TICK FEVER IN EAST PERSIA.

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On November 17, 1919, whilst touring the upper sections a wire was received from the A.D.M.S. asking for an investigation into an outbreak of fever in a company of Indian Pioneers working on the road at Sharifabad, north of Turbat, and that influenza was suspected.

On arrival at Turbat eighteen cases from this company were found in hospital under the care of Captain Haji, I.M.S. This officer stated that he first suspected the early cases of being sandfly fever. Firstly, on account of the history, that they had been bitten by insects; secondly, on account of the symptoms, which were those of frontal headache and pains referred to the limbs and back; and thirdly, owing to the fact that blood films were negative both to malaria and relapsing fever. Some of the later cases had marked chest symptoms with frothy sputum and he was debating in his mind whether he should diagnose these as influenza. One case had been diagnosed relapsing fever and spirochætes had been found in the blood.

On going round the wards, it was observed that all of the cases, including the one with spirochætosis, presented the same symptoms during their attacks of fever, namely, severe headache, frequently frontal in type, pains in the loins and down the backs of the limbs or generalized pains all over the body. The majority had palpable spleens and a few had a superadded bronchitic condition. Several of the cases had normal temperatures at the time of inspection and it was noted that their temperatures had come down by crisis and a certain proportion were just commencing a relapse.

On further investigation, it was found that the patients complained of having been bitten whilst living in a serai at Sharifabad and the majority were able to produce proof in the form of well marked healing or healed scars of bites which were usually sited on the wrists, ankles, or neck. Only two or three of the men had seen ticks in the serai and none of them knew the cause of the bites, as they were bitten at night, and being Pioneers doing hard work slept heavily. All cases were provisionally diagnosed tick fever and the daily examination of the blood, using thick drop films, was commenced. The total number of cases admitted into hospital at Turbat from this company was twenty-two and spirochætes were eventually found in four cases.

On November 20, 1919, Sharifabad was visited. This is a village
Tick Fever in East Persia

situated in a narrow elongated valley twenty-three miles south of Meshed at the junction of the East Persian and Tehran-Meshed trade routes. During the winter the cold is severe, chiefly on account of the winds which sweep down the narrow valley. In the village are several old Persian serais which afford accommodation to the personnel of the numerous Persian donkey and camel caravans.

From the information gathered at Sharifabad, it appeared that three platoons of a Mahratta Company of Pioneers arrived at Sharifabad on October 24 to do work on the road and being down-country Indians complained of the severity of the cold. In consequence of these complaints, the officer commanding the company took over and billeted the men in one of the Persian serais after thoroughly cleaning it out and disinfecting the floors of the rooms with cresol. Fires were then lighted in the rooms and a few days later the men commenced to see occasional ticks and complained of being bitten. However nobody apparently connected the ticks with the bites.

The first case of fever reported sick on November 5, twelve days after the occupation of the serai and within the next five days twenty-five more cases occurred. On November 11, No. 14 platoon, strength then thirty-nine, left for Turbat, and whilst on convoy an additional twelve men developed the disease. In all twenty-two cases were admitted to hospital in Turbat from No. 14 platoon. The officer commanding the company at this time began to think that there might possibly be some connection between this disease and the serai, and on November 15 he moved Nos. 15 and 16 platoons into camp, leaving the sick and sick attendants in the serai. The total strength of Nos. 15 and 16 platoons was 110 men; of these, 50 contracted the disease and, out of the 60 effectives left, 24 only were unbitten.

On visiting the serai with the officer commanding the company and the serai keeper it was seen that it was of the usual Persian type, namely, of some considerable age, built of burnt brick, and enclosed within four walls in the form of a quadrangle, the gateway in the centre of one of the walls. The living rooms, some of which were being used for housing the sick, were built against the three inside walls facing the gateway, on a brick plinth about three feet six inches in height. Each room possessed an outside verandah space with which it communicated by means of an open archway. In the centre of the serai was a clear space for the accommodation of the animals belonging to caravans.

