Proceedings of conference of medical specialists of Eastern army held in March 1943.

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PROCEEDINGS

OF

CONFERENCE OF MEDICAL SPECIALISTS

OF

Eastern Army held in March 1943

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MEETING OF MEDICAL SPECIALISTS HELD AT THE LORETO CONVENT, CALCUTTA, FROM THE 15TH TO THE 18TH MARCH, 1943.

(NOTE.—In putting together the proceedings of the conference it has not been possible for the compilers to refer illegible and ambiguous matter to the writers and they have had to use their own judgment in blue pencilling prolixity. They have endeavoured to produce a correct version of the proceedings of the conference and they apologise for any errors or omissions which might have occurred.)

LIST OF OFFICERS WHO ATTENDED THE MEETING.

1. Major-General T. O. Thompson, C.B.E., late R.A.M.C., D.D.M.S., Eastern Army.
2. Brigadier H. L. Marriott, late R.A.M.C.
3. Colonel G. F. Taylor, I.M.S., Consulting Physician, Eastern Army.
4. ,, W. J. Robertson, A.M.S.
5. ,, F. C. K. Austin, A.M.S.
6. ,, J. Ainslie, I.M.S.
7. Lieut.-Col. C. M. Seward, R.A.M.C.
8. ,, S. H. Dimson, R.A.M.C.
9. ,, E. D. Mackworth, I.M.S.
10. ,, M. H. Shah, I.M.S.
11. ,, R. N. Tattersall, R.A.M.C.
12. ,, G. A. Ransome, I.A.M.C.
13. ,, A. Meneces, R.A.M.C.
14. ,, Browning, R.A.M.C.
15. Major F. Ayrey, I.M.S.
16. ,, H. H. Corrigall, R.A.M.C.
17. ,, H. P. Jameson, R.A.M.C.
18. ,, P. C. Dhanda, I.M.S.
19. ,, J. P. W. Dunlop, R.A.M.C.
20. ,, H. B. Lal, I.M.S.
21. ,, B. A. Lamprell, I.A.M.C.
22. ,, F. McCay, I.M.S.
23. ,, P. A. Mathew, I.A.M.C.
24. ,, H. A. Mullen, R.A.M.C.
25. ,, G. V. S. Murthi, I.M.S.
26. ,, J. P. J. Paton, R.A.M.C.
27. ,, M. H. P. Sayers, R.A.M.C.
28. ,, L. S. F. Woodhead, I.M.S.
29. ,, M. Ziaullah, I.M.S.
30. Captain C. A. Gavan Duffy, R.A.M.C.
31. ,, P. H. Birks, R.A.M.C.
32. ,, N. S. Clark, R.A.M.C.
33. ,, J. H. Gibbens, R.A.M.C.
34. ,, K. R. Graig, R.A.M.C.
35. ,, M. A. Khan, I.M.S.
36. ,, A. M. M. Payne, R.A.M.C.
37. ,, J. C. Shee, R.A.M.C.
38. ,, A. A. White, R.A.M.C.
39. ,, Willatt, R.A.M.C.
40. Lieutenant R. T. Bowes, R.A.M.C.
41. ,, G. A. Kiloh, R.A.M.C.—Secretary.
42. ,, E. G. Rhind, R.A.M.C.
43. Major J. H. Rogan, R.A.M.C.
44. Captain H. M. Rao, I.M.S.
45. F./O. N. S. Khan, I.M.S.

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PROCEEDINGS
OF
CONFERENCE OF MEDICAL SPECIALISTS.

RESUME OF THE PROCEEDINGS OF THE MEETING OF THE MEDICAL SPECIALISTS OF EASTERN ARMY, INDIA, HELD AT THE LORETO CONVENT, ENTALLY, CALCUTTA.

First day (*March 15th, 1943*).

Major General T. O. Thompson, D.D.M.S., opened the meeting of the Medical Specialists of Eastern Army, India, at 9 A.M. on the 15th March 1943 at the Loreto Convent, Calcutta, and made the following introductory remarks :

" Gentlemen, it is very pleasant to welcome such a large crowd of distinguished people here and I have great pleasure in opening this meeting which Taylor has been very busy getting prepared. In an area like this there is obviously a very great deal to learn and I look forward eagerly to the papers that will be read to us. But one thing I would like to impress on you before you start off on the specialist side of medicine is that our job is essentially to keep the men fit in the first place, and secondly, when they fall sick to get them back to duty as early as possible. I say this because although there are very many interesting diseases and individual cases we must not lose sight of the fact that it is the trivial cases which are in greatest abundance and which actually produce the greatest amount of inefficiency from the point of view of fighting the enemy.

Last year there were 186,000 admissions into hospital in the Eastern Army. I emphasise the number of admissions because one knows that up in the Assam area a large number of men were never admitted into hospital, who were sick enough to be admitted had beds been available. Of the 186,000 there were about 53,000 British and the rest Indian troops. Incidentally, of the British troops, nearly 5,000 were officers. Of the 186,000 again, 83,000 were for malaria. We know that a large number of malaria cases were never admitted to the hospital at all ; we also know that a large number of malaria cases were not diagnosed as such.

In the last three months of the year, we evacuated 18,000 sick men from Eastern Army and the difficulty was to cope with the flood.

When you are going round on inspection, and teaching your medical officers, you must bear in mind that although other cases are much more interesting, it is the job of the M.O.'s to deal with the trivial cases and get them back to duty. Look at the map which the Eastern Army covers and just think for a moment of the types of diseases which are likely to occur there, and which the programme must include. A very large slice of attention must be given to the diseases of the area, diseases which are as important as the actual presence of the enemy. This is a point which we can stress, that although the enemy with whom we can deal is there, there is also the enemy in the form of the diseases of these particular areas, which are far more important and very much more difficult to deal with. So that any detail we can get of the diseases of the area will be of value. When you are instructing in your own hospitals use every bit of information you have acquired and pass it on to your G.D.Os.

I am glad to see that we are to hear something of Naga Sores, some of which are certain to produce a neuritis and subsequent paralysis. I saw in a note from the Middle East yesterday that the same thing has been occurring there.

I hope that in every hospital clinical meetings are now held, because, to my mind, they are of real value. They not only offer a chance for people who do know about the subject to impart knowledge to others, but they also afford an opportunity for officers or personnel from one hospital to come into contact with those of another, and to realise the state of affairs in other hospitals. I would like these clinical meetings to be fostered and continued as much as circumstances will permit ; there have been some extremely interesting ones and I have had the pleasure and honour of being invited to go and attend some of these. One quite unique one was held beyond Tamu in the jungle, on an afternoon about a month ago in an amphitheatre dug out. We had three most excellent papers read on Malaria. Obviously malaria is the outstanding problem from the preventive point of view, and we have some papers on this subject in the programme,

and one or two really new points which have been discovered about malaria. In addition to malaria we have other common conditions which will arise to be dealt with, such as dysentery, which are always distressing and nearly always devastating at certain times of the year ; a very common condition is hookworm anæmia which has to be borne in mind. We have papers on typhus, on jaundice, that extremely interesting condition the cause of which I would very much like to know. I have been interested in jaundice for at least 15 years out here and I think I know less about it now than when I started.

Leprosy is a condition of which we all fight shy of and it will be very nice to hear about it from a real expert.

Gonorrhæa is causing a considerable amount of difficulty in every hospital owing to the number of cases and the protracted nature of the disease when it does not get proper treatment.

Skin troubles have already been mentioned, but most skin troubles are due to causes which although trivial, do produce a very large amount of inefficiency. I counted up a group of men coming out of Burma under a year ago and at one time one in three of the men who went past me had some form of skin trouble of the limbs. We also hope to receive aid and comfort on the vexed question of medical boards from one who might practically be looked upon as our special correspondent. I hope he will be able to give help on the difficult points.

Dengue can become quite a serious condition. Back in 1939 there were 365 admissions for dengue among B.O.Rs. alone in Calcutta and Barrackpore, so that it is not a condition which can be neglected entirely.

One further aspect which I would ask you to keep in mind and that is the question of vitamin deficiency. We got trouble in the forward area where troops were certainly not getting the fresh food and fresh fruits to which they were entitled. It is largely a question of transport. When there is such trouble let us know at once if you notice signs of deficiency disease in the particular group or formation."

He then invited the conference to proceed with the agenda before them.

Brigadier H. L. Marriott read the following paper :

ILL EFFECTS OF HEAT.

In 1942 in India two thousand patients were admitted to military hospitals suffering from the effects of heat ; 136 of them died. Three quarters of the admissions were British troops. Very many other men, not ill enough to be sent to hospital, were sufficiently affected to diminish their efficiency.

The ill effects of hot weather are not only important in relation to healthy men, but also in regard to the sick. They may seriously complicate all kinds of medical and surgical conditions.

It is important that Medical Officers shall clearly understand the pathology, symtomatology, prevention and treatment of heat effects. The key to understanding is to think in terms of the mechanisms by which the body is damaged rather than in terms of nomenclature.

There are two main mechanisms by which the body may be seriously injured by heat, namely :—

(1) Loss of water and sodium chloride from sweating.

(2) Over-heating.

Cases due to the former mechanism are said to be suffering from " Heat Exhaustion ". This name, though sanctioned by usage, is an unfortunate one in that it tends to imply that the condition is something akin to fatigue and, therefore, probably not of serious importance. This is quite untrue, for Heat Exhaustion is often fatal. Cases presenting over-heating are suffering from " Heat Stroke ".

In any hot season there are about ten times as many cases of Heat Exhaustion as of Heat Stroke. The two conditions are easily distinguished by the high body temperature (more than 105°F.) of the latter. Both are due to heat and not to any peculiar effect of the light rays of the sun as suggested in the old-fashioned term " Sunstroke ". This does not mean that topees should not be worn in hot weather. The topee, by its shading effect, helps to diminish the general heating of the body.

Apart from Heat Exhaustion and Heat Stroke, transient vaso-motor manifestations, *e.g.* fainting, or neurotic phenomena may be encountered.

(1) *Loss of Water and Sodium Chloride from sweating* (*Heat Exhaustion*).—In hot

climates sweating is of enormous importance and the main means by which the body temperature is prevented from rising. Its efficiency in this respect is remarkable. Thus, when the atmospheric temperature and that of all inanimate objects, is 120°F. the body, itself a heat producing machine, manages by virtue of the evaporation of sweat, to maintain a temperature more than 20 degrees cooler than that of its surroundings.

If muscular work is being done, the volume of sweat, which must be secreted to keep down the body temperature, may be 2, 3 or 4 gallons (9-18 litres) per 24 hours. It is necessary in the tropics to think of fluid loss from sweating, and of necessary compensating fluid intake, in terms of gallons rather than in smaller measures.

Sweat is essentially a solution of sodium chloride in water. In Europeans its composition is approximately half an ounce of salt to the gallon. Recent Australian work suggests that the salt content of the sweat of natives of tropical countries, and of thoroughly acclimatised persons, may be lower than that of newcomers. This may explain the relatively much greater incidence of Heat Exhaustion in British as compared with Indian troops (about 50 : 1). The relative incidence of Heat Stroke is not so very different.

The main physiological function of sodium chloride is osmotic maintenance of the water content of the body fluids. If the salt content of the body drops, tissue dehydration and reduction of blood volume ensue.

The daily intake of salt in ordinary diet is about half an ounce and is more than is needed to maintain equilibrium under cold or temperate climatic conditions. The excess of sodium chloride is excreted in the urine.

Under hot conditions, if sweating exceeds 1–1½ gallons per day, it is obvious that salt depletion must occur unless there is a compensatory increased ingestion of salt.

The serious features of Heat Exhaustion are essentially those of circulatory failure due to diminished blood volume and may be due to :—

(*a*) Primary dehydration from simple water deprivation, *e.g.* men on the march in water-less country.

Much more often the cause is :

(*b*) Secondary dehydration (inability of the tissues to hold water) due to salt depletion, and seen in subjects who are drinking water freely.

The symptoms of Heat Exhaustion are :—

Weakness.
Giddiness.
Anorexia, Nausea, Vomiting } May be very marked and suggest some abdominal condition.
Headache.
Cramps.
Feeble pulse.
Low blood pressure.
Moist skin.
Temperature : sub-normal, normal, or may be raised up to 103°.
Urine diminished : NaCl absent or very scanty, *i.e.*, less than 0·3 per cent.
Blood : Hæmoconcentration, Diminished plasma NaCl, Raised blood urea.

The above manifestations closely resemble those of a crisis in Addison's Disease which is essentially also a condition of salt depletion.

The diagnosis of Heat Exhaustion should not present much difficulty. Particularly important observations are taking of the blood pressure and testing of the urine for NaCl.

A simple quantitative test for NaCl is as follows :—

Requirements : Test tube.
Fountain pen filler pipette.
20 per cent. potassium chromate solution.
2·9 per cent. silver nitrate solution.

Ten drops of urine are measured into the test tube. One drop of the potassium chromate solution, the indicator, is added. With the same pipette, the silver nitrate solution is now added a drop at a time ; the test tube being shaken after each drop. The end point is a sharp colour change of the whole mixture from yellow to brown. The

number of drops of silver nitrate solution needed to produce it equals the number of grammes per litre of NaCl in the urine tested. Normal urine, unless very dilute, contains from 1 to 20 grammes per litre. In hot weather, less than 3 grammes per litre in a concentrated specimen indicates depletion. In Heat Exhaustion less than 1 gramme per litre is usual.

Treatment.—The essential treatment is restoration of salt and water balance by the administration of normal saline (8·5 grammes per litre of NaCl). One or two gallons are required in the average case. In 1942 many cases were seen in hospital which had failed to clear up because saline had been administered in homeopathic doses of a pint or two. Such patients had sometimes been in hospital for several weeks with persistent low blood pressures. Some showed marked mental changes—confusion, depression, even gross delusions. All still had no NaCl in their urines, and quickly cleared up on its liberal administration.

The normal saline should, whenever possible, be given by mouth, but, if the patient is badly collapsed or vomiting, parenteral administration, rectal or intravenous, of the first half gallon is necessary. Such cases are urgent emergencies and the intravenous route is preferable. The rate of administration should be a pint per 20 minutes.

Treatment should be controlled by observation of :—

(*a*) The patient's general condition.

(*b*) The blood pressure taken half hourly.

(*c*) The urinary output and NaCl content measured four-hourly. The aim should be to attain an output of ½ pint four-hourly, and an NaCl content of 5-10 grammes per litre.

(2) *Over-heating* (*Heat Stroke*).—The essential feature of heat stroke is a high body temperature—105°—112°. If the temperature is 107° or more, the case is one of the desperate emergency and death is highly probable unless the temperature is lowered within a matter of minutes.

Heat stroke will occur in anyone if conditions are sufficiently severe and, under such circumstances, many men will present it. In general, however, it is seen in sporadic cases when conditions are not so extreme. Why do these men develop hyperpyrexia ? The usual reason is because *they have stopped sweating*. The stoppage of sweating is generally due to the presence of an infection. Infection automatically tends to set in motion the normal fever reaction—a reaction essentially consisting in inhibition of heat loss mechanisms. The infection may often be quite slight—a boil or a mild enteritis. Its fever reaction in a temperate climate might be no more than a temperature of 99·4° but under very hot conditions, cessation of sweating for even a few minutes means rapid rise of body temperature. The commonest precipitating infections in India are malaria and sand-fly fever.

Symptoms—

Temperature 105°—112°.
Skin usually dry and burning.
Mental confusion, delirium, mania or coma.
Bounding pulse.
Blood pressure normal or raised.
Cerebro-spinal fluid pressure raised.
Face congested, may be cyanosed.
Urine—NaCl usually present in normal amount.

Diagnosis.—The diagnosis of hyperpyrexia merely necessitates feeling the patient and taking his temperature.

Treatment.—If there is the slightest possibility of malaria being present, intravenous quinine should be given immediately.

The essential treatment of hyperpyrexia *per se* is to cool the patient AT ONCE AND WHEREVER HE HAPPENS TO BE. There must be no waste of time in transferring him to hospital unless it is immediately adjacent. What is done at once counts ten times more than what may be done in half an hour's time.

The most effective method of cooling a patient, unless atmospheric relative humidity approaches saturation, is by the evaporation of water from the skin, *i.e.*, mimicking the natural process of sweating. This is about eight times as effective as packing him

in ice ; the latter is only needed under rare conditions of high temperature with very high relative humidity.

The patient should be stripped naked and wrapped in a wet sheet. The sheet must be kept continuously wetted with tepid water (ice cold water is not desirable as it causes vaso-constriction and so diminishes heat loss). One or more fans should be kept vigorously playing on the patient so that maximum evaporation is secured. If fans are not available, then a draught must be created by relays of men flapping towels.

The body temperature should be taken every 10 minutes and the cooling stopped when it falls to 102°. For the next week the patient must be very closely observed as relapse, due to disorder of the heat regulating centre, may occur.

A particularly useful ancillary measure in the treatment of Heat Stroke is lumbar puncture, controlled by manometry, with reduction of the pressure (measured with the patient lying in the lateral position) to 100 mm.

Prevention.—The general principles of the prevention of heat effects among troops are set forth in Special India Army Orders which should be consulted. It is proposed here only :—

(*a*) To draw particular attention to the importance of adequate salt intake in hot weather.

(*b*) To indicate the special hazards to which sick patients are exposed.

(*a*) *Importance of adequate salt intake.*—The physiological consequences of salt depletion have been recognised for several years but there is still a tendency, except in certain industrial concerns, inadequately to apply the lesson.

Sedentary workers are unlikely, even in the hottest weather, to become seriously salt deficient, but men marching or doing muscular work, day after day, must suffer salt depletion unless their ingestion of salt is increased.

For such men, an increased intake, over the normal $\frac{1}{4}$ ounce per day, of $\frac{1}{2}$ to $1\frac{1}{2}$ ounces, according to the degree of sweating, is needed. This amount cannot conveniently be taken as a condiment. The simplest way to get it taken is to add $\frac{1}{2}$ ounce of salt per gallon to all drinking water and water used to make tea, coffee, etc. Taking a pinch of salt (perhaps 30 grains) once a day is quite inadequate. It must be remembered that there is no reserve of sodium chloride in the body, whose total salt content is about 5 ounces.

(*b*) *Special hazards in regard to the sick.*—In very hot weather it is easy for Heat Exhaustion to develop as a complication of any medical or surgical condition which causes a patient, through weakness, loss of appetite, vomiting, or other cause, to diminish his intake of fluid or food (and therefore of salt). There is particular danger in cases suffering from vomiting or diarrhœa, for not only is ingestion of water and salt limited but there may be gross extra loss.

In hot climates measurement of urinary output, and checking the NaCl content of the urine, should be routine for all seriously ill patients.—Patients suffering from any form of infection are peculiarly liable to develop heat stroke because of inhibition of sweating. When the weather is very hot, an inspection round of all patients should be made every two hours to detect the possible development of hyperpyrexia. It is not necessary to take the temperatures of all the cases. All that is needed is to feel their skins and to take the temperatures of the ones that feel hot. In hot weather, drugs of the atropine series, which inhibit sweating, should be used with the greatest caution. When patients are unconscious (not forgetting anæsthetised patients) care should be taken not to prevent their normal heat loss by over-covering them with bed clothes, rubber sheets, etc.

DISCUSSION.

Col. Taylor brought out two points : (1) The civilian Burma evacuees treated at the School of Tropical Medicine, Calcutta, were examined for chloride content of the urine. It was found to be deficient in all cases. (2) In Indian civil hospitals, heat stroke is extremely common after operation. Operations in the hot weather are avoided as far as it is possible because of this danger.

Major P. C. Dhanda said : " It was observed at 45 I.G.H. in case of a large number of patients, including up patients, that with the advent of warm weather they seemed to suffer from mild degree of anorexia, lassitude and lack of energy and enthusiasm for the evening games and recreation facilities provided, even though the weather was

not so hot. Extra ¼ oz. of salt added to the individual daily ration did definitely seem to improve the above symptoms, this being the only change made over the period. It is suggested that this might have been due to a sub-clinical degree of salt deficiency, on account of increased salt excretion in warm weather. These patients were originally on convalescent diet scale (I.I.) with a salt scale of ⅛ oz.

Col. Ainsley raised the point that really early treatment of heat stroke is important.

Major J. P. J. Paton asked : " Approximation of the blood pressure towards the crisis in lobar pneumonia is an indication of a good prognosis. Does the same apply in heat exhaustion ?"

Brig. Marriott. Yes.

Capt. J. C. Shee stressed the urgency of the treatment of hyperpyrexia. Rogers pointed out that if the period of unconsciousness is less than 1½ hours, only 8% die. If the period of unconsciousness lasts more than 3 hours, 70% die. Therefore a very large number of cases will be treated at F.As., to which specialists are not attached. Therefore efforts should be made to see that all F.As. medical personnel should be instructed in the emergency treatment of heat pyrexia.

Practical points arising from personal experience are : (1) Dehydrated patients suffering from diarrhœal diseases are particularly liable. (2) When dysenteric patients develop heat hyperpyrexia, the diarrhœa stops. This being presumptive evidence of dehydration, the patients should be given sips of salt water as soon as consciousness returns. (3) Rectal thermometer should not be left *in situ*, owing to danger of breakage during convulsions. The rectal temperature should be taken every five or ten minutes. (4) Personnel doing fanning should be carefully watched for evidence of exhaustion and should be frequently relayed. (5) Troops of all arms should be instructed in the causes and avoidance of heat exhaustion and hyperpyrexia. (6) The issue to and carrying of lumps of rocksalt by all troops, to be sucked during the day, is a useful prophylactic measure.

Lt.-Col. C. Seward said : " Brig. Marriott has emphasised the importance of adequate hydration of the soldier in the field, both in prophylaxis and in treatment. In surgical wards pails of drink are set between stretchers with rubber tubes to act as syphons. In the less dramatic but equally hot atmosphere of the medical wards the necessity for adequate hydration is often overlooked in cases of fever, vomiting and diarrhoea. The case often regarded as toxic is often suffering and may die chiefly from dehydration. The frequent sips administered by sister or orderly are quite insufficient and the patient may be too languid or weak to use a feeding cup.

In this hospital we have set up drip cans and blood bottles hung just above the bed with a rubber tube leading to the mouth where a bent glass tube, such as dental surgeons use, hooks on to the lower teeth. A clip on the tube at the patient's hand enables him by slight pressure to feed himself. "

Lt.-Col. S. B. Dimson said : " There are just a few personal experiences I would like to record as illustrating Brig. Marriott's most interesting and lucid paper. I treated 10 cases of heat stroke while working in a B.G.H. in Central Command. There were no deaths. Our routine was to place the patient naked on a spring charpoy and sprinkle him with water, cooled to about 70°F. by ice, from a watering can. Water much colder than this defeated its object by producing violent shivering and vaso-constriction. The rectal temperature was taken every ten minutes. Blankets and hot water bottles were provided at 102°F.

Two of my heat stroke cases became violent, cyanosed and then comatose for some hours. Hæmatemeses totalling 2—3 pints occurred which we considered served the purpose of a venesection. To my knowledge this symptom has not before been recorded.

A most interesting case of heat exhaustion occurred in a B. O. R. convalescing from malaria who had already been several days in hospital. He collapsed, vomited copiously and sweated profusely with a temperature of 95°F. and blood pressure of 80/50. He looked like an adrenal crisis and when albuminuria was found his blood urea was done and found to be 160 mg. per cent. Next day it was 50 and the day after 25. During the whole of this time he received copious saline drinks. I related this case to Brig. Marriott who considered the sudden reduction in blood volume accounted for the high

blood urea. This case is also interesting as showing how a man while receiving a normal hospital diet can still get a poor salt intake and develop alarming symptoms of heat exhaustion.

The Chairman said that officers should keep an eye to see the early signs and symptoms of heat exhaustion in those who are actually working with them and who are not apparently complaining of anything

"About the extra salt, I was one of the first to introduce it in Ferozepore Fort I came to the British cook house and asked the head cook how he was managing about it. He with a very pleasant look said that he did it very nicely and had saved 60 lbs." (Laughter).

Brig. Marriott answered the queries and summed up.

Col. G. F. Taylor then read his paper as follows:

SOME MEDICAL PROBLEMS OF THE EASTERN ARMY.—

The main problem is malaria. We, at this conference are more directly concerned with clinical features and treatment. We have all seen more severe and curious types of malaria than ever before, comparable to the epidemics of Macedonia in 1916-17-18, and of Ceylon and Brazil recently. Because of the large numbers of relapses during, and shortly after treatment many medical officers in Assam have questioned the value of anti-malarial drugs, especially Mepacrine and asked whether the standard army treatment is long enough. Major Rogan was therefore sent to Assam to try out the I.C.I. Mepacrine used in the army, against Bayer's atebrin. He has shown that their action is identical. Dr. Napier at the Calcutta School of Tropical Medicine used mepacrine in monkey malaria and found it to have the same action as atebrin. Finally there is the assurance that the two drugs are chemically identical. Recommendations to lengthen and intensify treatment always arise during severe epidemics. In Macedonia in 1918, up to 120 grains of quinine were given daily, for long periods without stopping the frequent relapses. The Army Blue Book treatment, a short course of quinine, mepacrine and pamaquin, is based on the League of Nations report of "The Treatment of Malaria"—1937, in which a mass of work in malarial treatment is summarised. A longer course of treatment is advocated by some whose views are given in "Transactions of the Royal Society of Tropical Medicine", August, 1942, and earlier numbers.

The army policy is to treat both fresh and relapsed cases with this short treatment. An enlarged spleen is a response of the reticulo-endothelial system needing no special treatment, other than the usual treatment of the acute attack of fever, and of any resulting anaemia. Whether this is the correct policy needs discussion and possibly further work.

Owing to Major Rogan's work, we think that many relapses must be due to men not taking drugs prescribed. This state of affairs appears to be very common, as most hospitals report frequent failures. Has anyone any suggestions how this state of affairs can be put right?

Colonel Afridi has pointed out that some of these early recrudescences of fever are due to multiple infections, but these do not explain all the failures. This is based on James' work on experimental malaria, in which he showed the difference between the primary and the relapse attack of fever.

It is reported that both British and Indian troops refuse to take mepacrine because they fear it will cause impotence. As far as it is known, there is no basis in fact for this belief. In the last war the idea that chlorination of water caused impotence, was said to have been spread by the Germans. This conference may be able to decide how prevalent such ideas are and recommend methods of dealing with them.

At least twelve deaths have occurred in Eastern Army as the result of intravenous quinine being given in excessive doses, too quickly, in cases of cerebral malaria. The army booklet advises 6 grains in 10 cc. of water injected slowly. In the fatal cases up to 12 grains have been given in a few minutes. A circular is needed giving exact instructions of dose, dilution, and speed, because correctly given intravenous quinine is safe. The Blue Book treatment of cardiac syncope needs revision, one of the subjects which I hope we may discuss.

All M.Os should keep in mind the fact that malaria may complicate all other diseases. In endemic areas any infection such as pneumonia or typhoid may bring on a malarial relapse. It has been advised that all such cases receive anti-malaria treat-

ment as well as the specific treatment. Major Shah in his series of *post mortem* examinations has shown that meningitis may be masked by the diagnosis of cerebral malaria, the subject of a recent D. D. M. S. circular. Also a chronic malarial infection may be present without any acute attacks, causing symptoms of anaemia, etc. I have been wondering if it would be useful to use the cultural methods for malarial parasites in such cases, the technique of which is used at the School of Tropical Medicine, Calcutta.

Arsenic in the after treatment of malaria fell into disuse when atebrin and plasmoquin were introduced. Sinton at Kasauli had shown that arsenic injections were useful in acute attacks and relapses. The D. D. M. S. has issued instructions to treat a series of malarial relapses with two or three injections of arsenic in addition to ordinary treatment.

Because of the difficulties in preventing malarial relapses, there is a strong case for a special centre to investigate this problem. Such treatment as a longer course of plasmoquin (Manifold in 1930 was using it for 21 days), the possibilities of immuno-transfusions with blood or serum from immune cases, and of a vaccine from sporozoites based on the recent work of Mulligan, Dikshit and others, could be tried. Major Rogan has shown the value to the army of such special investigations.

The paper by Captain Birks on the clumping of red cells in some cases of malaria in Assam, so called auto-agglutination, will interest everybody. The condition has been observed by Sayers, Rogan and others and should be further investigated.

A beginning has been made to investigate malarial anaemia in Eastern Army. An officer at the 47th B. G. H. has had training in modern haematological methods from Dr. Napier. It is too soon to come to any conclusions. Evidence is collecting in hospitals that anaemia persists as long as the underlying cause, which may be chronic malaria, amoebiasis, hookworm or malnutrition, remains untreated. Once the underlying cause is removed cases recover as quickly with or without the " mass treatment " that has been recommended. Further investigations with modern methods are needed in one or two centres for British and Indian troops.

The extent of ancylostomiasis is unknown in Eastern Army. Some months ago it was arranged that officers in charge of laboratories should examine cross sections of Indian troops for hookworm. Preliminary reports indicate that many units are heavily infested. We need to discuss whether all Indian units should be examined, and if a special officer should be appointed for this. Dr. Napier raised the point that a low degree of infestation was unimportant. But for troops even a small number of worms may impair their efficiency, and with malaria, make them more liable to anaemia.

During the evacuation of the sick last year, there was much malnutrition due to men being on half rations in forward areas. Full rations could not be carried over roads damaged by monsoon rains.

There were but few cases of marked deficiency diseases, a few cases of beri-beri, and some mild cases of scurvy. This state of semi-starvation was partly the cause of the severity of malaria and the high relapse rate.

We, as medical specialists are not directly concerned with army policy, but I feel it is our duty to point out where we can, that a fighting force will be destroyed by sickness when exposed to severe malaria with short rations, as we experienced last year.

Many people question the vitamin content of the rations issued to the British and Indian troops, Vitamin A in Indian troops, Vitamin B in British, and Vitamin C in both. The D. A. D. M. S. (nutrition) G. H. Q., is investigating these problems, the result of which we shall hear.

Bacillary dysentery has not as yet been a serious problem, but may well be in the future. Sulphaguanidine has not been available for extensive use, and this is one of the most serious drug shortages. M & B 693 is being used with good results, although bacillary dysentery has not usually been of a severe type in Eastern Army.

Dehydration in cases of dysentery, typhoid and continued fevers was to be found in all Indian hospitals with alarming frequency. The main cause of this was that the M.Os. did not realize the seriousness of this condition, and did not train their nursing staff to give large quantities of fluid by the mouth, nor did they give intravenous saline early enough in sufficient quantities. The test for chlorides in the urine should be introduced into all hospitals, and extra salt given to all cases where chloride is lacking. When heat stroke begins to occur, cross sections of troops must be examined for chloride deficiency, and where required extra salt should be supplied with daily rations.

The use of mixed saline and serum needs investigating for medical and surgical cases. Possibly one of the transfusion units could take this up, and also find out the quantity of saline (hypertonic and normal) needed for heat stroke cases. Most of the stills in use in hospitals are without baffles, one of the causes of reactions after intravenous saline. Baffles are being provided through the field transfusion unit in Calcutta.

Since the Burma evacuation there has been a much higher incidence of amoebic dysentery. There have been the usual difficulties in diagnosis. We must bring to the notice of M.Os. the need for continual care that the stools are examined fresh. Amoebic hepatitis and liver abscess have been frequent, and unusual cases such as strictures of the colon, localised peritonitis, and amoebic masses mistaken for carcinoma have been seen. The disposal of amoebiasis cases is always difficult, as they tend to relapse within a few months. Cases of hepatitis very often need several courses of emetine over a period of some months. Tachycardia due to emetine has been seen far too frequently, and we need to be continually on the watch to see that emetine is given at correct intervals, and the patient is in bed during treatment, and if necessary afterwards. The supply of drug has been short. Recently a small amount of emetine bismuth iodide has been obtained for use in resistant cases in Calcutta hospitals. The meaning of amoebic cysts in soldiers who have not had dysentery has not been decided, and also their significance in some convalescent cases which resist treatment. Much chronic ill-health is due to amoebiasis, which has not shown any symptoms of dysentery. A routine stool examination is desirable in all medical cases where time permits. The Chicago epidemic of amoebic dysentery proved that cysts can be water-borne and it is essential therefore that we do our best to eradicate the common fly, and satisfy ourselves that the water used by the troops is fit to drink. There are still many cook houses and latrines which are not fly proofed, and we must also remember that permanganate solution does not kill cysts on fresh fruit and vegetables. Dr. Das Gupta, Director of the Calcutta School of Tropical Medicine, has offered his help in an investigation in amoebiasis.

