FURTHER OBSERVATIONS ON 'TRENCH FEVER':
A RELAPSING FEVER OCCURRING WITH THE BRITISH TROOPS
IN FRANCE

(A Report to the Medical Research Committee)

BY G. H. HUNT AND J. W. MCNEE

THE disease now known to our armies as 'trench fever', which has been met with among the troops in France since the early summer of 1915, has in recent months been the subject of published investigations, in which both of us have taken part (Hunt and Rankin, *Lancet*, Nov. 20, 1915, and McNee, Renshaw, and Brunt, *British Medical Journal*, Feb. 12, 1916). Since these observations were published further work has been carried on, leading to results which we now propose to give. The points not hitherto discussed, or on which additional evidence has been collected, may be stated at once to show in what way the details now given amplify our previous experience and add to our knowledge of the disease as a whole.

These points are—

1. The duration of the disease, and its importance as a source of wastage in our armies.
2. Definite outbreaks of the disease in medical units.
3. Its means of transmission.
4. Its probable incubation period.
5. Attempts at specific treatment.

Symptomatology.

A brief account of the disease as it exhibits itself in the winter months will have some value, as in neither of the previous papers referred to was a very full account of the symptoms given. The following description, written by a patient himself, is so typical a picture of the illness as seen at present, that we cannot do better than quote it in full. This account was drawn up unaided, from notes the patient had kept in a diary.

'On Monday morning I felt ill. The general symptoms were a hot, drowsy, powerless feeling, accompanied by dull pains up the front of the legs. We had to go to the trenches at night, and on arrival I collapsed and slept in a dug-out all night. Tuesday morning I felt a lot better, and did not report sick, but on

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Tuesday night pains began again, and on Wednesday I reported sick. I described the symptoms and had my temperature taken, which was high, and that night saw me in the hospital at A——, labelled "influenza". Thursday, Friday, and Saturday morning my temperature was normal though the pains were still there, and on Saturday afternoon I was sent to the hospital at S——. My temperature was taken there, which was 101 as far as I remember, and after describing the pains, &c., I was sent to bed labelled "trench fever". All day Sunday my temperature was still up, and the pains up the legs and in the head most violent. On Monday morning my pains got a lot better, and with it my temperature became normal and remained so all day Tuesday. On Wednesday morning my temperature rose again to 100, and at night was somewhere about 102, and the pains in my legs and head again became very bad. This continued all Thursday, and during the night my pains got much easier. On Friday my temperature was normal, and also on Saturday morning. On Tuesday (i.e. the next week) I was sent to this hospital at M——. My temperature remained normal and my pains very slight until the morning of the 23rd. During the afternoon of this day the pains in my legs and head again became very bad, and that night my temperature rose to 101, and remained high until the morning of the 26th, when it became normal and the pains decreased in violence. During the next three days the pains were much easier, and my temperature each night registered a little over 99. On the afternoon of the fourth day (29th) the pains became very bad and my temperature rose again to over 100 and remained so until the morning of the 2nd, when it became normal. During this attack my pains were more violent than in any of these attacks, and it was impossible to sleep. They stretched from the bottom of the legs right up the thighs, accompanied with a headache and a slight pain in the back. I may say that in the interval between my previous attacks the pains in the legs and head were always there, but to a much slighter degree. But after this (my fifth and last attack to date, in which the pains were more severe than any before), the pains completely died away and were not felt by me for about sixteen days, after which I felt them again slightly for three to four days, during which time my temperature registered a little over 99. Since which time (four days ago) I have not felt them, and my temperature has been normal. During the attacks I felt very weak and could hardly walk; I am now a lot stronger, but any undue exertion such as running, carrying anything, shows this weakness up.

This description illustrates almost all the characteristic points, particularly the site of the pain, and the alleviation or complete disappearance of symptoms which accompany the fall of temperature. The onset with weakness and drowsiness is typical of one class of case, whereas in others sudden dizziness or a 'shivery feeling' usher in the disease. More rarely a feeling of *malaise* lasting a day or two precedes the attack. Certain symptoms, in view of our more numerous observations, may be referred to a little more in detail. Headache is invariable, usually frontal, and a very common complaint is of pain behind the eyes, increased by movement of them. Less commonly the headache is universal, and may be most intense in the nape of the neck; in two cases, indeed, pain and stiffness in this region were so intense that lumbar puncture was performed to exclude meningitis. Another important diagnostic point is the absence of any nasal or bronchial catarrh. The bowels are generally constipated during the pyrexia, and vomiting has sometimes occurred, possibly as a result of this. Diarrhoea is never seen, and its spontaneous occurrence would exclude a diagnosis of the disease.

