The DIFFERENTIATION of NON-LOUSE-BORNE FEVERS of the TYPHUS GROUP occurring in the UNITED PROVINCES, INDIA.

A Thesis submitted for the Degree of M.D.

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1. THE THESIS.

This thesis is that the non-epidemic cases of typhus fever which occur sporadically in the United Provinces, India, do not constitute a single disease entity. In a series of twenty cases analysed six can be classified in the scrub typhus-tsutsugamushi disease group. Four of these were cases of the latter condition, which is now regarded as mite-typhus, a condition which has not been described previously in India. In the remaining fourteen cases two distinct types of serological reaction are found, and these correspond to some extent to differences in epidemiology and clinical type. Whether they are due to viruses of different type, or to different strains of the same virus is discussed. Analogies with other typhus group diseases are drawn and appear to indicate that both these groups are tick-borne.

2. INTRODUCTION.

During the past fifteen years, particularly during the latter part of this period, the non-epidemic forms of typhus fever have been the subject of widespread investigations, both in tropical countries and in temperate climates where these diseases are found during the hotter months. Sporadic forms of typhus fever have occurred during this period in localities where previously such diseases did not exist. At a recent meeting of the Royal Society of Tropical Medicine and Hygiene Dr. W. Fletcher described how the typhus fevers of the types he has investigated appeared as a new disease in the Federated Malay States about 1924; he and Sir Malcolm Watson, both of whom had been in the country for over twenty years, could affirm this with confidence. Evidence of the similar appearance of typhus-like fevers in parts of India, where previously they were unknown, can be adduced. The problem in India, the Federated Malay States, and also in other parts of the world, has presented a changing front since its inception by virtue of an alarming increase in the mortality of the disease, which was shown by earlier observations to take a negligible toll of human life. In many parts of the world, for example in South Africa, the United States of America, and the countries bordering on the Mediterranean, investigations have shown that these non-epidemic typhus fevers can be differentiated into certain forms which are tick-borne and others which are flea-borne. It is known that Japanese river fever or tsutsugamushi disease, a typhus-like fever, is mite-borne. In the Federated Malay States a clear differentiation based on considerations of epidemiology and serological reactions has been established. No satisfactory classification of non-epidemic typhus-like fevers occurring in India has so

far been made. Evidence that they can be subdivided is adduced in this thesis.

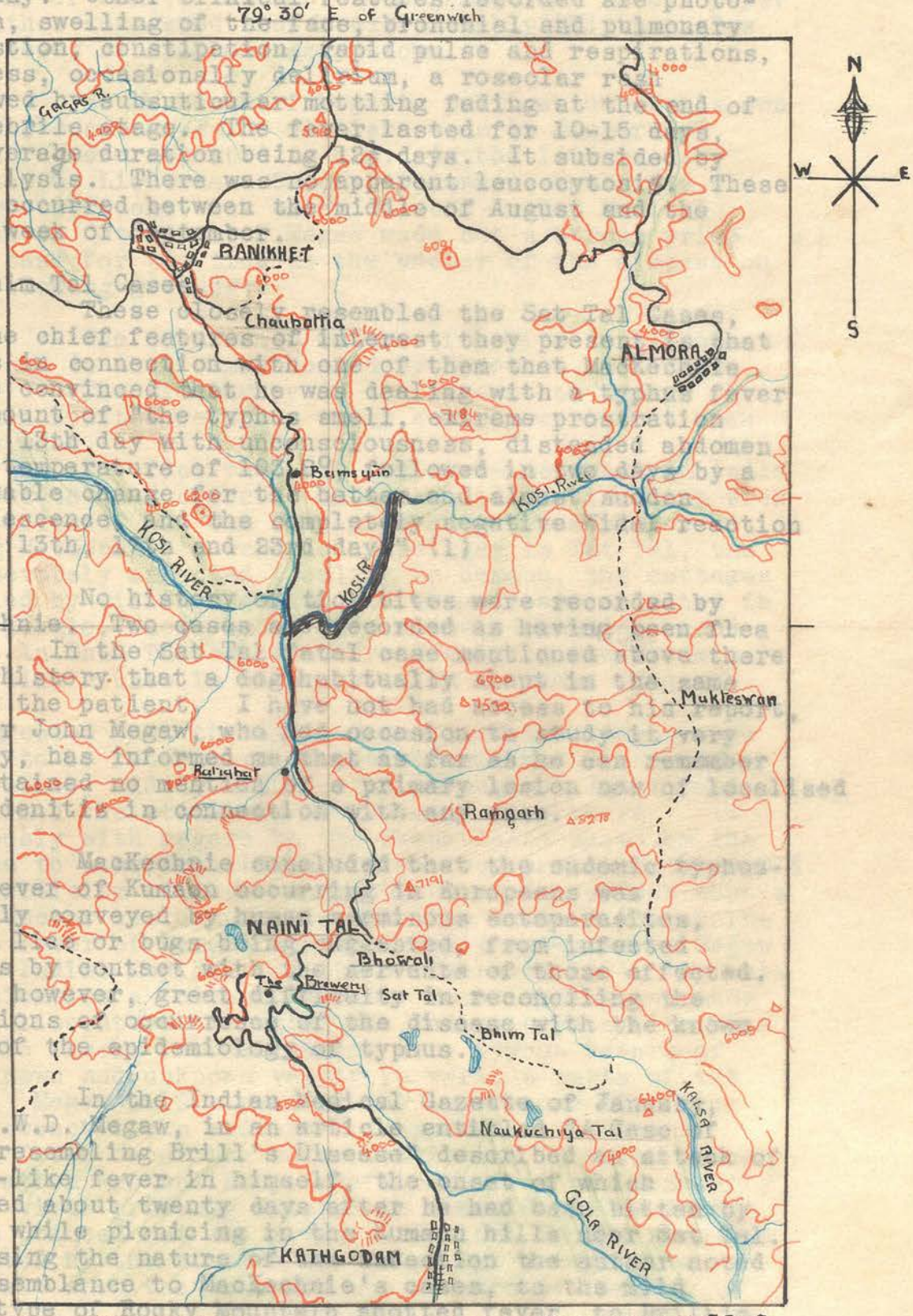
3. HISTORY OF NON EPIDEMIC TYPHUS-LIKE FEVERS IN INDIA.

In 1913 the Government of the United Provinces deputed Major MacKechnie, I.M.S. to investigate certain fevers which had been prevalent for some years among European summer visitors at Bhim Tal and Sat Tal in the Kumson lake area (see map). These are summer hill resorts situated at an altitude of 4500 feet and within easy reach of the plains. Bhim Tal is situated on one of the main bridle path trade routes between India and Tibet. Sat Tal is close to it about two miles off the beaten track. Both are small communities, with cottages occupied by summer residents set in the heart of forest and scrub jungle, with only a small clearing of these, and situated in each case near a lake or "tal". In Bhim Tal there is a village and some houses, including a hotel used by Europeans, built on cleared land. MacKechnie found that Sat Tal was the more severely affected locality. In Bhim Tal practically all the cases of fever in Europeans occurred among the residents of cottages set in the forest. A neighbouring military furlough camp situated in the lower part of a broad valley leading from Bhowali to Bhim Tal was free from the disease, and similarly the somewhat large community of Naini Tal, the summer headquarters of the Provincial Government, situated at an altitude of 6500 feet about six miles distant. The Indian population did not appear to be seriously affected, and most of the cases occurring in Indians were among the servants of the European visitors. In assessing the nature of the fever of unknown origin he had investigated between July and October, 1913, and after elimination of enteric group and various other continued fevers, MacKechnie concluded that "There were left only typhus fever, Brill's disease and the spotted fever of the Rocky Mountains among the continued epidemic fevers which did not yield blood cultures" (1).

As the majority of one group of cases to be described later in this thesis were contracted in the Kumson lake area at the same season of the year, a few observations on the cases dealt with by MacKechnie may be of interest. MacKechnie's report was never published other than departmentally, and for details I have drawn upon the reference to his work and extracts from it by Megaw (1) (2).

The Sat Tal Cases.

There were only eight cottages in this locality in every one of which one or more cases occurred in the years 1912 and 1913. Three clinical charts given show fever of 14-15 days duration. in two of these the temperature climbs steadily to a fastigium in the region of 102-103° and of about seven days duration, followed by a fall of the temperature to a slightly lower level for three days and then by rapid lysis; in the third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Bhowali
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case there was typhoid state, high ontinued fever followed by crisis on the 13th-14th day, but the patient did not recover consciousness and died on the 18th day. Other clinical features recorded are photophobia, swelling of the face, bronchial and pulmonary congestion, constipation, rapid pulse and respirations, deafness, occasionally delirium, a roseolar rash followed by subsuticular mottling fading at the end of the febrile stage. The fever lasted for 10-15 days, the average duration being 12½ days. It subsided by rapid lysis. There was no apparent leucocytosis. These cases occurred between the middle of August and the first week of September.

The Bhim Tal Cases.

These closely resembled the Sat Tal Cases, and the chief features of interest they present is that it was in connection with one of them that MacKechnie became convinced that he was dealing with a typhus fever on account of "the typhus smell, extreme prostration on the 13th day with unconsciousness, distended abdomen and a temperature of 103.8°, followed in two days by a remarkable change for the better and almost sudden convalescence, and the completely negative Widal reaction on the 13th, 17th and 23rd days" (1)

No history of tick bites were recorded by MacKechnie. Two cases are recorded as having been flea bitten. In the Sat Tal fatal case mentioned above there was a history that a dog habitually slept in the same bed as the patient. I have not had access to his report, but Sir John Megaw, who had occasion to study it very closely, has informed me that as far as he can remember it contained no mention of a primary lesion nor of localised lymphadenitis in connection with any case.

MacKechnie concluded that the endemic typhus-like fever of Kumaon occurring in Europeans was probably conveyed by human verminous ectoparasites, fleas, lice or bugs being suggested, from infected natives by contact with the servants of those affected. He had however, great difficulty in reconciling the conditions of occurrence of the disease with the known facts of the epidemiology of typhus.

In the Indian Medical Gazette of January, 1917 J.W.D. Megaw, in an article entitled "A Case of Fever resembling Brill's Disease" described an attack of typhus-like fever in himself, the onset of which occurred about twenty days after he had been bitten by a tick while picnicing in the Kumaon hills near Sat Tal. Discussing the nature of the infection the author noted its resemblance to MacKechnie's cases, to the mild Idaho type of Rocky Mountain spotted fever, to Brill's disease, to the typhus-like fever occurring near Pretoria and described by McNaught (3) and to the macular fever of Tunisia. He suggested that the infection was probably conveyed by a tick or some other

biting insect, from man to man or from animal to man. The tick which had bitten him had been discarded at the time of removal and not identified, but in his paper the author suggested that it was probably Rhipicephalus sanguineous or Hyalloma aegypticum.

As a result of Megaw's publication of his own case the occurrences of similar cases in Nagpur and Bangalore were reported to him. In the latter case, reported by Lieutenant Colonel Sprawson, there was a history of recent tick bite. In the Indian Medical Gazette of October 1921 Megaw made out a strong prime facia case for the tick as the vector of the disease on the following grounds:-

(1) The occurrence of the tick bite in his own case, and in that communicated by Sprawson.
(2) The similarity of the disease to Rocky Mountain spotted fever in which a tick vector had been established.
(3) The fact that all the cases reported in India appeared to have occurred under conditions in which tick infestation of man was likely to have taken place. Citing MacKechnie's work he noted that in Sat Tal, the most severely affected locality in Kumaon, the cottages occupied by visitors during the summer were situated in dense jungle, there being only a small clearing round each. In Bhim Tal cases occurred only in individuals inhabiting houses in close relation to dense jungle.

He suggested that the small mammals of the jungle were likely to be reservoirs of the virus, that the disease was probably widely distributed throughout India, and reaffirmed the statement he had made four years previously with regard to the resemblance shown by the disease to other conditions in various parts of the world. Some criticism of these suggestions to the effect that a louse vector was compatable with the known facts of the typhus fever of Kumaon was adequately answered by Megaw in the Indian Medical Gazette of February 1924. In this communication a further valuable contribution was made to the literature, bringing the Indian typhus-like non-epidemic fevers into alignment with typhus fevers of both known and unknown vector in various parts of the world. Megaw laid stress on the importance of taking into account ticks and mites as possible vectors of typhus fever occurring under conditions in which louse infestation was unlikely, reaffirmed that the reservoir of the virus probably existed in mammals of the jungle, and he pointed out the great variations in the symptoms presented by the disease rendering its recognition difficult when the observer was unaware of these.

Some confirmation on Megaw's views on the aetiology of non-epidemic typhus fevers in India accrued as a result of an outbreak which occurred in February 1924 among troops encamped for manoeuvres in the vicinity of Saugor, a military station in Central India at an elevation of 1500-2000 feet above sea level. The cases are described by Megaw, Shettle and Roy in the Indian Medical Gazette of February 1925. In the nine cases observed there was no evidence of louse infestation, case to case infection could be excluded and the disease in each case was contracted under conditions rendering tick bite likely, but no history of this was given in any of the cases. Commenting on this Megaw stated that the only other vector likely was a mite, but pointed out that was a primary sore and localised lymphadenitis, described in association with mite typhus, were absent in all cases, this was unlikely. In the same communication Megaw reports details of seven other cases records of which had been communicated to him, In three of these there was a history of tick bite within the limits of the incubation period of the disease. He suggested that "tick typhus of India" or "tick typhus" would be the most appropriate provisional designation for the disease.

In their review "Tick Typhus and other Sporadic Fevers of the Typhus Group" published in the Indian Medical Gazette of June 1928 Megaw and Sundar Rao reported further cases, accounts of which had been submitted to the former from various parts of India. In all the diagnosis was clearly established. In the minority a history of tick infestation was given, and no actual species had been identified. In the great majority of the remainder infection had been contracted under circumstances in which tick infestation might be presumed to have occurred without its being observed by the host. This communication contains a map showing the distribution of typhus-like fevers in India which were considered to be carried probably by ticks. The authors, however, did not regard their tick vector theory as established; they merely suggested that an arthropod of the wilds conveyed the infection from a reservoir in rodents, and that all cases should be investigated with special reference to ticks, mites and other arthropods. The review showed that the Weil Felix reaction had been tested in a large proportion of the cases. A positive reaction was only recorded in two of these, and this in the low serum dilution of 1:80. The authors quote, however, certain comments by one of them, Dr. S. Sundar Rao, on a case which occurred at Saugor in 1927 to the effect that the Weil Felix reaction, although negative on the 9th and 16th days, showed a weak positive reaction on the 21st. Attention was drawn to the lateness in development of agglutinins, to the necessity for the test to be made with various

types of Proteus X and carried out up to one month from the onset of the disease.

Two interesting cases were recorded in the Indian Medical Gazette of November 1928 by Ghose. In both cases primary sores were present, associated in one with localised painful lymphadenitis. This appears to be the first case recorded in India showing these lesions. The patient was a middle aged European lady who kept seven long haired dogs. The case occurred at Allahabad.

A similar case in which there was a history of tick bite, definite evidence of a resulting sore and associated painful lymphadenitis occured in Delhi in February 1932 and was reported by Christian and Hepple (4). This patient was a lady who bred fox terriers, and gave a good deal of attention to their care. A guinea pig was inoculated intraperitonally from the patient's blood on the 8th day of the disease, and further animals inoculated with its blood on the 11th and 19th days after injection, and with a brain emulsion after killing the animal on the 19th day. Fever of varying duration was produced in all the secondarily inoculated animals, but none died. Scrotal lesions were absent in the animal originally inoculated, and no rickettsia bodies were seen in sections of the brain and testicle.

In a series of three cases occurring at Bangalore in 1931 and reported by Biggam (5) there was no history of infestation by ticks or other arthropods, but these cases had been exposed to conditions in the open country under which bites might have occurred. The Weil Felix reaction was tested in each case, and two showed weak positive results.

A series of cases occurring at Ahmednagar during 1933 was recorded by Blewitt (6). This locality does not feature as an endemic area in the map previously mentioned and published by Megaw and Sundar Rao in 1928, and the condition appears to have cropped up in 1932, when eight cases were reported, as a new disease. Blewitt reviewed thirteen cases of the disease which he observed in 1933. In two cases only there was a definite history of tick bite a few days prior the onset of the disease, but other cases were contracted in the same locality at the same time as those in which there was a history of tick bite. The series included four cases contracted in barracks and nine occurring outside. Blewitt attributed all cases to their having been in the vicinity of herds of domestic buffaloes which normally harbour the tick, human infestation from this source being facilitated by rank vegetation.

Early in 1933 the B. proteus emulsions issued

to Military laboratories in India were standardised as to types and strains used and their preparation by Bridges (7), and from this time onwards more significant results are apparent in the Weil Felix reaction. Blewitt found that the test was invariably negative during the first week of the disease, positive in 60% of the cases during the second week, and positive in all during the 3rd week of the disease. He states, "The curve rises rapidly in the second week, and by the third week has risen from a titre of between 1:125 and 1:250 in the second week to 1:500 and over; 40% of the cases, however, remain negative until the third week. The neight of the curve is maintained until somewhere between the fifth and sixth weeks, when it gradually commences to fall and by the twelfth week is well below the base line titre". This is taken as 1:125, as the serum of some normal healthy individuals tested was found to agglutinate the emulsions used in dilutions up to 1:50. The types used were OX2, OX19 and OXK, and it was noted that "X19 usually gave the earliest positive results and the highest and the most prolonged results; X2 gave the next best results".

An epidemic of much serological and clinical interest has recently been recorded by Macnamara (8). The cases occurred in the Simla Hills, where there is no record of the disease having been observed prior to 1932. In 1934 fifteen cases occurred in Europeans between the middle of August and the end of September. The Indian population appeared to be little affected. The serological interest lies in the fact that practically all the cases showed agglutination with O emulsions of B. proteus XK, some in dilutions suggesting strongly an analogy to, or identity with, the type of reaction found in scrub typhus of the Federated Malay States. The results of agglutination with emulsions of indologenic strains of B. proteus X are not recorded in any of the case notes given. The mode of infection could not be ascertained. Over one half of the cases gave a history of exposure to conditions in the wilds mainly as a result of exploring the neighbouring hills regularly on foot; two lived in quarters isolated from barracks; two of the cases had never left barracks within the limits of the incubation period. One of the sufferers, Lieutenant Colonel Covell, I.M.S., has pointed out that the appearance of the condition as a new disease locally corresponds roughly with the acclimitisation of the common Indian squirrel, which was originally brought to Kasauli for research purposes in 1924, and by 1930 had become established in the local fauna. It nests in the roofs of barracks and bungalows.

The series of cases collected for this thesis occurred in the United Provinces in the years 1932-1934. At the time when I commenced to collect notes on cases the opinion was widely held that in the typhus fevers of unknown vector, or of tick vector as some cases appeared

to be, the Weil Felix reaction was either negative or was position only in low serum dilutions. My main object at first was to have all cases tested serologically using O emulsions of the various types of B. proteus X available, care being taken to test the sera during convalescence in view of Dr. S. Sundar Rao's observation previously quoted, and also as Pijper and Troup (9) had reported that in tick-bite fever of South Africa, a disease they considered to belong to the typhus group, the highest titres are obtained many days after the patient is quite better. As evidence from the cases observed accumulated, it became clear that the Weil Felix reaction was almost invariably positive, provided tests were carried out during convalescence. A further feature of great interest shown in the results was that in some cases significant titres were only obtained with emulsions of B. proteus X Kingsbury, suggesting that the cases could be divided into serological varieties similar to those established by Fletcher and Lesslar (10) in Malayan tropical typhus. I was able to collect notes of four cases all contracted about the end of August in a locality about three miles distant from the scene of MacKechnie's work in 1913. These cases included two fatal cases which occurred early in September 1932 in healthy young adults. This constituted a unique record then in connection with Indian non-epidemic typhus fever of unknown vector, although at about the same time two fatal cases occurred at Sabathu in the Simla hills. All of the above four cases contracted in the Kumaon lake area showed a primary lesion and associated lymphadenitis, analogous to the similar lesions found in the tsutsugamushi disease, fievre boutonneuse and the tick-bite fever of South Africa. Evidence will be adduced to show that they were cases of the scrub typhus-tsutsugamushi fever group, showing the clinical features of the latter, a disease which has not so far been described in India, although Fletcher, Lesslar, and Lewthwaite, (11) had suggested that it probably occurs. The remaining cases are difficult to classify but the fact that many of them show serologically relatively high titres with O emulsions of B. proteus X2 raises interesting speculations as to their relationship to fievre boutonneuse and Rocky Mountain spotted fever. In some cases the clinical resemblances shown, particularly to the former, are very close.

It is a matter to be regretted that no analysis of the antigenic structure of the virus of any form of non-epidemic typhus fevers in India by agglutinin production in rabbits and cross immunity tests in guinea pigs has so far been published. In endeavouring to classify cases of the disease occurring in India we have to rely on considerations of epidemiology, the clinical condition and the serological reactions. As comparisons will be made later in the thesis with non-epidemic typhus-like fevers occurring in the Federated Malay

States, South Africa, the Mediterranean countries and the United States a preliminary survey of these conditions will be of assistance in the subsequent task of classifying cases of the disease group as they are found in India. The non-epidemic typhus fevers of other countries, such as Mexico and Brazil, will not be reviewed as no comparisons will be drawn from them.

4. NON-EPIDEMIC FORMS OF TYPHUS FEVER IN OTHER PARTS OF THE WORLD.

(a) The Federated Malay States.

In 1925 and 1926 Fletcher and Lesslar (10) described tropical tuphus as found in the Federated Malay States. They called the disease sporadic tropical typhus because it did not occur in epidemics, and occurred only in the tropics or in temperate climates during the hotter months. They defined the disease as an acute specific fever of sudden onset associated with severe headache and vomiting, rarely fatal and terminating by rapid lysis or crisis about the 14th day. A rash appears about the 5th day, and the condition is clinically indistinguishable from true typhus. The conditions under which it occurs, however, are vastly different, there being no evidence of case to case infection. Nervous symptoms, sleeplessness and delirium, are common, and they state that bronchitis occurs in nearly every case. In their reports they draw attention to he strong resemblance shown by the condition to similar fevers which had been described in other parts of Asia, in Africa, America, and Australia. They had also studied Megaw's reports on the condition occurring in India and called by him "tick typhus", and noted its close similarity to the tropical typhus of the Federated Malay States. They draw attention, however, to the difference in the reported results in the Weil Felix reaction, this being negative in the Indian cases but positive in Malayan tropical typhus.

The contradictory results of the Weil Felix reaction reported in other parts of the world in the investigation of cases clinically and in other respects resembling the typhus they had described were suspected by Fletcher and Lesslar to be due to the use of different strains of B. proteus X 19, or to the use of strains modified in their reactions by prolonged culture. The strain in use by them was one which had been brought to the Federated Malay States by Dr. A. N. Kingsbury in 1924 from the Bland Sutton Institute. It had been obtained from the National Collection of Type Cultures in 1921. In their earlier work on tropical typhus they used this strain alone, and found that with it a large number of cases showed positive reactions. The titres observed varied from 1:500 to over 1:10.000, and the maximum was reached about the end of the third week or a little later, i.e. during convalescence. After a large series

of control tests had been carried out on the sera of ordinary hospital patients, they reported that this organism was never agglutinated as a higher titre than 1:200 except in tropical typhus.

The strain in use in their earlier work, which they called B. proteus X Kingsbury, was found to differ from various other strains they received from different countries in that it did not produce indol in peptone water. In comparing its serological reactions in cases of tropical typhus with those of other an-indologenic strains and the indologenic strain, National Collection No. 66, they found that the sera of two typhus patients which agglutinated XK did not agglutinate the indologenic strain No. 67. Further tests showed that the sera of nine cases of tropical typhus which agglutinated XK at various titres above 1:1000 did not agglutinate indologenic strains from the National Collection above 1:60. This led them to modify the routine tests in use by them and from the beginning of 1925 they tested all their cases with emulsions of an indologenic strain from the National Collection, Warsaw or No. 67 in addition. During the first month they encountered two cases in which the indologenic strain was agglutinated at high titres, whereas agglutination did not occur with XK beyond 1:30. Similar results from other cases followed. As in the cases which showed positive reactions with XK. called by them Group K, so in those showing agglutinstion within indologenic strains, called Group W. agglutinins appeared about the end of the second week and increased up to about the beginning of the fourth week. In this way the two serological types of tropical typhus in the Federated Malay States became recognised.

Clinically the two disease resembled each other closely, but it was noted that in Group W the temperature declined by lysis more often, and the decline was more apt to be followed by a period of low, irregular fever and slow convalescence. In their report of 1926, however, the writers noted that there was probably an aetiological difference, as all the cases in a small outbreak in a camp were of Group K. Further observations of the writers at this time on the Group K. cases were that Europeans and Punjabis, the latter mostly bullock cart drivers, were affected out of all proportion to their relative numbers in the population, that the disease tended to occur in circumscribed areas, and that Megaw's conjecture that ticks carry the infection was probably correct. They had been unable to obtain a history of tick bite, however, in any of their cases.

In their later work, Fletcher and Lesslar, associated with Lewthwaite (11) described the epidemiology of the foregoing fevers. They called Group W "shop typhus", and group K "scrub typhus", the qualifying word in each case being the key note to the epidemiology. They show that shop typhus is a disease of indoor workers,

shop keepers being commonly affected, particularly those concerned in the handling of food and grain. Infestation by lice plays no part, and the uncleanly are not specially affected. In all these respects they noted the close resemblance to Brill's disease in the United States of America, XX and to the typhus-like fever of Australia described by Hone (13). They further noted that in all these three conditions the clinical condition is all most identical, and that the Weil Felix reaction is positive with indologenic strains only. In their further investigations of shop typhus they found no evidence to incriminate any particular insect as the vector.

