A CLINICAL STUDY OF TSUTSUGAMUSHI DISEASE WITH SPECIAL REFERENCE TO THE EFFECT OF PROPHYLACTIC VACCINE UPON CASES WHO WERE ALREADY INCUBATING THIS DISEASE.

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SECTION 1. INTRODUCTION.

This study of the Clinical Aspects of Tsutsugamushi Disease - Scrub Typhus - was undertaken in the course of duties as a Medical Specialist to a Forward Medical Unit while stationed in Mandalay, Burma, during the period from June to December of 1945.

For the major part of this period Field Laboratory facilities were one hundred miles distant, and this unfortunate circumstance limited the extent of the investigations which originally had been contemplated. In spite of this difficulty essential tests were performed, the specimens being conveyed by our shuttle service of ambulances to Meiktila.

Fortunately Nursing Sisters of the Q.A.I.M.N.S. were present to assist in the accurate recording of routine investigations and to supervise the all important nursing, which, in the main, was done by Indian Nursing Sepoys.

A special ward was reserved for all acute Scrub Typhus cases and a picked staff maintained in this ward.

The Literature on Scrub Typhus which has become available (and removed from the Secret List) since one's return to England will be referred to throughout this thesis by quoting the Author's name and the year of publication in the text, together with a Reference Number to further details in an extensive Bibliography appended finally.

Only those cases which were personally observed and documented throughout their illness have been described, and the programme of Scrub Typhus Inoculation which resulted in the cases to be described in Part II had been entrusted to the writer by the [redacted].D.M.S. XII Army.

The cases studied and recorded in this Thesis were drawn mainly from within Mandalay City Boundary, but about 25% were sent in from Units scattered up and down the Irrawaddy Valley, fifty to one hundred miles north and south of the city.

It is desired to acknowledge the help, encouragement, and permission to publish findings granted by the following :-

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SECTION II. GENERAL SUBJECT MATTER OF THESIS.

A Clinical Study of One Hundred and Thirty Cases of Scrub Typhus (Tsutsugamushi Disease) including Original Observations relating to the following aspects of the Disease :-

1. Epidemiological Data of the Mandalay Outbreak (1945), with Rainfall, Relative Humidity and Maximum and Minimum Temperature Charts, compared with Incidence Charts and discussed.
2. Observations on the possibility of Infection having been acquired indoors.
3. Records of Blood Pressure, showing rise above normal level in early convalescence.
4. Records of the Changes in the Deep Reflexes, with general increase in Convalescence and occasional ankle clonus.
5. Observations concerning Hepatomegaly.
6. Consideration of Tachypnoea, Defective Basal Aeration, Expiratory Dyspnoea

and Tympanites, as Signs.

7. The Relationship of Weil-Felix Titre to the duration of Fever, with Illustrative Chart.

8. Treatment: The use of Mersalyl, and the Limited value of Oxygen.

9. The use of Di-Butyl-Phthalate on Beds, Bedding and Floors as an additional protective measure.

10. Post-Mortem records of Nine Cases, consolidated system by system in the general text.

11. An account of the Effect Produced on Sixteen Cases of Scrub Typhus by their having Scrub Typhus Prophylactic Inoculations while they were Incubating the Disease.

12. Reference to a Search for Eschars on Healthy Troops.

13. An Extensive Bibliography (202 References.)

14. Commentary.

In order to give a complete picture of the Disease it has been presented in systematic form with sections added, complete with full references, on

History, Aetiology, General Epidemiology, and Blood Chemistry, all of which were outside the scope of personal observation.

SECTION III. HISTORICAL.

Scrub, or Mite-Borne, Typhus, sufficiently closely resembles the other forms of Typhus Fever in its Clinical Aspect to have rendered its differentiation quite a recent event.

This fog of uncertainty as to its true nature is reflected in the number of Synonyms by which it has been described : -

Tsutsugamushi Disease, Japanese River Fever, Mossman Fever, Queensland Coastal Fever, Rural Tropical Typhus, Scrub Tropical Typhus, Sumatra Mite Fever, Endemic Glandular Fever, Pseudo-Typhus, Pseudo-Typhoid of Deli.

It is now accepted that Scrub Typhus as described in this Thesis is identical in all essential respects with Tsutsugamushi Disease, or Japanese River Fever.

Credit of first description of this Disease is variously given to a Chinese writer of the third century, (by Megaw,(1945) ref.119) and to one of the sixteenth century, (Blake,Maxcy, Sadusk,Kohls and Bell,(1945) ref.14).

Both of these writers attribute the disease to the bite of 'a small red insect', a 'Sha-shi', Sand-Louse, or Mite, which was known to burrow in sand.

The disease was described in some detail by Hakiyu Hashimoto in 1810, and to this writer is attributed the giving of the descriptive title 'Tsutsugamushi' i.e. Dangerous-Mite(or Insect) Disease, thus showing his knowledge of the vector. In more recent times one of the earliest references to the Disease was made by Palm,T.A. in 1878, in a letter to the Rev.John Lowe. In this letter he gives "some account of a disease called Shima-mushi, or island insect disease, by the natives of Japan, peculiar (it is believed) to that country and not hitherto described." (Ref. 141.)

In several districts of the Malayan Peninsula and in the Pacific Islands the identity of the disease was for a time obscured by the inconstancy of the presence of the Dermal Lesion or Eschar. This latter had come to be regarded as the diagnostic physical sign of classical Tsutsugamushi disease as described by Japanese observers, so that many Typhus group fevers were

described and variously named.

"Rural Typhus" was described by Fletcher and Leslar (1925) and Fletcher and Field (1927) (Ref.204.) in Malaya, and in these cases was distinguished from the coincident cases of Tsutsugamushi Disease by the presence of a Bubo in the former disease and an Eschar in the latter.

This distinction was reaffirmed by Anigstein,(1933) (ref.5.) and it was not until the work of Lewthwaite and Savoor,(1940)(ref.101.) that the identity of Rural Typhus in Malaya with Classical Tsutsugamushi Disease was proved to the hilt by cross-immunity experiments.

Classification of the Typhus Group of Fevers in terms of their respective Vectors as suggested by Megaw, has greatly simplified their study and description.

While there are marked epidemiological differences in different members of the group, it is still upon the differing agglutinations of their sera against three strains of B.Proteus that precise diagnosis ultimately depends.

The pioneer work of Wilson (1909), and Weil Felix (1916), on the isolation of Proteus - like organisms from the stools of Typhus patients and their subsequent agglutination in high titre with the serum of patients suffering from Epidemic Typhus, was the basis of the still employed Wilson-Weil-Felix test. (Napier . 1943) (ref.201.)

This test was further studied and elaborated by Boyd (1935) (Ref.15.) when he showed that when the O X K strain of B.Proteus suspension was agglutinated in high titre and the O.X. 19 strain agglutinated in low titre, or not at all, with the serum of the patient, these findings were strongly suggestive of Scrub or Mite-Borne Typhus. (Tsutsugamushi Disease).

SECTION IV. AETIOLOGY.

The Typhus Group of Fevers have been known to be caused by Rickettsial Bodies ever since Rocha-Lima first described and named Rickettsia Prowazeki, the causal organism of Epidemic Typhus, in 1916.

There are a number of claimants tothe honour of first identifying the causal Rickettsia of Mite-Borne Typhus and these may be summarised as follows, each claimant having given a different name to the organism :-

Name Given.	Claimant.	Year.	Ref.
Theileria Tsutsugamushi.	Hayashi.	1920.	62.
Rickettsia Nipponica....	Sellards.	1923.	157.
Rickettsia Orientalis...	Nagayo.	1930.	133.) 140.) 136.)
Rickettsia Tsutsugamushi.	Ogata.	1931.	139.
Rickettsia Akamushi.....	Kawamura & Imagawa.	1931.	72.

Rickettsia Orientalis and Rickettsia Tsutsugamushi are now considered to be identical and the cause of the disease.

Infection can be transmitted in the laboratory to rabbits by injection of the Rickettsial

x (None of the above References have been personally verified.)

suspension into the aqueous humor of the eye resulting in pannus, with ultimate recovery in two to three weeks. (Nagayo et alia. 1931.) (Ref. 132,134.)

Intra-dermal inoculation of the Rickettsia into monkeys and apes produces an ulcer, febrile disturbance, leucopenia, and rise of agglutinins against an O X K suspension. (Napier 1943)(Ref.201).

Inoculation of a Rickettsial suspension into the testes of rabbits has also been used as a confirmatory diagnostic test. Rickettsial strains were isolated from the blood of some of the cases to be recorded herein, by Major S.Lal Kalra, I.A.M.C. of the Field Typhus Research Team.

The Vector of Mite-Borne Typhus in South-West Asia has been identified as Trombicula Deliensis. It is the Larval phase of this mite which becomes infected by its single tissue-meal from the animal reservoir and transmits its infection through the ova to its offspring. This in turn (when it has developed to the larval stage) passes the infection on to Man by a further bite and meal. (Lewthwaite and Savoor .) (Refs. 96 and 101.)

This mite is barely visible, reddish brown, and measures 0.25 mm.

It was not proved to be the actual vector in the present cases, but the Scrub Typhus Field Research Team working with us found this Mite to be present in the ears of rodents in the area, and from this mite isolated Rickettsial strains with antigenic structure closely resembling, if not identical with, those isolated from human cases.

The Life Cycle of a closely related Trombiculide "Akamushi", found mainly in Japan, has been fully worked out by Miyajima and Okamura (1917), * (Ref. 125), and an excellent description given.

The important points discovered were, that the larval form attaches to the host for three or four days, and, when fully fed, drops off and burrows underground. Here it Metamorphoses to Nymph form and may be maintained in moist surroundings feeding on the juices of vegetables, potatoes, melons, etc. It crawls around and comes to the surface at times, but finally burrows again to pupate.

The Imago emerges and is to be found in its natural habitat, mainly under fallen leaves, decayed vegetable matters, or in the grass over the fine sandy

mud precipitated by floods.

When exposed, the mites briskly seek their shelter in the earth. It is probable that they try to avoid direct sunlight and dessication. " In a certain uncultivated spot, they were found so abundantly that one bushel of earth covering one square yard contained about fifty specimens. " " In Nature, both the Nymph and the Adult seem to live on the juice of plants, e.g., Reed (Imperata arundinacea Cyr.) , Daisy (Artemesia Vulgaris L.) etc."

The natural reservoir of infection in the Mandalay Area, as in other parts of Burma and in Malaya, is the rodent population. The Scrub Typhus Field Research Laboratory workers, Major.S.Lal Kalra, I.A.M.C., and Dr. Browning, of the B.M.R.C., established that rats and bandicoots locally were markedly infested, and experimental white mice which they let loose in suspected areas round Mandalay Fort soon became infested. The mites were found readily in the external auditory meatus of the infested animals.

Blood taken from several suspected (and subsequently proved) human cases was inoculated into White Mice which died within 14 days and from their brains Rickettsial strains were subsequently isolated.

These workers further showed (Major S. Lal Kalra, in a personal communication) that the rodents suffered from the disease in two phases, one Active and Septicaemic, during which Rickettsia could be isolated from the blood, which was actively infective to a Mite taking a meal on it, and secondly, a Latent phase, when Rickettsia were not recoverable and the animal not infective.

SECTION V. EPIDEMIOLOGY.

The Geographical known extent of Scrub Typhus is in scattered areas throughout Southern and Eastern Asia, the Pacific Islands, Northern Australia, some portions of East and South India, Burma, Malaya, and part of North East Africa.

It has been known for long that Focal Endemic Areas are usual in this disease.

NAGAYO (1923) (reference 130) called them * "Yudokuchi" meaning " Poisonous Places", and this characteristic first noticed in Japan holds good for Malaya and Burma as well.

Clasically the type of country which is dangerous is, as the common name for the disease implies, Scrub Land, i.e. areas where low bushes and coarse grass abound, especially where jungle

land has been cleared then subsequently allowed to become over-grown. Swampy ground near rivers and lakes or by the sea is specially liable to become infested.

Swampy conditions following the subsidence of the waters of flooded river valleys during the Monsoon season are ideal for the survival of the Vector. (Blake Maxcy, et alia. 1945) (Ref.14).

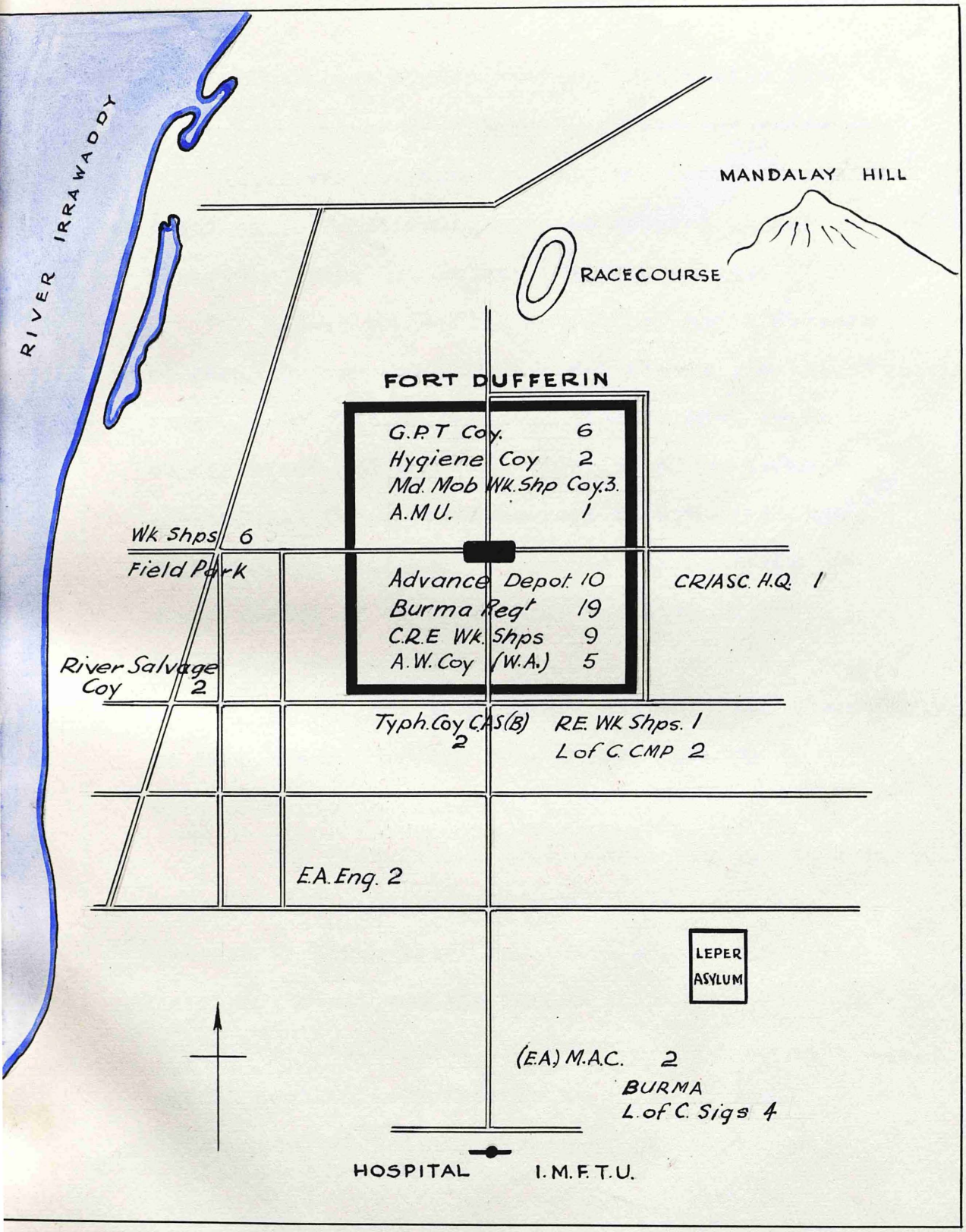
The Larval form of T.Akamushi in Japan is said to emerge from the soil at a Temperature of 20 degrees Centigrade (68 degrees F.).

At Temperatures of 65 degrees Farenheit and above it becomes active and it can cause infection (McCulloch, 1944) (Ref.117).

Men moving about in an infested site are much less likely to be infected than those who stand or sit about. Further, it is well recognised that newcomers to an infested area are much more susceptible to the disease than the indigenous peoples, who, presumably, have acquired immunity owing to attacks earlier in life.

The presence for even a few days of a body of troops in an infested area may be productive of a sudden crop of cases at the conclusion of the Incubation Period. This became a military problem of

DIAGRAM 1



SKETCH MAP of MANDALAY

SHOWING TYPHUS SITES

JUNE - DECEMBER 1945

ii. Epidemiology In Mandalay and District - June - December, 1945.

As was mentioned above, the Local Vector was found to be T.Deliensis and the natural animal reservoirs were Brown Rats and Bandicoots.

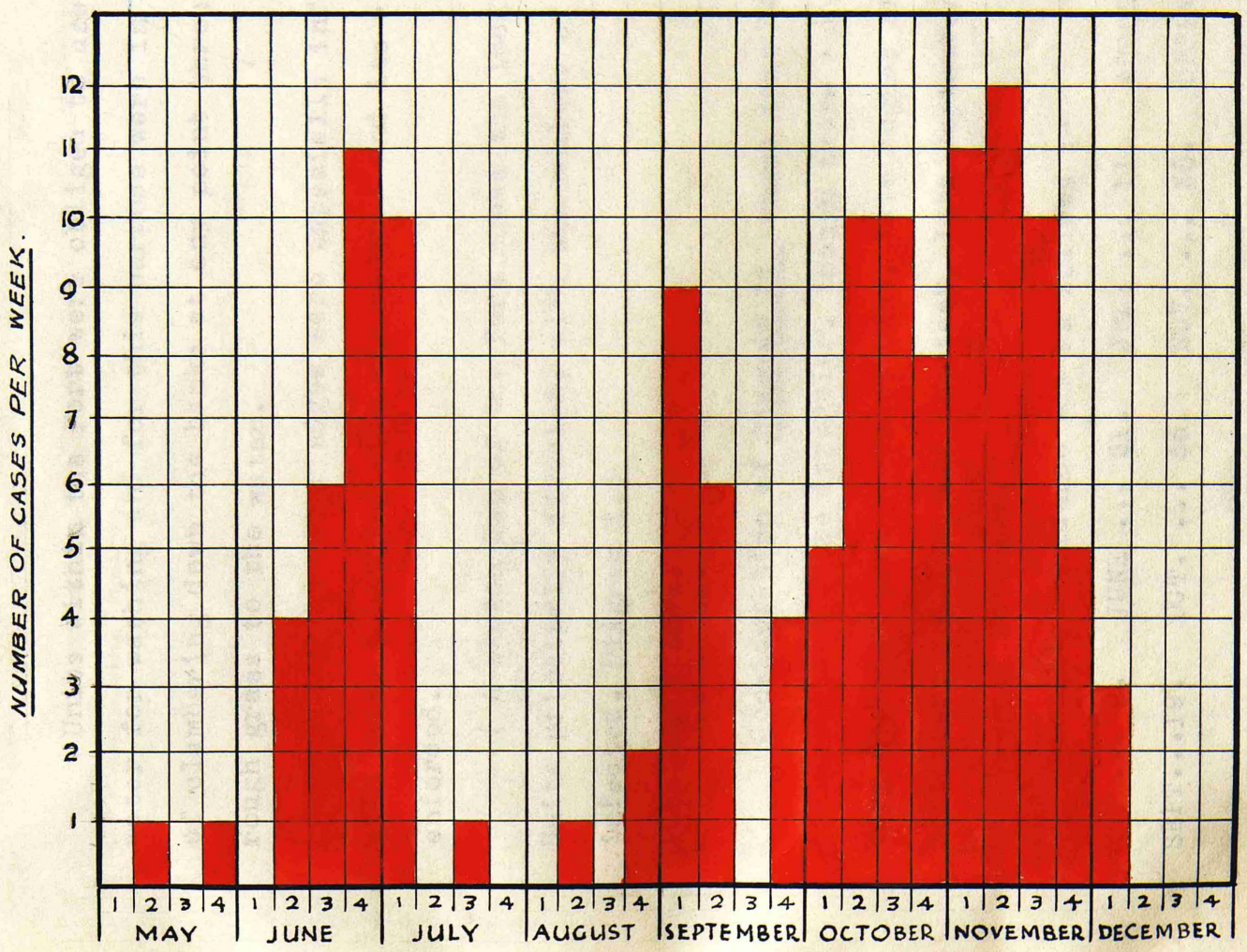
Mandalay District has always had a measure of Scrub Typhus Endemic, but not always recognised as such, so that an outbreak such as that about to be described had not been experienced by Burmese physicians. These civil doctors thought that the Japanese had suffered from a similar outbreak during their period of occupation of the City but this could not be confirmed.

Of the one hundred and thirty cases observed no less than fifty-one (31%) came from Units stationed within the Fort, Mandalay.

The Fort is one mile square and was left in a devastated condition by the Japanese on their retreat in March 1945. Practically no buildings remained intact and the former areas of park-land and lawns were allowed to become over-grown with lush grass, particularly around the edges of the Moat which is situated around the perimeter of the Fort.

DIAGRAM II

CHART SHOWING INCIDENCE OF SCRUB TYPHUS CASES FROM MAY - DECEMBER 1945 IN MANDALAY



Units within the Fort were obliged to use Moat water for washing and for this purpose were in the habit of clambering down the banks at any point through the rough grass to the water.

Since the water edges were especially infested with rats, a bathing site was cleared and its use enforced.

(A sketch Map of the Fort shows the locations of Units principally affected, with the numbers of troops infected. Diagram 1.)

iii. Incidence.

Consideration of Diagram II shows that Case Incidence was quite irregular, though there were three very definite peak periods; June, late August and early September; and last and greatest, late September with all October and November.

Monthly Incidence was as follows :-

MAY ... 2.	JUNE ... 21.	JULY ... 11.	AUGUST ... 3.
SEPT...19.	OCT. ... 33.	NOV. ... 38.	DECEMBER.. 3.

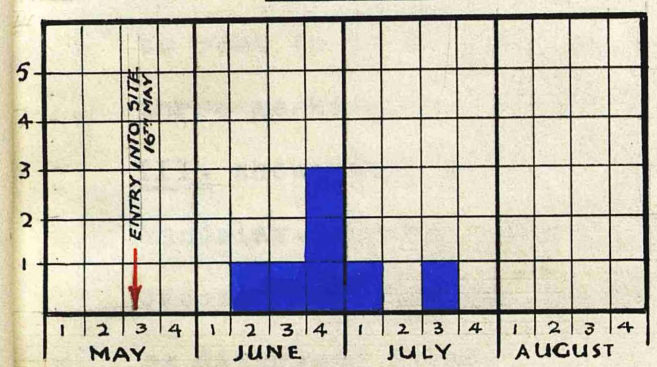
iv. Incidence by Unit, Nationality, and Occupation.

When Incidence was considered Unit by Unit

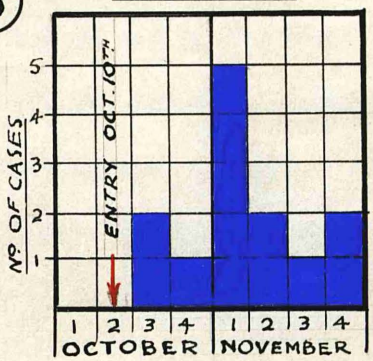
DIAGRAM III.

GRAPHIC REPRESENTATION OF NUMBER OF CASES WEEKLY ADMITTED TO HOSPITAL WITH SCRUB TYPHUS FROM SIX DIFFERENT UNITS IN MANDALAY, SHOWING BY ARROW (RED) DATE OF ENTRY TO CAMP SITE.

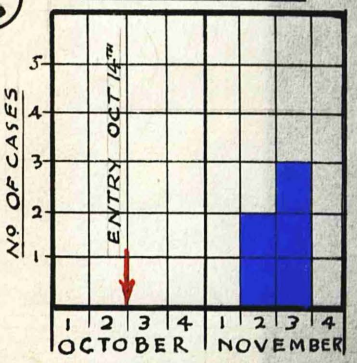
G.P.T. COY.



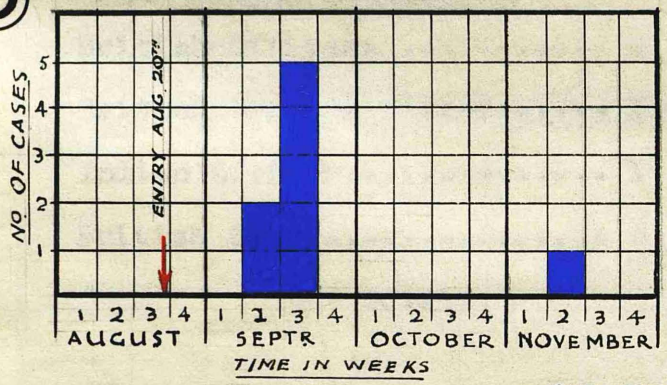
B ENG. BN. I.E.



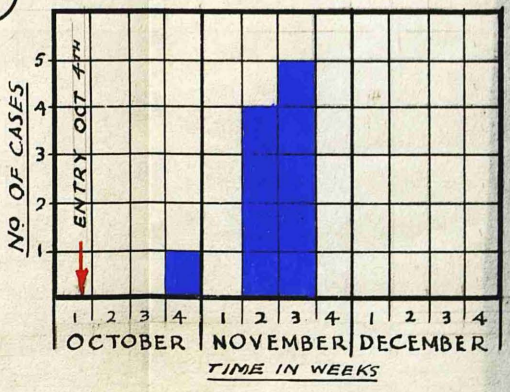
C A.W. COY. (W.A)



D ADVANCE DEPOT BURMA.

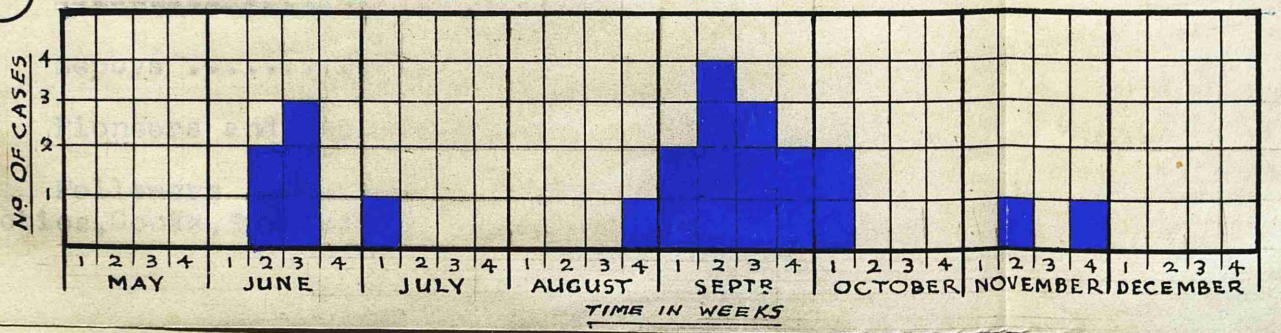


E C.R.E.



F 2ND BURMA REGT

UNIT PERMANENTLY ON SITE



It must be added that the great ma[illegible] in

it immediately became evident that the incidence of cases in point of time was very definitely related to the entry of fresh troops into an infested site.

Within three weeks from their entry cases commenced to come in in a wave, and after a period of a further three weeks almost as abruptly ceased to appear. Diagram III. shows this for several units stationed within Fort Mandalay. Further stay on the same site failed in most cases to produce any further cases. (This point will be discussed later.)

The Nationalities of Cases :-

British Officers	2	African O.R.s.....	7
British Nursing Sister.....	1	Indian NCO.s.....14	
Indian Officer.....	1	Indian O.R.s.....99	
British O.R.s.....	4	Civilians,Burmese.....	2
Totals.	8		122.
		Grand Total.	130.

Occupation of Indian Cases.

Sepoys	51.
Pioneers and Sappers....	26.
Followers ..... (Dhobies,Cooks,Sweepers.)	22.
Total.....	99.