There have been a few cases of sprue with no unusual clinical features. I think the main problem here is the disposal of cases, as they tend to relapse in spite of modern treatment and where it is possible I think they should be sent to England.

The epidemics of typhus and anterior poliomyelities and epidemic hepatitis have been interesting, but have presented no unusual problems except the question as to whether poliomyelitis is attributable to military service, a query put up to G.H.Q. which is as yet unanswered. A number of cases of encephalomyelitis have been seen which is fairly common in India.

There has been an unusuallly large number of cases of multiple peripheral neuritis. Some of these apparently have been due to diphtheria contaminating the common " Naga Sore ". A very few have been beri-beri, and others of unknown origin, similar to those described by Critchley as progressive toxic peripheral neuritis. During this summer an investigation is needed into the pathology, prevention and treatment of " Naga Sore ", and the possibility of diphtheria borne in mind.

Kala-azar has occurred in Indian troops and is beginning among the British. The technique of the aldehyde and stibamine tests has been faulty in many hospitals, and the meaning of these tests misinterpreted. Napier in the Indian Medical Gazette, October 1939, has put the matter clearly, as also has Major Pasricha in the Medical Directorate G.H.Q. letter Z25496/1 DMS 5(c), dated 18th September 1941 to all hospitals.

Lt. Col. Browning is giving a paper on the modern treatment of gonorrhoea which stresses the need for a revision of the treatment laid down in the army book " Venereal treatment ", 1941. Eastern Army needs a consultant dermatologist to improve the standard of treatment. The D.D.M.S. has laid down the policy of treatment in a recent circular. There have been a great many cases of all types of ringworm. These have been treated in the usual way, also by the American treatment of equal parts of pure carbolic and camphor which has been very successful. Otitis externa is extremely common in the hot weather, and without stopping bathing, it is difficult to prevent it.

No new treatments of any importance have been tried during the past year. There is a case for the use of convalescent serum in typhus, typhoid, and small-pox. Dr. Grant at the All-India Institute of Hygiene, has arranged to prepare these, and I hope they will be available to all hospitals.

Treatment of blackwater fever has in some cases been unsatisfactory, as sufficient lkalies were not given to make the urine alkaline and so prevent the formation of acid

haematin. The recommendations for treatment of incompatible blood transfusions apply. 150 c.c. of 3% sodium citrate solution are run into a vein rapidly, then 450 c.c. of the same solution is mixed with 2,400 c.c. of 5% glucose and given by a continuous drip infusion taking 24 hours. In milder cases 8 grammes of sodium citrate can be given by mouth followed by 2 grammes, 2 hourly for 24 hours. When the urine is alkaline the colour turns from dark brown to the pink of haemoglobin. Possibly the transfusion units could supply bottles of this solution to all hospitals.

I want to re-emphasise that the main problem of treatment in Eastern Army is the treatment of malaria and its relapses to which I have already referred. We need continually to emphasise that all cases of malaria receive full treatment and that the treatment is continued and completed when evacuation is taking place.

Major Sayers has spent much time on his paper on medical boards, and I hope, is issuing a pamphlet to advise us on this difficult matter. We need to decide the disposal of such cases as sprue, blackwater fever, chronic amoebiasis, chronic malarial relapses and anxiety states. And also the grounds for recommending transfer of cases to England. There have been differences of opinion of the attributability on some diseases to military service ; in the case of infantile paralysis G.H.Q. have been asked for a ruling.

Although the question food in hospitals and units is not directly our concern, it is obviously of vital importance. The consensus of opinion is that the rations themselves are in most cases good, but very often the cooking is really very bad, the diet hopelessly monotonous, and in some cases the quantity is deficient. Some organization for the inspection and improvement of these conditions is urgently needed.

It is hoped that this conference will be repeated, and I think we should consider some way of circulating the opinions, findings, and difficulties of specialists, possibly by a local journal. Finally it will be helpful if this meeting can come to some conclusions as to our needs and how to deal with them, in order that definite proposals may be put up to G.H.Q.

DISCUSSION.

Lt.-Col. M. H. Shah said : " With regard to the diet and feeding of patients there are several difficulties. G.H.Q. circular on malnutrition has provided an excellent basic diet for the feeding of acutely ill and febrile patients. It is however unsuitable for the convalescing patient who generally clamours for the type of food he is used to. In considering the problem of diets and malnutrition it is important to remember that it is not only the adequacy of caloric and vitamin values which matter, but that the proper quantity should actually reach the patient and actually be consumed by him. A solution has then to be found to overcome the following difficulties :—

1. Proper dieting on an individual basis requires the intelligent integration of a large number of extras in the diet. This leaves the patients too much at the mercy of junior medical officers. I suggest that the hospital diets should be standardised on the basis of a weekly menu in order that the necessary change and variety are provided in the meals. This has been done in the B. wing of my hospital with considerable success and requires to be undertaken on the I. side.

2. The average cook in the Indian wings of the hospitals has had no training. Most of them have never cooked meals before in their lives. I feel something should be done to secure their training.

3. With the posting of non-medical quartermasters there is a great need for another non-medical person who could constantly supervise the quantity, quality and variety of items issued by the quartermaster and generally guide and direct the cooking.

I should also like to make a plea for the inclusion of buttermilk popularly known as ' lassi ' in the diet of Indian patients. If the dairies are not in a position to prepare curd and ' lassi ' for use in the hospitals the buttermilk, which is often available and is generally thrown out after the removal of butter, should be secured for the patients.

Capt. G. Duffy commented on the relatively unprotected state of the army as regards small-pox. Contacts in a ward vaccinated recently with four points vaccination had 59 per cent. positive takes, not including immediate and accelerated reactions. A medical officer vaccinated successfully with one point contracted small-pox one month later. Other instances were quoted. These facts suggest the necessity for much more

care when doing routine vaccination. Failure to "take" means inefficient vaccination as often as it implies immunity.

Major F. Ayrey asked if particulars might be given of the centre referred to from which sera for the treatment of typhoid and typhus might be obtained. Col. Taylor had referred to this mode of treatment as being in the experimental stage. While this was true, there was evidence on clinical grounds that in the case of typhoid the blood of convalescents was beneficial.

He quoted two cases of typhoid treated in Egypt, the first with convalescent whole blood, the second with whole blood of a B.O.R. inoculated with T.A.B. three months previously. 1 to 1½ pints of blood were given in each case by drip method. Both cases appeared to benefit considerably from the treatment; both showed an appreciable fall in temperature and in addition to general improvement in the one case (an R.A.M.C. Sergeant) a troublesome bowel incontinence ceased; in the other the temperature rose from 103° to 105° following the transfusion, dropped to subnormal, then rose to 100°; coincidentally the patient's delirium, which had lasted for over two days, ceased. Both cases, which could be classed as severe, made good recoveries.

Recently in Rawalpindi he had given 100 c.c. of convalescent Typhoid Serum by split intramuscular injections to a child aged 5 suffering from typhoid and amoebic dysentery. On the eighth day, the T O titre was O, three days after the serum injections the T O titre had risen to 1/640. (Tests made by Major Bhatnagar, I.M.S., District Laboratory, Murree.) When the serum was given two unfavourable prognostic signs were present, severe meteorism and right sided parotitis. There was a definite clinical improvement coincident with the rise of the T O titre and the child made a good recovery.

Unfortunately in the three cases quoted it has not been possible to correlate the clinical observations with scientific investigation. The observations were mainly clinical and to be of value any similar investigations ought to be made with the full collaboration of a laboratory. The results he noted might have been due, not to any immuno-reaction, but to something in the nature of non-specific protein shock. The question of whether to give whole-blood or serum, the amounts required and careful following up of titres were but a few of the observations necessary.

Nevertheless the speaker considered the results sufficiently encouraging to warrant further extended trial.

Whilst it might be useful to have a central laboratory for the provision of sera, it should be borne in mind that it was within the reach of most hospitals to provide their own blood or serum at short notice. Usually one or two typhoid convalescent patients were within reach. If none was available there was always a large accessible population who had had T.A.B. inoculations. Felix had pointed out that the highest degree of immunity was conferred by the disease itself, all the tissues taking part in the response. On theoretical grounds the blood of a convalescent patient was preferable to that of a T.A.B. inoculated person, but in the event of the former not being available there was clinical evidence that the latter was not without its value.

If every hospital could submit reports on the treatment of even a few cases each, in, say, six months and twelve months' time, the results might throw useful light on the efficacy of this form of therapy. He considered it a unique opportunity for determining whether the method marked a real step forward in the treatment of typhoid fever.

Col. Ransome said: "I was delighted to hear Col. Taylor stress this question of cooking. It is a most urgent need in this army to have proper invalid cooking for the I.O.R. At the moment it does not exist, except by private initiative in a few hospitals. This is usually inadequate. The Indian hospital cooks are all village boys, many of them have only had a fortnight's training and though they can cook chapatis and rice quite well I would submit that this is not necessarily a good middle diet when a patient's powers of digestion are impaired by fever or by disease. It is this lack of a middle diet which causes so much invalidism among the more chronically ill I.O.Rs. The basic diet as supplied is excellent but it must be rendered fit for absorption by sick people.

Col. Taylor summed up and replied to questions.

Major Rogan then read his paper as follows.

INVESTIGATION INTO THE TREATMENT OF MALARIA IN ASSAM: December 1942—February 1943.

1. *Authority for the investigation.*—This investigation was authorised by D.M.S., India, letter No. 7333/1 (D.M.S.5(b)), dated 7th November 1942, to the D.D.M.S., Eastern Army, which stated that as some doubt had been expressed regarding the efficiency of the standard treatment of malaria, as laid down in G.H.Q., India, Memo. No. 7005/D.M.S.5(c), issued on 29th May 1942, in regard to cases of malaria in Assam, a preliminary investigation into the effect of the standard treatment would be started forthwith, in Assam, on a controlled series of British and Indian cases of malaria.

The Medical Directorate, G.H.Q., India, instructed the investigating officer to prepare a scheme whereby the action of the standard treatment could be effectively assessed. Modifications of the standard treatment were to be similarly assessed, including one in which atebrin (Bayer's) would replace mepacrin and plasmoquin (Bayer's) would replace pamaquin. Such a scheme was prepared and approved. He was further instructed to obtain as much information as possible about the conditions under which malaria had been treated in Assam.

2. *Site of the investigation.*—The 66th Indian General Hospital (Combined), located at Manipur Road, was chosen as the site for the investigation, as it appeared likely to afford the largest number of untreated cases of malaria, a considerable number of which would probably be freshly infected. Prior to the investigation, the prevailing local impression with regard to malaria was that the large majority of cases were infected with M.T. malaria of a dangerous type, which was resulting in a fatal termination in an unusually large number of cases. A high relapse rate was also attributed to this type of malaria. This impression was not substantiated by the findings of the investigation. The work of Lt. Col. Shah, O.C., Medical Division of the 66th Indian General Hospital (Combined), who arrived in Assam shortly before the investigation started, shed further light upon the high mortality attributed to malaria. The following extract from his specialist report for the period 4th November 1942 to 31st January 1943, is instructive.

> "The outstanding fact about this period has been the unusually high mortality. Post-mortem examinations have established the fact that a great majority of the cases which die, have a combination of emaciation, anæmia, hookworm infection, and malaria. These conditions provide the soil in which other diseases make their appearance.

Post-mortem findings / December 1942—January 1943.

Total of cases examined	140
Cause of death—	
Pulmonary disease	52
Dysentery	53
Malaria	16
Meningitis, etc.	14
Cases showing evidence of active or recent malaria	81"

Opinions on the standard treatment were sought from Officers Commanding hospitals in Assam, on the route to Manipur Road. They varied from ' very unsatisfactory ' to ' quite good '. One Officer Commanding a hospital stated that of the first 20 cases of malaria, of which he had kept careful records, 13 had relapsed within ten days of their completing treatment.

Although the routine of the investigation precluded travel in Assam, a considerable number of medical officers in transit were met in Manipur Road. General discussion with them on malaria and its treatment revealed that doubt as to the efficacy of the standard treatment was wide-spread. It was also found in some cases that officers were ignorant of the correct administration of the treatment they were condemning. Further, it must be recorded that ignorance of the most elementary facts about malaria and its treatment was all too frequently encountered.

3. *Scheme of investigation and results obtained.*

Series of cases.—Four treatments were used and each was employed on a fixed ratio of cases infected with B.T., M.T. and mixed infections, the ratio comprising a constant total. The treatments were :—

A. Standard treatment.
B. Standard treatment with atebrin replacing mepacrine and plasmoquin replacing pamaquin.

C. Standard treatment modified by giving quinine grs. x t.d.s. until the patient is afebrile.
D. Treatment in use in the Eastern Army when the investigation started, *viz.* :—

Mepacrin 0·1 gm. t.d.s. for 5 days, two days rest thereafter, and then Pamaquin 0·01 gm. t.d.s. for British troops and b.d.s. for Indian troops for 5 days. Mepacrin and pamaquin to be supplemented by quinine grs. x b.d.s.

The ratio of cases was fixed as follows and was largely determined by the relative incidence of the different varieties of infection.

Treatment.	I.O.R.						B.O.R.						
	B.T.			M.T.			Mixed including quartan.			B.T.			M.T.			Mixed including quartan.			
	F.	R.	Total.	F.	R.	Total.	F.	R.	Total.	F.	R.	Total.	F.	R.	Total.	F.	R.	Total.	
A	10	24	34	8	18	26	3	12	15	1	8	9	5	1	6	1	1	2	92
B	9	25	34	8	18	26	4	11	15	2	7	9	2	4	6	1	1	2	92
C	6	28	34	3	23	26	5	10	15	0	9	9	3	3	6	1	1	2	92
D	7	27	34	6	20	26	2	13	15	1	8	9	6	—	6	0	2	2	92
																Grand Total.			368

Note. F—Fresh infection.
R—Relapse.

Cases were recorded as fresh or relapse according to case histories which were accurate in British cases but somewhat unreliable in Indian cases.

The relatively high incidence of B.T. malaria will be noted and also the close correspondence of the B.T. to M.T. ratio in I.O.Rs. and B.O.Rs. The higher proportion of mixed infections among the I.O.Rs. indicates that they were more heavily infected than B.O.Rs.

A further 51 cases were treated, some of which were surplus to the ratio. Others had to be discarded from the ratio owing to intercurrent illness interfering with the criteria on which the efficiency of treatments was to be based. The latter were kept under surveillance as they provided information of value apart from the individual efficacy of each treatment.

Treatments A, B, C, and D were given in strict rotation until 200 Indians and 60 British cases had been taken into the series. Thereafter their application to cases was manipulated to a slight extent in order to secure the fixed ratio shown in the table above.

Selection of cases.

Indian.—Cases were selected in sequence from the detention ward of the hospital. The only cases rejected were those who showed evidence of cerebral or cardiac malaria (such cases were few and constitute a separate problem requiring special treatment. When the issue as to their survival is decided they do not show any abnormal response to treatment), and those who showed evidence of a dual pathology. Unfortunately the majority of cases had received variable amounts of treatment at their units, prior to admission, but the inefficiency and inadequacy of this treatment was clearly demonstrated by its absolute failure to control the infection. It was considered that differences in medication received before admission to hospital would average out over the series of cases selected. It was noted that in January there was a decline in the physique of patients admitted to hospital with malaria, and that cases from one unit preponderated markedly. This unit will be referred to latter in the report.

British.—Practically every B.O.R. admitted to hospital was included in the series, only those being excluded who had had a significant amount of treatment prior to admission. Such cases were very few.

Management of cases.

Indian.—Cases were, as far as possible, kept in bed until they had been afebrile for two days. In fact, great difficulty was experienced in achieving this aim. It was not uncommon to find patients with high fever wandering out into the jungle for natural purposes, when they were not under immediate surveillance.

British.—Cases were allowed up gradually after they had been afebrile for five days.

General.—Indian cases were admitted to the experimental ward in the afternoon and as many of them were sharply ill, one dose of quinine grs. x was given after admission. In the case of B.O.Rs. admitted in the evening, treatment was withheld until the following morning.

The administration of drugs was in every instance supervised by the pathologist or by the investigating officer. Even so, it was by no means easy to ensure that every patient received them. Indian patients were frequently absent from their beds during treatment rounds and a certain number of them attempted to retain tablets in their mouths, presumably with a view to their ejection later. Evidence that it is not enough to give the patient his treatment, without making sure that he is taking it, was provided by the fact that pyjamas, issued from the hospital store to patients, showed yellow mepacrin staining of the pockets on several occasions.

In view of the difficulty experienced in securing that patients took their treatment, when this was a vital part of the routine of the investigation and was rigorously supervised, the positive nature of the assurances received from certain quarters in Assam that treatment has been scrupulously carried out in the past is surprising. On the other hand, at least one O.C. hospital has frankly admitted that at the height of last malarial season it was quite impossible with the staff at his disposal to treat his cases of malaria adequately.

Both British and Indian cases were given ordinary hospital diet.

All cases were retained in hospital for fourteen days after the cessation of treatment, in order that recrudescences in that period could be accurately observed.

Mosquito nets were employed throughout the investigation. Very great difficulty was experienced in maintaining anti-malaria discipline which suggests that this discipline among units in the area was bad. This was not an isolated observation but was confirmed by the O.C. No. 9 A.M.U. which is situated in the vicinity.

Control of pyrexia.—Patients were rendered completely afebrile in from 1-7 days. In every case when pyrexia failed to respond normally to treatment, careful search revealed the presence of intercurrent disease. The clearance of parasites from the blood afforded a fair indication of the control of the malarial infection in such cases, and they responded to appropriate treatment for the intercurrent infection present. In none of them did malaria complicate their subsequent treatment.

Control of pyrexia achieved by the four treatments may be demonstrated thus :—

Treatment.	Cases treated.			Average duration of fever per case in days.		
	I.O.Rs.	B.O.Rs.	Aggregate.	I.O.Rs.	B.O.Rs.	Aggregate.
A	75	17	92	2·03	1·88	2·01
B	75	17	92	1·40	1·71	1·46
C	75	17	92	1·53	1·88	1·60
D	75	17	92	1·65	2·18	1·75

Malarial parasites in the peripheral blood.—The preliminary diagnosis was obtained by examining blood smears stained with Leishman's stain. The result was expressed as the species and form of parasite found and the number of positive fields present in ten consecutive fields examined, thus : B.T. rings, trophozoites and schizonts, 6/10. Thereafter thick drops were taken morning and evening and stained by Field's method. After 4 consecutive negative slides had been reported, the blood was regarded as clear of parasites. Two further thick drops were examined on the day after treatment was concluded. In none of these drops were parasites found. In every case where a temperature of 99 F. or higher was recorded, after the initial control of pyrexia, thick drops were taken morning and night and were supplemented by smears when malarial parasites were found.

The following table shows the clearance of parasites from the peripheral blood during the course of the four treatments :

Treatment.	Cases treated.			Average period required to clear parasites from per blood.		
	I.O.Rs.	B.O.Rs.	Aggregate.	I.O.Rs.	B.O.Rs.	Aggregate.
A	75	17	92	2·79	2·41	2·72
B	75	17	92	2·66	2·53	2·65
C	75	17	92	2·76	2·94	2·79
D	75	17	92	3·02	2·88	2·99

Comment on control of pyrexia and clearance of parasites from the peripheral blood.—Scrutiny of the tables demonstrating those functions of treatment reveals that no advantage is gained by employing very large doses of schizonticidal drugs as in treatment D.

The administration of quinine grs. x t.d.s. until the patient is afebrile, as in treatment C, does not achieve an earlier abolition of fever than quinine grs. x t.d.s. for 48 hours, followed by mepacrin or atebrin O.I. gm. t.d.s. as in treatments A and B.

It will be noted that control of fever was generally achieved slightly more quickly in Indian cases. This small difference may be due to the extra dose of quinine after admission and is a striking indication of the ineffectiveness of treatment in units prior to admission. This treatment, although it has achieved negligible therapeutic results, has nevertheless involved the wastage of very large amounts of quinine.

The longer period required in Indian cases to remove parasites from the peripheral blood suggests that they were more heavily infected with malaria.

The finding in Indians as compared with British cases, of a longer period during which parasites remained in the peripheral blood, is explicable in that the Indian cases were of two types. In the first type the patient had acquired a certain amount of tolerance to the infection, and in the second type he had progressed along the road to malarial cachexia and had failed to respond with an adequate febrile reaction to an infection which was gradually winning the fight against his progressively feeble resistance.

Relapse.—In explaining the basis of classification of the recurrences of fever due to malaria, which were encountered in this series, a brief outline of certain facts relating to relapses and immunity may be of value. These facts are of world-wide application but are of unusual significance when applied to conditions prevailing in Assam.

M.T. malaria has invariably a small relapse rate and relapses occur shortly after the original infection has subsided, so that " recrudescence " is possibly a better term to use for this phenomenon. The great majority of such recrudescences occur within 8 weeks after recovery from the primary attack.

B.T. malaria, in sharp contrast to M.T., has a high relapse rate. The relapses occur in two waves, early and late. The majority of early relapses which, as in M.T. malaria, may conveniently be called recrudescences, develop within two months after recovery from the primary attack. Relapses comprising the later wave develop between the sixth and tenth month after the primary attack. Treatment given during the latent phase between the primary attack and the relapse has apparently little or no effect in preventing the latter.

With regard to immunity, there is a large individual variation in resistance to infection. This influences both the primary attack and the development of subsequent relapses. Thus some individuals are strongly resistant and may have a mild primary attack and no relapse. Others may relapse several times and eventually acquire what can, for practical purposes, be regarded as immunity. Others again may drift into malarial cachexia, and eventually lose the power of an adequate febrile reaction to the presence of large numbers of parasites in the blood. It should be appreciated that the presence of parasites in the blood without pyrexia may be associated with

(*a*) the development of immunity, or
(*b*) the development of malarial cachexia.

These two conditions, which are diametrically opposite, can only be differentiated by a careful investigation of the case on a clinical basis.

Unfortunately, immunity in malaria is highly specific. Infection with one species fails to confer immunity against another species and infection with a single strain of one species seldom protects the subject against re-infection with a different strain of the same species. Further an M.T. infection superimposed upon an incubating B.T. infection, may suppress the latter, which may emerge later from its hiding place in the body to attack the patient in full force the M.T. infection having completely failed to provide immunity against the subsequent development of the B.T. infection. This phenomenon is frequent in areas where a large number of re-infections is occurring.

It will thus be observed that the recrudescences, both during treatment and after the completion of treatment, may arise from a variety of causes. In estimating the value of treatment, it is essential that such causes be carefully distinguished.

A true recrudescence is one in which the original strain of the same species which caused the primary attack reappears, *i.e.*, recrudescence due to the same strain of the same species.

Secondly, the recrudescence may be due to a species other than that causing the primary attack, *i.e.*, recrudescence due to a different species.

Finally, in areas such as Assam, where a large number of immunologically distinct strains of B.T. and M.T. malaria prevail simultaneously, recrudescence may be due to the appearance of a strain other than that causing the primary attack. Thus although the second attack is due to the same species it is brought about by a new strain *i.e.*, recrudescence due to a different strain of the same species.

A primary attack of malaria may be distinguished clinically by the following principal characteristics :—

1. Irregular fever at the onset, later assuming a quotidian and then a tertian pattern.
2. The blood slide. In B.T. infections the parasites are found at different stages of development. In M.T. infections normally only rings are found and are usually fairly numerous.

A true recrudescence shows the following differences from this picture :—

1. The pyrexial reaction is milder than that of the primary attack and usually assumes a tertian pattern from the outset.
2. The blood slide. In B.T. infections the majority of the parasites are at the same stage of development. In M.T. infections the number of rings are usually fewer than in the primary attack.

Recrudescences due to a different species or due to a different strain of the same species resemble a primary attack closely.

Two out of the six recrudescences were due to different species.

Excluding the two recrudescences due to a different species the total of recrudescences due to all other causes was 17 out of a total of 368, which amounts to 4·6 per cent. Out of this corrected total of 17 recrudescences 8 cases conformed so closely to the pattern of a primary attack that it is reasonable to presume that they were due to a different strain of the same species. The remaining 9 cases conformed to the pattern of a true recrudescence. It should be appreciated that treatment is only maximally effective in preventing true recrudescences.

It is of interest to note that among the B.O.Rs. there was only one recrudescence (It was considered to be due to the same strain of the same species.) This strengthens the evidence that reinfections were much commoner among the I.O.Rs.

The number of recrudescences is too small to be statistically significant from the point of view of assessing the relative efficiency of the four treatments. The results obtained cannot be regarded as unsatisfactory.

Effect of treatment on the spleen.—It has been shown by Afridi that the spleen of untreated monkeys, inoculated with *P. cynomolgi*, is enlarged during the course of the attack, that this enlargement continues for a short period while parasites are diminishing in the blood and is then followed by a reduction in size of the organ. This finding was

confirmed during this investigation in 25 per cent. of the cases which were receiving treatment. There is strong reason to believe that efficient treatment, in combination with the patient's reaction to the infection, increase the amount of reduction in the size of the spleen.

The following average reduction in the size of the spleen occurred during the four treatments :—

Treatment.	Number of cases.	Average reduction in size of spleen in finger breadths.
A	92	1·71
B	92	1·90
C	92	1·79
D	92	1·70

This table fails to demonstrate the fact that in a considerable number of cases in which, on admission, the spleen extended for three or four finger breadths below the costal margin, a very marked reduction in the size of this organ occurred by the end of treatment and in some instances it became impalpable. "Hard Bake" spleens of different sizes which were very few were not difficult to detect, in that treatment had little or no effect upon them. It follows therefore that any attempt to use the spleen of troops in their units as an indication of their saturation with malaria, and thus for evacuation, is quite unwarrantable, unless the troops concerned have had a full course of malarial treatment prior to examination of the spleen.

Absorption of drugs.—On the second day of treatment with quinine, and on the fourth day of treatment with mepacrin and atebrin, the urine was tested for these drugs using Tanret's test and the sulphuric acid test respectively.

In five cases Tanret's test gave a negative result. All were B.O.Rs. and they had voided the urine for testing before the morning dose of quinine. No negative result was obtained in testing for mepacrin and atebrin. In twelve cases the urine was tested daily for the presence of those drugs and they were detected in the urine for eight to ten days after the cessation of treatment. No difference in the persistence or intensity of excretion was noted between mepacrin and atebrin.

Toxic reactions to drugs.—No toxic reaction to mepacrin or atebrin was noted. One I.O.R. developed an acute hallucinosis towards the end of the quinine stage of C treatment. Had he been receiving mepacrin or atebrin it would have been difficult not to ascribe this mental disturbance to an atebrin psychosis.

Epigastric pain and cyanosis were noted in the case of one I.O.R. on pamaquin treatment. Three I.O.Rs. and four B.O.Rs. complained of epigastric pain while being treated with this drug and one B.O.R. showed cyanosis. In no case was the toxic reaction severe.

Mild degrees of cinchonism were met with in several cases.

Haematology.—In order to determine whether any of the treatments in use caused anæmia the following routine was adopted :—

A hæmoglobin estimation by Sahli's method was carried out as soon as the blood was clear of parasites. If the Hb. was below 75 per cent. erythrocyte count was carried out also. A further Hb. estimation was done at the end of treatment, and when the second estimation showed a fall in Hb. a further erythrocyte count was done.

Severe anæmia was not found among B.O.Rs. but was present among I.O.Rs. in a certain number of cases. The average initial Hb. estimation of all I.O.Rs. in the series was 67 per cent. and that of the B.O.Rs. 73 per cent. Complete blood counts did not reveal any unusual type of anæmia and the types encountered could all be fully accounted for by a varying combination of repeated attacks of malaria, hookworm infection and malnutrition. It seemed likely that many of the cases of malnutrition had been recruited in that state and had not improved during military service.

The hæmoglobin estimations carried out at the end of treatment failed to demonstrate that any of the four treatments caused anæmia. In fact, in cases free from hookworm, spontaneous regeneration took place to some extent. It would appear that

this regeneration is inhibited by the presence of hookworm infestation and this is demonstrated in the following table.

Species of infection.	Number of Species of infection.	Number of cases.	Average rise or fall in Hb.
			Per cent.
B.O.Rs.—			
(Hookworm found in only 2 cases)	B.T.	39	+4·4
	M.T.	26	+2
	Mixed	9	+0·9
I.O.Rs.—			
(*a*) Without hookworm	B.T.	40	+1·7
	M.T.	36	+1·2
	Mixed	16	+1·3
(*b*) With hookworm	B.T.	90	+0·25
	M.T.	65	—0·8
	Mixed	43	—2·6

Prevalence of hookworm infestation.—Stools were examined for hookworm in all Indian cases and in British cases with a Hb. below 75 per cent. The saturated saline flotation method was used and only one stool was examined from each case so that the findings may err on the low side. They are as follows :—

I.O.Rs.—

Cases examined	348
Positive	70·4 per cent.
A.P.C. Troops positive	85·3 per cent.
Other units I.A.	54·9 per cent.

B.O.Rs.—

Cases examined	37
Positive	2

Case histories.

Indian.—These revealed in the majority of instances that the unit treatment of malaria had been largely devoid of rationale, irregular and grossly wasteful of quinine. It was impossible to avoid the impression that all too frequently it had consisted of a reckless exhibition of quinine to all cases complaining of fever, irrespective of whether they had malaria or not. The quinine was often given in inadequate doses for long periods, thus failing to achieve cure and at the same time rendering the patient a highly dangerous carrier.

Typical histories are . . . { Quinine once daily for one month. / Quinine twice daily for 14 days.

In one instance a patient had been given quinine t.d.s. for 9 months and in two others b.d.s.—t.d.s. for 3 months.

Certain labour units had conceived the idea of giving all their troops quinine gr. x t.d.s. for 7 days as blanket treatment and were carrying it into practice. Some patients had had more than one such course.

British.—Very few B.O.Rs. were treated in their units but were sent to hospital when they were thought to have malaria.

General.—The history of one particular unit is deserving of study as it throws some light on the confused impressions prevailing in Assam with regard to the inefficiency of the standard or indeed any recognised treatment.

This unit, an A.P.C. battalion, was raised in February 1942 and was composed of Telugu, Malayan and Tamil troops. During training about 200 recruits were discharged owing to gross anæmia, refractory emaciation and other marked disabilities. The unit was not dewormed during training.

With a strength of 1279 it arrived on the 14th September 1942 at Manipur Road and the first night there was spent in the train at a siding. Twelve days later the sick parade of malaria cases only had risen suddenly to 240 and this figure increased to 52[illegible] by the seventeenth day.

Fourteen days after arrival this unit began to evacuate invalids and by the end of February, 826 cases had been evacuated and 43 had died.

The survivors were labouring for 11 hours daily with a mid-day break of one hour for food, 40 minutes of which were spent marching to and from their lines. They provided 75 out of the 300 Indian cases investigated and among this number there were 9 recrudescences out of the total of 19.

Lt.-Col. Shah has informed me that in November, when he was inspecting the unit, he found 25 cases suffering from malarial rigors among a detachment which had just marched in from duty.

A unit such as this has obviously been heavily and repeatedly infected with different strains of malarial parasite, and to expect results uniform with those obtained in a less heavily infected community is futile, however well designed and efficiently administered the treatment may be. This statement must not be interpreted as a counsel of despair. If every case in heavily infected units is treated with the maximum of efficiency there is no reason why they should deteriorate into the state which has just been described.

Intercurrent disease during treatment and convalescence.

British cases.—Only three cases showed evidence of intercurrent disease. One developed a cellulitis of foot during convalescence and showed a recrudescence of M.T. malaria of similar species and the same strain thereafter. The other two suffered from what were probably typhus and caecal amoebiasis respectively.

Indian cases.—A considerable number of I.O.Rs. developed pyrexia during treatment and convalescence, not due to malaria, but to intercurrent infection, which responded to appropriate treatment. The commonest cause of fever was respiratory disease, sometimes occurring with relatively few signs in the chest. Severe cases responded well to sulphapyridine. Unless blood examinations had been carried out in combination with careful clinical examination, many of those cases might easily have been mistakenly regarded as relapses, as they frequently showed a sharp rise of temperature with a rigor at the onset.

The high incidence of respiratory disease is not surprising. Many of the patients affected were of poor physique and in a poor state of health. In early December when very cold nights were experienced, many I.O.Rs. were admitted to hospital with inadequate clothing. In hospital they had to be content with two blankets until after 15th December 1942, when authority for the issue of three blankets was given.

It is of interest to note that the incidence of intercurrent disease among cases from the unit whose history has been given above was 28 per cent., while the figure for all other Indian cases was 19 per cent.

4. *Summary and conclusions.*—The type of malaria encountered in Assam does not differ in any essential respect from the malaria met with in many other parts of the world, either in its manifestations or in its response to treatment. It would be untrue to suggest that it does not present a very grave problem to the troops in this area, but the first essential in dealing with this problem is to understand it.