Scrub typhus was found to occur under different conditions. They have shown that this a disease of open field workers, affecting labourers on plantations, cowherds and bullock cart drivers. Indoor workers are not affected. The disease is usually contracted in untilled open country, particularly on land that has been cleared of jungle and cultivated, but later neglected, becoming overgrown with scrub and weeds. They found that some cases were contracted in waste, swampy land. Other interesting features in connection with outcrops of cases were shown.m The disease was found to occur in circumscribed areas. In the Oil Palm estate outbreak reported by them (11) which occurred in 1926 - 1927, the cases occurred mainly in an area of 1000 acres which had been originally cleared in 1922 but had not been kept clear of weeds and undergrowth during the economic stress of the subsequent bad years. On two adjacent parts of the estate, one in which the development of weed and scrub had not taken place owing to the previous planting of a cover crop, and the other on which clearing was not commenced until 1926, very few cases occurred, and these were confined to the former area. No cases occurred on neighbouring estates evacuating sick to the same district hospital. The disease occurred at about the same time as some of the Europeans on the estate contracted the tsutsugamushi disease, and none of these subsequently contracted scrub typhus. The authors suggested that the former probably conferred immunity to the latter. The majority of the cases of scrub typhus had been working on the estate for less than one year, and those who did not go out to work were not attacked.

In their work published in 1929 these authors state "The disease is very rarely fatal except in those who are already debilitated, and though patients

XX Note:- The group of cases referred to were those described by Maxey (12) in the Southern States, now classed as endemic typhus.

sometimes appear to be so ill as to be on the point of death yet they almost always recover". Fletcher (14), however, has since reported that in 1931 there was a sharp rise in the incidence of the disease accompanied by a mortality of 12%.

Serological investigation of the cases contracted on Oil Palm estate confirmed the results of the authors' earlier work. A positive Weil Felix reaction was marked with XK, but the reaction with X19 was negative.

Fletcher, Lesslar and Lewthwaite concluded that the virus of scrub typhus was in some way connected with weed and undergrowth and possibly with rats which live among these. They noted its close similarity to Megaw's cases, but found no evidence of tick bite in any of their cases. They suggested that sporadic typhus occurring in India was probably not one disease, but more than one, and drew attention to the close similarity of a case described by Ghose, previously mentioned in this thesis, to tsutsugamushi disease.

In the same work Fletcher, Lesslar and Lewthwaite drew attention to the relationship between scrub typhus and the tsutsugamushi disease of the East Indies. Clinical features common to both are the prominence and rapid development of nervous symptoms, stupor by day, and restlessness or actual delirium at night, the loss of the knee jerks and deafness in the later stages. The rash in both occurs about the fifth day and is similar. Splenic and a slight generalised lymphglandular enlargements are common to both, and also bronchitis. The outstanding clinical feature in which they differ is that in scrub typhus there is no primary lesion and associated lymphglandular swelling of a grosser nature than the generalised enlargement, whereas in the tsutsugamushi disease, these are always found. Lesser divergent features are the mode of onset, sudden in scrub typhus and insidious in tsutsugamushi disease. In the former the fever is at its height the 8th or 9th day, and is more remittent than in epidemic typhus and terminates by crisis or quick lysis. Convalescence is rapid. In tsutsugamushi disease the fever shows all the variations of typhoid, subsides by lysis and convalescence is slow, consciousness not becoming normal until the patient has been convalescent for several days. Serologically they found that cases of tsutsugamushi disease show a positive agglutination with XK, but in a much lower titre than in scrub typhus, the maximum titre varying from 1:60 to 1:240. The writers stated, however, that the tsutsugamushi disease is the only condition apart from scrub typhus which shows an agglutination with XK in a dilution of over 1:200.

Epidemiologically the conditions under which the two diseases occur were found to be closely similar. Tsutsugamushi disease also occurs in workers on land which has been cleared and subsequently become overgrown with long jungle grass and bushes. The writers were so impressed with the similarity in the epidemiology of the two conditions that they concluded the origin must be similar, and as mites have been shown to act as vectors of the tsutsugamushi disease, they suggest that mites are also responsible for conveying infection in scrub typhus.

Since the work described above, Wolff (15) has shown that the results of the Weil Felix reaction in Sumatran cases of the tsutsugamushi disease are indistinguishable from those found in scrub typhus. Similar observations have been made in the Federated Malay States by Martin (16) Further, Lewthwaite and Savoor (17) have demonstrated cross immunity between the viruses of the two diseases.

(b) The Typhus Fevers of South Africa.

Pijper and Dau (18) (19), who have carried out extensive observations on the typhus fevers, state that three forms of this disease group have been studied by them in South Africa. These are:

(1) Epidemic, louse-borne typhus.
(2) Tick-bite fever, and
(3) Sporadic or "mild" typhus".

Epidemic, louse-borne typhus.

A note on the subject of epidemic or louse-borne typhus, not other wise dealt with in this thesis, is necessary in order that a clear conception of the typhus fevers of South Africa be given. Pijper and Dau (18) report that the Weil Felix reaction in this disease does not show the high titres for B. proteus X 19 found in epidemic typhus elsewhere. The reaction appears to be of the nature of a group agglutinin response.

Tick-bite fever.

This appears to have been the condition described by McNaught (3) to which reference has been made in connection with Megaw's work on the non-epidemic typhus fevers of India. It is a disease contracted in the open veldt, and Pijper and Dau (18) have shown that the infecting agent is a larval tick. They believe that a reservoir of infection exists in rodents. The disease is characterised by bite mark exactly similar to the tache noire of fievre boutonneuse and to the primary lesion of tsutsugamushi disease. The regional lymph glands are swollen and painful. Fever lasts for 8 - 10 days, and a rash comes out in successive crops commencing about the fifth day. This may be macular or papular, blotchy, diffuse or discrete. Headache and conjunctival suffusion are marked, and swelling of distant lymph glands has been noted in

some cases. Mild abortive forms showing only bite mark and local lymphangitis are common. The white blood cells are not increased, and the differential count shows a relative lymphocytosis.

Agglutination tests with O emulsions of B. proteus X19, X2 and XK show a positive reaction. The highest titres are obtained during convalescence about the fourth week, but very high titres are not found although agglutinins persist in the blood for a long time. As a rule there is a rising titre for all three variants used. XK may show a more marked reaction than X19, and the serum of one case may at one time agglutinate X19 in a higher dilution than XK and later show a reversal of this.

Sporadic or "mild" typhus.

This condition is sharply differentiated clinically from tick-bite fever by the absence of bite and painful localised lymph glandular swelling. It is a disease of towns. Infestation by lice and case to case infection play no part in its incidence, and the uncleanlyare not specially affected. The clinical condition shows a characteristic papular rash. The severity of the fever varies from a mild range in ambulant types to continuous fever extending over 12-14 days.

Serologically positive results are obtained with the Weil Felix test. Pijper and Dau (19) state that "most cases give significant reactions and some of them more than that. On the whole X19 and X2 reacted better than X Kingsbury, but this was not always the case. The most striking feature of the table is that X2 reacted at least as well as X19".

The virus of this disease has been studied by the above observers in guinea pigs and rabbits and has been found in consequence of the results to belong to the typhus group. Compared in cross immunity tests with the virus of South African epidemic typhus and the virus of tick bite fever, the virus of sporadic of "mild" typhus shows the same reactions as a typhus-like virus isolated by them from rats in Potchefstroom, Transvaal, where cases of the sporadic of "mild" typhus they describe have been known to occur for many years. Pijper and Dau (19) conclude that "this constitutes evidence that South African "mild" or "sporadic" typhus comes from rats, and is communicated to man by rat fleas". "So far, however, no work has been done on rat fleas to prove that they harbour or transmit the virus".

Pijper and Dau have analysed the antigenic structure of all three South African typhus viruses by the production of agglutinins in rabbits and cross immunity tests in guinea pigs. The results indicate a close relationship in antigenic structure, and this agrees with the observations of the agglutination reactions in patients suffering from the three varieties

of typhus described by them. If these results are confirmed it will be evident that the louse and flea-borne varieties of typhus fever found in South Africa are not identical with similar diseases in other parts of the world.

(c) NON-EPIDEMIC FORMS OF TYPHUS FEVER IN THE MEDITERRANEAN COUNTRIES.

Professor Charles Nicolle (20) has classified the typhus fevers found round the Mediterranean littoral as follows:-

(1) old world typhus conveyed by lice.
(2) benign typhus conveyed by fleas.
(3) fievre boutonneuse, or macular fever, conveyed by ticks.

Of these old world typhus as found in its classical form in this part of the world does not concern us in this thesis.

Benign typhus.

This is a mild form of typhus fever occurring in man in mild epidemics or, more commonly, endemically under conditions of living or occupation associated with rat infestation. The disease is primarily one of rats. The condition is described in the next section of this thesis.

Fièvre boutonneuse.

This disease was originally described in Tunis by Canor and Bruch (21) in 1910. Numerous cases occurring in and around Marseilles and other parts of the South of France, in Italy, Spain, Portugal, Greece, Rumania, Morocco, Algeria, Tripoli, Egypt and Syria, have been described in the last ten years. In addition to the name fièvre boutonneuse, given to the condition by Ganor and Bruch on account of the feeling imparted to the fingers on palpating the cutaneous lesions, the condition appears in literature under the names macular fever, eruptive Mediterranean fever and fievre exanthématique.

The clinical condition presented by the disease is usually clearly differentiated from benign typhus by the presence of a bite mark, the "tache noire", a scabbed puncture 4-10 mm. wide and usually associated with some swelling to the neighbouring lymphatic glands. The disease is always endemic, and cases occur only during the hotter months of the year. The general reaction is more severe than in benign typhus. The fever may rise sharply or slowly and remains high at about 101° with slight morning remissions. A pulse rate of about 100 at this stage is frequent. The conjunctivae are suffused, and the pharynx is red and slightly swollen.

this frequently causing complaint of difficulty in swallowing. Constipation is usual, and a slight bronchitis is frequently present. The rash appears in outcrops commencing about the second to the fourth day on the trunk and limbs and spreads in the course of the next two days over the whole of the skin surface. It consists of slightly raised, irregularly shaped macules, at first pink but later undergoing a transformation into darker shades, red then purple, at which stage they do not disappear entirely on pressure. The spots may become purpuric. Professor A. Lemierre (22), upon whose work I have drawn for this description of the disease, states that "in no case is the intelligence impaired or drowsiness present". Other writers, notably Olmer (23), state that restlessness and delirium may occur, but that patients rarely pass into stupor. The temperature usually begins to fall as soon as the rash is complete, usually about the fifth to the eighth day, and remains at a lower level of about 99^{9} - 100° for about four days after which it subsides by lysis, becoming normal on the twelfth to the fifteenth day. During defervescence of the fever the rash fades and gradually disappears, but traces may be evident as a residual staining for varying periods up to several months, Complications occasionally noted are myocarditis, phlebitis, congestion of the lungs, nephritis and meningism. Convalescence is gradual. The mortality is less than 2%.

Atypical forms of the disease occur. The "tache noire" may be absent, and febrile conditions resembling the disease and showing this lesion may show no rash. Some of these appear to be abortive attacks to which the term "formes frustes" has been applied.

The earlier attempts to establish the value of the Weil Felix reaction in the dianosis of fièvre boutonneuse yielded confusing results. Durand (24) however, showed in 1932 that, if O emulsions of X19, X2, and XK are used, significant titres are found with the two former strains, either solely or predominantly for one or other or for both in relatively equal amount. The maximum titres are not found until late in convalescence, in fact significant titres may be absent until the fourth or fifth week after the onset of the disease. The titres obtained are markedly lower than those found in epidemic louse-borne typhus. No reaction with B. proteus XK is found.

Fièvre boutonneuse has been shown by Durand and Counsiel (25) to be conveyed to man by the bite of a tick, Rhipicephalus sanguineus, which is found on dogs. Durand (26) has shown that dogs are immune to the disease, but that young pups kept free from ticks, can be inoculated with the disease in an inapparent form.

Young pups are therefore considered an important reservoir of the virus, as also are rodents which harbour Rhipicephalus sanguineus. Durand regards the tick itself as an important reservoir, and, as it reaches man via the dog, the latter is a factor of great importance in the transmission of the disease.

Nicolle (20) states that although benign typhus and fievre boutonneuse may each present a definite clinical picture which distinguishes the one from the other there is no diagnostic feature of universal application for this purpose. Guinea pig inoculation, however, provides a ready means of differentiating the two diseases. If the blood of a patient suffering from the disease called by Nicolle "benign typhus" is injected into a guinea pig intraperitoneally a severe condition known as the Neill-Mooser reaction results. This will be described in connection with endemic, murine or flea-borne typhus. Similar procedures with the blood of patients suffering from fievre boutonneuse have been reported by Troisier and Cattan (27) and Caminopetros and Gontos (28) to cause a varying type of reaction. The animal may react with fever only. It may show fever and scrotal oedema, the latter less marked than in the Neill-Mooser reaction, or it may develop an inapparent infection.

(D) NON-EPIDEMIC FORMS OF TYPHUS FEVER IN THE UNITED STATES.

Non-epidemic typhus fevers are found in the United States in three forms.

(1) Brill's disease.
(2) Rocky Mountain spotted fever.
(3) Endemic typhus.

Brill's disease.

This form of typhus fever as it occurs in New York was described by Brill (29) in 1898. Brill noted that the condition was much milder than epidemic typhus and that it differed from this condition epidemiologically. The condition only concerns us in this thesis because of the analogies drawn by MacKechnie and Megaw between it and Indian cases of non-epidemic typhus. Until comparatively recently Brill's disease was considered to be the same condition as the endemic typhus of the Southern States. Guinea pig inoculation, however, has shown that the viruses of the two conditions are different, that of Brill's disease being identical with the louse-borne virus of epidemic typhus, the other being the virus of murine typhus. Recently Zinsser (30)

has conducted an epidemiological survey of the disease in New York and Boston, and has found that 94.8% of the cases which came under review occurred in immigrants from European countries where louse-borne typhus is epidemic or endemic. He has confirmed Brill's thesis that the disease is a mild form of true typhus, not spread by contact or lice. Zinsser regards Brill's disease as a recrudesence of infection in individuals who have previously been infected with true typhus.

Rocky Mountain spotted fever.

This is a typhus-like fever originally described as having a patchy distribution in the Rocky mountain regions of Montana, Idaho, Wyoming. The condition closely resembles louse-borne typhus, but the duration of the fever tends to be longer and the rash is usually much more conspicuous. The fever in a well marked case is high, lasts about three weeks and subsides by lysis. During the defervescent stage there is often a period of intermittent fever. The pulse rate is high. The rash appears on the second to the fifth day, is first noticed as a rule on the wrists and ankles and later becomes generalised. It usually extends to the face, palms and soles, and purpuric change is frequent. Splenic enlargement and jaundice are common. Bronchitis occurs, but less frequently than in louse-borne typhus. Abdominal distension, albuminuria, delirium and toxaemic myocarditis with consequent low blood pressure are similar to the corresponding manifestation in true typhus. In severe forms of the disease necrosis of the skin of the toes, fingers, ears, prepuce, and scrotum have been recorded. A brown staining often persists at the site of the rash for several weeks after recovery. Remarkable regional variations in mortality occurs. In some valleys a mortality of 70% has been recorded, whereas at the same time the mortality in other valleys has been less than 10%.

A well marked primary sore and associated lymphadenitis are not found in Rocky Mountain spotted fever, but occasionally small cutaneous scars and slightly enlarged adjacent glands have been observed.

The disease is contracted by man chiefly in the wilds, in open wooded country at an altitude of 3000-4000 feet. It is conveyed to man by the bite of a tick, Dermacentor andersoni, the wood tick which feeds on small rodents, and of certain other ticks. A definite history of tick bite is found in the majority of cases. The disease occurs chiefly in spring, when the ticks are active after winter hibernation. Within recent years cases have been recognised in practically all of the Western States and also in the Eastern States, where the tick vector is Dermacentor variabilis. Milam (31) reported eighteen cases occurring in North Carolina during 1933. He affirmed the previously existing views

that small wild rodents formed the reservoir of infection. The virus, however, has not been found in any of these. The vector ticks as larvae and nymphs feed on them and become infected thereby. In the adult stage they prefer the dog as hosts and are in this way brought into cntact with man. The dog does not appear to harbour the infection. Continuity of the virus is effected through the eggs of the adult female tick. Milam reports that the disease appears to be on the increase in North Carolina.

The earlier investigations of the Weil Felix reaction in Rocky Mountain spotted fever yielded negative results with emulsions of B. proteus X19, but in 1929 Kirlee and Spencer (32) tested the sera from a few cases and found agglutinins for X19 and XK together in one serum and separately in others. X19 reacted significantly in a minority of cases and the titres of agglutination were low. Moreover agglutinins for X2 and XK were present in a considerable proportion of the cases. Significant agglutins for OX2 were observed by Spencer and Maxcy (33) in 1930. The reaction was further investigated by Davis and Parker (34) in 1932. In the summary of their work these writers state

"The relatively high titres obtained with OX2 are to be noted.

Agglutination of proteus X strains occurs in a considerable proportion of cases of Rocky Mountain spotted fever. The number of strains necessary to secure agglutination in sufficiently high titres to be of possible diagnostic significance and the irregularity with which the results are obtained indicate that with the available strains the agglutination tests cannot be regarded as a diagnostic procedure in a measure comparable to agglutination tests in certain other diseases".

They recommend that the serum be examined on the tenth to the fifteenth day, again seven to ten days later and finally during convalescence.

Guinea pigs inoculated with the blood of patients suffering from the disease show a severe fabrile reaction and the infection conveyed is fatal. The post mortem appearances include scrotal lesions, enlarged glands and spleen and hyperplasia of the bone marrow. A milder type of virus not causing a fatal reaction in the guinea pig has been described by Reimann, Ulrich and Fisher. (35)

Endemic typhus.

This disease was first reported in the United States in 1923 by Maxcy and Havens (36) in Alabama. Since then the incidents of the disease has shown a remarkable increase and it is now widely distributed over the south eastern states. Originally a disease of towns it has spread to country districts in recent years. It is a flea-borne disease primarily affecting

rats and is dealt with in the next section of this thesis.

5. ENDEMIC TYPHUS (Syn. FLEA-TYPHUS, MURINE TYPHUS).

At the time when Megaw was endeavouring to bring the Indian typhus-like fevers he has investigated into alignment with other typhus fevers of unknown vector in other parts of the world, he noted reports on fevers resembling mild typhus by Wheatland (37) and Hone (13) in Australia and by Maxcy and Havens (36) in the United States. The cases described by Wheatland in Queensland were mostly farmers in mouse infested districts. The outbreak of cases appeared to be preceded by a high mortality among mice, and the name "mouse disease" was applied to it. Hone's cases in Adelaide were mostly associated with rats and grain stores. In 1926 Maxcy (12) reported a large number of cases from Alabama. He observed that cases tended to occur in the summer and autumn, that persons handling food were specially liable to infection, that overcrowding and louse infestation played no part in the spread of the disease, that case to case infection did not occur, and that negroes appeared to escape infection. He suggested a rodent reservoir of the virus and an arthropod vector other than the louse.

In 1917 Neill (38) reported that if the blood of a patient suffering from a typhus fever, now known to be endemic typhus, is injected intraperitoneally into a male guinea pig a severe febrile reaction with swelling of the tunica vaginalis and periorchitis results. The importance of this was not recognised until eleven years later when Mooser (39) investigating the disease as it occurs in Mexico described the same changes and affirmed that they were specific for the virus he was investigating. In addition to the macroscopic change mentioned above the endothelium of the tunica vaginalis was found to contain many rickettsia bodies and the fluid in the sac to possess a high degree of virulence. This reaction in the male guinea pig is now known as the Neill-Mooser reaction, and it has proved of great value in differentiating endemic, flea-borne typhus from tick and louse-borne varieties of the disease.

In 1931 and 1932 Dyer and his co-workers (40) in America showed that an emulsion of fleas taken from rats in areas where numerous cases of endemic typhus had occurred produced the Neill-Mooser reaction when injected intraperitioneally into male guinea pigs. By the same method Mooser, Castaneda and Zinsser (41) in Mexico showed the presence of the virus of endemic typhus in the brains of wild rats caught in endemic areas. Dyer and his co-workers have further shown that the rat flea, Xenopsylla cheopis, can convey infection from rat to rat, that the virus multiplies in the flea,

and that the faeces of the flea are infective. Dyer concludes that "the rat flea, Xenopsylla cheopis, as the vector of endemic typhus meets the requirements of the epidemiological evidence".

The modern conception of endemic typhus is that it is primarily a disease of rats with a wide distribution throughout the world. It appears to occur in epidemics which leave the majority of the infected animals immune. Even in localities where the rat population is heavily infected cases may only occur sporadically in man. This would appear to be due to the fact that the disease does not kill the rats. Wheatland's observation previously mentioned that outbreaks of the disease were preceded by a high rodent martality is unique in this respect. The rat flea, therefore, is not driven as in the case of its host dying of plague to seek an alternative host; it tends to remain on the rat or in its nest. The disease, however, may be transmitted to man by the bite of the rat flea. On this account it is sometimes called "flea-typhus". As the disease is primarily one of rats some authors, particularly certain French writers, apply the term "murine typhus" to the disease in the rat and in man. The "shop typhus" of the Federated Malay States described by Fletcher and Lesslar is now regarded as this disease.

Jame and Aujalea (42) describe the clinical features of endemic typhus, called by them murine typhus, as follows:

The disease may be epidemic or endemic, and the incubation period is six to fourteen days; The onset is sudden with headache, anorexia, flatulence, nausea and constipation. Conjunctival suffusion and pharyngeal congestion are occasionally present. Slight enlargement of the spleen may be detected. A morbilliform, macular or maculo-papular rash, not disappearing completely on pressure, appears about the fourth or fifth day of the disease. It does not affect the face, and frequently avoids the palms and soles. Occasionally it becomes purpuric. The rash disappears in about a week. The temperature is usually continued and fever usually persists for about ten to fourteen days after which it subsides by crisis. The pulse rate is slow in comparison with the temperature, and the blood pressure is seldom depressed. The urine is diminished but rarely shows albuminuria. The patient is never very ill, and the mortality in otherwise healthy subjects is negligible.

Milam (43) in a comparative table of the features of Rocky Mountain spotted fever and endemic typhus in America states that in the former the fever subsides by lysis, the rash appears first on the wrists and ankles and then becomes general, including the palms and soles, and that the pulse rate is higher; in endemic typhus the fever is lower and ends by crisis at the end

of the second week, the rash appears first on the trunk and flexor surfaces of the limbs and is rarely found on the face, palms and soles and that the pulse rate is slower.

The Weil Felix reaction in endemic typhus is positive with B. proteus X19 but the titres are not so high as those shown by cases of epidemic, louse-borne typhus. Moreover agglutinins are not demonstrable in the blood until about the end of the pyrexial period or even later. Spencer and Maxcy (32) state that in the test only the strain X19 need be considered.

6. THE CASES.

Classification.

For the purposes of discussion the cases are provisionally classified mainly on epidemiological basis as follows:

Group A.

Case Nos. 1, 2, 3, 4, 5 and 7 (vide appendix) Total 6.

Four of these Nos. 1 - 4 were contracted in the Kumaon lake area during the season of heavy rainfall, i. e. from about the middle of July to September. One case, No. 7 was contracted on the plains during the rains, and is serologically closely related to this group.

Group B.

Cases Nos. 8, 9, 10, 11, 12 and 13 (vide appendix) Total 6.

All of these were contracted in the Ranikhet area of the Kumaon hills during the summer season proceding the heavy rains, i.e. from the middle of April to the middle of July.

Group C.

Case Nos. 6, 14, 15, 16, 17, 18, 19 and 20. (vide appendix) Total 8.

These cases were contracted in the plains between September and March, i. e. during the cooler and drier part of the year.

ANALYSIS OF AND COMMENTS ON THE CASE RECORDS.

Group A.

In grouping these cases together I have been prompted by the following considerations:-

Two officers, cases 2 and 3, proceeded on ten days leave together from the 17th to the 27th August, 1932 to fish at Naukatchiya Tal in the Kumaon lake area. They returned to their plains station, where one fell ill on the 28th August and the other on the 4th September. Both showed the features of a typhus-like disease associated with a primary sore and adjacent painful lymphadenitis. Case 2 died after a severe illness, on the twelfth day of the disease. Another officer, Case 1, who had been shooting at Sat Tal in the same area at exactly the same time, fell ill on the 6th of September, and showed a clinical condition almost exactly similar to Case 2 and also resulting in death on the twelfth day of the disease. There is strong prima facie evidence that all three were cases of the same disease, for although the rash and the general reaction differred in Case 3 from that in the other two, nevertheless it was a typhus-like disease associated with what appeared to be a primary lesion and associated painful localised lymphadenitis. A year later another officer from the same unit as cases 2 and 3 went to Naukatchiya Tal to fish on the 20th August and spent about 10 days there. On the 5th September he developed a severe typhus-like disease also associated with a primary lesion and adjacent painful lymphadenitis, although the rash present was scantier and disappeared earlier.