At the time of inspection the sick, eighteen in number, were being moved from the serai, and it was seen that they exhibited the same symptoms as the cases in hospital at Turbat. Respiratory complications, however, were not so prevalent amongst them. Whilst looking at the cases the Sub-Assistant Surgeon in charge brought to our notice a sick attendant who complained of having been badly bitten on the neck during the previous night. The bites on his neck were fresh and bleeding and of
the same character as produced by ticks. On looking through his bedding, four ticks were found, one an *Argas persicus* and three ticks of the *Ornithodoros* species which since have been identified at the Agricultural Research Institute, Pusa, India, as *Ornithodoros lahorensis*. One of the *Ornithodoros* ticks was seen to be gorged with blood. In all five ticks of the *Ornithodoros* species and one of *Argas persicus* were obtained in the serai. In this connexion it should be remembered that the *Ornithodoros* is more frequently seen during the daytime than the *Argas persicus*.

These ticks were shown to the serai keeper and to certain local inhabitants, who were unanimous in stating that both species were dangerous to "ferungis" or foreigners such as ourselves. The *Ornithodoros* was said to be "karab" or bad, and gave rise to a fever of some days' duration, but that the *Argas persicus* was "khaile karab," extremely bad, and would cause some weeks of fever and possibly death. We were also informed that the reason why Persian travellers did not contract these diseases was because each traveller before entering a new serai wet his finger in his mouth and with it picked up some of the dust off the ground and ate it. The "nauak" or salt in the dust afforded him protection.

So much for local beliefs.

On arrival at Meshed next day the officer commanding at the general hospital stated that it had been reported to him that several cases of influenza with marked chest symptoms had arrived from Sharifabad. On visiting the wards it was found that the patients were suffering from the same disease as seen at Turbat and Sharifabad but that bronchitic and chest symptoms were much more marked. These complications had probably been aggravated by exposure during evacuation by camel convoy. A large proportion of the cases had enlarged spleens and normal temperatures, having recovered from their first attack of fever *en route*. Bite lesions were observed on the extremities of the majority, and, in one case only had spirochetes been discovered. The records of temperatures at Sharifabad and past histories of the patients were handed over to the officers in charge and further observation, and in some instances the finding of the parasite soon convinced them that they were dealing with a fever of a relapsing type having many points of difference between it and the relapsing fever which they had been accustomed to encounter in Meshed.

**GENERAL ASPECT OF THE DISEASE.**

In June, 1919, one of us, viz., C. H. H. H., had the opportunity of seeing nineteen cases of tick fever contracted in serais in Jinnuk and district. The clinical picture and subjective symptoms of all these cases were the same and as briefly described in connexion with the cases in the hospital at Turbat. Their temperature charts were all of the same type and usually showed a short initial fever of a moderate intensity of one to five days' duration followed by numerous spiky relapses which rarely lasted.
for more than one day. The temperature of the patient during a relapse as a rule reached 104° F., and the crisis was usually accompanied by sweats and a moderate degree of collapse. Chest symptoms did not predominate, probably because the outbreak occurred during the hot weather.

In the Sharifabad outbreak, 72 cases were admitted to hospital, 50 at Meshed and 22 at Turbat. The first sixteen cases arriving at Meshed and several of the Turbat ones showed signs which at first pointed rather to influenza as a diagnosis, viz., more or less generalized pains all over the body, cough and bronchitis, and frothy sputum which in some instances was bloodstained.

During the febrile stages all the Jinnuk and Sharifabad cases presented identical symptoms and clinical signs, but the outstanding feature of this last outbreak was undoubtedly the extraordinary variations in the character of the fever that the individual cases displayed.

**Symptomatology.**—The symptoms of the disease were those of fever and headache, usually frontal in type, and in certain cases photophobia was observed. This localized headache was more common during the initial attack of fever and in well marked spiky relapses with high temperature. In cases showing mild relapses, or, with a continuous type of fever, the headache was more diffuse. The patient as a rule complained of pains in the small of the back and down the backs of the limbs. Generalized pains all over the body were observed as a rule in cases showing periods of continued fever. In bronchitic cases, pain was at times referred to the region of the sternum. Patients during the febrile stages looked ill and felt very miserable. The constitutional disturbance was not so severe as in the cases of Indian relapsing or Jinnuk tick fevers.

**Rigors.**—In the low abortive and irregular types of fever rigors were not observed. It was only in the cases in which the rise of temperature was considerable that the onset of fever was preceded by a rigor. At the time of decline of temperature profuse sweating and collapse were rarely seen.

**Pulse.**—During the febrile stages the pulse was usually full and the pulse rate ranged between 100 to 120 per minute. During the apyrexial periods the pulse maintained its normal rate.