When seen during a febrile period the patient looks flushed, but the eyes are clear and bright. He frequently does not look as ill as the high fever would lead one to suspect, and various patients have been discovered reading at a table with temperature up to 104° F. Less commonly the sense of weakness is much more profound, and the patient looks seriously ill. Such cases have come under grave suspicion of belonging to the enteric group, until the negative bacteriological examinations and the occurrence of typical short relapses proved them otherwise.

The tongue is often somewhat furred during the fever, but never becomes dry. Routine examination of the heart, lungs, and abdomen has never revealed anything abnormal. The spleen has not been found enlarged, although special attention has been paid to this point in some hundreds of cases. Albuminuria, even in cases with very high fever, has never been observed.

Course of the Disease.

Two clinical varieties of the disease were distinguished in a previous paper (McNee and Renshaw), and named (1) the short type, (2) the long type.

The short type. This type, when the disease first began to be recognized, was certainly much the predominant one, but this is no longer so. In one account of the disease (Hunt and Rankin) thirty cases, mostly of this type, were described; in the other (McNee and Renshaw) all but twenty of the cases observed fell into this group.

The characteristic temperature chart shows a period of pyrexia lasting six to eight days. In a number of cases there is an intermission, in which the temperature may come down to normal or almost normal, but without much, if any, relief from the symptoms. Such an intermission, when it occurs, is met with between the third and fifth days, and is of short duration. Coincident with the fall of the temperature to normal about the end of a week, all symptoms disappear at once, and the patient feels perfectly well. A single relapse follows, usually after an interval of two to four days. During the relapse all the previous symptoms return, but are never so severe as before. This relapse marks the end of the illness, and the patient is generally fit for duty almost at once. A number of such cases have been observed for weeks, and some even (R.A.M.C. personnel) over a period of months thereafter, without the least return of pain or fever, so that there can be no question (as has been suggested to us) of additional relapses occurring when the patient is not under observation, in this type of the disease.

The long type. This type, from being one of comparative rarity, has now become during the winter months the commoner variety of the disease. Here the illness takes on the character of a true relapsing fever, and as many as five or six relapses may be met with extending over a period of several weeks. The symptomatology is identical with that of the previous type, the only distinction

being that the initial bout of fever is short (frequently about three days), and the relapses usually as severe as the original attack. No definite periodicity in the relapses can be traced from the examination of many charts.

Usually the first relapse occurs four or five days after the temperature has fallen to normal, but the intervals between subsequent relapses vary between three and thirteen days. During these intervals the temperature may remain normal, but more frequently it rises slightly above normal in the evenings.

After the last definite relapse, as indicated by a distinct spike on the temperature chart, has occurred, the patient is frequently by no means cured. Oscillations of temperature, with return of pains and headache, may recur over a period of weeks or (rarely) even months. During such recurrences the temperature is always found elevated, generally to about 99° F. or about 100° F. Such men are quite unfit to return to duty at once, and are practically all evacuated to the base, and many to England.

Duration of the Disease.

This is one of the most important considerations for armies in the field, where every source of wastage counts. We wish, therefore, to draw attention definitely to the fact that 'trench fever' as seen during the winter and spring months cannot be classed as a short disease. The longer, relapsing type prevails, and the average duration of a number of recent cases is certainly not less than *four to six weeks*, during which time and generally longer the man is unfit for active duty. This represents a period of loss but little short of that brought about by the milder cases of the enteric group and many wounds.

We have in addition charts which show relapses, or oscillations of temperature accompanied by definite symptoms, for a much longer period, in which the men remained unwell for nearly three months.

Thus the disease, which is now widespread among the troops in France, would seem, from the point of view of wastage alone, to merit every attention.

Outbreaks of the Disease in Medical Units.

Several such outbreaks have come more or less under our direct observation, and especially one at a casualty clearing station to which one of us was attached (G. H. H.). As such cases were so completely under control from the outset, they were studied with care, especially with regard to factors which might throw light on the means of infection, the incubation period, &c.