I examined cases 1, 2 and 4 in the course of their illnesses, and case 2 shortly after death. In case 1 on admission to hospital there were two papular sores about 3 mm. in diameter and with punched-out ulcers with red inflamed margins at the site mentioned in the case records. In case 2 at the time of death the central portion of the lesion described consisted of a black scab about 3-4 mm. in diameter with a surrounding area of inflamed red skin about 1" in diameter. In Case 3 on the fifth day of the disease the lesion mentioned was smaller, namely a papular sore with a punched-out crater, the ulcerated surface being 1-2 mm. in diameter. The margins were not so red as in cases 1 and 2. Case 4 on admission showed a raised red sore about 6 mm in diameter with a dried necrotic centre, but when I examined the patient six days later the central portion had been shed, the lesion was healing and the glandular inflammation previously present had subsided. In each case the adjacent lymph glands were enlarged and painful on admission, and the inflammation showed a tendency to subside a few days later. The question was raised whether these lesions were ordinary infected sores such as might arise from scratching mosquito or bed bug bites, and whether the glandular swellings were a simple lymphadenitis of septic origin resulting from such. In cases 1, 2 and 4 the patients showed very numerous other skin lesions of this nature, particularly on the wrists, forearms and around the knees, but these

were distinct in character from those considered to be the primary lesions of the disease in that they were slightly purulent and showed no clear-cut ulcerated crater nor black necrotic centre with red margins, such as were shown by the lesions described in detail above. Further the glandular swellings were in each Case related to the lesions described as primary lesions. In Case 2 it is worthy of note that the lymphadenitis affected the left inguinal glands. The lesion described as the primary sore was on the lower left quadrant of the abdomen. The femoral glands were not enlarged, although there were numerous septic sores with no specific characters around the knee.

One reason for laying stress on the above features of Cases 1, 2, 3 and 4 as a factor warranting their grouping together is that such lesions are rarely found in the non-epidemic typhus fevers of India. I have only found two records of cases showing their presence, namely one of the cases described by Ghose, and that reported by Christian, both of which have been previously mentioned. Sir John Megaw has informed me that the latter case was the first case in which he saw such lesions, although it occurred in 1932. I had occasion to examine this case with Captain Christian on the 8th day of the disease. The primary lesion on the thigh was then a lesion very similar to that described in case 4.

The recognition of a typhus-like fever associated with primary sores and adjacent lymphadenitis immediately suggests an analogy to three conditions, namely:

(1) tick bite fever of South Africa.
(2) fièvre boutonneuse.
(3) Japanese river fever or tsutsugamushi disease.

Of these the two former conditions are associated with a low mortality, practically negligible in healthy adults below middle age; the third may show a mortality as high as 60%. As two out of the four cases in question died, a suspicion is raised that they were either cases of tsutsugamushi disease or of a similar tuphus-like fever which has not so far been described. Attention therefore is at once directed to a comparison of the epidemiological factors, clinical condition and serological reactions of these cases with the corresponding factors in tsutsugamushi disease.

Epidemiological factors.

In Japan cases of tsutsugamushi disease occur between June and October. In Sumatra and the Federated Malay States the incidence is less strictly seasonal. In Japan the incidence of the disease is chiefly upon

workers in fields flooded during seasonal heavy rains. The vector of the disease is a mite, chiefly Trombicula akamushi, which normally infests rats and mice. Certain features of the epidemiology of the disease in the Federated Malay States have been mentioned in a previous section of this thesis, namely its occurrence on land which has been cleared and subsequently become overgrown with long jungle grass and bushes.

In the Kumaon lake area the rainfall between the middle of July and the end of August is very heavy, and the water level of the lakes rises, covering much surface weedy and marshy during the long dry season. In many places the forest and jungle scrub come right down to the edge of the lakes, paths through them are narrow, and fishing in August entails scrambling through much undergrowth and long grass, frequently over a marshy surface. Within the past twenty years the district as a hot weather resort has declined in popularity, partly perhaps as a result of its ill repute as a "plague spot", and now the chief European visitors are a few officers who visit Naukatchiya Tal in August to fish. Much of the ground cleared many years ago round the few houses frequented by Europeans is now overgrown with long grass. The restricted area in which the four cases occurred is noteworthy. The village of Bhowali five miles distant attracts quite a large number of summer residents whose sole means of exercise during the rains is walking along the narrow forest paths, picnicing and bathing when circumstances permit. No similar case was reported amongst the hotel residents in Bhowali during the years 1929-34. Case 1, however, lived at Bhowali during his leave, but it appears likely that he contracted the disease in the Kumaon lake area during his shooting expeditions. A close resemblance, therefore, is shown between the conditions under which the three Naukatchiya Tal cases occurred and those associated with the tsutsugamushi disease.

The clinical condition.

For the purpose of comparison I have consulted four of the most well-known text books on tropical diseases in the English language. XX The presence of primary lesions and associated glandular swellings has already been noted. The mode of onset of the disease

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XX Manson's Tropical Diseases 9th Ed. Edited by Manson.Bahr. Tropical Medicine. Rogers and Megaw, 2nd. Ed. The Diagnostics and Treatment of Tropical Diseases. E. R. Stitt. 5th Ed. The Practice of Medicine in the Tropics. Edited by Byam and Archibald. Vol. 111.

with chilly sensations succeeded by a period of continuous fever, the latter well illustrated in Case 4, is seen in all cases. A comparatively slow pulse rate during this period is seen. The profuse macular eruption becoming confluent in Cases 1 and 2 is compatible with a diagnosis of tsutsugamushi disease, but the late appearance of the rash in Case 2 on the 8th day is more in conformity than its earlier appearance in case 1. The type and distribution of the rash in all cases is compatible with the variations recorded in the text books consulted, and a suggestive feature is the absence of petechial change in Cases 1. 2. and 4. This is common in less severe forms of typhus fever endemic in India, and its absence in cases 1, 2, and 4 is therefore noteworthy. An interesting feature of case 4 was the scanty, macular rash appearing mainly on the trunk on the sixth day and disappearing in about five days. Mention of this variation in the rash of tsutsugamushi disease is made by Stitt. Other features of the cases, the facies, appearance of the tongue, the early splenic enlargement, the lymphglandular enlargement, other than the regional bubo, the diarrhœa in cases 1 and 2, the typhoid state and nervous symptoms, all have their exact counterpart in descriptions of tsutsugamushi disease. Cases 1, 2 and 4 were complicated by severe myocarditis of which the two former died, and this mode of death corresponds. Finally the death of Cases 1 and 2 on the twelfth day of the disease, about the same time as cases of tsutsugamushi disease usually succumb, and the mortality of the cases constitute strong evidence that the cases can be classified as tsutsugamushi disease.

With the exception of the mildest case, number 3, none of the cases show in the blood examinations recorded the leucopenia which figures prominently in the descriptions of the disease from Japan. The observations, however, of Kouwenaar, Snijders and Wolff (44) to the effect that in the Sumatran form of the disease they have only observed this in 10% of cases goes far to reconcile this apparent discrepancy.

Serological Evidence.

For reasons mentioned in connection with the work of Fletcher and Lesslar in the Federated Malay States of comparing their Weil Felix reaction results with those recorded in other parts of the world in connection with fevers resembling their tropical typhus, the Weil Felix reaction as carried out in Military laboratories in India prior to 1933 cannot be regarded as entirely satisfactory. The type strains used, emulsions of which are issued from the Enteric Convalescence

Depot, Kasauli, had been there for many years. O emulsions of X2 were not issued, but another strain called "Multesar" was used in conjunction with X19 and XK. For the history of this strain reference may be made to Bridges' (45) work. I understand he has since shown that it is a strain of X19. The Weil Felix reactions of cases 1, 2 and 3, all of which occurred in 1932, need not be considered seriously for those reasons, although the titre of 1/300 in XK recorded during convalescence in Case 3 on the 38th day is suggestive. Further, Cases 1 and 2 ended fatally on the twelfth day, at which period of the disease significant titres could not be expected. Case 4, however, was fully investigated after Bridges had introduced new cultures from the National Collection of Type Cultures for the preparation of the suspensions issued. The results were significant, namely.

Day of disease.	OX19.	OX2.	OXK.
5.	Nil.	Nil.	Nil.
10.	1/25.	1/25.	1/500.
14.	1/25.	1/25.	1/2500.
18.	Nil.	Nil.	1/5000.

This shows conclusively that case 4 was one of the scrub typhus- tsutsugamushi fever disease group, and as a well marked primary lesion and associated glandular swelling were present, the nature of the case must be considered to be tsutsugamushi disease, and the others were in all probability of the same nature.

Before dismissing Cases 1, 2, 3 and 4 I am tempted to speculate whether or not the disease from which they suffered was the same as the fevers occurring in the same district at the same time of year, which MacKechnie investigated in 1913. As previously stated Sir John Megaw who had occasion to study MacKechnie's report very carefully, and who published extracts from it twice (1) (2), assures me that as far as he can recollect the report contained no mention of a primary lesion nor of associated buboes. It has been mentioned that Fletcher, Lesslar and Lewthwaite, in the Oil Palm Estate outbreak described by them in the Federated Malay States, reported cases of the tsutsugamushi disease occurring in the same area and at the same time as scrub typhus, and suggested that the former disease conferred immunity to the latter. It appears to me that, if primary lesions and associated lymphadenitis were absent in MacKechnie's cases, these were probably cases of scrub typhus.

I have included case 5 in Group A. This patient was also an officer, who gave a history of two shooting expeditions within the limits of the incubation period of the disease. The case was contracted in

September in the hills of the United Provinces in a locality which is far removed from the Kumaon lakes, and in which the occurrence of typhus-like fevers had not previously been reported. This case showed a typical primary lesion in the left infraclavicular region and an enlarged tender gland in the posterior triangle of the neck on the same side. The rash was exactly similar to that seen in case 4 and disappeared early. Further, a fairly severe typhoid state was present. The diagnosis of a typhus group fever was not borne out, however, by a positive Weil Felix reaction, although the emulsions used were similar to those used in case 4. An element of doubt, therefore, arises as to the merits of the case for inclusion in this group. The case was undoubtedly one of the non-epidemic typhus group of fevers common throughout India, and the fairly severe typhoid state, and scanty rash disappearing early were considered to be more suggestive of this group than of the others.

As tsutsugamushi disease is now commonly grouped with scrub typhus, largely on account of the serological reactions they show in common with B. proteus XK, I have included one other case in this group which showed significant titres with B. proteus XK.

Case 7 was examined by me during convalescence. The patient was an Indian sepoy in whom a rash would have easily escaped notice, and the manner in which the diagnosis was made is interesting as it illustrates the value of the Weil Felix reaction in elucidating the nature of fevers occurring in India, which, in the absence of the test, would probably be diagnosed clinically as enteric group infections. The history of pain in the right axilla on admission and subsiding two days later was very definite, and I suspected it to have been due to an enlarged gland secondary to a primary lesion. I could not find any scars suggestive of this, however. The case cannot be accepted as one of scrub typhus apart from grouping of this condition with tsutsugamushi disease.

Although the series of cases does not include any typical case of scrub typhus, evidence is accumulating that this disease occurs in India. I understand on high authority that, although Macnamara does not state the results of agglutination tests with B. proteus X19 and X2 in his recent communication on cases observed in the Simla hills previously mentioned, the Weil Felix reactions were typical of scrub typhus.

Group B.

In this group Cases 8, 9, 10 and 13 developed a typhus-like disease in the Ranikhet area of the Kumaon hills during the months April to July, and case 12 showed a similar disease about twelve days after leaving the area. Cases 8, 9 and 13 were soldiers who had not left the immediate vicinity of barracks within the

limits of the incubation period of the disease, taken as five to twenty days. Case 13 gave a history of contact with a sick dog. Case 12 had spent four nights in bivouac during a journey by road to railhead. Case 10 was a nursing sister who bred fox terriers which were frequently in her quarters. She had been for a walk in the jungle five days before the onset of her illness, and on return had found on her thigh a small tick, apparently a nymph or larval form. She stated that it did not appear to be engorged with blood, but on examination after the onset of the disease a small papular lesion was observed close to where she had found it, and one adjacent femoral gland was slightly swollen. Neither the papular lesion nor the gland swelling was so marked as in cases 1, 2, 3, 4 and 5 of group A. Case 11 was a nursemaid whose only contact with jungle conditions was during a picnic she had attended six days prior to the onset of her illness.

The clinical condition in these cases with the exception of case 13 was similar. There was fever of eleven to thirteen days duration subsiding by lysis, headache and joint pains were more or less severe, rigors and sweating occurred, a bright red macular rash appeared about the third to the fifth day of the disease, and was noticed in most cases first on the limbs, in others on the trunk. It showed successive outcrops over a period of two to three days, and spread to involve the limbs and trunk, being rather more profuse on the former, the palms and soles in all cases, and the face in the majority. Petechial change was noted in one case only. The temperature showed a tendency to fall when development of the rash was complete. The rash underwent colour transformation to a deeper shade of red, then purple. It commenced to fade shortly before defervescence of the fever was complete, and there was residual staining during convalescence at the sites affected. The tongue was coated (white) in the early stages, and later brownish in the more severe cases. All cases were flushed, and showed conjunctival suffusion and sore throat. Constipation, a generalised slight lymphglandular enlargement, and enlargement of the spleen were reported in some cases. Mental symptoms consisted of a moderate degree of drowsiness and restlessness. In case 10 mild delirium was recorded, and also a moderately severe degree of myocarditis indicated by a fall in the systolic blood pressure. Phlebitis of the right femoral vein occurred as a complication in case 11 after decline of the primary fever.

The serological reactions of these cases show significant titres for B. proteus X19, more marked for the strain Multesar in cases 8 and 9 in which this was used in addition to strain Warsaw. It is a matter to be regretted that type X2 was not used in these cases, as it figures prominently in the results

of the 1933 cases following the use of Bridges' emulsions prepared from type cultures from the National Collection.

Case No.	Day of Disease.	X19.	X2.	XK.
10	7	Nil.	Nil.	Nil.
	25.	1/2500.	1/2500.	1/50.
11	7	1/85.	Nil.	1/50.
	14.	1/1200.	1/1200.	1/35.
	17.	1/6000.	1/3000.	1/35.

Agglutinins for X2 were, however, absent in case 12, which showed the following results.

Day of disease.	X19.	X2.	XK.
5.	Nil.	Nil.	1/17.
9.	Nil.	Nil.	1/25.
13.	1/1000.	Nil.	1/50.
18.	1/2500.	Nil.	1/50.

The results are similar to those described by Durand in fievre boutonneuse, and previously mentioned. They differ from those found in Rocky Mountain spotted fever and tick bite fever of South Africa in that they show no significant agglutination with type XK.

Case 13 is of interest in that it was associated with the foregoing cases as to place and seasonal incidence. It appeared to be definitely a mild typhus-like disease associated with a bubo in the groin which began to subside shortly after admission. This could not be attributed to local septic infection, and the short course and early subsidence excluded lymphogranuloma inguinale as the nature of the lesion. Unfortunately the Weil Felix reaction in this case had to be carried out with old emulsions owing to auto-agglutination in the test with the fresh supplies of those received at the time. Clinically the case is suggestive of the "formes frustes" of fievre boutonneuse.

A comparison of the epidemiology of these cases with the known facts of the epidemiology of fievre boutonneuse is of interest. The latter disease occurs only in the hotter months, is not contagious, is much more common in rural areas than in towns, there is occasionally a history of tick bite and almost always

a history of the presence in immediate contact with the patient of dogs, sometimes of sick dogs which have been heavily infested with ticks.

Cases such as these recorded in this group occur sporadically at Ranikhet each year between the middle of April and the middle of July. Cases do not seem to occur after the heavy rains are well established in the latter month. The European population consisting of British troops and their families is usually between 2000 and 2500 at this time, and the total number of cases reported in the five years 1930-34 was seven, of which four occurred in 1933 and two in 1932. No evidence of case to case infection has ever been observed, and the cases have been nursed in the general wards of the hospital without spread of the disease occurring. Dogs tend to become tick infested to a mild extent; isolated cases of tick bite in man are very rarely reported. The barracks abut upon the jungle. The dog population of barracks is large, as a dog is commonly kept by the soldier, and as dog-owners proceeding to the hills in summer frequently take with them the dogs of comrades remaining on the plains. Practically every soldier living in barracks comes in contact with dogs in the course of his every day life. In the series of six cases in group B we find special mention of close contact with dogs in two, and it may be safely assumed that contact occurred in three of the others.

The conditions of occurrence of the cases of Group B are similar to those of fievre boutonneuse, the serological reactions recorded resemble closely those reported by Durand in this condition, and the clinical condition present is a fever of similar duration, showing closely similar features, similar complications, and is approximately of the same average severity of reaction. The outstanding feature in which the cases differ from fievre boutonneuse is that bite mark and associated glandular swelling are very unfrequently reported.

Group C.

A study of these cases shows that epidemiological, clinical and serological features are less uniform than in the previous group. Two cases, Nos. 18 and 19, are, however closely related in all these respects, and provide some structural basis for an analysis of the others.

Case 18 developed in the latter part of October 1934. and case 19 a month later. Both occurred in Meerut, a station where no similarly developed cases had been previously observed. The two cases had nothing in common as to previous movements, and the barracks in which they lived were half a mile apart.

No clue could be found pointing to a vector concerned in the transmission of the disease, but a small papular lesion lacking a cleanly-cut central ulceration or scab, and not associated with local glandular swelling, was found in case 19. This patient gave no history of contact with dogs, but he was a keen cricketer and his activities in this game took him out on to playing fields where cattle had grazed a good deal about a month prior to his infection.

Clinically the differences shown by cases 18 and 19 when compared with those of group B are:-

(1) a longer duration of fever, namely 16 days; the fever show a more definite stage of fastigium lasting about 4-6 days after the appearance of the rash during which further outcropping of this occurs, and which terminates about the tenth day, when there is a dramatic amelioration of symptoms. This is followed more definitely than in the cases of group B by a phase of lower temperature lasting about three days and preceeding a phase of definite lysis during which the temperature is mildly intermittent.

(2) the rash is maculo-papular at the onset, distribution and spread are the same as in group B, but colour transformations are less marked, and the rash disappears entirely during the phases of fever above mentioned following the fastigium.

(3) signs of bronchitis and pulmonary congestion are recorded in case 19 commencing on the ninth day.

A very careful examination of the total and differential white blood corpuscle count was made in these two cases, and the results were as follows:

Case No.	Day of Disease.	Total.	Polys.	Lymphos.	Momos.
18.	7.	6,200.	53.	39.	8.
	14.	6,000.	64.	33.	3.
19.	7	5,600.	58.	36.	6.
	13.	6,000.	65.	30.	5.

Serologically a rising titre for all three types of B. proteus X is seen in case 19, and for X19 and XK in case 18. The highest titres are seen with X19, but these are markedly lower than those recorded in cases 10, 11 and 12, with which they are comparable as they were carried out with the same emulsions.

An examination of the other cases in the group shows that cases 6 and 17 resemble these two cases.

Case 6 occurred at Bareilly in October 1932, was clinically mild, although the fever lasted for 16 days, and showed well marked development of agglutinins for XK on the twenty first day. The recorded titre for X19 is 1:150, and as I have regarded all titres above 1:125 as significant, this case has not been classified with group A as one of scrub typhus. Further, I have avoided as far as possible laying stress on the Weil Felix reaction titres, in cases where this test was carried out prior to the introduction of Bridges' work in 1933.

Case 17 occurred at Bareilly in March 1933. The patient had been in camp for eight days and fell ill two days after his return. The onset was acute, and a suggestive symptom recorded at this period was pain in the groin. This appears to have disappeared rapidly, as it is not subsequently mentioned, and the results of examination directed towards determining the cause of the pain are not reported. This symptom is suggestive of tick bite, but in making this statement I am assuming that the condition was not one of lymphadenitis of septic origin. The clinical condition shown is similar to that seen in cases 18 and 19. The fever lasted for eighteen days, but its subsidence was followed by a short period of irregular fever. Outcropping of the rash occurred over a longer period than in case of group B, signs of pulmonary congestion were present as in case 19, but appeared earlier. Symptoms referable to the cardio-vascular and nervous systems appear to have been rather more severe than in cases 18 and 19, and dissimilar clinical features recorded are the residual staining left by the rash, the splenic enlargement and the white blood corpuscle count, which was as follows:-

Day of disease.	Total.	Polys.	Lymphos.	Monos.	Eosins.
4.	14,200.	76.	18.	6.	-
14.	12,450.	71.5.	23.	5.	.5

The Weil Felix reactions reported in cases 17, 18 and 19 were:

Case No.	Day of Disease.	X19.	X2.	XK.
17.	4	1:17.	1:60.	1:70.
	8	1:17.	1:60.	1:25.
	12	1:125.	1:275.	1:175.
	16	1:175.	1:275.	1:300.
	25	1:85.	1:175.	1:250.
18.	5	Nil.	Nil.	Nil.
	7	Nil.	Nil.	Nil.
	15	1:250.	Nil.	1:250.
	22	1:500.	Nil.	1:125.
	29.	1:250.	Nil.	1:25.

Case No.	Day of Disease.	X19.	X2.	XK.
	7	Nil.	Nil.	Nil.
	10	1:50.	Nil.	Nil.
19.	20	1:250.	1:25.	1:125.
	26	1:1000.	1:250.	Nil.
	30	1:500.	1:125.	Nil.
	37	1:400.	1:250.	Nil.
	41	1:250.	1:125.	Nil.

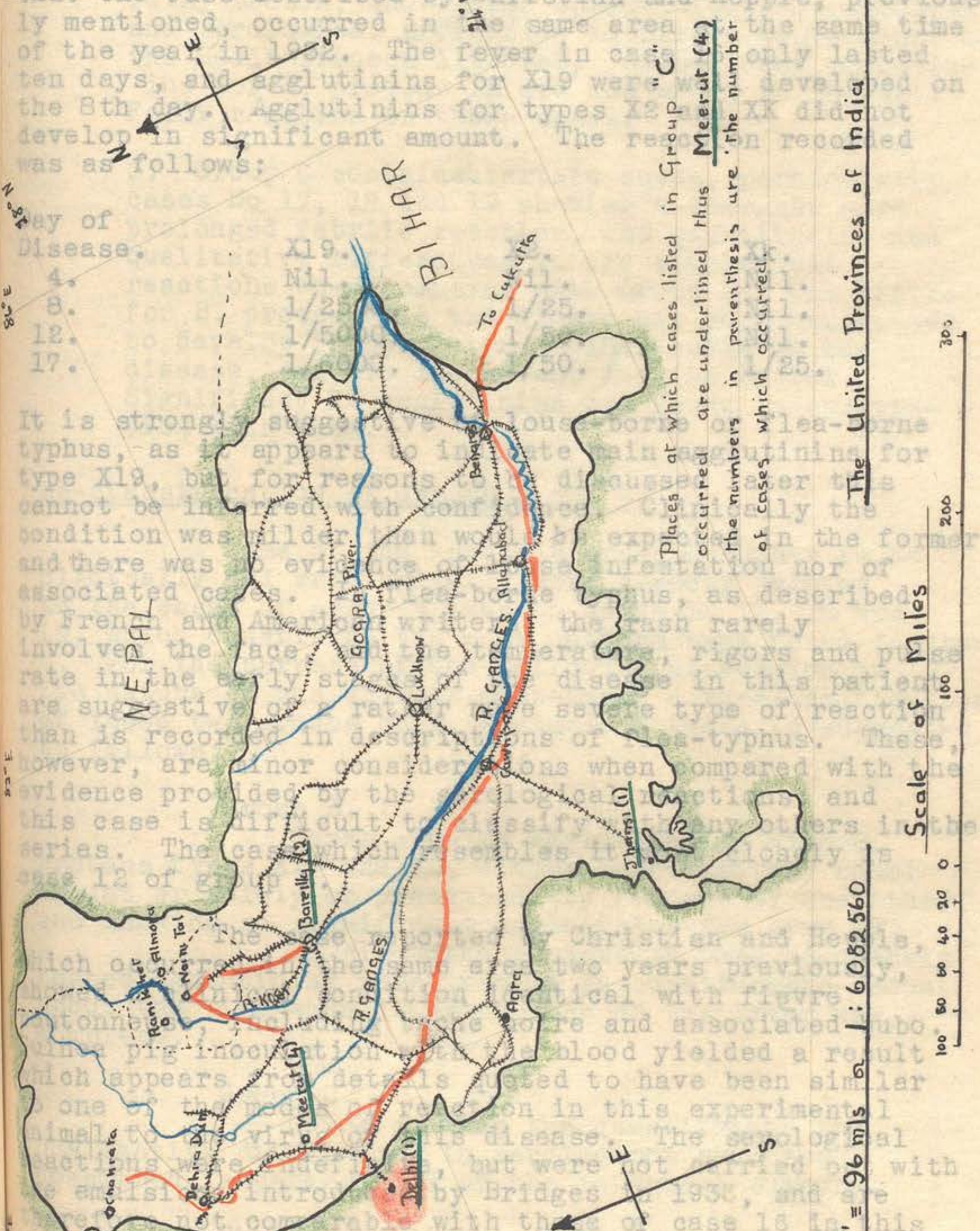
The type of reaction seen in these three cases is similar to that reported by Blewitt in connection with the cases he observed at Ahmednagar in 1933. It is also similar to the reactions observed in Rocky Mountain spotted fever and the tick bite fever of South Africa. The general clinical reaction is more severe than in tick bite fever of South Africa, from which it also differs in the absence of bite mark and lymphadenitis. When compared with Rocky Mountain spotted fever we find that the duration of the fever, the high initial fever in case 17, the tendency to irregular fever at the end of lysis in all cases, and following it in case 17, the marked amelioration of symptoms about the 10th day in cases 18 and 19, and the pulmonary symptoms recorded, are very similar to what is commonly found in ~~Rocky Mountain spotted fever~~ this disease, which these cases closely resemble, although no mortality is shown, and the patients were never dangerously ill. Apart from the serological reactions, however, the difference in symptoms shown by these cases when compared with those of group B is mainly one of degree, with minor differences of kind such as the presence of bronchitis. The results of guinea pig inoculation reported in case 17 do not assist us in drawing analogies with other diseases as the particulars reported do not show whether any infection resulted from the inoculation or not.