There is reliable evidence that the unsatisfactory situation with regard to malaria, prevailing in Assam, is due to a variety of factors which will be described in sequence.

Units.—Unit medical officers have frequently shown a poor understanding of malaria. Among certain units they have on occasion concurred in the attitude that patients with malaria should be given sufficient quinine to control fever, and should thereafter return to work, apparently oblivious of the fact that inadequately treated cases constitute a constant danger to their fellows in areas where there is a high transmission rate.

Hospitals.—The diagnosis of malaria by laboratories and in hospitals has at times been superficial and unreliable. The pressure of work on laboratories must, presumably, have been too heavy for accurate work to be possible, but instead of pointing out this fact, indifferent work has been carried out which has rendered official statistics of little value. The refusal of higher authorities in certain cases to accept a diagnosis of clinical malaria has provided a great temptation in times of stress to fabricate diagnosis.

Hospitals have laboured under grave disadvantages of shortage of staff and trained personnel in spite of their representations in the matter. They have had to utilize valuable medical officers in arranging transit to the detriment of efficient medical work. In one hospital, for instance, which had an establishment for 700 beds, weekly admissions averaged 3,000 cases with an average stay in hospital for each case of 3-4 days. Apart

from the O.C., six medical officers were on its strength, including the Pathologist. In another hospital, an unqualified dispenser was carrying out all dispensing for over 1,000 hospital patients and for units totalling 35,000 men.

The quality of subordinate staff has been adversely affected by war expansion. A considerably number of nursing sepoys are ignorant and inexperienced and not infrequently those responsible for temperature and pulse charts are not in possession of the most elementary timekeeper.

When it is realised that atebrin is being sold in the black market at Rs. 2 As. 8 per tablet, it would be idle to pretend that theft of drugs does not occur on occasion.

Lines of communication.—Thousands of malaria cases have passed along the L. of C. ostensibly during their treatment for malaria. To secure correct continuity of treatment under the conditions prevailing during evacuation is difficult at the best of times, and at rush periods in the past no one can seriously maintain that efficient malarial treatment has been carried out.

Evacuation of the four treatments investigated.—With regard to treatment, it is emphasised that all four treatments gave satisfactory results and that no superiority of one over another could be demonstrated. Similar results cannot be obtained unless it is rigidly ensured that every patient swallows the drugs prescribed.

Treatments such as treatment D involving the use of large amounts of schizonticidal drugs, have no justification for their use. Further, the employment of treatment C which employs more quinine than treatments A and B cannot be recommended. As the proprietary forms of the drugs employed in treatment B are unobtainable, treatment A, *i.e.*, standard treatment, remains as the treatment of choice.

It might be appropriate to conclude this report with an extract from the Official History of the War dealing with malaria in Macedonia :—

> " Many statements have been made as to the peculiar severity of the malaria in Macedonia and some have even sought to discover some special feature in the malaria parasites themselves to account for this.
>
> It is true that in 1916 the mortality was fairly high for malaria but it must not be forgotten that the great outbreak came as suddenly and unexpectedly as a Macedonian Summer thunderstorm and that the arrangements for dealing with such a large number of sick were at first inadequate. The roads along which the patients were brought to the base were at the time in a very bad condition and it is only surprising that the mortality was not higher. In 1917 and 1918 with greatly improved conditions of transport and treatment the mortality was much lower, though the malaria to which the troops were exposed was the same. The feature of the malaria of Macedonia, therefore, which made it so serious, was the very large number of cases and not the greater proportion of severe cases among them."

DISCUSSION.

Major H. B. Lal said : " As recently as October last year, when the shortage of quinine both for military and the civil use had begun to manifest itself, a series of letters appeared in the Indian papers especially expressing views as to the correct use of quinine.

Having read the whole correspondence I was rather confused as to the real situation and have only been waiting for an opportunity to have the question settled. Before an opinion is expressed one has to solve a few of the following problems :—

1. Does quinine act as a protoplasmic poison directly on the malarial parasite or does it act by stimulating some form of body defensive mechanism ?
2. Does quinine act in the plasma or in the RBCs, or is it absorbed by the reticulo-endothelial system and act in these cells by stimulating them to greater action ?
3. At what stage is the malarial parasite most effectively acted upon by quinine ?
4. What form does the immunity against malaria take ?

As to the mechanism of the anti-malarial action of quinine, the position is rather confused. While many observers hold that cure by quinine is possible only through stimulation of the inherent defensive mechanism of the body, the weight of clinical observations supports the assumption that quinine acts directly on the plasmodia, being comparable to the effect of emetine on *E. histolytica.*

The fact that the malaria parasites after the addition of quinine saline solution of 1 : 10,000 concentration are still infective after 12 hours at body temperature supports the former view. But it has been objected that *in vitro* the conditions are entirely different. In support of the view that a direct action is displayed the fact is adduced that quinine

influences only certain stages of development, namely the free forms and young parasites till attached to the red cells.

It may be assumed that in complete cures both actions come into play but the more important of the two is the direct action. This conclusion can be drawn from the quick and often life saving effect of intravenous quinine.

There are moreover two variables in the problem :—

(*a*) Variations in the virulence of the strain of the parasite. To quote an example it is now recognized that the Italian strain of *P. falciparum* requires 8 times as much quinine to stop the attack as the Indian strain. In India itself there is a large number of strains which markedly differ in their reaction to anti-malaria therapy.

(*b*) Variations in the acquired or racial resistance of the patient, even in acquired resistance. James found extraordinary individual differences enabling him to classify his patients into very refractory, normal, and usually susceptible.

Ignorance concerning the influences of these two variables has often led to much bitter controversy. Practitioners frequently base their opinions on experiences limited to a specified region, and each is probably correct in the presentation of fact.

To return it is clear that the presence of a certain concentration of quinine is necessary in the plasma before and after the schizonts break up into the most susceptible form —the merozoites. It has also to be borne in mind that merozoites cannot be destroyed by one exposure to quinine, otherwise there would never be a second or third rise of temperature after exhibition of the drug. Moreover there is always the possibility of a double or triple infection. It is also obvious that the concentration of quinine required to kill the merozoites *in vitro* is very low but it must be prolonged, not only to kill as many of the young parasites as possible, but also to paralyse them and delay or inhibit further successful entrance into the RBCs and development into schizonts.

What the mechanism of immunity is, has not yet been settled. On clinical grounds one feels that the immunity is just a manifestation of compensatory hypertrophy of the reticulo-endothelial system of the spleen and the liver and that the acute phase of malaria is the period in which this compensation has not yet come into play and that chronic malaria is merely the minimal persistence of the malaria parasite in spite of the destructive activity of the endothelial system.

So far army personnel have led, relatively speaking, a more protected life and with proper housing and efficient anti-malaria measures in every cantonment, chances of reinfection were few. Moreover the standard army treatment given early enough and carried out conscientiously usually prevented any cases going into the chronic stage. The army's attitude has been to prevent the occurrence of chronic cases rather than provide treatment for them.

Usually chronic cases were seen in individuals who either possessed very little natural resistance or were exposed to repeated infections. Both these factors have in this war begun to manifest themselves in the deep forests of Burma, and the base hospitals have begun receiving large numbers of cases with immensely enlarged spleens, persistent anæmia, muddy complexion, and emaciation. And thus the need for an efficient treatment of chronic cases has arisen in the army.

Major G. V. S. Murthi said : " Standard army treatment is a very satisfactory type of treatment from a practical point of view. Any one disappointed with it should carefully check up that it has been actually carried out. The dosage of quinine at grs. x t.d.s. is a reliable and efficient dose. This was verified by Sinton, a distinguished malariologist working with a controlled army population. It requires no revision unless some one is prepared to produce properly controlled statistical evidence. The time of administration of quinine before or after the rigor is immaterial. It is a satisfactory state of affairs if the drug is in fact given, no matter when, or how exactly the drug acts —in the serum or r.b.c. or r.e. system.

The word relapse is loosely used with reference to malaria and reinfection is confused with it. What are really reinfections are deemed relapses and the type of treatment or the potency of the drug may there be seriously discredited.

Immunity in protozoal infections has not yet been established. In malaria immunity has no practical significance.

Lt. Col. R. N. Tattersall said : " Working in a hospital only 120 miles from Major Rogan's research unit, I have made some observations which are not always in accordance with his findings :

1. With regard to the abdominal pain after mepacrine, we have found that nearly 50 per cent. of I.O.Rs. complain of this symptom and eventually we had to institute the giving of an extra ration of bread with the morning tea.

2. Our relapse rate of patients under treatment is 2 per cent. Usually this occurred during the latter part of the pamaquin course. We have not sufficient beds to observe the patients, after the completion of their course and we discharge them to duty with a recommendation for 7 days attend " B ". I can produce no exact figures to prove my point but I feel certain that if Major Rogan had examined his patients during the period of observation he would have had a higher relapse rate. I suggest that his research gives a false picture of the relapse rate on active service.

3. Major Rogan stated that he had expected to find an unusual type of malaria in Assam and that he was surprised to find that it was not typical. I have found that a number of symptoms—hæmorrhage in particular—are unusually frequent in their occurrence, hæmoptysis, epistaxis, hæmaturia and blood in the stools. All these symptoms appear to be associated with this infection and even when the blood slide is negative and investigation shows no other cause of this hæmorrhage, these cases respond rapidly to a standard course of anti-malarial treatment.

Lt.-Col. S. B. Dimson said : " Before making any comment, I would like to take this opportunity to congratulate Major Rogan on his brilliant and painstaking piece of malarial research. The question which is of great interest now is the comparative value of the standard army treatment. My experience in West Africa was distinctly favourable as my relapse rate in primary M.T. cases was only 1 per cent. against 8 per cent. in controls treated by quinine only.

In India war-time conditions make an estimation of the relapse rate much more difficult. Cases received in our base hospital ex-convoy do not add much to our knowledge because (*a*) large numbers are hurriedly evacuated and so treatment is often incomplete ; (*b*) cases are evacuated only if convalescence is likely to be prolonged, *e.g.*, if suffering from anæmia, splenomegaly and malnutrition. A large percentage of these will relapse or have already done so. (*c*) Patients are returned to their depots and beyond an entry in the field medical card, following up is almost impossible.

Local cases, however, are much more suitable for prolonged study. The units are static for considerable periods, their strength is almost constant, malarial admissions always come to the same hospital and reinfections do not, in the non-malarial season, complicate statistical results to any extent. The first pre-requisite is to distinguish between fresh and relapse cases as it is my experience that treatment often fails to prevent further relapses. I cannot help feeling that Major Rogan's criteria, using only the temperature chart and blood films, are a little too simple. At Horton, only 80 per cent. of B.T. cases had an irregular temperature and these were primary, not fresh cases. It is unlikely that in Assam, especially army I.O.Rs. there can have been many primary cases. Many B.T. relapses do not show a tertian periodicity partly due to prompt treatment. More M.T. cases show a typical plateau curve whether primary, fresh or relapse. I find that it is exceptional to find parasites in B.T. relapses all at the same stage of development. In fact and in parenthesis I believe many B.T. rings are mistakenly called B.T. rings because it is not known by many pathologists that a M.T. ring when old is as large and fat as a B.T., though it is true that there are fewer M.T. rings seen in relapses this criterion is no help in an individual case.

This differentiation between fresh and relapse cases is most difficult and in the malarial season almost impossible. But now, when few fresh cases are occurring at bases, one can get some help by taking the following points into consideration when discharging a patient from hospital : (*a*) Did any attack occur within the previous 3-4 months ? (*b*) Were gametocytes seen early in the present attack ? (*c*) Has the patient still got an enlarged spleen ? I think by these means I can achieve up to 80 per cent. accuracy. Each case is indexed and a local unit register compiled. We therefore know the morbidity and relapse rates of each unit, and if a unit moves will send the list to the M.O. in charge for submission to the local hospital.

During the 40 days I have worked in the Eastern Command, I have discharged 230 cases of which 20 per cent. had relapsed after quinine, mepacrine, plasmoquine : although I have a bias towards the superiority of this treatment I am reserving judgement until I have studied many more cases and made absolutely certain that, as Major Rogan has emphasised, the treatment is carried out in its entirety.

Lt.-Col. Shah said : " I think after what Major Rogan has said there is little room for doubt that the standard army treatment for malaria is efficient both from the point of view of controlling the pyrexia as well as in preventing relapses. I think the point that we should now consider is, how can we ensure that every case of malaria in Assam receives this treatment. Obviously hospitalisation would be the best but if, due to the shortage of medical manpower, there is any doubt, the company commander should be made personally responsible for the men of his company being regularly paraded to receive medicine. As the units tend to look at the course of malaria treatment as being unduly long, and are generally reluctant in releasing their men for that period, I wonder if we could not compromise without impairing the efficiency of treatment by overlapping quinine administration over the first two days of the mepacrine course.

With regard to the toxic symptoms of mepacrine administration in dealing with a large number of Indian cases I have not had any spontaneous or voluntary complaints such as were mentioned by Lt.-Col. Tattersall. I have however never asked the patients. Instructions already exist to the effect that mepacrine should not be given on an empty stomach.

Lt.-Col. Ransome : " Major Rogan has made as one of his chief points the absolute necessity of ensuring that every patient gets his medicine. He has stressed the need for ocular demonstration of this point. May I suggest a way of checking up on this which I have found very useful. The quinine after the patient has swallowed it is blocked in blue on the chart and the atebrin in red. I use this method, not an original one, with all controlled drugs so that one can see at a glance where the drug has commenced to act, how long it has been going, how late in the disease it has been applied, all without having to stoop down too near the bed to read each chart minutely, a very important point when one is making a round of some 500 or 600 cases in a week as a divisional officer. Every case of malaria or dysentery becomes then a pharmacological experiment as it were. I find it of great advantage in teaching the young medical officers the action of these basic drugs, an action which is not appreciated so readily if one is not quite certain when the patient was put on and when he was taken off, as one looks at the chart.

Major Paton : " In order to ensure that patients receive the treatment ordered, it is suggested that all anti-malarial drugs, and drugs of the sulphonamide group, be impregnated with Methylene Blue, the urine being inspected after the administration of the drug for the presence of the dye.

The Chairman : " From the remarks of the last few speakers the high importance of ensuring that treatment is actually being taken is clear and this must be firmly impressed upon all medical officers. As an example, I recollect our giving prophylactic quinine on board ship to men about to arrive in Basra. Later we found the whole of the quinine tablets lying on the deck.

Major Rogan in summing up the discussion, re-emphasised that mepacrine should never be given on an empty stomach. Observation of this rule would prevent the development of colic in cases being treated with this drug.

He pointed out that case histories had only a very limited value in assessing whether or not a malarial attack was a true relapse.

Dealing with the recent newspaper correspondence about the effectiveness of very small doses of quinine in curing malaria, he stated that the advocates of such doses had entirely misinterpreted work on experimentally induced malaria in which the strain used was of low virulence, tending to spontaneous cure. Such infections might be ' cured ' by a small dose of quinine (grs. v) but they bore no relation to the strains commonly met with in India. A dose of quinine grs. x t.d.s. might on occasion be slightly in excess of requirements but bearing in mind that absorption may be hindered by various factors, it would be obvious to the meeting that it was better to overtreat a few cases slightly than to undertreat many.

Captain Birks then read his paper as follows :

A NEW APPROACH TO MALARIA.

The intention of this paper is as follows :—

1. To describe and discuss the observed phenomenon of auto-agglutination of red cells in malarial subjects.
2. To record some microscopical observations on the action of (*a*) quinine, and (*b*) adrenaline, on fresh blood cells.

3. To record some clinical observations on the conjunctival vessels in malaria cases and some other vascular signs in malaria.
4. From the above to discuss the mechanism of the malarial relapse and frequent failure of the therapeutic attack.
5. To discuss the potential humoral defence against the malarial parasite.
6. To postulate a possible method of increasing the humoral defence and to produce a true immunity.
7. To suggest a mechanism and pathology for blackwater fever.

Auto-agglutination of blood cells in malaria.—In November of 1942 it was observed quite by chance that a patient suffering from sub-tertian malaria auto-agglutinated his blood cells in thick film producing an identical picture to that seen in wrong cross typing for blood transfusion. Following this up it was found to be present in greater or lesser degree in a high proportion of malaria subjects. Usually it is visible to the naked eye but microscopical observation shows up the slighter degrees of auto-agglutination and confirms the naked eye appearance. It is not a constant finding and is often absent in initial attacks of malaria but it is constant in my experience, in all cases showing enlargement of the spleen. The following two cases are reported in detail as being the most significant and important.

(1) **Corporal O.**—In June 1942, he had a severe bout of M. T. malaria accompanied by vomiting. He made a good recovery and was quite fit until January 1943, when he came to me complaining of daily shivering attacks but protested that he was quite fit in the mornings and again at night but between 12-00 and 16-00 hours he felt ill and shivery. On examination the spleen was enlarged two fingers, a thick blood film was negative for M. T. but showed a moderate degree of clumping; he had no fever. Quinine grs. x t.d.s. were given on D1 and D2. On D3 at 12-30 hours he had a violent rigor, the spleen was enlarged to four fingers and tender. A thick blood film, taken at 13 00 hours just after the rigor had abated, showed an almost instantaneous gross clumping of red cells.

After staining, the film was found to be full of rosettes M. T. actually in the process of sporulating. It should be mentioned that the serum of this case had a curious milk and water appearance. The urine showed no abnormality. After running a fever of 101 for twelve hours there was an abrupt crisis and no further fever occurred. His appearance on D4 was unforgettable. The skin was of transparent white appearance and the infra-orbital skin looked black. The eyes were sunken and he looked very gravely ill but on talking to him he responded vigorously and said that he was doing well. He made a steady recovery.

(2) **Lieutenant F.**—He came to me asking for his second T. A. B. inoculation which was given, but having given it he told me that his other in oculation was still painful and on examination an extensive venous thrombosis was seen extending from the cubital fossa to the axilla. I rebuked myself for being so precipitate with the second T. A. B. and noticed that he looked pinched, cold, ill and depressed. On enquiring into his recent health it was found that he had had M. T. malaria in June treated by quinine alone for seven days. A thick film produced no malarial parasites but a gross auto-agglutination and watery serum. He was ordered to bed. The temperature was sub-normal. On D1 he received nothing, there was no fever and the spleen was not palpable though he was slightly tender under the costal margin.

On D2 a venous thrombosis occurred in the other arm identical to the first. He was given 1 grm. mepacrine t.d.s. No fever occurred. Quinine was deliberately omitted as blackwater fever seemed a not remote possibility in view of the gross auto-agglutination.

On D3 he was removed to hospital and continued his treatment.

On D10 he was seen walking about and a dramatic change was noted in his appearance. He was alert, jocular and clearly quite a different man from the depressed individual I had seen on D1.

Auto-agglutination of blood cells in my experience to date is as a rule more marked and constant in Indian sufferers from malaria. This may be due to their frequent bouts of fever which go untreated, or it may be that the blood group "O" to which most Indians belong and which has both agglutinins alpha and beta is responsible for it.

The exact mechanism and significance of this reaction is not certain but it is reasonable to suppose that it is a defence mechanism by the serum of the patient against abnormal red cells, *e.g.*, those that contain parasites or malarial pigment (Haemazoin). The objective of the defence being to prevent the parasite sporulating.

The action of quinine on fresh blood cells.—On adding a drop of intravenous quinine solution to freshly drawn blood an instantaneous haemolysis takes place to naked eye

and on microscopical examination this is found to be correct but it is also observed that some cells do not haemolyse but clump. This difference is presumably dependent on the age of the red cell and the normality or otherwise of its pigment.

The action of adrenaline.—If a drop of 1/10,000 adrenaline is added to red cells a similar action to the above appears to the naked eye but on microscopical examination it is found to be incorrect, the blood cells are intact, shrunken in size and no clotting occurs. Fine granules are also found in the serum after this reaction. In a few cases actual haemolysis does take place.

The action of quinine in malaria.—I believe the action of quinine is as follows : It causes haemolysis of all cells containing malarial parasites that it comes in contact with, thus rendering $\frac{1}{4}$, $\frac{1}{2}$ and $\frac{3}{4}$ grown parasites harmless, but should the quinine be taken when there is a large number of parasites in a mature state it may liberate them in great numbers and should the quinine be stopped, the patient is worse off than he was before. The cause of failure in quinine therapy is discussed later in relation to the malarial relapse.

Some clinical observations.—In December 1941, my attention was arrested by a paragraph in Manson Bahr's "Tropical Diseases" quoting Goldfedder—"The conjunctival blood vessels are darker, more superficial and have a wavy outline when the eye is turned forward." In the ensuing months this sign was looked for and found most valuable. It seemed especially interesting because the conjunctiva is the only place where one can directly observe blood vessels. This is a positive sign in 90 per cent. of British cases, in Indian cases the natural darkness of the conjunctiva makes the sign unreliable. The following observations are recorded :—

1. They often remain long after treatment.
2. They are often incompressible.
3. A conjunctival ecchymosis has been seen in two cases spreading from one of these vessels.
4. In Gnr. T., a patient who has had ten relapses B. T., I actually observed an alternating spasm and contraction in one of these vessels while the fever was 102.

Case 1.—A very severe conjunctivitis with great oedema though no fever. The condition differed from acute conjunctivitis of infective or traumatic origin ; there was a large number of thick red superficial vessels and extreme bogginess of the conjunctiva. A thick blood film showed B. T. rings and amoeboid forms. The condition cleared while taking a standard course.

Case 2.—Similar to the above case, he improved very slowly and was incompletely cured after ten days on silver nitrate drops. There was no purulent discharge. A smear was negative for the gonococcus. A thick film on D11 showed B. T. rings. Quinine was given on D12 grs. x t.d.s. On D13 the eye was much worse, but there was no purulent discharge. Quinine grs. x was given again.

On D14 there was a striking improvement and a steady return to normal from that day. Three weeks later the condition recurred and the standard course was given without any local treatment. The condition cleared on the third day. Five weeks later it recurred again but this time associated with purulent discharge and local measures only, cleared the condition. The characteristic vessels were absent.

Some other vascular signs.

Case.—Gnr. H. He had had two relapses B. T. in two months and came to me complaining of swellings of the ankles and shins. On examination a diffuse erythema with central area of oedema over the medial aspect of the ankle and two smaller swellings on the skin over the tibia were found. They itched but were not painful. B. T. rings and amoeboid forms were seen in thick film. The condition recurred on three successive nights. After the third day of standard treatment there were no more swellings. Six months later a similar condition occurred and responded again to anti-malarial treatment.

Case.—Dvr. A. He had B. T. malaria in June 1942. In November 1942 he complained of blisters recurring on three successive nights on his skin, also feeling hot in the afternoon. Thick film showed B. T. amoeboid forms. On examination there was nothing to be seen or felt but he assured me that they were there the night before. A standard course was given. On D1 he said that the blisters recurred but subsequently there were no further swellings.

Case.—Dvr. F. complained of swelling of the eyelid and mouth. He was seen by me in August 1942. He had a marked giant urticarial swelling of the right lid closing the right eye. He said that he had had them off and on for a week. He also complained of frontal headache. Blood film showed B. T. amoeboid forms. A standard course was given and no further swellings occurred until November

when he was seen again with a typical urticarial swelling of the lip. Blood film showed B. T. amoeboid forms again. No further swellings occurred after standard treatment.

In none of these cases was there any personal or family history of asthma, urticaria, or hay fever.

It is not suggested that these swellings are necessarily caused by the malarial parasite but that they are a manifestation of the auto-agglutination reaction to abnormal cells actually taking place in capillaries. It would be interesting to know whether asthmatics auto-agglutinate their cells during their attacks.

Haemorrhagic symptoms.

Case.—Dvr. S. complained of abdominal pain and diarrhoea for 3 days. On examination temperature was 97 and pulse 100. He was acutely tender in the right loin, especially in the renal angle. Spleen was not palpable, urine a trace of albumen and on microscopical examination showed 30 red cells to a field. Thick blood film—M. T. rings +. Standard treatment was given. On D3 and 5 there was a slight elevation of temperature; on completing the course he had returned to normal health.

Case.—Pte. X. complained of coughing up blood and pain over the upper three ribs on the left side. On examination temperature was 97·4 and pulse 85. He was a deep chested muscular subject; the chest moved equally *on respiration*. There was no abnormality of resonance, voice sounds, or breath sounds. No adventitious sounds were heard. Sputum collected in 24 hours showed four teaspoonfuls of heavily blood stained non-purulent substances. Thick blood film revealed M. T. rings. A standard course controlled his symptoms and restored him to normal health.

The following cases have been seen and discussed at clinical meetings in 45 I.G.H.; all with positive blood slides for M. T. malaria :—

(*a*) Subarachnoid haemorrhage.
(*b*) Haematuria.
(*c*) Bleeding from urethra.

The following two cases lend weight to the capillary agglutination theory.

Case.—Tpr. L. came to me complaining of pain at the end of his right index finger. On examination there was an erythematous patch on the dorsal aspect of the terminal phalanx. On D1 the arm was put in a sling, on D2 the terminal phalanx had cleared but the erythema had spread proximally involving the middle phalanx. On D3 there was an erythema on the adjacent finger confluent with the index skin erythema and it had spread on to the proximal phalanx and dorsal aspect of the hand. The erythema was cold and there was no oedema, the epitrochlear gland was enlarged but not tender. On D3 blood was taken from the centre of the erythema and the film was found to be packed with large lymphocytes, polymorphs, and amoeboid forms of B. T. He showed the typical conjunctivae of malaria and after starting quinine he complained on D2 of a mid-day fever and frontal headache with pain in the back and his temperature rose to 100. The erythema subsided on that day. Three months previous to this an identical case had been seen but its pathology was unrecognised.

The condition resembles nothing that can be found in text books. Erysipelas of a low virulence was the only diagnosis that could be made but it was manifestly impossible because of its extremely slow progress.

The mechanism of this skin condition can be explained as follows :—

The malarial parasite enters the skin capillaries in large numbers. In response to cold the capillary contracts shutting off the malarial nest, auto-agglutination takes place and for a time the development of the parasite is arrested. When the circulation is re-established in that capillary the parasite sporulates, rupturing the capillary wall; haemazoin escapes into the tissue spaces, and the pigment sets up an inflammatory reaction and is itself removed by scavenging cells to the glands draining that area.

The following case is worth recording, not that it is conclusive, but suggestive.

Case.—Sigmn. R. had two attacks of M. T. malaria in August and September 1942. In February 1943 he ran a bamboo splinter into the back of his hand and developed two ulcers at the site, the inflammatory action was slight and pus formation nil, and there was no lymphatic involvement. The ulcers spread slowly for ten days in spite of flavine and sulphonamide powder. On D10 they showed a clean floor, white devitalised sides rising steeply from the floor, the surrounding skin looked grey and unhealthy. On D11 the ulcers were packed with crushed mepacrine. On D12 the ulcers showed a healthy dry scab and a surrounding inflammatory zone, subsequent healing was uneventful.

It is dangerous to draw conclusions from one case alone but the following case is the most important and the most conclusive of all.

Case.—Dvr. C. M.T. malaria in October and an unspecified attack in January. In February he came to me complaining of fever and headache on the day before; at that time there was no fever. The tip of the spleen was palpable and thick film showed auto-agglutination and M. T. amoeboid forms. 30 grs. of quinine were given on that day and at 12-30 hours on D3 he ran a high fever 104, later developing a cough with heavily blood stained gelatinous sputum. A film was made of his sputum and stained by Leishman. On microscopical examination, it was a difficult film to examine on account of the sputum debris, but the impression received was of a large number of parasites. This diagnosis was not accepted until several parasites had been clearly found within the outline of a red cell, both M. T. rings and B. T. amoeboid forms were seen. On D4 after passing water a small clot came away from the urethra. This was stained and an identical picture to the sputum was found. It should be mentioned in addition that the spleen showed a marked enlargement on D5, being palpable 2 fingers beneath the costal margin.

Discussion on the malarial relapse and failure of therapy.

The following physiological facts are recorded :—

(*a*) The cross section of the capillary bed is larger than that of the arteries and arterioles.
(*b*) Only a proportion of capillaries are at any time in active operation.

(c) The liberation of adrenaline rises (i) in response to cold, and (ii) in response to hard physical exercise.

The following observation is re-stated: Adrenaline in contact with fresh blood cells reduces their size with the formation of a granular substance in the serum. On microscopical observation the cells lie loosely in the fluid medium without any agglutination or clotting.

The mosquito bite.

The injection of sporozoites is liable to infinite variation. She likes to bite into a vein and if successful the subsequent fever is inevitable, but she may bite into a capillary and the response of a capillary to trauma in occlusion and that of the blood is clotting. In thinking of a malarial invasion one has to consider the dosage and effect which may be as different as that between one-sixth gr. morphia and one grain. If the infection be heavy the defence has no time to react and the patient is overwhelmed in seven to 14 days by an acute fever. If the invasion is small or impeded by capillary occlusion the parasite is only liberated by violent exercise or great heat, when large numbers of blood vessels are opened. They may, on the other hand, be liberated in small numbers together with their metabolic waste products, haemazoin and red cell debris. Such small liberations produce no symptoms recognizable as malaria but provide the defence with an opportunity to develop its only possible reaction, agglutination of damaged cells. With every successful sporulation an increase of auto-agglutination occurs and when the parasite enters a capillary where the blood flow is slow, that agglutination takes place, surrounding the malarial parasite and adhering it to the capillary wall, from there they are dislodged by these anti-agglutination factors:—

(1) By violent exercise which liberates adrenalin.
(2) By intense cold which also stimulates adrenalin secretion.
(3) By intercurrent infection, cholera or T. A. B. inoculation which deviate the complement defence away from the malarial parasite to the fresh invader.

Remembering that a large proportion of capillaries are not constantly in action, it is reasonable to suppose that some parasites are for long periods non-effective, particularly if the agglutination is strong. It will be seen that quinine and the body defence are contradicting factors, quinine is attempting to haemolyse the abnormal red cell, the defence is tending to prevent it. This provides a rational explanation of the well-known fact that if the initial attack of malaria is not promptly and efficiently treated it is extremely difficult to eradicate the infection. This is because the capillary auto-agglutination prevents the parasite from ever coming into contact with the anti-malarial drug.

It is known that adrenalin diminishes the relapse rate and this is to be expected as it releases the parasite from the complement defence and provides a greater number of parasites for destruction. It is seen that the natural defence is inadequate and though it lessens the likelihood of an attack it impedes treatment.

The defence against the malarial parasite is necessarily incomplete because the invading organism is intracorpuscular and the products of its metabolism which are evidently toxic in themselves (as shown by the anæmia far beyond that which could possibly be achieved by the sporulating parasite) are rapidly stored in liver, spleen, and bone marrow. It is probable that most of the malarial symptoms are caused by the malarial pigment rather than the parasite itself. This is suggested by the cases that run high fevers without showing malarial parasites in the blood. Also by observing that many afebrile malarias become febrile towards the end of treatment. It also explains the differences between *P. falciparum* and *P. vivax* which is difficult to understand on the assumption that the intracorpuscular parasite itself causes the fever. It is reasonable to suppose that the chemical formula of the pigment is different in each case. It is possible to recognise cases with violent local symptoms due to the mechanical sporulation in association with a severe systemic reaction with no peripheral parasites. Thus the frequent finding of abdominal pain in malaria is an expression of distended capillaries; similarly some of the graver cases of malaria show only scanty parasites which indicates a large liberation of pigment from some local malarial nest.

The following case is of great interest and worth recording:

Case.—An Indian nurse complained of dizziness and of severe frontal headache on the evening of D1. On D2 she ran a fever of 104 sustained 12 hours, dropping to 100 and rising on D3 to 103, falling to normal on D4. There was a slight rise on D5 and D6 but on D7 there was no fever. Repeated blood films were negative for M. P. On D8 she complained of intense headache and developed a distressing hiccough which lasted 24 hours. She was drowsy, expressionless, and a bilateral ptosis was observed. Lumber puncture produced a clear fluid not under pressure and showed 16 lymphocytes per cmm. Intravenous quinine 10 grs. was given on D8 and repeated on D9, D10, D11 and D12, the hiccoughs ceased on D9 and the ptosis disappeared. She rapidly returned to normal and on D16 she was up and about but on D22 there was again frontal headache, unasea and a midday temperature of 100. No M. P. were seen but the condition cleared completely on oral quinine.