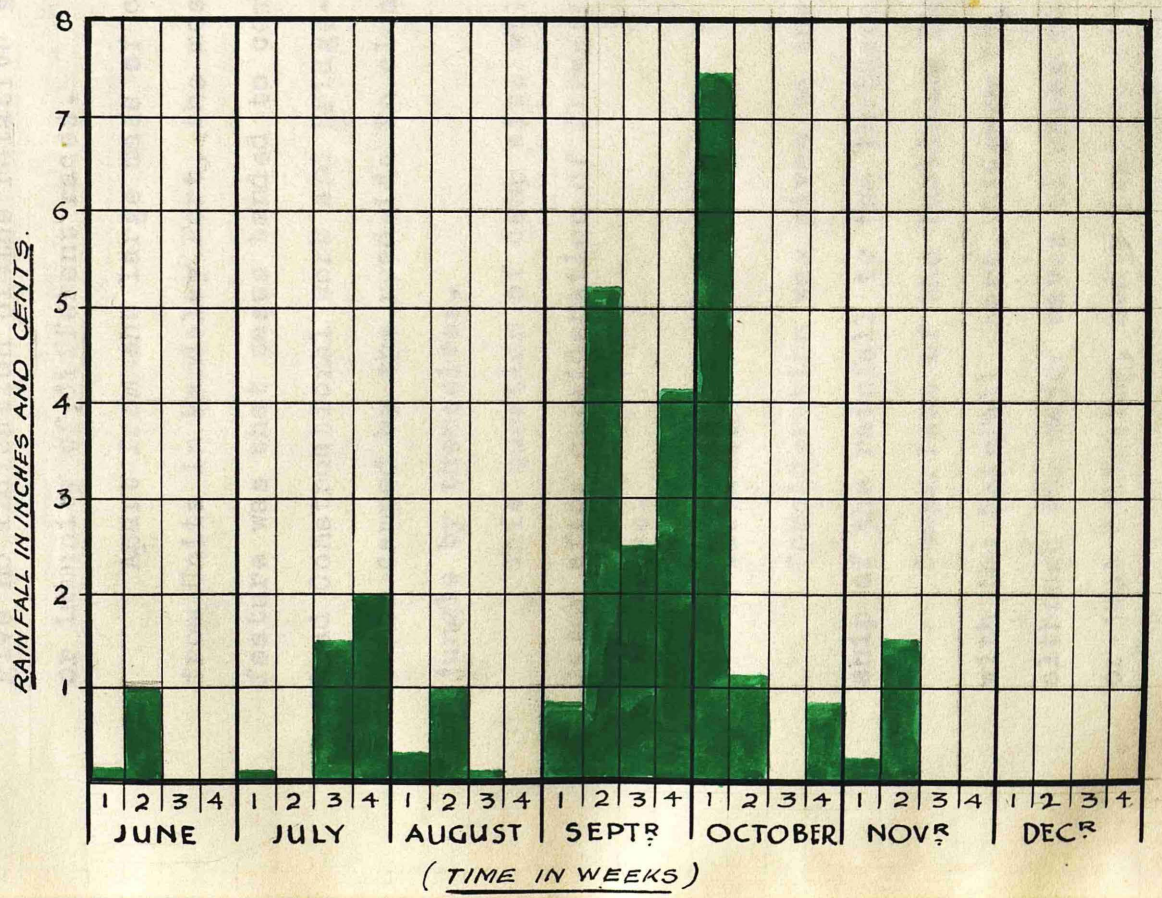
It must be added that the great majority of the troops in

DIAGRAM IV

RAINFALL RECORD FOR MANDALAY.

WEEKLY TOTAL JUNE - DEC. 1945.

(TOTAL RAINFALL IN YEAR 1945 = 41-79 INCHES)



the district were Indian so that the above figures give no indication of the relative susceptibility or immunity of different races.

Apart from the large mass of cases which came from Units in Mandalay Fort, the most noticeable feature was that cases tended to come from Units on Road Constructional work and Bridge-Building. These Units camped by the roadside in clearings made in the jungle by themselves.

This question of camp site will be taken up again later after consideration of Climatic effects on incidence.

v. Rainfall.

Consideration was given to the possible relationship of the rainfall to the incidence of Scrub Typhus.

Comparison of the Incidence Chart, Diagram II, with the Rainfall Chart, Diagram IV, shows that although the major waves of cases occurred during, or just following, heavy periods of rainfall, the cases continued to appear in increasing numbers for quite a month after practically all rain had ceased.

From consideration of this fact it was thought that this could only be one of several factors influencing the life and development of the Mite, and

DIAGRAM V

RELATIVE HUMIDITY- MEIKTILA DISTRICT.

JULY TO NOVEMBER 1945

(AVERAGE OF EACH 3 DAYS RECORDED)

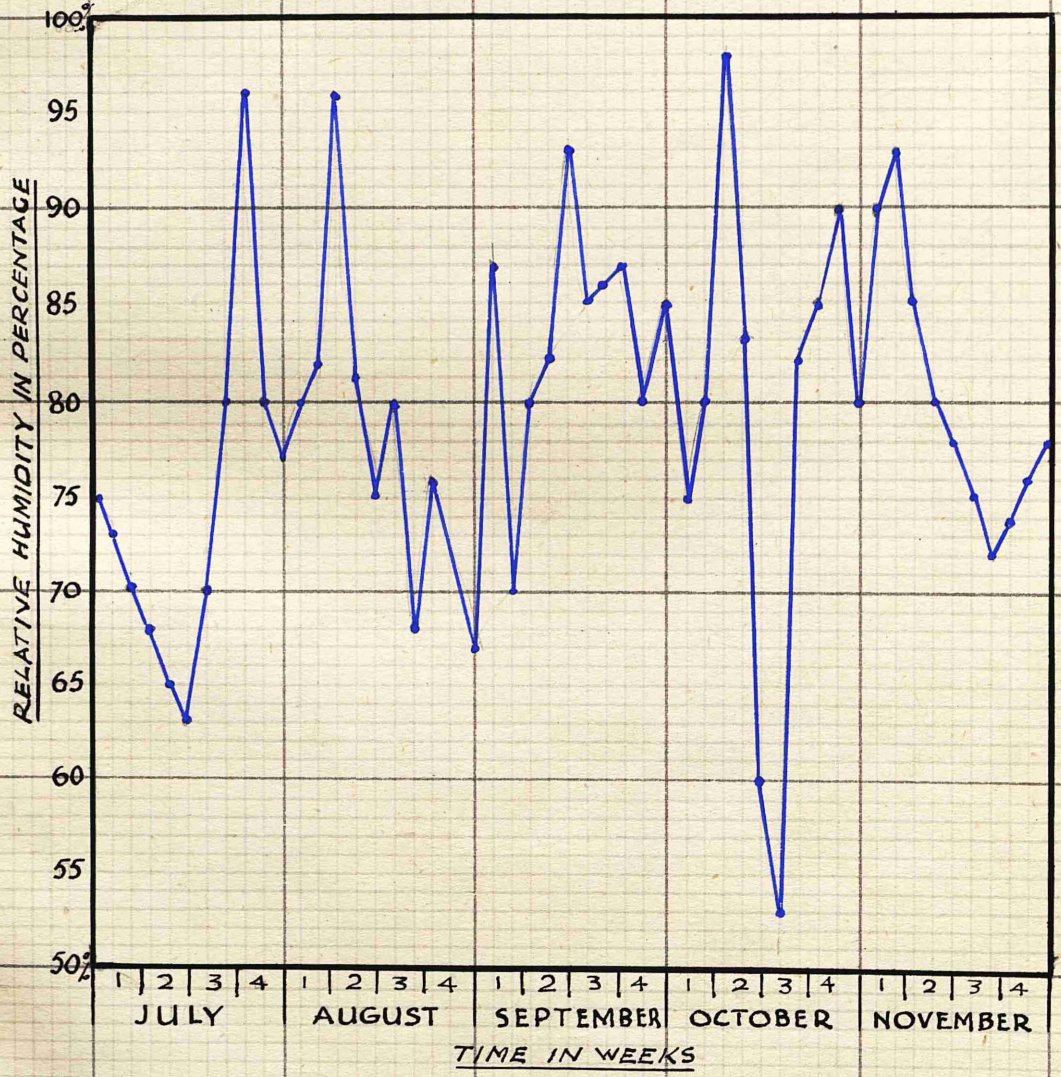
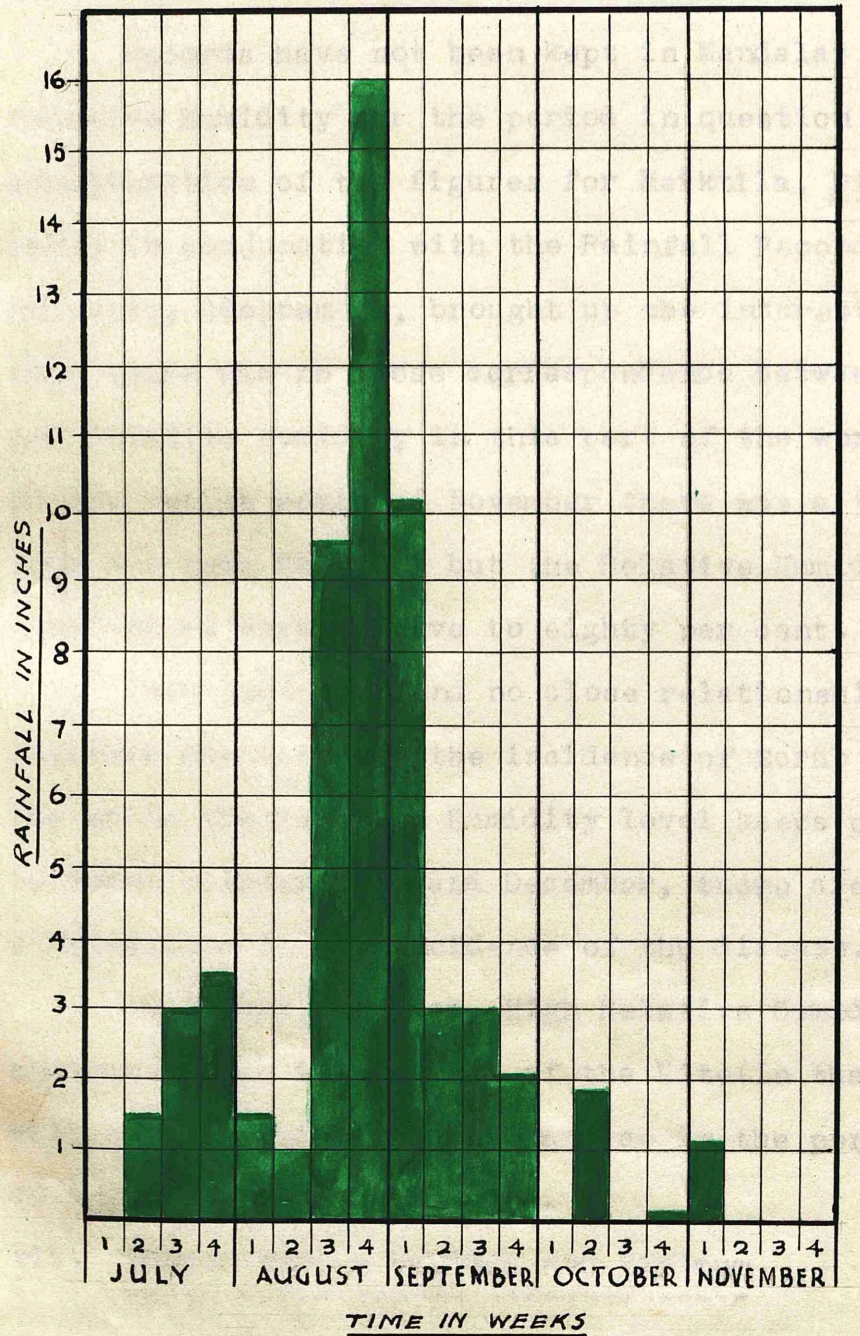


DIAGRAM VI.

RAINFALL OF MEIKTILA (BURMA)
JULY TO NOVEMBER 1945.
(WEEKLY TOTALS)



so affecting the spread of infection.

vi. Relative Humidity.

Records have not been kept in Mandalay of the Relative Humidity for the period in question but consideration of the figures for Meiktila, Diagram V., taken in conjunction with the Rainfall Record for Meitkila, Diagram VI, brought up the interesting point that there was no close correspondence between Rainfall and Relative Humidity in this part of the world. e.g. In the entire month of November there was a total of only one inch Rainfall but the Relative Humidity remained at seventy-five to eighty per cent.

Here again we find no close relationship between Relative Humidity and the incidence of Scrub Typhus, for while the Relative Humidity level keeps pretty constant between June and December, there are violent fluctuations in the incidence of the disease.

Doubtless, however, High Relative Humidity is another factor in survival of the Mite(in that dessication will kill it quite readily) and so in the persistence of infection in a given area.

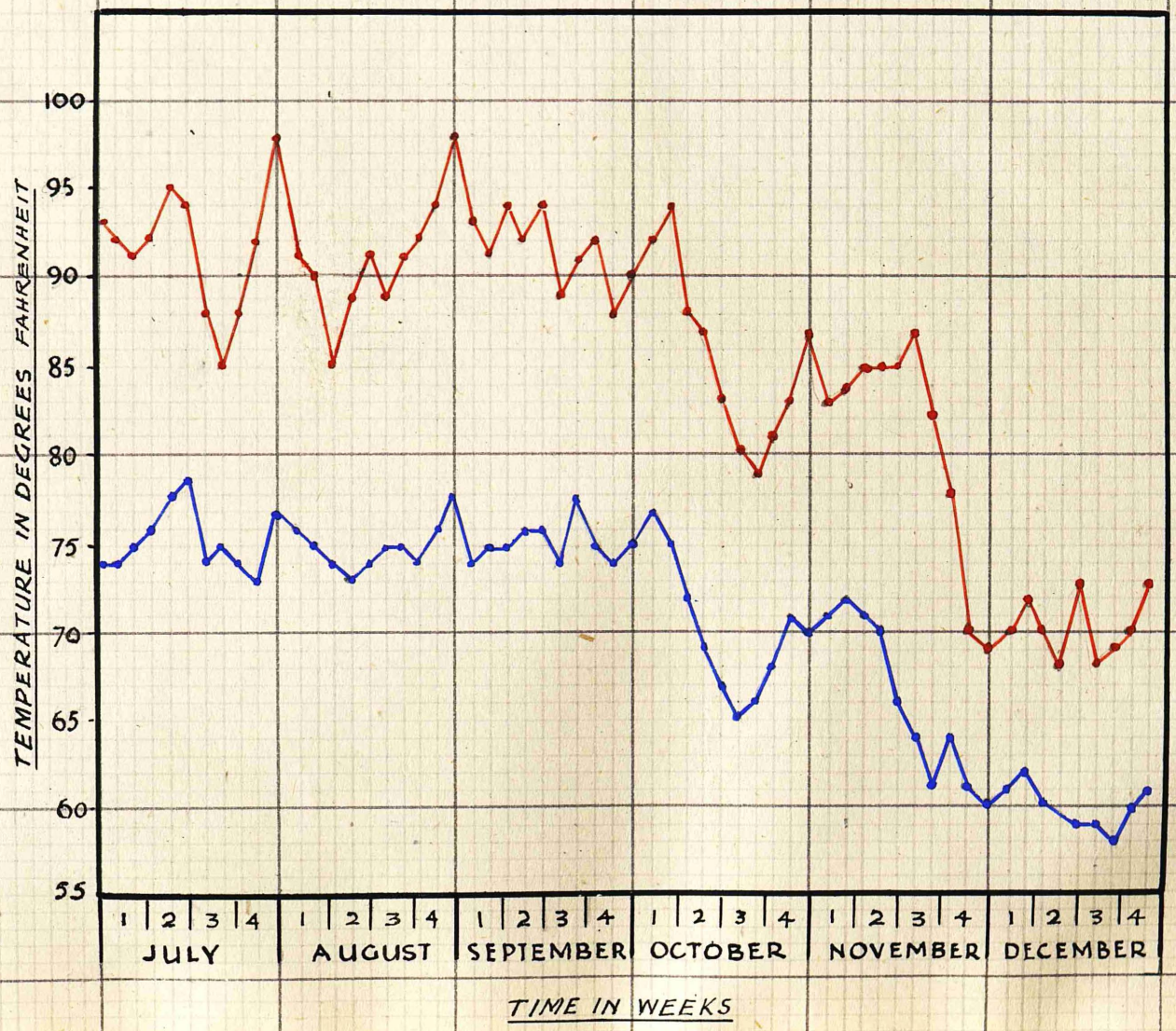
vii. Temperature - Maximum and Minimum.

By comparison of the Chart of Maximum and Minimum

DIAGRAM VII

MAXIMUM & MINIMUM TEMPERATURES IN MANDALAY DISTRICT JULY TO DECEMBER 1945.

(AVERAGE OF EVERY THREE DAYS RECORDED)



Temperatures with the Incidence Chart,(Diagrams VII & II) it will be seen that while the relatively steady Maximum and Minimum figures for July to October (Max. 95 degrees F. Min. 75 degrees F.) bore no relationship to the ebb and flow of the Incidence of the disease, the fall in both Maximum and Minimum Temperatures to around Max. 70 deg.F. and Min. 60 deg. F. in November appeared to be a factor in cutting short the outbreak.

Doubtless the Mite was made sluggish by the falling Temperature (Ref.117.)

viii. Infested Quarters.

Since it had been noticed that a majority of the cases in the first wave of Scrub Typhus came from Units sited within Fort Mandalay, a general instruction had been issued urging care in avoidance of grassy and scrub areas, weekly application of Di-Butyl-Phthalate, and the clearance of camp sites of all scrub and grass. Indeed, a notice was put up at each of the four gateways to the Fort announcing, " Scrub Typhus Danger Area, Keep to the Paths, Typhus Kills ." Whether this notice was wise is debatable, for the British patients who were unfortunate enough to contract the disease were certainly very much alarmed when they eventually discovered the nature of their illness.

It had been agreed by the Authorities that each Unit entering the Fort would be informed at once of the special danger, and accordingly take preventive action.

In spite of the above measures, and, in some cases, the additional precautionary measure of burning all grass and scrub in the camp site with Malariol, two fresh Units were infested within three weeks of their entry to the Fort.

These two Units will serve to illustrate a point which had been suspected in earlier cases, namely, that many troops appeared to have contracted their infection, not out-of-doors in grass or Scrubland, but in-doors in their Quarters and in all likelihood while lying upon their beds.

A. Advance Depot Burma. (See Diagram IIID)

On 20th August, 1945, Advance Depot Burma entered their site in Fort Mandalay and proceeded to clear the area of grass and Scrub for themselves, local labour not being available at that time.

From this Unit between the 10th and 14th of September 1945 five out of six of the occupants of one tent were admitted, and from the same Unit a further five cases were admitted within the period 3rd to 18th of September. Although they remained on

this same site for another two months only one further case presented, in a British Officer.

The strength of this Unit was 250 officers and men.

It was established that the five cases from one tent mentioned above (all Sikhs) had been employed in clerical duties and none had taken part in clearing the scrub. They gave the dates of onset as 7th,9th, 9th,10th, and 13th September.) Curiously enough the sixth member of this tent was admitted about the same time - but he was suffering from Gonorrhoea.)

Just as surprising was the fact that none of the personnel actually employed in clearing the scrub in this instance did develop Scrub Typhus.

Little was thought of these facts until, shortly afterwards, a similar finding was made in respect of another Unit.

B. C.R.E.Workshops.

The Advance Party of a C.R.E.Workshop Company entered the site two hundred yards from the above - named Unit (on the South Site of the Palace, Mandalay Fort) on the 28th September, 1945, and commenced to prepare the Officers' Mess Bungalow for occupation.

The Bungalow was situated twenty yards from a metalled road and approached by a gravel drive.

It had not been occupied since the departure of the Japanese, about six months previously, and was rather derelict.

Certain essential joinery works were performed in this building by a group of African Sappers from an Artisan Works Company (W.A.), and they slept in the building. Of those so employed four were admitted with Scrub Typhus, the dates of onset being 9th,10th,13th, and 16th November 1945.

In addition the following other personnel employed in this Bungalow were infected :-

The Civilian Plumber,	with onset	21st November.
The Officers' Mess Cook.	..	14th ..
Civilian Clerk.	..	19th ..
The British C.O.	..	14th ..
Second I/C.	..	12th ..

The latter two Officers appeared to have contracted the disease very shortly after entry to the Bungalow.

It appeared then that within twelve days, nine cases of Scrub Typhus had developed in persons of widely varying rank and occupation, the only factor in common being that they had lived in one particular Bungalow

during a period prior to onset greater than the Incubation period of the disease.

All of these nine cases had slept on low charpoys or Camp Beds.

There were four other cases from this Unit of two hundred Officers and Men within the same twelve days, but in these cases the connection with the Officers' Mess Bungalow could not be established with certainty. Their Ranks and Dates of Onset were :-

Sepoy.	16/11.	1/N.K.	16/11.
M/W.	19/11.	W/S.	21/11.

This site, with the one two hundred yards away, was clearly a "Typhus Island," and here again was the strong suspicion that the infection was contracted by the men while in their living and sleeping quarters rather than in the fields and grass around.

All of the patients mentioned above denied having walked or having sat down in the grass having been strictly enjoined not to do so, and they all insisted that they had used the special bathing place provided. It was not necessary for them to walk through grass to the latrine, and there was no reason why they should have been exposed unduly during duty hours to infection, but there was no guarantee that they had not been so exposed

during their off-duty hours.

In this instance also the cases occurred in a wave lasting fourteen days (plus one isolated case) and eventually the Unit moved out of the site on Medical advice. (See Diagram III,E.)

ix. Discussion Arising from Above Observations.

In the whole series of 130 cases including the above, on questioning, 25% were very definite that they had never had any occasion to walk or lie on grass within the fourteen days prior to admission. Since most of these were officers or of the clerical class, it can be well understood that all that many of them did was to walk from their Quarters to the office and back again.

It was reported by all Units entering the Fort that the area was infested with rats and that on their entry the Camp Sites and Buildings remaining were swarming with them.

Trapping was done quite extensively by a Hygiene Section and large numbers of Brown Rats and Bandicoots were caught and the bodies burnt after dropping them into kerosene.

It is unlikely that this measure in itself constituted a danger for it is thought that the Mites will not transfer from a dead rat (Kohls,G.N.,et alia,1945.) (Ref.79.-),

and they cannot be persuaded to do so in the laboratory. Moreover it is remarkable that none of those employed in rat-catching became infected, though of course they had been instructed to take every known precaution.

It is known now that Mites only crawl up from the ground when attracted by the immediate proximity of a host, and do not, as was formerly thought, get brushed off grass or low shrubs by the passer by.

Their speed of travel has been estimated to be five inches per minute on wood, as against one inch per minute on muslin, and two inches per minute on some other varieties of cloth.

They are equally active by day and by night.

(Kohls,G.M. et alia. 1945.)(Ref. 79.)

While it is true that the Mites die readily on dessication it appears just possible that the outdoor rats came into tents or buildings, in search of food, or because of the wholesale clearance of the scrub which had been their natural habitat, and brought the Mites in with them. In view of their relatively rapid rate of travel upon wood, the Mites may have reached their victims while they were lying in bed.

Further support was given to this view by the result of consideration of the distribution of the

position of the eschars on the body. Of the eschars seen 56% were found to be upon the upper part of the body, and, in particular, only 5% were seen upon the thighs below the gluteal fold and only one was found below the level of the knee.

One further point worth mentioning is that although the Field Supply Depot and C.B.I.D. were within three hundred yards of the sites mentioned above and would be expected to have attracted large numbers of rats, in point of fact no cases came from these Units.

As a result of the conviction that infection was occurring to some extent at least in doors, extra instructions were issued advising that, in addition to using Di-Butyl-Phthalate on clothes, it should also be sprayed on charpoys, beds and bedding, and, if possible, on floors at weekly intervals.(By this time the Typhus Research Team had left us or we would have asked their Acarologist to examine samples of the dust from tents and floors etc. for insect counts.)

x. Preventive Measures Employed.

In addition to the use of D.P.B., frequent bathing with soap and water was advised with special instructions to pay extra attention to the axillae and crutch, sites of election of the larval Mites possibly on account of

their warmth and moisture.

Dr. Kenneth Mellanby of the B.M.R.C. told us that Benzyl Benzoate Emulsion 5% was more effective in killing Mites, but this was not available to us.

Evacuation of a site as a measure designed to prevent further cases seemed rather useless in view of the spontaneous cessation of incidence within about three weeks or less, by which time all the cases likely to get the disease seemed to have contracted it.

It was difficult, however, to avoid advising evacuation if an alternative site could be pronounced free from infection and safe. This was unfortunately a real difficulty, for although there were known hyper-endemic foci there were also scattered cases coming from all over the entire district in ones and twos wherever there was a body of troops stationed, and apart from the hill station of Maymyo, forty miles away, no area could be pronounced to be safe.

As will be related in Part II, prophylactic inoculation was tried later in the Season.

SECTION VI.

Clinical Features of Scrub Typhus in Mandalay.

The outstanding features of the disease essentially conformed to the classical description of Scrub Typhus elsewhere.

First of all a review of the features of the disease will be given and then each system will be considered separately.

(a.) Incubation.

The Incubation period in these cases could not be assessed accurately because of the period of exposure to infection was equal to or greater than the incubation period but the outside - limit was less than twenty-one days.

It is known from the Port Moresby cases (Blake, Maxcy, et alia) (Ref.14.) that the incubation period is usually ten to twelve days.

Within this period, and usually about five days before the onset of symptoms, a papule may have been seen, but, being painless, and producing no itch, occasioned no interest or concern to the patient, and, indeed, in most cases he was quite unaware of its existence prior to examination.

This papule became the Eschar, characteristic of the disease, which has been thought by some to be produced by the stylostome of the larval Mite being left in the skin.

(b). Prodromal Symptoms and Onset.

During the last few days of incubation there was usually complaint of lassitude, anorexia, insomnia, vague malaise, a definite severe frontal headache, aching limbs, and the lymphatic glands, especially those related to the site of the eschar, became palpable and tender.

On completion of the Incubation Period the onset was sudden, ushered in with shivering, possibly a rigor, and rapid rise in temperature reaching a 103 Deg.F. within forty-eight hours, and, apart from small remissions of one or two degrees lasting only a few hours, remaining at that level.

Intense frontal headache and retro-orbital pain were usual accompaniments, and a short hard unproductive cough with pains in chest, back, and limbs were common.

Vomiting, though occasionally an early symptom, was more commonly seen in the second than first week of illness.

Within a few days there was usually suffusion of the

eyes with congestion of the conjunctivae, and in the first week congestion of the pharynx was usual.

This suffusion of the eyes accompanied by drowsiness and a curious appearance of immobility was so characteristic that, after experience of these cases, one could enter a ward and, looking round from one end pick out the probable fresh Typhus Cases. They gave the impression of being present in body but absent in mind.

Within the first week the lymphatic glands of groin, axilla, and neck, were found to be enlarged and the largest of these was usually an excellent guide to the position of the Eschar, when there was one present.

Since anti-malarial treatment was given routinely to all cases (by Army Order) the failure of fever to respond within a few days helped to eliminate Malaria as a possibility.

Somewhere between the fourth and sixth days of illness a maculo-papular rash was occasionally seen (18% of cases), the tongue became furred, dry, and cracked, while fever continued without remission, or with remissions of two degrees lasting only a matter of hours. Marked apathy with complete lack of interest in food and surroundings made close nursing attention essential.

(c). Second Week.

By the beginning of the second week the cough had become most troublesome, hard, persistent, and unproductive, with rales, rhonchi, and inspiratory spasm. Some cases by this time were showing cyanosis, central and peripheral.

Progress of the disease was steady and remorseless, the face became bloated and besotted looking, the patient spent his days in a torpid state and his nights in great restlessness.

Usually by this time he was querulous, though he evinced little or no interest in his illness, and although obviously ill, rarely looked as seriously ill as his Temperature Chart would have led one to expect.

His breath was foul, and the presence of a number of such patients in a room produced a peculiar unpleasant odour noticeable on entering. The most constant attention to Oural Hygiene failed to prevent sordes from collecting on lips and teeth and some complained of persistent thirst.

By this stage the Spleen was easily palpable and possibly tender, while the Liver was occasionally palpable but rarely tender.