**Respiratory System.**—Cough and bronchitis were very common respiratory complications in the Sharifabad outbreak, being present in sixty-eight and sixty-four per cent of cases received in hospital at Turbat and Meshed respectively. In four cases the sputum was bloodstained. In the Jinnuk outbreak, which occurred in the hot weather, only ten per cent developed bronchitis, which became worse during the periods of pyrexia and cleared up concurrently with the disease after salvarsan injections.

**Hæmorrhage.**—No cases of hæmorrhage occurred amongst the cases in hospital at Turbat. At Meshed four cases with hæmorrhagic sputum were observed. One case developed hæmorrhages from the bowel, two cases had
profuse epistaxis, and one bleeding from the gums. The number of cases with haemorrhages was eleven per cent of the total cases. In the Jinnuk outbreak ten per cent of the cases had haemorrhages.

**Alimentary System.**—The appetite was, as a rule, good, and the tongue clean during the a pyrexial periods. The bowels tended to be constipated, but in two cases severe diarrhoea occurred. Enlargement of the liver was rarely found, and when present it was not to any appreciable extent; and no case developed jaundice. In the Jinnuk outbreak five per cent of cases developed jaundice.

**Spleen.**—On palpation the spleen was usually found to be enlarged, rather soft and painful to the touch, and at times the patient complained of very exquisite pain in this region. This enlargement became as a rule more marked during or at the termination of a febrile stage. At Meshed the spleen was enlarged in sixty-eight per cent of cases, and at Turbat in sixty-three per cent. Of the cases in which spirochetes were found thirty per cent had no palpable splenic enlargement. Spleen puncture was performed on four occasions with negative results, as no spirochetes were recovered.

**Bacteriology.**—Bacteriological examinations were confined to the examination of blood slides, as appliances and animals for other investigations were not available.

**Blood Examinations.**—The blood of all cases with fever was examined daily for the presence of spirochetes by means of the thick drop method. Total blood counts could not be carried out owing to the absence of apparatus, and differential counts presented no constant feature, but there appeared to be a tendency to increase in the mononuclear elements.

**Spirochetes.**—The same difficulty in finding the parasite was experienced in these cases as in the Jinnuk outbreak. The spirochete was rarely found, and when present it was only in very small numbers. At Meshed spirochetes were observed in 14 per cent, and at Turbat 18 per cent of the cases. Of the positive cases, spirochetes were found in 20 per cent during a pyrexial periods, in 20 per cent during the initial fever, in 50 per cent during the first relapse, and 10 per cent during the second relapse. In no thick drop film were more than six spirochetes ever observed, the usual number being one or two, and the presence of the parasite during a pyrexial periods was contrary to all expectations. These findings offer a marked contrast to the louse-borne variety of Indian relapsing fever, in which numerous clumps of organisms may be frequently seen during the height of the fever in thick-drop preparations, and in no instance during a pyrexial periods have spirochetes been observed by us.

Spirochetes were usually found in cases with definite relapses, with a spiky type of temperature chart, and it is interesting to note that in the Jinnuk outbreak in which all cases were of this type spirochetes were found in forty-two per cent of the cases. It was also observed that the parasite-
could easily be found during relapses in cases which had previously given positive results, especially in those in which they had been seen during an apyrexial period.

*Morphology of the Spirochaetes.—* In a previous paper on this disease one of us, C. H. H. H., gave as his opinion that the spirochaete might be said to be longer, a little coarser than the Indian variety, and that its spirals were more regular and deeper; the Indian variety being less regular and possessing open flexures. The Persian variety was also said to average from eighteen to twenty-two microns in length without showing divisional characters, and short forms were rarely seen. On one occasion a spirochaete thirty-five microns in length was seen, without any attempt at division being visible in the protoplasm. Looped and figure-of-eight forms were occasionally met with. These observations in regard to the morphology of the spirochaete seen in the Jinnuk outbreak were confirmed by Captain A. S. Fry, I.M.S., Captain J. H. C. Walker, R.A.M.C., and Captain K. Venugopal, I.M.S.