On the 8th day of disease in this case the diagnosis was agreed amongst four doctors as acute encephalitis, a fifth doctor dissenting on the grounds of the temperature chart and all agreed that quinine should be given. In fact all doctors were correct in their symptomatic observations, the fifth nominated the pathology. The condition can be explained by the following mechanism. A malarial nest sporulated in the corpus striatum liberating haemazoin into the circulation, rupturing capillaries and allowing pigment to enter the brain substance, producing the picture of acute encephalitis. The headache was an expression of distended capillaries; drowsiness, hiccough, and ptosis were due either to an anæmia of the part, or to the presence of malarial pigment in the brain substance. The quinine reached a high proportion of the parasites but left a few locked in capillaries to reappear at a later date.

The Humoral defence.

Kala-azar and malaria are the only diseases of acute invasive type that produce a violent reaction in the body and which allow at the same time the continued existence of the patient without

the production of a specific immunity. Other diseases of an equivalent violence, pneumonia, small-pox, scarlet fever, typhoid and typhus, overwhelm the patient or they are themselves overcome by the specific defence. Malaria and kala-azar are the only diseases which show evidence of a symbiosis. The reason for this failure of the defence is the inability of the defence mechanism to attack directly the intra-corpuscular parasite. The best that it can do is to develop a defence against abnormal red cells of an indiscriminate and non-specific type.

Considering the possible antigens of a malarial parasite we find :—

(*a*) The red cell with its intra-corpuscular parasite.

(*b*) The malarial pigment liberated on sporulation.

(*c*) Red cell detritus.

The malarial pigment produced by the various types of parasite is probably different and they are tabulated as follows :—

P. falciparum = HX 1.
P. vivax = HX 2.

If blood is allowed to haemolyse in distilled water after being withdrawn at the height of the fever it will contain :—

1. Extra corpuscular ring forms.
2. HX 1, or HX 2, or both.
3. Red cell envelope.

If this is now reinjected into the patient subcutaneously all the substances have to be collected and carried *via* the lymphatic system into the circulation. The idea is speculative but not without reason and it is hoped that a specific defence will be established thereby.

Sixteen cases have actually been treated by the injection of 2 ccs. of haemolysed blood. Of these, eight have a six months history, 7 have been free from malaria. Five of which previously had four or more relapses. The eighth which was the first done received only ·75 ccs. and though he is an apparent failure he is the most instructive of the lot. He has had two exceedingly trivial relapses in which the temperature rose to 100 on one day only. The other eight are too recent to be of value.

Observations following injection.

The author has injected himself twice with haemolysed blood taken from acute febrile cases. On the first occasion 5 ccs. from a B.T. case. There was no local reaction, but an enlargement of the epitrochlear gland, slight enlargement of the axillary glands and of the posterior cervical group. Seven days later ·3 ccs. from a mixed B.T. and M.T. case were injected. There was a brisk local reaction, an inflammatory zone with a central white wheal appeared within five minutes. The epitrochlear gland was enlarged within an hour and the posterior cervical group was slightly enlarged and there was some pain in the left side of neck on the following day. A blood film taken proximal to the site of injection 24 hours later showed many polymorphs and large lymphocytes filled with brown pigment.

Summary.

After observing the phenomenon of auto-agglutination of red cells in a high proportion of malaria cases together with the more constant observation of dark thickened incompressible blood vessels in the conjunctiva, also some symptoms of haemorrhage and urticaria it is considered probable that the malaria parasites spend much of their time in terminal blood vessels in nests of agglutinated blood cells. In these capillaries they may set up various symptoms relative to the site of the vessel. In the brain they may produce every type of headache, in the abdomen they can produce pain of varying intensity and location. In the skin in association with trauma, they can produce indolent ulcers and it is believed by the author to be the basic cause of ulcus tropicum (syn. Naga sores), not to be confused with Oriental sore.

The auto-agglutination is presumed to be a complement defence against abnormal and damaged red cells. That defence is released by anything that stimulates the excretion of adrenaline *e.g.*, extreme cold, and muscular exercise, also by intercurrent infections that deviate the complement defence. All these factors may produce a malarial relapse. It is further believed that quinine and other anti-malarial drugs fail because they never reach the parasites locked in non-functioning capillaries.

It is suggested that a specific defence may be stimulated by the injection of haemolysed blood containing malarial parasites. A number of cases are recorded which are too small to be of any definite value but there is nothing to discourage and a little that is suggestive.

In addition to a possible great improvement in the treatment of malaria this paper opens up new ideas on the treatment of asthma and other allergic diseases in which the specific sensitising substance cannot be found. The signs described in malaria are believed to be due to the pigment of the parasite which is taken up by new red cells in bone marrow rendering them abnormal with a tendency to haemolyse and producing as a defence mechanism the auto-agglutination described. A similar abnormality of pigment is not unlikely in asthmatics. Moreover the action of adrenaline as a relief in this disease is interpreted differently in that it appears to enter into chemical combination with the pigment of the red cell, or the red cell envelopes thus releasing the auto-agglutination reaction.

A rational explanation of blackwater fever is also possible with the above data. It is suggested that after prolonged infection with the sub-tertian parasite, the bone marrow and other haemopoietic tissues become saturated with malarial pigment, and every new red cell turned out is abnormal. A gross auto-agglutination reaction is stimulated which prevents haemolysis but in the presence of intercurrent infection or exposure to chill with a sudden rise in the excretion of adrenaline this auto-agglutination reaction is released and a massive haemolysis occurs. Similarly quinine taken at this critical state when there are a large number of red cells containing abnormal pigment will cause a wide-spread haemolysis with all the symptoms of blackwater fever.

Conclusions.

1. Auto-agglutination of red cells is a frequent finding in cases of malaria.
2. The state of the conjunctival vessels and other vascular signs suggest that this reaction takes place within the lumen of small blood vessels during life.
3. The injection of haemolysed or whole blood taken from the patient at the height of the fever has been tried in eight cases with histories lasting six months and the results are not discouraging. It is now being tried on a larger scale.
4. Remembering the similarity of the auto-agglutination reaction to that seen between incompatible red cells and sera, and the resemblance of blackwater fever to the reaction of a patient to incompatible blood, some close connection seems feasible between blackwater fever and auto agglutination.

DISCUSSION.

Capt. J. C. Shee said that in common with others, he had observed the phenomenon of auto-agglutination in Assam. It must be an unusual phenomenon, as it is not generally known to malariologists. This phenomenon was observed in thick film from six patients one morning. All cases were relapses, all were heavily infected, four were B. T. and two were M. T. It was a particularly cold morning, and bearing the possibility of cold auto-agglutination in mind, the room temperature was taken and found to be 52°F. During the next four days, thick films were done each day, the phenomenon grew weaker and disappeared as the films became negative for parasites. At the same time the weather was gradually becoming warmer, and morning temperature was 60°F. on the fourth day of examination. The question therefore is, did the phenomenon disappear owing to rise in external temperature or to elimination of parasites ?

Auto-agglutination has been described as a diagnostic sign in trypanosomiasis, but abandoned as totally unreliable.

It is felt that the phenomenon needs much further investigation. Auto-agglutination is unlikely to be related to blackwater fever, since it is seen in both B. T. and M. T. infections, but in the present state of our knowledge of the reaction, very much more work is required, before even tentative conclusions can be safely drawn.

Col. Taylor said that a number of officers in Assam have reported the phenomenon. It can be seen better in a thick film and has been seen by Sayers at midday in a warm climate. It has not been seen in blackwater fever cases, thousands of which must have been examined in detail in various parts of the world. It seems to be a subject needing more detailed examination. The School of Tropical Medicine, Calcutta, are prepared to do this and I suggest that Capt. Birks arranges to bring a few cases down with him to the 47th where the School of Tropical Medicine could do the details.

Major J. M. Rogan said that he had noted the phenomenon of auto-agglutination among cases investigated by him. This phenomenon had been described before and occurred in many acute infections other than malaria. Marked instances of auto-agglutination in which it was impossible to produce the phenomenon by mixing the fresh blood with Hayem's, Tyson's and sodium citrate solution were probably due to cold agglutinins.

He had been quite unable to confirm Capt. Birks' observations that enlarged and dilated conjunctival vessels persisted after the control of an attack of malaria.

In his opinion any attempt to theorise about the aetiology of malaria on the basis of this phenomenon and that of auto-agglutination was absolutely unwarrantable.

Ascoli's treatment of chronic malaria with adrenaline and antimalarial drugs was one largely discredited as it depended on the theory that adrenaline causes contraction of the spleen which drives the parasites out of this organ into the peripheral blood.

In fact adrenaline causes splenic contraction if this organ is not grossly fibrose but the parasites remain *in situ* as can be demonstrated by parasite counts.

The conference met again at 9 A.M. on the 16th March, at the Calcutta School o Tropical Medicine.

Major M. H. P. Sayers described and demonstrated the details of technique fo the preparation and staining of thin and thick films as follows :

PREPARATION AND STAINING OF BLOOD FILMS.

To clean slides.—The first essential is clean slides. Used slides should be boile in soapy water for some hours. They must then be *very thoroughly* washed in runnin water to remove all trace of alkali. If no running water is available several change of clean water must be used. Slides, wrapped in paper packets of fives or tens, can b stored in a box, or they can be kept in rectified spirit in a glass jar with a ground glas lid.

If slides are very dirty and soiled with grease or balsam they may be soaked ove night in glass cleaning fluid (1 part each of potassium bichromate and commercial sul phuric acid with 10 parts of water). After rinsing thoroughly, proceed as above.

Before use, slides are well polished with an old clean cotton or khaki drill cloth holding the slide within the cloth without touching it with the fingers. Always hol slides by their edges, and avoid handling the surface.

To prepare thin films.—Take two or three polished slides and lean them upright near at hand. Select a slide for a spreader with a smooth even end. For a pricker us a straight cutting needle. Flame the needle and prick the finger. A deep prick i unnecessary. Take a slide and invert the end on to the small bead of blood as it appear being careful to avoid touching the finger with the slide. Place the slide on a flat whit surface (piece of paper on the table) so that the end with the blood on it is towards th right. Immobilize the other end by holding the edges with the left fore-finger and thumb and apply the spreader at an angle of 45 degrees, somewhere about the centre of th slide. Bring the spreader into contact with the blood, and wait until the blood run by capillary attraction between the spreader and the slide. The film is spread jus before the blood has reached the margins of the spreader. It is very important tha the blood should follow the spreader, and that the spreader should not push the bloo in front of it.

Each film should be labelled by writing the patient's name and the date across th film with the point of the needle.

To prepare thick films.—Time and trouble are saved once confidence is gained i the thick drop. This will often reveal parasites, where they are missed in the thin film The time taken in examination is very much less, but it is sometimes difficult to be sur of the species.

Three drops of blood, each the size of a drop for the thin film, are pooled with th point of the needle into an even thick film, rather less than half an inch square. Th slide is then placed on a flat surface to dry. It is best to leave the thin and thick film side by side till the latter is thoroughly dried. During this time they should be covere up (saucer) or flies will spoil the films. The two should then be placed together, film facing, and wrapped in a piece of paper on which is written the patient's name and date

Leishman's stain.—1. It is absolutely essential for good results to use fresh distille water of neutral or faintly alkaline reaction in order to dilute the stain. But for wash ing the films after staining, ordinary tap water can usually be used.

A simple method of checking and if necessary correcting, the reaction of distille water is as follows :—

Place 5 c.c. of the distilled water in a test tube and add to it five drops of 0·04 per cent. water solution of bromo-cresol purple * as indicator. If the water is faintly acid, as is usually the case, will turn a pale yellow colour. In this case add very cautiously, drop by drop, a 1 in 1,000 water solution of sodium carbonate. The water turns a purple-violet colour. At this point stop at onc and now use the water thus prepared for diluting the stain. Excess of soda solution must not be used. (The faint trace of indicator present will not affect the staining.)

* Obtainable at the Bengal Industrial & Scientific Works, 112, Chittaranjan Avenue, Calcutta MESSRS. BAIRD & TATLOCK (LONDON), LTD., *Agents* :—BALMER LAWRIE & CO., LTD *103, Clive Street, Calcutta.*

2. *Preparation of Leishman's stain.*—Scrupulously clean a ground glass stoppered bottle, a 100 c.c. (or 50 c.c.) graduated cylinder, and a glass (not porcelain) pestle and mortar. Then rinse them out with pure methyl alcohol. Weigh out 0·15 grammes (2·25 grains) of Leishman's powder, and measure out 100 c.c. of methyl alcohol in the graduated cylinder. Put the weighed Leishman's powder in the glass mortar, add a little methyl alcohol from the cylinder, and grind. Pour the dissolved stain from this into the glass bottle. Repeat with successive quantities of alcohol until all the powder has been dissolved. Do not filter. If possible keep the bottle over-night in a warm dark cupboard or in the incubator.

3. The stock solution so prepared should be kept in a dark cupboard. For use the stain should be poured into a perfectly clean drop bottle. Always ensure the stopper is turned so as to exclude air when not in use. Finally, never insert a pipette into the stain unless it is clean and dry.

To stain a thin film with Leishman's stain.—1. Lay the film on a staining rack. A convenient rack is made by fixing two pieces of glass tubing with plasticine across an enamel tray. *The rack must be dead level.*

2. Drop the Leishman's stain from a drop bottle on to the film until the whole surface is covered. Leave for *half a minute.*

3. At the end of half a minute drop on to the slide approximately double the quantity of pure distilled water from a drop bottle. If the whole slide was covered in step 1 the correct amount of distilled water to add will be just short of the amount required to overflow the edge, which must not occur.

The water and the alcohol of the stain will automatically mix, but this can be facilitated by blowing gently up and down the slide for a moment. If the stain has been properly prepared and diluted, a golden green scum will rise to the surface after one or two minutes. Stain for 7-10 minutes.

4. The diluted stain should then be flooded off with a gentle stream of running water, from a wash bottle or tap. The washed slide should look pale mauve in colour when held up to the light. Do not tip off the stain.

5. Do not blot, but lean the slide upright to drain and dry, film side inwards.

NOTES.— (i) If there is doubt about the staining, before putting oil on the slide, examine under a $\frac{1}{12}$th objective. If the nuclei of the leucocytes are well stained, malaria parasites can be presumed to be well stained also. If understained, the slide can be restained using the same technique.

(ii) Deposit tends to occur :—

(*a*) If too long an interval has been allowed to elapse before diluting with distilled water.
(*b*) If staining is prolonged over 20 minutes.
(*c*) If the stain is old.

To stain thick films.—A simple method for routine purposes, is to cover the thick drop with a 1 in 15 dilution of Leishman's stain in distilled water. Allow the stain to act for about half an hour. The slide is then carefully washed as described under thin film technique.

NOTES.—The washing must be carried out very gently, otherwise the film will wash off the slide. If the slide is kept for an hour or so before staining, there is less tendency for this to occur.

To stain thick and thin films on the same slide.—Separate the thick and thin films by drawing a line across the slide with a grease pencil. Place the slide on the staining rack and de-haemoglobinize the thick drop with enough distilled water to cover it. Carefully flood the thin film with Leishman, and leave for half a minute. Then add distilled water to cover the whole slide, the dilute stain overflowing onto the thick film, but not over the edge of the slide. Leave for 10-15 minutes. Wash carefully and dry as described above.

Examine the thick drop first, parasites if present, are readily seen. With practice the species can usually be determined. If in doubt confirm by examination of the thin film. The latter can be dispensed with as confidence in the thick drop is gained.

Staining by Fields technique.—(Extracted from Trans. of the Royal Soc. of Trop. Med. & Hyg., Vol. XXXV, No. 1 of 3-7-1941).

The chromatin of malarial parasites is only faintly stained by methylene blue. Counterstaining with eosin has little further effect. Romanowsky showed that the effects of these two stains are modified if the methylene blue is exposed to the action of alkali, or is matured by age ; the chromatin then stains a deep red. This effect was

next shown to be due to decomposition products of methylene blue, now usually termed methylene-azure, or polychrome methylene blue. The staining of the chromatin is a dual effect of the methylene-azure and eosin ; the basic azure mordants the chromatin and the acid eosin stains it.

Preparation of Fields stain.—Two solutions are used—methylene-blue-azure, and eosin—both in isotonic solution adjusted to pH 6·6. Isotonicity and the correct pH are determined by the amount and proportion of the acid and alkaline phosphates which the stain contains.

Solution A—

Methylene blue (Medicinal)	0·8 grammes
Azur 1	0·5 ,,
Disodium hydrogen phosphate, anhydrous	5·0 ,,
Potassium dihydrogen phosphate, anhydrous	6·25 ,,
Distilled water	500·0 c.cs.

Solution B—

Eosin, yellow, water soluble	1·0 grammes
Disodium hydrogen phosphate, anhydrous	5·0 ,,
Potassium dihydrogen phosphate, anhydrous	6·25 ,,
Distilled water	500·0 c.cs.

The phosphates are first dissolved then the stain added. Solution of the granular azur 1 is aided by grinding in a mortar with a small quantity of the phosphate solvent. The solutions of the stain should be set aside for 24 hours, when, after filtration they are ready for use. The addition of 0·1 per cent. formalin helps to prevent bacterial contamination. The same solutions may be used for weeks continuously without apparent deterioration, but the eosin should be renewed when greenish from the slight carry-over of the methylene blue. The stains are kept in covered jars, of depth about 3 inches.

Should azur 1 be unobtainable a methylene blue-azure mixture, of undefined composition, but serving equally well, may be prepared as follows :—

(i) Dissolve 1·3 grammes of medicinal methylene blue and 5·0 grammes of anhydrous disodium hydrogen phosphate in 50 c.cs. of distilled water.
(ii) Bring to the boil, and then slowly evaporate in a water bath almost to dryness. This takes some hours if a flask is used.
(iii) Add 6·25 grammes of anhydrous potassium dihydrogen phosphate.
(iv) Add 500 c.cs. of distilled water, stir until the stain is completely dissolved, and set aside for 24 hours. Filter before use. This represents solution A.

Field's stain is only used for thick drop staining. Drops should be about the size of a shilling and not too thick ; the thickness of the dried film should not be so thick that the hands of a watch cannot be seen through it. Films are ready to stain as soon as dry, and stain better when freshly prepared than after keeping for some days.

Procedure.—(*a*) Dip the (unfixed) film in solution A for one second.
(*b*) Remove from solution A and immediately rinse in clean water by waving *gently* for a few seconds until the stain ceases to flow from the film and the slide is free from stain.
(*c*) Dip into solution B for one second.*
(*d*) Rinse again gently in clean water as at (*b*).
(*e*) Place vertically against a rack to dry.

* The staining times may need slight adjustments to suit different batches of stain. Varying periods of from one to five seconds may be tried until results are optimal.

Staining by Simeons' modification of Boye's technique.—(Extracted from I. M. G. December 1942).

Preparation of stain.—1. The stain consists of two solutions, prepared as follows :—

Solution 1 (Eosin solution)—

Eosin pure	1·0 gm.
Distilled water	1000·0 c.cm.

Solution 2 (Stevenel's blue)—

(i) Medicinal methylene blue	1·0 gm.
Distilled water (Dissolved completely.)	75·0 c.cm.
(ii) Potassium permanganate	1·5 gm.
Distilled water (Dissolved completely.)	75·0 c.cm.

(iii) Mix (i) and (ii) in flask. A massive precipitate forms at once.
(iv) The flask is kept in a water-bath at boiling point for half an hour during which the precipitate re-dissolves.
(v) Filter. The stain is now ready for use, it requires no further dilution.

2. For staining single slides, use small glass cylinders 1½ inches in diameter and 3½ inches high which, when not in use, are closed with greased watch-glasses to prevent evaporation. The contents of these cylinders decrease very slowly through the lifting out of wet slides. The loss is replaced by adding from stock. The more the stain is used the better it appears to become.

3. *To stain thin films—*

(i) Fix by immersion in spirit	1 minute
(ii) Rinse with tap water	4 seconds
(iii) Immerse in Eosin solution	10 ,,
(iv) Rinse with tap water	4 ,,
(v) Immerse in Stevenel blue	15 ,,
(vi) Rinse with tap water	4 ,,
(vii) Immerse again in Eosin solution	10 ,,
(viii) Rinse with tap water	4 ,,
Total time required	1 min. 52 secs.

Allow to dry in upright position.

To stain thick drops—(original technique)

(i) Dehaemoglobinize by immersion in tap water in beaker No. 1	1 minute
(ii) Immerse in Eosin solution	20 seconds
(iii) Rinse by dipping into tap water in beaker No. 2	4 ,,
(iv) Immerse in Stevenel's blue	30 ,,
(v) Rinse by dipping into tap water in beaker No. 3	4 ,,
(vi) Immerse again in Eosin solution	10 ,,
(vii) Rinse by dipping into tap water in beaker No. 2	4 ,,
Total time required	2 mins. 12 secs.

4. *Notes.*—It must be remembered that this method is still in the experimental stage and no doubt improvements as a result of modification in technique will be made. Capt. J. W. Lacey, R.A.M.C., has found the following modification to give very fair results for thick films, particularly if neutral distilled water is used for washing :—

(i) The dried thick drop is immersed in the methylene blue solution direct, with no previous dehaemoglobinization, for 5 seconds.
(ii) Wash thoroughly in neutral distilled water, waving the slide to and fro for about 5 seconds.
(iii) Immerse in the Eosin solution for 7 seconds.
(iv) Wash again in distilled water for 5 seconds, dry.

It is important that the " thick drops " should be fresh and not too thick.

Advantages of the method described—

(*a*) The stain itself is " home-made ".
(*b*) It contains no alcohol.
(*c*) It is suitable for staining by immersion instead of flooding.
(*d*) It does not appear necessary to be fastidious about the pH of the distilled water employed in its manufacture.
(*e*) It improves with use.
(*f*) It reduces the time required for processing drops and films to a matter of seconds.
(*g*) The results are perfectly satisfactory for all routine clinical work.

Dr. S. Sen then gave a description of the malarial parasites with the help of screen projections. He also demonstrated the taking of blood from a malarial patient for blood culture ; also the aldehyde test.

Major Murthi asked the use of the blood culture method, and whether the method Dr. Sen was demonstrating was a modified one.

Dr. Sen said that it was a modified method and that blood culture was hardly necessary in most of the cases.

Major Rogan asked Dr. Sen what conditions other than kala-azar gave a positive aldehyde test.

Dr. Sen replied that trypanosomiasis did so but as this condition was not met with in India, it did not complicate the test in this country.

The Chairman then thanked Major Sayers and Dr. Sen for their demonstrations and invited Dr. Lowe to give his lecture on leprosy.

LEPROSY.

Dr. John Lowe demonstrated the examination of lepromatous lesions of various kinds in patients and the taking of smears for microscopical examination, and spoke as follows :—

General.—With the recent rapid expansion of the Indian Army leprosy is not uncommonly found in its personnel, and particularly in men recruited from areas where leprosy is common. These areas include Madras and other parts of South India, Orissa, Bengal, Bihar and parts of the United Provinces, Central Provinces, and Bombay. Leprosy is also not uncommon in hill people such as Gurkhas.

In India the *mild neural type* of the disease predominates, and many cases are very slight. In the diagnosis of these cases, little help is given by standard text books of medicine, which describe mainly the severer cases less commonly seen in India, and particularly in the army.

Types of leprosy and their manifestations.—By far the commonest type is the neural type and it shows itself in either or both of the following ways :—

(*a*) The occurrence of one or more patches in the skin showing usually a definite margin, some loss of pigment, diminution in cutaneous sensibility, sometimes thickening and erythema of the margin of the patch or occasionally of the whole patch, and not infrequently thickening of the cutaneous nerve branches supplying the patch.

(*b*) Areas of diminished skin sensation and later trophic changes, deformities, and ulceration in the distribution of the peripheral nerve trunks of the limbs, the affected nerve trunk often being thickened and tender. Almost any peripheral nerve trunk may be affected in this way, but the commonest are the ulnar and the peroneal nerve branches and less often the tibial nerve. Involvement of these nerves later causes trophic changes in the hands or feet, claw hand, foot drop, trophic ulcer of the sole, etc.

The *lepromatous type* is less common particularly in the army and shows itself by infiltration, thickening and sometimes nodulation of the skin, particularly of the face and ears, but frequently there is slight diffuse infiltration of most of the body. Some anaesthesia and nerve involvement may be present but are usually not marked. There is often some involvement of the mucous membranes, particularly of the nose.

Diagnosis.—Bacteriological methods of diagnosis are of very little use in the neural cases which form the great majority, since these cases are usually negative to all ordinary methods of bacteriological examination. In lepromatous cases, which are rarely seen in the army, bacteriological methods may be of some use, but diagnosis is usually easy even without it.

The diagnosis of leprosy usually depends on thorough clinical examination of patients for the detection of either or both of the following signs :—(*a*) impairment of skin sensation, (*b*) definite thickening of nerves.

Impairment of skin sensation is usually demonstrated by testing the sensation of light touch. Impaired sensation may be found in patches of the skin and/or in the distribution of the affected nerve trunks.

Thickening of nerves may be detected in the cutaneous nerves supplying the anaesthetic patches and /or in the nerve trunks supplying anaesthetic areas in the limbs.

A nerve should not be stated to be thick merely because it can be felt for many normal nerves are palpable particularly when they run over a bone. A nerve is thick only when it is thicker than the same nerve on the other side of the body, or, if both sides are affected, thicker than it is in a normal person of corresponding size and build.

To repeat : proper clinical examination will make diagnosis possible even in slight cases, whereas bacteriological methods are usually of little or no use.

Bacteriological examination, if done, should be done by taking up a fold of suspected skin between thumb and forefinger, maintaining pressure to prevent bleeding, making a little slit into the corium with a sharp scalpel, scraping the sides and the bottom of slit with the point of the scalpel to obtain tissue fluid, and making a smear with this on a slide. Examination of the nasal mucous membrance is much less reliable, but if it is done, an actual fragment of mucous membrance must be removed from the nasal septum for making smears.

In cases of *neural* type, both these methods of examination nearly always give negative results.

ANCYLOSTOMIASIS.

Lt. Col. M. H. Shah then read his paper on ancylostomiasis as follows :

" I am posted to a place where patients have been dying like flies no doubt from diseases like malaria, dysentery and pneumonia, but chiefly because they were grossly malnourished and heavily infected with hookworms.

Extent of the disease.—Ancylostomiasis is a disease of the tropical and sub-tropical countries. In India its prevalence is already considered to be widespread. Even in peace time there was hardly a station where the medical wards did not produce 4—5 cases a month. Now on account of the considerable expansion of the Indian Army the state of affairs must be very akin to that of the general population in India. South Indians and the Gurkhas are the most heavily infected, with a rate of about 90%.

In the 66 I.G.H. the following data have been obtained :—

1. *Examination of the stools.*—(*a*) These were first carried out in November in State Labour patients by the Field Laboratory. A figure of 53·7% was obtained where a high assessment had been made on clinical grounds.

(*b*) In December Major Rogan began his investigations and in the (i) A.P.C. Units consisting of South Indians, Bengalis, Biharis and a few Punjabis, reported 89·6% (ii) Indian Army Units, he found infection in 53% cases.

2. *Post mortem examination* of a series of 100 consecutive cases revealed :

	Total.	Positive.	Percentage.
Indian Army	9	7	77·7
A. P. C.	15	11	75
State labourers	76	73*	95

(*Two of the 3 negatives had been dewormed.)

These figures can be taken as a clue to the magnitude of the problem of ancylostomiasis in the Army.

II. *Type of infection.*—Both *ancylostoma duodenale* as well as *Necator americanus* are known to be present in this country.

III. *Forms of the disease.*—(*a*) Period of invasion is characterised by the appearance of intensely itchy papules over the site of infection. These papules which apparently appear within a few hours of exposure are commonly seen over the feet and particularly in between the toes. The itching is generally intense that the victim is so obsessed with a desire for scratching that he often has to prick them to induce bleeding in the hope of securing relief.

In South India I have been told this lesion assumes the appearance of a fungus infection. This may be due to the massive and repetitive nature of the infection and due to the infected skin getting sodden from prolonged work in the paddy fields. The ground itch described in the text books as consisting of erythema, dermatitis and vesicles may really be a combination of allergy, scratch dermatitis and secondary infection.

During the few weeks following the appearance of the papules in a proportion of cases the individuals have been known to develop a mild persistent wheeziness. As this complaint does not persist beyond the monsoon season, it may presumably be related to the period when the larvae are making their way to the duodenum and pass through the lungs and the respiratory passages. The appearance of mild asthma in the monsoon may thus be an evidence of the individual having been infected with this disease.

(*b*) Cryptic form of the disease which is really a carrier condition and comprises the bulk of the cases of this disease. In this condition the hookworms though present in the jejunum rarely produce any overt disturbance, and although the victim is often slightly anaemic and due to his lowered resistance is an easy prey for other diseases he remains generally unaware of his condition. It is usually not until after deworming that he begins to appreciate the difference in his physical and mental vigour which follows this treatment.

(*c*) The third form of the disease, *i.e.*, anaemia, as the presenting symptom occurs in a relatively small proportion of cases. These have been variously estimated at 2—3% of those actually infected. In these the victim presents the picture of a rapidly progressive

anaemia which unless treated in time generally proves fatal either from myocardial failure or from some superadded disease like dysentery or malaria.

IV. *Recognition of the disease.*—The presence of itchy papules in between the toes and the subsequent appearance of asthmatic symptoms during the monsoon may be considered as evidence of the individual having been infected with this disease.

The cryptic form of the disease can be easily recognised from the presence of pigmentation of the tongue. In the 99 patients I left in one of my wards it was present in 28. The pigmentation is generally of a dark brown colour appearing as pinpoints over patches of the papillae and though almost always present at the edges it sometimes extends over the dorsum and in a few cases may be seen under the tongue and even over the palate. In the well established forms of the disease the pigmentation tends to disappear hence the tongue has been perhaps aptly described as the " white blotting paper tongue ". The cryptic condition could also be suspected from the presence of eosinophilia. In a recent series of 10 differential counts of patients admitted for various complaints the findings were :

1 case	1 per cent.
3 cases	2 ,,
1 case	6 ,,
2 cases	7 ,,
2 ,, ...	8 ,,
1 case	10 ,,

This is however not a sufficiently practical method for dealing with a large number of cases and by itself cannot be employed as conclusive evidence of the presence of this disease.

Examination of the stools by the flotation method as recommended in the army appears to be highly accurate. Although the *post mortem* figures of the A.P.C. unit were 73% only, perhaps due to the much smaller number of cases, Rogan's positive stools from these units were 89%.

The recognition of the well established disease may also be difficult. This is firstly due to the apparently well nourished condition of these individuals. (2) Due to the frequent lack of realisation which characterises even this form of the disease the individual often continues to work unconcerned until puffiness of the face or actual eodema appears on his feet. (3) Neither the conjunctivae due to occasional pigmentation nor the nails due to a relatively more opaque appearance provide reliable indications regarding the extent of anaemia.

If however the tongue is examined as recommended for the diagnosis of cryptic cases the white blotting paper appearance particularly if any residual smudges are present will generally provide sufficiently reliable evidence of the disease. On the whole it may be said that in India hookworm anaemia is so common that every anaemia of an apparently idiopathic nature should be considered as being due to the hookworm unless it is proved to be definitely otherwise.

The haematological picture of the disease is that of a secondary microcytic anaemia and there is nothing distinctive about it except for the frequent presence of eosinophilia. In cases complicated by nutritional deficiency the blood picture may actually be that of a macrocytic type.

V. *Sources of infection.*—As the chief mode of infection is through the contact of the body with infected soil, the sources of infection in the men lie in their houses which chiefly being in villages have no sanitary arrangements. In the army on account of superior sanitary arrangements and due to the protection afforded by boots the possibility of fresh infection is so materially reduced that " join the army to escape the hookworm " will not be a bad recruiting slogan. Indeed even if deworming is not carried out the army life itself and the boots which the soldier continues to wear on leave in his village even if only to show off, so considerably reduce the chances of reinfection that due to the self limiting nature of the disease, it so cures itself that the best examples of Indian manhood are to be seen only among the army.

VI. *Prophylaxis.*—1. Mass deworming of the troops to eliminate the carriers. This already exists in the form of an order for all the newly recruited men in the army.

2. Sanitation and discipline. Men should be compelled to use the latrines and the excreta at no stage of its disposal should be permitted to come in contact with the superficial layers of the soil. In the temporary camps either bore-hole or deep trench latrines should be used.

3. Camp sites should be carefully selected and areas suspected of having previously been occupied by the civilian population and the neighbourhood of villages should be avoided.

4. Personal protection is provided best by wearing boots and by avoiding the unnecessary contact of the body with the soil. As there are possibilities of acquiring the infection through the mouth raw vegetables and fruits should be carefully washed in salt water or some other suitable disinfectant and the water supply should be adequately protected.