Deep Reflexes were diminished or lost and superficial slightly diminished. Vomiting was occasionally serious to a degree necessitating Intra-Venous or Rectal feeding. Hiccough, when present was usually most severe and intractable and Tympanites might have appeared by the end of the second week. By this time the Rash, where present had usually faded and Constipation was usually absolute.

(d). Crisis.

If Defervescence had not occurred earlier, the Twelfth to Sixteenth days of illness were most critical.

By then Toxaemia was at its height and the patient was immobile, unresponsive, refusing even fluids. The tongue was perpetually dry, the eyes lustreless and expressionless, and there were signs of bronchitis or patchy consolidation in both lungs, accompanied by marked Dyspnoea.

The pulse was rapid and of small volume (in contrast to the earlier Bradycardia), Blood pressure low to the point of collapse, and in some cases oedema of legs or sacrum complicated matters.

(e). Decline.

(e). Decline.

Usually at the sixteenth day or thereby events took a turn for the better, but, if not, rapid decline occurred with death in a few days.

In the latter cases, incontinence of urine and faeces, muttering delirium, circulatory failure with hypostatic ordema of the lungs, presaged coma and death.

(f). Recovery.

Recovery was by lysis, remarkably rapid, accompanied by a marked diuresis and commonly with drenching sweats. Blood pressure rose, reflexes became increased, and physical signs in heart and lungs rapidly cleared up.

Brightness and awareness rapidly returned and sleep resumed its normal rhythm.

In a few cases when recovery seemed assured complications arose which greatly lengthened the fever and prolonged convalescence.

(g). Convalescence.

Five to six weeks later the patient had but slight glandular enlargement, blood pressure was normal or above, deep reflexes usually increased, and superficial

reflexes normal. Heart and lungs were now normal and the patient regaining strength slowly. By seven to eight weeks he was getting around comfortably and by ten weeks was usually ready for evacuation to Convalescence.

A small proportion of cases were distinctly milder and fit for Convalescence in five to six weeks, and fit for duty in two months. The average case was unfit for three months, and the more serious cases for six months.

(h). Physical Signs considered in Detail.

1. The Eschar.

This, the Primary Dermal Lesion, the most helpful single sign in early diagnosis, was seen in 72% of cases, and was solitary in all but two cases where two lesions at approximately the same stage of development were found.

The distinct impression was gained that the more thorough research the higher would be the percentage of cases found to have Eschars. Three cases in this series who had eschars would have been missed for lack of complete examination because, one British and one Indian Officer and one European Catholic Priest,

each had an eschar on his penis or scrotum and modesty had hindered their thorough examination by the admitting Medical Officer.

As has been said, the patient was usually entirely unaware of the presence of the Eschar and was equally unable to account for it though some rational explanation was attempted.

The few who had noticed it thought that it had come about five days prior to the fever and none of them apparently had noticed the accompanying glandular enlargement.

Appearing as a papule (only observed in one case) it proceeded to pustulation, the stage at which it was usually seen on admission, and then usually became umbilicated, oval in shape, 5 - 7 mm. in diam., and 1 - 2 mm. deep, surrounded by a red areola of inflamed skin.

In warm, moist areas the surface of the pustule broke down and the lesion presented as an ulcer with a sloughing yellow base, which, on the scrotum and penis, tended to heal rapidly (by the twelfth to the fourteenth day) leaving very little trace, while on dry or exposed areas it became crusted with a dark coagulum. This, if left to separate spontaneously, did so in the third week, but, if picked off, an indolent

ulcer remained for four to six weeks leaving a much more noticeable scar than would otherwise have been the case.

On dry skin surfaces the Eschar crust normally separated in the third to the fifth week leaving a pale flexible scar surrounded by an area of pigmentation which was much more noticeable in European than in dark skins.

In only one case was the Eschar observed to abort at the papular stage without even pustulation, and this was in a case modified in all respects by the administration of Scrub Typhus Vaccine to the patient while he was actually incubating the disease.

No Eschar became the site of serious secondary infection nor was there any related lymphangitis noted.

Excision of the Eschar in a few cases had no effect on the general course of the disease or on O X K Titres.

The distribution of the Eschars on the body surface was puzzling when considered in relation to what is known of the Etiology and Epidemiology of the disease.

In 94 cases who exhibited Eschars it was as follows :-

Neck 9%.	Shoulder. 14%.		Axillae. 22%.		Chest 10%.		
Groin 13%.	Scrotum.) Penis.) Perineum.)	16%.	Flank.) Thigh.) Leg.) Feet.)	15%.	Arm.) Hand.)	1%.	

One curious point was that while in the first hundred cases of those with Eschars only five were found to have them on the scrotum, penis, or perineum, but in the last thirty cases no fewer than nine such were found.

This probably bears out the suggestion made above that the genitalia were not sufficiently thoroughly searched in the earlier cases.

Only one Eschar was noted distal to the knee - joint, none distal to the elbow - joint, and only one on the lateral surface of the arm over the deltoid. Approximately only five per cent were found below the level of the gluteal fold and this caused some speculation as to how the Mite came to bite at such a high level in the body, coming as it did from the ground.

It is known that it can and does travel upward toward warmth and moisture, and tends to settle on areas such as the genitalia and axillae for its tissue meal, but still it is surprising that it does not achieve penetration at lower levels

than indicated by the above figures. This appeared to confirm the view that in many cases the infection was contracted when lying down on the ground or when in bed.

One case had a typical Eschar behind the ear and as mentioned above no less than nine per cent were found to be upon the neck. Next to the moist areas the pressure points seemed slightly more liable to be points of election.

Some recent work by Philip and Kohls (1945) (Ref.144 and 79.) reporting on an epidemic in a small island of the Purdy Group called South Bat Island, states that some troops slept on hammocks and some on cots raised on wooden boards from the ground, and that none of those who slept in hammocks were affected. They state that insufficient numbers were involved to prove this suggestion of infection while in bed but it confirms the above findings. In this case rats were reported to be found everywhere crawling around the beds and the species was Rattus Concolor Browni. (Here also Mites were reported to have been found on pigs and on birds called Rails.)

The presence or absence of an Eschar appeared to have no influence on the severity of the disease and the removal of an Eschar produced no noticeable effect

upon the course of the illness. (Also c.f.Machella 1945). (Ref.107.).Lipman, (1944)(Ref.103) has described appearances on section of an Eschar:- The Ulcer base extends into the lower corium and consists of necrotic tissue infiltrated with polymorpho-nuclear leucocytes and lymphocytes. There is also mild perivascular infiltration of the vessels of the corium with monocytes.

2. The Rash.

A Rash was observed in only 23 (18%) of cases.

This rather low percentage is in part accounted for by the fact that only seven cases were met with in light-skinned Europeans, the remainder being Indian, African, and Burmese, in whom the rash is less easily detected visually but may be felt on light palpation.

The Rash most commonly appeared in macular form though less often the elements were markedly papular developing between the third and tenth day.

The macules and papules were deep rose colour, sparse, and blanched on pressure. The rash was centrifugal, commencing on the lower trunk and then spreading to the face and proximal portions of the limbs on both flexor

and extensor surfaces equally. In only one case the rash became partially petechial, remaining visible for four days and disappearing with lycis. The rash disappeared in reverse order from its appearance.

The intensity and duration of the rash appeared to bear no relationship to the severity of the disease.

In no case was it seen to involve the mucous membranes.

3. Skin.

In this series it was exceptional for a patient to perspire as freely as one would expect with a sustained fever: on the contrary, the skin was intensely dry and burning, and occasionally a fine, bran like, desquammation was to be seen. Possibly this was part of the mechanism evident in this disease for the conservation of chlorides. It is true, however, that in the critical days just prior to lysis, drenching night sweats were occasionally seen.

4. Adenitis.

The entire reticulo-Endothelial-System is severly affected so that within a few days of onset,

and certainly by admission, a few discreet, very small, rubbery glands were usually palpable, and occasionally visible in the Posterior Triangle of the Neck.

As the disease progressed, ninety per cent of cases showed significant enlargement of superficial lymphatics with a definite, tender, large, " sentinel" gland indicating the area of drainage in which to look for the Eschar.

This (general) adenopathy persisted into the third or fourth day of disease, and in those cases which came to Post-Mortem it was seen that this enlargement also involved glands of the mediastinum and mesentery.

In no case did the glands suppurate or lymphangitis appear. Excision of the Eschar did not cause the glands to disappear.

MICROSCOPICALLY :- the glands are reported by whom? to be very congested with their sinuses filled with macrophages, small round cells, and Red Blood Corpuscles.

5. Fever.

Though preceded by a period of malaise the onset of fever was quite sudden, usually reaching 102 degrees F. in 48 hours and 103 degrees F. within a further twenty-four hours.

The onset was only rarely accompanied by a rigor and the characteristic periodic remissions of Malaria were absent though lesser daily remissions of one to two degrees were common.

Several variations in the pattern of fever chart were seen, but there was a basic uniformity and the average duration of fever for all cases was (17.38) seventeen ~~to thirty-eight~~ days - Resolution was by lysis.

Most commonly the first few days showed daily remissions of two degrees to be followed by a period of continued fever lasting about tend ays. (See Temp.Chart 1.) Normally defervescence occurred about the seventeenth day but occasionally it was much delayed. Where the disease had not seemed sufficiently severe to be responsible for this prolongation of fever it was usually found to be due to super-added secondary infection and these cases responded well to Penicillin treatment. Examples

of this prolongation of fever may be seen in Chart 1. where the cause was an abscess in the thigh, (due to an injection of Convalescent Serum becoming septic) and Chart 2. Banta Singh, who developed Broncho-pneumonia. This latter chart is also interesting in that it illustrates peripheral collapse occurring on the 12th. day of illness (when Blood Pressure fell to 70 m.m. Hg. Systolic and 50 m.m. Hg. Diastolic.)

Although the more severe cases tended to have a longer fever, the most acute of all passed to a fatal termination within fourteen days of onset. (See Page 103).

It was noticed that there was a tendency for cases which commenced with a high, swinging, remittent fever, subsequently levelling out at 103.6 or 104 deg. F., to become exceptionally serious or fatal. (Charts of Kartar Singh, (Masters, and Manickam Nos. 5, and 10.)

Hyperpyrexia was occasionally met with but of itself was no great problem, responding as it did quite readily to simple hydro-therapeutic measures. Temperatures of 106 - 107 deg. F. were sometimes recorded, with subsequent recovery.

Occasionally a Pseudocrisis occurred on

the 6th. - 10th. day, only to be followed by a resumption of fever and the former symptoms. (See Temp. Chart 4.) Not only did the fever subside but for a brief twelve to twenty four hours the general condition of the patient was greatly improved.

Recovery from illness followed by Relapse was not seen, but Machella (1945) reports one case of true relapse. (Ref. 107.)

Another type was the case which ran a short course but while fever lasted was very severe. (See Charts of Muthisa-6, and Cotte-7.)

There was frequently occasion to remark that the patient did not look as ill as his lengthy and dramatic temperature chart would have led one to expect, and this seemed specially noticeable to visitors, lay and medical.

This feature was outstanding in the Inoculated cases (described in Part 11) and is usual in cases of Kala-Azar, where, however, there is a bright mental state in contrast to the lethargy of Scrub Typhus.

TABLE I.

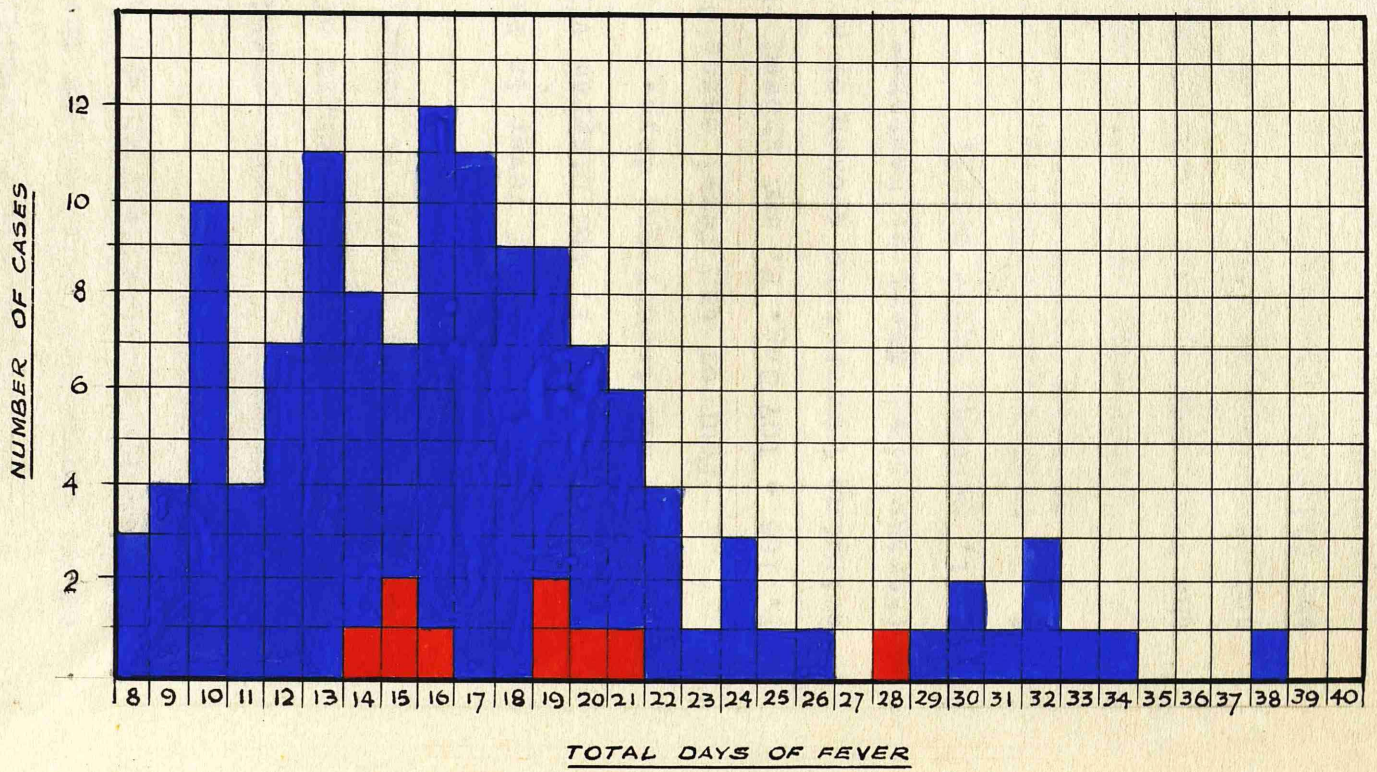
O X K Agglutinations and Length of Illness in Fatal Cases.

Name.	Case No.	Age.	Days III B.A.	Day of Death.	AGGLUTINATIONS. 7.	14.	21.	28.	Date of Death. 1945	Eschar.
Masters.	20.	25.	2.	19.	50.	100.	250.	-.	7/7.	L.Thigh.
Andi.	24.	30.	5.	14.	25.	125.	-	-.	9/7.	Nil.
Dalwar Khan.	33.	28.	4.	20.	50.	100.	(19) 150.	-.	12/7.	R.Groin.
Kartar Singh.	55.	35.	4.	21.	25.	250.	500.	640.	23/7.	Nil.
Nanku Das.	60.	22.	3.	16.	-	80.	320.	2500.	28/9.	Scrotum.
Bantu.	67.	50.	3.	28.	160.	-	-	-	16/9.	Axilla L.
Sankar Nair.	76.	21.	2.	15.	-	160.	640.	-	13/10	L.Chest.
Manick -am.	80.	30.	10.	19.	-	80.	0.	-.	11/11	L.Axilla.
Koya- Muslier.	92.	38.	7.	16.	40.	160.	-	-	7/12.	R.Scapula.

DIAGRAM VIII.

NUMBER OF CASES FOR EACH GIVEN LENGTH OF FEVER (FOR 130 CASES)

NUMBER OF DEATHS ON GIVEN DAYS OF FEVER



The height and continuity of the fever was of no prognostic value though the length of fever was usually proportional to the severity of the infection.

Diagram VIII shows graphically the number of cases which had a given length of fever and the days upon which death tended to occur. (None in this series died afebrile).

The length of fever in Fatal Cases will be seen from Table I. and Diagram VIII to vary between fourteen and twenty-one days.

Four of the fatal cases died in Hyperpyrexia T. 106 - 107 deg. F. and showed the violent swinging Temperature spoken of above (P.46). (Kartar Singh Chart 5: Manickam, Chart 10: Masters : Andi, Sankran Kutty Nair).

6. WEIL-FELIX REACTION.

This test was carried out as a routine on the 7th., 14th., 21st., and 28th., days of illness and occasionally later, for the confirmation of the Clinical Diagnosis.

An agglutination of the OXK strain of Bacillus Proteus by the patient's serum at dilutions of I/I25 and above was taken to be diagnostic of the disease.

TABLE II.

Table Illustrating Tendency for Titre of O X K to Rise in Inverse Ratio to the Length of Fever in Days.

(a). SHORT SHAPP FEVERS RAPID EARLY RISE IN TITRE.

Name.	Length of Fever.	Agglutinations.	Severity.	Temp. Chart No.
Muthisa.	9 days.	1/2,500 (10th day).	Mild.	6.
Cotte.	12 days.	1/320 (10th day).	Mild.	7.
Pipot Raj.	10 days.	1/3,200 (10th day)	Mild.	12.
Ramzan.	13 days.	1/5,120.(12th day)	Mild.	11.

(b). LONG FEVERS - SLOW RISE AT FIRST - RAPID IN CONVALESCENCE.

Bose.	22 days.	240 (21st). 5,000 (27th) 10,000 (40th).	Fairly Severe.	14.
Petchai.	25 days.	40. (13th). 80. (20th). 160. (25th),	Very Severe.	15.
Simeon.	28 days.	50. (14th). 160. (27th). 640. (40th).	Very Severe.	13.
Nagiah.	38 days.	25. (12th). 125. (30th). 640. (49th).	Very Severe.	9.

This titre was met with as early as the 5th day but more commonly much later, between the 14th and 21st days.

A few (12%) cases which were quite definite with full clinical picture including rash and Eschar (10% out of 12%), never reached a diagnostic level at all. (This was possibly due to the serum being spoilt by travelling 100 miles).

It was unusual to find much increase in titre of O X 19 (such as appears in Epidemic Typhus) above 1/40, but in one case Sep.Lachman Singh, O X K and O X 19 both agglutinated in rising titres thus:-

(See Temp.Chart 8.)

12th day ... O X K ... 1/125 O X 19 ... 1/250

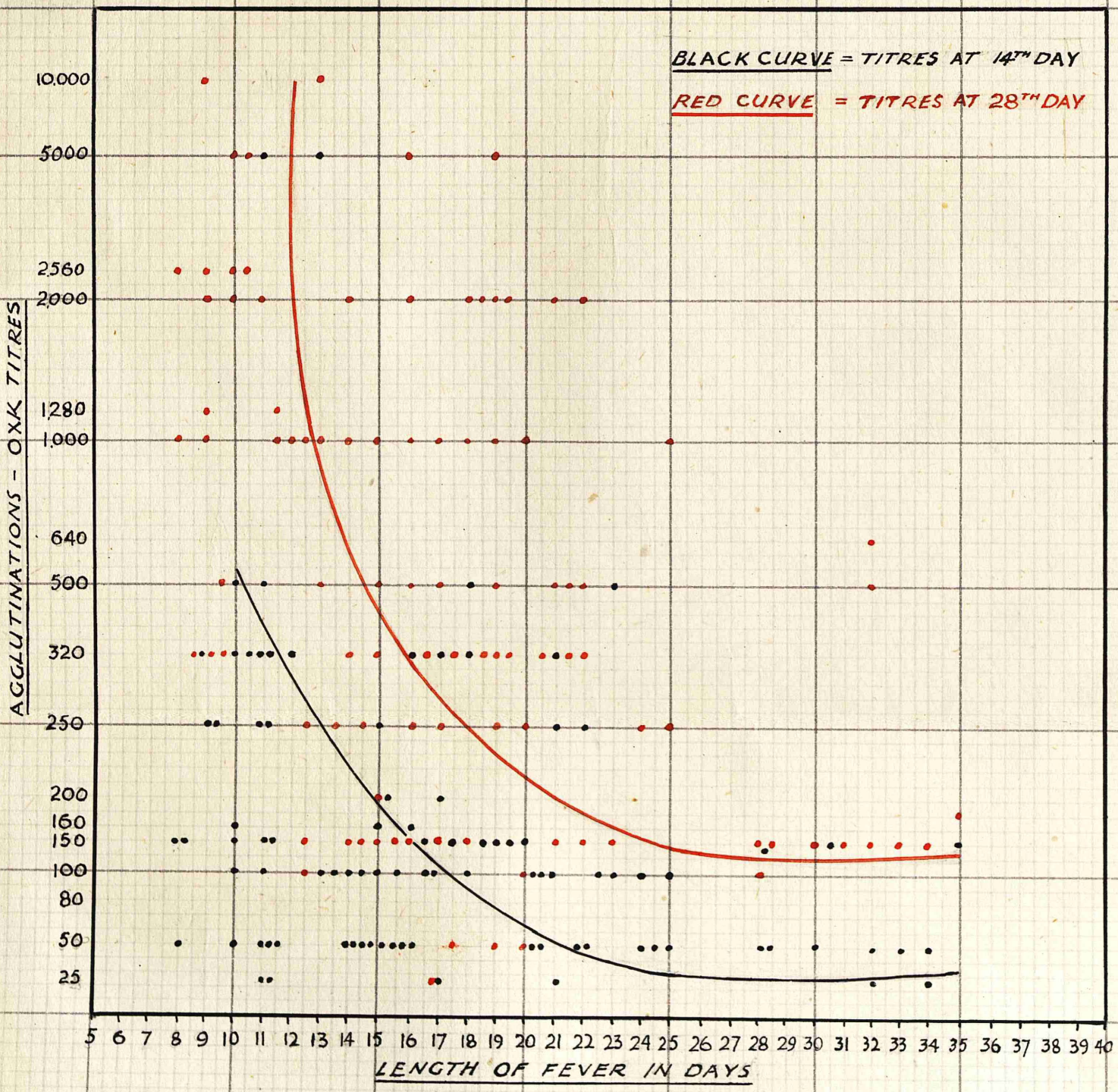
18th day ... O X K ... 1/500 O X 19 ... 1/500

The fever in this case lasted 18 days and in falling the O X 19 titre came down first. In all other respects this case was classical. In only one other case did O X 19 rise as high as 1/80.

Severe cases, and cases which terminated fatally, showed a late rise in O X K titre, in the former case only becoming Diagnostic in convalescence, and in the latter, only Diagnostic just prior to death.

DIAGRAM IX

SCATTERGRAPH SHOWING AGGLUTINATIONS AGAINST OXK ON 14TH • AND 28TH • DAYS OF ILLNESS ARRANGED ACCORDING TO LENGTH OF FEVER IN DAYS. (FOR 96 CASES)



One fatal case (Manickam Chart 10) only reached a titre of 1/80. (See Tables I & II. Cases 5 - 8.) (See also Scattergraph, Diagram IX.)

This tendency of the titre to rise in inverse ratio to the length of the fever in days, was most noticeable.

Patients who showed a rapid, favourable, though sharp reaction to the disease, invariably showed an immediate high titre rise. (See cases I - 4 Table II. Also Scattergraph, Diagram 9.) (Temp. Charts 6 , 7 , 11,& 12.)

From these and similar results it was deduced that a rapid and early rise in titre was a very favourable prognostic sign, and, as might have been expected, a slow rise was evident of a poor immune body response.

This conclusion was followed up and the agglutinations on the 14th and 28th day were plotted against total length of fever in days, for 100 cases producing the Scattergraph, Diagram IX.

It will be seen that in just the very cases where a confirmatory significant agglutination would be of importance, one finds that a rise in titre is so late in developing as to be of merely academic interest proving a case which is by then quite obvious when the patient is convalescent or moribund. In

a majority of cases maximum titres were not reached until the 28th day, and some even as late as the 45th day.

Slide Agglutination Tests.

These were carried out for all the early cases. (In accordance with instructions laid down in Memorandum No.12 of Medical Directorate, Allied Land Forces, S.E.A. dated 19th Feb.45). The tests were done in conjunction with Weil-Felix Reactions but were found to be so much less sensitive, and, as has been indicated above, the latter themselves were not too helpful, so slide agglutination methods were accordingly abandoned.

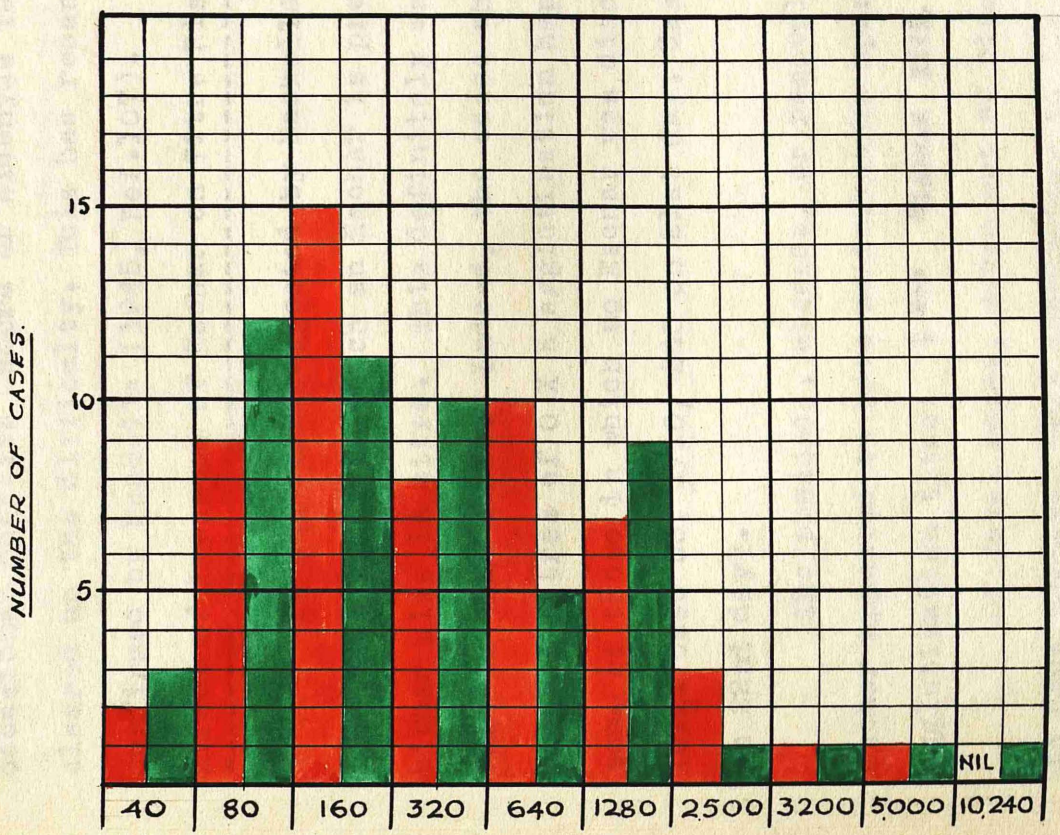
False Positives were rare, and in this group there was only one case. This was a Weil's Disease which came in the midst of a group of Scrub Typhus cases and was not immediately recognised, in that the early O X K titre was 1/320, but the jaundice and polymorphonuclear leucocytosis gave the correct diagnosis.

In Kala-Azar there is a rise in the titres of all three Proteus Suspensions. This fact gave rise to some difficulty to the writer during an epidemic of this disease in Chittagong, East Bengal, in the Winter

DIAGRAM XIII

DIAGRAM SHOWING THAT PRESENCE OF AN ESCHAR DOES NOT AFFECT TITRE.

(TITRES TAKEN ON 21ST DAY)



of 1944-5, but in no case did the titres rise to diagnostic level and the finding of the Leishman-Donovan Bodies in Spleen, or Sternum, with an occasional positive Chopra or Aldehyde Test, cleared up the difficulty. This has recently been confirmed by Machella (1945, Ref.107).

Effect of Presence of Eschar on Titre Rise and Severity.