In regard to the spirochaetes found in the Sharifabad cases, H. D. W. states it is difficult to give any definite opinion owing to the small number of organisms seen, and as the exclusive use of the thick-drop method resulted in the spirochaetes taking on a somewhat "pulled out" appearance. In one case the organisms were not longer than fifteen microns, whilst in another they reached as great a length as thirty microns. The average length of the spirochaete was about twenty microns, and the shorter forms tended to be thicker than the longer forms, which were fine. Similar variations have been noted in the spirochaete of Indian relapsing fever, but the extreme length of the organism has not been so great. The spirals in the Persian spirochaete would appear to be more open than those of the Indian variety, but in no instance could it be definitely stated which form of spirochaete was present.

H. D. W. confirms the observations in regard to the average length of this organism, but it would be interesting to know if he attributes the more open spirals to his so-called "pulled out" appearance resulting from the employment of the thick-drop method. It must be agreed, however, that in no film is it possible to identify definitely the variety of spirochaete present, but the spirochaetes seen in a thick film at Turbat by C. H. H. H. were of the same type as the ones observed in the Jinnuk outbreak.

*Incubation Period.*—In the Jinnuk outbreak all cases were bitten on the one night, and developed the disease within a few hours of each other on the same day, namely, on the eighth day after infection. This outbreak occurred during the hot weather, when ticks are more active, and they were seen within an hour or two of the occupation of the serai. In the Sharifabad outbreak which occurred during the cold weather ticks were not seen for the first few days. In all probability they were hibernating in cracks in

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1 *Journal of the Royal Army Medical Corps*, vol. xxxiv, No. 6, p. 484.
the walls, etc., and did not appear until the warmth due to the lighting of fires and the regular occupation of the rooms attracted them. This has been noted during the winter in other Persian buildings.

The first case reported sick at Sharifabad on November 5, 1919, and the greatest number admitted to hospital on one day was on November 9, 1919, twelve and sixteen days respectively after the occupation of the serai. The sick attendant, Yankat Mani, was on duty with the sick in the serai after the evacuation by Nos. 15 and 16 platoons, and was bitten by ticks during the night on November 19, 1919. He was admitted to hospital with tick fever on November 27, 1919, on the eighth day after infection, and no man developed the disease at a later period than eight days after the evacuation of the serai.

Fever.—This subject has already been touched upon under a different heading, but owing to its great importance it requires to be more fully dealt with. As previously mentioned, the outstanding feature of the Sharifabad infection was the extreme diversity in the type of fever presented by the individual cases, and it may be briefly stated that the fever varied from a mild attack of a few days’ duration, without subsequent relapses, to a severe continuous rather irregular type of fever lasting upwards of fourteen to sixteen days, which in some instances was followed at irregular intervals by short spiky relapses. The greatest number of relapses seen in any one case was seven, and in all cases as the disease progressed an attempt to reproduce a spiky type of chart similar to the one seen in the Jinnuk outbreak occurred. Vide Charts I and II. As a rule apyrexial periods were much longer and more irregular than in the Jinnuk cases, in which the period was usually a matter of a few days only. In the Sharifabad cases apyrexial periods were very prolonged, the longest period on record being forty-one days.

The records of temperature, etc., of the cases at Turbat whilst at Sharifabad and during evacuation by camel convoy are unfortunately not available, but the histories and charts submitted indicate the type of fever, etc., and are sufficiently complete for grouping purposes. In order to ensure greater accuracy, the complete Meshed charts have only been used and reproduced.

The cases of the Sharifabad outbreak may be roughly grouped as follows:—

(a) Cases in this group developed an initial fever lasting two to six days. It was usually of a low continuous type and not the high continuous fever seen in louse-borne relapsing fever. This was followed by an afebrile period varying from two to fourteen days, which was succeeded by short periods of fever, frequently, of only one day’s duration. In one case seven relapses were noted. Into this group, in which the cases are of the Jinnuk type, thirty-two per cent of cases fall, and in blood films spirochaetes were more easily found.

One case, Chart No. II, is particularly deserving of note. The patient
after a preliminary attack of fever and an afebrile interval of two days developed a relapse of two days' duration. During the succeeding afebrile period he was admitted to hospital, and spirochetes were found in the blood five days after the relapse. Two days later he was given 0.6 gramme of neo-kharsivan intravenously, and twelve days afterwards a second relapse occurred in which spirochetes were again found in the blood. Hyperpyrexia of a 106° F. was noted in two cases, in one after an injection of neo-kharsivan. Of cases in which the spirochetes were found, seventy-two per cent are present in this group.
(b) In this group the initial fever was low and the apyrexial period short, lasting from one to six days. Following this was a period of somewhat irregular continued fever from four to eight days in duration. Relapses were not common. One case showed a spiky relapse after eleven days, and another three short spiky relapses at intervals of one, three and forty-one days. Twelve per cent of cases fall into this group, and in none of these were spirochaetes found.