5. *Education.*—While the war lasts full scale education of the troops is perhaps not very feasible but if the men could only be told about the horrors of this disease, the mode of its spread and the case of its treatment I am sure much would be gained.

VII. *Treatment.*—Our existing instructions for the treatment of this disease appear to be sound and practical. Tetrachlorethylene due to its low toxicity is the drug of choice. My experience is however chiefly confined to the use of carbon tetrachloride with which even during the recent months I must have treated more than a thousand cases. 45 m. of the drug in two ounces of a saturated solution of mag. sulph. on an empty stomach first thing in the morning is not only a convenient method of treatment but if used when contra-indications like heart, kidney, liver disease, or the presence of a very advanced degree of anaemia are not present, it is free of any risk. By using it in this way I have never had any fatality. The only case of acute yellow atrophy we have seen at *post mortem* was the one who had not been dewormed. I have therefore not been able to bring any personal experience but I am certain that the deworming of troops with this drug is absolutely safe.

The addition of m 15 of ol. chenopodium is absolutely necessary in the case of units which are also infected with round worms. In a recently treated series of 12 state labourers the addition of chenopodium m 15 lead to the expulsion of round worms in 5 cases. Carbon tetrachloride given alone to another 9 did not expel any round worms.

The use of carbon tetrachloride is dangerous when the anaemia has advanced to the stage of puffiness and oedema, and in such cases it is wise not to take risks with carbon tetrachloride. Iron sometimes helps to improve such cases sufficiently to stand the treatment later.

I need hardly add that deworming should be followed by a course of iron and stools examined every 10 days. If ova continue to appear in the stools a second course of carbon tetrachloride should be repeated after a period of 3 weeks.

I do not know if there is any real shortage of these drugs in the country, but if it is so, could not the time-honoured thymol be used for the treatment of hospital cases.

Col. Taylor said that for the last three months laboratories have been investigating the incidence of ancylostomiasis in the Eastern Army. Their reports show that hookworm is widespread in some Indian units. It is suggested that a touring unit is needed to examine and when necessary treat units on a mass scale. Also the evidence suggested that when time permits all Indian cases in hospital should have a routine stool examination, which is the practice in most civil hospitals in India.

Major P. A. Mathew said : " Carbon tetrachloride should not be given in cases who had recently recovered from jaundice, as it is a hepatic toxin and a flare up or recrudescence is possible and fatal results have occurred in mass treatment. The army instruction of 3 weeks interval is not absolutely essential, although it is safer. I have treated a large number of cases, 90% of the population in the area where I come from (Madras coastal area) being infected. The interval I have allowed is only 10 days. Minimum number of days for ova to reappear is about 7 days after a course of carbon tetrachloride, one or two days being allowed for re-examination of stools. No untoward effects have been noted in more than 1,000 cases so treated. "

Lt. Col. Shah in winding up the discussion said : " The changes in the heart are of the type usual to a state of advanced anaemia. The heart in the advanced case is enlarged, flabby and dilated.

Carbon tetrachloride is given as a dose of 3 c.cs. in two ounces of saturated mag. sluph. The mixture is prepared on the spot and thoroughly shaken up to emulsify before administration.

I have no experience of having cured an established state of asthma by deworming. "

DYSENTERY.

Capt. I. D. Willatt, R.A.M.C., then read his paper on Dysentery as follows :

" From the month of May 1942 to December 1943 inclusive, a period of eight month, 1,672 cases of dysentery passed through the Davidian Hospital. It was found that the majority of these cases were suffering from amoebic dysentery.

The percentage of each type of dysentery was as follows :

(1) 49% of the cases were amoebic in type. This figure includes cases of amoebic hepatitis which comprised 1% of the total of all cases of dysentery.
(2) 34% of the cases were bacillary in type.
(3) 2% only were mixed infections of bacillary and amoebic dysentery.
(4) 15% of cases were grouped as clinical dysentery. They exhibited an indefinite type of exudate in which no amoebae were found on repeated examination and from which no organism of bacillary dysentery was cultured.

These figures show amoebic dysentery to be half as common again as bacillary among the troops admitted to the Davidian Hospital.

It might be postulated that a large proportion of the 15% of clinical dysenteries were really of a mild bacillary character and this seems feasible in view of the fact that only 2% of this group were ever readmitted as ' Dysentery protozoal '. Even if this should be so, however, the figures for amoebic dysentery are still in excess of those for bacillary dysentery.

The relative proportions of amoebic and bacillary dysentery are of interest when compares with the work of J. Cunningham (1923) who found that " 86% of the dysentery in the jails of Eastern Bengal was bacillary ". Acton and Knowles found in 1920 to 1923 " that in Calcutta bacillary dysentery was at least five times as common as amoebic ".

All diagnoses of amoebic dysentery in the series quoted above were made on the finding of the vegetative form of *Entamoeba histolytica* in the stools (apart from some of the cases of amoebic hepatitis).

It appeared that recent arrivals in the country were particularly susceptible to both forms of dysentery. The case notes of 200 cases of amoebic dysentery were investigated. Of the 200 cases 128, or 64% of the total, had served in India for 6 months or less. Recent arrivals also seem to be susceptible to bacillary dysentery.

With regard to stations from which individuals suffering from dysentery were admitted, Calcutta, Dum Dum, Deula, Jessore, and Cuttack appeared to be the most frequent.

Investigations were conducted on a group of 200 cases of amoebic dysentery and 170 cases of bacillary dysentery. It was found that the percentages of admissions from each station bore a fairly close approximation in the amoebic and bacillary groups.

	Amoebic dysentery. per cent.	Bacillary dysentery. per cent.
Calcutta	37·5	43·0
Dum Dum	24·0	10·0
Jessore	6·0	5·0
Cuttack	4·5	2·0
Deula	6·0	5·0
The five station comprised	78·0 of total	65·0 of total

These figures are influenced by such factors as troops movements, which tend to raise the figures for Calcutta for instance, but nevertheless they seem very suggestive of a common factor being the major cause of spread.

The seasonal incidence of each type of dysentery is quoted here as some approximation in the rise and fall of the monthly incidence is found. This again appears to suggest a common medium for the spread of infection.

	May.	June.	July.	August.	Sept.	Oct.	Nov.	Dec.	Jan.
Bacillary dysentery	17	33	100	139	48	66	68	91	52
Amoebic dysentery	7	23	150	149	112	154	107	102	47

It will be noted that a marked rise occurred at the time of the monsoon in July of both types of dysentery. July and August were the months in which most dysentery cases were treated.

Bacillary dysentery is unlikely to be spread by flies at the time of the monsoon and amoebic dysentery is accepted as being a water borne disease. The suggestion is put forward that both bacillary and amoebic dysentery occurring among troops in this area are contracted from water supplies in very many cases. It seems difficult to explain the peak incidence during the rainy season in any other way.

There was a dramatic fall in bacillary dysentery in the hot month of September, whereas the incidence of amoebic dysentery showed a more gradual fall.

Amoebic dysentery.—A straightforward case of amoebic dysentery, diagnosed on the day of admission, remains in hospital for at least 19 days. When he has received his " ten days excused duty " on discharge he has been away from his duties for 29 days. Amoebic dysentery is thus rather a serious cause of incapacity.

At first a course of emetine hydrochloride total grs. xii by injection was given for cases of amoebic dysentery. Treatment with carbarsone was instituted if *E.H.* cysts were found in the stools while carrier tests were being done. It is now the custom to give carbarsone tablets i B.I.D. to every case of amoebic dysentery. Treatment with carbarsone is initiated on the 2nd day of rest in the emetine course and is usually continued for 8 days. Carbarsone seems to have an excellent effect in eradicating *E.H.* cysts, which are commonly found in the stools after emetine alone has been given. 126 cases of amoebic dysentery were treated with emetine injections and carrier tests for *E.H.* cysts were done.

93 cases = 74 per cent. remained cyst free throughout.

33 cases = 26 per cent. had cysts at some stage and required treatment with carbarsone.

The 26 per cent. of cases showing cysts in the stools all became cyst free when carbarsone tablets i B.I.D. was administered. In no case was there failure to obtain 6 negative carrier tests in this series.

I can recall a few cases in which carbarsone given orally for 8 days failed to eradicate *E.H.* cysts. In these cases carbarsone enemata 2 per cent. were given daily and had the desired effect. The value of routine carbarsone is apparent from these results. In my opinion it has a definite prophylactic value in getting rid of *E.H.* cysts from the bowel. We are all familiar with the patient who has five consecutive negative stools but where the sixth test contains *E.H.* cysts, but what about the seventh, eighth, ninth or subsequent stool of the patient discharged following six negative carrier tests ? While the standard of cure (6 negative carrier tests) laid down in Regs. M.S.I. is very satisfactory in my opinion when hospitals are apt to be so full, a routine course of carbarsone would seem of definite value in eradicating any carrier who may elude the test. It is thus a useful prophylactic measure.

The relapsing case of amoebic dysentery, which is appearing now more and more commonly, constitutes rather a problem. A number of cases have been encountered throughout in which the vegetative *Entamoeba histolytica* is still found in the stools after a full course of emetine has been given. This is particularly apt to occur in relapsing cases, the entamoeba either being present in the stool throughout or appearing again a few days after the end of treatment. Emetine bismuth iodide is difficult to obtain and in view of this the practice has been tried of giving a further eight daily injections of emetine gr. i commencing a fortnight after the cessation of the original emetine course. With this second emetine course a daily retention enema of 2½ per cent. chiniofon (Yatren) is given and continued for eight days. In the limited number of cases in which this method has been tried, it has proved successful. Not only are negative stools obtained

but extensive amoebic lesions have been observed, by sigmoidoscopic examination, to heal up rapidly.

Two such cases are quoted :—

(1) Name G. H. Age 32. Service in India 1 year and 4 months. History of favour previous attacks of amoebic dysentery, the last being 10 weeks ago. On admission vegetative *E. H.* in the stools.

Treated with emetine and carbarsone.

28th day in hospital—Stool contained vegetative E.H. ++++++in spite of the fact that he had completed his course of treatment less than a fortnight before.

Sigmoidoscopy on the 35th day showed numerous small amoebic ulcers.

From the 38th to the 45th day he was given 8 injections of emetine eath of gr. i and a chiniofon retention enema daily.

Twelve negative carrier tests were obtained after this course add sigmoidoscopy on the 56th day 3 weeks after the original one showed a normal rectum to a distance of 5 inches.

(2) Name A.B. Service in India 9 months.

Gave a history of two previous attacks of amoebic dysentery

His stool contained vegetative *E. H.* on admission and he was treated with emetine injections and carbarsone. After the 9th injection the stool still contained vegetative *E. H.*

Sigmoidoscopy on the 31st day in hospital showed numerous small amoebic ulcers 0·2 to 0·4 mms. in diameter mainly on the left and right lateral folds of the rectum.

Eight furthur injections of emetine and chiniofon enemata were started at this time.

On the 52nd day sigmoidoscopy showed an almost healed ulcer on the left lateral fold only.

18 negative carrier tests were obtained from the 42nd day in hospital onwards.

Unpleasant symptoms complained of by patients receiving treatment for relapses were persistent diarrhoea during the first emetine course—often not associated with failure of amoebae to disappear and dizziness due to a marked fall of the blood pressure. Relapsing cases who had received emetine before, seemed more sensitive to the toxic effect of the drug.

Relapse rate worked out on a basis of cases readmitted to the Davidian Hospital was 5 per cent. from May to December 1942 (total of 804 cases treated). The figure should probably be higher because a number of the relapsed cases would not be readmitted to Davidian Hospital.

Of a series of 200 cases 10 per cent. were relapses, 1 per cent. had relapsed for the second time. The average service in India of the relapsing cases was seven months only.

The incidence of relapses arising from the five stations of Calcutta, Dum Dum, Deula, Jessore and Cuttack was found to resemble the percentage figures obtained for fresh cases of amoebic dysentery.

	Fresh cases. per cent.	*Relapses* (20 cases). per cent.
Calcutta	37·5	50·0
Dum Dum	24·0	20·0
Jessore	6·0	0·0
Cuttack	4·5	5·0
Deula	6·0	0·0

This series is not very conclusive as the right hand column is based on 20 cases only but from the above figures, category C would not seem particularly advantageous for chronic relapsing cases. I am in favour of invaliding such cases to a temperate climate where their services can be retained and where they will prove useful. I would recommend this in any case in which more than three relapses have occurred.

.11 out of 562 cases suffering from bacillary dysentery were subsequently admitted to the hospital with amoebic dysentery. This figure of 2 per cent. only shows that an attack of bacillary dysentery does not seem to render the bowel liable to an amoebic infection.

Bacillary dysentery.—The commonest type of causative organism found in this area is the *Bacillus dysenteriae Flexner.*

An analysis of 125 cases showed organism in the following percentages :—

	per cent.
1. Flexner	62
2. Shiga	0·5
3. Sonne	14
4. Schmitz	9
5. Boyd	10

Sulphapyridine has been used largely in this hospital in the treatment of bacillary dysentery. The total dosage given is grms xi and this has proved sufficient. Sulphapyridine 0·5 grms 4-hourly is given for 36 hours, the patient being wakened during the first night only for his 4-hourly doses. Sulphapyridine 0·5 grms 4-hourly is then given for 24 hours.

I wish to emphasise the importance of giving large quantities of fluids and alkalies with the sulphapyridine for the unpleasant complication of haematuria is apt to result after a comparatively small dosage.

I think that this is due to the marked dehydration occurring in bacillary dysentery, with the result that the formation of M & B crystals is favoured.

M & B treatment possesses the following advantages over saline treatment :

(1) The diarrhoea is rapidly brought under control and this has a good psychological effect. When M & B is administered at 18·00 hours the patient often states that he feels much better on the following morning.

(2) No long starvation period is necessary. On the day following the day of admission the patient can take a light diet of minced chicken, steamed fish, bread and butter, etc., without ill effect.

(3) The period in hospital is definitely reduced.

84 cases treated with salines spent an average stay of 11 days in hospital.

86 cases treated with drugs of the sulphonamide group averaged 8 days in hospital only.

(4) M & B is of particular value in the choleraic dysentery cases. Such a case has extremely frequent stools of rice water type, muscular cramps, a low blood pressure and may show such dehydration that intravenous saline is necessary.

It would seem unwise to increase the dehydration in such a case by giving saline purges, wheras M & B rapidly checks the diarrhoea.

DISCUSSION.

Lt. Col. Dimson said : " In opening this discussion on amoebic dysentery, I am aware that, having seen only 300 cases myself since last May, there must be many here who have had three or four times that number under their care. It is therefore with much diffidence that I place before you what I have learnt. I will be brief omitting all theoretical considerations and as the subject is so vast, many important aspects of the disease.

The great majority of my patients were B. O. Rs. who came from the Eastern Army to the 14th B.G.H. at Bareilly. They were sent to us often before the first emetine course was completed, but many, arriving with diarrhoea or malaria, developed amoebic dysentery later. Any special interest my cases may have lies, therefore, in providing some information concerning what happened in the interval between the primary course of treatment and the discharge of patients as so-called cure to their depots. But I would greatly appreciate an answer to the question which is of absorbing interest to me, namely, how many of our cures may have relapsed.

Diagnosis.—With an efficient laboratory service and training of medical, nursing and ward personnel, difficulty was experienced in only few instances. The routine in these difficult cases (showing generally frequent loose stools with an occasional trace of mucus or indefinite exudate) was that, after at least six negative fresh stool

examinations had been recorded, recourse was had to sigmoidoscopy. This was sometimes successful in showing amoebic ulcers but more frequently all that could be seen was a reddened mucous membrane bleeding easily. If the diarrhoea persisted, three emetine injections were then given, and continued if the response was satisfactory. If all these measures failed, amoebic dysentery could be excluded. Little reliance could be placed on the temperature chart, W.B.C. count (except in hepatitis) or absence of Charcot-Leyden crystals.

Our dysentery wards produced five cases of sprue, two of mucous colitis, one of T.B. enteritis, one of chronic bacillary dysentery and three of chronic enteritis. In the local I.M.H., chronic enteritis was more commonly found, sometimes with co-existent amoebic dysentery. The presence of giardia was always recorded and most of these cases proved in time to be suffering from amoebic dysentery. Some, however, were undoubtedly primary and showed the gastric symptoms, coated tongue, and pale frothy stools, associated with this condition. Mepacrine was given with excellent effect. It was also used in cases of doubt as a diagnostic test, but even in proven amoebiasis it often reduced the number of stools during the tests for cure and afterwards.

A source of difficulty in some cases was the presenting symptom of bacillary dysentery, generally Flexner. My one fatal case started off with Flexner A2 and was treated first with salts and then with M & B 693 without any result. When I saw him, his caecum was thickened and tender and the next stool showed *E.H.* vegetative forms in large numbers. He died towards the end of his emetine course, which had failed to relieve his distressing symptoms, and *post mortem* showed that perforation and general peritonitis had occurred. His caecum was bathed in anchovy sauce pus, and the large bowel showed numerous amoebic ulcers. The patient had died of hyperacute amoebic dysentery.

Treatment.—All cases when first diagnosed were treated with emetine injections on the scale of 1 gr./stone body weight. Routine B.P. readings were among the indications whether a pause in the course should be instituted. When we overcame our initial acute shortage of amoebicidal drugs other than emetine, kurchi bismuth iodide with alkalies was given as well in cyst cases, either with or following the emetine course. In relapses, other drugs used were E.B.I., carbarsone, stovarsol, and enterovioform, but we had too little to allow of an accurate estimate of their efficacy. Amoebiarson was used solely in retention enemata. In vegetative E.H. relapses it was combined with emetine and K.B.I. and in cyst relapses with K.B.I. alone and proved effective. I gained the impression that stovarsol was valuable only in alleviating emetine depression that E.B.I., carbarsone and enterovioform were equally useful by mouth in resistant cases, and that K.B.I. alone in doses of either 5 or 10 grs. b.d. was promising in cyst cases. Hypertonic saline and eusol retention enemata, kaolin, and isapghul were mere palliatives. Bacillary dysentery complicated 10 per cent. of our cases, often in the latter half of a course. When treated with M & B 693 within 36—48 hours of the onset it cleared up dramatically.

In the early days after the withdrawal from Burma, emetine was our only drug and there was therefore undue haste in giving relapses a second course too soon after the first. One unhappy consequence was the occurrence of peripheral neuritis in 6 B.O.Rs. which fortunately cleared up completely after 4—6 weeks. But a more serious result was a death which I consider was indirectly due to a second course following the first after only seven days. A newly arrived M.O. did not appreciate the need for a minimum interval of 3-4 weeks and when I saw the patient he had bronchopneumonia following a mild upper respiratory infection. His persistent vomiting and dysphagia had not been recognised as grave symptoms of emetine intoxication. He died 24 hours later.

Prognosis.—Cases when first diagnosed gave the proportion of vegetative to cyst forms of E.H. as 3 to 1. Out of 250 B.O.Rs. approximately 50 per cent. were cured with one course of emetine. But of these successes there were nine vegetative to one cyst form *i.e.*, 60 per cent. of all vegetative cases and 20 per cent. of all cyst cases were cured by emetine alone. A further 15 per cent. of all cases were cured by a combination of emetine and K.B.I. as a primary course.

Great care was taken to detect relapses by means of stool charts, inspections, and examinations, and sigmoidoscopy, after tests of cure. No case was considered cured unless the stools numbered two or less daily and were macroscopically as well as microscopically normal. This rigid rule naturally varied with the enthusiasm of the M.O.

but in general it was followed. One illustrative case can be cited. A patient convalescing at Ranikhet after apparent cure had 1-2 stools daily for two weeks and only once was mucus seen. A week later I returned him to Bareilly for sigmoidoscopy before his discharge. Amoebic ulcers were seen and, resisting further treatment, he is now awaiting trans-shipment.

Our relapse rate came to 35 per cent. but this time the ratio of vegetative to cyst forms of E.H. was one to four. A second course of treatment was given and 4/7 of these cleared up, leaving 3/7 (15 per cent. of all my cases) as chronic relapses.

These chronic cases could be subdivided into two groups, 1/3 being convalescent cyst passers (5 per cent. all cases) and the remainder (10 per cent. all cases) showing symptoms and usually resisting whatever treatment we had available. A third course of emetine ± K.B.I. was hardly ever successful.

Disposal.—Higher authority laid it down that symptomless cyst-passers should be returned to their units. Although pleased to see those too-familiar faces go, I feel convinced that it is not the correct policy. These men cannot be regarded as 'healthy' carriers, like most sweepers, and will almost certainly develop symptoms sooner or later. In the meantime they are a menace in forward units where hygiene may be imperfect. These men, together with chronic relapsing cases, will henceforth, I believe, be treated here where better facilities are available. Should treatment fail, invaliding them is, in my opinion, the only course open to us.

There remains for consideration the much more numerous class of so-called cures. Since Regs. M.S.I. lay it down that, after test for cure, stools should be examined weekly for six weeks, it is my opinion that not only should ex-patients be kept at their depots for this purpose but, if necessary, they should be placed temporarily in category C for three months to ensure that forward units will not be burdened with them.

The problem is rather different with Indian troops and followers because a much higher proportion of 'healthy' carriers exists and the active disease is much less frequent. It is reasonable therefore to return to their units untreated cyst-passers with no history of dysentery but whose existence was detected by routine examination (*e.g.* for ova). But those who have had active disease should, after thorough treatment has failed, be boarded out as is the line suggested to be taken for B.O. Rs. It goes without saying that cyst-passers should not do cookhouse duties or remain mess servants. In I.O.Rs., where no other work for them is possible, they should in my opinion be boarded out.

SIGMOIDOSCOPY.

Lt. Col. Ransome then read his paper on sigmoidoscopy as follows:

"I am going to confine my attention to day to the immediate diagnosis of acute amoebic and bacillary dysentery by the use of the sigmoidoscope. When I use the word sigmoidoscope many of you will have visions of something pushing its way precariously into the pelvic colon groping for above the valves of Houston. I would disabuse you of this. In the vast majority of cases an examination of the rectum is all that is required to make a diagnosis, but as this instrument must never be passed blind, a glass window and insufflator are needed. Proctoscopy would be the correct term in the majority of cases. An analogy from midwifery is the use of forceps. Most forceps cases are low, but one should be able to use the same instrument high if necessary.

When I left the Tropical School fresh from the influence of the master (Manson-Bahr) I had a great respect for the mysteries of sigmoidoscopy, regarding the instrument with awe, an instrument only to be used in difficult cases and not for making an early diagnosis. However in Singapore in Professor Hawe's clinic one soon learnt its very great value in the early diagnosis of both amoebic and bacillary dysentery. He had a very fine dysentery ward going and although within a few yards of it there was an excellent clinical laboratory, sigmoidoscopies—or shall we call them proctoscopies—were done on the patients there, if there was the slightest doubt of the diagnosis and by this means a positive diagnosis was made in the majority of cases. Very very few remained undiagnosed after the first 24 hours. Of course in the early days, exudates alone had been used, but it was found by experience that the intelligent use of the combined method proved far more accurate. Many hundreds of these examinations were done without a single fatality.

One should regard the examinations as not unlike looking at the throat in cases of sore throat—one would be horrified at merely taking a swab from the throat through a half-opened mouth without actually looking at the tonsils! It is the same with the

disease of the lower bowel. The days of ocular demonstration have come, and by it a diagnosis can be made with about the same accuracy as by inspecting the throat, with the same advantage that you can take a swab under direct vision.

Now, perhaps some of you will wonder—should this instrument ever be passed when the patient is actually having many stools and tenesmus, such as he may have when the first comes into the hospital ? My answer to this is, if in doubt of the diagnosis, Yes. In bacillary dysentery, the only dysentery where there is likely to be much pain, the instrument is only passed just into the rectum.

Acute amoebic dysentery and acute bacillary dysentery are sometimes most difficult to differentiate, and nowadays when we have a specific remedy such as M & B 693 or sulphaguanidine, it is essential to begin the treatment of bacillary dysentery at once. Every hour lost may mean damage to the mucosa of the colon and what is more important, to the lower reaches of the ileum. This question of the immediate accurate diagnosis of bacillary dysentery is a burning one. I am constantly seeing wrecks of men with bloated bellies and chronic diarrhoea who have been dallied with from the start and labelled sprues, while many bacillary dysenteries diagnosed on exudates have come to me and on sigmoidoscopy prove to be amoebic. The latter experience has occurred far too often. The practice of purging with salts is possibly responsible for this. The amoebae don't like it. They become refractory, precyst and look like macrophages.

You will find that in bacillary dysentery, every single case has lesions in the rectum, while in acute amoebic dysentery 70 per cent. have lesions. Notice, I say, the rectum not sigmoid. If I said sigmoid, I should add another 20 per cent. This means that in acute bacillary dysentery one should be 100 per cent. accurate by inspection of the rectum during life and in fact one very nearly is so. If the patient has clinical dysentery and has no ulceration in his rectum but the mucosa is healthy, for practical purposes he is almost certainly amoebic and in the Eastern Army should be diagnosed and treated as such.

I shall not dilate on sigmoidoscopic appearances. They are well described in the books, but for those of you who are not familiar with them I would say, in passing, keep in your mind the pathology of the other fundamental orifice. Amoebic ulceration is characteristic. The early lesion looks exactly like those little peptic ulcers we used to get as children on the inside of our cheeks in summer—apthous ulcers, a brilliant yellow base with surrounding ring of erythema on a normal mucosa. The most perfect illustrations of the amoebic ulcers are to be found in Sir Leonard Rogers' drawings of *post mortem* specimens. They are better than those in the more modern text-books. In bacillary dysentery the whole mucosa is involved, reddened and often oedematous, very much like streptococcal sore throat, remembering always that even streptococcal throat can become phlegmonous. Sometimes of course there is a mixed infection, in which case there are punched out ulcerations on an inflamed mucosa. It would be well to point out in this connection that because the appearance and exudates are in favour of bacillary dysentery it does not absolve us from having repeated stool examinations on the chance that there may be amoebic infection also. I am convinced that there is a greater need for the use of this instrument of precision in the Eastern Army. It is far too much in the hands of the surgeons and consequently is not employed often enough, nor are the physicians given the chance to learn its use. I feel that every single place where dysentery is treated should have an instrument and that the instrument should be kept in the ward. To learn its use is not difficult providing one starts on cases which are normal and then on cases of proved amoebic dysentery. One should remember that it should never be passed blind, just past the internal sphincter, the obturator should be taken out and then insufflation should be commenced. I know that in one week one could become really useful with it, having taught many people to use it in the past.

On visiting some area hospitals in the Eastern Army I was struck by the number of cases which were diagnosed as clinical amoebic dysentery, and in whom the E.H. vegetative forms had not been found. For instance there was one hospital of 400 beds which had been functioning for three months and had only found the amoebae twice. I know from experience that many of these cases were amoebic and could have been most easily proved so with the instrument rather than treated expectantly. I am going to quote to you some figures from the Eastern Army. All of these are cases which have passed through my hospital from other hospitals. There are 36 cases in the series, all

cases of proved amoebic dysentery. They might be taken as a cross section. The average time in hospital before diagnosis was 10·3 days. One third were diagnosed during the first 3 days, one third were diagnosed after 10 days, but after 3 weeks 6 still remained undiagnosed, this represents 300 treatment days lost.

Now, I feel that out of these 36 cases if proctoscopy had been done early, all would have had the emetine within 3 days rather than being plagued with salts until such time as a diagnosis was made. Do not, for a moment believe that I am advocating sigmoidoscopy as a complete replacement of clinical side room methods, one augments the other. Both should be used, the better the side room bandobast the less the sigmoidoscope will have to be used. But if the side room is inefficient and if for any reason one really wants to know in a hurry what is the answer, with a sigmoidoscope and your microscope you can give it at once in nearly a 100 per cent. of cases ; even if there is no microscope you will be right 9 times out of 10 using both, the errors of both tend to cancel one another.

In conclusion, I would point out that in this room at the moment there are in a tin box 5 specimens of large gut, all showing the ulceration of amoebic dysentery ; all had ulcerations extending to the rectum. All could have been diagnosed easily with a sigmoidoscope and all are dead. The specimen that I brought with me was called bacillary dysentery on the exudate, this in spite of the fact that a catheter was passed into the rectum and mucus from its eye examined.* I have no doubt that had these patients been sigmoidoscoped early and emetine commenced some of these interesting specimens would not be here now. I feel their owners might have been willing to submit to the risk, risk which in my opinion is no greater than that of general anaesthesia and which was as you see small compared with that of leaving the case untreated.

*In some of these cases there is a proctitis for the first inch or so of the anal canal. This can give rise to a " bacillary picture ". The double infection has already been mentioned.

Case history 1.—Amoebic dysentery. Sgt. A.W.

August 1942. Bowels open 6-8 times daily. Nausea after stools. Slime and blood 2 days. When sick admitted to B.M.H. Meerut. In-patient 4th to 17th August. Given anti-dysenteric serum.

After discharge, stools again became loose. Readmitted September and given same treatment. In-patient two weeks.

Two weeks later readmitted. No serum, no emetine. Eusol enemas.

Patient rejoined unit and came down to Patna. Slight diarrhoea all time. Two days before admission bowels open 6-7 times daily, some slime and blood. 3 stools examined ; bacillary exudate reported in each. Sigmoidoscopy with typical amoebic ulcer. E.H. recovered from sigmoidoscope scraping. Large bowel showed no evidence of previous bacillary infection.

Although this is a chronic case of amoebic dysentery, it illustrates the fact that a bacillary exudate can be reported by a competent person. This was the laboratory Jamadar, the probable explanation being proctitis.

Case history 2.—Amoebic dysentery. Gnr. C.

11 weeks griping and abdominal pain, right iliac fossa. Diarrhoea off and on lasting about 3 days, formed stools in interval. No slime and blood noticed by patient until just before admission when he noticed a little blood. There was tenesmus during these two days.

Admitted 17-10-42. Two examinations. No amoebic cysts or amoebae. Sent by hospital ship to 67 B.G.H. Salines given.

26-10-42. Sigmoidoscopy : Mucosa, folded, normal colour. A few petechial haemorrhages the size of lentil seeds, were seen at 6 inches, the haemorrhagic areas appeared to be raised from the surface. No definite ulcer was seen but the appearances were suggestive of early amoebic lesions. Subsequent stool showed E.H. vegetative forms.

This case illustrates the point that there was, except for one small lesion, a normal mucosa but the patient had had dysenteric symptoms. If he had been bacillary the whole bowel would have been reddened.

Case history 3.—Example of where a case was lost through failing to do a sigmoidoscopy and relying on reports of " bacillary exudate " done by a competent laboratory trained Jamadar.

A certain patient was admitted with mild dysentery. He was passing a little slime and blood. Associated with it was what seemed epidemic jaundice, and in fact probably was. Patient passed from 4-6 stools a day and many of these stools were examined, it being a routine in that particular ward to examine every stool passed during the day time by a patient with diarrhoea. The reports came back negative for amoebae, labelled bacillary or indefinite exudate. The patient was put on salts and usual ladder diet, he was given for his liver condition adequate glucose. After about a week the diarrhoea appeared to be better, no slime or blood appeared and one felt that he was getting on fairly well as many of these patients do, the jaundice had begun to fade.

Quite suddenly within a period of 24 hours the patient's condition changed for the worse. He became semicomatose and confused. It seemed to me obviously that for some reason he was going to die. I suspected cholaemia. In view of the fact that he was practically moribund I did not sigmoidoscope him but gave him in pious hope emetine, having asked myself the question : is there any disease such as amoebic dysentery which might respond to a specific drug and which I might have overlooked ? In due course as I had expected the patient died, and I undertook a complete autopsy

including the brain. I was unable to find the exact cause of death but concluded that he died from cholaemia. His bowel showed amoebic ulcers which I could have reached with a sigmoidoscope and could have diagnosed a week before the onset of coma. In view of the fact that it is probable that this patient died from septic absorption from his ulcers with a liver unable to detoxicate, the conclusion is obvious. *Post mortem* showed a proctitis for the first inch of the anal canal; above this was a normal mucosa with typical amoebic ulcers.

Case history 4.—The body of a B.O.R. was brought by river steamer to the hospital in which I worked. This patient had been diagnosed first bacillary dysentery and later carcinoma of the bowel. He had had no specific treatment and been placed on the ship, a journey which took 4-5 days. He complained of abdominal pain on the ship and there was also a history of some haemorrhage from the rectum. It was called carcinoma of the rectum and he was going to be buried as such. This meant, quite apart from the fact that the diagnosis was wrong, that his wife would get no pension. On these grounds I was able to obtain a *post mortem* and I found that he had amoebic dysentery and ulcerations in the rectum, and that the cause of death was a perforation of a ulcer in the ascending colon.