Between July 13, 1915, and January 2, 1916, thirteen men of the unit referred to above were affected with typical attacks of the disease. At first the cases developed with long intervals between them, i.e. between July 13 and October 5 four men fell sick at different times. During the second week of October two men fell ill, and in the months of November and December eleven

men (about one-tenth of the total strength) were admitted to hospital suffering from the disease. Both the short and the long type of cases occurred, and certain of the latter group must be referred to individually.

In investigating the outbreak special attention was paid to the following points:

1. Had the men affected been nursing patients suffering from the disease, or had they been in contact with other men in the unit who developed it?

2. Had they been bitten by lice, or noticed them on their clothes?

3. The point whether a man can have two separate attacks of the disease came up for consideration for reasons considered below.

(a) All but three (Ptes. C., Ch., and G.) had been attending cases of 'trench fever'. Pte. C. slept with Lance-Corporal T., and developed the disease six days after the latter fell ill. Pte. Ch. was never in the wards, nor did he sleep beside any of the men who fell ill. His duties were concerned with the cleaning of the hospital blankets, and the question at once arose as to whether he was infected by contact with the blankets, and if so, in what way. Pte. G. was a stretcher-bearer, and thus came into closer contact with the clothes and blankets of the patients admitted to hospital than with the patients themselves.

(b) Although every facility possible is given to men of the unit for bathing and changing their clothes, it is inevitable that their close contact with men from the trenches should lead to occasional infection with lice. Seven out of the thirteen men who fell ill stated that they had found lice from time to time on their clothes, and positive evidence on this matter is of greater value than a negative reply, since a few lice on the clothes may readily pass unnoticed unless a careful search for them is made.

(c) Three men (Sergt. M., Pte. N., and Pte. S.) were in hospital on two occasions, and the question whether they were suffering, on the second admission, from a new infection or a recurrence of the first, is of such importance both with regard to the duration of the disease and the question of immunity from fresh infection, that the cases will be described in some detail.

Sergt. M. had two typical attacks, the first from July 14 to July 26, and again from October 5 to October 12. Between the bouts of fever he was never really well, being easily tired and complaining from time to time of slight attacks of headache and pain in the legs. After the second pyrexial period symptoms continued to recur at intervals, and in February, 1916, eight months after the first infection, he still complained of them occasionally. During this month his temperature was taken regularly, night and morning, for eighteen days, when it was found that his temperature touched 99° F. on four evenings, and twice reached 99·4° F. It seems almost certain that the second febrile attack in October was a recurrence of the first in July, and not a new infection from without, and this case moreover seems to afford an example of the effects of the fever persisting for eight months.

Pte. S. was in hospital from September 11 to September 20, and again from November 26 to December 6. During the interval he complained from time to

time of aching pains in the legs, and the second attack must again be put down to a revival of the original infection.

Pte. N. was in hospital between November 5 and 14, and later between December 17 and 29. Between the two attacks he felt perfectly well, and was free from all symptoms suggestive of the disease. Here, if the second attack is to be considered dependent on the primary infection, it is an example of the virus lying absolutely dormant for a period of thirty-three days.

The Means of Transmission of the Disease.

Little evidence with regard to this was available at the time of the previous papers. The experimental evidence of McNee and Renshaw, however, which went to show that the virus was one contained in the corpuscular elements of the blood, pointed strongly to the infection being introduced by a parasite. We think sufficient proof has now been obtained that the body louse is the parasite concerned. Absolute proof is lacking, as we have been unable to carry out actual transmission experiments with lice from infected cases, but the indirect evidence given below seems to build up a good case for our view.

First of all with regard to the outbreaks in casualty clearing stations. It is noteworthy that in a small ward containing ten beds, three orderlies who have been attending cases of the disease for many months have never become infected. Thus close personal contact alone appears insufficient for infection. In another casualty clearing station, where four of the ward orderlies had typical attacks, the conditions were different. The ward was a large one, and often contained over a hundred patients, mostly slight cases of illness, and some of whom were certainly lousy when admitted. The men with 'trench fever' were kept more or less together on one side of this ward. Other men of the personnel or clearing stations affected by the disease have included:

1. The attendant of the Thresh disinfector.
2. The attendant of the incinerator.
3. A stretcher-bearer.
4. The man who had charge of the removal of soiled blankets.