Examining the case records of group C for further cases showing similar serological reactions to the foregoing, we find a rising titre for all three types of B. proteus used in case 20. In this case the titre for X19 is much higher and appears earlier than in the other cases, the same applies to X2 and a well-marked late rise in XK is seen. The case occurred at Meerut in October 1934. The patient was an Indian clerk who was employed in the office of a mule transport unit and who lived in the bazaar. Both these places were about two miles distant from the barracks for British troops where cases 18 and 19 occurred, and it can be stated that apart from general location and time of year, case 20 was epidemiologically quite distinct from these. Clinically there was no evidence of bite mark, the disease was comparatively mild, as is shown by the normal blood pressure record on the eigth day, the temperature was of the plateau type and fell by crisis, and the rash did not involve the face. In my opinion this case clinically

suggests endemic, murine or flea-borne typhus, and although the serological reactions are quite inconsistent with those recorded in connection with this disease where it occurs, with the exception of South Africa, they are consistent with the type of reaction recorded by Pijper and Dau in connection with the sporadic or mild typhus described by them.

Consideration of Case 20 leads up to Case 15, one which occurred in the same locality three weeks previously in a sowar of an Indian cavalry regiment, the barracks of which adjoined the lines of the unit where case 20 was employed. This patient presented a puzzling clinical picture to the medical officers who saw him, diagnosis of measles and enteric group were suggested at different times, and it was solely due to the carrying out of the Weil Felix reaction during convalescence that the nature of the disease was established. Although the febrile reaction was moderately severe, the disturbance of general health recorded was slight. This, in conjunction with the absence of the rash on the palms, soles and face, raises a suspicion of endemic, murine or flea-borne tuphus, but reference to the Weil Felix reaction results shows a highly significant titre of agglutination solely for type X2. X19 agglutinins were recorded in quite insignificant amount, and XK agglutinins were entirely absent. It is extremely difficult to find a qualitative reaction of this kind in the serological observations recorded in connection with endemic typhus. Similar reactions occur occasionally in fievre boutonneuse, and also in Rocky Mountain spotted fever. Both of these are tick-borne diseases.

Case 14 occurred near Jhansi in November and appeared to have been contracted during a march through jungle country. The patient was admitted to hospital on account of a pneumonic condition. Whether this was part of the typhus infection or not was doubtful. The typhus rash was observed for the first time on the tenth day after admission, and, as it was prominent before the sixth day in all the other cases of groups B and C, it would appear that a typhus-like disease became superimposed on a pneumonic infection contracted during the incubation period of the former. On the other hand pulmonary congestion occasionally complicates the non-epidemic forms of typhus fever, as has been noted in connection with fievre boutonneuse and in cases 17 and 19, and well marked development of agglutinins for B. proteus X19 and X2 were present on the thirteenth day of reckoning the time of onset of the typhus as that of the appearance of earliest symptoms necessitating admission to hospital. The symptoms during the three to four days prior to the appearance of the rash, and the course of the disease afterwards, are very similar to what is seen in the cases of group B, and the serological reactions appear to indicate a close affinity of this case to those of Group B.


The United Provinces of India
Places at which cases listed in Group "C" are underlined thus Meerut (4). The numbers in parenthesis are the number of cases which occurred.
Scale 1" = 96 mls or 1:6082560
Scale of Miles
100 80 60 40 20 0 100 200 300
NEPAL
BIHAR
To Calcutta
Benares
Allahabad
Lucknow
Jhansi (1)
Bareilly (2)
Meerut (4)
Delhi (1)
Agra
Dehra Dun
Chakrata
Naini Tal
Almora
Ranikhet
R. Gogra
Gogra River
R. GANGES
R. Kosi
24° N
28° N
80° E
N
S
E
W

Case 16, occurring at Delhi in February 1934, was not associated with any others, but it is noteworthy that the case described by Christian and Hepple, previously mentioned, occurred in the same area at the same time of the year in 1932. The fever in case 16 only lasted ten days, and agglutinins for X19 were well developed on the 8th day., Agglutinins for types X2 and XK did not develop in significant amount. The reaction recorded was as follows:

Day of Disease.	X19.	X2.	Xk.
4.	Nil.	Nil.	Nil.
8.	1/2500.	1/25.	Nil.
12.	1/5000.	1/50.	Nil.
17.	1/6000.	1/50.	1/25.

It is strongly suggestive of louse-borne or flea-borne typhus, as it appears to indicate main agglutinins for type X19, but for reasons to be discussed later this cannot be inferred with confidence. Clinically the condition was milder than would be expected in the former, and there was no evidence of louse infestation nor of associated cases. In flea-borne typhus, as described by French and American writers, the rash rarely involves the face, and the temperature, rigors and pulse rate in the early stages of the disease in this patient are suggestive of a rather more severe type of reaction than is recorded in descriptions of flea-typhus. These, however, are minor considerations when compared with the evidence provided by the serological reactions, and this case is difficult to classify with any others in the series. The case which resembles it most closely is case 12 of group B.

The case reported by Christian and Hepple, which occurred in the same area two years previously, showed a clinical condition identical with fievre boutonneuse, including tache noire and associated bubo. Guinea pig inoculation with the blood yielded a result which appears from details quoted to have been similar to one of the modes of reaction in this experimental animal to the virus of this disease. The serological reactions were indefinite, but were not carried out with the emulsions introduced by Bridges in 1933, and are therefore not comparable with those of case 16 in this series.

Summary of Analysis of the Cases.

1. Evidence is adduced to show that the cases of Group A, occurring in the Kumaon lake area in August, i.e. during the season of heavy rainfall, belong to the scrub typhus-tsutsugamushi fever group, and two other cases have been classified with them, one on clinical, the other on serological grounds.

2. The cases of Group B, which were contracted in the Kumaon hills prior to the onset of the rainy season, show close epidemiological, clinical and serological affinities to fievre boutonneuse of the Mediterranean littoral. Significant agglutinins for B. proteus XK are not shown in the Weil Felix reaction in these cases.

3. Group C contains certain cases, particularly cases No 17, 18 and 19 showing a somewhat more prolonged febrile reaction, and quantitative and qualitative differences in the serological reactions when compared with Group B. The titres for B. proteus X19 and X2 are not so high, appear to develop rather later in the course of the disease, and are inconstant for the latter. Significant XK agglutinins are found in association with them.

Re-classification of Groups B and C.

Some of the cases in group C appear to be clinically and serologically more closely related to the cases of group B than to cases No 17, 18 and 19, which constitute the most uniform type found in group C. For the purpose of the following discussion on the nature of the viruses concerned, a re-classification of these two groups on a serological basis is suggested as follows:-

Group B.

Cases showing agglutination with B. proteus types X19 and X2, either in relatively equal amount or solely or predominantly for one or the other, and showing no significant agglutinins for type XK.

In all these cases which were adequately tested agglutinins were present in considerable amount about the time when defervescence of the fever was complete.

Group C.

Cases showing the quantitative and qualitative differences in serological reaction described in paragraph 3 of the foregoing summary.

This classification relegates cases 14, 15 and 16, to Group B, which case 14 resembled clinically. In places in different categories cases 15 and 20, the two Indian cases which had a good deal in common epidemiologically. Case 20, however, remains an anomaly in Group C owing to the high titres of agglutination recorded comparatively early in the course of the disease.

7. Nature of the Viruses Concerned in the Cases.

The serological reactions of cases 4 and 7

show clearly that the virus concerned in these was that of the scrub typhus-tsutsugamushi fever disease group, and clinical and epidemiological considerations point to the other cases of the group having been of a similar nature. In the present state of our knowledge of the non-louse-borne varieties of typhus fever this group can be regarded as a distinct entity. To what extent, however, the serological reactions of groups B and C, as reclassified, indicate any relationship with other known diseases of the typhus group, or even indicate any essential difference in the two groups themselves, is difficult to determine.

It has been observed that the serological reactions of Group B correspond closely to the results observed by Durand in fievre boutonneuse, and those of group C to those observed in Rocky Mountain spotted fever. Felix (46) had advanced the view that the results recorded in these conditions can be explained by the differentiation of what he terms "main" and "group" agglutinins, the characters of which he summarises as follows:

Main agglutinins.	Group Agglutinins.
Reaction almost invariably positive.	Reaction irregular often negative,
Titres high.	Titres low.
Appearance of agglutination early.	Appearance late.

In the same work he shows that it is not always possible to determine from agglutination reactions whether an antigenic factor can be classed as "main" or "group", and that analysis of antigenic structure requires experimental production of agglutinins in rabbits, and cross immunity tests in guinea pigs. In case 16, however, the agglutination results, as previously indicated, tend to show that type X19 is a main antigenic factor, but the possibility of this case having been one of endemic, murine or flea-borne typhus has been considered. To a somewhat lesser extent the serological reactions of cases 11 and 14, showing well marked development of agglutinins for types X19 and X2 before defervescence of the fever was complete, suggest that one of these was a main antigenic factor. As the agglutinins for the two types were present in relatively equal amount, however, it seems safer to assume that they were group agglutinins. All that can be inferred from the serological reactions of group B, therefore, is that they are due to strains of virus possessing predominant group antigens of type X19 or X2 or both.

Felix has also shown that group agglutinins are not invariably formed in infections by a virus containing corresponding group antigens. In an analysis of the antigenic structure of B. proteus XL, a strain isolated by Dr. Lima from a case of non-epidemic typhus in San Paulo, he showed that its main antigen corresponds to type X19 and that it contained group antigens corresponding to type X2 in greater quantity than the old

world strain of X19, and also group antigens of type XK. Agglutinins for types X2 and XK, however, were not constantly present in the sera of patients suffering from the disease, nor in the sera of rabbits immunised with strain XL. Commenting on Durand's observations on the serological reactions in fievre boutonneuse, Felix states "It is true that antibodies are not invariably formed against all the antigenic compounds of an infecting organism or of a vaccine used for immunisation, and this is especially the case with minor antigenic factors such as group antigens". This raises the questionwhether there is any essential difference in typebetween the cases of groups B and C as reclassified. The resemblances shown in the serological reactions in group B to those reported by Durand in fievre boutonneuse has been frequently noted. A wider survey of this disease, however, shows that the absence of XK agglutinins reported by this observer is not invariable. Cavaletti (47) and Picori (48), testing the sera of cases of "febbre errutiva", the name applied to the disease in Italy, found significant agglutinins for type X19 in human cases of the disease acquired naturally, but Reitano and Bonicelli (49) found agglutinins for all three types in patients experimentally infected from ticks. The extent, therefore, to which cases of Groups B and C can be attributed to different types of virus or to different strains of the same virus is doubtful. Further, in the absence of cross immunity tests no statement as to identity of the virus in either group with the virus of any other typhus disease can be made.

8. Evidence of Vectors Concerned.

In group A the established identity of the cases with the scrub typhus-tsutsugamushi fever disease group permits of an assumption that a vector was a larval mite. Although the causal relationship of mites with scrub typhus has never been proven, cross immunity between it and the virus of tsutsugamushi disease has been shown and the main antigenic factor of the virus is identical in the two conditions. The absence of skin lesions in cases of scrub typhus raises doubts as to whether some other vector may not transmit the virus without altering its antigenic structure. The bulk of the cases in group A, however, showed the skin lesions and associated buboes characteristic of tsutsugamushi disease, in which a larval mite vector is the established mode of transmission. Moreover the epidemiological conditions present, namely heavy rainfall and a waterlogged condition of the ground surface, which appear for some reason to result in larval mites leaving their normal rodent hosts, lends additional support to the assumption.

In Group B there was a history of tick bite five days prior to the onset of the disease in case 10, and evidence of a primary lesion on admission of the case to hospital. Most of the other cases were

epidemiologically, clinically and serologically similar to this case, and it may be assumed that infection occurred in a similar way. Megaw, in advancing his views on the tick as the most probable vector of such cases in India, has pointed out that a tick bite is painless, and that the smooth human skin and the friction of clothes thereon leads to early dislodgment of the tick when it infests the human body. These circumstances, and the fact that the average individual does not look for ticks, tend to lower the proportion of cases in which a history of tick infestation can be obtained. Local sores and ulcers are rare in the case of a bite by a fully developed male tick in many parts of the world including India, although such lesions are common after infestation with larval or nymph forms. This may explain the presence of a primary lesion in case 10, and its absence in the others. In fievre boutonneuse, in which Rhipcephalus sanguineus has been proven to be the vector concerned, a history of contact with dogs is almost invariable, but a definite history of tick bite appears to be absent in the majority of cases. The epidemiological, clinical and serological resemblances shown in this group to fièvre boutonneuse lends some support to an assumption of a common vector, Felix (50) has drawn attention to the special importance of type X2 agglutinins in tick borne varieties of typhus fever, although whether they are a major or a minor antigenic factor is not yet determined. These figure prominently in 2/3 of the cases in this group which were adequately tested. On the other hand type X2 reacted equally well as type X19 in the sporadic or mild form of typhus of South Africa described by Pijper and Dau, the transmission of which they ascribe to a rat flea. This latter observation, however, is so far unique in the realm of flea-borne typhus fevers, and we may say that an assumption of a tick transmitting vector concerned in the cases of group B finds considerable support in the following:

(1) evidence of tick infestation in one case to which others were epidemiologically, clinically and serologically similar,

(2) the prominence of X2 agglutinins in the serological records of 2/3 of the cases which were adequately tested,

(3) the close similarity shown by the cases of this group to fievre boutonneuse, in which a tick vector is established.

In group C the only clinical evidence suggestive of tick bite was a history of pain in the groin at the onset of the disease in one case, and a papular lesion of doubtful nature and not associated with local glandular swelling in another case. Two of the cases appear to have been contracted in the immediate vicinity of barracks; one gave a history of exposure to conditions

of camp life. In the earlier records of sporadic forms of typhus fever occurring in India, a history of exposure to conditions prevailing in the wilds was often stressed as indicating a tick vector and wild rodent reservoir of the virus. The more recent reports of series of cases, however, such as t ose of Blewitt and Macnamara previously mentioned, show that those living in such communities as barracks are by no means immune. Blewitt was able to adduce fairly strong evidence of a tick vector in the cases he examined, and the serological results reported are very similar to those found in this group. These moreover, closely resemble those found in Rocky Mountain spotted fever and tick bite fever of South Africa, both of which are tick-borne diseases. Reference to a table drawn up by Felix (50) and showing the present state of our knowledge with regard to the typhus group of fevers, shows a subgroup of undetermined type in which a group agglutinin response in the Weil Felix reaction involving types X19, X2 and XK is found. The diseases in which the vector is known and which are represented in this type are all tick-bornw, with the exception of epidemic and endemic typhus of South Africa. This constitutes the main evidence warranting an assumption that a tick was the vector concerned in the cases of group C.

Although a knowledge of the vector concerned in the transmission of the typhus group of diseases is of great importance from a hygienic standpoint, it does not necessarily add to our knowledge of the antigenic structure of the viruses concerned, which is the only satisfactory basis of scientific classification. The work of Pijper and Dau, previously referred to, shows that the viruses of the South African typhus fevers are closely related if not identical in antigenic structure. They are, however, transmitted by three different vectors. This shows that the typhus group of fevers cannot be classified on a vector basis, and therefore the fact that the viruses of groups B and C were probably both transmitted by ticks does not indicate that they are the same. Further, the possibility that the same virus may have been transmitted from the same reservoir by a different vector, e. g. the flea, cannot be discounted in the present state of our knowledge of the typhus group of fevers.

9. CONCLUSIONS.

1. Case records of twenty cases of non-epidemic typhus fever occurring in the United Provinces, India, have been analysed.

2. Evidence has been adduced to show that six of these cases belong to the scrub typhus-tsutsugamushi disease group, and that four of these were cases of tsutsugamushi disease, a condition the occurrence of which in India has not been described previously. The

nature of the main antigen of the virus in these cases is of type XK, and the transmitting vector is assumed to be a larval mite.

These cases occurred during the season of heavy rainfall, i.e. from the middle of July to the end of September.

3. The remaining cases show two main types of serological reaction namely

(a) a well marked development of agglutinins for B. proteus types X19 and X2, either in fairly equal amount or solely or predominantly for the one or the other. Significant agglutinins for type XK are absent in these cases.

(b) a less marked agglutinin response, tending to occur later than that described under (a), and involving all three types X19, X2 and XK. In the case of X2, agglutinins are not constantly present.

The cases showing these reactions were contracted in ths hills during the dry summer season between April and July, and in the plains during the dry season commencing after the cessation of the rains in September for a period extending from then until March, All the cases contracted in a localised area in the hills and adequately tested serologically gave the type of reaction described under (a). Analysis of the cases occurring on the plains show both types of reaction.

4. The cases showing the reaction described under 3 (a) show epidemiological, clinical and serological affinities to fièvre boutonneuse of the Mediterranean littoral. The cases described under 3 (b) show clinically similar symptoms differing in degree only from those of group 3 (a) and approximating more closely to that described in connection with Rocky Mountain spotted fever. The serological reactions in the cases classified under 3 (b) are similar to those found in this disease.

5. Definite evidence of tick bite associated with infection is found in one case only of those described under (3), but the nature of the serological reactions and the resemblances shown to typhus fevers in which a tick vector is the established mode of transmission appear to indicate that both groups described under (3) are tick-borne.

6. The relationship of the viruses of the groups described under 3 (a) and 3 (b) to each other, and to the viruses of other diseases of the typhus group, to which they show epidemiological, clinical and serological affinities cannot be established on the serological and other evidence provided in the case records.

7. In one case classified under group 3 (a) the serological reactions appear to indicate that type X19 is a main antigenic factor, and the possibility of this case being of the nature of endemic, murine or flea-borne typhus has been considered.

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APPENDIX.

CASE RECORDS.

NOTE. Temperature charts relating to cases accompany the text of each case. None of the cases were complicated by the presence of malarial parasites in the blood, and in all of them clinical records show that blood examinations were carried out on more than one occasion after admission, and in most cases on the occurence of rigors at irregular intervals in which these were a feature of the clinical condition. Case records also show that routine chemical and microscopical examinations of the urine were carried out at least once shortly after admission, and in most cases at other times later. The only abnormality noted was the presence of albuminuria in cases 2 and 4 as stated in the narratives of these.

Case 1. Lieut. D. aged 24. 3rd./8th. Punjab Regt.

Admitted to hospital on 11/9/32 complaining of headache, shivering and pains in the joints. Duration of complaint, 5 days.

Patient had been shooting in the region of Sat Tal near Bhowali in the Kumaon hills since the middle of August. He gave no history of having noticed ticks on his body, but stated he had been tormented by biting insects in the jungle, and in machans. Two papular sores about 3 mm. in diameter with punched-out ulcers in the centre were present on the right leg below the knee. In addition there were numerous septic abrasions resulting from bites on both knees and wrists.

A local practitioner at Bhowali, called in to see the patient when he fell ill, had reported the presence of a rash (further particulars not obtained) on 8/9/32.

On patient's admission to hospital the face was very flushed and the eyes suffused. The tongue was heavily furred over its entire upper surface with a shaggy, brownish white fur. Enlarged tender lymph glands about the size of a hazel nut were present in the right femoral region. This inflammation subsided in a few days after admission. In addition, the lymph glands in the posterior triangles of the neck, epitrochlear and left axillary regions showed slight, but painless, enlargement. The effects of the toxaemia appeared to be chiefly on the muscle of the heart and of the bowel. On the 10th day the position of the apex beat, previously in normal position, was noted to be $4\frac{1}{4}$" from the mid-sternal line. Pulsation was diffuse, and there was also pulsation visible over the 4th interspace above and internal to the apical pulsation. The first sound in the mitral

Case 1. (continued)
area was short and soft, and the blood pressure 90/60 mm. Hg. The following day there was marked cyanosis and dyspnoea, which steadily increased. Muttering delirium was first reported on the 10th day and increased in severity, but intervals of fairly clear consciousness, during which the patient could talk rationally, were present up to within a few hours of death.

The rash became practically confluent on the trunk by the 10th day, when it was still a bright rosy red. On the arms it commenced to show signs of fading before this, and a bright coppery hue was brought out on pressure. The eruption showed no petechiae.

WHITE BLOOD CELL COUNT. Day of disease, 6th. 14,600 per c. mm. Polys. 69%. Lymphs. 28%. Monos. 3%.

WEIL FELIX REACTION

Day of disease	OX19	OX Multesar (x)	OXK
6	nil	nil	nil
8	nil	1:18	1:60

WIDAL REACTION (last inoculation within the previous 18 months)
(Expressed in terms of Standard Agglutinin Units)

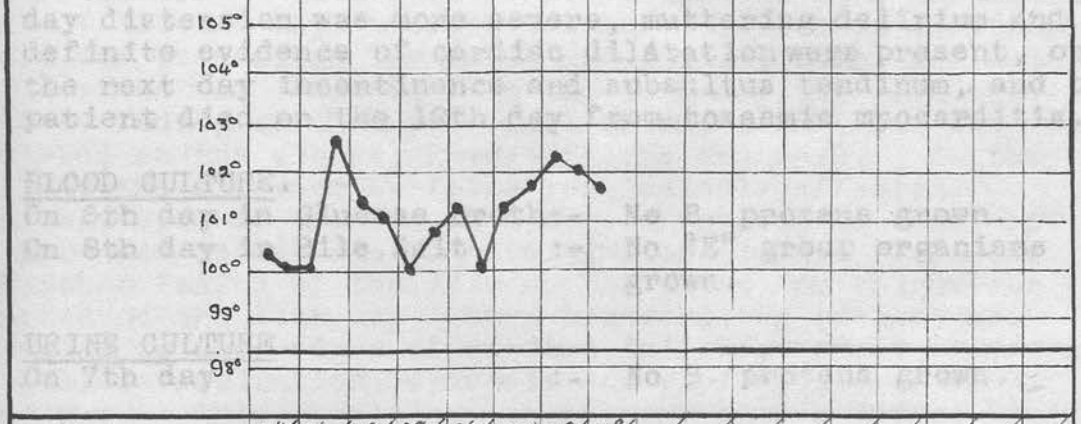
Day of disease	T	A	B	TO
8	7	16	55	1:17

There was complaint of sore throat, and marked faucial and pharyngeal congestion. The spleen was easily palpable on inspiration, and tender. There was a profuse bright red, discrete, macular rash present on the chest, abdomen, back and arms, and to a lesser extent on the face and extensor aspects of the forearms. On these sites, however, it became well marked the following day, when it was also noted to be present, but to a lesser extent, on the extensor surfaces of the legs. No involvement of the palms nor of the soles was ever observed.

The course of the fever is shown on the chart. The splenic enlargement subsided and could not be detected after the 9th day of the disease. Other clinical features were drenching sweats throughout, difficulty in swallowing,

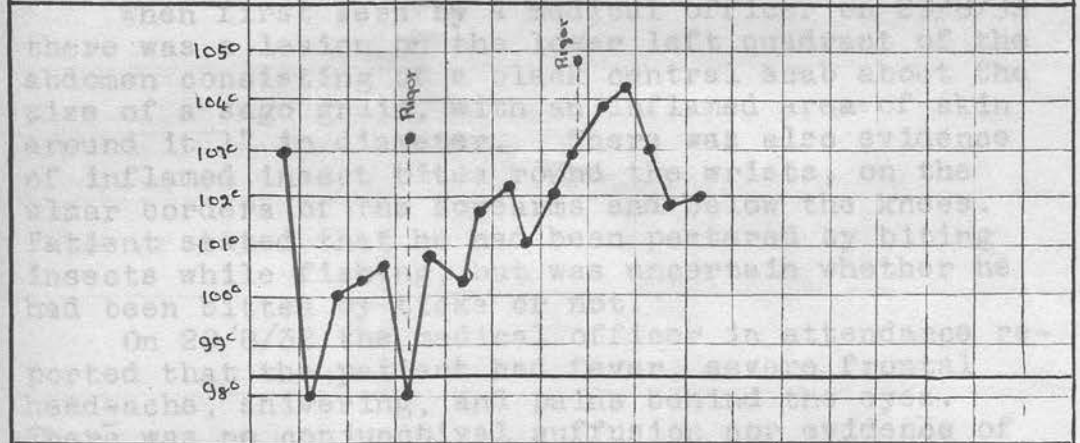
Case 1.

Dates of observation	11	12	13	14	15	16	17	18
Day of Disease	5	6	7	8	9	10	11	12
Pulse	104/96	86/84	88/96	88/84	96/104	120/120	128/136	148
Respirations					32/36	36/36	48/48	48
Motions	•/2	•/2	1/4	8/2	•/1	2/1	1/1	



Case 2.