This case illustrates the paramount need for early treatment with emetine, and its obvious corollaries.

DISCUSSION.

Major Sayers: "The sigmoidoscope should not be allowed to overshadow the importance of the clinical side room diagnosis of dysentery. We have found difficulty in teaching the correct use of the microscope. A number of oil immersion lenses have been damaged by careless use. The consequences of careless manipulation with the sigmoidoscope might be even more serious.

The important thing in the diagnosis of dysentery is the repeated examination of fresh stools, especially in the acute phases of the illness. A bacillary exudate in an acute case, which does not show definite amoebae inspite of repeated examination, can be taken to exclude coexistent amoebic infection. Examinations must be repeated because the excretion of amoebae tends to be intermittent and therefore they may be missed unless this is done. In the chronic case the sigmoidoscope may be a very useful ancillary diagnostic measure, but again the failure to find amoebae on repeated examination will usually safely exclude amoebic infection.

The exudate.—In the acute phase of bacillary dysentery, the type of exudate is diagnostic. The highly cellular character and the absence of faecal matter and bacteria are the striking features. 90 per cent. of the cells are of the polymorphonuclear type, while the remainder is made up of macrophages epithelial and perhaps an occasional eosinophil cell. Red cells are scattered among the inflammatory cells and do not occur in clumps, though rouleaux formation may be seen.

In the later stages, the character of the exudate changes and the red cells tend to disappear. The polymorphs show signs of degeneration, while the mononuclear cells increase. This type of exudate is called 'indefinite' and resembles the type of exudate seen in amoebic dysentery.

There is no exudate which can be taken as diagnostic of amoebic infection. Diagnosis depends on the finding of motile trophozoic amoebae. The exudate in amoebic dysentery is less cellular in character, red cells occur in clumps and not in rouleaux and Charcot-Leyden crystals may be seen. These features may be taken as pointers in diagnosis, but without the demonstration of motile amoebae, the diagnosis is unconfirmed.

Thus we should speak of two types of exudate only, the characteristic 'bacillary exudate' of acute bacillary dysentery, and the 'indefinite exudate' of the later stages of this disease and of amoebic infection. In the latter case there may be indications of amoebic dysentery, the definite diagnosis of which depends on the demonstration of trophozoic amoebae. It should never be necessary to have to resort to the diagnosis of a case from what may be *thought* to be dead amoebae.

Capt. A.M.M. Payne: "May I endorse Lt. Col. Ransome's remarks on sigmoidoscopy and may I put in a plea for the C.C.S. which is not equipped with a sigmoidoscope.

I was interested to hear of Lt. Col. Dimson's case of perforation of the caecum. I have seen five similar cases, three of which had a laparotomy. Two of these closely mimicked acute appendicitis and at operation, no perforation was present but there was obviously extensive amoebic ulceration in the caecum and sigmoid with a plastic peritonitis. They both did very well. One obvious perforation was opened but nothing could be done owing to the friable state of the caecum which had a perforation the size of a sixpence. Both the other two cases died with obvious perforations, one with haemorrhage from the rectum in addition. The other showed very extensive ulceration

with a large caecal perforation at autopsy. He was suffering from M.T. malaria and had had no dysenteric symptoms. The stools had been examined with negative results. One of these cases perforated on the 6th day of emetine therapy, and the other on the 4th day.

I have recently made some observations on the carrier rate in my unit after 8 months in India.

Findings :

Total number of B.O.Rs. investigated	95
Known cases of amœbic dysentery whose stools could not be examined.	4
Number of men examined—two stools each	91
Showing vegetative *E. histolytica*	2
„ E. coli cysts	12
„ E. histolytica cysts	15
„ Charcot-Leyden crystals (No E.H. or cysts)	1
	per cent
Total number of proven E. histolytica infections	21= 22·1.
Number of cases of amœbic dysentery	9= 9·5 .
Number of cyst passers (excluding those who are passing vegetative forms and those whose stools could not be examined).	15 out of 89 or 16·85.

22·1 per cent. of the unit are known to have been infected by *E. histolytica*, 9·5 per cent. have had amœbic dysentery and 12·6 per cent. are passing cysts but have not had amœbic dysentery. Of those 9 men who have had amoebic dysentery three have left the unit owing to the resistant nature of their dysentery, three are still passing cysts but are symptom free, and two are under treatment. One man has been detached and his stools have not been examined, he is known to be symptom free.

Consideration of the time lost from work gives information about the relative morbidity of amœbic dysentery, the amœbic carrier, and other forms of dysentery and diarrhoea.

Each day in hospital is counted as 1 ; attend C (excused duty) on the sick report is counted as 1 ; attend B (light duty) as ½ ; attend A (attendance with full duty) is not counted.

In eight months.

21 men infected with E. histolytica have lost	561½ days.
Average= 26·8 days per man.	
74 men not infected with *E. histolytica* have lost	168½ days.
Average—2·28 days per man from diarrhœa or bacillary dysentery.	

Further analysis shows that by far the greater time was lost in clinical attacks of amoebic dysentery :

Days lost in clinical attacks	491
Days lost apart from clinical attack *i.e.* from apparently simple diarrhœa	70½
Two groups of men contributed to this last figure :	
1. 9 men who had had, or later developed, amœbic dysentery, lost	19½ days
2. 12 cyst-passers lost (4·25 days per man)	51 days.

Comparing this figure, 4·25 days per man, with the figure of men not infected with *E. histolytica*—2·28 days per man, it is evident that significant diarrhœa is nearly twice as prevalent among the cyst passers. Six of the cyst passers lost no time whatever.

Thus we can divide cyst-passers into three groups :

1. Those who have had amœbic dysentery.
2. Those who have reported sick with apparently simple diarrhoea.
3. Those who have never reported sick.

The relapsing nature of amoebic dysentery is well-known, five out of nine cases from this unit have relapsed. A cyst-passer who has once had amœbic dysentery seems to be very likely to have further attacks.

The cyst-passers who have had simple diarrhœa have lost an average of 8·5 days per man, compared with the control 2·28 days per man. In addition personal enquiry shows that they are liable to attacks of loose stools and occasional passage of slime not sufficient to cause them to report sick. In this group the infection is evidently active and it seems reasonable to assume that they may develop amœbic dysentery should their resistance become lowered or should they acquire a superadded bacillary infection. Probably at intervals these men pass vegetative amœbæ. Two such cases were

discovered in the course of this routine search. Both men had had mild diarrhoea for a few days but had not intended to report sick. In both the stool was of the consistency of porridge and careful inspection showed mucus with microscopic blood intimately mixed with fæces. Vegetative amœbae were present. Both stated they were not feeling up to the mark and had vague abdominal discomfort.

The six cyst-passers who have lost no work all state that they feel well and have no abdominal symptoms, that their bowels are regular and that they have noticed no slime in their motions. This is of little significance since deep trench latrines have been used. In 4 out or 6 a trace of mucus was present on examination. All had had mild diarrhœa for a day or two on arrival in India and again early in the monsoons, but had been well ever since. In these men the infection seems to be almost a symbiosis at present. The standard of sanitation and hygiene in the unit has been good except for a period at the start of the monsoons. At this time an attempt was made to incinerate the dysenteric faeces from patients but owing to the wet and shortage of fuel and use of unsuitable type of incinerator, the attempt was ineffective and large numbers of flies bred in the faecal matter running from the incinerator. This was rectified by use of an Ottway Pit, but the men's cookhouse was invaded by flies and it seems likely that it was at this time that the infection was spread since it was about one month after this that cases of amoebic dysentery occurred, seven within a space of 14 days.

The general applicability of these findings is limited by the obvious sanitary defect which seems to have been responsible for the outbreak. However other reports on the carrier-rate show that the figures do not greatly exceed the percentage anticipated. Dobell in England found 7·1 per cent. among 3,146 civilians. Boeck and Stiles found 8—10 per cent. among 8,039 persons in America. Manson-Bahr states that there are no reliable statistics of the carrier rate in India. Reports by MacAdam on Indian troops in Mesopotamia showed the rate to be 5—20 per cent. according to the history of dysentery or diarrhœa, an average of 16·3 per cent. among 946 Indians. Dunbar and Stephens give the carrier rate among Indians in Madras as 21·9 per cent. Acton and Knowles report a carrier rate of 10 per cent. in 233 routine examinations of patients in Calcutta. Among the personnel of No. 12 I.G.H. in Mesopotamia Acton found a 6 per cent. carrier rate in 1916 and 20 per cent. in 1918.

In America figures as high as 53·7 per cent. have been reported.

Acton and Knowles estimate a general figure of 15 per cent. for the tropics and point out that the more often and more carefully the stools are examined the higher becomes the incidence. In this series 12 carriers were detected at the first examination and three more were found at the second. Military circumstances prevented further examinations.

The disposal of the amœbic carrier presents a difficult problem. He is a danger both to himself and to others. It is perhaps not out of place to emphasize that the sufferer from amœbic dysentery is not infectious during the acute stage, he becomes a danger to others when treatment has ceased and cysts appear in his stools and he is free from symptoms. In general, the treatment of the acute attack is satisfactory, though resistant cases occur. It is the relapsing case and the carrier for whom treatment is both prolonged and unsatisfactory. Ever present is the danger of secondary amoebiasis and an acute abdominal catastrophe which may occur without any dysenteric symptoms.

The days lost as a result of amœbic infection represent a serious loss of man-power; in this unit it has been 2·42 per cent. over a period of 8 months. Practically, this can only be reduced by reducing the number of fresh infections since eradication of the infection is so difficult, and this can be done only by reducing the chances of exposure.

As long as carriers are present exposure will occur unless sanitation and hygiene are perfect. However if 10-20 per cent. of the army are carriers it seems impracticable both to detect and remove them all, and even then local sources of infection remain. It is evident that apart from special groups of men in the army the solution must lie in improved sanitation. No cyst carrier should be allowed to handle food, eating utensils, or be concerned in the supply of drinking water, and a search for carriers should be made in any unit in which amœbic dysentery is prevalent. The importance of personal hygiene is obvious. Flies and contaminated water are the two other principal sources of infection. Anti-fly measures laid down in the Army Manual of Hygiene and Sanitation are very effective if properly carried out. In India, however, special watch should be kept for Indians defaecating on the ground in the neighbourhood of the camp thus providing both a breeding place for flies and, quite probably, a supply of amoebic cysts.

Contaminated water is not made safe by chlorination. Yorke and Adams have shown this and also that potassium permanganate so often used to sterilize vegetables and fruit is ineffective in concentration of 1 in 100—far in excess of that generally employed. Human night-soil is used as a manure in India and salads must often be contaminated.

Chemical methods of killing cysts in water would make it undrinkable.

Filtration and heat are effective if properly carried out. 50°C. for 5 minutes is lethal to cysts. In an endemic area, if contamination of the water supply is suspected, filtration or boiling is necessary. Proper education of the officers and men is essential if sanitary measures are to be carried out effectively.

The significance of the carrier state in amœbiasis is still uncertain. The carrier rate in England seems to be about 7 per cent., yet endemic amœbic dysentery is extremely rare. There are two main theories to account for this, firstly that there are two varieties of *Entamoeba histolytica* which are morphologically in distinguishable, one being pathogenic, the other non-pathogenic; and secondly that some secondary invading organism enables a symbiotic protozoon to become pathogenic. Whichever theory is correct, it seems that some infected people show no clinical signs and are in good health, whereas others are liable to intermittent disturbances of the bowels, attacks of dysentery, secondary amœbiasis and various degrees of ill-health.

This investigation does not cover a long enough period to show whether this is a real or artificial division. A division is certainly suggested—15 infected men have had symptoms and 6 have not. It would be interesting to see whether this state of affairs continues throughout their stay in the tropics.

Colonel Taylor had asked me how often I had found amœbiasis in cases of dysentery showing a bacillary exudate. My impression was that it occurred frequently. I have since looked up my records.

Total number of bacillary exudates considered	52
Number showing vegetative amœbae (E. H.)	9
Number showing amœbic cysts (E. H)	5
Number showing Charcot Leyden crystals	1

Thus 26·9 per cent. of bacillary exudates showed vegetative or cystic forms of *Entamoeba histolytica.*

Analysis: Five cases showed cysts only, vegetative forms were never found. It seems probable that these were cases of bacillary dysentery in men who were "cyst passers", and that the amœbic infection was of no ætiological significance.

Nine cases showed vegetative forms. Four of these presented the clinical picture of bacillary dysentery—acute febrile onset, 12—24 stools per diem with colic and tenesmus, non-fæculent stools at first, dry furred tongue, general abdominal tenderness. All four cases gave a history of occasional attacks of diarrhœa in the past, and one case had proved amœbic dysentery before.

These cases appear to have been amœbic "carriers" in whom a superadded bacillary infection caused a flare-up of the amœbiasis. Two of these cases showed further evidence of bacillary dysentery. One developing conjunctivities and arthritis, the other presenting the late sigmoidoscopic picture of chronic bacillary dysentery.

Five cases had a history of several days increasing diarrhœa, macroscopic blood and mucus appearing after a week or more, colic, little or no tenesmus, no fever. They were not actually ill on admission.

It is suggested that these were primarily cases of amœbic infection, and that the appearance of the exudate was due to secondary infection of the amœbic ulcers.

Conclusions.—The finding of a bacillary exudate is strong presumptive evidence of bacillary dysentery. In view of the high carrier rate double infections are common and bacillary dysentery may excite an existing quiescent amœbic infection. Bacillary exudate may be closely mimicked in primary amœbic dysentery with secondary infection of the ulcers, but the clinical picture is that of amœbic dysentery.

This matter has been thoroughly investigated in the past notably by Hanghwort in 1924. He concluded:—

1. Bacillary exudate is characteristic of bacillary dysentery.
2. Absence of macrophages and evidence of toxic necrosis of leucocytes excludes bacillary dysentery.
3. The cellular exudate in amœbic dysentery is largely determined by the degree of bacterial infection.

Capt. J. H. Gibbens thought that there was a lot of nonsense talked about " cyst-passers "—doctors were by no means clear about the life history of *Entamoeba histolytica*. What happened briefly was this. When E. H. cysts were swallowed, the keratin coating was dissolved by the acid gastric juice, and the amœba settled down happily to histolyse the mucous membrane of the gut. When conditions of life in the gut were unfavourable, the amœba simply curled up into a ball and was passed into a new world. This explained the periodicity in passing cysts, to which a previous speaker had referred. In what might be called stage 1 of the disease, as fast as the amœba histolysed the mucous membrane of the gut, the body cells were able to repair the damage. There were no symptoms—the parasite was said to be living " in harmony with his host ". This he proposed to call amœbic infection. In stage 2 when the patient's resistance was sapped perhaps by malaria or bacillary dysentery or overwork in the Eastern Army, the amœba gained ground and histolysed the tissues at a greater rate, the power of repair lagging behind. Symptoms and signs were (1) grumbling feelings in the abdomen, (2) a tendency to loose stools, and (3) E. H. cysts, with possibly a very occasional live amœba in the stools. This we called amœbic diarrhœa. In the third stage, the amœba was gaining ground even more quickly, powers of repair were virtually nil, and now there was fresh blood and mucus and active amœbæ in large numbers in the stools. This and this only should be called amœbic dysentery.

Now comes the point, what should be done about treatment and here Capt. Gibbens suggested that the situation could best be visualised by taking a personal view. So far he had not had the disease, but what was he going to do if he did ? If a pathologist found cysts in his stools at the moment, he proposed to have no active treatment whatever, and as to his " official disposal ", he said he would just carry on quietly with his job, with perhaps greater care about washing his hands. If stage 2 was encountered, he said he did *not* intend to have emetine, though possibly he might revise this opinion after a longer stay in India. He thought his general resistance must have got low and he proposed to apply for leave and go away for several weeks' cold and convalescence in the hills. If however he had the bad luck to reach stage 3, he was a case for bed and emetine.

Finally he asked if one of the first speakers would explain why emetine injections were said to kill active amœbæ but not cysts ; while E. B. I. was said to kill cysts but not amœbae. This seemed to him complete nonsense. Once encysted, the amœba was no longer dangerous ; in all cases all that mattered was the treatment of the active amœba histolysing the gut. Surely both emetine and E. B. I. must attack the amœba *in situ* ; any effect on the daughter cysts must be secondary.

Major L. S. F. Woodhead pointed out that during the months May—December 1942 out of about 400 cases of dysentery admitted to the B. M. H., Shillong, 248 were amœbic. This is roughly 62 per cent. of the cases.

In those amœbic and bacillary cases with severe hæmorrhage P. R. Congo Red (1 per cent.) was given intramuscularly with very good results. The site of injection was the buttock and 10 c.cs. was given first day, 10 c.cs. next, and 5 c.cs. next. All bleeding stopped after first injection.

Congo Red as above was also given coupled with 5 per cent. retention enemas in cases of severe dysenteric diarrhœa and the number of stools were either completely stopped or greatly reduced.

Lt. Col. E. D. Mackworth : "I would like to describe a 'snag' case which I recently encountered. A sepoy came in with a history of one day's fever (103°F) and a rigor the previous day. He also complained of pain around Murphy's area. On examination he was found to have a three finger enlargement of the spleen and of the liver, the latter being very tender. B.T. ring parasites were found—a fairly heavy infection. Standard treatment was commenced. By the end of the sixth day there was no change in the temperature which had ramained almost continuously at 102°-103°F. The medical officer had considered the possibility of amœbic hepatitis. The stools were negative for amœbæ and cysts on three occasions. Careful interrogation failed to reveal any history suggestive of amœbic dysentery. I was called to see the case on the 7th day. The liver remained very tender and three fingers enlarged. I started the patient off on a course of 12 injections of emetine hydrochloride and the effect was excellent. The patient, who had been unable to sleep owing to the hepatic pain, got a good night's sleep and the temperature came down the following day and stayed flat. The rest of the blue book

antimalaria treatment was completed when the course of emetine had finished. He made an uninterrupted recovery and was discharged fit to duty.

I feel entitled to say that the diagnostic therapy of emetine cured a coincident amœbic hepatitis in this confusing case."

Lt. Col. Dimson summed up the discussion as follows :

" This most interesting symposium and the impressive lists of figures will take time to digest, yet there remains much which we have barely touched upon and much which would require further discussion which time unfortunately does not permit at present.

That bacillary dysentery often complicates amœbic dysentery is surely added evidence that dysentery organisms may cause a flare up of latent E. H. infection and this should make people consider carefully the subsequent history of their bacillary dysentery cases. In fact when an " indefinite " exudate is seen I find myself inclined to regard it as a pointer towards amœbic dysentery.

There is little doubt that sigmoidoscopy should be more often used but its dangers, especially in acute cases and even in experienced hands must be considered. Two deaths have recently been reported in the civil hospitals as a result of it.

Capt. Willatt has asked me to answer the question of one speaker regarding the time interval between admission of a case and diagnosis. It is the same day or the next. Lt. Col. Ransome however fixed the delay as being much greater, only 1/7 of 36 cases being diagnosed in the first 3 days. My own experience is that while cases presenting symptoms for the first time are usually diagnosed within the first 3 days, where a course has already been given and a relapse is possible, diagnosis by stool examinations alone takes at least a week on the average.

As regards treatment we are all impressed by Manson-Bahr's figures and would like to use his routine treatment for chronic cases. We hope supplies of E. B. I. and yatren will be available, at least in this hospital (47th B. G. H.) for trial.

The question of prevention has been stressed by Lt. Col. Meneces and Maj. Genl. Thompson and I can fully endorse their remarks, having done hygiene inspections of various units. I would like to see incinerators abolished and septic tanks constructed for dysentery wards at least, but in the meantime we can do a lot to improve matters with the means at our disposal. If we do not insist on a radical improvement in personnel and unit hygiene, we must certainly expect the epidemics of amœbic dysentery which previous speakers have forecast."

AMOEBIC HEPATITIS.

Capt. C. A. Gavan Duffy then spoke on amœbic hepatitis as follows :

" When we consult the text books we find that amœbic hepatitis affects Europeans rather than Indians and particularly those Europeans who have been a long time in the country. It was also thought that alcoholism was a predisposing factor.

Now it seems that while Indians are by no means immune, this is still predominantly a disease of Europeans, but our patients are recent arrivals and they are not alcoholics ; in spite of this the disease appears much as it was described by the original investigations. I will tell you what we have been seeing here.

My first contact with liver abscess was 10 years ago when in London, Manson-Bahr demonstrated the signs in chest and right hypochondrium, but I am afraid that not even his eloquence was able to interest me in what I regarded as a clinical monstrosity, something which I did not expect to come across again, but I have seen it here several times, and that is a bad thing : the soldier deserves an earlier diagnosis.

It was five years before I again came in contact with amœbiasis, and this time it presented itself as " lumbago ", until examination disclosed fluid at the right base, which proved to be " anchovy sauce ". The patient, I remember, had a large and exceedingly tender liver which disappeared rapidly with emetine.

And then within a few days of arrival in this country, I encountered for the first time the tender epigastric swelling which is at times so very like carcinoma of the stomach. We are not likely to confuse them here, but it should be realised that many of the British troops will take their amœbæ home with them, and in the future it will be well to remember that a tender mass in the epigastrium sometimes yields to emetine. (And, in passing amœbiasis provides a perfect imitation of carcinoma of the rectum, and in the R. I. F., it can cause all sorts of difficulty.)

I think the form we most often see here is a febrile disease with pain below the right costal margin and an enlarged tender liver, and this does not cause much trouble in diagnosis, but I come now to the first of the problems, the question as to whether the disease is above or below the diaphragm, whether it is pneumonia or hepatitis. Of course, the most important thing is to be "Hepatitis-minded". This immediately simplifies matters.

One should consider the lung and the liver in turn, and look for discrepancies. Are the temperature, pulse-rate and respirations just what one would expect for pneumonia? And if they are, remember that an inflamed diaphragm, whatever the cause, can cause shallow and hence increased respirations, and that it is common for hepatitis to be accompained by right basal crepitations of fluid.

Are the signs at the right base such as one would expect for the day of the disease?

And then one examines the liver, looking carefully for subcostal or intercostal tenderness and trying the effect of compression. It is a good plan to sit the patient up and let him lean back against you until his abdominal muscles are relaxed, when you should pass the right hand under the costal margin and upwards, at the same time asking for a deep breath. Hepatitis may occur without any history of diarrhœa, but recent or concurrent diarrhœa are suggestive, and I use the term diarrhœa in preference to the more usual 'dysentery'. It is also common to find isolated patches of tenderness along the line of the colon particularly in the caecal region. There are three aids of great value — a leucocyte count and differential, a skiagram and, having completed the investigation, the therapeutic test.

There is leucocytosis with both conditions, but with pneumonia, a leucocyte count of say 18,000 will have 90 per cent. granulocytes, whereas with hepatitis the normal 65 per cent. —70 per cent. remains unaltered. Rogers pointed this out forty years ago and it has been amply confirmed.

Screening shows diminished to absent movement of the right side of the diaphragm, and the more usual skiagram may show:

A less clean-cut diaphragmatic shadow which is usually somewhat raised.
A more acute cardiophrenic angle.
A flat plateau or upward bulge which drops sharply to form an acute costo-phrenic angle.
Extension of inflammation into the lung.

Having done all one can to arrive at a diagnosis, one gives sufficient emetine to cause a definite fall in the temperature. On the first day, I usually give two injections of gr. 1 each and thereafter gr. 1 a day up to grs. viii, after 4 days' rest four more doses of gr. 1 each are given. Even in the presence of an abscess, there will be an early and considerable drop in the temperature and leucocyte count, because these are dependent on the amœbic infected tissue round the abscess rather than on the abscess itself.

I need scarcely remind you that innervation of the diaphragm is such that irritation of the dome may cause pain in the shoulder, while peripheral irritation is referred to the abdomen. I have seen a patient with pain in the right shoulder (which was worse when lying on the left side) and a few toxic aches being treated with sodium salicylate, while another was given heat and massage to the trapezius. There should be less difficulty with abdominal pain, because here one is more likely to palpate a tender liver and the pattern of the disease should exclude any surgical condition. Unhappily many medical officers have never learnt these patterns and you will too frequently meet with an unwarranted diagnosis of appendicitis.

I now come to another problem, that of a P. U. O., for pyrexia can go on for a considerable time without hepatic signs. The common mistake is to regard it as belong to the enteric group, a mistake which a leucocyte count should prevent. On the back of our temperature charts, there is an excellent plant for the investigation of this condition, and, if we follow it, while paying attention to the history and the possibility of colonic tenderness, and remembering the value of the therapeutic test, we would not go far wrong.

I have not mentioned malaria. Osler said he had never encountered a liver abscess that had not been soaked in quinine, and it is still common enough, particularly where clinical malaria is a frequent diagnosis. The more exact diagnosis of malaria is going to provide an earlier diagnosis of hepatitis. These diseases have much in common and

one must remember that the malarial liver is often tender and sometimes palpable, a feature which is much neglected in the text books.

I have spoken of amœbic hepatitis as of a febrile disease, which may or may not have hepatic signs, but recently I saw a man who had a pain in the R. I. F., and then below the costal margin and a couple of days later, in the right shoulder. He was afebrile, and did not appear ill but the leucocyte count (with the characteristic differential) was 18,000 and the B. S. R. 78. A skiagram showed a small abscess which appeared about to penetrate the diaphragm.

And again, one of our own orderlies, following a few days' diarrhœa, had very severe pain below the right costal margin and in the right shoulder, with a tender liver, but he was afebrile, and, in addition had a normal leucocyte count and a normal B. S. R. Clinically it was hepatitis and there was a good response to emetine.

And recently, we admitted a patient with a surgical condition intraperitoneal rupture of an amœbic abscess.

I shall conclude by saying that, as a rule, amœbic hepatitis is straightforward, but one must be prepared for it to break every rule and for successful diagnosis, one must use every available diagnostic method, while not relying too confidently on any one of them.

Treatment :—

Hepatitis—Emetine.
Abscess—Emetine.

It may be necessary to aspirate, but quite large abscesses will absorb and should be given a chance to do so. Where aspiration is essential, it must always be preceded by a short course of emetine to get rid of the congested state of the liver. Neglect of this precaution may lead to dangerous bleeding. I have noticed that the people with most experience of this disease are inclined to say—" Try another course of emetine ".

Disposal.—Depending on the severity of the condition, we have placed our patients in category B or category C for six months.

Major P. A. Mathews : " I have seen at least 150 cases of liver abscess in the course of 1938-42 in one civil hospital. There was no X-ray in my hospital till late in 1942. Abscence of movements of the diaphragm is a definite finding in liver abscess and is best demonstrated in fluoroscopy but the case can be demonstrated at the bed side by percussing out the upper border of the liver in both inspiratory and expiratory phase and it will be found to be almost nil. Another point which I want to emphasise is that all these 150 patients were treated without aspiration. Aspiration must be reserved for the chronic walled abscess not going down with emetine."

Lt. Col. E. D. Mackworth : " In my opinion this case of liver abscess which has just been shown by Capt. Duffy should be aspirated for the following reason if no other. I look on this case as being analogous to a case of empyema which has been treated with a sulphanilamide but the sterile pus left *in situ*. No one would consider it correct to leave a large collection of pus in the pleural cavity in view of the damage to the lung that would inevitably occur. Similarly, I feel it would be wrong to leave untouched this large collection of pus—free of amœbæ and bacteria though it probably is for it would inevitably result in still further hepatic damage."

Major F. Ayrey agreed with Capt. Duffy's remarks on the diagnosis of this serious condition. The X-ray films shown demonstrated fully developed liver abscess excellently, but the diagnosis of amœbic hepatitis or early abscess was often extremely difficult. The speaker attached great importance to two tests :—

1. The " prodding " test, carried out by pressing the fore-finger firmly against the chest wall at various points over the liver. Tenderness could usually be elicited and in some cases the site of the maximum degree of tenderness was a pointer to the position of an early abscess.
2. X-ray screen examination (if the patient were fit enough) which usually showed a diminished excursion of the right dome of the diaphragm, sometimes immobility.

He had not seen the resulting skiagram after lipiodol injection into an aspirated cavity but Col. Cameron (Consulting physician, Southern Army) had been able to demonstrate the size of an abscess cavity by air injection following aspiration.

A point for particular emphasis, especially to medical officers newly arrived from U. K. and meeting the disease for the first time was the importance of the case history. In cases in which amœbic hepatitis or abscess was suspected failure to elicit a history of dysentery too often led to the diagnosis being abandoned. It was important in such cases to interrogate thoroughly on the occurrence of previous attacks of diarrhœa and their nature. Even in the absence of any history of dysentery or diarrhœa the possibility of amœbic hepatitis or abscess should not be abandoned.

Major Ayrey quoted two cases of amœbic abscess which terminated fatally in Egypt. Both patients denied any history of dysentery and one denied the occurrence of even a transient attack of diarrhœa during his two years service in the Middle East. In both cases there was sudden rupture of the liver abscess into the peritoneal cavity.

He fully agreed with Capt. Duffy on the advisability of regarding all cases admitted as right-basal pleurisy (with or without effusion) and right basal pneumonia as possible cases of amœbic hepatitis or abscess and investigating accordingly.

Medical officers of forward units ought to be enjoined not to give suspicious cases morphine injections before sending them back to base hospitals. One of the fatal cases referred to had been given two injections of morphine gr. ½ before admission for supposed right-basal pneumonia. 12 hours elapsed before it was possible to obtain a coherent statement and a few hours later an acute abdomen had developed.

Major Dunlop said that Capt. Willatt's figures on the incidence of amœbic dysentery in hospital corresponded closely with the figures obtained at the field hospital in which he worked. The latter are as follows :

A. Of the first 100 cases passing through the B. O. R. Dysentery Ward in January and February 1943.
- 48 were amœbic dysentery
- 29 were diarrhoea
- 6 were clinical dysentery
- 1 was bacillary dysentery
- 2 were gastro-enteritis
- 9 were malaria
- 3 were other medical diseases
- 2 were N. A. D.

No doubt many of the cases labelled diarrhœa were actually recovering from bacillary dysentery as many were received late in these months.

B. Of 50 exclusive cases of amœbic dysentery :
- (1) 44 were fresh cases
  - 6 were relapses.
- (2) The diagnosis was determined by :
  - Presence of active amœbæ in 44
  - Presence of cysts in 5
  - Sigmoidoscopy (in the absence of amœbæ and cysts) 1
- (3) Treatment (12 day course of emetine gr. i daily and K. B. I. powder gr. x b.d. per mouth)
  - Apparent cure (symptom & cyst free) 21
  - Persistence of cysts 27
    (in which 11 were symptom free)
  - Unhealed bowel (sigmoidoscopy) 2
- (4) Average stay in hospital of the 21 successful cases was 29 days.

With regard to the examination of stools Major Dunlop said : " In my opinion the microscopic examination of the stools should be carried out by the M. O. himself in the clinical side room. Otherwise results will be vitiated by delays and muddles in transit between the sweeper, the orderly and the laboratory.

Relapsing cases.—Cases that have spent most of their previous 6 months in hospital with amœbic dysentery are too frequently seen in forward areas. I suggest that a patient who has had two or more relapses should be temporarily lowered in category and kept near his depot or in the more severe cases invalided home.

The exudate.—Surely it would be preferable for the laboratory report, to state the type of cell seen in the exudate rather than to label it ' bacillary ' or ' indefinite '.

I agree with Major Sayers that the appearance of the exudate in bacillary dysentery depends entirely on the stage of the disease. The older it is, the more the red cells tend to be pigmented and clumped and the less evident do the macrophages become.

Major Frank McCay : " There are two points that I would like to mention : The first is the incidence of mixed dysentery which I have found in private practice during

the last 12 years in Calcutta to average about a third of all my cases of dysentery. I think that the incidence of amœbic, bacillary and mixed cases are all about the same in spite of the great differences between the two parasites. This is compatible with common ætiology. If a case of dysentery does not respond to emetine or bacteriophage after say four or five days treatment I have another stool examination done and usually find that I then have to treat the other type of dysentery as well. The second point is the exhibition of saline for all cases of dysentery. I think this a crime and is breaking one of the basic laws of good therapeutics in that it is stimulating an inflamed organ. It is really worse and goes back to those bad old days when bleeding was considered to be the correct line of treatment for all diseases, as by giving purgatives to dysentery cases the blood loss is increased. So is the dehydration and shock from which the patient is already suffering. Cholera is similar clinically to serve bacillary dysentery and yet no one dares give purgatives in this disease. I am sure that the average reasonably mild case of dysentery can safely be left to get rid of the contents of the large intestine by himself and severe ones are crying out for rest. I therefore give opium and belladonna and not saline purges to my dysentery cases.

