibility of louse transmission, for this form of the disease is due to a different organism which does not indiscriminately use either vector. Clinical evidence in favour of the tick-borne variety included the sparse appearance of spirochaetes in the peripheral blood, the infrequency of jaundice, the shorter duration of primary

fever, and the greater frequency of relapses. Hamilton pointed out that the greater frequency of iridocyclitis in Tobruk than in Syria was curious, as this complication is commoner in the louse-borne type of the disease. The Tobruk series was, however, small, and the spirochaete is known to be a very mutable organism both with regard to the symptoms it produces and its immunological characters. The actual circumstances in which men were infected overwhelmingly pointed to tick transmission; ticks were found on the men, and they or their larvae infested many of the endemic areas, in North Palestine and Syria particularly. Adler and others in 1937 had previously described a series of forty-five cases from North Palestine, thirteen of which arose from infection in a single cave. Two medical men investigating the outbreak were attacked by larval ticks in the same cave and contracted the disease. One interesting episode during 1941 was the occurrence of relapsing fever in four Australian soldiers who had not been recently outside an area in Southern Palestine, hitherto believed to be free of the disease. Enquiry showed that they had on the same day visited a cave some miles away from any military camp.

It was believed that the tick vector in Palestine was the *Ornithodorus papillipes* (*tholozani*), and the organism the *Spirochaeta sogdianum,* possibly *S. persica.* The tick vector in North Africa was *O. erraticus* and the spirochaete *S. berbera.* The exact identity of the vector and spirochaete responsible for infections seen in the A.I.F. was not certainly established, despite the assistance of experts in the Hebrew University, for the difficulties of collection and transmission of specimens at the time were considerable. In the desert ticks were found in crevices and hollows of rocks, in Syria they frequented rocks and particularly caves. Both adult and larval ticks transmitted the infection, and as pointed out above, in spite of their lengthy feeding times, the larvae in particular were often not discovered for some time by reason of the painlessness of the bites.

TREATMENT

Treatment was not very satisfactory. It is interesting that during the 1914-1918 war arsenic earned a reputation as a specific, but in 1940-1941 its effect was on the whole disappointing. Arsphenamine was given in the form of "Neosalvarsan". The official instruction advised successive intravenous injections of 0.45 gramme, 0.6 and 0.6 gramme on the first, fourth and seventh day. It was thought better not to administer the drug during an actual paroxysm. Arsenic injections did not appear to prevent relapses so far as observation went. Accurate figures concerning the frequency of relapses and indeed the after history of patients have been difficult to obtain since the men were infected in widely separated areas, and frequently treated in numbers of different medical units. It was the general opinion of physicians that arsenic was not very successful in the local varieties of the disease, even allowing for the greater resistance to this treatment known to be a feature of the tick-borne disease when compared with the louse-borne variety. Therefore, as there was a prevailing shortage of arsenical drugs, the course given was usually limited to three doses.

Bismuth was used in some later series in 1942, eight injections being given alternating with five of arsenic. Limited experience suggested that this was perhaps of some value. There was no evidence that malaria lessened the liability to recurrences of relapsing fever.

In 1941-1942 A.I.F. hospitals in the Middle East treated 382 men with relapsing fever with no deaths; their average stay in hospital was 42 days. When men were free from symptoms and neither blood nor cerebro-spinal fluid showed any abnormality, and no fever had occurred for two or three weeks, they were considered to be convalescent and were treated as such.

REFERENCES

S. ADLER et alii, *Army Trop. Med. & Path.*, Vol. XXI, 3 Apl. 1937.
E. L. COOPER, *Med. Journ. Aust.*, 6 Jun. 1942.
J. B. HAMILTON, *Brit. Journ. Ophth.*, Feb. 1943.
R. B. SCOTT, *Lancet*, 30 Sept. 1944.
D.G.M.S., Army, *Tech. Instr. M.E.*, No. 16.