Dates of observation	30	31	1	2	3	4	5	6	7	8
Day of Disease	3	4	5	6	7	8	9	10	11	12
Pulse.	80	40/64	68/44	62/68	80/88	90/90	42/42	88/92	100/120	
Respirations		22	24/24	20/22	20/24	24/22	22/44	40/40	60/60	
Motions		1	2/2	1/1	•/1	•/2	3/3	12/2	2	



Case 1 (continued).
a drowsy looking, bloated face, with heavy-lidded congested eyes and swollen lips. Severe diarrhoea associated with the presence of vegetative forms of Giardia intestinalis in the stools was present on the 7th and 8th days, and there was vomiting on the 9th, when some degree of abdominal distension was also noted. The following day distension was more severe, muttering delirium and definite evidence of cardiac dilatation were present, on the next day incontinence and subsultus tendinum, and the patient died on the 12th day from toxaemic myocarditis.

BLOOD CULTURE.
On 6th day in Glucase Broth:- No B. proteus grown.
On 8th day in Bile Salt :- No "E" group organisms grown.

URINE CULTURE.
On 7th day :- No B. proteus grown.

Case 2. Capt. H., aged 33. 12th Fd. Bgde. R.A.

History of infection contracted in the same locality of the Kumaon hills as Case 1, namely at Naukatchiya Tal, where he stayed on a fishing holiday from 17-27/8/32. Symptoms developed on 28/8/32 after his return to Meerut.

Patient stated he was a subject of haemophilia, this having been discovered in the course of two previous operations, one for haemorrhoids and the other for appendicitis.

When first seen by a medical officer on 29/8/32 there was a lesion on the lower left quadrant of the abdomen consisting of a black central scab about the size of a sago grain, with an inflamed area of skin around it 1" in diameter. There was also evidence of inflamed insect bites round the wrists, on the ulnar borders of the forearms and below the knees. Patient stated that he had been pestered by biting insects while fishing, but was uncertain whether he had been bitten by ticks or not.

On 29/8/32 the medical officer in attendance reported that the patient had fever, severe frontal headache, shivering, and pains behind the eyes. There was no conjunctival suffusion nor evidence of pharyngitis. There were enlarged, painful lymph glands rather larger than a hazel nut in the left inguinal region.

The patient was admitted to hospital the following day suffering as described above. The face was congested, and the tongue was coated with a brown fur, but was clean at the edges and tip. Beyond notes regarding restlessness at night and conjunctival suffusion on 3/9/32, the case records merely show the above symptons severe and continued up to that date.

Case 2 (continued).
Albuminuria was present. On 4/9/32, the 8th day of the disease, a rosy red macular rash, fading on pressure, was noted on the abdomen and chest. The macules varied in size from small spots to irregular blotches about 1 cm. in diameter. Conjunctival suffusion was more marked. The following day the rash was more profuse on the trunk, and was present on the face, arms, legs, palms and soles. Diarrhoea was present. On the 10th day the rash appeared to be fading on the upper part of the trunk, but was well marked on the elbows, knees, thighs and back. On the limbs the extensor surfaces were chiefly affected. Drowsiness was present to a degree verging on coma, and there was severe diarrhoea with incontinence of faeces. Further fading of the rash on the chest and thighs was noted on the 11th day, when, however, the patient commenced to show signs of cardiac failure, namely dyspnoea, shallow respiration, cyanosis and rapid pulse of small volume. This condition became more severe and he became completely comatose and died the following day.

BLOOD
WHITE CELL COUNT. Day of disease, 6th. 6,400 per c.mm.
Polys. 56%. Lymphs. 33%. Monos. 11%.

WEIL FELIX REACTION.

Day of disease	OX19	OX Multesar	OXK
11	1:125	nil	1:35

WIDAL REACTION. (Date of last inoculation within the previous 18 months).
Expressed in terms of Standard Agglutinin Units.

Day of Disease	T	A	B	TO
7	7	8	12	nil

BLOOD CULTURE.
On 7th day in Bile Salt)
On 9th day in Bile Salt) No "E" group organisms grown.

URINE CULTURE.
On 8th day :- No Enteric group found.
On 10th day :- No B. proteus found.

Captain H. (case 2) was accompanied while on leave fishing by Major M. (case 3).

Case 3. Major M., aged 45. R.H.A.

This patient ~~was~~ returned to Meerut with Capt. H. whom he had accompanied for the period spent at Naukatchiya Tal. He was well up to 4/9/32. On this evening he complained of headache, general malaise, fever and shivering. The following evening he had a temperature of 101°, but on the morning of the 6th this was normal. He was admitted to hospital on 7/9/32, complaining of severe headache, nausea, and vomiting. The tongue showed a white fur, but was clean at the edges and tip. The face was flushed, and the conjunctivae suffused. The case notes state that he had no sore throat at this time. Nothing abnormal was noted in the examination of the chest, abdomen and urine. On the left leg there was a papular sore, with a clearly punched-out crater, the ulcerated surface being 1-2 mm. in diameter. One left femoral gland was enlarged and tender. On 8/9/32 two rosy red papules were found on the abdomen, and conjunctival suffusion was more marked. The following day a scanty rosy maculo-papular rash was present on the face, neck, abdomen, back and arms. Patient now complained of sore throat in addition to severe headache and restlessness at night. On 10/9/32, i.e. the 7th day of disease, the rash was noted on the extensor aspects of the arms and legs, and on the palms. In addition there was a fresh outcrop on the chest and abdomen. Headaches were now rather less severe. Vomiting occurred five times in the course of the next three days, during which time further eruptions of rosy red maculo-papules appeared on the trunk and arms, and petechiae were noted in the original outcrop. On 12/9/32 the rash appeared more profuse still on the trunk and forehead, but showed signs of fading on the forearms. The patient vomited again twice on this date. The following day showed marked abatement of the symptoms. The entire rash was definitely fading, and profuse sweating occurred. Four days later the rash had almost entirely disappeared, but it left a brown staining which was quite visible two weeks later.

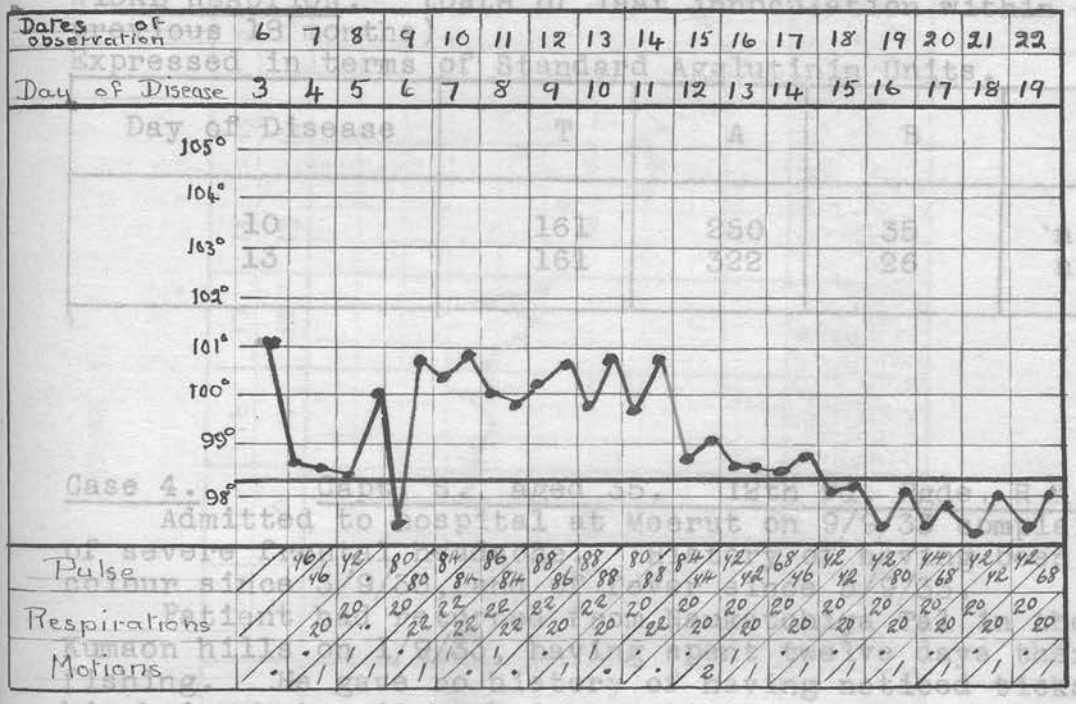
Convalesence was rapid, and the patient recovered normal capacity for work two weeks after defervescence of the fever, although a physical examination of the heart showed a soft systolic mitral bruit not observed on admission.

WHITE BLOOD CELL COUNT. Day of disease, 8th. 4,400 per c.mm. Polys. 68%. Lymphs. 25%. Monos. 5%. Eosins. 1%. Basiphils 1%.

Case 3 (continued).
WEIL FELIX REACTION.

Day of disease	OX19	OX Multesar(x)	OXK
4	nil	nil	nil
10	1:17	1:85	1:85
38	1:125	1:150	1:300

Case 3.



Case 3 (continued).
WEIL FELIX REACTION.

Day of disease	OX19	OX Multesar(x)	OXK
4	nil	nil	nil
10	1:17	1:85	1:85
38	1:125	1:150	1:300

WIDAL REACTION. (Date of last innoculation within the previous 18 months).
Expressed in terms of Standard Agglutinin Units.

Day of Disease	T	A	B	TO
10	161	250	35	nil
13	161	322	26	nil

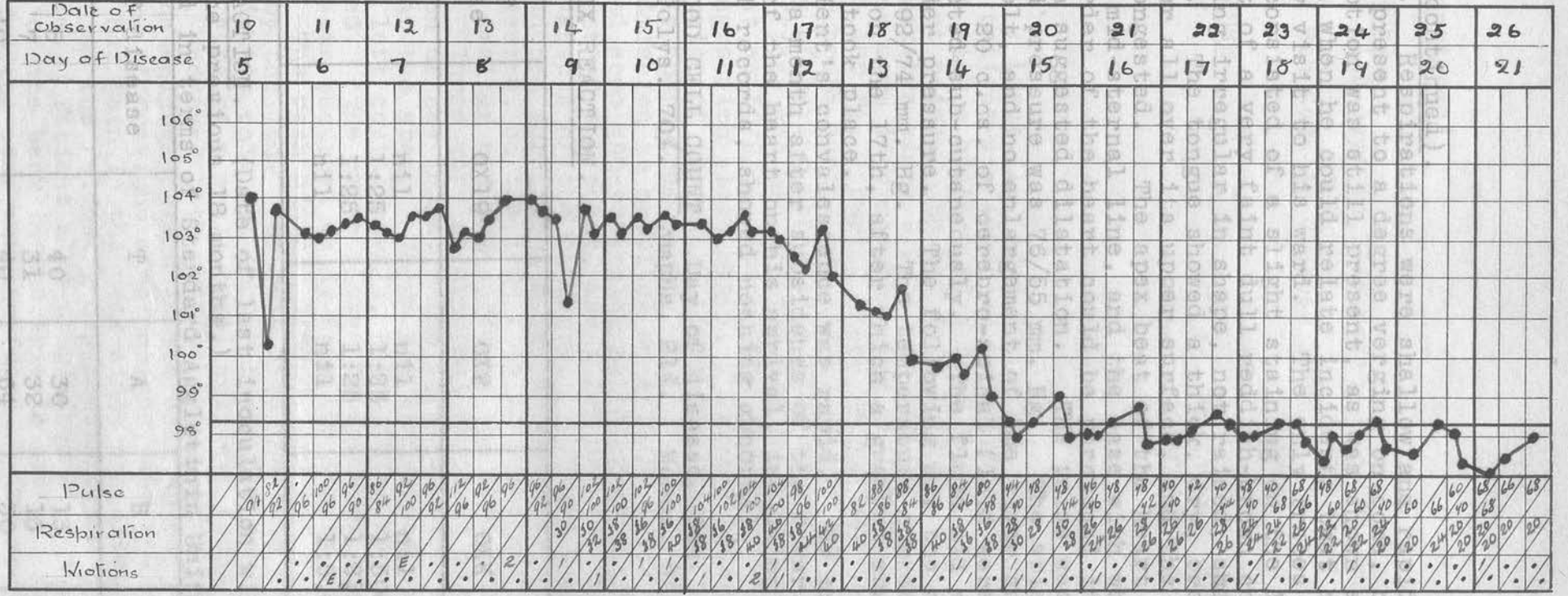
Case 4. Capt. S., aged 35. 12th Fd. Bgde. R.A.

Admitted to hospital at Meerut on 9/9/33 complaining of severe frontal headache. History of having been off colour since 3/9/33, and of fever since 5/9/33.

Patient had returned from Naukatchiya Tal in the Kumaon hills on 1/9/33, having spent twelve days there fishing. He gave no history of having noticed ticks on his body, but said hevhad been bitten by leeches and various insects. When first examined there was a slightly raised red sore, about 6 mm. in diameter, and with a necrotic centre, on the left leg.

On admission the patient showed a very flushed face with suffused eyes. The tongue was heavily coated with a thick brown fur. An enlarged tender lymph gland abouth the size of a large hazel nut was present in the left femoral region. On 10/9/33 a few rosy red macular spots were observed on the chest, arms and abdomen. The following day these had faded slightly, but a scanty fresh outcrop was seen in the same situations. The spleen was palpable and tender, and there was marked apathy and drowsiness. The rash was more profuse on the 12th, and on that day urine examination showed a trace of albumin. The rash was still apparent the next day, and a systolic murmur heard over the mitral area was recorded in the case notes of that date. I examined the patient two days later, i.e. on 15/9/33, when he presented a very severe toxic state. He was flushed, with heavy-lidded, congested eyes, and slightly

Case 4.


Date of Observation
Day of Disease
10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
106°
105°
104°
103°
102°
101°
100°
99°
98°
Pulse
Respiration
Motions

Case 4 (continued).

cyanosed. Respirations were shallow and rapid. Drowsiness was present to a degree verging on coma, but function of perception was still present, as was shown after his recovery, when he could relate incidents that had happened during my visit to his ward. The only traces of a rash present consisted of a slight staining on the left side of the chest of a very faint dull reddish-brown colour, the areas being irregular in shape, not raised, and 4-6 mm. in diameter. The tongue showed a thick, dry, brownish, shaggy fur all over its upper surface, and the throat was deeply congested. The apex beat of the heart was 4½" from the mid-sternal line, and the ease with which the right border of the heart could be percussed in its normal situation suggested dilatation. The pulse was dicrotic. The blood pressure was 76/55 mm. Hg. The spleen could not be felt, and no enlargement of the liver could be detected. 20 c.cs. of cerebro-spinal fluid were withdrawn and injected sub-cutaneously. The fluid did not appear to be under pressure. The following day the blood pressure was 92/74 mm. Hg. The temperature commenced to fall by lysis on the 17th, after which a gradual abatement of symptons took place.

Patient's convalescence was rapid. He proceeded to the U.K. a month after subsidence of the fever, and examination of the heart on his arrival, including electrographical records, showed nothing abnormal.

WHITE BLOOD CELL COUNT. Day of disease, 6th. 8,400 per c.mm. Polys. 70%. Lymphs. 21%. Monos. 8%. Eosins. 1%.

WEIL FELIX REACTION.

Day of disease	OX19	OX2	OXK
5	nil	nil	nil
10	1:25	1:25	1:500
14	1:25	1:25	1:2500
18	nil	nil	1:5,000

WIDAL REACTION. (Date of last inoculation with T.A.B. within the previous 18 months.)
Expressed in terms of Standard Agglutinin Units.

Day of disease	T	A	B	TO
5	40	30	13	nil
7	31	32	13	nil
10	40	64	30	1:50

Case 4 (continued).

BLOOD CULTURE.
On 5th and 11th days in Bile Salt:- No "E" group organisms grown.
On 5th and 8th days in Glucose Broth:- No B. proteus grown.

URINE CULTURE.
On 7th day :- No Enteric group organisms grown.

Case 5. Lieut. L., aged 30. The Black Watch.

This patient was admitted to hospital at Chakatra on 4/10/34 with a history of 6 days' fever, headache and severe joint pains. He had left Kashmir on 7/9/34 and been in Chakatra since 9/9/34, except for two shooting expeditions down into neighbouring valleys at a height of about 5,400 ft. During these he had sat down for about four hours during the middle of the day. He gave no history of having observed a tick on his body. The medical officer who had treated him in his quarters stated that on 30/9/34, apart from sweats, a whitish furred tongue with clean edges, a flushed appearance with suffusion of the eyes, there was nothing abnormal objectively apart from fever.

On admission to hospital on 4/10/34 a few rosy red macules and some sub-cuticular mottling were observed on the front of the chest, and a few macules on the extensor aspects of the forearms. There was a small raised reddened sore about 8 mm. in diameter, with a necrotic centre, on the left side of the chest, and a number of smaller healing sores on the legs, the results of bites. There were no abnormal physical signs on examination of the lungs. The first sound of the heart was soft at the apex. There was tenderness on pressure under the left costal margin, but nothing abnormal could be palpated. The urine showed no abnormal constituents. Severe sweats occurred daily from the 4th to the 8th October. The rash did not extend, and had almost disappeared by the 7th. On this date the case notes show that a slightly enlarged tender posterior cevical gland, about the size of a small hazel nut, was found on the left side, and that both epitrochlear glands were palpable. The enlarged gland in the neck appears to have been missed at previous examinations, and the patient stated he had had pain in the neck since the onset of the disease. On the following day headache and joint pains were severe. Patient also complained of pains in the left side of the back in the splenic area. He was flushed, and the eyes were suffused. The tongue was heavily coated with a brownish-white fur, but was clean at the tip and adjacent edges. The throat was con-

Case 5 (continued).
gested. I saw him the following day when his condition was unaltered. He was very drowsy and exhausted, but answered all questions with precision. I could not detect any signs of cardiac enlargement, but the first sound at the apex was soft and short, and the blood pressure was low, 92/76 mm. Hg. The epitrochlear glands were still palpable, and the more grossly enlarged gland behind the left sternomastoid could still be felt enlarged, but it was not tender. The only evidence of rash on the trunk was the presence of very faint brownish stains, irregular in outline and about 5 mm. in diameter, on the left side of the chest. Nothing appeared to remain of the rash on the forearms, the extensor aspects of which were much discoloured by sunburn. It was considered that the severe toxaemia, flushed face, suffused eyes, congestion of the throat, appearance of the tongue, enlarged glands, the history of a rash, severe headache, joint pains and sweats enabled a diagnosis of typhus fever to be made with confidence. This, however, was not confirmed by serological examinations later.

Marked improvement took place in the patient's condition two days after the above examination. He sweated profusely on the 10th October. On this date joint pains were still present. The temperature fell by lysis and reached normal on 15/10/34. There was some evidence of bronchitis on 14/10/34, which persisted for three days. Low blood pressure persisted for ten days after the fever had disappeared, but otherwise convalescence was satisfactory.

WHITE BLOOD CELL COUNT. Day of disease, 7th. 4,800 per c.mm. Polys. 58%. Lymphs. 42%.
Day of disease 9th. 5,200 per c.mm. Differential count not recorded.

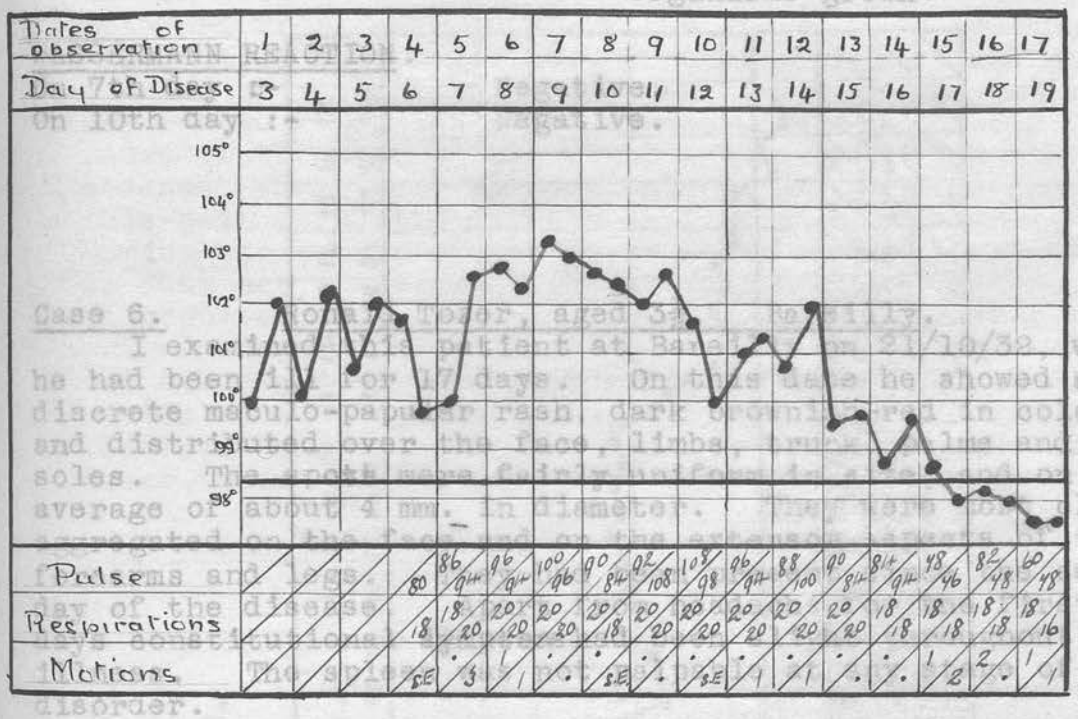
WEIL FELIX REACTION.

Day of Disease	OX19	OX2	OXK
12	1:17	nil	1:17
19	1:25	nil	nil
22	1:25	nil	nil
28	nil	nil	nil

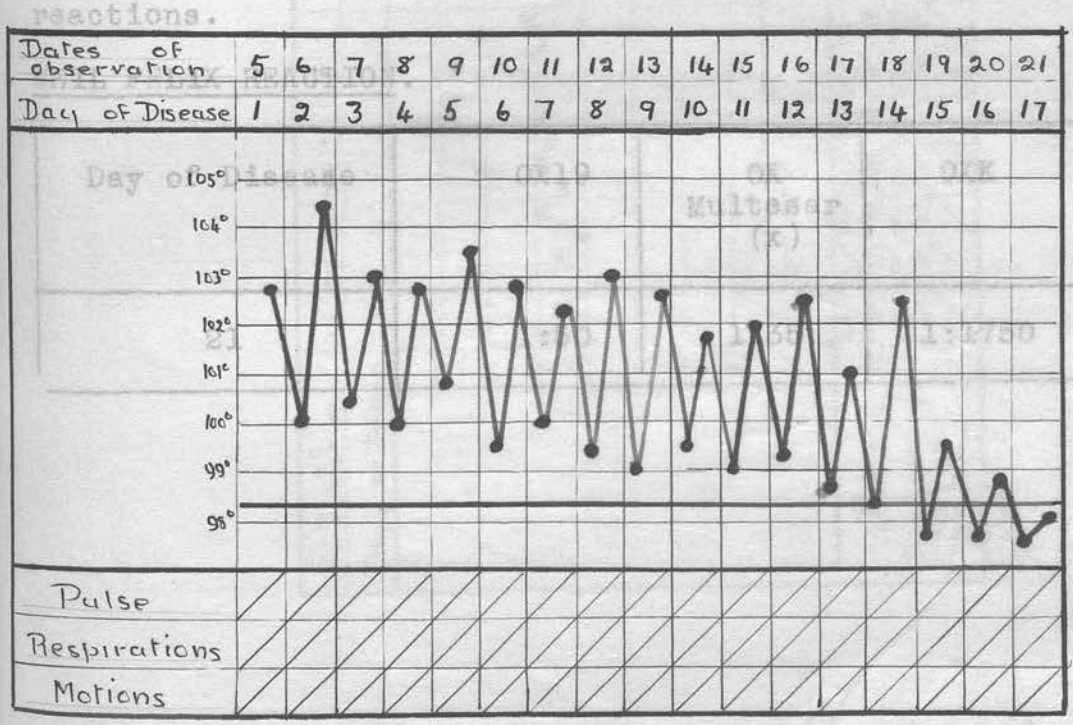
WIDAL REACTION (date of last inoculation with T.A.B. within the last 18 months).
Expressed in terms of Agglutinating Titre of Sera.

Day of Disease	T	A	B	TO
8	1:135	1:60	1:250	nil
12	1:175	1:60	1:300	nil

Case 5.


Dates of observation
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
Day of Disease
3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
105°
104°
103°
102°
101°
100°
99°
98°
Pulse
80 86/94 96/94 100/96 90/84 92/108 108/98 96/94 88/100 90/84 84/94 48/46 82/48 60/48
Respirations
18 18/20 20/20 20/20 20/18 20/20 20/20 20/20 20/20 20/20 18/18 18/18 18/18 18/16
Motions
S.E. 3 1 . . S.E. . S.E. 1 1 . . 1 2 2 . 1 1

Case 6.


Dates of observation
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Day of Disease
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
105°
104°
103°
102°
101°
100°
99°
98°
Pulse
Respirations
Motions

Case 5 (continued).

BLOOD CULTURE.
On 7th, 8th and 10th days in Bile Salt:- No "E" group organisms grown.

WASSERMANN REACTION.
On 7th day :- Negative.
On 10th day :- Negative.

Case 6. Ronald Tozer, aged 3½. Bareilly.

I examined this patient at Bareilly on 21/10/32, when he had been ill for 17 days. On this date he showed a discrete maculo-papular rash, dark brownish-red in colour, and distributed over the face, limbs, trunk, palms and soles. The spots were fairly uniform in size, and on an average of about 4 mm. in diameter. They were most clearly aggregated on the face and on the extensor aspects of the forearms and legs. They had been present since the second day of the disease. Apart from headache for the first few days constitutional symptoms had been slight throughout the illness. The spleen was not palpable at any stage of the disorder.