It has been suggested by Machella (1945, Ref. 107) that cases in which an Eschar is present show a higher rise in titre. This definitely was not the case in this series. Indeed, the cases which had the highest titres of O X K agglutination happened to be some of those in which no Eschar was discovered. (e.g. Case 53, 1/10, 240 on 21st day; Case 23, 1/5000 on 22nd day).

The presence, absence, or removal of the Eschar appeared to have no influence upon the agglutination titre. (See DIAGRAM XIII.)

Of fatal cases, seven out of nine were found to have Eschars. This corresponds to the overall finding of Eschars in 72% of all cases. Machella's statement (Ref.107) that the presence of pneumonia does not affect the titre was confirmed.

SECTION VII. (i) RESPIRATORY SYSTEM.

one of the helpful early symptoms of Scrub Typhus is a persistent, hard, unproductive cough, which greatly aggravated any headache which was present. Fully 90% of patients complained of this within the first week and this often gave the hint that a case was Scrub Typhus rather than Malaria.

Less important and less frequent (45%) in appearance, was a mild sore throat which on examination showed slight injection of the fauces and pharynx.

Toward the end of the first week it was noted that aeration became very defective in both bases. This sign was so constant as to be regarded as definitely suggestive of Typhus.

Next, within the few days following appeared medium sized rales and a few rhonchi, more in the apical than other fields.

Another interesting sign appearing about the 7th to 10th day of illness was an intermittent Tachypnoea, variable from time to time throughout the day, and in the more serious cases becoming constant, troublesome, and characteristic, in that chest

movement was almost entirely apical and Vital Capacity seemed to be greatly impaired. Although the bases seemed to be very little aerated yet they did not necessarily become congested and rarely were consolidated.

This Tachypnoea was doubtless in part due to Raised Body Temperature, External Moist Heat, and the Anoxic process resulting from the Specific Vasculitis, but probably the principal cause was a direct toxic action on the Respiratory Centre in the Lower Pons and Upper Medulla.

Insufficient additional Oxygen is taken up in the over-ventilated area to compensate for the Incomplete Saturation in the under-ventilated Alveoli so the blood is liable to be Oxygen Deficient. (Samson Wright, 1940).(Ref.202). Anoxia due to such shallow breathing tends to set up a vicious circle which tends to aggravate the original condition.

As the disease progressed into the second week, a frank diffuse Bronchitis developed in 55% of cases with the production of muco-purulent, tenacious sputum, rarely tinged with blood, and in no great

quantity.

A further 10% went on to the development of a patchy pneumonitis with ill-defined consolidation and "Rusty Sputum".

Two only developed Lobar Pneumonia and one of these went on to an empyema, from which Staphylococci were isolated.

This complication cleared very satisfactorily with local and parenteral Penicillin.

Pulmonary Infarct was suspected in one case and two cases developed a severe Acute Laryngitis.

Hypostatic Congestion developed at some stage in all very severe cases.

Post Mortem Appearances. (Nine cases.)

All cases except one showed intense congestion of both lungs with marked injection of the mucous membranes of trachea and bronchi. Muco-purulent secretions, in a few instances blood-stained, were contained. The bases were Oedematous.

Four cases showed patchy red hepatisation but in each of these cases the segment of lung affected floated in water.

Two cases showed multiple pulmonary abscesses, mainly peripheral in distribution, each

abscess quite small and discreet and giving rise to no recognisable physical sign in life. These may have originated in infarcts. In only one case were the lungs noted to be macroscopically normal at P.M., and this was the more remarkable in that there had been the usual Bronchitic signs with diminished basal aeration clinically, in life.

Pleurae. Apical adhesions involving visceral and parietal pleurae were noted to be almost universal in P.Ms. on Indian subjects and in only one of the nine cases did the pleura permit the lungs to be removed easily.

One case showed small sub-pleural haemorrhages in the lungs and two cases were found to have each a few ounces of serous effusion in the pleural space.

Ulceration of the Larynx has been described to occur (Maj.Miller, A.A., R.A.M.C.) in this disease but was not met with.

SECTION VII (ii). Circulatory System.

The Pulse Rate during the first week showed a relative bradycardia in a majority of cases.

During the second week of illness this disparity evened out, and, if the case proceeded into a third week of fever the pulse was likely to rise to one hundred and twenty to one hundred and thirty per minute, and to become thready and feeble.

Accompanying this increase in rate was a steady fall in systolic and diastolic blood pressure, or in a few cases, a sudden fall in systolic and diastolic pressures to 80/50 m.m. Hg. in a Cardio-Vascular collapse, both Ventricular and Peripheral.

In such a collapse the patient was cyanosed, cold, clammy, and pulseless at the wrist, resembling a case of Neurogenic Surgical Shock.

The Cyanosis was of a peculiar character with central and peripheral components, and the general effect in appearance was a "blue-grey pallor" of the skin, of the face and extremities especially, and less well seen on the trunk. It did not necessarily accompany peripheral collapse and was seen on occasion apart from this condition and where there was no pneumonitis. The phenomena seemed to be the result of toxic action on the neurogenic control of

DIAGRAM X

DIAGRAM SHOWING COURSE OF BLOOD PRESSURE IN SCRUB TYPHUS – FOR SIX CASES – (NUMBERED)

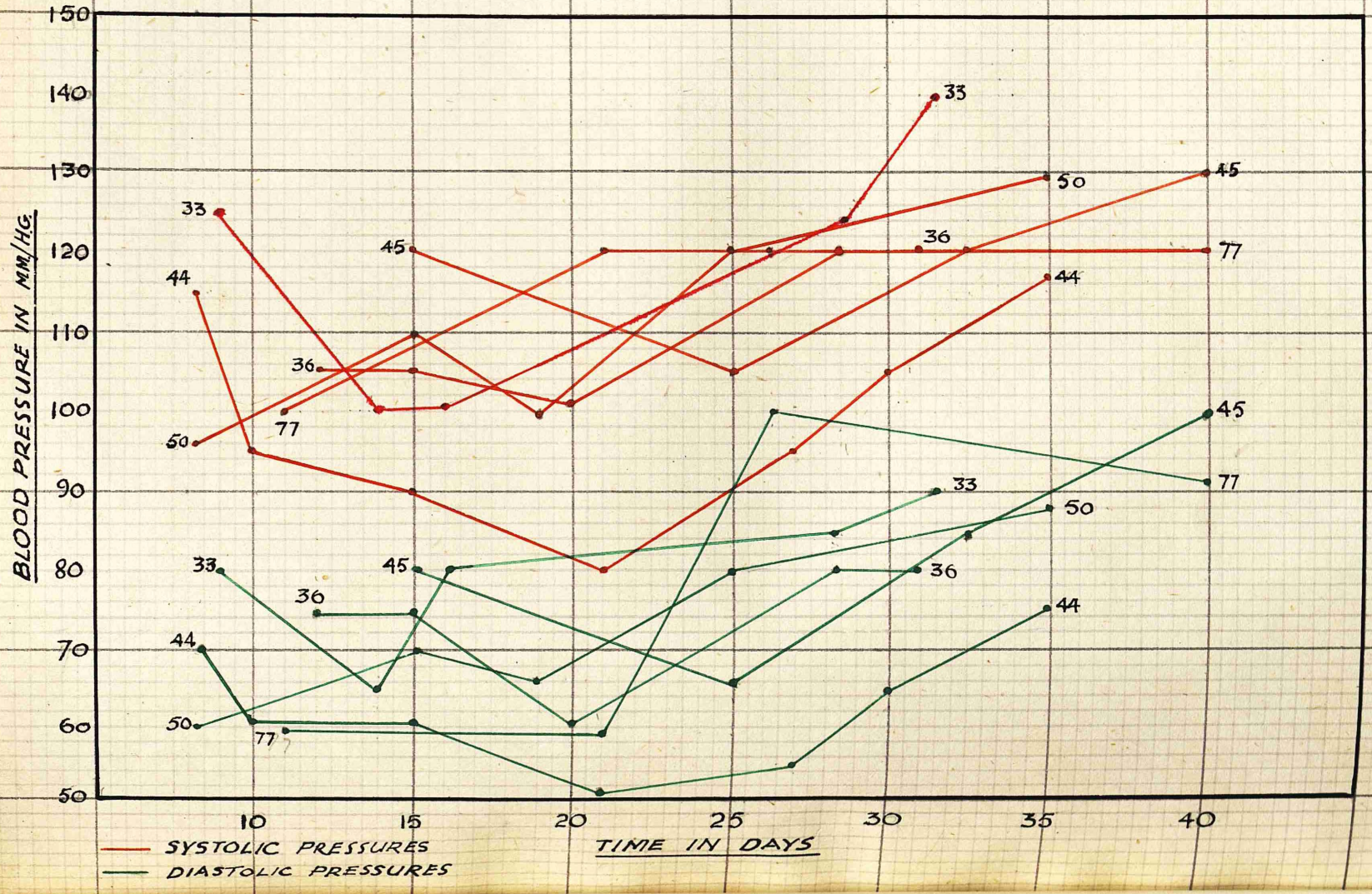


TABLE III.

SHOWING TENDENCY TO RISE IN BLOOD PRESSURE DURING CONVALESCENCE.

(Four Series of Ten Cases as Samples).

Case No.		Admission.	1st Week.	2nd Week.	3rd Week.	Discharge.
	S	105.		95.		118.
1.	D	75.		60.		85.
	S	120.		100.		135.
2.	D	80.		65.		100.
	S	100.		90.		130.
3.	D	70.		60.		90.
	S	100.		100.		120.
4.	D	70.		65.		85.
	S	110.		100.		140.
5.	D	80.		70.		95.
	S	110.		95.		130.
6.	D	80.		70.		80.
	S	120.		105.		135.
7.	D	80.		75.		100.
	S	120.		100.		140.
8.	D	80.		70.		100.
	S	120.		110.		150.
9.	D	70.		65.		100.
	S	105.		95.		125.
10.	D	75.		65.		85.

	S	95.	110.	100.	130.	120.
50.	D	60.	70.	65.	90.	90.
	S	105.	120.	110.	90.	110.
51.	D	70.	80.	75.	65.	80.
	S	110.	100.	90.		100.
52.	D	75.	65.	60.		75.
	S	120.	120.	100.		110.
53.	D	80.	80.	70.		80.
	S	90.	95.			110.
54.	D	65.	65.			80.
	S	120.	110.	90.	80.	
55.	D	80.	70.	65.	50.	Died.
	S	120.	110.	100.		120.
56.	D	60.	70.	65.		80.
	S	110.	110.	105.	95.	120.
57.	D	65.	65.	65.	55.	70.
	S	110.		80.	110.	110.
58.	D	60.		50.	75.	80.
	S	100.	110.	105.		120.
59.	D	65.	50.	50.		80.
	S	110.	100.	90.	110.	125.
60.	D	70.	60.	50.	60.	85.

TABLE III (CONTINUED).

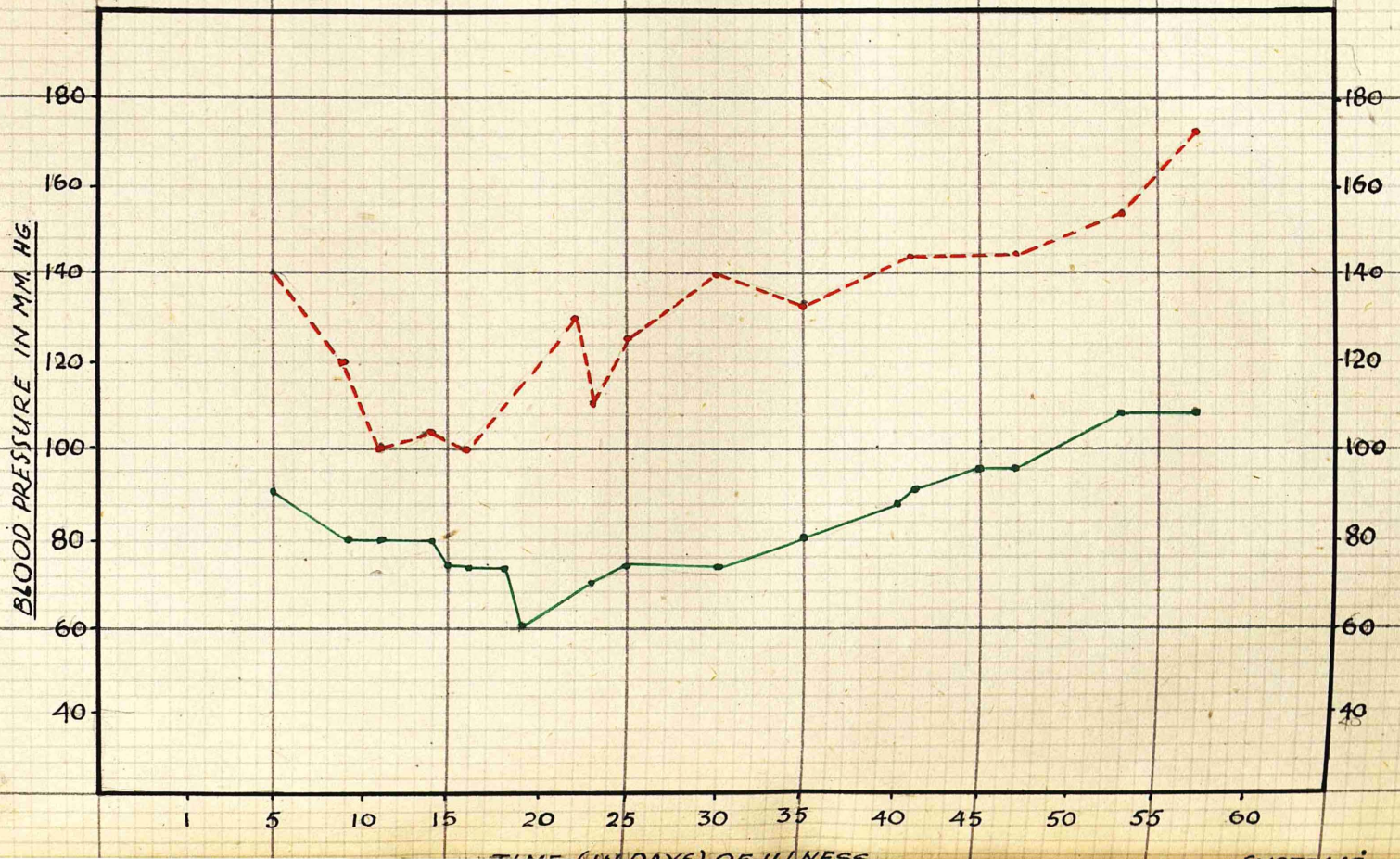
Case No.	On Admission.	1st Week.	2nd Week.	3rd Week.	Discharge.
	S : 95.	85.	100.		120.
100.	D : 55.	45.	60.		80.
	S : 130.	115.			120.
101.	D : 75.	70.			80.
	S : 120.	110.	75.		
102.	D : 75.	70.	45.	DIED.	
	S : 110.	100.	85		120.
103.	D : 60.	50.	45.		80.
	S : 110.		100.	140.	140.
104.	D : 65.		70.	80.	85.
	S : 110.	110.	100.		135.
105.	D : 60.	70.	70.		90.
	S : 100.	100.	110.	110.	110.
106.	D : 70.	70.	70.	50.	70.
	S : 95.	90.	80.		120.
107.	D : 55.	55.	45.		80.
	S : 90.	95.	80.	100.	120.
108.	D : 60.	60.	50.	60.	70.
	S : 100.	90.	90.	90.	110.
109.	D : 70.	50.	60.	60.	80.

	S : 110.	100.	85.	100.	130.
70.	D : 60.	65.	60.	70.	90.
	S : 100.	80.	70.		
71.	D : 65.	50.	45.	DIED.	
	S : 100.	85.	90.	100.	110.
72.	D : 70.	60.	60.	80.	80.
	S : 100.	95.		110.	130.
73.	D : 60.	55.		90.	90.
	S : 110.	110.			125.
74.	D : 65.	60.			85.
	S : 100.	110.	100.		120.
75.	D : 65.	65.	70.		80.
	S : 140.	120.	100.	100.	175.
76.	D : 80.	75.	80.	70.	110.
	S : 100.	110.	120.	125.	135.
77.	D : 60.	65.	80.	90.	95.
	S : 100.	100.	100.	105.	125.
78.	D : 60.	50.	55.	60.	85.
	S : 90.	100.	80.	80.	115.
79.	D : 65.	65.	50.	50.	80.

DIAGRAM XI

BLOOD PRESSURE CHART – HARI SINGH (CASE 76)

(REPORTED IN FULL IN APPENDIX "B")



Extensive oedema of the legs and sacral cushion were indications of threatened heart failure and usually signified a grave state, but a few cases were seen where it appeared quite suddenly in the absence of any sign of cardiac or renal failure and disappeared equally mysteriously. This condition is considered further on pages 85 and 86.

Blood Pressure.

Variations in blood pressure were particularly observed in all cases. The results were charted and a selection of these is recorded graphically in Diagrams X, and X1, and the remainder in Table III.

The results briefly stated are these:-

On admission, Systolic and Diastolic levels were within normal limits or had already commenced the slow steady fall which appears in most cases with the development of the disease in intensity.

In a few cases, as has been described above, there was sudden peripheral collapse during which figures of 75 - 80 / 35 - 50 mm.Hg. were registered. (See Temp.Charts 2, 3, & 8ii).

During the recovery phase both Systolic and

Diastolic Pressures rose steadily and by the fourth week from onset had regained their former level.

Next followed a period of reaction during which Systolic, and to an even greater extent Diastolic, pressures rose above the level maintained prior to illness, so that readings of Systolic 140 - 150 m.m.Hg., Diastolic 95 - 100 m.m.Hg., were common.

In the fifth and later weeks, both Systolic and Diastolic tended to remain high and most cases passed out to Convalescence at the end of nine to ten weeks with Blood Pressure still raised above admission levels.

It is usually stated (Napier 1943.Ref.201) that once recovery has been made there are seldom any after effects in the circulatory system, and, in general, this appears to be the case.

In two cases however of rather above average age (44 and 50), the cardiac condition gave rise to some concern during recovery and all the signs of acute myocarditis were present.

After removal from the Acute Ward when afebrile,

it was necessary to bring one of them back once, and the other twice, for greater care and attention on account of extreme breathlessness on the slightest exertion, and both of them were evacuated after ten and twelve weeks respectively, as "Lying cases" recommended Discharge from the Service.

Several cases developed a Cardiac Neurosis, well named by Blake and Maxcy (1945) (Ref.14.) "Neuro-circulatory Asthenia".

Histo-pathology.

The basic Histological change in Scrub Typhus is known to be endothelial thickening in the finest bore capillaries. Since this affects most organs, ultimately, all the well known signs can be attributed to this process.

The arteries and arterioles show a focal vasculitis and perivasculitis which produces the various symptoms and signs. "Typhus Nodules" have been found in various tissues including heart and brain.

Post Mortem Appearances.

Macroscopically no change was noted in the Blood Vessels. The Heart was only found to be enlarged in one case, the remaining eight being normal, or slightly smaller, in size, and in systole. The one which was found enlarged showed right sided dilatation. In a few cases the muscle was flabby but in the others apparently quite normal, valves were competent and sound and the coronary arteries patent. The only abnormality was the presence of tiny sub-pericardial haemorrhages in five cases. Surprise was always expressed at the apparent normality of the organ.

The Pericardium.

In two cases the Pericardial space contained a few ounces of serous fluid,.

SECTION VII. (iii). Gastro - Intestinal System.

i. The Tongue Within the first few days the tongue became dry and centrally furred, the coating in the first place being whitish, and later brownish in colour. As the disease progressed

the dryness increased and the tip tended to become raw first of all, and in some severe cases, the entire tongue gradually became like "raw meat".

In other severe cases the tongue looked shrunken and dry, or cracked and leathery, coated with sordes, defying the best efforts of the Nursing Staff to keep it moist.

ii. Abdomen.

It is commonly stated that the abdomen is retracted in this disease, but in this outbreak it was not so: indeed, on the contrary, one of the most troublesome and persistent signs was Tympanites. (c.f.Williams & Sinclair, 1944).(Ref.184). This was preceded and accompanied by severe constipation, and neither condition was materially relieved or effectively prevented, by any amount of attention to evacuation. Each patient had ten to twelve and even more pints of fluid measured out to him daily, was given a saline or vegetable purgative, had frequent saline bowel wash-outs and rectal flatus tubes passed. In the most severe cases these measures were entirely ineffectual in

preventing constipation, and in 40% of all cases, Tympanites appeared and was most troublesome.

In some it was a serious factor, ballooning of the bowel having become so marked as to hinder free movement of the diaphragm, and so still further diminishing Vital Capacity. 'In one case it was felt that this was the precipitating cause of death. Pituitarin and Acetyl-Choline were tried in varying dosage for this complication with little effect.

Bowel stasis was probably a factor in the reduction of Plasma Chlorides, in the rise in Blood Urea, and in the production of an Alkalaemia.

Diarrhoea.

This was uncommon (eleven cases) and easily controlled when present.

Hiccough.

This symptom was present in twenty two cases. It was a serious sign developing usually during the second week of illness, persistent and not at all amenable to treatment. One Typhus Research worker (Dr.Browning of the B.M.R.C.) who had been working with us subsequently contracted Scrub Typhus and had

to be placed on the " Dangerously Ill" List purely on account of the severity of this symptom. It was generally thought to indicate incipient Uraemia, but this did not seem to be the case invariably. Carbon Di-Oxide and Oxygen Inhalations seemed to help.

Vomiting.

This symptom was less common but equally persistent and resistant to treatment. Stomach lavage and Ryle Tube per-nasal feeding was necessary and very satisfactory for those who had neither the will nor ability to feed. (Rectal and Intravenous alimentation were given up as much less satisfactory.)

Abdominal Hyperaesthesia, - was marked in five cases.

Palpable Splashing Caecum, - was noted in twenty cases, but investigations of stool were negative for vegetative Amoebae Histolytica.

Post-Mortem Appearances.

Small sub-mucosal haemorrhages were noted in the stomachs of three cases, and, of Fatal Cases, all but two showed ballooning of the stomach, small

intestine, and to a greater extent Transverse, Ascending, and Descending Colon, collapsing with an audible hiss on being punctured. One case showed a large, long standing, Amoebic Type ulcer one inch in diameter and irregular. This was situated in the ascending colon two inches above the caecum, showed signs of recent haemorrhage and was probably responsible for a preterminal haemorrhage from the bowel.

The only other abnormality noted was petechial, sub-mucosal haemorrhage in the ileum of one case.

SECTION VII.(iv). Genito-Urinary System.

No symptoms referable to the Reproductive System were met with but it is stated (Blake, Maxcy et alia, 1945) (Ref.14.) that Orchitis with tubular atrophy may occur.

Urinary involvement was first evidenced by decrease in output during the acute phase of the disease followed by a diuresis accompanying defervescence.

This gave the curious effect of the appearance of a rapid loss of weight at a time when the patient was obviously on the way to recovery. (See Section on Fluid Balance . (Page 85 and 86.)

In spite of an intake of Sod.Chlor. gr.xx in

each pint of fluid, and a fluid intake of eight to twelve or more pints, daily, it was found that Urinary Chloride levels were constantly diminished proportionately to the severity of the disease. Readings of 2-3 gms. per litre were quite usual in severe cases. (Simultaneous records of Serum Chlorides levels were taken and these likewise were found to be low, (350 - 370 mgm/100 cc.) but the Pathologist felt that the only technique available was not sufficiently reliable to place any stress on the results.)

Retention of Urine necessitating repeated catheterisation was met with in one case as a late neurological complication. Fortunately lysis had occurred prior to its development or it would have produced a fatal termination in all probability, for this British Major had been in a very critical condition.

Frequency of Micturition was met with in a few of the severe cases but never seemed to be of much consequence in itself.

Of the nine fatal cases it was thought that two died in Uraemia: Urinary Output decreased to Nil and the Blood Urea climbed to as high as 354

mgm./100 cc. before death. (Kartar Singh.)

It was thought strange that in only a very few cases were significant changes found in the urine. Albuminuria was by no means constantly present in even prolonged fevers. This finding was doubted, tested, and proved personally on several occasions to be so. Rarely, hyaline casts were found.

The condition seen in the severe cases resembles closely the state of affairs produced by Renal Anoxia which has recently been described by Macgraith,B.G., Havard,R.E., and Parsons,P.S. (Ref.110.)

Post-Mortem Appearances.

Macroscopically, Pelves, Ureters and Bladder showed no abnormalities.

The Kidneys were found to be normal, or slightly increased in size, some pale, some congested and in a few cases, the cortex was thinner than normal. The capsule stripped readily in each case.

Subacute Glomerular Nephritis has been described (Lipman 1944) (Ref.103.) but was not detected

macroscopically in these cases.

Section VII. (v). Central Nervous System.

Symptoms and signs of Central Nervous involvement were to be found in practically every case. Most prominent among symptoms was Headache, which was severe in 55% of all cases. This headache was of a most persistent and intense character, chiefly frontal or behind the eyes, which themselves were suffused, injected with a distinct inter-palpebral band, and painful on movement. The headache was usually relieved by Salicylates and in any event tended to improve after the second week.

The one outstanding and constant physical sign was the marked reduction or loss of Deep Reflexes during the Acute Phase, with their return in the fourth week, and increase in fifth and sixth weeks and later, even to the extent of ankle-pseudo-clonus which was found in 12% of all cases at some point in their illness.(See Table below.) This pseudo-clonus persisted from the fourth to the seventh week and the late increase in deep reflexes for considerably longer.

The State of the Deep Reflexes at Three Stages in Scrub Typhus. (100 Cases.)

State of D.R.s.	On Admission.	3rd. Week.	6th Week.
Normal.	56.	18.	23.
Diminished.	34.	74.	2.
Increased.	10.	8.	75.

Superficial Skin Reflexes were found to be unaltered unless when coma threatened, when they were absent.

The Eyes.

As has been said elsewhere, the eyes were early suffused, with marked injection of the inter-palpebral band, (c.f. Col.Walker, I.M.S., unpublished paper) photophobia, and occasional sub-conjunctival haemorrhages.

The Optic Fundi of many patients were examined but apart from retinal engorgement no other change was noted by the writer or reported by our Ophthalmic Consultant.

(Blurred Discs with 1-2 dioptres oedema has been reported by Machella and Forrester 1945).(Ref.107.)

Tremors.

Tremors and twitchings of the limbs and especially of the fingers were notable in all severe cases. These signs increased with voluntary movement and appeared in cases which were showing muscular weakness. The movements were irregular and of considerable amplitude, not fine and rapid as in anxiety states. Incoordination was marked at times, to the extent of preventing patients who were otherwise making a good recovery from feeding and attending to themselves. This tremulous state lasted long into recovery, or, in fatal cases, passed into the pre-terminal carpofloggia.

Carpo-Pedal Spasm, and a Tetany-like condition were seen in five severe cases. In appearance it resembled closely the signs seen in the Tetany and Carpo-pedal spasm associated with rickets in children, but Chvostek's and Trouseau's signs were not able to be elicited. Lipman (Ref. 103) groups these cases with Cerebral Scrub

Typhus and states that in these the Blood Calcium was found to be normal. (Vide infra section on Alkalaemia.)

Paraesthesiae.

Lt.Col. G.A.Ransom's sign of " Tender Toes " was looked for but found positive only in about ten per cent of cases, and even then, in a late, rather than an early phase of the disease, so that it was of little diagnostic value.

Pain in the Metatarsal Joints and over the metatarsals was complained of by three patients, in all three during the recovery phase, and persisting about a week. To judge from their fear of having their feet touched the pain must have been intense.

Neuritis.

Pains of a severe neuritic type were met with in four cases, two of the shoulder muscles accompanied by some wasting, one of the upper arm, and one of both legs with patchy sensory loss.

Dysarthria.

Dysarthria due to inco-ordination of the labio-glossal musculature was seen in a few of the most severe cases prior to development of muttering delirium

and a terminal typhoid state. Where recovery occurred speech became normal gradually.

Deafness.