Major G. V. S. Murthi said that the cyst carrier should neither be completely ignored nor should he be invalided. It is best to make an official note of his condition when it has been competently diagnosed and not to give him any engagement in the cook house.

Malarial dysentery exists but it is rare and no one should retain the impression that it is frequent and overlook cases of amœbic and bacillary dysentery which are the commoner diseases.

The value of sigmoidoscopy as a routine measure in the diagnosis of dysentery should be carefully considered. Microscopic examination in the clinical side room should be the mainstay for diagnosis. The ulcerations seen by the sigmoidoscope are inconclusive. Sigmoidoscopy is of undoubted value in the investigation of obscure cases but should never be used in an acute case of dysentery.

Major P. C. Dhanda : " A useful point needs stressing in the diagnosis of amœbic dysentery particularly when searching for amœbic cysts in subacute or chronic cases. Apart from the individual values of the two diagnostic aids—sigmoidoscopy to look for the characteristic ulcer, and microscopic examination of stools for detection of cysts, the two methods when combined by taking a direct swab specimen from the suspected ulcer for microscopic examination, will not uncommonly enable one to find cysts when they may not have been detected with ordinary stool examination. Cysts it was seen sometimes tend to appear with irregular periodicity in stools, also even with a cyst positive stool, no ulceration may be found on sigmoidoscopy, presumably on account of the amœbic lesions more commonly being located in the cæcum and ascending colon.

At times I have detected amœbic cysts in the stools of cases presenting as chronic dyspepsias without any history of dysentery or even diarrhœa in the past, though the latter statement could not be considered absolutely reliable. The treatment for amœbiasis cured or considerably improved the dyspeptic symptoms. It is suggested that amœbiasis widely prevalent as it is in India may sometimes have an atypical symptomatology. Three cases seen by me were diagnosed and treated with much effect as ' Hypochlor-hydric dyspepsia ' and on amœbic cysts being found in the stools and appropriate treatment instituted, the symptoms improved."

(Third day, March 17th, 1943)

The conference met again at 9 A.M. at the Loreto Convent on the 17th March, 1943.

Lt. Col. C. Seward read the following paper :

EPIDEMIC JAUNDICE & HEPATITIS.

Physiology.—The modern classification of jaundice is based upon the relationship of bilirubin to the liver cell.

It will be remembered that bilirubin is formed from the breakdown of the R. B. Cs. by the Kuppfer cells of the reticulo-endothelial system in the marrow and spleen and to a small extent in the liver.

In passing from the blood stream through the polygonal cells of the liver into the bile capillaries the bilirubin undergœs a change, not yet understood, which is demonstrable by the Van den Bergh test and which seems to lower its renal threshold.

One might usefully refer to the two forms as alpha-bilirubin before and beta-bilirubin after its passage through the liver cell. The lesion in a case of jaundice may lie *before*, *in* or *after* the liver cell.

In *haemolytic jaundice* such as occurs in Acholuric jaundice and malaria, bilirubin is produced in excess in the blood ; it passes as usual through the liver into the bile capillaries and colours the stool normally, whilst, though this alpha-bilirubin is in excess in the blood, the renal threshold for it is high and it does not appear in the urine. The lesion here lies, so to speak *before* the liver cell.

The Van den Bergh reaction is indirect.

In *obstructive jaundice* bilirubin is produced in the blood and secreted normally by the liver cells.

The lesion is *after* or *beyond* the liver cell and may be a stone in the common duct or a carcinoma of the head of the pancreas or an occlusion of the hepatic duct by enlarged glands in the porta hepatis, etc.

The secreted bilirubin (beta-bilirubin) is dammed back into the blood stream through the bile capillaries.

It is able to pass the renal threshold and so darkens the urine, whilst the obstruction results in clay-coloured faeces.

The Van den Bergh of this beta-bilirubin is direct.

In *toxic* or *infective jaundice* the lesion is *in* the liver cell, the condition is a hepatitis.

The Van den Bergh reaction is usually biphasic, varying because the alpha-bilirubin (though produced in normal amount) is in excess in the blood, for it is not fully secreted by the *damaged* liver cells.

The beta-bilirubin which has been secreted by the *undamaged* liver cells is dammed back into the blood because the bile capillaries are occluded in the swollen liver tense within its capsule.

The former gives the indirect Van den Bergh such as occurs in hæmolytic jaundice ; the latter gives the direct Van den Bergh of obstructive jaundice.

The sum of the two reactions is the biphasic reaction.

The urine and faeces should vary according to the degree of the obstructive element.

Causes of jaundice.—Time excludes from this brief review anything more than a mention of :

Weil's Disease or *Leptospirosis.*—In this there is a leucocytosis rather than a leucopenia and an agglutination reaction against the leptospira develops as early as the third and is always present by the 10th day. We have done half a dozen such tests, all with negative results.

Infective Mononucleosis.—We have not met the cases described as occurring with jaundice (which I suggest may be due to enlarged glands in the porta hepatis) but the leucocytosis, with high proportion of monocytes, the glands, angina and Paul Bunnell reaction will serve to exclude this condition.

The *French* describe a *type* of jundice with rheumatic pains, urticaria and migraine. We have not encountered it but I mention it for U. S. A. observers of epidemic jaundice mention this evidently allergic phenomenon as occurring in 20 per cent. of their cases. This is probably a variety of the epidemic hepatitis which is the subject of this paper.

Pamaquin or *mepacrin staining* may occur in treated malarias and can be tested for in the urine.

Then there are the true *obstructive* and *haemolytic jaundices* already mentioned.

Yellow Fever.—This has not occurred in India and has other features such as hœmorrhage.

The jaundice of the *Bilious Remittent Fever* form of malaria and that of *Blackwater Fever* can be distinguished by the history, blood slide, urine and response to quinine.

And finally, the subject of this paper, in which such varied symptoms as fever, malaise, depression, along with an acute gastric upset and enlarged liver, are usually but not always accompained by jaundice.

In the absence of jaundice this syndrome may have to be distinguished from the various fevers, gastritis, cholecystitis and amœbic hepatitis and, in children, from acidosis and " bilious attacks ".

The Etiology of Epidemic Jaundice.—Epidemics of jaundice have occurred in many perhaps in most wars. In the American Civil War there were 22,000 cases with 160 deaths ; in the Franco-Prussian War 800 cases occurred ; in the South African War

5,500, and in the last war epidemics of jaundice occurred on both Eastern and Western fronts.

In the present war jaundice has occurred in epidemic form in Europe among the enemy as well as among ourselves, in the Middle East and in India.

Findlay has pointed out that the character of the earlier outbreaks up to the last war cannot now be determined for only in 1915 was the condition known as leptospirosis separated off.

Apart from this condition the English teaching (in accordance with the views of Hurst) is that as well as the occasional case of jaundice, which we have long been in the habit of diagnosing at home as " catarrhal jaundice ", there is an epidemic form of catarrhal jaundice, and also epidemic hepatitis.

We know that cases of catarrhal jaundice, that is of cholangitis rather than hepatitis, do occur.

There is the much quoted case of Eppinger of a girl who died from falling out of a window on the 7th day of an attack of jaundice.

The liver was found to be normal but the mucous membrane of stomach and duodenum were swollen, the ampulla of Vater was prominent, and the mouth of the common duct was completely blocked by inflammatory swelling of its wall so that the contents of the gallbladder could not be squeezed out.

Such is a pure catarrhal jaundice.

Now Hurst found in the duodenal contents of nine cases in the Gallipoli campaign turbid fluid and very numerous coliform bacilli. He therefore considered that catarrhal jaundice occurred in *epidemic form* as well and such is still the teaching of the text books.

As Findlay says however, apart from this Gallipoli outbreak, the etiology of which cannot now be determined any more than can that of jaundice before the discovery of the leptospira, there is no record of a true catarrhal jaundice ever appearing in epidemic form and clinically there are no symptoms by which catarrhal jaundice and infective hepatitis can be distinguished.

He says that laboratory tests have failed to separate the two conditions, though Hurst states that the levulose tolerance test shows marked hepatic insufficiency in hepatitis but is normal in catarrhal jaundice. We would certainly expect this in the first week before liver damage had become marked.

When then these conditions cannot or can scarcely be distinguished it seems unsound to postulate two kinds of epidemic jaundice in addition to leptospirosis which we are not considering.

Catarrhal jaundice occurring as a single case secondary to duodenitis and gastritis—Yes.

But not an *epidemic* catarrhal jaundice, for such would imply an epidemic duodenitis. Did such occur one would expect an epidemic wave of jaundice to coincide with outbreaks of influenza, respiratory and gastro-intestinal conditions. It has been pointed out in the Klinische Mediginische Wochenschrift (Jan. 1942) that no such correspondence exists.

Recollecting the numerous cases of gastritis and duodenitis that one has seen I think an ascending cholangitis and catarrhal jaundice must be a rare complication but we must regard it as occurring sometimes (as in Eppinger's girl) and such are true cases of catarrhal jaundice.

But I do not believe that it occurs in infective form, sporadically or epidemically, and I think that the cases we used to see at home were in most instances examples of epidemic hepatitis.

It was Hurst and Simpson who in 1934 gave us this entity, Epidemic Infective Hepatitis which, I believe, includes the cases which Hurst described as cases of epidemic catarrhal jaundice.

Although the mortality is low opportunities have occurred recently of examining cases which died in accidents and one striking case of a child of five who came from a village in which jaundice was prevalent. She came into hospital for tonsillectomy ; after 24 hours she developed jaundice and on the 4th day after operation had a fatal hæmorrhage.

In these cases—in contrast to the case of Eppinger—the stomach, duodenum and bile ducts were normal whilst hepatitis was present with degenerative changes and cloudy

swelling in the parenchymatous cells and round celled infiltration in the portal spaces. The early changes consisted in necrosis of the central parts of the liver lobules.

It seems however from examination of the livers of persons who have died of accident after recovery from jaundice that the repair of hepatic damage is prompt and complete.

Causal organism ?—That the condition is caused by a virus is likely for Findlay states that some 44 cases of jaundice followed 60-80 days after the giving of filtered and bacteriologically sterile serum from measles convalescents.

This pooled serum must have contained a filterable agent.

Further the leucopenia suggests a virus infection as does the lasting immunity from further attacks though this is questioned by Newman from the experience of the Lavant Valley outbreak ; and we have had one or more instances of 2 attacks.

It appears to be spread by droplet infection and the incubation period is about one month ; most authorities put the limits at 20-41 days. Such a long incubation period is again suggestive of a virus infection.

Infectivity.—Cases appear to be most infectious in the pre-icteric stage and some cases of hepatitis occur without icterus so that isolation will not prevent though it may reduce the spread of infection. The young and the new arrival in an endemic area seem the most susceptible.

We have had at least 2 instances in which the condition was probably caught in hospital but we have only lately practised isolation though this was advised some time ago, in fact by Pope Zacharias who occupied the See of St. Peter A.D. 741-752. Perhaps after this 1,200 years warning we should have taken the advice of His Holiness. We now isolate cases from the moment of diagnosis for at least a week.

Whilst probably infective in the latter part of the incubation period and in the pre-icteric stage it is not clear how long this persists through the icteric stage.

The symptoms and signs as described by different observers vary greatly and I have endeavoured to compare these with our own findings.

We have been seeing cases of jaundice, undoubtedly infective, in considerable numbers and from October 1942 to February 1943 we have averaged some 35 such cases at any one time on the medical side of the hospital. As their stay was about 3 weeks we estimate that we have seen about 200—300 cases.

Our cases did well on symptomatic treatment and their icterus was clearing when, after some 3 weeks, they were sent to a convalescent depot. Some, however, without being particularly ill developed profound icterus and took months to lose this.

Only in the last two or three weeks have I given these cases more attention so that I might have some data to give you at this meeting. I arranged a questionnaire and examination and a few tests to be carried out by the specialists and myself and I will give you our meagre findings to date and will compare them with those of Hurst, of the U. S. A. workers, the findings of the Lavant Valley outbreak in 1941 and others.

Clinical Findings.

Others in *man's Unit* with *Jaundice.*—We frequently obtained a positive answer to this question. I had concluded from this fact and the rareness with which it appeared in Hospital that the condition was highly infective in the early stages only. With however an incubation period of 21-40 days and the fact that our patients as a whole are here or only 2-3 weeks such a conclusion was not justifiable and it became apparent that we must isolate patients at least in the early stages.

Day on which *Jaundice first appeared.*—Hurst states that in this disease Jaundice is the first symptom, *i.e.*, that it appears on the first day of disease—

In our first series it appeared on the 4th day on the average and in a recent series of 50 cases it was on the 6th day.

Others report 1st to 8th day and as late as the 12th day.

Symptoms and their *frequency.—Icterus* occurred first in about 5 per cent. of our cases. It varied in intensity from faint staining to an intense orange yellow and lasted usually some 21 days but sometimes persisted for 2-3 months. Bates found icterus to be absent in 10 per cent. of 65 cases. It is thus very common but not invariable.

Pyrexia.—The frequency of this as a presenting symptom could not be determined as cases entered Hospital as a rule on the 5th day, *i.e.*, on the appearance of the jaundice. As the duration of the pyrexia is 3-6 days (though occasionally up to 14 days) it had frequently gone by the day of admission.

Hurst says that the temp. is slightly raised ; U. S. A. workers that pyrexia is absent or slight ; Cameron regards pyrexia as invariable in the pre-icteric stage ; in the Lavant Valley outbreak some cases were afebrile but some rose to 102-105 per cent. ; ours usually shewed a brief pyrexia.

Bad taste in the *Mouth* is a valuable symptom, 20 of 32 having it.

Furred Tongue.—One observer states that a clean tongue is the rule ; we think a furred tongue is usual.

Malaise was present in half the cases and in 72 per cent. of Cameron's.

Headache occurred in 40 per cent. of ours and 50 per cent. of Cameron's.

Itching we did not have an example of ; Cameron had 5 per cent. of cases.

Joint Pains occurred in 20 per cent. of the U.S.A. cases but only in a few of our series.

Urticaria.—This occurred and preceded onset of jaundice in 2 cases.

Anorexia is an important symptom being almost invariably present—in 94 per cent. of ours and 86·5 of Cameron's cases.

Vomiting was a minor symptom with us but occurred in 46 per cent. of Cameron's cases.

Nausea and *Epigastric discomfort* or *pain* occurred in 84 per cent. sometimes amounting to severe pain, burning, stabbing or colicky, and occasionally under rt. costal margin and so simulating cholecystitis for which cases are sometimes sent in.

Diarrhœa or rather loose stools (though one mimicked bacillary dysentery) occurred in 18 per cent. ; Cameron's series 7 per cent.

Constipation was well defined in 38 per cent. of ours and in 25 per cent. of Cameron's cases. Whilst thus either may occur the bowel function is frequently quite undisturbed.

Pale stools were observed by the patient in 43 of 50 cases ; the average day of first observation of this was 4-5th.

Dark Urine is probably invariable and was first noticed by the patients on 3rd day on average. It is a striking symptom and valuable. We have not yet been able to obtain Para-aminobenzaldehyde to test the doubtful or early cases for urobilinogen.

Liver enlargement and tenderness.—The U. S. A. workers found it in 20 per cent. We found one or both in 83 per cent. ; Cameron found enlargement in 57 per cent. and tenderness in 64 per cent. It may persist long after jaundice, pale stools or any other symptoms have disappeared. I have recently seen a British officer with Sprue who had Infective Hepatitis 6-7 months previously and who still had a large liver. I believe alcohol is one of the causes of the persisting enlargement.

Splenic Enlargement.—Hurst says it is often palpable. Only 10 per cent. of our cases had splenomegaly and of these half gave a history of Malaria.

Col. Cameron found 27 per cent. of 170 with enlarged spleens.

Bradycardia.—This is stated by Hurst to be marked. Cameron says that it is a noticeable feature of the phase following development of jaundice but it is absent during pyrexia. It is probably the bradycardia that follows all infections with a virus such as Sandfly Fever and Dengue.

We did not observe it carefully but certainly found heart rates in the 40s and 50s commonly.

Albuminuria was found in the febrile stage of those with more severe constitutional disturbance.

W. B. Cs.—On admission these varied from 4000 to 7000, a number being normal but I think early leucopenia is the rule. Such is Cameron's view and he points out that leucocytosis is never present and so test is valuable.

B. S. Rate appears to be normal.

Van den Bergh reactions were done in a number and all shewed a direct positive but it seems to be biphasic early and direct during icteric phase as one would expect.

The quantitative V. D. B. was always increased averaging 5-6 units, the normal being 0·2—0·5 unit.

The *Histamine Test* is worth remembering (0·1 per cent. of a 1 per cent. solution intradermally) in puzzling cases which have not yet or which do not develop Icterus and we have managed to remember it in time to get one positive result.

A Word upon Treatment.

This is at present non-specific though convalescent serum has been used in severe cases.

As to *diet*, recent experimental work seems to show that, whilst restriction of fat is necessary in hepatic damage, restriction of protein, though it has been advised is not only unnecessary but actually harmful.

What emerges from this work is the necessity for a low fat and high carbohydrate and high protein diet (P 100, F 20, C 450 gms).

Of proteins, casein is important as it contains the amino-acid methionine from which choline, essential for fat metabolism in the liver, is derived.

Skimmed milk and cheese should therefore be included in the diet.

As to vitamins, K is called for if hæmorrhage occurs in liver disease.

The fat reduction makes the addition of A and D advisable, such as adexolin or in this country Fish liver oil.

Essential to proper liver function is a component of the vitamin B complex which can be given by the addition of yeast, one or more ounces daily.

In this disease, as in amœbic hepatitis, it is clearly good counsel to forbid alcohol for three months, and what has been said should apply to all forms of hepatic damage.

These findings, and opinions are based upon too few cases to be of great value and are subject to review, after we have had the opportunity to observe critically a far greater number of cases.

When this paper was written I was unaware of Col. Cameron's definitive work upon the same subject; as the findings and the views expressed correspond closely with his they are perhaps, for this reason of greater value.

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DISCUSSION.

Brig. Marriott remarked that the authority on jaundice in this country is Col. Cameron who had made an extensive investigation of the subject.

Major Ayrey gave a report of one of his observations.

Capt. Birks stated that he had had ten cases of jaundice following sub-tertian or mixed M.T. and B.T. infection. Eight showed all symptoms of obstructive jaundice. Two showed normal stools with bile in urine.

He asked for advice upon the pathology of this jaundice following malaria, believed to be due to excessive red cell destruction with liberation of large amounts of pigment in the blood stream producing (*a*) clinical icterus, and (*b*) liver saturation with obstruction from excessive secretion.

Lt. Col. Seward thought the jaundice was due to occlusion of bile ducts from swelling of the liver within its capsule, the swelling being partly due, like of the spleen, to disintegrated red cells.

Capt. Payne "I had the opportunity of investigating an epidemic of 74 cases of infective hepatitis last autumn. The general picture was similar to that already described. There are however a few points I should like to make.

Firstly the incubation period. I have been fortunate enough to read Col. Cameron's paper and it is a magnificent work. Apart from the question of the incubation period, my findings were, as far as they went, similar. He states that the incubation period is 32 days and stresses that this is the minimum time and that the appearance of the disease may be delayed for months until some other factor, alcohol, fatigue and exhaustion, or other disease has lowered the general or local resistance and rendered the liver

susceptible. In the cases that I saw the incubation period was about 20-40 days which is the usual figure given. Of course we do not know the length of the infective period and final agreement on the limits of the incubation period, cannot be reached until that is known, since most studies are based on case to case intervals. I was looking for accessory factors such as Col. Cameron mentions and generally was unable to find them. Thus only two cases had coincident malaria, two amœbic dysentery in five cases the onset was related to a route march, in 4 to cholera vaccination. This did not seem a significant number under the circumstances. Alcohol, however, did seem to play a part, 7 cases, all officers, related the onset to the taking of alcohol, a high proportion considering how few had been able to obtain any.

There are some curious features in the eipdemiology of this disease that have not yet been adequately explained. When a family or group of people is exposed to infection, they do not all always develop the disease together, but fall sick one after another at intervals of one month. Examples of this are frequent in the literature and are beautifully illustrated in Newman's delightful paper. Pickles attempted to explain this by suggesting a very short or even intermittent infective period, although he has recorded transmission of the disease 8 days before the onset and 7 days after the appearance of icterus. Newman suggested that the periodicity of the gastro-intestinal functions might be responsible, such as the level of gastric hydrochloric acid and the potency or otherwise of the ampulla of Vater. However Col. Cameron has found that the gastric HCl is generally within normal limits or even raised in some. I suggest that the factors which Col. Cameron suggested determined the onset of the disease, are of importance in determining infection, and the presence or absence of these factors is responsible for the unusual behaviour of the disease. The occurrence of gaps in a chain of infection is also well known. Col. Cameron's theory would explain this. But I made observations which would also account for it, namely that mild abortive cases were quite frequent. These men have a few days malaise, anorexia and nausea, often with slight enlargement and tenderness of the liver and sometimes a trace of conjunctival icterus. They do not report sick since their symptoms are so mild. If I am correct in my diagnosis and if they are really as common as I felt, they are of enormous epidemiological importance, and I suggest that they fill the gaps in the chains of infection.

Transmission of the disease is generally believed to be by droplet infection but no very convincing evidence has as yet been brought forward. An interesting comparison could be made in this epidemic. Two units, A and B, arrived from England at the same time, crossed India in the same train and pitched tents alongside each other under the same clump of trees. Early in the monsoons unit A had a high sick rate 30-40 per day, whereas unit B only had 10-15. Most of the cases in unit A were of diarrhœa and a cause was soon found in defective sanitation. The deep trench latrines of unit A had been dug in clay soil with the result that they flooded and alarming numbers of flies appeared. Unit B had better drainage. The defective latrines were replaced and sanitation and hygiene became good with the expected drop in sick rate. Now unit B never had a single case of hepatitis, whereas unit A has 15 cases up to the end of October. 6 cases had occurred before the improvement in sanitation. This improvement seems to make no difference to the progress of the epidemic. Considering other possible methods of transmission, flying insects were presumably the same for both units. Body lice did not occur. Rats were common in both units. Army rations were drawn in the same lorry. Drinking water was properly chlorinated and drawn from the same tank. Washing water however was drawn from different wells and used unchlorinated. The colonel of unit A kindly consented to chlorinate all washing water. This appeared to make no difference to the progress of the epidemic. I was able to obtain clear histories of 19 contacts apparently in causal relationship. There were many others but they were multiple and not clear. Although I can only bring negative evidence, it seems that droplet spray is the most likely method of transmission.

The clinical picture has already been well described. I think the non-icteric and abortive cases will be found to be much more common than is generally realized. Bradycardia occurred in only 50 per cent. of cases and has no obvious relationship to the intensity of icterus nor to the severity of the disease.

I observed that in 9 out of 13 cases the blood pressure showed a fall below 110 m.m. of mercury between the 7th and 14th days. The lowest was 80/50, the average 96/60. In most cases it had risen to normal by the end of the 4th week, but in 3 it persisted until

the 6th week. These three cases appeared to have signs of myocardial weakness which ultimately cleared completely. Col. Cameron describes vascular changes in the heart at *post mortem* which might be the cause of this. (Brig. Marriott suggested chloride deficiency as a possible cause).

The output of chloride in the urine was not checked. In 16 out of 22 cases there was definite albuminuria ; 6 out of these were decidedly more than could be accounted for by fever. Newman and others have recorded this. Casts are evidently unusual though I found a few granular casts. I would relate this to Col. Cameron's finding of tubular damage.

In 4 cases I found an increased proportion of polymorphonuclear leucocytes on the 1st day. Except in one case, which recorded 80 per cent. on the 6th day and which I was unable to follow up, all within a day or two commenced to show the leucopenia generally described reaching its maximum about the 10th-24th day.

I would like to endorse Brig. Marriott's remark on the importance of inspecting the stools. In this series 40 per cent. were clay-coloured, 40 per cent. were pale and 20 per cent. normal throughout.

Finally Col. Cameron has made observations suggesting that cirrhosis of the liver may be a late complication of this disease.

Brig. Marriott asked whether the blood pressure was low in Capt. Payne's cases.

Capt. Payne answered yes, it was.

Lt. Col. Seward. Was there an enlarged spleen ?

Capt. Payne: Only in 3 per cent.

Col. Taylor: Working in North-western India for the last dozen years the following points were noted :—

1. Epidemics of epidemic jaundice commonly occurred in September.
2. The common occurrence of diarrhœa and pale stools in British and Indian population.
3. Two cases of epidemic jaundice were at autopsy indistinguishable from acute yellow atrophy.
4. Lævulose tolerance tests in 12 mild cases were normal.
5. The frequency with which emetine was given by the civil practitioner.
6. Duration of jaundice was usually a few weeks but one case was seen in which bile pigments were present in the urine and skin for 5½ months.

Lt. Col. Ransome : " Col. Seward spoke on the differential diagnosis between leptospiral jaundice and epidemic hepatitis. So far in this country though I have been on the lookout for leptospiral jaundice I have not seen a case. At the Tan Tock Sen Hospital in Singapore we had 66 cases of the disease in 4 years and all of us became familiar with the syndrome so that it could often be diagnosed before the jaundice came on. For those M.Os. who have not yet seen leptospiral jaundice I would stress the following points :—

First, the onset. This is nearly always sudden and the patient takes to his bed very early within the lapse of a few hours. This was particularly dramatic among the Chinese who are very game and will usually not go to bed unless they are very ill indeed.

Secondly, during the third to fifth day period before the onset of jaundice the patient is very ill.

Thirdly, the eyes are injected. By the third to fifth day (often the stage when the patient was admitted) the patient could either be one of the typhus group, specially tsutsugamushi, or leptospirosis. A third possible diagnosis in two Europeans was very severe dengue. A diagnostic feature at this stage is the extreme tenderness of the muscles which in the severe case is almost always present. One gives the muscle a gentle squeeze and the patient will leap out of the bed with pain. This was most striking and led to the diagnosis of many of these cases.

There are several other small points worth mentioning. The white count is always up, 12,000—16,000 with a polymorphonuclear leucocytosis which differentiates it from dengue or epidemic hepatitis. The skin is flushed so that one can readily imprint the mark of a hand on the chest. This is a red flush, not the somewhat cyanotic flush seen in severe cases of typhus.

Jaundice occurs about 4th to 5th day and is of the colour of Australian gold compared with the ordinary yellow gold of Europe. This reddish tinge of the jaundiced skin is very characteristic and can be explained by the erythema already mentioned. The

urine, by about the second day, contains albumen and casts. Casts are far more numerous than in catarrhal jaundice and r.b.s. are often found in the centrifuged-deposit, which emphasizes the hæmorrhagic nature of the disease.

In concluding, I would again stress that the essential feature to keep in mind is the tenderness of the muscles which should be looked for in every febrile case from an endemic area.

Major Rogan confirmed the presence of muscle tenderness as an important diagnostic point. With regard to infective hepatitis, he described briefly an outbreak of about 50 cases in Singapore in the spring of 1941. Cases came from units widely scattered throughout the island, two or three from each unit. The only common source of infection appeared to be the water supply. No cross infection took place in the wards which may have been due to the fact that the virus possessed a low infectivity.

Lt. Col. Seward answered the queries and summed up.

POLYNEURITIS

Capt. C. A. Gavan Duffy then spoke on polyneuritis as follows :—

" I am going to show the meeting some patients with polyneuritis, and I will start with two instances of a condition with which we are only too familiar—post-diphtheritic paralysis.

The first man had a sore throat last October, and a throat swab being negative, he was not given any antitoxin. During the second week his voice became slightly nasal, and later on, while attempting to swallow fluids, he sometimes regurgitated them through his nose. This of course was due to palatal paralysis.

About the fourth week, he noticed a peculiar disturbance of his vision. Although seeing quite clearly everything at a distance of more than a few feet, anything close to him, such as print or his food, appeared blurred.

And then, about the sixth week, he first became aware of tingling in the tips of the fingers, soon to be followed by pins and needles, tingling and numbness of all the extremities as high as the elbows and knees. At the same time, his arms and legs became weak.

It was somewhat later that I first saw him, and he presented a pitiable sight. Unable to move his limbs and with wasted muscles, he had to be propped up in bed, because his trunk and neck were also involved. Added to this, he was unable to feel anything below the elbows or knees and, his larynx being affected, he could not even complain. He was indeed fortunate that the exotoxin did not attack the phrenic nerves, and that the heart escaped—clinically. This disease shows a strong tendency to recovery, and now he is up, though not very strong.

The second man presents a similar picture—sore throat, palate paralysis and peripheral neuritis—though not so severely affected. He denied having any trouble with his vision, but when I gave him a book to read, he held it at arm's length.

Now I come to two men who, instead of a sore throat, had jungle sores, and you will see that they have the same nervous lesions (with the exception of palate paralysis) as the patient with faucial diphtheria. One of them, while stationed near Cuttack, contracted ten sores which took 2-3 months to heal, in spite of his being sent to a hospital quite early. While there he found here was unable to read, although his vision was unaffected for objects at more than a few feet. He reported it to the doctor, who told him he had been reading too much. He then developed peripheral neuritis, a gradual onset of sensory disturbances in the fingers and toes, eventually reaching the elbows and knees. This was accompanied by muscular weakness, and the time I saw him, there was considerable wasting. He is now much improved.

The other man acquired his sores (eight about the feet and ankles) the other side of Chittagong, and, in spite of early evacuation, they took a couple of months to heal. Then he too had peripheral neuritis, and a similar disturbance of vision, though a recognised specialist in opthalmology told him there was nothing the matter with his eyes, and even made a note to that effect in his A.B.64. I have stressed the eye lesion, because it is so characteristic of diphtheria, and makes it clear that these patients have diphtheritic infection of the sores and not avitaminosis, which is the usual diagnosis. There is paralysis of the ciliary muscle, so that the patient is unable to accommodate for near objects. Test type can be read, and the pupils contract normally to light, and on convergence ; unless the patient is asked to read print, the lesion may be overlooked.

I should like to know more about the bacteriology of jungle sores : what proportion are infected with K. L. Bs. and what other organisms are present. Col. Taylor is arranging an investigation. Antitoxin hastens healing of the sores, but is of no value for established paralysis.

I am now going to show you a patient who had jungle sores which had healed by last October, when he was sent back to his unit near Cox's Bazaar. There the greater part of his time was occupied in leading a mule through the jungle, and the management of a mule is a full time job. The rations consisted of bully-beef, biscuits and tea, with an occasional sausage, and after ten weeks of this life, he contracted malaria and dysentery, and, after four days' illness, he woke one morning to find he could barely move his arms and legs. When I saw him, 10 days later, he had well developed peripheral neuritis and he weighed 7½ stones (normal 12 stones).

I do not think this was diphtheritic because the interval of 10 weeks after healing of the sores was too long, and the onset was too rapid.

There was no loss of accommodation, on the other hand he had, I believe, been on a diet deficient in vitamin B_1; he had been working hard enough to deplete his store of this vitamin, and he had malaria and dysentery which are recognised as precipitating factors in beri-beri, for such I believe it to be. Most important of all was the rapidity with which he improved when given injections of Benerva. Now the reflexes have returned and he has gained 3 st. 8 lb.

I shall not detain you long over the next two patients, who have bilateral external popliteal neuritis, the one following typhus fever, the other typhoid fever. There is bilateral 'foot-drop' with blunting of sensation over the appropriate area, the lower half of the antero-external aspect of the legs, the dorsum of the feet and the toes with the exception of the terminal phalanges, which are supplied by the plantars. The knee-jerks and ankle-jerks, which are activated by other nerves, are normal. We give these patients massage and electricity, but are careful to impress on them that active movement is much more effective.

Now this last patient presents something of a problem as to the aetiology. During January he is said to have had clinical malaria, and was given the standard treatment. About three weeks after the onset, and having been afebrile for a considerable time, he developed pain in the right side of the neck and, two days later in the right arm, and about this time, noticed some weakness in it.

Today one finds that he has paralysis and wasting of the right biceps and brachialis (musculo-cutaneous nerve C5, 6) and loss of sensation along the outer border of the forearm, the skin area supplied by the same nerve. He flexes the elbow by means of the brachioradialis, which is supplied by the musculo-spinal nerve.

The right supraspinatus and infraspinatus (suprascapular nerve C5, 6) are also paralysed, and deep hollows can be seen above and below the spine of the scapula. What little external rotation remains is due to the Teres Minor.

The group of internal rotators is similarly affected (subscapularis C5, 6 and 7) and on attempting to adduct the arm against resistance it is clear that there is no contraction of the muscles of the posterior axillary fold, and if one places one's hand on the side of the chest and asks the patient to cough, it is interesting to notice the absence of contraction of the affected latissimus dorsi.