There was no history of a tick bite nor of any painful enlarged lymph glands. A similar case had occurred in an adjacent bungalow in October 1931.

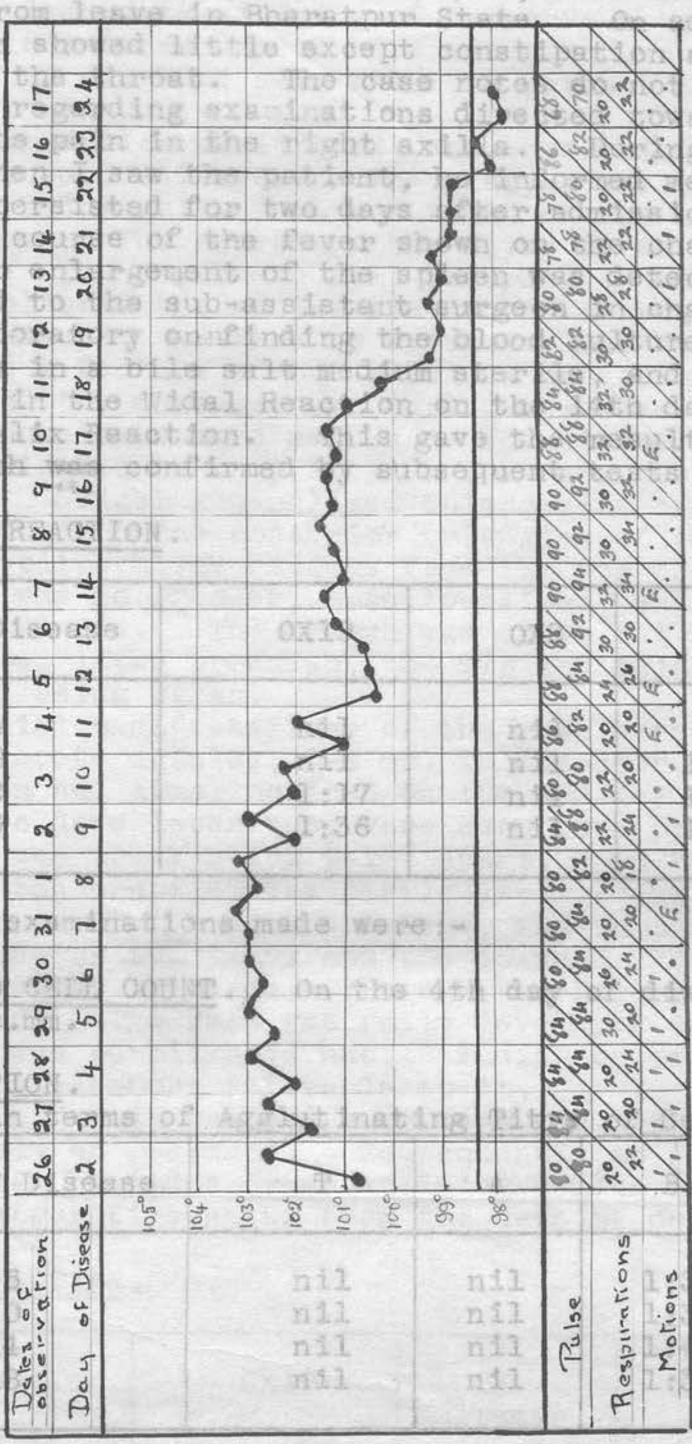
The case is quoted on account of the serological reactions.

WEIL FELIX REACTION.

Day of Disease	OX19	OX Multesar (x)	OXK
21	1:50	1:35	1:1750

Case 7. L/NK., R.S., aged 28.

This patient, an Indian sepoy, was admitted to the Indian Military Hospital, Bareilly, on 26/7/34, complaining of fever, weakness and pain in the right axilla. He had been in Bareilly since 16/7/34, when he had returned from leave in Bharatpur State. On admission examination showed little except constipation and congestion of the throat. The case notes do not contain any record regarding examinations directed towards the cause of the pain in the right axilla. During convalescence, when I saw the patient, he informed me that this pain persisted for two days after admission. During the course of the fever shown on the chart on the preceding page no rash nor enlargement of the spleen was detected. It occurred to the sub-assistant surgeon in charge of the brigade laboratory on finding the blood culture taken on the 6th day in a bile salt medium sterile, and no diagnostic use in the Widal Reaction on the [illegible] day, to test the Weil Felix Reaction. This gave the results shown below, which was confirmed by subsequent tests as shown.



WEIL FELIX REACTION.

	Day of Disease	OX19	OX2	OXK
Case 7.	14	nil	nil	1:5,500
	18	nil	nil	1:10,000
	22	1:17	nil	1:12,000
	26	1:36	nil	1: 7,000

Other examinations made were:-

WHITE BLOOD CELL COUNT. On the 4th day of disease:- 4,320 per c.mm.

WIDAL REACTION.
Expressed in terms of Agglutinating Titre of Sera.

Day of Disease	[illegible]	[illegible]	[illegible]	TO
[illegible]	nil	nil	1:[illegible]0	1:17
10	nil	nil	1:[illegible]0	1:20
14	nil	nil	1:[illegible]5	1:20
18	nil	nil	1:[illegible]0	nil

Case 7. L/NK., R.S., aged 28.

This patient, an Indian sepoy, was admitted to the Indian Military Hospital, Bareilly, on 26/7/34, complaining of fever, weakness and pain in the right axilla. He had been in Bareilly since 16/7/34, when he had returned from leave in Bharatpur State. On admission examination showed little except constipation and congestion of the throat. The case notes do not contain any record regarding examinations directed towards the cause of the pain in the right axilla. During convalescence, when I saw the patient, he informed me that this pain persisted for two days after admission. During the course of the fever shown on the chart ~~below~~ on the preceding page no rash nor enlargement of the spleen was detected. It occurred to the sub-assistant surgeon in charge of the brigade laboratory on finding the blood culture taken on the 6th day in a bile salt medium sterile, and no diagnostic use in the Widal Reaction on the 14th day, to test the Weil Felix Reaction. This gave the results shown below, which ~~was~~ were confirmed by subsequent tests as shown.

WEIL FELIX REACTION.

Day of Disease	OX19	OX2	OXK
14	nil	nil	:3,500
18	nil	nil	1:10,000
22	1:17	nil	1:12,000
26	1:36	nil	1: 7,000

Other examinations made were:-

WHITE BLOOD CELL COUNT. On the 4th day of disease:- 4,320 per c.mm.

WIDAL REACTION.

Expressed in terms of Agglutinating Titre of Sera.

Day of Disease	T	A	B	TO
6	nil	nil	1:30	1:17
10	nil	nil	1:30	1:20
14	nil	nil	1:45	1:20
18	nil	nil	1:30	nil

Case 8. Pte. J., aged 24. 1st Bn. The Ches. Regt.

This patient fell ill on 13/5/32, complaining of headache, pains in the joints and chest, nausea and loss of appetite. He had been stationed at Chaubattia for five weeks prior to the onset, and during this time had not left the immediate vicinity of barracks. No history of a tick or any other insect bite was given, nor was any evidence of the same seen when the patient came under observation.

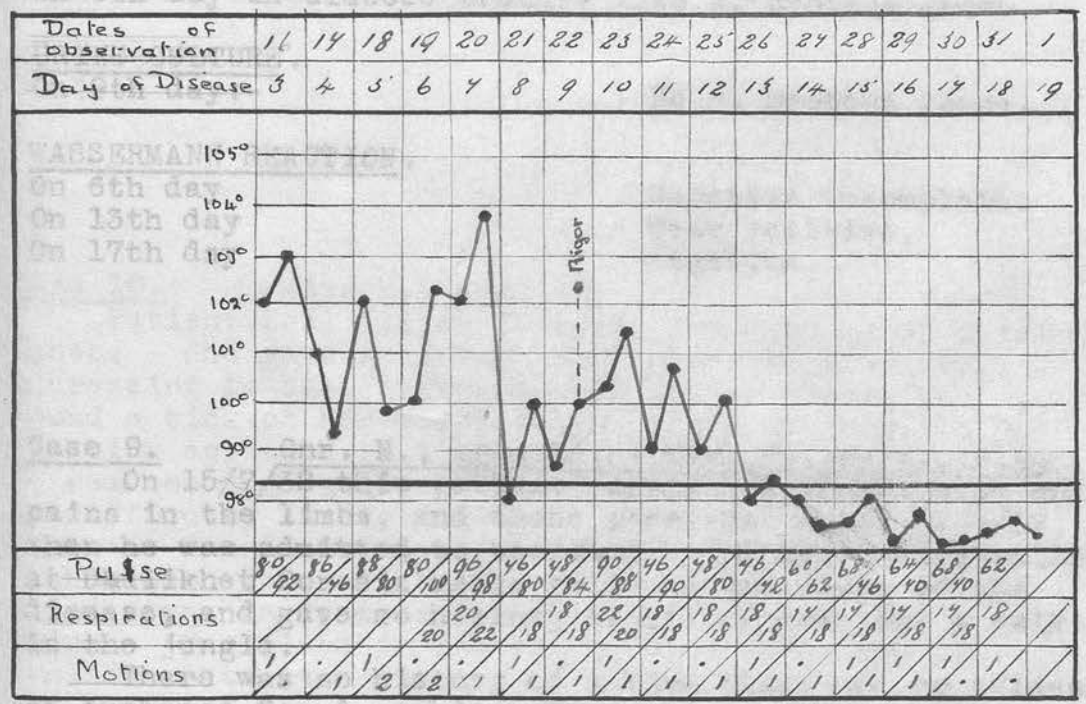
He reported sick on 16/5/32, and on examination was flushed, with suffused eyes. The pharynx was congested. A faint dull red macular rash was found on the abdomen, chest and arms. The course of the fever is seen on the chart on the following page. The prominent fall recorded on the night 20-21/5/32 followed the administration of aspirin for the relief of headache. Rigors at irregular intervals and sweating were a feature of the clinical condition up to the 9th day of the disease, and during the same period apathy and drowsiness were marked. The tip of the spleen was palpable on deep inspiration from the 6th to the 8th day. Slight generalised enlargement of lymph glands was noted in the posterior triangles of the neck, axillae and epitrochlear regions from the 6th to the 12th day. There was no grosser, more localised, enlargement of the lymph glands. The tongue was moist but furred, at first white, later brownish, the tip and adjacent lateral edges being clean.

The initial manifestations of the rash were a few dull red, discrete macules, 3-4 mm. in diameter, on the chest, abdomen and arms, noticed on the 3rd day of the disease. Two days later they were much more profuse, the spots on the trunk being ½-1½" apart. On the 5th and 6th days the eruption was particularly marked on the extensor aspects of the arms and legs, and on the 6th day it was observed on the palms and the soles. The face and scalp were not involved, although the former was deeply flushed. The rash was fully developed on the 7th day, when it was purplish in hue. Fading on pressure was complete. There was no discomfort referable to it. About the 10th day it assumed a coppery hue, and failed to fade completely on pressure. Subsequently it faded gradually, but left behind a brown staining, which was plainly visible for about five weeks from the date of onset.

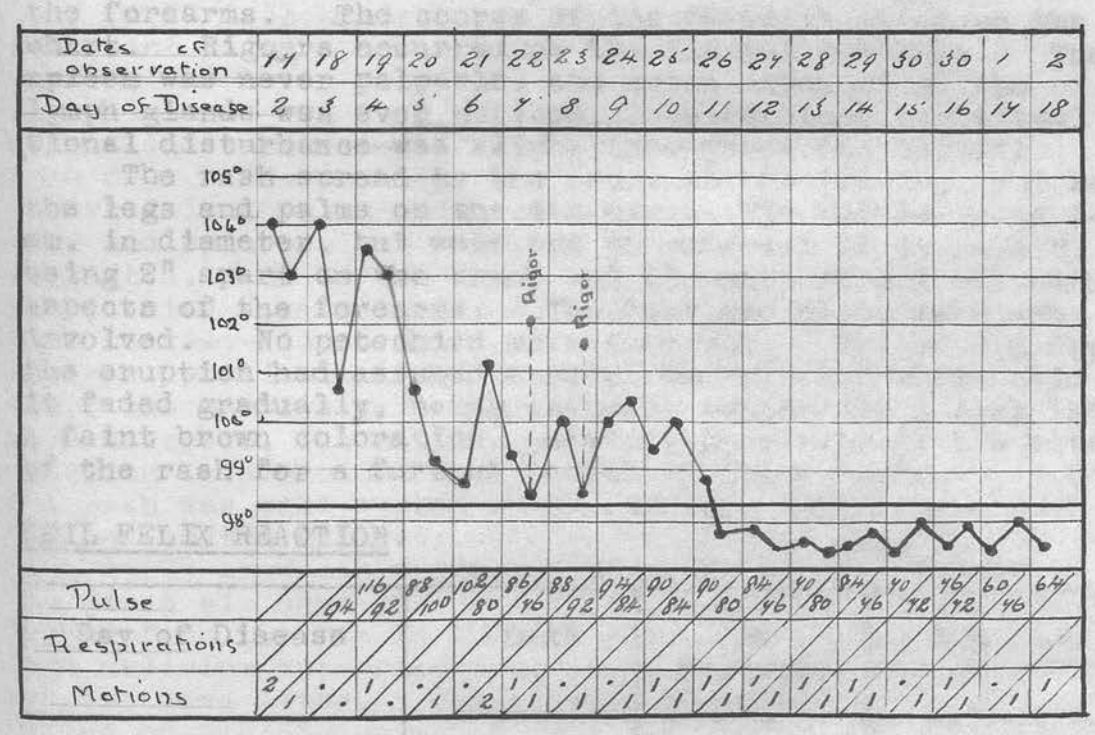
WEIL FELIX REACTION.

Day of Disease	OX19	OX Multesar	OXK
6	nil	nil	1:17
13	1:250	1:250	1:25
17	1:500	1:700	1:25
27	1:250	1:1000	1:25
45	1:175	1:500	1:25

Case 8.


Dates of observation
11 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 1
Day of Disease
3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
105°
104°
103°
102°
101°
100°
99°
98°
Rigor
Pulse
80/92 86/96 88/80 80/100 96/98 96/80 98/84 90/88 96/90 98/80 96/92 60/62 68/96 64/90 68/90 62/
Respirations
20 20/22 18/18 18/18 22/20 18/18 18/18 18/18 14/18 17/18 17/18 14/18 18/
Motions
1/. ./1 1/2 2/2 ./1 1/1 1/1 ./1 1/1 ./1 ./1 1/1 ./1 1/1 1/1 1/. 1/.

Case 9.


Dates of observation
17 18 19 20 21 22 23 24 25 26 27 28 29 30 30 1 2
Day of Disease
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
105°
104°
103°
102°
101°
100°
99°
98°
Rigor
Rigor
Pulse
94 116/92 88/100 102/80 96/96 88/92 94/84 90/84 90/80 84/96 90/80 84/96 90/92 96/92 60/96 64/
Respirations
Motions
2/1 ./. 1/. ./1 ./2 1/1 ./1 ./1 1/1 1/1 1/1 1/1 1/1 ./1 1/1 ./1 1/

Case 8 (Continued).

BLOOD CULTURE.
On 6th day in Glucose Broth:- No B. proteus grown.

URINE CULTURE.
On 9th day:- No B. proteus found.

WASSERMANN REACTION.

On 6th day	Negative incomplete.
On 13th day	Weak positive.
On 17th day	Negative.

Case 9. Gnr. N., aged 23. 49th Fd. Batt., R.A.

On 15/7/32 this patient complained of headache and pains in the limbs, and these peraisted until 17/7/32, when he was admitted to hospital. He had been stationed at Dhulikhet for six weeks prior to the onset of the disease, and gave no history of having gone for a walk in the jungle.

There was no history of a tick bite, and no evidence of such was found on his body on admission.

When first examined on 17/7/32 he was flushed, with suffused eyes. The tongue was slightly furred in the centre, and the throat was congested. On 18/7/32 a dull red macular rash was noted on the extensor aspects of the forearms. The course of the fever is shown on the chart. Rigours occurred on the 7th and 8th days. The spleem was never palpable, and no enlargement of the lymph glands was ever noticed. Generalised constitutional disturbance was slight throughout the illness.

The rash spread to the trunk on the 3rd day, and to the legs and palms on the 4th day. The macules were 4-6 mm. in diameter, but were not so numerous as in case 8, being 2" apart on the trunk and 1" apart on the extensor aspects of the forearms. The face and scalp were not involved. No petechiae were observed. By the 7th day the eruption had assumed a purplish hue, and after this it faded gradually, being scarcely noticeable a week later. A faint brown coloration, however, persisted at the site of the rash for a further period of three weeks.

WEIL FELIX REACTION.

Day of Disease	OX19	Ox Multesar	OXK
6	1:50	1:50	1:25
16	1:250	1:1000	1:35
36	1:50	1:500	1:17

Case 9 (Continued).

BLOOD CULTURE.
On 5th day in Glucose Broth:- No B. proteus grown.

URINE CULTURE.
On 14th day:- No B. proteus isolated.

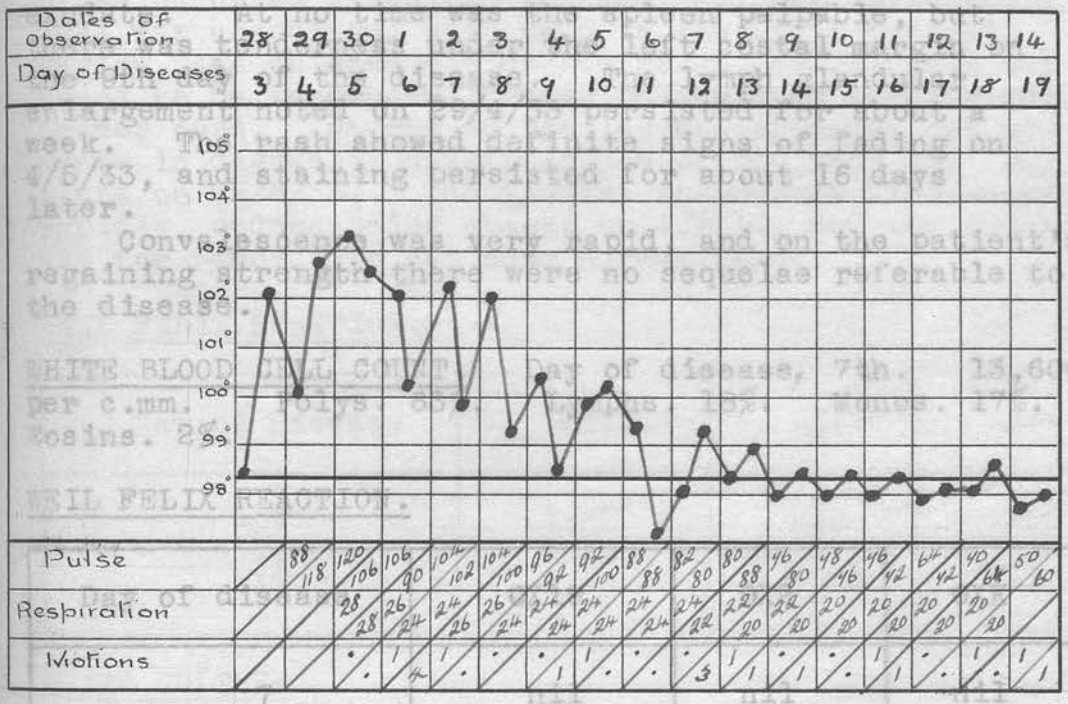
Case 10. Miss M., aged 49.

Patient fell ill on 25/4/33, complaining of chilliness. She gave a history that about 20/4/33, on undressing to bathe after a walk in the woods, she found a tick on her right thigh. Her description of the tick appeared to indicate that it was a larval form. It was not engorged with blood on removal, and she had no difficulty in dislodging it. On examination no mark was found on the site indicated as that from which it had been removed, but there was a small red papule about 2 mm. in diameter on the outer aspect of the right thigh. One gland in the right groin was slightly swollen, but not tender.

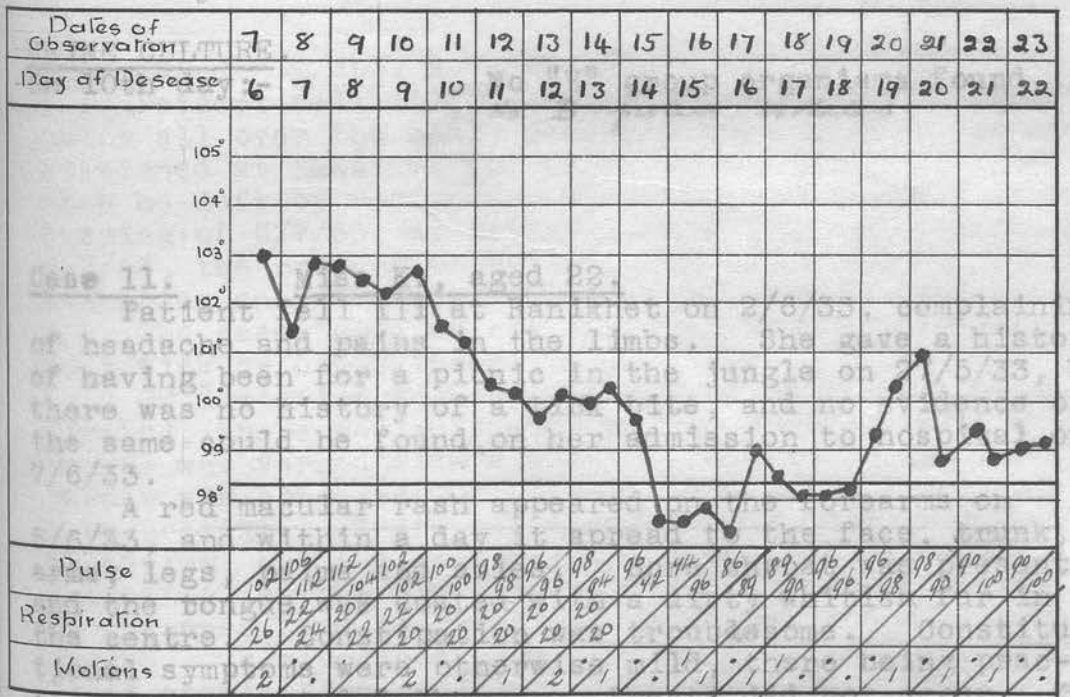
Patient was a breeder of fox terriers, and she was in the habit of giving much personal attention to their care. They were frequently in her quarters. She had lived at Ranikhet for one month prior to the onset of the illness.

On 27/4/33 headache, pains in the back of the neck and joint pains, particularly in the wrists, were very severe, and these persisted through the febrile stage of her illness. On 29/4/33 a macular rash appeared on the wrists and ankles and spread to her arms and thighs the same day. Examination then also showed a few slightly enlarged lymph glands in the posterior triangles of the neck and epitrochlear regions, and the throat was deeply congested. On 30/4/33 the rash spread to the trunk and face, which appeared bloated and congested. The eyes were heavily-lidded and suffused. The rash was very profuse, particularly on the arms near the shoulders, where the macules were confluent. On the trunk they were discrete, but there was considerable subcuticular mottling in addition. No petechial characters were seen. The rash was well marked on the palms. The tongue was dry and coated all over with a fur at first white, later of a dirty brownish white colour. Sweats occurred during the first six days of the disease, and mental torpor was marked from the 7th to the 9th days, during which period mild delirium was present at night. Drowsiness persisted for two days later. The abdomen became slightly distended on 3/5/33, on which date a systolic blood pressure of 104mm. Hg. was recorded. Two days previously this had been 114 mm. Hg. There was no nausea nor vomiting. Distressing features of the illness were severe headache, sore throat causing great pain on swallowing, joint pains

Case 10.



Case 11.



Case 10 (Continued).
and tenderness of the skin where the rash was marked. The throat showed marked congestion but no visible exudate. At no time was the spleen palpable, but there was tenderness under the left costal margin on the 9th day of the disease. The lymph glandular enlargement noted on 29/4/33 persisted for about a week. The rash showed definite signs of fading on 4/5/33, and staining persisted for about 16 days later.

Convalescence was very rapid, and on the patient's regaining strength there were no sequelae referable to the disease.

WHITE BLOOD CELL COUNT. Day of disease, 7th. 13,600 per c.mm. Polys. 63%. Lymphs. 18%. Monos. 17%. Eosins. 2%.

WEIL FELIX REACTION.

Day of disease	OX19	OX2	OXK
7	nil	nil	nil
25	1:2,500	1:2,500	1:50

BLOOD CULTURE.
On 7th day in Glucose Broth:- No B. proteus grown.

URINE CULTURE.
On 10th day:- No "E" group organisms found.
No B. proteus isolated

Case 11. Miss K., aged 22.

Patient fell ill at Ranikhet on 2/6/33, complaining of headache and pains in the limbs. She gave a history of having been for a picnic in the jungle on 27/5/33, but there was no history of a tick bite, and no evidence of the same could be found on her admission to hospital on 7/6/33.