Deafness of the Inner Ear type was found in twenty-eight per cent of all cases. The incidence was distinctly higher for severe cases than for the remainder. Deafness commenced early and persisted well into recovery. In a few cases deafness was almost absolute, but even in the worst case there was great improvement before transfer to Convalescence. Quinine was not employed for Routine Anti-Malarial Treatment in this series so could not be in part responsible for the deafness as has been suggested by Kleine (1945) (Ref. 78).

Tinnitus : Not noted.
c.f. Mendell, T.H. (1946)(Ref.203). in 49% of cases.

Reversal of the Sleep-Rhythm.

This was troublesome in many cases during the second to fourth weeks of illness. This was one of several functions of the Hypothalamus disturbed by the disease. (Sleep Centre is in Sylvian Aqueduct of 3rd Ventricle.)

Coma.

Of the nine fatal cases, two died in a

coma which was thought to be Uraemic in origin. Blood Urea levels of 200/364 mgm./100 cc. blood were recorded prior to death.

The cerebral changes accompanying this coma were probably such as accompany increased intra-cranial pressure, in that they were not irreversible and could be relieved by 20 cc. of Intravenous Glucose 20% thereby restoring the patient to temporary consciousness. Cases dying in Coma are termed 'Cerebral Scrub Typhus' by Lipman (Ref.103.)

Cerebro-Spinal Fluid.

Facilities only permitted of this examination in a few cases though Lumbar Puncture was employed regularly for the relief of severe headache.

In such cases a rise in Cerebro-Spinal Fluid pressure was usual up to 250 mm. of water. In the few cases in which fluid was examined no notable abnormality was found. (Williams,Sinclair and Jackson 1944) (Ref. 184.) report a decrease in Cerebro-Spinal Fluid Chlorides below 700 mgm./100 cc. in 31 of 52 specimens examined. This decrease was more marked in severe cases, and twice as frequent where neurological signs were present.)

Post - Mortem Appearances.

Macroscopically, the surface of the brain was in all cases oedematous, the vessels of the pia-arachnoid were congested but no haemorrhages were observed on the brain surface or, after section, in its substance.

Microscopically, Round Cell and Plasma Cell "Perivascular Cuffing" is described, (Williams 1944) (Ref.184.) resulting in gliosis. This makes up the Typhus Nodule. There is endothelial proliferation and the vessels are plugged with leucocytes. (Lipman 1945) (Ref.103.)

Section VII.(vi). The Blood Cytology.

Red Blood Corpuscles.

No specific effect was noted to be produced upon the R.B.C.s in this disease. Cases which ran a long course inevitably showed varying degrees of hypochromic anaemia with a reduction of Haemoglobin to 11-12 grams per 100 c.c. of blood. There were no marked abnormalities in cell form.

Leucocytes.

The leucocyte count was insufficiently constant

to afford any guide as to diagnosis, though, in general, the tendency was toward a leucopenia with a slight relative lymphocytosis. If a secondary infection supervened, such as bronchopneumonia the picture changed to a polymorphonuclear leucocytosis. In two hundred and twenty Total White Blood Counts and an equal number of Differential White Cell Counts the following figures were obtained :-

T.W.B.C.

Above 6,500 / c.m.m..... 33%

6,500 / c.m.m. and below.67%

Polymorph Counts.

Above 70% of Total 26%

70% of Total and below.. 74%

Lymphocyte Counts.

The figures were the inverse of polymorph counts.

Eosinophils.

Tended to increase with recovery.

Williams, Sinclair, and Jackson pointed out recently (1944) (Ref.184) that a rise in the Lymphocyte Count heralds an improvement in the clinical condition, and that failure of this response

TABLE IV.

REPRESENTATIVE WHITE BLOOD COUNTS IN FATAL CASES.

During "A": First Ten Days: "B" 2nd Ten Days.

Case.		T.W.B.C.	Polys.	Lymphs.	Monos.	Eosins.	Day of Death.
Banta.	A.	4000/. c.m.m.	78%	18%	2%	2%	28th.
60.	B.	4,600. "	60.	38.	-	2.	-
Koya-Muslier.	A.	8,000. "	49.	46.	5.	-	15.
102.	B.	20,000. "	77.	23.	-	-	-
Manick-am.	A.	3,400. "	60.	37.	3.	-	19.
80.	B.	4,000. "	56.	41.	2.	1.	-.
Nanku-das.	A.	5,300. "	53.	44.	3.	-	16.
71.	B.	4,800. "	56.	41.	2.	1.	-.
Kartar-Singh.	A.	7,400. "	70.	29.	1.	-	21.
55.	B.	5,800. "	60.	30.	2.	-	-
Dalwar-Khan.	A.	6,800. "	74.	24.	1.	1.	16.
88.	B.	8,800. "	67.	30.	1.	2.	-.
Masters.	A.	7,400. "	65.	32.	2.	1.	19.
20.	B.	6,500. "	53.	41.	3.	3.	-.
Sankran-Nair.	A.	13,400. "	67.	32.	1.	-	9.
92.	B.	9,200. "	54.	44.	1.	1.	-.
Andi.	A.	5,000. "	51.	47.	2.	1.	13.
24.	B.	4,500. "	50.	46.	2.	2.	-.

occurs in fatal cases.(Also Blake and Maxcy,1945), (Ref.14).

This was not borne out by an analysis of the White Counts and Differential Counts early and late in Fatal Cases in this series. (See Table IV).

Section VII.(vii.) Reticulo-Endothelial System.

The Reticulo-Endothelial System was markedly affected in all cases. Evidence of this was seen in the enlargement of lymphatic glands in all parts of the body, along with increase in the size of SPLEEN and LIVER. Also in changes in the endothelium of all capillaries. These endothelial changes resulted in an increase in the permeability of the vessels giving rise to tissue oedema and petechial haemorrhages.

As has been mentioned above, the lymphatic gland in whose drainage area lay the eschar invariably showed the greatest increase in size and so served as a "Sentinel" pointer. It was Tender, discrete, and of soft, rubbery consistence. Other lymphatic glands tended to show the same changes in lesser degree, and, in severe cases, the glands were often visible as well as palpable in situations such as the posterior

triangle of the neck.

Post-Mortem Examination showed similar changes in the glands of the Mediastinum and Mesentery.

The Spleen.

Enlargement of the Spleen was almost invariable at some point in the disease, and the following is a brief account of its progress.

During the First Week of disease the spleen rapidly increased in size so that its lower border became palpable and it felt soft and was tender to examination.

This increase was continued into the second week to become maximal at the end of the second week.

The Third Week brought regression in size and by the end of the Fourth Week the spleen border was palpable only in an occasional severe case, or possibly in one subject to chronic Malarial enlargement.

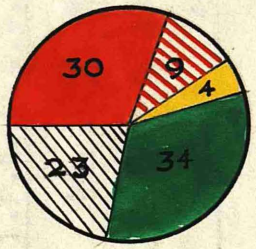
The percentage number of cases at three different stages of increase are represented in Tabular Form beneath. In this series of cases Malaria was a rare complication and could be discounted as a cause of Splenic enlargement except where the spleen was initially and finally increased.

DIAGRAM XII A & B

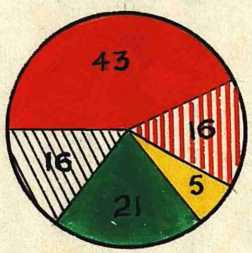
DIAGRAMS SHOWING RELATIVE CHANGES IN SIZE IN SPLEEN & LIVER.

A. SPLEEN

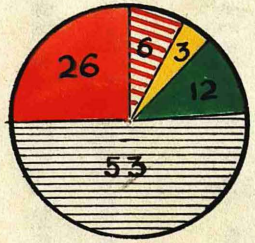
1ST & 2ND WEEKS



3RD WEEK



4TH & 5TH WEEKS

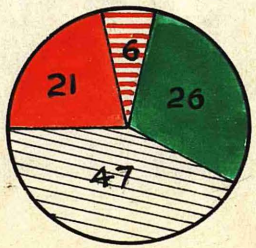


KEY

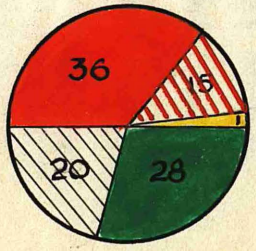
= N.P
= J.P
= 1FB
= 2FB
= 3FB

B. LIVER

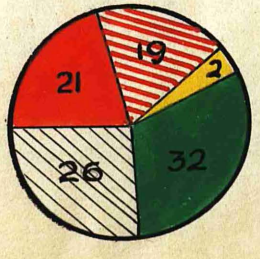
1ST & 2ND WEEKS



3RD & 4TH WEEKS



5TH & 6TH WEEKS



Weeks.	N.P.	J.P.	1.F.B.	2.F.B.	3.F.B.
1 & 2.	23.	34.	30.	9.	4.
3.	15.	21.	43.	16.	5.
4 & 5.	53.	26.	12.	6.	3.

For Graphical presentation of same findings see Diagram XII.

Liver.

Meantime the Liver was increasing but at a slower pace than the Spleen and about one week behind in relative size. The increase was general and after two weeks was just palpable below the costal margin to the extent of "one Finger-breadth". By the end of the fourth week it was commonly " two Finger-breadths," and, at six weeks, was often still "two Finger-breadths", or even more, enlarged.

Regression in size was equally slow and in many cases on evacuation in the ninth week and later, the Liver was still palpably enlarged.

The edge was usually firm in consistence and very seldom tender. Tenderness at once raised

the suspicion of coincident amoebic hepatitis, and this was well founded in six cases all of whom responded well to Emetin leaving the Typhus condition untouched; liver tenderness disappeared but fever continued unabated.

The above noted changes in Spleen and Liver seemed to be part of the Reticulo-Endothelial response to Rickettsial Infection.

The Liver changes in size seem to have been unremarked hitherto possibly because:-

(a). The Liver is not tender and occasions no complaint.

(b), In Fatal Cases the Reticulo-Endothelial Response is not so good and there is little enlargement seen at P.M.

(c). The increase in size is relatively late in onset and is best seen in convalescence.

The Rate of Increase is shown in Tabular Form beneath and in Diagram XIII. (for 100 cases). Figures in percentages.

Weeks.	N.P.	J.P.	1.F.B.	2.F.B.	3.F.B.
1 & 2.	47.	26.	21.	6.	0.
3 & 4.	20.	18.	36.	25.	1.
5 & 6.	26.	32.	21.	19.	2.

Post - Mortem Examination. Spleen and Liver.

The Spleen was found to be enlarged in all nine cases and its consistence seemed to depend on the previous presence or absence of chronic Malaria. Usually it was soft, dark red, mushy and engorged with blood, but in a few cases it was hard and friable. One case showed a fibrinous peri-splenitis.

The Liver was usually found to be enlarged, externally regular and smooth. On section it was seen to be engorged with blood, slightly fatty, and in a number of cases had a typical "nutmeg" mottled appearance.

In only one of nine cases was it slightly reduced in size and this case showed a greater degree of fatty change.

Microscopic Appearances.

Major McGovern, Pathologist, reports (Sangster, C.B.& Kay, H.B.1945) (Ref.153.) that the main change in the Liver is Cloudy Swelling with varying degrees of Central Lobular Necrosis.

Lipman B.L.et alia 1944 (Ref.103.) describes the microscopic changes in Liver, Spleen and Lymph Glands as follows :-

Liver.

Changes vary from Diffuse Cloudy Swelling to Fatty Degeneration of Hepatic Cells: Minimal to Advanced Focal Monocytic Infiltration of Hepatic Parenchyma with a few Polymorphonuclear neutrophils about the peri-portal spaces. The connective tissue spaces about the larger bile ducts showed similar cell infiltration ranging from normal to pronounced. Sinusoidal Spaces contain many plasma cells and mononuclear leucocytes. The Kuppfer Cells are swollen and sometimes their cytoplasm is vacuolated.

Spleen.

Extreme congestion. The Lymphoid Follicles swell and are diffusely infiltrated with polymorphonuclear neutrophils.

Two cases of Splenic Infarct were found in Two Hundred Cases.

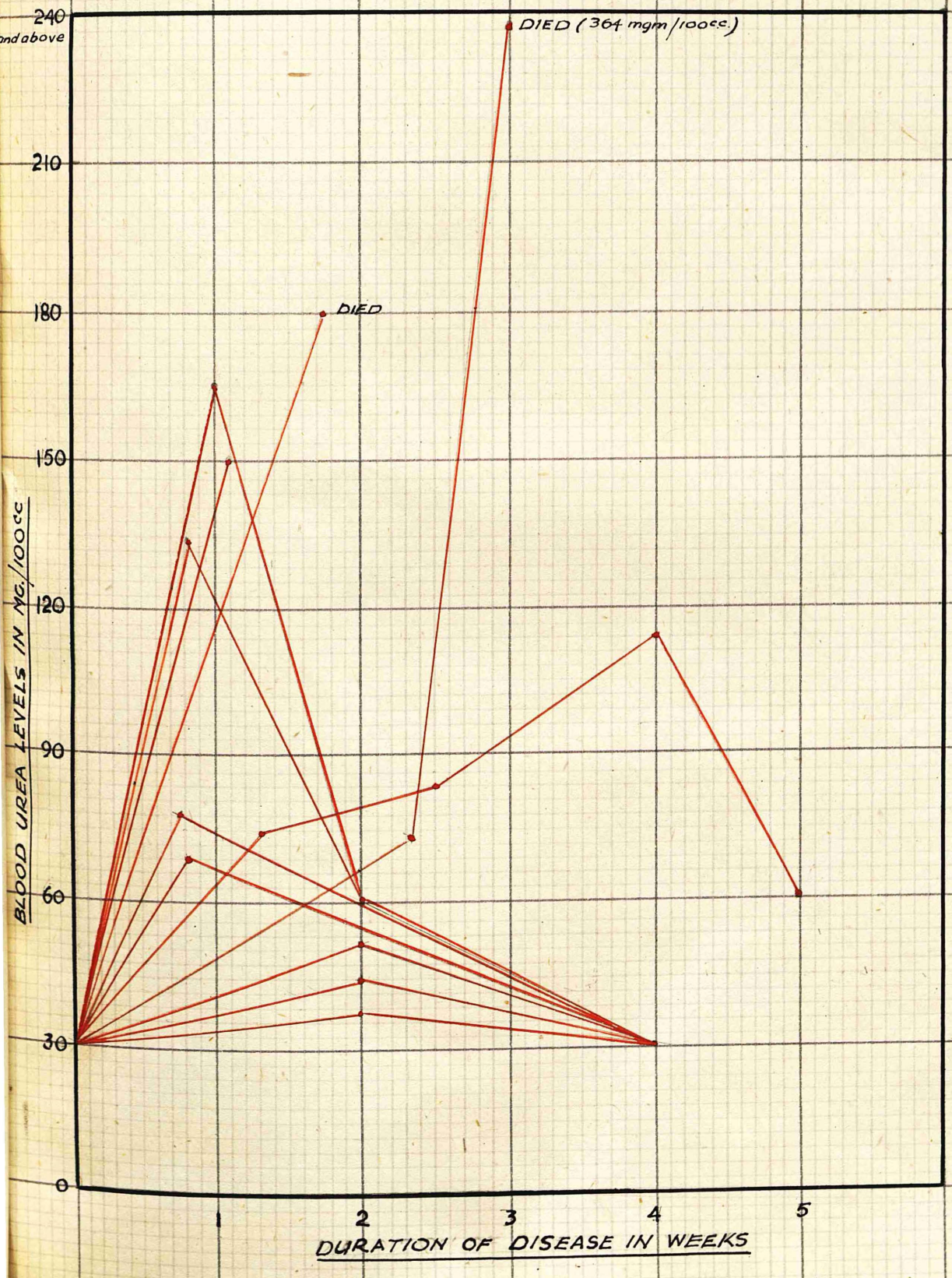
Lymph Nodes.

These are soft, greyish pink in section, and show areas of focal necrosis with dense polymorphonuclear neutrophil infiltration. The Sinuses contain many mononuclears and the Reticulum is crowded with Lymphoid Cells.

The capsule shows pronounced

DIAGRAM XIV.

BLOOD UREA LEVELS IN SCRUB TYPHUS. (11 SPECIMEN CASES)



monocytic infiltration.

Section VII. (viii). Blood Chemistry.

Facilities were available for only a limited number of estimations of Blood Urea and Serum Chlorides.

Blood Urea.

This was found to rise slowly and steadily during the course of the disease, and, in cases terminating fatally, suddenly increased toward the end reaching a figure in one case of 364 mgm. per 100 c.c.blood.

Diagram XIV shows some typical results. Carpo-Pedal Spasm and Tetany were probably in some ways connected with this rise. Lipman B.L. et alia 1944 (Ref.103) state that Non-Protein-Nitrogen rises to 74 mgm/100 c.c.blood.

Serum Chlorides.

Those which were done gave constantly low figures, but, unfortunately, our Pathologist placed no reliance on their accuracy because of local technical difficulties. Blake and Maxcy confirm that Plasma Chlorides are lowered. (Ref. 14.)

Serum Proteins.

Serum Proteinsare reported by Mc.Govern (Ref.153) to be reduced to 5.I to 5.4 gm. per 100 Millilitres, and Blake and Maxcy report (Ref.14) that there is a further steady decline in the Albumin / Globulin Ration, in that while Globulin decreases Albumin increases in amount. Lipman (1944)(Ref.103) states that serum proteins are normal unless there is a severe albuminuria. Plasma Fibrinogen is stated to fall in the second to third week showing impairment of Hepatic function. (See observations above upon Liver changes).

It has been established (Blake and Maxcy 1945) (Ref.14) that there is no increase in Pro-Thrombin time and therefore no lack of Vitamin K. The bleeding diathesis which sometimes appears in Scrub Typhus must therefore be attributed to Vascular Endothelial damage with increased permeability. There is an associated fall in Serum Calcium (Ref.153). McGovern gives the figures as averaging between 7.6 and 8.0 mgm. per 100 Millilitres. (Lipman 1944) (Ref.103) states that

Serum Calcium values are normal even in convulsive cases). Clotting Time has been variously reported to be Prolonged (Ref.78.) and Normal (Ref.103.)

Alkalaemia.

Facilities were not available to estimate the pH of the Blood but during the acute phase of the disease the clinical symptoms strongly suggested that they were fundamentally being produced by an alkalaemia, Loss of Appetite, Headache, Irritability, and other changes in the Mental State, Nausea and Vomiting resulting in Tetany, Renal Insufficiency resulting in Uraemia and Death in Coma. It was mentioned above that Carpo-Pedal Spasm was seen in Five Cases. Lipman, 1944 (Ref.103.) states however, that Blood Calcium was found to be normal in such cases.

Fluid Balance.

After seeing a number of cases it became obvious to the observers that during the acute phase of the disease there was marked retention of fluid in the tissues. As a routine measure large quantities of fluids were administered to every case (10 - 16 pints daily). Accompanying this,

and added to all fluids, Sodium Chloride was given in the proportion of gr.xx to each pint.

Urinary output during the first two weeks was greatly diminished in qhantity but immediately improvement in the patient's general condition became imminent a great increase in output was noted: that is to say,a critical diuresis occurred (c.f. Megaw,J.W.D. 1945) (ref.119)+(Army Med.Dept.Bull. No.41, 1944) (~~Ref.109~~.)

Retention of fluids during the first two weeks produced the appearance of no loss of weight, or indeed, a very slight general tissue oedema with rounded contours.During recovery, marked diuresis produced the appearance of marked loss of weight, to a degree sufficient to be visible to all and a worry to the patient who was by this time sufficiently recovered to be taking an interest in his condition.

Marked Tissue Oedema appeared in Twenty Cases of whom Sixteen recovered. It was thought to be of three types (a) General, due to (i) Renal Insufficiency and (ii) Capillary Permeability and (b) Peripheral, due to Cardiac Insufficiency.

Excessive sweating resulted in Salt Depletion and Secondary Dehydration, but the main cause of

TABLE VI.

CASE 57. FLUID BALANCE SPECIMEN CHART.

Time.	Sun.		Mon.		Tues.		Wed.		Thur.		Fri.		Sat.	
Date.	15.		16.		17.		18.		12.		13.		14.	
	In:	Out.	In:	Out.	In:	Out.	In:	Out.	In:	Out.	In:	Out.	In:	Out.
0800.	50	10.							10		36	10	48	10.
1200.	18	14.							10	10.	36	10	42	12.
1200.														
1600.	77	20.							90	35.	78	32.	8	10.
1600.														
2000.	42	22.							28	33	38	30.	992	22.
2000.														
2400.	36	12.							16	25	40	42	16	12.
2400.														
0800.	16	20.							16	12				
Total														
Pints	12	4.							8	5	16	8	15	5.
Ozes.	5	16							2	5	4	6	0	16.

Time.	Sun.		Mon.		Tues.		Wed.		Thur.		Fri.		Sat.	
Date.	16.		17.		18.		19.		20.		21.		22.	
	In:	Out.	In:	Out.	In:	Out.	In:	Out.	In:	Out.	In:	Out.	In:	Out.
0800.														
1200.	56	28.	42	14.	40	25.	28	18.	42.	30.	32	21.	25.	18.
1200.														
1600.	28.	20.	50	17.	24	16.	40	13.	42.	10.	30	12.	34.	21.
1600.														
2000.	32	22.	36	32.	57		46	10.	54.	10.	42	11.	36.	18.
2000.														
2400.	24	8.	27	21.	39	11.	48	22.	36.	12.	26	12.	28.	14.
2400.														
0800.	22		30	5.	33	13.	28		16.		32	12.	22.	10.
Total.														
Pts.	8	3.	9	4.	8	3.	9	3.	9.	3.	8	3.	7.	3.
Ozs.	2	18.	5	9.	13	5.	10	2.	10.	2.	2	17.	5.	18.

Figures in Tables represent ounces unless otherwise stated.

dehydration seemed to be the diuresis of recovery.

As has been mentioned, routine estimations of Urinary and Serum Chlorides during the acute phase gave constantly low figures for both, and that in spite of pushing the salt intake with all fluids. It was a mystery how the chloride seemed to disappear so readily out of the circulation, presumably into the tissues.

The earlier cases were treated as routine during the acute phase with Intravenous Glucose-Saline, but it was found that this placed too great a strain upon the Circulation and in some cases caused pulmonary oedema. This was abandoned in favour of Rectal Glucose-Salines and later this was replaced by Trans-nasal Intra-gastric Drip feeding from a reservoir and this proved eminently satisfactory.

Five cases were given Dried Reconstituted Plasma but this was badly received in each case with rigors or collapse so its use was not continued. (Faulty Storage was blamed.)

A Four-Hourly Chart of Intake and Output of Fluids was kept for all cases and from this the progress of the patient could be judged. (One such record is reproduced in Table No.VI.)

Section VII.(ix). Mental Changes.

The characteristic appearance of the Typhus Case has been commented upon earlier in the Thesis and it was the Mental State of the patient which mainly contributed to this appearance of immobility. There were several factors in its production. Apathy, complete and absolute as to their state was quite usual. Gradually they became vegetative, sinking into a torpor with vacant unseeing stare. The threshold for auditory and visual stimuli appeared to be raised, so that no attention was paid to a visitor to the Ward and if the doctor was answered at all it tended to be a monosyllabic reply. Other factors doubtless contributing to the immobility were the very severe retro-orbital eye ache and frontal headache aggravated by movement, also the photophobia from which so many of these cases suffered causing them to keep their eyes shut for a large part of each day.

Some of the milder cases were unduly optimistic and showed complete unconcern throughout.

In recovery they were all anxious to get back to work far in advance of their strength.

Many were very irritable, a few depressed, and a few confused and delusional during the toxic phase, but none of these changes were permanent in any of the cases seen.

Two Negro patients became delusional and manic so had to be forcibly restrained and given 8 c.c. Paraldehyde intra-muscularly to induce sleep.

Any serious mental changes seemed to have all cleared by the end of the third week but prolonged rest seemed to be essential for final mental and physical fitness.

Section VIII.

COMPLICATIONS.

A. Respiratory.

i. Bronchitis.

This was the commonest of all complications occurring in 48% of cases, indeed, it was really regarded as a symptom, being present in some small measure in practically every case.

The usual remedies had little effect on this complication and this fact gave rise to the suspicion that it was Rickettsial in origin. In

10% ofcases it passed into a

ii. Broncho-Pneumonia.

of a patchy, ill-defined type, again showing no response to Sulphonamides and Penicillin, which were tried in every case. In those cases which showed a polymorphonuclear leucocytosis, secondary infection was presumed and Penicillin pushed with a favourable response.

iii. Lobar Pneumonia.

was met with in only two cases and in each of these the question arose as to whether these were not really the result of

iv. Pulmonary Infarcts.

Both recovered, so it could not be proved, but one of them went on to

v. Pyo-thorax necessitating rib resection and instillation of Intra-Pleural Penicillin, with complete recovery as a final result.

vi. Pulmonary Abscesses were seen scattered throughout the lungs of two cases which came to Post Mortem. The abscesses were small and situated peripherally.

None of these had been recognised Clinically in life and here again the impression was gained that possibly infarcts were the cause of these scattered septic foci.

vii. Oedema of the Lung.

Oedema, indistinguishable from Hypostatic Oedema, appeared in severe cases during the second or third week but it seemed to be of less serious prognostic significance than when appearing in other diseases. It was associated sometimes with cyanosis of central origin and marked inspiratory dyspnoea. Oxygen administered in a special tent appeared to benefit these cases.

viii. Expiratory Dyspnoea.

In most cases Dyspnoea when present was of an inspiratory nature but in seven cases, all severe, in their later stages dyspnoea became expiratory in pattern and all the usual anti-spasmodics and Oxygen failed to give any relief.

ix. Acute Laryngitis.

This was seen in only three cases and lasted from four to seven days.

Major.A.A.Miller,R.A.M.C., has reported a

specific ulceration of the larynx in Scrub Typhus. (Personal Communication.)

B. Cardio-Vascular Complications.

i. Peripheral Vascular Failure.

This complication was met with in 12% of cases, it has been described on pages 57 and 59.

ii. Extra-Systoles were noted in 8% of cases. They appeared usually about the third week of disease, commonly remained quite un-noticed by the patient and were no indication of severity.

iii. Heart-Block of 2; 1 pattern was seen in only one case in his fourth week of illness. He was critically ill for a few days but made an excellent recovery.

iv. Myocarditis.

Myocarditis was seen in only five cases associated with triple rhythm and this was a passing phase as may be seen from the fact that only two cases were evacuated with special precautions on account of this complication.

v. Thrombo-Phlebitis.

Eight cases of thromb-phlebitis were seen.

One of these was remarkable in that every vene-puncture resulted in thrombosis both proximal to and distal to the level of the puncture. These thromboses were of saphenous or femoral veins, ran the usual course, and were a most troublesome complication.

vi. Epistaxis was common appearing in most severe cases. The usual form was one or two profuse bouts.

vii. Sub-conjunctival Haemorrhages appeared in many of the severe cases and ran a normal course.

viii. Haematemesis and Melaena were each met with in one case, the latter of which on Post Mortem was shown to have an old Amoebic Ulcer which was probably the source.

C. Gastro-Intestinal Complications.

i. Diarrhoea was, in our experience, rare, and appeared incidentally in only eleven cases.

ii. Hiccough and iii. Tympanites are discussed on pages 63 and 64.

iv. Ascites was found in only one case in association with a small pleural effusion and no cause other than Typhus could be found. Both effusions cleared up in the fifth week of illness.

v. Acute Parotitis was found in two cases, bilateral in one and unilateral in the other. In the first of these the parotitis was the first sign, and the only complaint made on admission. It was wrongly diagnosed prior to admission as Mumps. (A similar case was described by Patterson H.S. (1944) (Ref.142).

D. Uro-Genital Complications.

i. Retention.

Two cases requiring catheterisation for two and three days respectively, were seen. These cases occurred when recovery was taking place. The Prostate was normal in size in both cases and both made a good recovery. It appeared to be in the nature of over-action of the sympathetic nervous system.

ii. Frequency occurred in a few cases, again during recovery and of nervous origin.

iii. Acute Diffuse Glomerular Nephritis has been described by several writers but was not seen in any of our cases.

E. Central Nervous Complications.

i. Deafness of Inner Ear Type.

Slight in 18%

Severe in 10%

All cases showed great improvement if not full recovery prior to evacuation.

ii. Peripheral Neuritis.