These four men were never in contact with patients, but always in proximity to the clothes or blankets of cases admitted, and therefore very liable to infection with lice.

Of thirteen men in a clearing station who developed the fever, seven admitted they had seen lice from time to time on their clothes. It is further of interest that the chief outbreak in this hospital occurred three weeks after the battle of Loos, at which time many hundreds of sick and wounded were passed through in a short space of time, and attention to patients as regards lousiness was necessarily less complete than in ordinary circumstances.

Almost all the men affected by the disease state freely that they have been bitten by lice, and indeed lice have been taken off many typical cases in field ambulances and dissected, in the search for a plasmodial virus. Officers

and men are affected by this disease in about the same proportion, and for the trench zone the same holds as regards the presence of lice.

The point brought out in a previous paper that only two classes of men are affected, those from the trench zone and men of the Royal Army Medical Corps, is very important, and favours our view. Apparently this distribution, after the disease has been continually present in our troops for over a year, must be somewhat modified, as fresh infections have recently been met with further from the front. This is of course not surprising, when the movements of troops are considered along with the frequency of the disease and the prevalence of lice.

At first it was impossible to say whether some flying insect such as the mosquito, &c., might not be the carrier of the virus, but any such view has been negatived by the persistence of the disease unchecked throughout the whole winter. Lice are really the only common parasites found abundantly at all seasons of the year. It is a curious and interesting fact, when the nature of the billets in barns is considered, that fleas appear to be scarce. They are seldom found, and are never complained of by the men themselves.

From the above evidence, necessarily not complete by the absence of experimental transmissions, it seems almost certain that the body louse must be considered the means of transmitting the disease in nature.

Incubation Period.

The only direct evidence bearing on this question is the result of the experimental inoculations. In these the period varied from six to twenty-two days. The shortest intervals followed the *intravenous* injection of 'whole blood', the *intramuscular* method being employed where the illness developed after twenty-two days. It seems feasible to suppose, if the louse be the means of transmission, that much more of the virus may be introduced by an injection of 5 c.c. of blood than can be transferred by the bite of a small parasite. We believe, from a number of observations in different cases and collections of cases, that the incubation period in nature is a fairly long one, somewhere *between fourteen and twenty-four days*. It is impossible to give in detail a list of all the observations which have led us to define this time, but an example may be given to show the type of evidence on which we have had to depend.

Sergt. B. stated that he knew himself to be lousy on May 5, but then got rid of them by bathing and changing his clothing. Thereafter he was not in the trenches, and was free from lice until May 21, when he was admitted to hospital with an attack of 'trench fever'. Sixteen days thus elapsed between the time when he was lousy and the onset of his illness.

Treatment.

Before the identity of the disease was established experimentally, the treatment was naturally purely symptomatic. *Quinine*, 30 grs., along with *sodium salicylate*, 90 grs. (or sometimes *aspirin*), was given daily to reduce the temperature and relieve pain. Both of these drugs were found definitely of much value for the effects named, but it was soon obvious that neither drug cut short in the least degree the course of an attack.

Attempts were then made to find some more specific remedy, and in view of the experimental evidence pointing to the infective virus being always in the blood, arsenic was tried in the form of *salvarsan* intravenously, while *Fowler's solution* was also given to some cases by the mouth. The *salvarsan* was given in doses of 0.3 grm., and was administered (1) at the onset of a relapse just as the temperature was rising, (2) after a febrile period was over, to prevent a further relapse. No beneficial effect was attained, the course of the disease continuing unchecked.

Antimony, in doses of 1/50 grain intramuscularly, was given daily for a week, but the relapses followed as before, while *mercury* given by inunction and sometimes combined with *iodide of potassium* proved equally useless.

In one severe case *eusol* was given intravenously (75 c.c. of a 0.5 per cent. solution) without influencing the fever in any way.

Considering the possibility that, as occurs in other diseases, antibodies to the virus might be developed in the course of spontaneous cure, and have a therapeutic value, two cases were treated with the *serum of a carefully chosen convalescent*. Twenty cubic centimetres of blood were withdrawn from this patient ten and twelve days after his last relapse. After separation of the serum, this was injected four hours later into the veins of two patients who were just beginning to relapse on these two days. In both patients the course of the relapse was in no way altered, and subsequent relapses occurred in both men.

Thus, to sum up, no treatment hitherto tried has been in the least successful, except as regards the control of symptoms.

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