A red macular rash appeared on the forearms on 5/6/33, and within a day it spread to the face, trunk, arms, legs, palms and soles. Sore throat was present and the tongue was coated with a dirty whitish fur in the centre. Constipation was troublesome. Constitutional symptoms were otherwise mild, there being practically no mental lethargy. Sweats did not occur. The spleen could not be felt at any stage of the disease. Slight enlargement of lymph glands in the posterior cervical, epitrochlear and left axillary regions was noted when she was first seen on 5/6/33, and for about three days later. Sore throat disappeared by 10/6/33,

Case 11 (Continued).
and the rash commenced to fade the following day. The temperature was normal on 16/6/33, but recrudescence of fever occurred rising to 101 deg. F. four days later. This was associated with pain in the right femoral region, and on examination the right femoral vein was found to be thrombosed, being palpable as a thickened, tender cord. Oedema of the leg was present, but moderate in degree. Disappearance of the rash was complete on 22/6/33. The femoral thrombosis cleared up rapidly, oedema being absent on 4/7/33. and the patient fit for removal to her home a week later.

WEIL FELIX REACTION.

Day of Disease	OX19	OX2	OXK
7	1:85	nil	1:50
14	1:1200	1:1200	1:35
17	1:6000	1:3000	1:35

URINE CULTURE.
On 8th, 9th, 10th, 11th, 12th, 13th, 14th, 15th days) No B. proteus found.

Case 12. L/cpl. M., aged 25. R.C. of Sigs.
Patient fell ill on 16/7/33 complaining of aches and pains all over the body, headache and rigors. He had been stationed at Ranikhet for three months prior to 5/7/33, when he left by road. He bivouacked at Bumsaon on the evening of 5/7/33, at Ratighat on 6/7/33, at Bhowali on 7/7/33, the Brewery on 8/7/33, and entrained for Meerut at Kathgodam on 9/7/33, arriving at his destination on 10/7/33.
The case notes do not mention any history with reference to a tick or other insect bite.
On admission to hospital on 18/7/33, the face was flushed, there was suffusion of the conjunctivae, the tongue was furred with a thick brownish coating and the throat was congested. Constipation and insomnia also were present. There was tenderness in the left hypochondrium, but the spleen could not be felt. The following day there was severe headache, pain referred to the eyes, and conjunctival suffusion was much more marked. A rigor occurred, followed by profuse sweating. Blood examination revealed no malarial parasites. (NOTE. There was a history of malaria B.T. in Feb., 1932). Mentally the patient was quite alert, but he was very restless on the night 19-20/7/33. The next morning a rosy red maculo-papular rash was observed, most marked on the limbs around the joints, but also present on the trunk.

Case 12 (Continued).
A few spots were found on the face, and there was mottling of the palms and soles. Marked prostation was noted in the case sheet on the 21st. On the 22nd the rash was more definitely macular, and showed petechial characters. The spleen was just palpable, but not tender, and the throat slightly congested. On the 23rd the rash was more marked on the chest, abdomen and back, but that originally noted on the limbs was duller and brownish in colour. In type the rash on the trunk was now macular, with petechiae more marked. Mottling was still present on the palms and the soles. During the day the patient was lethargic, and at night restless. Drowsiness was increased on the following day, and the petechial characters of the rash more pronounced, but this was not observed on the fresher outcrops. On the 25th the rash commenced to fade, and it assumed a coppery hue. The spleen was palpable up to the 31st, on which date very faint staining indicated the sites of the rash on the chest, abdomen and back, and to an even lesser extent on the limbs.

Convalescence was rapid and uneventful, except that on 7/8/33 the patient complained of acute pain over the right shoulder and in the forearm, with numbness of the fingers. Objectively, nothing abnormal was noted on examination. The pain lasted most of the day and recurred to a slight extent the following day.

WHITE BLOOD CELL COUNT. Day of disease, 5th. 9,200 per c.mm. Polys. 56%. Lymphocytes, 28%. Monos. 16%.

WEIL FELIX REACTION.

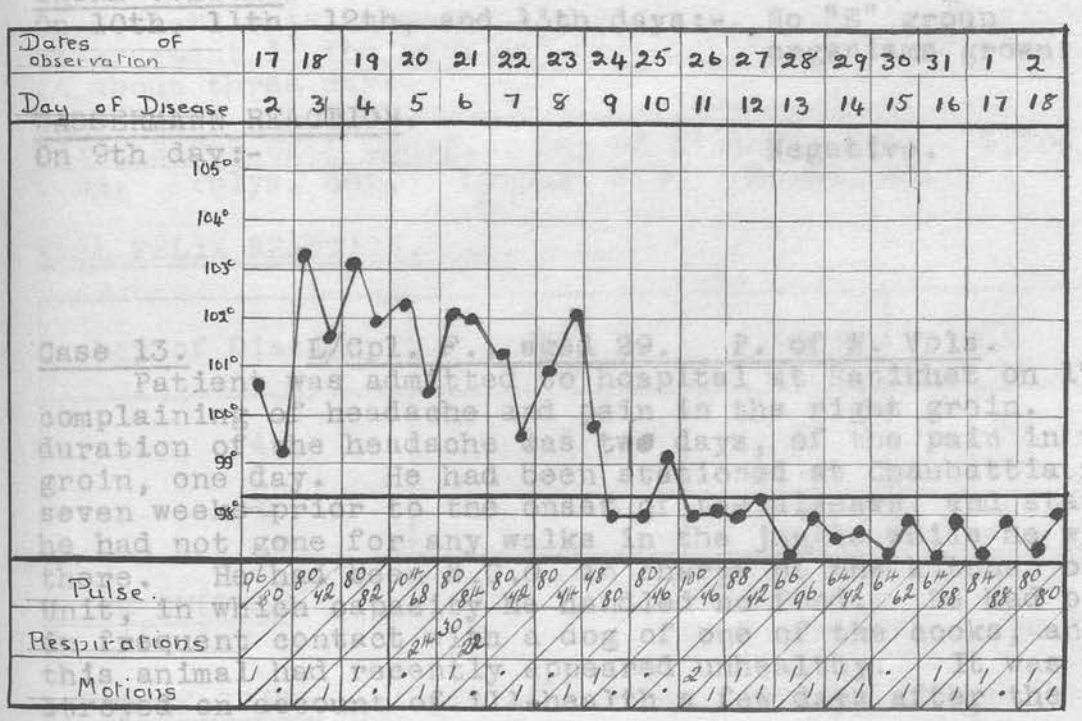
Day of Disease	OX19	OX2	OXK
5	nil	nil	1:17
9	nil	nil	1:25
13	1:1000	nil	1:50
18	1:2500	nil	1:50

WIDAL REACTION. (Date of last inoculation with T.A.B. May, 1933).
Expressed in terms of Standard Agglutinin Units.

Day of Disease	T	A	B	TO
5	15	100	115	nil
13	19	129	50	nil

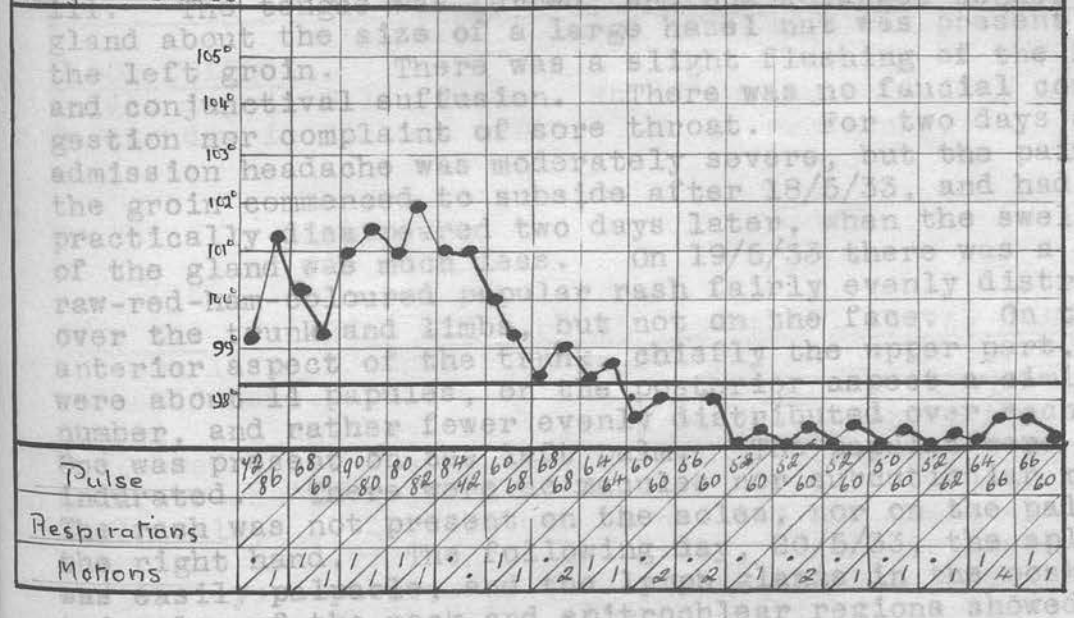
BLOOD CULTURE.
On the 5th and 9th day in Bile Salt:- No "E" group organisms grown.
On the 5th day in Glucose Broth:- No B. proteus grown.

Case 12.



Dates of observation	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	1	2
Day of Disease	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Pulse.	96/80	80/42	80/82	104/68	80/84	80/42	80/44	48/80	80/46	100/46	88/42	66/96	64/42	64/62	64/88	84/88	80/80
Respirations				24	30	22											
Motions	1/·	1/1	1/·	·/1	1/·	·/1	·/1	1/·	·/·	2/1	1/1	1/1	1/1	·/1	1/1	1/·	1/1

Case 13.



Dates of observation	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	1	2
Day of Disease	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Pulse	72/86	68/60	90/80	80/82	84/42	60/68	68/68	64/64	60/60	86/60	58/60	52/60	52/60	50/60	52/62	64/66	66/60
Respirations																	
Motions	·/1	1/1	1/1	1/1	·/1	1/1	·/2	1/1	·/2	·/2	·/1	·/2	·/1	·/1	·/1	1/4	1/1

Case 12 (Continued).

URINE CULTURE.
On 10th, 11th, 12th, and 13th days:- No "E" group organisms grown.

WASSERMANN REACTION.
On 9th day:- Negative.

Case 13. L/Cpl. F., aged 29. P. of W. Vols.

Patient was admitted to hospital at Ranikhet on 17/5/33 complaining of headache and pain in the right groin. The duration of the headache was two days, of the pain in the groin, one day. He had been stationed at Chaubattia for seven weeks prior to the onset of the disease, and stated he had not gone for any walks in the jungle while he was there. He had been N.C.O. in charge of the kitchen of his Unit, in which capacity he handled no food. He had been in frequent contact with a dog of one of the cooks, and this animal had recently appeared unhealthy. It was destroyed on account of ill-health a few days after the patient was admitted.

Previous Medical History:- Malaria, B.T., Oct., 1928, June, 1929, and June, 1930. Sandfly-fever at Landikotal, August, 1932. (Note. There was some evidence to show that some fevers diagnosed as "Sand-fly fever" at Landikotal at that time were probably fresh infections with malaria).

On admission to hospital the patient did not appear ill. The tongue was furred, and one enlarged tender gland about the size of a large hazel nut was present in the left groin. There was a slight flushing of the face and conjunctival suffusion. There was no faucial congestion nor complaint of sore throat. For two days after admission headache was moderately severe, but the pain in the groin commenced to subside after 18/5/33, and had practically disappeared two days later, when the swelling of the gland was much less. On 19/5/33 there was a scanty, raw-red-ham-coloured papular rash fairly evenly distributed over the trunk and limbs, but not on the face. On the anterior aspect of the trunk, chiefly the upper part, there were about 14 papules, on the posterior aspect a similar number, and rather fewer evenly distributed over each limb. One was present on the left palm. The papules were not indurated. There were no macules nor subcuticular mottling. The rash was not present on the soles, nor on the palm of the right hand. The following day, 20/5/33, the spleen was easily palpable, and the lymph glands in the posterior triangles of the neck and epitrochlear regions showed slight enlargement. On 21/5/33 the patient felt much better and had no complaint.

The temperature was normal on the morning of 24/5/33, the eighth day of the disease. The rash commenced to fade

Case 13 (Continued).
on 22/5/33. and disappeared completely in the following ten days. The splenic enlargement persisted up to 30/5/33. No anti-malarial treatment was given. The lymph glandular enlargement in the neck and epitrochlear regions disappeared in about three days.

WHITE BLOOD CELL COUNT. Day of disease, 5th. 5,200 per c.mm. Polys. 60%. Lymphs. 37%. Monos. 3%.

WEIL FELIX REACTION.

Day of Disease	OX19	OX2	OXK
4	1:17	nil	1:35
7	1:25	1:17	1:60
21	1:150	1:35	1:35

URINE CULTURE.
On 14th day No B. proteus grown.

WIDAL REACTION. (Date of last inoculation within the last 18 months).
Expressed in terms of Standard Agglutinin Units.

Day of Disease	T	A	B	TO
4	38	20	74	1:40
14	35	14	74	1:25

BLOOD CULTURE.
On 4th day in Bile Salt:- No "E" group organisms grown.
On 4th day in Glucose Broth:- No B. proteus grown.

Case 14. Bdr. C., aged 24. 64th Fd. Batt. R.A.

On 15/11/33 this patient noticed pains in the calves, and stiffness. His unit was marching from Allahabad to Jhansi, and had been 19 days en route. During the march he looked after a dog, which slept in his tent, and he went out shooting in the jungle adjacent to the route a good deal. At no time had he noticed any ticks on his body, nor any evidence of the same. After he became ill the dog was examined for ticks, with negative results.

The patient reported sick on 17/11/33 complaining of dizziness, headache, nausea, pains in the limbs and fever with rigors. He was admitted to hospital at Jhansi on 18/11/33. On admission he was very flushed, with suffused eyes. The tongue was moist, and coated with a white fur.

Case 14 (Continued).

He had a short dry cough, and examination of the chest showed dullness at the base of the right lung, distant breath sounds and increased tactile fremitus. Symptoms continued to be severe, and on 20/11/33 fine crepitant rales were heard over the base of the right lung. Some tenacious muco-purulent sputum was now being coughed up, and pneumonia was diagnosed. The following day there was bright red blood in the sputum. Case notes of the next two days mention marked restlessness at night, and on 24/11/33 sore throat and profuse sweats were reported. The following day there were signs of resolution of the pneumonia, namely redux crepitations, the cough was looser, but he was still very drowsy. On 26/11/33, 1.e. about the 10th day of his illness, a rosy macular rash was observed distributed all over the body with the exception of the scalp and an area of the chest to which antiphlogistine had been applied. It was well marked on the palms and soles, and some of the spots on the trunk and arms showed petechial characters. The rash did not irritate. Headache and pains in the limbs were very severe, and the calves were tender on pressure. The tongue was still moist and was coated thickly with a white fur. The rash was more profuse the following day, but no further outcrops were reported. It commenced to fade about 5/12/33, and a week later it was very faint on the trunk, legs, palms and soles. At other sites which had been involved it showed as a faint brown staining. A week after this it was still visible on the extensor aspects of the legs and on the soles, but was completely absent elsewhere. On 30/12/33 it was very faint at these sites, and on the trunk a faint brown mottling could be demonstrated by allowing the surface of the body to become cold.

WHITE BLOOD CELL COUNT. Day of disease, 10th. 9,200 per c.mm. Polys. 74%. Lymphs. 22%. Monos. 4%.
Day of disease 13th. 9,500 per c.mm. Polys. 73%. Lymphs. 21%. Monos. 5%. Eosins. 1%.

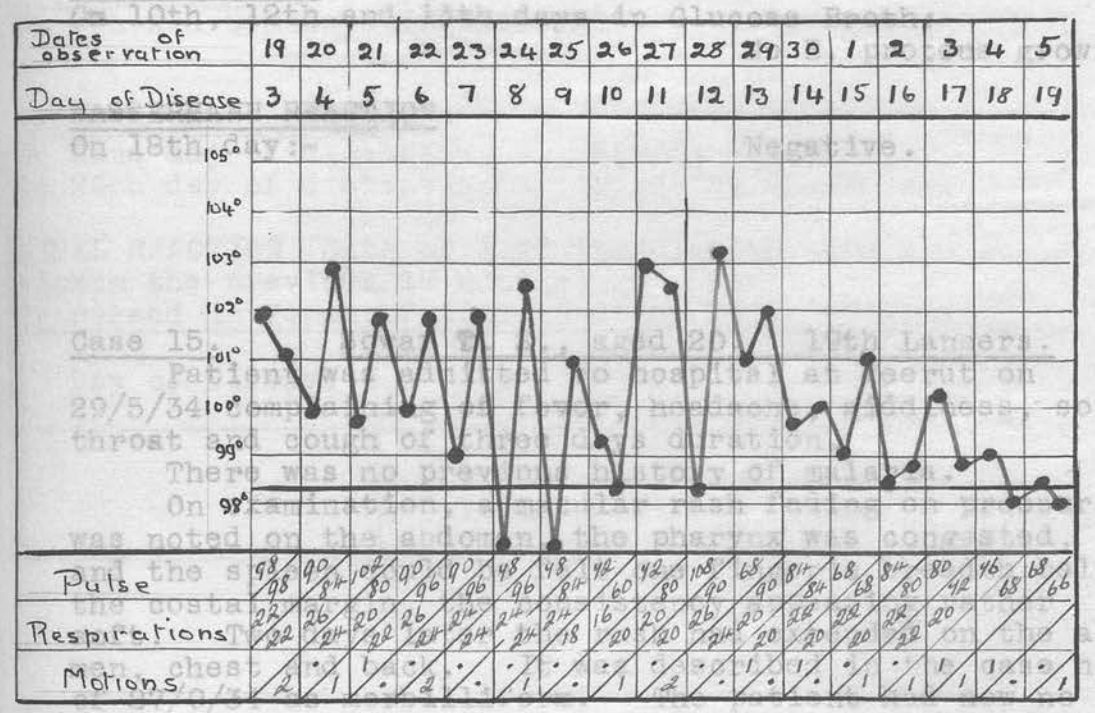
WEIL FELIX REACTION.

Day of Disease	OX19	OX2	OXK
10	nil	nil	nil
13	1:1500	1:1500	1:50
54	1:500	1:1000	1:50

WIDAL REACTION. (Date of last inoculation with T.A.B. within the previous 18 months).
Expressed in terms of Standard Agglutinin Units.

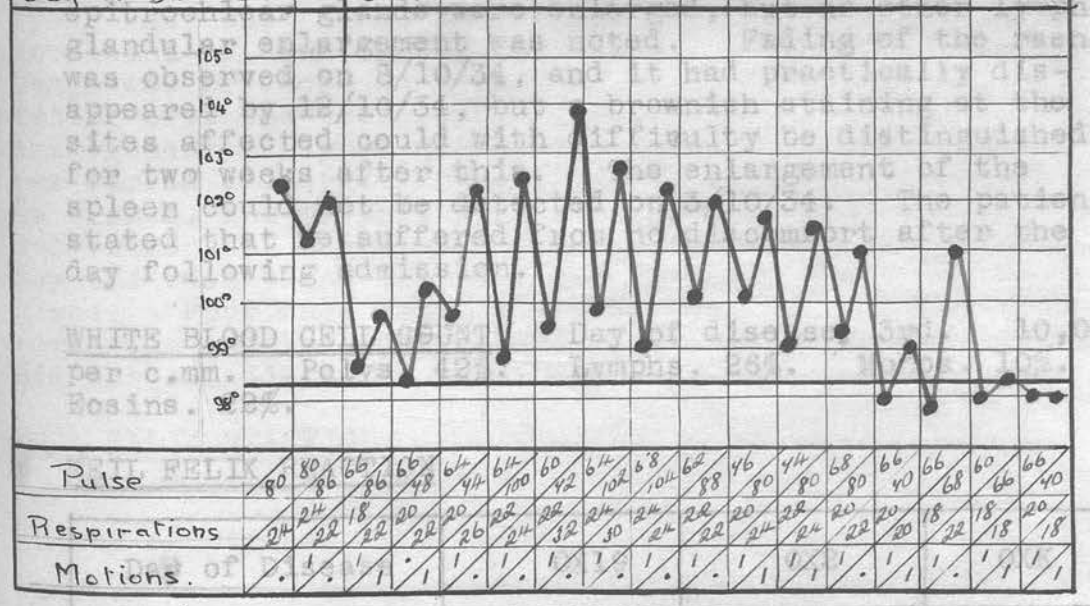
Day of Disease	T	A	B	TO
10	35	64	56	nil
14	70	100	64	nil
22	62	100	64	nil

Case 14.



Dates of observation	19	20	21	22	23	24	25	26	27	28	29	30	1	2	3	4	5
Day of Disease	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Pulse	98/98	90/84	102/80	90/96	90/96	48/96	48/84	42/60	42/80	108/90	68/90	84/84	68/68	84/80	80/42	46/68	68/66
Respirations	22/22	26/24	20/22	26/24	24/24	24/24	24/18	16/20	20/20	26/24	20/20	22/20	22/20	22/22	20/	/	/
Motions	2	1	·	·	2	·	1	·	1	2	·	·	1	·	1	1	·

Case 15.



Dates of observation	23	24	25	26	27	28	29	30	1	2	3	4	5	6	7	8	9
Day of Disease	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Pulse	80	80/86	66/86	66/48	64/44	64/100	60/42	64/102	68/104	62/88	46/80	44/80	68/80	66/40	66/68	60/66	66/40
Respirations	24	24/22	18/22	20/22	20/26	22/24	22/32	24/30	24/24	22/22	20/24	22/24	20/22	20/20	18/22	18/18	20/18
Motions.	·	1/·	1/1	1/·	1/·	1/·	1/·	1/·	1/·	1/·	1/1	1/1	1/·	1/1	1/·	1/1	1/1

Case 14 (Continued).

BLOOD CULTURE.
On 10th, 12th and 13th days in Glucose Broth:-
No B. proteus grown.

WASSERMANN REACTION.
On 18th day:- Negative.

Case 15. Sowar T. S., aged 20. 19th Lancers.

Patient was admitted to hospital at Meerut on 29/5/34 complaining of fever, headache, giddiness, sore throat and cough of three days duration.

There was no previous history of malaria.

On examination, a macular rash fading on pressure was noted on the abdomen, the pharynx was congested, and the spleen could be felt one finger's breadth below the costal margin, the consistency appearing rather soft. Two days later the rash had extended on the abdomen, chest and back. It was described in the case notes of 27/9/34 as morbilliform. The patient had now no complaint nor disturbing symptoms. Four days later, i.e., on 1/10/34, an extension of the rash to the upper limbs, and, to a lesser extent, the lower limbs, was noted, and it was more extensive at the sites previously affected. Five days after this the rash, still described as morbilliform, was well marked on the trunk and upper limbs, it was scanty on the lower limbs, and had been absent throughout on the face, palms and soles. The epitrochlear glands were enlarged, but no other lymph glandular enlargement was noted. Fading of the rash was observed on 8/10/34, and it had practically disappeared by 12/10/34, but a brownish staining at the sites affected could with difficulty be distinguished for two weeks after this. The enlargement of the spleen could not be detected on 3/10/34. The patient stated that he suffered from no discomfort after the day following admission.

WHITE BLOOD CELL COUNT. Day of disease, 3rd. 10,000 per c.mm. Polys. 42%. Lymphs. 26%. Monos. 10%. Eosins. 22%.

WEIL FELIX REACTION.

Day of Disease	OX19	OX2	OXK
22	1:25	1:2500	nil
29	1:25	1:1000	nil
40	nil	1:500	nil

Case 15 (Continued).

BLOOD CULTURE.
On 7th and 8th days in Bile Salt:- No "E" group organisms grown.

WASSERMANN REACTION.
On 22nd day of disease:- Strong Positive.
On 29th day of disease:- Negative Incomplete.

WIDAL REACTION (Date of last inoculation with T.A.B. within the previous 18 months).
Expressed in Terms of Agglutinating Titre of Sera).

Day of Disease	T	A	B	TO
3	1:600	1:60	1:60	nil
7	1:600	1:150	1:60	nil

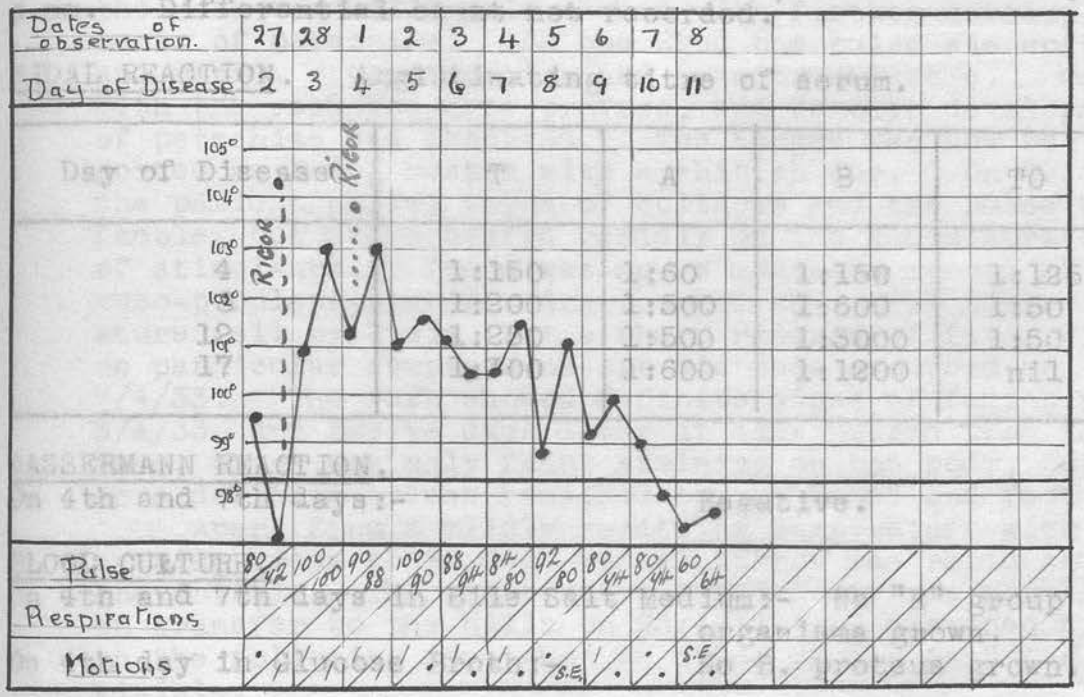
Case 16. L.Cpl. L., aged 23. The K.O.Y.L.I.