As already described on page 72 the manifestations of Peripheral Neuritis were, Anaesthesia, Hyperaesthesia, Paraesthesia, Paresis, Tender Toes, Painful Meta-tarsals and Joints, Shoulder-girdle pain and wasting.

iii. Meningismus with Nuchal Rigidity

was present in eight cases all of which were severe or fatal. (So called Cerebral Scrub Typhus).

iv. Encephalitis may have been the cause of death in some of the cases who died in coma. "Focal Typhus Nodules" have been described to have been found in the brains of patients who died of Scrub Typhus. (Blake and Maxcy, 1944). (Ref.14).

v. Abdominal Hyperaesthesia was noted in five cases but its significance was not clear.

F. Splenic Infarct.

One patient described sudden severe

pain in the splenic region causing suspicion that an infarct had occurred, but this could not be confirmed.

G. Septic Complications.

i. Abscesses in arm and buttock, sterile, as result of Penicillin or Convalescent Serum Therapy.

ii. Suppurative Otitis Media. Four cases.

iii. Pustular Follicular Dermatitis.

Four cases of infection of the Axilla and two of the beard region were seen. One involving the beard region was specially severe, appeared overnight with great swelling of the face (a Sikh patient) but cleared in three days with local and parenteral Penicillin.

iv. Dental Abscess severe enough to call for special treatment in two cases.

v. Periostitis has occurred in one case (known to the writer) not actually included in this series.

H. Ariboflavinosis was seen in three cases and Acute Glositis in five cases, in spite of a liberal supply of supplementary Vitamins.

I. A Pigmented Hairy Mole was seen which showed signs of extension and inflammation during the disease.

J. Sialorrhoea appeared in one case during the second week. This was transient and was presumably a hysterical manifestation.

K. Alopecia of a patchy type was not seen but there was a marked general thinning of hair in many cases.

L. Concurrent Diseases.

i. Malaria.

Malaria was found incidentally in only five cases on routine examination for parasites. Of these, two were Benign Tertian, two were Malignant Tertian, and one was Mixed Tertian. The presence of Malaria had no noticeable effect on the course of the disease. In any event, by Army Order, all cases of fever lasting more than forty-eight hours were receiving Full A.M.T.

ii. Amoebic Hepatitis.

Amoebic Hepatitis was considered to be coincident in six cases and all responded well to Emetin. Active Amoebic Dysentery was not found as a coincident infection.

iii. Bed Sores.

Bed sores occurred in two severe cases with deep sloughs down to bone, both over the sacrum. They gave the impression of being due to deep local thrombosis followed by sloughing. These cases were grossly emaciated but recovery took place after a lengthy illness. Penicillin was instrumental in clearing the infection, administered locally and parenterally.

iv. Helminthiasis.

Ankylostomiasis and Ascariasis were found coincident in 10% of cases.

Section IX. Differential Diagnosis.

In an endemic area where cases are known to be occurring there is not likely to be any trouble about the diagnosis. Awareness of the possibility of a case proving to be Scrub Typhus ensures that the diagnosis will not be missed.

The combination of rash, eschar and lymphadenitis (The Triad) is characteristic, and confirmation is eventually afforded by a positive Weil-Felix Reaction.

Briefly, the differential points for the main diseases which might cause confusion are as follows:-

In every case epidemiology is most helpful.

I. Malaria.
- i. Absence of the triad(above).
- ii. Presence of Malarial Parasites.
- iii. Presence of regular remissions.
- iv. Negative W.F. Reaction.

2. Dengue.
- i. Absence of Eschar.
- ii. Otherwise strong resemblance in early symptoms.
- iii. Rash centrifugal tending to macular and erythematous. Typhus rash centripetal.
- iv. Temperature falls by crisis seventh day.
- v. Negative W.F. Reaction.
- vi. Even more acute onset with sudden prostration in Dengue.

This is the disease most likely to be confused in the early days with Scrub Typhus for above and other reasons.

3. Typhus: Flea - Louse - Tick - Borne.
- i. Weil-Felix Reaction.
- ii. Absence of Eschar.
- iii. Only Flea-borne is found in the same areas.

4. Typhoid, Para A. and B.
- i. Typhus is more sudden in onset.
- ii. Serological. Widal. Positive.
- iii. Absence of eschar and related glands.
- iv. Characteristic rash.
- v. Blood and Urine Cultures.

5. Weil's Disease.

i. Absence of Eschar.
ii. O X K agglutination in low titres only (False, Positive).
iii. Presence of Jaundice.
iv. Finding Leptospirae in Blood or Urine.
v. Animal Inoculation.
vi. Specific agglutinins.

One such case appeared among the Scrub Typhus Cases and gave rise to some confusion through the false positive O X K reaction (1/360).

6. Kala-Azar.

i. Absence of triad.
ii. Weil-Felix may rise only to titre of 1/160(False Positive).
iii. Leishman-Donovan Bodies present in Spleen, Liver or Sternum.
iv. Chopra and Aldehyde Reactions may be positive.
v. Marked Leucopenia present.
vi. Characteristic Temperature Chart. Classical double rise in twenty-four hours.

7. Glandular Fever.

i. Absence of triad.
ii. W.F. negative.
iii. Presence of Mono-nuclear Leucocytosis.
iv. Paul-Bunnell Reaction Positive.

8. Mumps.

i. Usually bilateral, rarely suppurates.
ii. Absence of triad.
iii. Serological reactions negative.

9. Meningitis.

i. Eliminated by Lumbar puncture.
ii. Leucocytosis.

10. Measles.
    i. Presence of Koplik's spots.
    ii. Absence of Eschar.
    iii. Weil-Felix is negative.

11. Plague.
    i. Bacillus Pestis is found by Gland Puncture or Blood Culture.
    ii. Absence of Eschar and Weil-Felix negative.

12. Amoebic Hepatitis.
    i. Absence of triad.
    ii. Presence of Polymorphonuclear Leucocytosis.
    iii. Tender Liver border with response to Emetin.
    iv. Weil-Felix Reaction Negative.

13. Secondary Syphilis.
    i. Absence of Eschar.
    ii. Characteristic coppery rash.
    iii. Wasserman or Kahn positive.
    iv. Weil-Felix Negative.

Section X. Prognostic Indications.

During the course of this small outbreak in Mandalay it was noticed that the Virulency of the disease decreased as the season advanced, while in the neighbouring district of Meiktila (one hundred miles away) the reverse was the case.

This decrease in virulence is reflected in the gradually diminishing death rate month by month.

Deaths occurred on:-

July:	7th, 9th, 12th, and 23rd.
August:	Nil.
September:	16th and 29th.
October:	13th.
November:	11th.
December:	12th.

During the months September to December however, many very severe cases were dealt with who but narrowly escaped with their lives, but, taken as a whole, there were a larger percentage of less severe cases during those months.

In this series the Mortality was NINE cases. (or seven per cent.)

The average Mortality is stated by Megaw to be five per cent, varying from one per cent in fit men to twenty per cent in debilitated persons. (Mendell , 1946 , 2.7% of 75 cases.) (Ref. 203.) (Philip et alia , 1946 ,4.5% in 222 cases.) (Ref.204.)

Lipman has analysed two hundred cases (Ref.103) and points out the large increase in mortality with increasing age, as follows:-

Over-all Mortality	10%
Average age of entire group	25.7 years.
" " " patients who died	30.9 "
" " " those who recovered	25.1 "

Proportion of patients aged 30 or over	14.5%
" " " aged 30 or over who died	40%

The nine deaths in this series gave a representative scatter but it has to be remembered that the group at risk is very much selected when dealing with a body of troops.

Age at death for the nine cases:-

21, 22, 25, 28, 30, 35, 38, and 50 years.

All nine died between the fourteenth and twenty-eighth days of illness, the distribution being:

14th, 15th, 16th, 16th, 18th, 19th, 19th, 21st, 23th.

Earlier in the Campaign it was evident that the longer a patient was ill unattended, the less his chances of recovery, but in these cases most were admitted very promptly.(Admitted on 2, 2, 3, 3, 4, 4, 5, 7, 10th days of illness).

It was noticeable however, that cases who were admitted obviously seriously ill tended to go on to a fatal termination in spite of every attention.

Unfavourable Signs.

The following signs and symptoms were noted to be unfavourable.

1. Persistent Hiccough.
2. Persistent Vomiting.
3. Grey Cyanosis (Peripheral).
4. Haemorrhagic Symptoms. Epistaxis, Sub-conjunctival and P.R.Haemorrhage.
5. Tympanites, marked in practically every severe, and in all fatal cases.
6. Marked Fall in Urinary Output.
7. Slow rise in O X K titre.
8. Sudden Peripheral Collapse.
9. Rise of Pulse Rate above 120 per min.
10. Rise of Respirations above 36 per min.
11. Oedema of Extremities and Lumbar Cushion.
12. Triple Rhythm.
13. Carpofloggia, Severe muscular tremor, Carpo-pedal spasm.

Favourable Signs.

Among favourable signs were:-

1. Reversal of the above Symptoms and signs, including
2. Lysis in second week.
3. Diuresis immediately preceding fall in Temperature.

4. Rapid Rise in O X K Titre.

Of those who recovered the ultimate prognosis was good provided that they were given sufficient rest before resuming duty. After eight to twelve weeks in Hospital they were ready to proceed to Convalescence, where, after a further one to three months, they were ready to return to duty.

All cases required special feeding-up to replace protein loss and as far as these patients could be followed up they appeared to suffer no serious after effects of their illness.

TABLE Va.

HIGH CALORIE FLUID DIET FOR FEBRILE PATIENT.

Hours.			CALORIES.
0600.	Tea with plenty of milk and sugar.(½oz.)	8 oz.	90.
0800.	Eggs (2).Flip in milk (with brandy)(2 dr)	10 oz.	350.
1000.	Ovaltine, Bengers,Horlicks,Vegamite.	8 oz.	200.
1200.	Cream Soup thickened with ground rice. or Atta and Flavoured with Tomato etc.	10 oz.	200.
1400.	Milky drink flavoured with Vegamite etc. and Brandy ½ oz added.	8 oz.	200. 50.
1600.	Tea with plenty of milk and sugar.(½ oz)	8 oz.	90.
1800.	Soup as at 1200 hours.	10 oz.	200.
2000.	Egg(2) Flip in milk with sugar.	10 oz.	350.
2200.	Horlicks, Ovaltine,Bengers or Vegamite.	10 oz.	200.
0200.	Milk with brandy (½ oz).	8 oz.	250.
	Total.	90 oz.	2180.Cals.
		= 4½ pts.	

At every odd hour give 8 oz fruit juice with ½ oz. sugar.

Total.	4 pts.	600.Cals.
	8½ pts.	2780.Cals.

TABLE Vb.

HIGH CALORIE DIET FOR CONVALESCENTS AFTER FEVER.

Hours.		Calories.
0800.	2 Eggs boiled, poached or scrambled on toast with butter or dripping.	250.
	1 Slice of bread,(or substitute) with honey or jam.	170.
	1 Cup of tea with milk and sugar.	40.
1200.	1.Cream (thick) soup with pureed veg.8 oz. and seasoning.	80.
	2.minced boiled or curried chicken 4 oz. With Rice or Dahl Chapatties. 8 oz.	500.
	3.Curds - Dahl - with fresh or tinned fruit.	400.
1600.	Tea, Milk, Sugar, biscuits, Roti Honey or Jam.	200.
1880.	As at 1200 hours.	1000.
		2640.

At 1600 hours,1000,1400,2000,2200 hrs. give alternately

Fruit Drinks with Sugar and Ovaltine (Bengers,Horlicks,

Vegamites Cocoa.) 200
In Milk 8 oz.) 250.

Calories. 3090. approx.

* On subsequent days mutton, liver, fish, may be substituted.

To Increase Caloric Value add Cheese Bhajia at 1200 hours and Halva (toffee) at 0600 hours (800 cals.)

Section 11. Treatment.

The general principles of treatment closely followed the instructions laid down in the Medical Technical Memorandum No.6 published by The Medical Directorate of 11th Army Group, S.E.A.C., dated 1st.August, 1944.

This instruction placed the greatest stress on the importance of Nursing, a High Fluid Intake (10-16 pints daily), adequate salt intake, the use of Fans and Punkahs, and adequate protein intake.

Nursing was considered of primary importance, and very devoted service was given by a small band of Q.A. Nursing Sisters, under really difficult conditions.

Special attention was given to the replacement of the marked protein wastage and the diets appended in Table V were devised for this purpose; Va, a fluid diet suitable for intra-nasal feeding, and Vb, a light highly nourishing diet.

Fresh yeast was obtained from the local bakery and given with six Multivitamin Tablets daily to all cases to cover deficiencies in the diet and previous deficient intake. (Each tablet contained:

Vitamin A, 5,000 I.U., Thiamin, 1 mgm., Riboflavin, 2 mgm., Nicotinic Acid., 10 mgm., Ascorbic Acid.30 mgm.)

Intra-venous Glucose Saline (Isotonic) was given freely to the earlier cases but later it was felt that more satisfactory results were obtained by Intra-nasal feeding in difficult, or semi-comatose patients, with no risk of aggravating or producing pulmonary oedema.

Oxygen.

An Oxygen Tent was improvised out of stout blue impervious sheeting into which were set celluloid windows, in each side, and in the roof. This was done because Scrub Typhus cases seemed to tolerate the B.L.B. mask very badly. Dyspnoeic patients and cyanosed patients were placed in the tent for one to two hours at a time and observed. Although all seemed to show objective improvement by reduced dyspnoea and cyanosis, very few admitted that any benefit was received.

Much use was made of the tent, however, because the phenomenon of tissue anoxia seemed to be so prominent a sign and to be at the root of many symptoms of the disease.

Routine Anti-Malarial Treatment, was given by 14th Army Order to all patients suffering from fever lasting more than 48 hours, but in the Mandalay District this proved unnecessary because suppressive Mepacrine treatment kept the incidence of Malaria down to a minimum. Routine Treatment consisted of Mepacrine Tabs. 0.I g., tabs.iii, t.d.s. on the first day, b.d., on the second day, and once daily for the following five days.

Convalescent Serum.

It was hoped that frequent small doses of the serum of patients who had made a good and rapid recovery might be beneficial if given intra-muscularly to patients early in the disease, by stimulating Immune-Body Formation. Doses of 5 c.cs were given daily from the 7th to twelfth day of illness to forty cases without any evidence of benefit being obtained, so the method was accordingly abandoned.

N.A.B.

In four cases only an attempt was made to abort the disease with injections of N.A.B. 0.35 g. Intra-venously. There was no evidence of benefit, indeed the cases upon which it was tried appeared to be slightly worse rather than better so this method

also was discontinued.

Sulphonamides.

Sulphonamides were used freely and often in any case where there was reason to suspect a secondary infection, and only then was there any appreciable benefit received.

Penicillin.

Was similarly used with benefit when any secondary infection was suspected. In later cases, since the supply was in excess of demand, it was used in preference to Sulphonamides because of its lack of toxicity. It was given Intra-Muscularly every three hours in doses of 15-20,000 units to a total of 500,000 units.

Symptomatic Treatment.

Sedatives. Restlessness was treated with " Three fifteenths Mixture" or Phenobarbitone gr.I.

For wild delirium and Mania, Paraldehyde 8-10 c.cs intra-muscularly was the treatment of choice.

Stimulants. Peripheral collapse was treated with Intra-Venous Glucose, 10-20 c.cs of 20%, and Intra-Muscular Ephedrine. Central failure was treated with Coramine and in a few cases, in spite of much controversy on this point, Digoxin 0.5-0.75 m.g.m. was given Intra-Venously with undoubted benefit. This latter, in view of the controversy was only given to cases which appeared to be desperately ill.

Oedema.

Where it could be shown that the oedema was not of Renal Origin it was thought worth while trying the effect of giving Mersalyl 1-2 c.cs I.M. after previous saturation with Ammonium Chloride. The resulting Diuresis was most satisfactory and helpful in restoring the body fluid balance.

Tympanites, was treated with High Washouts, Rectal Tubes and I.M. injections of Pitressin and Acetyl-Choline in large doseage, with little evident benefit.

Hiccough was most intractable but seemed to be helped by Carbon Dioxide and Oxygen Inhalations.

Headache was treated if very severe by Lumbar Puncture; otherwise, large doses of Salicylate

seemed to benefit.

Marked Wasting, was treated during the recovery phase with an Intra-Venous Drip of Protein Hydrolysate 200 c.cs and was well tolerated.

Bed Sores were treated with local and general Sulphonamide or Penicillin, each with excellent effect.

Alcohol in the form of Brandy was used in small frequent doses to all patients on exclusively fluid diet with considerable benefit as a soporific and stimulant and a useful addition to the calorific value of the diet.

Para-Amino-Benzoic Acid.

It has been reported recently by Lt. Nicholas A. Tierney, U.S.N.R. (Ref.205.) that Para-Amino-Benzoic Acid has been used with some success in the treatment of eighteen cases of Scrub Typhus. These cases were at an I.G.H. in Ledo , Assam . Of the eighteen cases so treated all recovered and it is claimed that,the symptoms were less severe , there were fewer days of Fever , and that Convalescence was shortened. The only ill effect was the tendency to a fall in the Total White Blood Count , the differential Count remaining unaffected. The drug was given by mouth in an initial dose of 8 Gm. (in 10c.c. 5% Sod. Bic. Soln.) followed by 3 Gm. every two hours. Treatment to be effective had to be commenced within the first week of disease.

P A R T II.

An Account of the Effect produced on Sixteen Cases of Scrub Typhus by their having Scrub Typhus Prophylactic Inoculations while they were Incubating the Disease.

Section I. Introduction.

In anticipation of an intensive 1945 Campaign against the Japanese in Malaya, it was decided by the War Office that the production of Scrub Typhus Vaccine, as prophylactic against the known risks in this terrain, should receive very high priority.

By May 1945, a Laboratory was set up at Frant, Sussex, under the auspices of the "Wellcome" Veterinary Research Station and prepared to start large scale production of Scrub Typhus Vaccine.

Great speed was essential so that one and a half million doses of vaccine might be ready in time to give protection before the projected offensive in the late summer of 1945.

The lungs of Cotton Rats were found to be the best medium for the culture of the Rickettsiae so these rats had to be imported by air from America. (Buckland 1945) (Ref.18).

It was impossible to spare the time for testing the vaccine out clinically on a large scale, but it had been proved to confer immunity upon mice which were exposed artificially to infection, and so the team of Bacteriologists were obliged to put the vaccine into full scale production without the benefit of a proving on human material.

As events proved, the Japanese Campaign ended precipitately and the vaccine was not so seriously required as had been anticipated.

Section II. Distribution.

Supplies of the Vaccine were available for clinical use in Burma early in autumn, and, since the main focus of Scrub Typhus in Burma at that time centred round Mandalay, it was decided that all troops in the Mandalay Area should be inoculated prophylactically.

The initial decision was to inoculate half of each company so as to have adequate controls, but various considerations, including the attitude of the Commanding Officers to the "experiment", demanded that all the men in each company should be done.

Seven and a half litres of vaccine were used in the inoculation of two thousand five hundred troops, 1 c.c. being given to each on three occasions, at weekly intervals.

It happened that the arrival of the vaccine coincided with the peak incidence of Scrub Typhus in Mandalay district (November 8 - 14) so that the Commanding Officers of Units became thoroughly alarmed and willingly agreed to prophylactic inoculation for their men.

It had been noted that the highest incidence of the Disease was to be found among Engineering and Road Building Companies, so that it was decided to inoculate these troops first.

All local Medical resources were mobilised to ensure the inoculation of the entire two thousand five hundred troops weekly, for three consecutive weeks, and the Medical Officers were requested to do a skin inspection at the same time for any lesion which resembled an Eschar.

Returns regarding Numbers, Names, and Units of personnel inoculated, and the presence or absence of an eschar, were centralised to our hospital for correlation before being passed on to Headquarters.

The Effect of Inoculation.

a. Local. A slight, temporary, tingling lasting five minutes due to the Formalin Vehicle.

b. General. No constitutional reaction was reported in any case as an immediate result, though fever following within a few days was reported by a number of cases to be reported more fully below.

Section III. The Search for Eschars in Healthy Troops.

It had been suggested that the bite of a Mite could produce an Eschar whether the Mite was infected with Rickettsiae or not, and therefore, that routine examination might be expected to show Eschars in completely healthy troops.

Of all the troops examined no case was found where a healthy man had a classical Eschar with related lymphadenitis. (The search was not as efficient as could have been desired as the subsequent cases will show.)

The search was extended to include a special examination of all admissions to hospital, and no eschars were found in cases not otherwise suspected of

being Scrub Typhus.

The Efficacy of the Prophylactic Vaccine in preventing the onset of Scrub Typhus has yet to be proved after the passage of time, for the writer was posted home at Christmas 1945 and this part of the work had to be left to a successor.

Section IV. Inoculations Given to Cases During Incubation Period.

The following record concerns those troops who fortuitously received their inoculations, one, or more, while actually incubating the disease. All of these were inoculated between the 10th and 18th of November 1945.

Sixteen such cases were received between the 12th and 30th of November, from 5 different Units, though half of the cases came from one C.R.E.Company, and four more from a Unit supplying this Company, with ancillary services and working on the same site. (These same cases are included in the discussion on Epidemiology).

The British Commanding Officer and his Indian Second-In-Command were among the patients and a British Officer from a Unit stationed one hundred yards away made a third. Four African Artisans were included and the

remaining nine were Indians. Of these sixteen, fourteen lived and worked in Fort Mandalay.

Attention was first drawn to the matter by a rumour which not unnaturally caused some alarm; that the inoculation of an R.E. Unit against Typhus had given some of the men this disease.

An immediate personal investigation was made on the 17th November and it was found that at that time there were three cases in hospital suspected of having Scrub Typhus who had been inoculated recently. These were, the Second-In-Command of the C.R.E.Company, who had been admitted the previous day, and two African Sappers admitted on the 12th and 16th November respectively. Enquiries at this C.R.E.Unit showed however, that a number of men had reported sick, and, by the 22nd November, seven cases including the Commanding Officer, had been admitted with a provisional diagnosis of Scrub Typhus.

The rumour then appeared to have some factual foundation in that all these men had been inoculated on the 12th or the 14th with Scrub Typhus Prophylactic Vaccine.

Careful examination of the first, and subsequent

fifteen cases, showed that no less than fourteen of them had typical eschars and lymphadenitis of the related glands.

This was most fortunate for the writer, for, anxious and angry Senior Officers had to be faced with a very definite opinion as to the cause of this outbreak, and these physical signs afforded sufficient proof for one to be confident that the disease had been contracted in spite of, rather than as the result of, Inoculation.

A reasoned explanation with such proof as could be adduced was fortunately accepted by these officers and the scheme of Inoculation was proceeded with throughout the Area.

These cases were of course proved later by serological tests.

The outcome of inoculation of individuals within the period of their incubation of the disease was awaited with some interest.

Of the sixteen cases, twelve had received only 1 c.c. of the vaccine prior to the development of symptoms, two had received two weekly injections of 1 c.c., and two had, during and overlapping the incubation period, received three injections of 1 c.c. of the vaccine.

TABLE VII.

TABLE OF AGGLUTINATIONS. Of Inoculated Cases.

GROUP I.

Case No.	7th day.	14th day.	21st day.	Fever in days.	Eschar.	Toxicity.
1.	80.	320.	1280.	32.	+	Late, Mild.
2.	Nil.	40.	1280.	34.	+	Late, Severe.
3.	40.	80.	320.	17.	+	Slight.
4.	Nil.	80.	1280.	26.	+	Slight.
7.	40.	160.	320.	8.	-	Toxic, Early.
11.	Nil.	80.	160.	14.	+	Moderate, Early
12.	40.	160.	320.	18.	+	Moderate, Early

GROUP II.

5.	40.	80.	640.	15.	+	Moderate.
6.	80.	1280.	-	12.	-	Moderate.
8.	40.	80.	320.	17.	+	Slight.
9.	40.	80.	320.	16.	+	Toxic, Early.
10.	40.	80.	640.	13.	+	Slight.

GROUP III.

13.	40..	80.	Lost.	12.	+	Very Slight.
14.	40.	80.	Lost.	30.	+	Very Slight.

GROUP IV.

15.	40.	80.	Lost.	10.	+	Absent.
16.	40.	80.	160.	9.	+	Absent.

Classification into Four Groups.

For descriptive purposes the sixteen cases have been divided into four groups according to the number of doses of vaccine administered and the length of the interval between administration and the development of symptoms, since these two factors, separately or in combination, appeared to modify the course of the illness.

Group I. Cases Inoculated two Days or Less Prior to Onset of Symptoms.

Cases: 1,2,3,4,7,11,12.

For Case Notes see Appendix C except case 1 which is reported here as sample of the group.
See also Table VII of Agglutinations and Length of Fever.

Case 1. 3392 Major.B., O.C."X" C.R.E. aet.34.

Admitted on November 18th 1945, giving a history of not feeling quite fit since his Prophylactic Inoculation of 1 c.c.Scrub Typhus Vaccine on 12th November, and expressing indignation that he should have thus been made ill.

Slight headache and a small amount of fever had been present since the 14th November,

but he had managed to carry on his duties until the 17th. He was most unwilling to be admitted to hospital, and after admission had to be ordered to bed. At this time all systems were normal on physical examination and the only abnormality noted was an eschar on the scrotum with enlarged left inguinal glands, which he had first noticed in his bath four days previously. No rash was seen. The patient's general condition was excellent and his spirits high, indeed, he was optimistic, regarding the whole of his illness as an intolerable nuisance. On Admission his SPLEEN was just palpable and LIVER not palpable. The Blood Pressure was 125/75 m.m.Hg., the Circulatory and Respiratory Systems were both found to be normal and the Deep and Superficial Reflexes were all present and normal. Total White Cell Count was 5,000/c.m.m. and Differential Count, Polymorphs, 52% , Lymphocytes 44%, Monocytes 4%, Eosinophils Nil. Urine was normal and there were no digestive disturbances.

Progress.

During the first week of illness there were practically no objective signs other than fever which rose daily to 102 degrees F. then dropped a degree but never reached normal at any point in the 24 hours.

His spirits remained high, the only symptom was a very slight headache, and it was with some difficulty that he was persuaded to remain in bed. (See Temp. Chart A1.)

O X K Titre on the seventh day was 1/80 and Blood Pressure was 100/60 m.m.Hg.

The Second Week opened with little difference in his condition except that a few rhonchi were heard at each base, but coughing was negligible. Fever was now maintained swinging between 102 - 104 degrees F., with the tendency to an evening rise. (See Temp.Chart A.) O X K was now 1/320, Spleen 1 F.B. increased, and Liver margin Just Palpable. All this time he had protested that he felt quite fit, sat up in bed, and ate all his meals. Cerebration was normal and permitted of reading technical books.

The Third Week. Apart from an appearance of tiredness there was no visible change in his condition, though the fever continued to swing between 101 - 104 degrees F. daily. There was now slight insomnia added to the headache and cough, Titre was now O X K 1/1280, and Blood Pressure 120/70 m.m.Hg., Deep Reflexes were absent and Superficial Feebly present. The Total

White Blood Count was 4,200 / c.m.m. and Differential Count, Polymorphs, 65% : Lymphocytes, 35% : Monocytes 0% : and Eosinophils, 12%. Spleen was 1 F.B. increased, and Liver J.P.

Between the 22nd and 26th days of illness a few toxic signs appeared: ashen pallor with the faintest degree of cyanosis, extra-systoles, and irritability. He continued to sit up in bed and enjoyed his meals though he read less and found he could only manage to cope with 'light' literature. There was no sign of loss in weight and, even at this point, on questioning he stated that he felt quite well though he looked a shade anxious. This mild course was maintained until fever settled by lysis on the 32nd day of illness. On the 24th day a mild degree of tympanites appeared and remained for three days.

The Spleen at the end of fever was Just Palpable and the Liver was 1 F.B. increased. G.I. System was normal. Deep Reflexes were increased, and the G.U. System was normal. Two months Convalescence was granted and this was without incident.

Comment on Cases of Group I.