(c) In this group cases showed a preliminary low fever followed by a short apyrexial period and then a long irregular fever of upwards of fourteen days' duration. Succeeding relapses, when they occurred, were of the spiky variety. Of the cases in which spirochaetes were seen eighteen per cent are included in this group, which comprises twelve per cent of the total cases.

One case in this group, which is referred to towards the end of the paper, requires special mention. This case showed an initial low form of fever followed after an apyrexial period of two days by a period of continuous but irregular pyrexia of fourteen days' duration; no spirochaetes were observed during this relapse, and two injections of kharsivan totaling
Tick Fever in East Persia

0.9 gramme were administered intravenously. A short spiky relapse of one day's duration occurred after twenty-seven days, and spirochætes were found in the blood.

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**Chart IV.**

(d) Saddle-back charts, somewhat resembling the one seen in cases of seven-day fever, were observed in four per cent of cases, and in one of these a relapse was recorded after an apyrexial period of sixteen days.

**Chart V.**
(e) One case showed no less than four relapses, during which the fever was of a very low type. These relapses were followed by a period of high continued fever cut short by injection of neo-kharsivan.

CHART VI.

(f) One case showed a very irregular fever resistant to neo-kharsivan.

CHART VII.

(g) This group of cases developed an initial rather irregular continued fever lasting from eight to ten days. Subsequent relapses were rare, and when they occurred they were of the usual short spiky variety. These cases, which comprise eighteen per cent of the total number, were markedly resistant to neo-kharsivan, and of the ones in which spirochaetes were seen nine per cent are included in this group.

(h) The remaining eighteen per cent of cases fall into this group. They call for no special comment, clinically and symptomatically they cannot be differentiated from any of the other cases, they required no special treatment, and after the one attack of fever of short duration they became convalescent. No relapse occurred in this type of case and in none of them were spirochaetes seen.
Tick Fever in East Persia

Treatment.—In our experience injections of salvarsan or neo-salvarsan have always been rapid and unfailing specifics in dealing not only with the Indian but also with Jinnuk varieties of relapsing fever. As a rule one injection of 0·6 grammes given at the height of the fever has proved to be efficacious with perhaps at the most two or three exceptions. In the Sharifabad outbreak in many cases injections totaling 1·5, 1·8 and in one instance 2·4 grammes of kharisan or neo-kharisan were found necessary to effect a cure.

In regard to this resistance, it must be admitted that frequently these injections were administered during an apyrexial period, and that the initial doses were too small to effect a cure. Still spirochaetes were being found during apyrexial periods, and in the Jinnuk cases small doses of kharisan 0·3 to 0·4 grammes administered at the height of the fever were found to possess as great a curative value as the larger ones. In spite of these objections there is no doubt that this infection was more resistant to the action of salvarsan products, and, in cases with periods of continued fever, markedly so.
Concluding Remarks.—The Sharifabad outbreak impressed upon all observers the great variability of Persian tick fever, and it is evident that the diagnosis of isolated cases may present a problem of no small difficulty unless the case be one with a clear history of tick bites or of the same type as the Jinnuk cases.

Ever since the Jinnuk outbreak of June, 1919, medical officers on the lines of communication, East Persia, have been on the look-out for cases of fever of that type, but only one or two cases have been reported, and these amongst Indians.

Attached to this force as auxiliaries are levies who for the most part are locally enlisted Persians or Hazaras and are treated in the lines of communication hospitals. The duties of the levies take them continuously into Persian serais and buildings and though they are quite frequently attacked by Indian relapsing fever in no instance has Persian tick fever been observed. On the only two recent occasions that Indian troops contrary to Standing Orders have sheltered in Persian serais forty-one and forty-six per cent of the men have become infected. This would seem to indicate that the Persian has an early acquired or an inherent natural immunity to this disease which is not enjoyed by the European or his comrade in arms the Indian. Perhaps the two most difficult conundrums to try and solve are:

1. The cause of the great variation in the Sharifabad cases and their relative resistance to salvarsan.

2. Why, in the case of certain infections, notably in the Jinnuk outbreak, the temperature charts are all of the same type, show more definite spiky relapses, rigors, sweats and collapse are more common, debility and constitutional disturbance are more severe and spirochætes are more numerous or more readily found? Do these differences indicate the presence of more than one infection, possibly of the same group, or is it due to one infection being modified through being transmitted by a different species of carrier?