This patient fell ill on 26/2/34 complaining of shivering, severe headache and pains in the chest. He was admitted to hospital at Delhi on the following day. On 28/2/34 a macular eruption was observed on the chest, abdomen and limbs. There were also a few spots on the face, but none on the palms nor soles. The case notes of this date state that he was flushed with suffused eyes, that the fauces were congested but there was no complaint of sore throat, and that a moderately severe cough was present, some rhonchi being audible on auscultation over the left lung. There was also slight enlargement of lymph glands in the neck. The tongue was furred and dry. On 1/3/34 the rash was petechial in places, and on this date a rigor occurred, and enlargement of the spleen was detected. The following day the rash began to fade, and symptons generally to abate. Four days later scarcely any trace of the rash remained, and the patient felt well, although the fever did not subside until the following day.

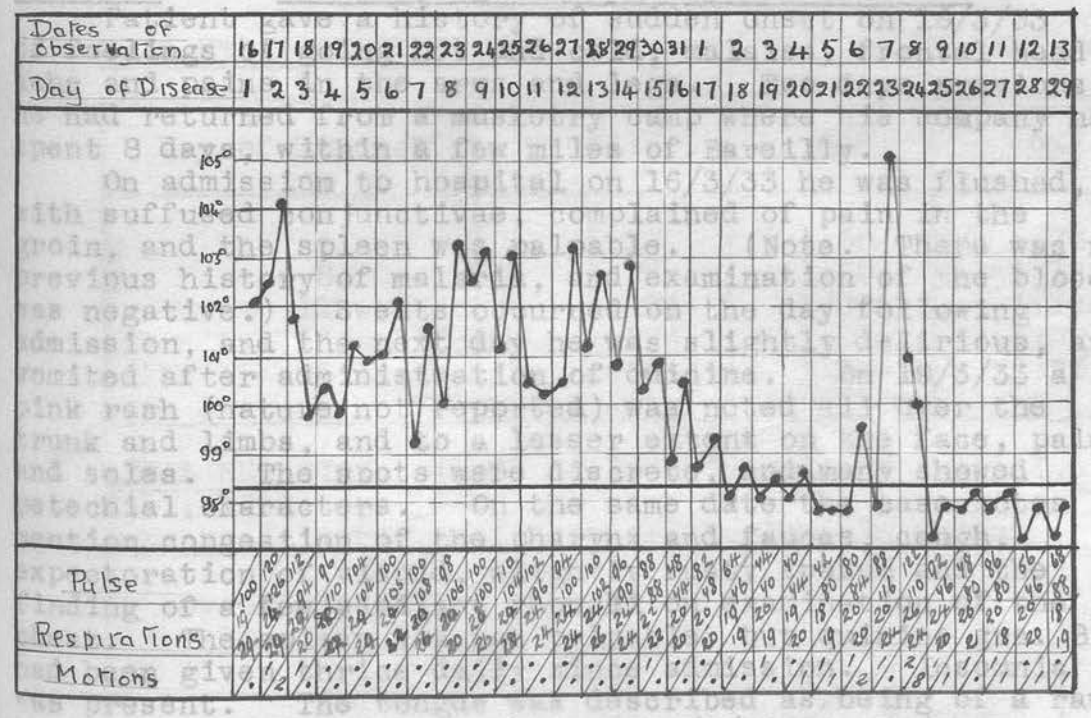
WEIL FELIX REACTION.

Day of Disease	OX19	OX2	OXK
4	nil	nil	nil
8	1:2500	1:25	nil
12	1:5000	1:50	nil
17	1:6000	1:50	1:25

Case 16.



Case 17.



Case 16 (Continued).

WHITE BLOOD CELL COUNT. Day of Disease, 5th. 8,200 per c.mm. Differential count not recorded.

WIDAL REACTION. Agglutinating titre of serum.

Day of Disease	T	A	B	TO
4	1:150	1:60	1:150	1:125
8	1:200	1:500	1:600	1:50
12	1:250	1:500	1:3000	1:50
17	1:300	1:600	1:1200	nil

WASSERMANN REACTION.
On 4th and 7th days:- Negative.

BLOOD CULTURE.
On 4th and 7th days in Bile Salt Medium:- No "E" group organisms grown.
On 4th day in Glucose Broth:- No B. proteus grown.

Case 17. Pte. D., aged 23. 1st Bn. D.C.L.I.

Patient gave a history of sudden onset on 16/3/33 of feelings of going hot and cold, malaise, frontal headache and pains in the arms and legs. Two days previously he had returned from a musketry camp where his company had spent 8 days, within a few miles of Bareilly.

On admission to hospital on 16/3/33 he was flushed, with suffused conjunctivae, complained of pain in the groin, and the spleen was palpable. (Note. There was no previous history of malaria, and examination of the blood was negative.) Sweats occurred on the day following admission, and the next day he was slightly delirious, and vomited after administration of quinine. On 19/3/33 a pink rash (nature not reported) was noted all over the trunk and limbs, and to a lesser extent on the face, palms and soles. The spots were discrete, and many showed petechial characters. On the same date the case notes mention congestion of the pharynx and fauces, cough, expectoration of viscid, slightly rusty sputum and the finding of a few sibilant rhonchi on examination of the chest. The spleen was not palpable, but quinine grs. 8 had been given thrice daily since admission. Insomnia was present. The tongue was described as being of a raw red appearance with no fur. On 20/3/33 little change was recorded except that mild delirium was present, congestion of the fauces was less, and the rash was more

Case 17 (Continued).
petechial. On 21/3/33 there was no delirium, and on the following day the cough had eased off greatly, but the rash was still well marked with further developments of petechiae. On the 22nd the pulse was soft and rapid. Constipation had been troublesome. On 24th the rash was more profuse, and further development of petechiae was observed. The tongue was now reported as being coated with a whitish fur. On 25/3/33 the patient showed signs of collapse and the pulse was feeble, but he recovered rapidly on the administration of stimulants. There was now a moderate amount of muco-purulent sputum being coughed up. The temperature fell by lysis, but a sharp relapse of fever with no particular symptoms except diarrhea occurred on 7/4/33. The rash showed definite signs of fading on 3/4/33, and twelve days later it disappeared from the face, there was only faint staining on the body, but more definite traces remained on the hands and feet.
Apart from a mildly remitting temperature with evening rises to 99 deg. convalescence was rapid and uneventful. The temperature settled down to normal on transfer to the hills on 23/4/33. I examined him on the following day, when no trace of the rash was visible.

WHITE BLOOD CELL COUNT. Day of disease, 4th. 14,200 per c.mm. Polys. 76%. Lymphs. 18%. Monos. 6%.
Day of disease 14th. 12,450 per c.mm. Polys. 71.5%. Lymphs. 23%. Monos. 5%. Eosins. .5%.

WEIL FELIX REACTION.

Day of Disease	OX19	OX2	OXK
4	1:17	1:60	1:70
8	1:17	1:60	1:125
12	1:125	1:275	1:175
16	1:175	1:275	1:300
25	1:85	1:175	1:260

WIDAL REACTION. (Date of last inoculation with T.A.B. Feb., 1932.
Expressed in terms of Standard Agglutinin Units.

Day of Disease	T	A	B	TO
4	71	19	36	1:50
8	71	38	72	1:85
12	71	48	333	1:85
16	63	62	717	
25	75	62	286	1:50

Case 17 (Continued).

BLOOD CULTURE.

On 4th day in Bile Salt:-	No "E" group organisms grown.
On 4th day in Glucose Broth:-	No B. proteus grown.
On 6th day in Glucose Broth:-	No B. proteus grown.

URINE CULTURE.

On 7th, 16th, 17th, 18th, 26th and 27th days:-	No "E" group organisms grown.

WASSERMANN REACTION.

On 14th day:-	Negative.

A guinea pig was injected interperitoneally with 5 cc. of the patient's blood taken on the 6th day of disease.

The animal showed no rise of temperature apart from normal variation and remained in good health.

Weil Felix Reaction carried out with its serum on 22nd day ~~of~~ after infection showed the following result:-

	OX19	OX2	OXK
Experimental Guinea-pig	nil	1:17	1:73
Control No. 1	nil	nil	1:38
Control No. 2	nil	1:25	1:38

Case 18. Tpr. P., aged 22. The Royals.

This patient was admitted to hospital at Meerut on 28/10/34, complaining of headache, abdominal discomfort, and a feeling of numbness in the arms. He had been off colour for four days and feverish for two days. He had been living the ordinary life in barracks locally for the previous three months. He did not own a dog, but had been in contact with a number belonging to his fellows.

He gave no history of a tick bite, and no evidence of such could be found on his body.

On the day of admission the patient had two rigors and sweated a good deal. He was flushed, and the conjunctivae were suffused. Apart from a severe headache, furred tongue and restlessness at night the case records contain no entry of note until 31/10/34, when he complained of a sore throat, and a rosy red maculo-papular rash was observed on the abdomen, chest, and soles of the feet. On 1/11/34 he perspired profusely. I examined him the following day, when he complained of pain on swallowing, and the rash was well marked all over the trunk, face and

Case 18 (Continued).
limbs, including the palms and soles. The throat was very congested, and the tongue was covered with a brownish white fur, except at the tip. There was slight enlargement of lymph glands in the neck, epitrochlear regions and axillae. The following day he appeared very apathetic and tired, complained of headache, aching in the limbs and joints, sore throat and abdominal pain. Examination of the chest and abdomen showed nothing definitely abnormal apart from the rash. On 4/11/34 symptoms began to abate rapidly, and the rash to fade. Four days later the patient felt quite well. The rash had entirely disappeared by 10/11/34.

WEIL FELIX REACTION.

Day of Disease	OX19	OX2	OXK
5	nil	nil	nil
7	nil	nil	nil
15	1:250	nil	1:250
22	1:500	nil	1:125
29	1:250	nil	1:25

WIDAL REACTION (Date of last inoculation with T.A.B. within the previous 18 months).
Expressed in terms of Agglutinating Titre of Sera.

Day of Disease	T	A	B	TO
5	1:500	1:60	1:300	nil
15	1:600	1:300	1:30	nil
22	1:600	1:300	1:550	nil

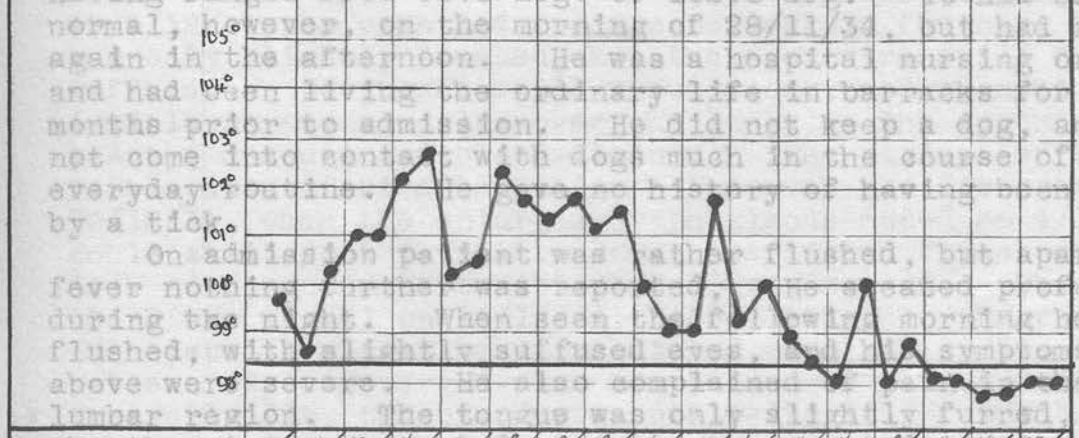
BLOOD CULTURE.
On 5th day in Bile Salt:- No "E" group organisms grown.
On 9th day (for medium see note at foot of page):-
No B. proteus grown.

WASSERMANN REACTION.
On 15th day:- Negative incomplete.
On 22nd day:- Negative.

NOTE:-
For the blood culture for B. proteus the blood was collected in sterile tubes and cultured according to the technique described by Felix ("Serological types of typhus virus and corresponding types of Proteus" published in Transactions of Royal Society of Tropical Medicine and Hygiene, Volume XXVII, No. 2, July, 1933).

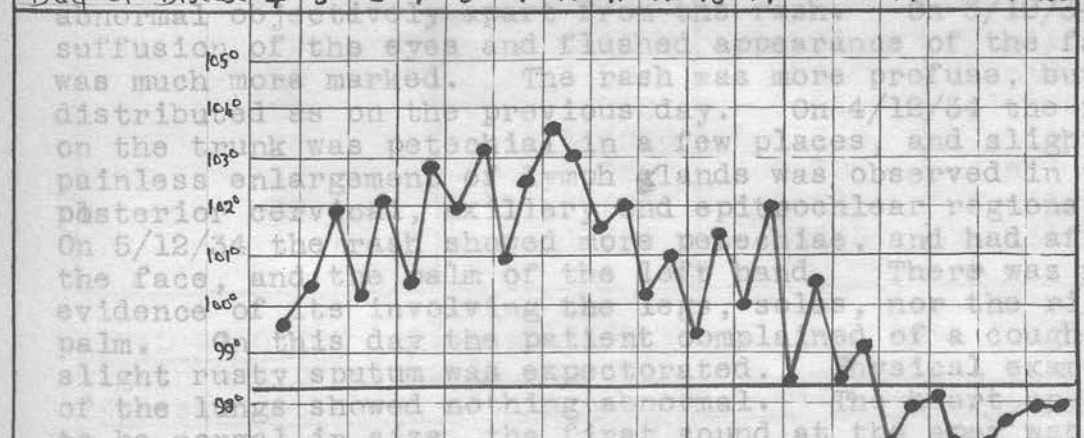
Case 18.

Dates of observation	28	29	30	31	1	2	3	4	5	6	7	8	9	10	11	12	13
Day of Disease	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Pulse	88	96/68	80/84	96/108	90/84	108/98	100/96	98/96	86/90	96/88	86/96	96/76	100/76	98/76	74/68	64/60	60/60
Respirations												26	24/32	26/24	24/24	24/22	24/26
Motions	·/1	·/·	2/·	·/·	·/S.E.	·/·	·/S.E.	·/·	·/S.E.	1/1	1/1	1/3	1/·	·/1	1/·	1/·	1/·



Case 19.

Dates of observation	30	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Day of Disease	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Pulse	96/92	100/88	86/100	92/80	98/80	100/90	92/92	88/80	84/76	76/84	72/76	76/68	72/60	68/68	68/64	60/68	64/68
Respirations				30	22/24	24/32	24	26	24	20/28	24/24	24/20	24/20	20	16/18	18	
Motions	·/·	·/1	·/6	1/·	·/1	1/1	·/·	2/·	·/·	1/1	1/·	1/·	·/1	·/2	1/1	1/2	



Case 19. Pte. M., aged 29, The Green Howards.

Patient was admitted to hospital at Meerut on 30/11/34 complaining of severe headaches, shivering and pains in the joints, particularly those of the hands and fingers, the knees, ankles, and right shoulder. He stated that he had had fever for four days prior to admission, his temperature having ranged from 99.8 deg. to 102.8 deg. It had been normal, however, on the morning of 28/11/34, but had risen again in the afternoon. He was a hospital nursing orderly, and had been living the ordinary life in barracks for three months prior to admission. He did not keep a dog, and did not come into contact with dogs much in the course of his everyday routine. He gave no history of having been bitten by a tick.

On admission patient was rather flushed, but apart from fever nothing further was reported. He sweated profusely during the night. When seen the following morning he was flushed, with slightly suffused eyes, and his symptoms as above were severe. He also complained of pain in the left lumbar region. The tongue was only slightly furred, and the throat was congested. A scanty rosy red papular rash was present on the trunk, chiefly the upper part, and shoulders. There was a small papular sore 2-3 mm. in diameter, on the left calf, but there was no enlargement nor tenderness of lymph glands in the popliteal, femoral nor inguinal regions. Patient again sweated profusely on the night 1-2/12/34, and on the following morning the rash, now maculo-papular, was well marked on the trunk, where it was most profuse, the arms, forearms, and, to a lesser extent, the thighs. On the abdomen the macules were $\frac{1}{2}$-1$\frac{1}{2}$" apart. Symptoms continued to be severe, and he was very restless during the night 2-3/12/34. He complained at this time of severe pain in the right shoulder, which showed nothing abnormal objectively apart from the rash. On 3/12/34 suffusion of the eyes and flushed appearance of the face was much more marked. The rash was more profuse, but was distributed as on the previous day. On 4/12/34 the rash on the trunk was petechial in a few places, and slight, painless enlargement of lymph glands was observed in the posterior cervical, axillary and epitrochlear regions. On 5/12/34 the rash showed more petechiae, and had affected the face, and the palm of the left hand. There was no evidence of its involving the legs, soles, nor the right palm. On this day the patient complained of a cough, and slight rusty sputum was expectorated. Physical examination of the lungs showed nothing abnormal. The heart appeared to be normal in size, the first sound at the apex was soft, and the systolic blood pressure was irregular, varying between 102 and 98 mm. Hg., the diastolic being 66 mm. Hg. Constipation was severe, but the tongue was moist and only slightly furred. The following day there was a marked change in the patient. Symptoms as on admission, severe up to the previous day, had abated almost completely, and headache in particular was absent. The face was much less flushed, and the eyes less suffused. The rash showed no fresh petechaie, and it had faded a little. Mottling of

Case 19 (Continued).
the soles was, however, observed for the first time on this date, there was a slight involvement of the extensor surfaces of the legs, and the maculae on the left palm were more definite. The blood pressure had risen, the systolic being variable between 108 and 104 mm. Hg., and the diastolic being 64 mm. Hg. A soft systolic mitral bruit was observed. On 7/12/34 the rash had faded considerably further, the face was only slightly flushed, but the eyes were still very suffused. Cough was still troublesome, and rhonchi were audible on auscultation over the lungs. The sputum was scanty, mucous, and blood-stained. The patient suffered little discomfort after this. The rash had disappeared on 10/12/34, when the enlarged lymph glands noted on 4/12/34 could still just be felt. Cough persisted for about two days more, and expectoration of sputum ceased. The temperature was normal on 13/12/34. Convalescence was rapid. The systolic mitral bruit persisted until 21/12/34, the patient was discharged from hospital on 27/12/34 feeling perfectly fit, the blood pressure being 124/80 mm. Hg. The spleen could not be palpated and was not tender at any period of the illness.

WHITE BLOOD CELL COUNT. Day of disease, 7th. 5,600 per c.mm. ~~Lymphs~~. Polys. 58%. Lymphs. 36%. Monos. 6%. Day of disease 13th. 6,000 per c.mm. Polys. 65%. Lymphs. 30%. Monos. 5%.

WEIL FELIX REACTION.

Day of disease	OX19	OX2	OXK
7	nil	nil	nil
10	1:50	nil	nil
20	1:250	1:25	1:125
26	1:1000	1:250	nil
30	1:500	1:125	nil
37	1:400	1:250	nil
41	1:250	1:125	nil

WIDAL REACTION (Date of last inoculation with T.A.B. within the previous 18 months).
Expressed in terms of Agglutinating Titre of Sera.

Day of disease	T	A	B	TO
7	1:300	1:60	1:275	1:50
10	1:300	1:60	1:275	1:50
27	1:300	1:300	1:550	nil
30	1:300	1:300	1:550	nil
37	1:300	1:300	1:300	nil

Case 19 (Continued).

BLOOD CULTURE.

On 8th day in Bile Salt:- No "E" group organisms grown.

On 8th and 10th days (for medium see note at end of case):- No B. proteus grown.

URINE CULTURE.

On 10th, 11th, 12th, 13th, 15th, 18th, 19th, 20th, 22nd, 23rd, 24th, and 25th days :- No B. proteus grown.

NOTE:-

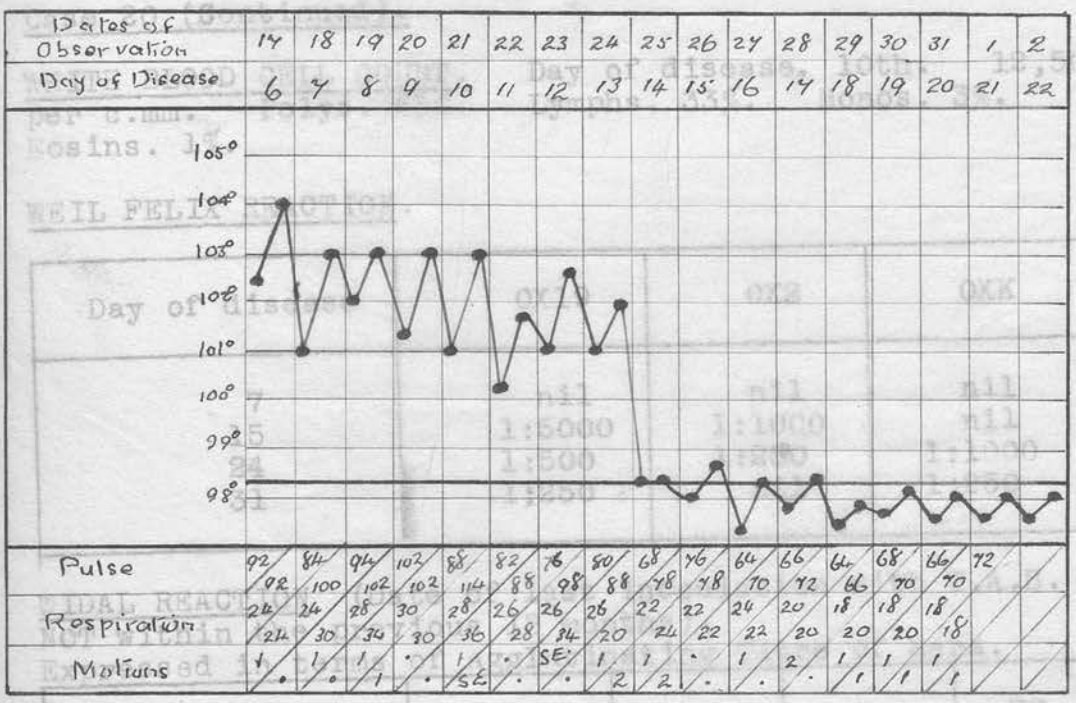
For the Blood Cultures for B. proteus the blood was collected in sterile tubes and cultured according to the technique described by Felix ("Serological types of typhus virus and corresponding types of proteus" published in Transactions of the Royal Society of Tropical Medicine and Hygeine, Volume XXVII, No. 2, July, 1933).

Case 20. Indian Clerk, N. H., aged 36. A.T.T. Coy.

This patient was admitted to hospital at Meerut on 17/10/34 complaining of fever, with shivering and sweating, headache, pains in the joints and cough, all of six days' duration. He gave no history of having been bitten by a tick. He suffered from malaria one year previously.

Clinical notes state that on admission he showed fever, a brownish furred tongue, flushed face, conjunctival suffusion and congestion of the throat. The following day a maculo-papular rash was found on the chest, abdomen and, to a lesser extent, the upper arms. A few spots were also present on the palms, and these could be rendered more prominent by pressure above the elbows. Patient still complained of severe headache and joint pains. On 19/10/34 the rash extended to the forearms. On the following day the headache and joint pains eased off, but the tongue was dry, showing a brownish incrustation. Examination of the heart and lungs showed nothing abnormal, and the blood pressure was 125/80 mm. Hg. The epitrochlear glands were noted to be slightly enlarged. The rash was now definitely macular. It did not involve the mucous surfaces of the mouth. Conjunctival suffusion and lethargy were noted up to 22/10/34, and on the same date the spleen could be palpated on deep inspiration. Fading of the rash was noted on 21/10/34, and in the course of the next four days the colour underwent a brownish transformation. On 29/10/34 it had disappeared. The spleen could not be felt on 24/10/34 nor subsequently. Convalescence was rapid, but complicated by a right-sided conjunctivitis which persisted for ten days.

Case 20.



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Case 20 (Continued).

WHITE BLOOD CELL COUNT. Day of disease, 10th. 12,500 per c.mm. Polys. 63%. Lymphs. 33%. Monos. 3%. Eosins. 1%.

WEIL FELIX REACTION.

Day of disease	OX19	OX2	OXK
7	nil	nil	nil
15	1:5000	1:1000	nil
24	1:500	1:250	1:1000
31	1;250	nil	1:250

WIDAL REACTION (Date of last inoculation with T.A.B. NOT within the previous 18 months).
Expressed in terms of Agglutinating Titre of Sera.

Day of disease	T	A	B	TO
7	nil	nil	nil	nil

BLOOD CULTURE.
On 3rd day in Bile Salt:- No "E" group organisms grown.

WASSERMANN REACTION.
On 8th day of disease :- Negative.
On 15th day of disease:- Strong positive.
On 24th day of disease:- Positive.
On 31st day of disease:- Negative incomplete.