On examination of Cases in Group I the two outstanding modifications of the usual course of the disease are :-

1. A marked lengthening of the fever (average 21.5 days, as against the average for the complete series of 17.38 days and of Group II of 14.5 days).
2. The delay in development of Toxicity in some cases and its relative diminution in others. This was a remarkable feature in view of the long fevers, (32 days in Case 1, 34 days in Case 2, and 26 days in Case 4.) and in view of the relatively high Temperature reached daily (103 - 104 degrees F.) (See Charts A,B,C, and Table VII.)

After one had been shown their Temperature Charts by the Sister in the Ward Side Room it was very surprising to see all but Case 2 sit up in bed to read and enjoy meals. Case 1 became toxic after 24 days, Case 2 after 16 days, and Case 4 not at all. Headache, retro-orbital pain, and respiratory signs when present, were minimal in all but Case 2 . Cases 3 and 4, in spite

of fever, both looked and felt surprisingly well.

Of all sixteen cases Case 2 alone showed visible loss in weight. Insomnia was unusual.

Of Group I, case 7 had the shortest fever of this sixteen.(14 days) . This case did however have a more rapid development of symptoms and was temporarily more acute than the others, having severe headache, cyanosis, and cardio-vascular collapse (See Chart D) on the 12th day. Recovery in this case was unusually rapid so that on the 19th day of illness he was fit for transfer to another Hospital.

Cases 11 and 12 both West Africans, the first of whom showed moderate, early toxicity with rapid and complete recovery, while the second had a coincident Amoebic Hepatitis which responded well to the exhibition of Emetine but left the underlying Typhus untouched. The response to treatment was well seen in the fall of the Leucocyte Total and Polymorph Counts.

It is perhaps noteworthy that in Group I the cases which proved to have the longest fevers (34, 32, and 26 days,) reached the highest Agglutination Titres in the series, as recorded on the 21st day of illness. Cases 1,2, and 4, all had O X K Titres of 1/1280. (This was the reverse of the

finding for the entire series. See Tables I and II and Diagram 1X).

Group II.

Cases who had received 1 c.c. of Scrub Typhus Vaccine Three or more Days Prior to Onset of Symptoms.

Cases Nos. 5, 6, 8, 9, 10,

For Case Notes See Appendix "C" except Case 9 which is reported here as sample of the Group. See also Table VII of Agglutinations and Length of Fever.

Case 9. 55333 Spr. D. A.W.Coy. (W.A.). aet.25.

Admitted on 19th November giving a history of not feeling fit since 17th November. He had received 1 c.c. of Scrub Typhus Vaccine on the 10th November.

On admission, he complained of severe headache, retro-orbital pain and retro-sternal pain, also some cough with a small amount of muco-purulent sputum.

On physical Examination : the throat was injected, the eyes suffused, and a few rales and rhonchi were present in the upper zones of both lungs. Blood Pressure was 100/70 m.m. Hg. , and there was slight epigastric tenderness.

An Eschar was found on the anterior wall of the

left axilla and the related axillary glands were greatly enlarged, rubbery, and tender. Other lymph nodes, especially posterior cervical were also enlarged and tender. The Spleen was 1 F.B. increased, and the Liver 1 F.B. increased and tender. No rash was seen. (See Temp. Chart.F.1.) Fever rose within 48 hours to 104 degrees F. and remained swinging between this and 102 degrees F. daily, never reaching normal. Deep and Superficial reflexes were normal, urine was normal. He lay quietly in bed and had lost the usual buoyancy of the West African. The Total White Blood Count was 5,600 / c.m.m.m. and the Differential Count, Polymorphs, 58%: Lymphocytes 38% : Monocytes 2%: and Eosinophils 2%.

Progress.

During the first week of illness the above mentioned signs and symptoms all increased in intensity. Bronchitis developed severly and the headache became most intense, Blood Pressure remained at 100/70 m.m.Hg. and Pulse Rate did not exceed 110 / minute. He lay very quietly in bed obviously rather frightened. On the seventh day his O X K Titre was 1/40, his deep reflexes were abolished, and he was complaining of mid-abdominal pain.

The Second Week.

Fever continued unabated with continuation of headache, and bronchitic signs. To these was now added dyspnoea with a respiratory rate of 46 / minute, Blood Pressure recorded 95/50 m.m.Hg., and Urinary Chlorides fell to 3 gms. per litre. By now the Spleen had increased to two and a half F.B. and the Liver to one and a half F.B. Further complaints were of pain in the right elbow joint with slight swelling and both knee joints. Acute laryngitis with complete loss of voice was also present and the O X K Titre was now 1/160. At this stage slight delirium with maniacal behaviour appeared and had to be dealt with by intramuscular injections of paraldehyde. On the 15th day resolution by lysis commenced and there was a sudden cessation of all symptoms and gradual clearing of all physical signs.

Recovery was very rapid and he was fit to be transferred to another hospital on the 18th day of illness.

Deep reflexes now returned and became exaggerated, Blood Pressure returned to 110/70 m.m.Hg., Total White Count rose to 6,500 / c.m.m. with a Differential Count of Polymorphs 46%; Lymphocytes 48%; Monocytes 4%; and

Eosinophils 2%. The Spleen had become 2 F.B. palpable and the Liver also 2 F.B. palpable, while the O X K Titre had now arisen to 1/320.

Comment on Cases of Group 2.

Cases of this Group seemed to be less affected in their course by inoculation than those of other groups. It did seem however that in these five cases the course of the illness was probably shortened, (Average length of Fever for these cases 14.5 days as against 17.38 days for the complete series.) and only one case, described above, showed toxicity for a short period followed by unusually rapid recovery.

Group III. Cases who had received 2 X 1 c.c. of Scrub Typhus Vaccine during or overlapping their Incubation Period.

Cases 13, and 14.

Case 13. 89867 W/S. A.R. of "X" C.R.E. Fort Mandalay.aet 30

Admitted on the 28th November 1935 complaining of slight headache and chilliness since the 21st of November. He had been inoculated with 1 c.c. of Scrub Typhus Vaccine on the 14th November and again on the 21st. No other complaintwas made.

On physical examination (7th day of the disease) the only abnormalities detected were an Eschar on the

ventral surface of the penis, with a lymphadenitis of the groins, and a slight injection of the fauces. No rash was seen. Blood Pressure was 110/70 m.m.Hg. Deep and Superficial Reflexes were present. No abnormality was noted in heart or lungs. Spleen was increased to 2 F.B. on the 7th day, and the Liver at this time was Just Palpable. The Total White Cell Count was 6,200 /c.m.m. and the Differential Count;Polymorphs 65%; Lymphocytes 32%; and Monocytes 3%. There was no abnormality found in Gastro-Intestinal or Genito-Urinary Systems. The O X K Titre on the 7th day was 1/40. Fever swung between 101/103 degrees F. daily. (See Temp.Chart.H.) During the first three days after admission the patient lay quietly in bed, ate well, slept well, and made very little complaint of any discomfort.

The Second Week.

On the 12th day fever resolved by lysis with cessation of all symptoms. On the 14th day Spleen was 1 F.B. increased, and liver 1 F.B. increased, while by the 21st day, the Spleen was Just Palpable and the Liver was 1 F.B. still.increased.

On the 12th day, Blood Pressure was 100 /65 mm.Hg.,

on the 16th day, 110/70 m.m.Hg. and on the 21st day 115/80 m.m.Hg. Deep Reflexes became very feeble on the 12th day but had returned briskly by the 21st. On the 14th day the O X K Titre had risen to 1/80, but unfortunately further reults were lost in a fire which gutted the Laboratory.

A second T.W.B.C. on the 14th day gave a reading of 4,500 c.m.m. with a Differential Count : Polymorphs 50%; Lymphocytes 45%; Monocytes 2%; and Eosinophils 3%.

Case 14. 212782 Spr.W.K. Eng.Bn. I.E. aet.45.

Admitted on 27th November 1945, on 4th day of illness, having been inoculated against Scrub Typhus on 18th and 25th November. On admission his only complaint was of slight frontal headache and aching limbs for the past four days. Temperature was swinging between 100 and 103 degrees F. (See Temp. Chart G.1.) and rather irregular, though tending to rise in the evening.

On examination an Eschar was found on the ventral surface of the scrotum on the right side and the right inguinal glands were much enlarged and tender. No rash was seen. Circulatory and Respiratory Systems were normal. Deep and Superficial

Reflexes were likewise normal, and Blood Pressure was 105/70 m.m.Hg., the Spleen was 3 F.B. increased and the Liver 1 F.B. increased. There were no other abdominal signs. The Genito-Urinary System was normal. The Total White Blood Count was 3,000 / c.m.m. with Differential Count of Polymorphs 56%, Lymphocytes 41%, Monocytes 3%, and Eosinophils 0%. No Malarial Parasites were seen. Throughout the first week the patient made no complaint except of a very mild frontal headache.

By the 7th day the Blood Pressure had fallen to 95/65 m.m.Hg. and the O X K Titre was 1/40. The patient felt wonderfully well, and, in view of all the signs, Chopra's Test and the Aldehyde Test were done and found to be negative. Likewise Splenic and Sternal Punctures revealed no Leishman-Donovan bodies.

He continued to sit up to take his food and slept well, and, apart from the increase in Liver and Spleen, the only thing which suggested that he was ill was the irregular fever swinging now from 99 to 103 degrees F. daily. Blood Pressure climbed steadily: 7th day 95/65 : 10th day 100/65 : 15th day 105/70 : 21st day 110/75:

30th day 120/85 m.m.Hg.

The Spleen gradually receeded in size but was still one and a half " " increased by the 21st day while the Liver had remained at 1 F.B. increased.

From the 14th to the 18th days a small degree of Tympanites was noted but the bowels continued to funtion normally. During this period also the Deep Reflexes were diminished but not quite lost. To one's surprise the fever continued, irregular, up to the 30th day, when it resolved by lysis. (See Temp. Chart G.2.) The O X K Titre rose to 1/80 on the 14th day, but here again the later tests were lost by fire.

At no time were there any respiratory or Circulatory symptoms or signs, and the entire course of the disease was characterised by a remarkable mildness when related to the irregular fever. Recovery once commenced, was rapid and complete. Although no malaria parasites were seen, there was a history of Chronic Malaria, and this was probably the cause of enlargement of Spleen and Liver rather than a coincident Kala Azar. A later T.W.B.C. done on the 21st day gave 5,400 / c.m.m. with a Differential Count of : Polymorphs 44%; Lymphocytes 50%

Monocytes 2% and Eosinophils 4%. Deep Reflexes returned and were equally increased by the 30th day.

Comment on Cases of Group III.

Despite the disparity of the length of fever in these two cases (12 and 30 days) the most notable feature of both was the extreme mildness and lack of toxicity. Neither was really ill, both sat up in bed throughout the illness and ate their food well and neither had any complications.

Group IV. Cases who had received Three X 1 c.c. of Scrub Typhus Vaccine overlapping their Incubation Period.

Cases 15 and 16.

Case 15. 213653. Spr. M.K. Eng.Bn. I.E. aet.29.

Admitted on 24th November 1945, on 3rd day of illness having been inoculated with 1 c.c. of Scrub Typhus Vaccine on the 6th, 13th, and 20th of November. (Three doses each of 1 c.c.) On admission, the only complaint was of shivering, and slight pain in the chest of two days duration.

On examination an eschar was found inthe right axilla and the axillary and inguinal glands

were enlarged and tender. The tongue was coated and dry and the fauces injected. The eyes were suffused and there was mild photo phobia. No rash was seen. Temperature on admission was 102 degrees F., and after remaining at that level for two days commenced a gentle swing from 100 degrees to 101 degrees F. daily, for the subsequent six days. (See Temp. Chart I.)

During the first week the patient made only slight complaint of cough and pain in the chest but continued to sit up and take nourishment throughout. Rales and rhonchi were found widespread in the right chest but no sign of Consolidation. The Total White Blood Count was 7,600 / c.m.m. with a Differential Count of Polymorphs 69%, Lymphocytes 29%, Monocytes 2%, and Eosinophils 0%.

On the 7th day the Spleen was not palpable and the Liver Just Palpable. On this day the Blood Pressure was 100/55 m.m.Hg. and the Deep Reflexes equally diminished. The O X K Titre was 1/40.

During the 2nd week of illness the signs and symptoms gradually cleared up and the fever gradually resolved on the 12th day by lysis, with complete cessation of all complaints. The patient did not lose weight or his appetite throughout the course of his illness and was fit for transfer on

the 16th day to another hospital for Convalescence.

On the 10th day his Spleen was Just Palpable and his Liver was not Palpable, Blood Pressure was 100/70 m.m.Hg. and Deep Reflexes still diminished. T.W.B.C. was 5,400/c.m.m. with a Differential Count of Polymorphs 56%, Lymphocytes 40%, Monocytes 2%, and Eosinophils 2%. By the 14th day his Spleen and Liver were Not Palpable and his Deep Reflexes fully returned. His O X K Titre was now 1/80 and his Blood Pressure 105/75 m.m.Hg.

The only other toxic symptom noted was very slight abdominal distension on the 12th day which responded to simple treatment at once. Recovery, once commenced, was very rapid and he was transferred on the 16th day of illness apparently well. (The final Agglutinations in this case were lost in a fire at the Command Laboratory.)

Case.16. 31186. Jem.F.S. Mob.Workshops. aet.25.

Admitted on 30th November, 1945, on the 5th day of illness, having been inoculated with 1 c.c. of Scrub Typhus Vaccine. on 12th, 19th, and 26th, November. On admission the only complaint was of slight fever and a slight frontal headache of

four days duration.

On Examination.:- an Eschar was found in the right inguinal region, with accompanying lymphadenitis. No rash was seen. Temperature on admission was swinging between 102 to 104 degrees F. daily, but immediately dropped to 99 to 102 degrees daily for the next three days, resolution by lysis commencing by the ninth day and finally becoming normal on the tenth day. This was the shortest fever of all the cases seen. (130 Cases.) (See Temp. Chart J.)

The eyes were slightly suffused. No abnormalities were found in heart, lungs, or abdomen. Reflexes were unaltered. It was difficult to persuade him to remain in bed since he maintained throughout that he felt perfectly fit, and, in fact, did continue to eat and sleep normally.

Spleen was just palpable and liver not palpable on the sixth day. Blood Pressure was 90/65, and Deep Reflexes normal. In the Weil-Felix Test the O X K Titre was 1/40, O X 19, 1/80 and O X 2.Nil, and the Total White Blood Count 7,000/c.m.m. while the Differential Count was:- Polymorphs 52%; Lymphocytes 40%; Monocytes 8%; and Eosinophils 0%.

On the Tenth Day Spleen was Just Palpable, Liver Not Palpable, and Blood Pressure 95/70 m.m.Hg. The O X K Titre was now 1/80, O X 19 also 1/80; and O X K 2 Nil. The Deep Reflexes were unaltered and Blood Pressure 95/70 m.m.Hg. By the 14th day the Spleen and Liver were not palpable, the Blood Pressure was 105/75 m.m.Hg. and the O X K Titre had risen to 160, O X 19 had fallen to 1/40 and O X 2 remained Nil.

All fever, signs, and symptoms had cleared by the 12th day, and the patient at his own urgent request was not sent on to Convalescence as was normal procedure, but was returned to his Unit on the 14th day with a recommendation for ' ten days excused duty'.

Comment on Cases of Group IV.

Fortunately, here again Eschars with accompanying Lymphadenitis were present to clinch the diagnosis in cases 15 and 16, particularly so since the final Agglutinations were lost by fire.

It was remarkable to see how fit these two cases kept throughout, and it does seem probable that, of all Groups, those who received three inoculations most benefited and therefore had the

shortest of all fevers without any noticeable toxicity as a result.

Conclusions Regarding Inoculation Cases.

The number of cases observed is much too small to permit of any generalisations but the following comment seems permissible.

On all Sixteen Cases only one (Case 2) could really be said to have been seriously ill, and even in this case the course of the disease was so modified that one is tempted to suggest that, but for the inoculation he would probably have succumbed.

This record compares very favourably with the over-all mortality of 7% and the fact that out of 130 cases fully 50% could be said to have been severely toxic at one stage of their illness.

No doubt was left in the writer's mind but that the inoculations profoundly altered the course of the disease in these patients for the better, and, in cases 15 and 16, almost aborted the disease.

Unfortunately the general prophylactic value of the Vaccine against Scrub Typhus could not be followed up by the writer, (owing to a Home Posting) and this has been left to a successor.

SUMMARY OF THESIS.

In this Study of Tsutsugamushi Disease certain aspects of the Disease came prominently to the notice of the observer, and, such as had not been emphasised previously, or had hitherto gone unremarked, have been specially stressed, in the course of an attempt to give a complete picture of the Disease.

Outstanding in the Clinical Picture, and possibly the key to the eventual successful specific treatment of the Disease, was the Anoxia of Tissues vital to the Economy due to the Specific Vasculitis. This state itself most readily observed as "Grey Cyanosis" is but part of a vi cious circle where a depressed circulation results in yet greater depression of the controlling Hypothalamic Centre. Possibly because of the above, and in any event aggravating the position, come further physiological and pathological changes: Tachypnoea, Extremely Defective Basal Aeration in the earlier weeks of the disease, and finally the frequent occurrence of Tympanites of a serious order rather late in the disease, all of which materially diminished Vital Capacity.

Another important symptomological group

were those which suggested that an Alkalaemia was basically the cause, viz: Anorexia, nausea, vomiting, headache, irritability, muscular tremor, carpo-pedal spasm and tetany. These symptoms were also noted to be related to a rise in Blood Urea and in some cases were followed by death in Uraemic Coma.

Changes in Blood Pressure and the Deep Reflexes have been followed in detail and it has been pointed out that in the period of early convalescence there is a reactionary increase is Systolic and Diastolic Pressures above average normal levels , while after the period of depression common to all toxic diseases, there is also a reactionary increase in Deep Reflexes, to such an extent that, in many cases Pseudo-Clonus was observed at the time of transfer to convalescence.

The integration and balance of Sympathetic and Parasympathetic Nervous System are said (by Samson Wright) to be controlled by a centre in the Hypothalamus (acting with the Posterior Lobe of the Pituitary) and it appears that this centre is specially affected by the Vasculitis.

Experimental stimulation of the Middle Hypothalamus is said to give Cardiac Slowing, Increased Gastric

Motility, Drowsiness, Torpor and Hypoglycaemia, (Samson Wright 1944) all of which are familiar signs in Scrub Typhus.

Attention has been drawn to Hepatomegaly which is regarded as part of the immunological response of the Reticulo-Endolethial System. This is deficient or absent in fatal cases, and probably on this account previously has been overlooked.

It was in the most serious cases who ultimately recovered that the three signs : Increased Blood Pressure, Increased Deep Reflexes, and Hepatomegaly, were most manifest.

An attempt has been made to establish a definite relationship between the severity of a case and its immunological response, as shown by the Weil-Felix rise in O X K Titre, and attention has been drawn to the prognostic implications.

From an Epidemiological point of view it was concluded that, in the aquisition of the disease, the entry of a fresh body of troops into an infected area was second only in importance to the maintenance of the pre-requisite level of Temperature and Humidity for the development of the Larval Mite.

Consideration of the cases arising from two special Units and other scattered cases led to the conclusion that many of the troops were infected while indoors and probably while sleeping, and, arising out of this observation, instructions were given that, in addition to other precautions, Di-Butyl-Phthalate should be sprayed on beds, bedding, floors, and night-clothing.

The problem has been raised of the undoubted tendency to a spontaneous drop in incidence of cases to zero after the first few weeks exposure to infection, but no satisfying solution is offered.

Treatment still leaves much to be desired; an increased use of Oxygen and Mersalyl is suggested.

In Part II a brief record has been given with Case Histories and Charts showing how Inoculation during the Incubation Period modified the Disease in the direction of prolonging the fever in some cases whilst at the same time reducing to a marked extent the Toxicity of the disease.

In the course of Mass Prophylactic Inoculation of a body of troops, a search made for Eschars in healthy men who had been exposed to risk of infection was entirely negative.

A Bibliography has been compiled after consultation with the recent comprehensive collection by **Blake, F.G. et alia (Ref. 14.) & Kohls, G.M. et alia (Ref. 79.)** and fifty-two recent recent references added thereto.

Seven Tables, Twelve Diagrams, and Temperature Charts of Twenty-Five Cases have been added in illustration of points raised in the Text.

APPENDIX "A"

THE COMPLETE CASE HISTORY OF A TYPICAL FATAL CASE.

2843 KARTAR SINGH aet 35 (L of C Ind.C.M.P.)

Direct admission to Hospital from a local Unit, on 6th July, 1945.

C/O. Fever, rigors, and severe headache of four days duration.

On Examination: A very well built man with obese abdomen.

Skin: An erythematous rash noted on abdomen, chest, shoulders and back, morbilliform in character.

Eschar: None detected.

Glands: Inguinal glands increased in size and tender.

Tongue: Lightly furred centrally. Ears, Nose and Throat all N.A.D.

Eyes: Suffused, pupillary reactions normal. Optic Discs normal.

C.V.S: Apex Beat $3\frac{3}{4}$" Lt. of Mid-Sternum in 5th.I.S. Heart Sounds, pure and regular, Pulse Rate 100 / min.

Blood Pressure, 120/80 m.m.Hg.

R.S: Excursion normal. P.N. normal. V.F. normal. No adventitious sounds. Resp.Rate 28 / min.

Abdomen: Obese, not distended, no ascites.

Liver: Not Palpable.

Spleen: Not Palpable.

U.G.S: N.A.D.

C.N.S: Deep Reflexes slightly and equally diminished Skin Reflexes: Abdom. + | + / + | + Cremasterics +

Plantars Rt. ↓ Lt. ↓

No Neck Rigidity.

Blood for M.P.s: Negative on six occasions.

T.W.B.C: 7,440 / cmm. Polys. 70%; Lymphs 29%; Monos. 1%.

Progress, Investigations and Treatment.

(See Temperature Chart 5 for entire course of Fever).

9.7.45. Referred to Medical Specialist who ordered transfer to Special Ward. Temp.Rising, Rigors every few hours, some Tympanites, Chest clear, Rash fading. T.103-104 deg.F. Pulse 118/ min.

Resp. 32/min.

Weil-Felix: OXK 1/25 OX19 1/25 OX2 Nil. Give Enema and Full Anti-Malarial Treat. Mist. Carminative 4 hourly.

12.7.45. Eyes still suffused, Inspiratory Rhonchi have developed at all areas. Give Acetylcholine 0.3 mgm. and Penicillin 15,000 Units 3 hourly.I.M.

13.7.45. More toxic, Pulse 120: Temp 104. Resp. 40/minute. ? Patchy consolidation in both lungs. Nurse in Fowler's Position.

Serum Chlorides .... 450 mgm./100cc.
Blood Culture... Sterile. Nikathemide 1 cc.S.O.S.
Placed on D.I.List.

Blood Urea ... 62 mgm./100cc.

Record Fluid Balance.

14.7.45. Very Toxic (See Chart V). Give Brandy 2 oz. 2 hourly. in continuous fluids. Inspiratory Rhonchi, patchy, Bronchial Breathing.

15.7.45. Above signs, with accentuated 2nd. pulmonic increase in Tympanites, very drowsy, eyes congested.

APPENDIX "A"

16.7.45. Slightly less toxic, 2nd. pulmonic sound less noisy. No increase in consolidation.

Weil-Felix. OXK 1/250 OX19 1/25 OX2 Nil.

Widal To 1/40 AO Nil.

T.W.B.C. 5,800 c/mm.

All treatment continued including Penicillin.

17.7.45.

Urinary Chlorides. 2 G. /Litre.

Give Oxygen in Tent 2 hours in eight.

Oedema of ankles and bases of lungs. More Tympanites. Respirations 60/minute.

Blood Pressure 90/65 mm.Hg.

Extremities warm, no sign of venous congestion.

Extreme myocarditis - Tic-tac rhythm, regular. Breathing very shallow and rapid, greatly impeded by extreme Tympanites.

Give:- Strychnine gr.1/60. 4 hourly alternatively with Pituitarin 1 cc.

Spleen 2 FB: +

Liver 1 FB +

Only complaint is of exhaustion. Still no Nuchal Rigidity. Kernig's sign Negative. Optic Fundi Normal, R. and L.

Deep Reflexes all absent.

Urinary output in 24 hours.. 28 oz.

18.7.45. Heart sounds of better quality. Discontinue Strychnine.

Less distressed. Oedema I.S.Q.

Continue all other treat.

Widal: TO/1/40. AO Nil. Give Digoxin 0.75 mgm.I.V.

Weil-Felix. OXK 1/500
OX19 1/25
OX2 Nil.

Serum Chlorides 250 mgm %. Give Ephedrine gr.i. I.M. t.d.s.

19.7.45. 09.00 hrs. Condition deteriorating. Stop Pituitarin.

P.136, T.102 deg. R.58/min.

Occasional Extrasystoles.

Tic-tac rhythm. No cardiac enlargement or Venous Congestion. Incontinence of urine. Blood Pressure 110/70 mmHg.

Subsaltus Tendinum present. Deafness marked.

Blood Urea: 76 mgm/100 cc. T.W.B.C. 10,400/cmm.

Widal: TO Nil. AO Nil.

Weil-Felix: OXK 1/500
OX19 Nil.
OX2 Nil.

16.00 hrs. Pulse reduced to 118/minute.

Repeat Digoxin 0.75 mgm. I.V.

23,00 hrs. Slight spasticity of muscles of arms and hands. Also neck rigidity. Frequent extrasystoles and extreme variations in

rhythm and volume of pulse. Resps. 60/min.

Fully conscious and makes no complaint. Oedema and Tympanites Increasing. Still taking nourishment well.

Atropin 1/100 gr. 4 hrly.
Repeat Digoxin 0.75 mgm.
(No need for intra-venous fluids).

20.7.45.

Pulse irregular and Dicrotic.

(See Temp.Chart V.)

Give Hypertonic saline by mouth.

Spleen 2 FB+: Liver:1½FB+

21.7.45.

Urinary Incontinence.

Otherwise slightly improved.

Less Tympanites, Less Oedema of legs and bases.

Carpo-pedal spasm present. Urine; S.G.1020 Albumin, a trace.

No sugar or Bile. Chlorides 2 Gm. / Litre.

22.7.45.

Volume and Tension of Pulse improved. Low muttering delirium and restlessness. Now obstructive and difficult to feed. Carpo-Pedal spasm apparently helped by Saline Orally. Subsaltus Tendinum marked. Lips Tremulous. Oxygen Continuous. Dullness Right Base and large rales.

Give Hypertonic Glucose-Saline Conc.20% in 60 cc - 20 cc. slowly I.V(10 Gm).

Poor Air Entry at both bases.

No Creps. Oedema of legs increasing,

No ascites.

Blood Urea: 364 mgm/100cc.

Urinary Chlorides: 2 Gm. / Litre.

Unconsciousness temporarily restored by I.V.

Glucose Saline Conc. 20 cc 20%.

Widal: TO Nil AO Nil. Weil-Felix: OXK/ 1/640.

08.00 hrs. Further deterioration, again semi-conscious.

Blood Pressure: 120/60 mm.Hg. Repeat Hypertonic Glucose 20 cc.
Slight cyanosis, as above.

Slapping 2nd.Pulmonic sound.

Faint systolic at base. No enlargement. Give Nikethamide and Brandy S.O.S.

23.7.45.

12.00 hrs. Again fully conscious,

Able to speak and recognise

people. Respiratory rate 68/min.

Pulse 160 / Min. 12.45 hours. Expired.
(on 21st day of illness).

POST - MORTEM REPORT.

Performed on 23.7.45 at 14.00 hrs.

Body of a well developed moderately well nourished male,

with distended abdomen and oedematous legs. Rigor Mortis not present.

Brain: Slightly oedematous, vessels of pia arachnoid congested but no petechial haemorrhages seen on section of brain.

Pleurae: About two ounces of serous fluid contained. Some Adhesion of parietal to visceral layers at right apex.

Lungs: Rt. and Lt. both intensely congested and oedematous, muco-purulent secretions expressed from bronchi and bronchioles. One patch of red hepatisation in right middle lobe, but in spite of all this all sections of both lungs float in water.

Pericardium: Normal.

Heart: Normal in size, muscle wall thickened and pale, valves competent and coronary vessels patent.