All the cases in the Jinnuk outbreak were absolutely free from lice. The later cases from Sharifabad showed a very light infestation, but as the earlier cases were free this can be ignored.

Then we have the statement of the serai keeper that the two species of ticks cause different types of fever. It is quite possible that this may be correct seeing that however prone the Persian may be to exaggeration he is usually fairly accurate when it comes to matters of common knowledge and everyday experience.

In the serai at Jinnuk both Ornithodorus and Argas persicus were present and all cases of fever contracted there were of the same type and reacted similarly to salvarsan. It is true that the outbreak occurred during the hot weather when the Argas persicus is more active. There is no doubt that all ticks do not equally convey infection seeing that thirty per cent of Nos. 15 and 16 platoons although bitten did not develop...
Tick Fever in East Persia

the disease. In the case of the sick attendant seen at Sharifabad, only one
gorged tick of the Ornithodorus species was found in his bedding but the
number of bite lesions seen indicated that he had been bitten by more than
one tick.

These differences also cannot be due to the number of tick bites, since in
the Jinnuk outbreak the type of fever was the same whether the man had
been bitten by three or fifteen ticks.

In the groups of cases showing periods of a more continuous type of
fever it is noticed that the fever tends frequently to become irregular and
to produce a spiky type of chart. This continued fever is undoubtedly not
due to a chest condition seeing that the majority of cases did not suffer
from respiratory complications. It may be possible that the Jinnuk and
"a" group cases are pure and that the other groups have a superadded
infection which is resistant to salvarsan. The case previously quoted in
group "c," Chart IV, in which spirochetes were eventually discovered
during a spiky relapse and the fact that eighteen and nine per cent of
positive cases are included in the groups "c" and "g" would appear to
disprove this theory.
There is one theory which appeals to us as worthy of consideration, namely, that all cases at Jimnuk were bitten on one particular night only and this inoculation or group of inoculations gave rise to an infection which manifested itself eight days afterwards. The cases at Sharifabad were bitten on several different nights and it may therefore be presumed that these repeated inoculations might give rise to their individual infections on succeeding days and so alter the character of the disease.

In addition, as these different infections have each their own particular cycle various broods of parasites may not all be equally affected by a single injection of salvarsan.

Chart No. IX has been included because to our minds it seems to convey the impression that the patient was suffering from a succession of infections and these developing consecutively produced a chart representing a type of continued fever.

However, in the absence of proof, deductions can only be regarded as pure conjecture and apart from indicating a possible field for research are of very little value.

In consequence of efficient and prompt treatment, no case suffering from this disease has died or has been invalided from East Persia, but there is ample evidence to prove that casualties did occur in the past amongst foreign civilians prior to the introduction of arsenical compounds by us.

Finally, although tick fever in East Persia under existing conditions does not cause loss of life there is no doubt that it merits serious consideration, seeing that patients suffering from the disease remain in hospital for periods varying from twenty-three to seventy-seven days, thereby entailing a considerable loss to the State both in efficiency and money.

In conclusion, the writers of this note tender their apologies for the many defects both in it and also in the investigation. The difficulties will be readily understood when it is realized that the investigation was carried out under field-service conditions; there was no laboratory available; the line of communication upon which these cases occurred is approximately 700 miles in length and solely dependent upon a road traversing most difficult country, with inferior motor facilities.

The onset of winter, the hibernating season for ticks, and the hurried departure of H. D. W. before the investigation of the cases and the writing of this paper could be completed gave rise to additional complications. Another attempt at continuing this investigation is planned for the coming spring when it is hoped that more fruitful results will be obtained.

An acknowledgment of our indebtedness is due to Captain Haji, I.M.S., or the very material assistance rendered by placing the records of his cases at our disposal and also to the Director of the Agricultural Research Institute, Pusa, India, for so kindly identifying specimens sent to him.