Liver: Very slightly increased in size, congested, nutmeg appearance, with an increase in appearance of fattiness.

Spleen: Increased in size by one half, consistence normal.

Stomach: A few submucous haemorrhages present.

APPENDIX "A"

Intestines and Pancreas: Both normal macroscopically, but distended with gas which rushed out with an audible hiss on gut being pricked.

Kidneys: Both normal in size, intensely congested, cortex reduced in depth, capsule strips readily.

Supra-renals: Apparently normal.

Urinary Bladder and Prostate, normal.

APPENDIX "B". Page i.

FULL CASE REPORT OF A VERY SEVERE CASE WHO FINALLY RECOVERED.

No. 54036. HARI SINGH. Age... 38. Rank..H/C.

Unit : Advanced Depot - Burma. Service - 10.

Disease :- RICKETTSIASIS - SCRUB. Station: MANDALAY.

12.9.45. Fever for past 5 days without remission and severe constant headache.

P.H. No Malaria or Dysentery. On Suppressive Mepacrine. Arrived in Fort Mandalay 20.8.45. D.B.P. used once.

O.A. T.104'. P.110. R.28. Well-built and nourished. Eyes Normal. Glands Nil. Tongue white, furred, margins sore. Throat N.A.D. Skin dry macular Rash, fading: Eschar: Rt. Ant.Axill Fold. CVS. A.B. 3½" Lt.Mid. Vth.I.S. Sounds pure and regular. B.Pr. 140/90 m.m.Hg. R.S. Poor air entry Lt. Base. No advent sounds. Abdomen N.A.D. Liver N.P. Spleen N.P. UGS. N.A.D. BRINE. N.A.D. C.N.S. Deep Reflexes very sluggish. Abdominals: + | +
+ | +

INVESTIGATIONS AND PROGRESS.	TREATMENT.
	Mist Alkali. 1 Oz.
	4 hourly.
B/S.3 Neg for M.P.s.	Glucose Soda Drink.
TWBC. 6/800/cm. Differential :-	
P.74%:L.24%: M.1%: E.1%:	
Widal TO.Nil. AO.Nil. Weil-Felix:	
OXK20: OX2:20 : OX19.20.	
15.9.45. A few inspiratory rales, and rhonchi at Poor entry/bases, has less toxicity.	
	Mist.Expect.Stim 1 oz.
16.9.45. Toxicity remains, pulse rapid, feeble.Slight tympanites.Spleen 1.FB. B.Pr. 120/85.	
	Stop Mist.Expect.Stim. and give Mist.Asthma 1 oz. 4 hourly.
18.9.45. Very much more toxic, grey colour, sweating. Rapid feeble pulse, marked dicrotism. T.105'. P.132. R.34. B.Pr. 100/80 m.m.Hg.Deep Reflexes lost. Blood Urea.Spoilt Rpt.	I.V.Glucose Saline continuous. Coramine 1 amp.4-hrly. Penicillin 15,000 U.s 3 hrly. Ca Gluconate in altern. pts to 5 pts. in all.
Widal Weil Felix OXK.20. OX19 20. OX2 20.	Discontinue Coramine.

19.9.45. Slightly improved. Less Toxic. Pulse. Better Volume. Tongue moist. T.103'. P.100. R.30. Tympanites.	Continuous Glucose Saline with Ca Gluconate in alt. pts. 5 pts. Continue Penicillin 3 hourly.
20.9.45. T.104'. P.120. R.40. Toxic but feels better. Very poor air entry. Rales and Crapes at bases. Tympanites worse, marked distension.	Acetyl. Chol..3 mg. 1. M. Saline washout. 2200 hrs. 2 pts Glucose Saline with 50 c.c. 30% Glucose - Ca. Gluconate 10 c.c. 10% in each pint.
21.9.45. Less toxic this morning, very exhausted. B.Pr. 105/80 m.m.Hg. Pulse feeble, Compressible - Tongue moist. Losing weight. Stool - No Exudate or Ova.	Acetyl Chlor..3 mg. 1 M. Pituitarin ½ c.c. bd. Saline washout. Rpt. above treatment.
21.9.45. TWBC. 8,800. DC.-P.67%. R.30%. M.1%. E.2%.	Glucose Saline with glucose 30%. 50 c.c. and Ca Gluconate 10 c.c. 10% in each pint. 4 pints in all. C.T.
22.9.45. More toxic again - pale greyish colour of skin.	
23.9.45. 0900 hrs. Much worse. Semiconscious, can barely respond. Deep reflexes abolished. Beyond complaining. Heart almost inaudible. B.Pr. 100/75. mm. Hg. 1800 hrs. Circulation improved. T. 103.4'. P. 106/m. R. 36.	

Tympanites Severe.Oedema of legs increasing.

24.9.45. Blood Urea. 56 mg.% Widal TO20:AO Nil.Weil-Felix OXK.80: OX2.40. OX19.40. Still critical but shade of improvement.

Continue I.V.Glucose Saline. c.Gluconate. 14 pints over 36 hrs. then stopped.

25.9.45. Central Circulatory failure. Oedema of hands;feet, legs extremities warm. B.Pr.110/75. Deep reflexes normal.Less Tympanites.1400 hrs. Very Toxic. Tympanites worse again. 2200 hours.Slightly less toxic.

Entirely fluids;milk and brandy 2 hrly. Push/Fluids (1 oz.Coramine 1 amp. 2 hrly.) Digoxin 0.75.I.V. Atropin Gr.1/100 stat. Mersalyl 1 c.c.(on trial) I.M.

26.9.45. 0900 hrs. Distinct improvement.Considerably less toxic.Oedema of feet persists. Extremities warm.Some reaction to Glucose Saline in tissues of Rt.Arm.Less Tympanites.B.Pr. 115/60 m.Hg.1800 hrs. Greatly distended again.

1. Hot Compress to Rt.Arm.
2. Brandy in milk oz.1. 2 hourly.
3. Coramine 1.75 mg.4 hrly.
4. Digoxin 0.5.mg.I.V.
5. Pituitarin ½ c.c.4 hrly.
6. Acetyl.Chol.3 mg.

Give Pituitarin 1 cc.stat.

27.9.45. 0900 hrs.Very exhausted. Oedema of extremities. Still

C.T. as above. Try oxygen 15 m.in 1 hr.

increasing.Crepes at both bases. Grey colour. Extremities bluish but warm.1800 hrs. Slight relief with Oxygen.	per B.L.B. mask. C.T. as above. 7. Repeat Mersalyl. 2 c.c. 1.M. 1.
28.9.45. 0900 hours. No air entry at bases. Colour a little better. Tympanites marked. Heart sounds regular,pulse 130 T.Remitting R.48. In general condition just a shade less critical. 1600 hrs. Slightly less toxic.Very exhausted. Good diuretic response.	1. Convalescent Serum.5 c.c. 1.M.
29.9.45.B.Pr.130/90.Is greatly improved. Pulse 88/m good volume regular R.28/cm. No distress.W.F.OXK.160.OX2.20. OX19.20.	Oxygen Cont. Pituitarin ½ c.c.bd.Coramine 1.75 mg.
30.9.45. 0900 hrs. B.Pr.115/70. Pulse fair volume and tension. Very drowsy as result of Sedative. Resp.28/mm.Oedema of legs greatly increased.	Given Paraldehyde 10 c.c. 1M at 0200 hrs.(by OMO.) Convalescent Serum 5.c.c.Digoxin 0.5.mg. Pituitarin ½ c.c. Mist. Caffein.Cit.oz.1.2 hrly.

URINE. S.G.1010/Alk.Alb.Trace Bile.Sugar Nil. Triple Phosphates. No Organic Deposits.

1.10.45. Less toxic, but very exhausted,drowsy,apathetic. Skin breaking over rt.buttock. Doubly incontinent. Urinary Chlorides 3 gms. per litre. TWBC.8,800. P.45%.M.3%. L.50%. E.2%. Differential.

2.10.45. B.Pr.125/75.mm.Hg.Drowsy, responds when roused.

3.10.45. Much less oedema of legs. Much more conscious,awake, responding. Pulse better quality and volume.96/min.Excreting large quantities of urine,becoming continent.T.falling.

4.10.45. Much improved.Taking interest in everything. Bladder under control.Continent, now passing quantities of urine.

Limit fluids to 5 pts. daily. (Present intake 12 pts. Out 7 pts.)
Salt free diet.
3.Convalesc.Serum.5.cc.I.M.
Digoxin 0.5.mg.once.I.M.
Mist.Caffein.Cit.oz.1.4 hrly.
4.Convalescent Serum. 5.c.c
C.T.Mersalyl. 2.c.c.I.M.
5. Convalescent Serum.5.c.c.

C.T.

Mersalyl 2.c.c.

7.10.45. Marked Improvement. Bed sores healed. Very little oedema of legs. Actively taking interest. No tympanites. Heart sounds improved.

8.10.45. TWBC.6,400/cmm.P.53%.L.41%.E.3%. M.3%. Slight fever last night. Bed sore has sloughed and now pus has formed beneath. Hypertonic Saline thrice daily to sore and Penicillin 30,000 Units 6 hrly.

15.10.45. Widal. T020.A0 Nil. Weil-Felix OXK40. OX2.Nil.OX19.Nil.

16.10.45. Reflexes - returning.

Liver : 2.F.B.+. Spleen.J.P.B.P.145/95 mm.Hg. mm.Hg.

25.10.45. Blood for Widal & Weil Felix.

30.10.45. B.Pr. 150/100. mm.Hg.

31.10.45. T.R.B.C.4,080,000. Patient is weak. P.120. Hb.12.3 gms/100 c.c. Mist Iron Tonic oz.1. Fluids.

3.11.45. Now fit to proceed to Maymyo for 1 month convalescence to be followed by 2 months sick leave if possible. — An almost fatal case of Scrub Typhus now left seriously debilitated,unlikely to be fit for service in less than another four months.

APPENDIX "C".

A SYNOPSIS OF THE REMAINDER OF INOCULATED CASES REFERRED TO IN THE TEXT.

GROUP I. CASE II. 10684. Capt.R.,C.R.E.Mandalay.Aet.27.

Admitted on November 17th 1945, complaining of headache and not feeling fit since 14th November 2 days after being inoculated with 1 c.c.Scrub Typhus Prophylactic Vaccine.

On Examination: no abnormality was detected save an Eschar on the ventral surface of the penis, glands in both groins enlarged and tender, and a faint Macular Rash, best seen, or rather, felt, over the trunk and shoulders. (Patient was very dark-skinned.) Although the patient was slightly apprehensive the only real indication that he was ill was his fever of 102-103 degrees F. daily, (See Temp.Chart B.i) but he sat up in bed, ate, and felt quite well.

On Admission his Spleen was not palpable, his Liver 1 F.B. increased, his Blood Pressure 100/60 m.m.Hg., Circulatory and Respiratory Systems were normal and Deep and Superficial Reflexes normal.

The Total White Blood Count was 4,600/c.m.m. and Differential Count, Poly. 67%, Lymphocytes 31%, Monocytes 2%, and Eosinophils 7%. Urine was normal,

and there were no digestive disturbances. The O X K Titre on the 7th day was Nil.

Progress :- During the entire first week following admission there was no material change in his condition from the above while Temperature was maintained at 102 - 104 daily, and on the 14th day almost reached 105 degrees F. Meantime there were neither chest, Circulatory or Respiratory signs.

By the 14th day the Spleen had become Just Palpable, the Liver 1½ F.B. increased, the Blood Pressure 100/70 m.m.Hg. and the O X K Titre 1/40. He was depressed but was eating well and sleeping reasonably well.

On the 15th and 16th days however, a change came over him and toxic signs commenced to appear. Respiratory rate increased to about 40 per minute and Pulse to about 140 per minute while Temperature remained sustained at about 103 degrees F. Bronchitic signs appeared with very poor aeration at both bases and a pallid or "grey cyanosis". Slight tympanites appeared on the 15th day but never as troublesome as in the un-inoculated cases.

Oxygen was administered in an Oxygen Tent and gave marked objective, though little subjective improvement.

His appetite had flagged and he was obliged to lie flat in bed; he was markedly despondent and slightly drowsy.

The next development was Cardio-Vascular Collapse with marked cyanosis on the 21st day of illness. (See Temp. Chart B.ii.) Blood Pressure dropped for 24 hours to 80/50 m.m.Hg. all deep reflexes were absent, marked tympanites had appeared, and O X K Titre had reached 1/1280. Temperature fell to subnormal, respirations reached 56 per minute and pulse rate 144 per minute. There was slight patchy consolidation at the Left Base. He was now obviously critically ill and was placed on the D.I.List. With continuance of Oxygen, Intra-Venous Glucose Salines, and Trans-Nasal Feeding he rapidly passed this crisis. Remittent Fever rising to 101 degrees F. daily now ensued and continued up to the 35th day of illness. Recovery was rather slow and accompanied by marked loss in weight. A trace of albuminuria noted on the 21st day. Blood Pressure had climbed to 120/80 mm.Hg.

by the 34th day. Deep Reflexes had returned and become markedly increased with some pseudo-clonus by the 30th day. On the 32nd day he developed a furuncle of the upper lip but this responded almost at once to Penicillin 15,000 Units three hourly to a total of 360,000 Units, Intra-Muscularly, thereby reducing the Temperature finally to normal on the 36th day of illness. (See Temp. Chart B.iii.)

Convalescence was prolonged and Discharge from the Service was recommended. This was the most serious of all sixteen cases who were inoculated. It appeared that the onset of Toxicity was probably delayed by the inoculation, but the toxicity could not be said to have been diminished.

CASE III. Cook Khasim. C.R.E.Mandalay. Aet.30.

Admitted on November 21st 1945, complaining of having had a rigor, headache and backache all dating from 14th November on which date he received an inoculation of 1 c.c. Scrub Typhus Prophylactic Vaccine.

On Examination the only physical signs were

an Eschar on the right lumbar region and some enlargement and tenderness of the right inguinal glands. In brief, the following indicates the course of the case :-

Continued Fever between 103-104 degrees F. for seventeen days resolving by Lysis.

(See Temp. Chart D.)

In spite of this high and continued fever the patient looked and felt surprisingly well throughout, and there were no subsequent complications. Changes in the physical signs may be tabulated as follows :-

	Admission.	2nd. Week.	4th Week.
Spleen.	1. F.B.	1.F.B.	J.P.
Liver.	1 F.B.	1.F.B.	1½ F.B.

Blood Pressure. On 7th,10th,12th,14th, 21st, 24th days of illness. 100/60, 95/55, 90/60, 95/65, 100/70, 110/80 m.m.Hg.

Total White Count and Differential Count.

On Admission : T.W.B.C. was 5,200/cmm.
Polymorphs. 77%. Lymphocytes 22%,
Monocytes 1%. Eosinophils.Nil.

On 16th day.Day.T.W.B.C. was 4000 /cmm.
Polymorphs. 75%. Lymphocytes.23%
Monocytes 2%. Eosinophils.Nil.

Agglutination Titres O X K.

7th day, 1/40. 14th day 1/80. 21st day 1/320.

Deep Reflexes. On Admission Normal; 3rd week diminished; On discharge - increased.

This patient was transferred on the 24th day from onset making an excellent recovery.

CASE IV. Abro. 600. Captain L., Burma Depot. Aet.23.

Admitted on 20th November 1945, the sixth day of illness, complaining of malaise, lassitude, slight headache and suffused eyes. He had received 1 c.c. Scrub Typhus Prophylactic Vaccine on the 12th November, 2 days prior to onset of symptoms. On Examination, he too proved to have an Eschar in an early stage on the Left Flank anteriorly and a morbilliform rash over all the trunk. There was, moreover, great increase in the left inguinal glands and they were tender. Fever on admission was 101-102 degrees F. daily and continued in type. (See Temp.Chart C.) Apart from the above mentioned, other signs were absent. This state of affairs continued for 26 days during which the patient sat up in bed and ate heartily every meal. He lost no weight, had no complications, and the only other

symptom was a mild degree of insomnia. One interesting feature was that the Eschar appeared to abort about the 10th day and never formed a proper necrotic coagulum, though it did leave a scar. This was the only case in the entire series in which the Eschar was seen to abort. Other findings during the course of the fever were as follows :-

	Admission.	2nd. Week.	4th Week.
Spleen.	J.P.	1.F.B.	J.P.
Liver.	J.P.	1.F.B.	1½ F.B.

Blood Pressure.

on 7th, 10th, 12th, 17th, 19th, 21st.

120/70, 110/65, 125/70, 110/65, 110/70 mm.Hg.

Total White and Differential Counts.

On Admission TWBC. was 5,000/cmm. Polymorphs.46%.Lymphs.51%. Monocytes 3%. Eosonophils. Nil.

On 21st Day. T.W.B.C. 5,400/cmm. Polys. 44%. Lymphs. 49%. Monocytes.7%.Eosons.Nil.

Agglutination Titres O X K.

On the 7th day, Nil. 14th day, 1/80. 21st day 1/1280.

Deep Reflexes. On admission Normal. 2nd week Lost. 4th week increased.

There was very slight tympanites on the 21st day.

It was most noticeable that toxicity was greatly reduced, and this was most remarkable in view of the sustained high fever. He was rather irritable but perfectly clear mentally throughout and was able to enjoy reading. There were no complications and in the end his recovery was quite rapid.

CASE VII. .95077. L/Nk.S.S., C.R.E.Coy. Aet.27.

Admitted on 22nd November 1945 complaining of six days headache, fever and pain behind the eyes.

He had received 1 c.c. Scrub Typhus Prophylactic Vaccine 2 days prior to the onset of symptoms.

On admission, in addition to the above complaints, he was constipated, had lost all appetite, and appeared acutely ill.

On examination : The eyes were suffused, the tongue dry and furred. No Eschar and no rash were observed, though there was a slight general increase in lymphatic glands, and temperature on admission was 103 degrees F.

There was slight tympanites and a small degree of cyanosis. From this it will be seen that he was admitted in a much more acute condition than any of the other cases. (See Temp.Chart E.) Other findings were as follows :-

	Admission.	2nd Week.	3rd Week.
Spleen.	N.P.	J.P.	N.P.
Liver.	N.P.	1 F.B.	1 F.B.

Blood Pressure.

On 10th, 12th, 13th, 14th, 16th, days of illness.

98/75,80/50,90/70,95/70,95/70 m.m.Hg.

Total White and Differential Counts.

TWBC. 6,400 cmm. Polymorphs 60%, Lymphocytes 37%. (on 11th day). Monocytes 2%, Eosinophils 1 %.

Agglutination Titres, O X K.

On 7th day, 1/40; 12th day 1/160; 19th day 1/360.

Deep Reflexes. On Admission,diminished equally;

2nd week, absent; 3rd week, returning, still feeble.

On the 12th day there was a severe circulatory collapse necessitating Intra-Venous Glucose Salines and Pressor drugs, but, as in other similar cases, recovery was rapid. He was fit for transfer to another hospital on the 19th day of illness.

CASE XI. 63074 Spr.A. 26 A.W.Coy.(W.A.) Aet.22.

Admitted on 16th November complaining of pain in the jaws and ears all the previous night and fever with headache for the past six days. He had been inoculated with 1 c.c. Scrub Typhus Prophylactic Vaccine on the day of onset of the fever.

On Examination : he was found to have an Eschar on the posterior surface of his scrotum and an inguinal adenitis, but no rash was discovered. There was a slight bronchitis and his Liver was slightly tender on the 12th day of illness.

Tympanites was present to a small extent on the 13th day and on the same day a little fresh blood was seen in the stools.

Fever was continued between 102 - 104 for fourteen days and subsided by Lysis. (See Temp. Chart .) Other findings in this case were as follows :-

	On Admission.	2nd Week.	3rd Week.
Spleen.	2.F.B.	4.F.B.	2.F.B.
Liver.	1.F.B.	1½.F.B.	2.F.B.

Blood Pressure.

On 7th, 12th, 14th, 17th days of illness.

100/75.90/60.95/60. 120/70. m.m.Hg.

Total White and Differential Counts :-

T.W.B.C. 8,400/cmm. Polymorphs 55%. Lymphocytes 43%.
(10th day.) Monocytes. 1%. Eosinophils.1%.

T.W.B.C. 7,400 /cmm. Polymorphs 58%. Lymphocytes 40%.
Monocytes 2%. Eosinophils.Nil.

Agglutination Titres O X K.

On 7th day Serum : 14th day, 1/80, 21st day 1/160.
Septic.

Deep Reflexes. were absent on admission but returned and were generally increased prior to transfer.

In this case there was moderate early toxicity with rapid and complete recovery and no complication other than rectal haemorrhage from haemorrhoids.

CASE XII. 53004. Spr.B., A.W.Coy.(W.A.). Aet.25.

Admitted on 12th November complaining of fever, frontal and occipital headache, and

cough, all of four days duration. He had been inoculated with 1 c.c. Scrub Typhus Vaccine on 10th November, two days after the onset of symptoms.

On Examination at Admission he was found to have an Eschar on the left scapula, also an axillary and cervical adenitis, but no rash was detected. A small degree of bronchitis was present; a cardio-vascular system was normal but there was a 1 F.B. enlargement of liver which was tender. Tympanites was noted on the 17th day but was not severe. The tenderness of liver combined with leucocytosis led to the diagnosis of a coincident amoebic hepatitis. This treated with emetin responded satisfactorily leaving the typhus unaffected.

Other findings :-

	On Admission.	2nd Week.	3rd Week.
Spleen.	N.P.	J.P.	N.P.
Liver.	1.F.B.(tender)	2.F.B.	1.F.B.

Blood Pressure.

On 7th,	10th,	14th,	18th,	25th.
105/65.	100/60.	95/55.	100/60.	110/70.

Day.	TWBC.	Polymorphs.	Lymphocytes.	Monocytes.	Eosoniphils.
7th.	9,400.	69 %	30 %	1%	0%
10th.	13,400.	51 %	48 %	1%	0%
14th.	12,600.	70 %	28 %	2%	0%
18th.	8,400.	66 %	37 %	2%	1%
25th.	7,100.	58 %	40 %	1%	1%

Agglutination Titre O X K.

7th day 1/40 : 14th day 1/160 : 25th day 1/320.

Deep Reflexes were diminished during the second week and increased at the end of the third week and later.

Fever was continued for the first 13 days and thereafter was irregular for the following 5 days. The presence of the coincident Amoebic Hepatitis probably made the case much more toxic than would otherwise have been the case. He made a fairly rapid and complete recovery. A course of Penicillin was given.

GROUP II. CASE V. 93262. Sep.H.K., C.R.E.Mandalay.Aet.20.

Admitted on 18th November complaining of slight headache, anorexia, constipation, and pain in the back of the neck, all of two days duration. He had received 1 c.c. of Scrub Typhus Prophylactic Vaccine on 12th November 4 days prior to onset.

On Examination he was noted to have an Eschar behind his right ear. (This was unique as to position.) The posterior cervical glands were enlarged and tender but no rash was discovered. No bronchitis or cardio-vascular affection was noted. Fever was continued for fifteen days then subsided by lysis. Slight Tympanitis was noted on the 11th day. Other physical signs were as follows :

	On Admission.	2nd. Week.	3rd Week.
Spleen.	1 F.B.	1 F.B.	J.P.
Liver.	J.P.	1 F.B.	1 F.B.

Blood Pressure. 7th day, 105/65. 10th day 100/65. 12th day 100/60.

Day.	TWBC. /c.m.m.	Polys.	Lymphs.	Monos.	Eosins.
7th.	7,200.	62%	39%	4%	0%
14th.	18,400.	46%	51%	2%	1%

Agglutination Titres of O X K.

On 6th day, 1/40: on 12th day 1/80. on 18th day 1/640.

Deep Reflexes.

On admission present; from second week until discharge greatly diminished.

After a period of moderate toxicity he recovered quickly and was fit for transfer on the 17th day after admission.

Slight broncho-pneumonic patches appeared on the 12th day and responded well to Penicillin Parenteral therapy.

CASE VI. Civil Clerk. Pillai.att.C.R.E. aet.25.

Admitted on 21st November, 1945, complaining of slight frontal headache and lassitude of two days duration, having been inoculated with 1 c.c. Scrub Typhus Vaccine on 14th November five days prior to onset.

On Examination. No Eschar or rash was discovered but interpalpebral congestion was marked and there was a mild general adenitis. The tongue was coated centrally with a thick white fur. Rhonchi were prominent at both apices and the bases were poorly aerated. Slight tympanites developed on the tenth day.

In view of the absence of both Eschar and Rash, it was fortunate for diagnosis that the O X K Titre rose early. Temperature was irregular and moderate, resolving by lysis after 12 days. Other findings were :-

	On Admission.	2nd Week.	3rd Week.
Spleen.	N.P.	J.P.	1.F.B.
Liver.	N.P.	1 F.B.	1.F.B.

Blood Pressure on named days of illness :-

9th 100/70 ; 11th 95/65 ; 13th 90/50; 17th 95/60;

21st 110/75 mm.Hg.

Day.	TWBC/C.m.m.	Polys.	Lymphs.	Monos.	Eosinophs.
8th.	7,400.	72%.	28%.	0%.	0%.
15th.	10,000.	74%.	22%.	2%.	2%.

Agglutination in Titres of O X K.

On 7th day, 1/80 ; on 14th day 1/1280. No other done.

Deep Reflexes.

Present on admission, diminished during second week, returned with great increase generally in third and subsequent weeks. The patient made an excellent recovery and was fit for transfer on the seventeenth day of illness.

CASE VIII. 241299. M/W.Chelliah. C.R.E. aet.25.

Admitted on 22nd November complaining of chilliness with frontal headache of three days duration. He had received 1 c.c. Scrub Typhus Prophylactic Vaccine on 14th November, five days prior to onset.

On Examination: An Eschar was found on the right flank with Inguinal,Axillary and Cervical Adenitis. No rash was noted. The eyes were congested, the tongue coated centrally, and rales and rhonchi were heard at all areas in both lungs.

A small degree of Tympanites developed on the 14th day, but was not serious or persistent. Temperature was irregular and lasted 17 days. Other findings were as follows :-

	On Admission.	2nd. Week.	3rd Week.
Spleen.	N.P.	J.P.	N.P.
Liver.	N.P.	J.P.	1.F.B.

Blood Pressure. on named days of illness :-
7th 95/60; 10th 100/65; 14th 95/60; 20th 100/70 m.m.Hg.

Day.	TWBC/c.m.m.	Polys.	Lymphs.	Monos.	Eosins.
10th.	6,000.	54%.	42%.	3%.	1%.
17th.	5,400.	50%.	47%.	1%.	2%.

Agglutination in Titres of O X K.

On 6th day 1/40. 12th day 1/160. 17th day 1/320.

Deep Reflexes were abolished in the second week and returned with slight general increase in the third week and later. Although thefever lasted 18 days there was very little toxicity indeed. Slight bronchitis and tympanites were the only complications.

CASE X. 56110. Spr.Welbeck. A.W.Coy.(W.A.) aet.23.

Admitted on 17th November 1945 complaining of fever, headache and dry cough all of oned ays duration. He had been inoculated with 1 c.c.Scrub Typhus Vaccine

on 10th November, seven days prior to onset.

On Examination : An Eschar was found on the Anterior fold of the Axilla and the corresponding axillary glands were very much enlarged and tender. No rash was observed. There was inter-palpebral congestion even greater than that usually seen in an African. A few rales were noted in the chest but no consolidation developed.

Other findings were as follows :-

	On Admission.	2nd Week.	3rd Week.
Spleen.	N.P.	J.P.	N.P.
Liver.	N.P.	J.P.	N.P.

Blood Pressure. on named days of illness :-

5th day 95/65 ; 10th day 90/60 ; 18th day 120/80 m.m.Hg.

Day.	TWBC./c.m.m.	Polys.	Lymphos.	Monos.	Eosinophs.
8th.	7,400.	48%.	44%.	6%.	2%.
16th.	6,200.	52%.	42%.	4%.	2%.

Agglutinations of O X K.

On 7th day 1/40 ; 14th day 1/80; 21st day 1/640.

Deep Reflexes were unaffected throughout.

Though this appeared to be a very mild case with no toxicity whatever, it will be noted that there was a considerable drop in Blood Pressure readings during the first and second weeks of illness. Recovery was rapid and complete.

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ADDENDA

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