This is not poliomyelitis, but a lesion of three separate nerves, one of which has a cutaneous distribution which is affected, and certain muscles supplied by the same root —Rhomboids, brachioradialis and pronator teres—are acting normally.

DISCUSSION.

Lt.-Col. Mackworth : " I would like to suggest that the last case of peripheral neuritis shown by Capt. Duffy may very well be a case of the Guilland-Barre syndrome. I have some experience of this syndrome having seen a dozen cases in Aberdeen 5 or 6 years ago. The case commenced with an unexplained pyrexia and the development of scattered palsies. The pattern of this case in the absence of any other ætiology being apparent, is highly suggestive and I think that the c.s.f. should be examined, especially to see if the typical high protein is not present. One is, of course, well aware that a raised c.s.f. protein is often a feature in peripheral neuritis due to other pathology but a protein of over 100 would, in my opinion, clinch the diagnosis. I also feel that the c.s.f. should be examined in Capt. Duffy's other case—that is the case showing winged scapula.

The pyrexia was never satisfactorily diagnosed in this other case and there also the correct diagnosis might, I feel, very well be Guilland-Barre syndrome."

Capt. Duffy : " Col. Mackworth has suggested that this may be the syndrome of Guilland-Barre (acute infective polyneuritis) which has a short febrile period, a latent afebrile interval followed by the sudden onset of polyneuritis. But it is usual for all the extremities to be involved, and the proximal muscles as much as or more than the peripheral ones.

This patient's condition differs in that only a limited number of muscles in one arm are involved and the c.s.f. does not show the great increase in protein (without increase of lymphocytes) which characterises the Guilland-Barre syndrome."

Lt. Col. Ransome : " I have been most interested in these cases of diphtheritic peripheral neuritis in which the clinical picture of this disorder has been so beautifully brought out. In diphtheritic peripheral neuritis the throat is not the source of infection, particularly in those cases which seem to take a very long time to clear up. Dr. Gordon Holmes stressed two points : He had two cases in which an antrum of Highmore was full of diphtheritic pus and did not improve until the source of infection was removed. The other place is a middle ear which may be infected though not discharging and which can be so easily overlooked when one examines with the auriscope unless one bears this in mind and examines every case of obscure peripheral neuritis as a routine in this way.

Capt. Birks referred to two islands in the Pacific : Island A has a large number of anopheline mosquitoes and malaria, Island B has no mosquitoes and no malaria. A has widespread Naga Sores and B has none. After 3 weeks in Assam 100 out of 400 got malaria and 30 others had sores.

Autoagglutination reaction, he believed, took place in the body, producing zones of devitalized tissue which in the case of skin have no defence against infection. The skin sloughs looking like the typical indolent ulcer which responds to no known antiseptic. Packing these ulcers with crushed mepacrine produces a startling regeneration of granulation tissue and rapid skin formation.

Capt. Duffy replied to the queries and summed up.

Major F. Ayrey then spoke on the relationship of peripheral neuritis and vitamin B_1 deficiency.

PERIPHERAL NEURITIS AND NAGA SORE.

Those who had read of the outbreak of beri-beri in the Mesopotamia and Dardanelles Campaigns of the last war would realise the importance of the nutritional factor in this present campaign. It was untrue to assume that because our knowledge of deficiency diseases had increased during the last 20 years the possibility of a disease such as beri-beri occurring now was remote. It might become increasingly difficult, if the campaign were protracted, to supply forward troops with a diet, adequate in all respects, and vitamin B containing foods in particular.

While it would be true to say that hitherto there had been no outbreaks of disease pointing to a gross deficiency, was there any evidence of minor degrees ? Several speakers had already referred to cases of peripheral neuritis complicating other complaints. Col. Taylor had referred to several cases of a chronic type of peripheral neuritis of unknown ætiology.

In Egypt in 1940-41 numerous cases were admitted to hospital from the desert with vague and varied symptoms difficult to name specifically ; these conditions included anorexia, lassitude, anæmia, swollen ankles, desert-sores, bleeding gums (found usually to be due to a Vincent's infection) and tinglings, ' pins and needles ' and parasthesias in the fingers and toes. From a caloric point of view their diets had been adequate. But the question of salt and water depletion and vitamin deficiency had to be faced.

These cases responded in the main to rest and good dieting with due attention to all factors including minerals and vitamins.

Major Ayrey gave a resume of an investigation he carried out in Edinburgh Royal Infirmary in 1936-37 on the therapeutic value of the parenteral administration of vitamin B_1 (which had then first been synthesised) in cases of peripheral neuritis of varying types. Most of them were of doubtful ætiology.

Sixteen cases in all were studied, all showing pronounced polyneuritis.

In two there was a demonstrable dietary deficiency of vitamin B_1 over a long period.

In all of the remaining 14 cases there was complete achlorhydria. There was in many cases something of a paradox for whilst there had been no inadequacy of vitamin B_1 in the diets, and though extra amounts of this vitamin in the form of Marmite had been tried without any benefit yet the cases responded often dramatically to vitamin B_1 when given parenterally.

The question therefore resolved itself into one of absorption. An investigation was quoted. Harris of Cambridge had about that time evolved the Rat Bradycardia test for the estimation of vitamin B_1 excreted in the urine and this was used by Harris as an index of adequacy or inadequacy of the person's diet with respect to this particular factor. 25 per cent. or more of the daily intake was excreted on a normal diet and low figures were an indication of vitamin B_1 shortage. The case in question was a woman with pronounced peripheral neuritis, anæmia and achlorhydria. Nutritious diet containing 1,000 units of vitamin B_1 daily were given and specimens of urine were examined daily by Harris for a week by the Bradycardia method. The excretion varied from 0 to 2 mg. considered by Harris as the Beri-beri level; this in spite of the large oral intake of vitamin B_1. Following injections of 500 units daily, the excretion quickly rose to 45 per cent. and from this time clinical improvement commenced. This investigation showed that adequacy of vitamin B_1 in the diet should not be assumed to indicate adequacy in the tissues, and that in chronic gastritis with achlorhydria the possibility of some malabsorption with resulting peripheral neuritis was a very real one.

The occurrence of polyneuritis in diseases often accompanied by achlorhydria was stressed. In sprue, pellagra, some cases of diabetes and gastric carcinoma, neuritic signs were often part of the clinical picture. Alcoholic neuritis had been shown to be due to B_1 avitaminosis, again due to a gastro-intestinal lesion with failure of absorption. And in the disease in which there was 100 per cent. achylia gastrica—pernicious anæmia—the first neural signs in untreated cases were those of a peripheral neuritis, usually before the nervous condition could be described as a "combined" degeneration.

It was emphasized therefore that in considering the ætiology of any case of peripheral neuritis the possibility of its being associated with a vitamin B_1 deficiency should not be abandoned simply because this factor was being taken in adequate amounts in the diet. A gastric analysis should be routine in such cases.

Another important factor in the production of avitaminosis was the toxæmic one. Fraser and Stanton's early finding that their coolies took about 90 days on a vitamin B_1 deficient diet to develop beri-beri had unfortunately led many into a sense of false security and delay in remedying the deficiency. Any known deficiency of vitamin B_1 should be corrected as early as possible. The work of Minot, Strauss et al had shown conclusively that a condition of hypovitaminosis could be precipitated rapidly into one of frank avitaminosis by the onset of a toxæmic illness. In forward units particularly there might be difficulties in providing consistently rations with adequate vitamin content, and the onset of a severe dysentery for example (with the combined factors of toxæmia and mechanical loss of minerals, vitamins, etc., from the bowel) might be the determining factor in producing an avitaminotic state, with little or no premonitory warning.

It has been stated by some observers that peripheral neuritis was not a common accompaniment of dysentery, malaria, etc. This may be true as far as cases showing severe clinical manifestations were concerned. In the speaker's view mild cases with tinglings and paræsthesia, etc., in the periphery were far more common than imagined but were not sought for and were frequently missed. Capt. Duffy had shown a case a few moments earlier in which (and in spite of history of sores) he (Capt. Duffy) did not consider the neuritis to be due to diphtheritic toxins. This man had admitted that though he had had vague symptoms of lassitude, headache, etc., sufficiently severe for him to go sick, it was the resulting attack of dysentery which had precipitated the neuritic symptoms—in this case of a severe degree. Capt. Duffy had noted the quick response to vitamin B_1 injections.

It was therefore of great importance that M.Os. of forward units should be alive to the possibility of toxæmic illnesses precipitating real or disguised beri-beri and any deficiency of vitamin B_1 in rations should be remedied either by the addition of appropriate foods or preparations such as Marmite, Vegamite, etc., with the minimum delay.

The speaker then referred to the misuse of vitamin B_1 parenteral preparations. The action of the factor was now known to be that of a co-enzyme, leading to the removal

from the blood of certain of the end-products of carbohydrate-metabolism ; these were known collectively as the bisulphite binding substances (B.B.S.), Pyruvic acid probably being the chief member. The blood level of these substances was raised in vitamin B_1 deficiency and they were believed to be responsible for the degenerative changes in the peripheral nerves. Strictly speaking the term " neuritis " was wrong as the pathological changes first affecting the myelin sheaths was degenerative in character and not inflammatory. For this reason the term " Neuropathy " had been suggested as more applicable. In brachial neuritis, sciatica, etc., there was a true interstitial neuritis, quite distinct in its pathology from polyneuritis. There was not a shred of scientific evidence that a vitamin B_1 deficiency was a factor in the ætiology of these conditions. The action of vitamin B_1 was clearly defined and strictly limited and the administration of scarce and expensive parenteral preparations in such conditions as sciatica, brachial neutritis, Bell's palsy, and even vague complaints such as anorexia, constipation, boils, etc., was to be deplored.

Major Ayrey stated that in the type of case shown by Capt. Duffy and in diphtheritic polyneuritis generally he had found vitamin B_1 injections disappointing and although the peripheral manifestations were similar to other well-marked types it was doubtful to what extent, if any, the vitamin under discussion was involved. Possibly we were dealing here with an exotoxin which had a truly toxic action on nerve-endings. The condition warranted further study.

The speaker wondered whether adequate steps were being taken to ensure the adequate supply of vitamin B foods and parenteral preparations. He knew of one brewery which for a long time had been throwing away daily 24 lbs. of yeast ; approximately 300,000 units per day. It was doubtful whether it was necessary to convert this into expensive preparations of doubtful keeping value, and possibly a simpler method of utilizing available yeast could be evolved for army use.

Major Ayrey summarised his remarks by suggesting that :

1. Medical officers should be alert to the occurrence of minor degree of ill-health which might be due to hypo-vitaminosis. Vitamin B_1 hypovitaminosis was evidenced by lassitude, anorexia, constipation, sometimes palpitation, and peripheral subjective sensory phenomena; it was important to recognise these phenomena before the fully developed picture of polyneuritis or beri-beri was produced.

2. In all cases of polyneuritis, mild and severe, the possibility of a vitamin B_1 deficiency should be considered. They would probably fall into four groups :

(*a*) Those due to B_1 avitaminosis, with demonstrable dietary deficiency.

(*b*) Those due to B_1 hypovitaminosis but precipitated into avitaminosis by toxæmic illnesses.

(*c*) Those due to failure to absorb vitamin B_1, specially evidenced in chronic gastritis with achlorhydria ; gastric analysis should always be done in doubtful cases.

(*d*) Those due to or associated with other diseases, *e.g.*, diphtheria (including Naga or Desert Sore), Diabetes, sprue, pernicious anæmia, etc.

It was considered that groups (*a*) and (*b*) were preventable by the provision of rations adequate in vitamin B_1 and medical officers of units especially in forward areas should be enjoined to see that necessary steps were taken to ensure that the required daily intake was provided, augmented with yeast, marmite, etc., if necessary.

3. The misuse of vitamin B_1, particularly parenteral preparations, should be prevented. Concentrated preparations of the latter should be reserved for :—

(i) the initial treatment of polyneuritis associated with achlorhydria.

(ii) severe cases in which the quickest possible improvement was desirable. A daily dose of 1,000 to 2,000 I.U. was usually required.

I must congratulate Major Ayrey on his very lucid exposition of the subject of vitamin B_1. He makes reference to the work of Strauss in which reserve storage of B_1 was mentioned as being particularly vulnerable in fever. The second point he stressed, which is extremely important, is the question of how much B_1 or any other vitamin the patient is actually absorbing. In cases of digestive disorder in this army I very frequently come across cases of vitamin deficiency though getting what is apparently an adequate dosage by mouth. Early in 1938 in Singapore an experiment was started during the typhoid epidemic in which 50 Chinese cases of typhoid were treated with large doses of prophylatic B_1 and 50 were to be taken and observed for the occurrence of

beri-beri. In the cases taken early, no beri-beri occurred but in the control cases beri-beri developed in a small number and was refractory to B_1, several patients losing their lives, so that we had to abandon the experiment and all cases were given B_1. The next step was that Prof. Hawes ordered that all febrile Chinese admitted to the Tan Tock Sen should have vitamin B_1 and by this measure alone reduced the mortality rate and pneumonia by 10-50 per cent., the mortality being by that time about 40 per cent. When M and B 693 became available mortality was further reduced to 8 per cent.

I am particularly worried about the lack of parenteral B_1 in the Gauhati area. Chinese troops are coming through and I feel certain we shall encounter Shoshin in the near future, a fatal disease in the absence of this drug."

TICK-BORNE TYPHUS

Lt. B.T. Bowes then spoke on tick-borne typhus and gave notes on cases admitted to 119 I.G.H. (B.T.) for January and February 1943.

The total number of cases were 30 (B.O.Rs.)+3 (B.Os.).

Incubation period.—All cases (except one from the Midnapore cyclone area) occurred in troops who had been training in the jungle at Chipadohar or near the Chaibasa road. The dates of onset lay between two and four weeks after the men arrived in the jungle. One man was in the jungle from 13th—21st January and the onset was on 30th January. One officer was in the jungle from 23rd January—5th February and the onset was on 12th February, and another officer from 1st February with onset on 27th February. These 3 cases limit the incubation period to 7—20 days.

Further, both officers say that they were bitten by ticks, one 9—10 days before onset and the other seven days. On the other hand none of the men had any recollection of being bitten, so that the occasion when the officers were bitten may not have been those on which they were infected.

Neither of these cases showed any primary lesion and in only one of the others was one present. It consisted of a dry scabbed sore on the forearm without any lymphangitis.

Onset.—The illness began with headache, shivering, general malaise, and aching and stiffness, particularly in the joints. Sometimes there were catarrhal symptoms.

After about a week the headache and pains passed off and the only complaint was of feeling hot. The patients were usually flushed and drowsy but never sericusly ill, even with prolonged high fever and profuse rash.

Conjunctival injection was always present varying from complete suffusion to a transverse band. There was no photophobia.

The tongue was furred and dry but became moist after about a week.

Rash.—The rash appeared usually on the 3rd or 4th day, beginning as a rule on the arms first and spreading rapidly. When fully developed it covered the limbs, trunk and face but not the scalp. It was more marked on the upper part of the trunk than the lower, and on the extensor surface of the limbs (particularly the back and top of the shoulder) than the flexor. The palms and soles and the face were nearly always involved. The milder the case the less marked was the rash. The lesions were maculo-papular and varied somewhat in size. On the body they were smaller, more discrete and papular, on the limbs larger and macular or sometimes almost nodular. On the feet and sometimes round the waist they were often petechial.

The rash was never irritating. It was pink at the onset, becoming a deeper red, then dusky and gradually brown, at the same time losing its raised quality. The staining persisted for weeks especially on the limbs where there was desquamation in the very profuse cases. Fading began first on the trunk, but the colour was usually still bright when the temperature fell.

There were no other consistent features. A mild bronchitis was frequently present, and sometimes the cervical lymph glands (especially in the posterior triangle) enlarged. The urine was normal and the bowels usually constipated. The liver and spleen were not enlarged and the blood counts were within normal limits.

Temperature.—The fever was usually remittent, sometimes with intermissions and with a maximum often of 104°. It was prolonged, falling by slow lysis to become normal about the 15th—18th day (less in the mild cases, but occasionally lasting even longer). The pulse was relatively slow.

Termination.—Improvement in the general condition usually began fairly suddenly about the 10th—13th day even though the temperature was still high and the rash profuse. Occasionally this change was dramatic. (Limits 6th—19th day.)

Complications.—Several cases had a concomitant attack of malaria accompanying the onset. One case during the stage of recovery had a sudden hæmoptysis with a small area of consolidation in the lower lobe and a small pleural effusion, all of which cleared up completely. At the same time he had a slate-blue colour. Two cases were tried, one with sulphapyridine and the other with sulphonamide, but both became cyanosed in 24 hours and the attempt at this treatment was discontinued.

Weil Felix Reaction.—The results of the test were very variable but all the cases showed a positive reaction of some kind.

OX2.—There were two distinct types of reaction, in one the titre rising to *1500—3500* (and in one case 30,000) and in the other not above *300*. The cases were about equally divided between the two types. Two cases showed no distinct rise at all. The two types were not related in any way to the clinical condition. The maximum occurred in the 3rd—5th week of the disease, usually the 4th and the rise was gradual, though occasionally sudden. The fall was always gradual and after 8 weeks the titre was still raised though less so than for OX19.

OX19.—The maximum titre was usually between *750* and *1500*, though three cases gave higher figures (3000, 7500 and 8500) and three lower (under 750). The latter were all mild cases (in one of which the rise was hardly appreciable).

The maximum was reached in the 4th or 5th weeks and occasionally the 3rd. One case had a titre of 7500 in the 2nd week and this fell rapidly again, and one reached its maximum only in the 6th week. The rise as with OX2 was usually gradual but sometimes sudden, while the fall was always gradual and after 8 weeks the level was still 150—750.

OXK.—There was very often no definite rise or fall and readings varied between 75 and 170 all through, though occasionally they were lower. Some cases showed a rise to 150 or 170 and a subsequent fall again and in one case the figure of 850 was reached in the 4th week.

The majority of the cases thus show a positive response to OX2 and OX19 and a doubtful one to OXK. There was no correspondence between the levels reached with the different antigens—both might be high, one only high, or both low. In the case in which 850 was reached with OXK, the figure for both OX2 and OX19 was 1700. On the whole the titre began to rise most markedly in the second week about the time when the fairly marked improvement in the general condition began. (The case which showed a titre of 30,000 in OX2 in the 2nd week (13th day) was one with a short sharp attack and, for the severity, the unusually low febrile period of 13 days.)

TREATMENT OF MALARIA

Brigadier G. Covell then spoke on the treatment of malaria as follows :—

General considerations.—There are two considerations which must be borne in mind when considering the treatment of malaria :—

(1) that, with the drugs at present available, there will always be a considerable proportion of chronic relapsing cases, however, long the period of treatment and however great the dosage prescribed.

(2) that in hyperendemic areas there are always a large number of mixed infections and reinfections. The fact that a patient has had a previous attack of malaria within the past few weeks should not be taken to indicate that his present attack is necessarily a relapse.

Prior to and during the war of 1914-18 it was customary to give quinine in massive doses and over long periods. The object of this was to diminish the number of relapses. It was known that quinine had a specific effect on the malaria parasite, and it was thought that its failure to prevent relapses must be due to insufficient dosage or too brief a period of treatment. One of the routine treatments tried in Salonika consisted of 30 grains of quinine by mouth and 30 intramuscularly daily for 12 days ; 60 grs. daily by mouth for the next 3 days ; 20 grains daily for the next 14 days ; a total of 1,180 grains in 29 days. The relapse rate among a series of 44 B.T. cases who received this course was 59 per cent. The dosage prescribed is in striking contrast to the present day army treatment which is equivalent to 210 grains of quinine followed by 5 days pamaquin.

There was formerly a Malaria Treatment Centre at Kasauli in which almost all the patients were chronic relapsing cases. A large number of different drugs were tried on these patients, every alternate man receiving a standard quinine treatment whilst the remainder were given the drug under trial. When plasmoquin was tried out under

hese conditions there was a marked and quite unexpected reduction in the proportion of relapses. This drug was subsequently included in the routine malaria treatment for the Army in India and as the result of this the Malaria Treatment Centre was closed down for lack of patients.

In addition to the work at Kasauli a great deal of investigation on the treatment of malaria was done at the Liverpool and Calcutta Schools of Tropical Medicine. In recent years a very extensive series of controlled experiments have been conducted in a number of different countries under the auspices of the League of Nations the results of which were summarised in the 4th General Report of the Malaria Commission. Further valuable knowledge regarding the use of antimalarial drugs has been gained during the administration of malarial therapy to cases of general paralysis.

At the result of all this work comparatively short courses such as the present standard treatment for the Army in India have come into general use. We now know that any dosage of quinine greater than 30 grains per day has not only no effect on the course of the disease but is bad for the patient's health, and similarly that to extend the course of quinine or atebrin (mepacrin) longer than the first week has no appreciable effect on the relapse rate. Plasmoquine (pamaquin) has a marked effect on the relapse rate, but it must be recognised that even when this is given there will always be a proportion of chronic relapsing cases, the number of these varying according to the species and strain of the infecting parasite, environmental conditions and other factors.

Intravenous versus intramuscular quinine.—The relative advantages and disadvantages of intravenous and intramuscular quinine have been the subject of much recent discussion and widely divergent views have been expressed. One view is that the use of intramuscular quinine is little short of criminal ; another, that it represents the method of choice for routine treatment. As we shall see, neither of these views is justified.

The objections to the routine use of intramuscular treatment are :—

(1) that it causes necrosis of muscle tissue and hence predisposes to invasion by organisms of tetanus, gas gangrene and streptococci. In wounded cases especially, showers of streptococci circulating in the blood may become localised in the thrombosed veins of the necrosed muscle tissue, causing a fixation abscess.

(ii) Sterile chemical abscesses, followed by fibrous nodules, may be formed. These cause considerable inconvenience and may possibly break down and suppurate years later.

(iii) Cases have occurred in which paralysis of a limb has followed when quinine has been injected in the vicinity of one of the principal nerves.

The opinion now generally held is :—

(A). Parenteral treatment should never be adopted as a routine practice but should be reserved for emergency conditions such as :

(i) where the patient cannot swallow quinine or atebrin.

(ii) hyperinfection (where more than 4 per cent. of R.B.Cs. contain parasites when more than 5 per cent. of infected R.B.Cs. show 2 or more parasites, or where pigmented asexual forms of *P. falciparum* are present in the peripheral blood.

(iii) Acute pernicious malaria (cerebral, cardiac or algid).

(iv) hyperpyrexia.

(v) peristent vomiting.

(vi) where, despite oral quinine in adequate dosage, asexual parasites persist in the blood or temperature fails to fall to normal in 3 or 4 days. (This usually indicates that the drug is not actually being taken.)

(B). If parenteral injections are decided upon, intravenous quinine is indicated unless (1) there are so many emergency cases to be dealt with immediately that there is no time to give it, (2) the patient is throwing himself about so that it is not possible to insert the needle into a vein, or (3) in children where it is sometimes difficult to do so.

Under such conditions intramuscular injections are indicated, preferably with mepacrin methane sulphonate (atebrin musonate) which does not cause necrosis.

Some clinicans prefer to give an intramuscular injection some hours after giving an intravenous in severe cases rather than give a second intravenous injection. The general rule in all cases is to get the patient on to quinine or mepacrin by the mouth as soon as possible.

Suppressive treatment.—This is an emergency measure designed to maintain a body of men on their feet for a limited period for some particular important task. The effects aimed at are :—

(i) Diminished morbidity, symptoms being masked in the majority of cases, provided that the drug is actually being taken in the prescribed dosage.
(ii) Reduction in severity of clinical attacks and consequent decrease in mortality.
(iii) Diminution in gametocyte carriers through a reduction in the asexual parasites from which they are derived.
(iv) Diminished tendency to blackwater fever.
(v) Cure of infection in some cases.

The chief cause of failure in suppressive treatment, as in curative treatment, is failure to ensure that the patient actually takes the drug in the required dosage.

The discontinuance of suppressive treatment should depend on :—

(i) Whether troops can be withdrawn to localities where the chance of reinfection is slight.
(ii) Whether the military situation is such that it will not be seriously affected if a considerable number of men go down at one time with febrile attacks.
(iii) Whether adequate hospital facilities are available.

In any case it is wise to discontinue the treatment in one unit first, so as to gauge the proportion of men likely to go down among the whole force, and thereafter to take the remainder off treatment by stages.

Suppressive mepacrin should be given in one dose immediately after the evening meal followed by a copious draught of water, in order to diminish the possibility of toxic effects. Such effects as do occur are of a minor character and tend to pass off after the first fortnight.

Relapses and Reinfections.—The frequent occurrence of reinfections has already been stressed. If a patient is told that he is suffering from a relapse, two effects are produced :—(1) he loses faith in the treatment and in doctors generally, and (2) he ceases to bother about any further measures of personal protection.

It is therefore wise to assure the patient that he is suffering from a fresh infection, unless there is definite and positive evidence to the contrary.

DISCUSSION

Col. Austin : " I shall report one small aspect of this enormous subject. In 1940 I was in Naushera. We were controlling the fever there with quinine, atebrin and plasmoquin. The fever came down and in those cases not a single one relapsed whilst a company which had been stationed at Ranchi was decimated ; these cases after my treatment still relapsed. It so happened that Brig. Covell was breaking journey at Naushera and so I asked him what he thought of it. He thought that it was due to the particular strain of parasites that attacked the troops at Ranchi."

Col. Taylor asked whether it was worth using methylene blue or not ? There have been various suggestions for a special centre for relapsing cases. In this connection he instanced 6 officers who were still relapsing. In the army there is a large number of cases of that sort. There is therefore a case for such a centre. Is there a case for the longer use of pamaquin ? Had Brig. Covell seen the phenomenon of auto-agglutination a few days after infection as reported in Capt. Birks' paper ? Col. Hayes has a record of 3,000 cases of intramuscular quinine given without any ill effect.

Brig. Covell : " I like the idea of a special centre. I have no personal knowledge regarding the longer use of pamaquin."

D.D.M.S. asked whether Brig. Covell thought that there was anything in the remarks of Capt. Birks, and whether men on sulphur by mouth were more or less immune to malaria because they were not bitten by the mosquitoes.

Brig. Covell : " I have not looked into Birks' paper. I am very interested in it. I do not know any work on that line, but Mulligan is working upon it. As regards sulphur by mouth I can test that out on monkeys. It would be actually prevention of the bite."

Lt. Col. Browning then gave his lecture which is summarised as under :—

TREATMENT OF GONORRHOEA

1. *On admission.*—A smear of the urethral discharge is taken at once on admission and the patient is placed on treatment as from the next 4-hourly tablet time.

2. *Diagnosis.*—If the original smear or any subsequent smear either of urethral discharge or of prostatic secretion shows the presence of gonococci, the diagnosis is gonorrhoea. If gonococci, are not found at any time, the diagnosis is urethritis V., that is urethritis as a result of sexual intercourse with an infected woman. The provisional diagnosis on admission therefore will be entered in pencil and the final one on discharge in ink.

3. *Treatment.*—The standard course of treatment will be by sulphaphyridine (M & B 693) tablets 0·5 grams given four-hourly day and night for 96 hours. Four tablets will be given the first time and thereafter two tablets. The course is thus :—

Day.	0200 hrs.	0600 hrs.	1000 hrs.	1400 hrs.	1800 hrs.	2200 hrs.
	Tabs.	Tabs.	Tabs.	Tabs.	Tabs.	Tabs.
1	4	2	2	2	2	2
2	2	2	2	2	2	2
2	2	2	2	2	2	2
4	2	2	2	2	2	2

The total course is thus of 50 tablets=25 grams. It can be started at any of the above times. In a case that has responded to treatment, the urethral discharge will have stopped and the patient will be quite dry. Tests of cure will then follow.

Irrigations of solution of potassium permanganate 1/20,000 will also be given b.d. of the preputial cavity and of the anterior urethra. The douche can for this purpose should be 3 feet above the level of the penis.

4. *Tests of cure—*

Day 5.—Prostatic massage, a smear being taken of the secretion expressed and examined microscopically.

Day 6.—Short sounds will be passed and hard nodules massaged out if necessary.

Day 7.—Prostatic massage as on Day 5.

5. *Patients responding to this treatment.*—If patients are quite dry and show nothing abnormal at the prostatic massages and the passage of short sounds, they will be considered to be cured and will be discharged to duty on Day 8. They will be given their original I, 1247 and told to report to their Unit M. O. with it on their arrival at the Unit. They will also be told :—

A. to report to their M. O. immediately if a urethral discharge recurs.

B. to become teetotallers for at least 3 months.

C. not to have sexual intercourse for 3 months.

D. to get a final test of cure and a blood test in 3 months.

6. *Patients not responding to initial treatment with sulphapyridine.*—These patients will not be dry on the fifth day. The routine for these cases will be :—

Day 5.—Prostatic massage, a smear being taken of the prostatic secretion expressed and examined microscopically.

Day 6.—Passage of short sounds and massaging of any hard nodules found.

A. A focus of residual infection will be found usually in the prostate, seminal vesicles or urethra.

B. Residual infection of the prostate and seminal vesicles will be treated by prostatic massage every 3 days for 15 days. Similarly residual infection in the urethra will be treated by passage of short sounds and massage over them for 15 days and continuing lavage of the anterior urethra with soln. pot. permang. 1/20,000 b.d.

C. If, at the end of 15 days, the condition is still present, the O.C. will be consulted as to the starting of a course of protein shock. Protein shock consists of giving T. A. B. vaccine *intravenously*. It should be noted that the Army Standard T. A. B. vaccine contains 2,000 million of bacilli per c.c. The following is a standard course :—

Day.	T.A.B.
1	50 million intravenously
4	100 ,, ,,
7	200 ,, ,,
10	400 ,, ,,
13	800 ,, ,,
16	600 ,, ,,
19	3,200 ,, ,,

D. It is hoped that the patient will be cured by this time. If not, the O. C. will be consulted forthwith.

7. *Points about the use of sulphapyridine—*

A. *Diet.*—Any ordinary or special diet may be given.

B. *Sulphur.*—Eggs, onions, sulphates and other things containing sulphur may be given in the ordinary way as required.

C. *Fluids.*—The importance of drinking as much fluid as possible cannot be overestimated. A convenient method of doing so is to give the patient ordinary Army tea ad. lib. At least a quart of fluid every two hours during the day should be drunk and the cook houses have instructions to provide tea to all comers at all times. Failure to drink enough fluid inevitably leads to toxic vomiting and may lead to haematuria, or anuria and possibly to death in consequence. The cause of death is found to be actual crystallisation out of sulphapyridine in the glomeruli and/or pelvis of the kidneys and/or in the ureters.

D. *Blue colouration.*—This condition may resemble the deep cyanosis of heart failure. It is due to a sulph-haemoglobinaemia and is of no significance. No action need be taken apart from reassuring the patient.

E. *Toxic vomiting.*—This is always due to defective fluid intake. It is only necessary to reassure the patient and give fluids ad. lib. forthwith. If necessary, morphia grains may be given as well.

F. *Haematuria.*—This is a danger sign of impending anuria and disaster. It is caused by the crystals of sulphapyridine formed in the kidneys and ureters as a result of insufficient fluid intake, actually lacerating those tissues and causing bleeding from them. Energetic treatment with large quantities of fluid by mouth, per rectum and, if necessary, intravenously will be started at once. Also a chart will be started of the amount of fluid intake and of urine passed. The O. C. invariably will be notified at once by the M. O. concerned.

G. *Anuria.*—This is the final warning of impending disaster and is a grave reflection on the M. O. concerned. Continuous intravenous saline (1 pint an hour) and fluids ad. lib. by mouth and rectum will be started forthwith. The patient will be put under the care of an orderly specially detailed for the case and none other. A chart will be started of the fluid intake and of the amount and characteristics of the urine passed. The O. C. invariably will be notified at once by the M. O. concerned.

H. *Agranulocytosis.*—A rise of temperature may occur during the course of sulphapyridine tablets. The possibility of its being due to the onset of acute agranulocytosis will always be investigated properly at once. A blood film for malaria parasites and a total white blood cell count will be done always and the O. C. consulted forthwith. If the white blood count is below 2,000, the treatment will be stopped and 10 c.c. of sodium pentnucleotide will be given hypodermically.

I. *Repeat courses of sulphapyridine.*—On no account will a second course of sulphapyridine be given until a differential white cell and a total white blood cell count have been done and until the O. C. has been consulted. As a matter of clinical experience it will be found that, if a patient has had a proper course of sulphapyridine and not responded to it, a further course of sulphapyridine is useless. Second course of sulphapyridine therefore will be given only to those cases in which there is a doubt as to whether the previous course was given properly.

Capt. White then read his paper on **Anxiety States** as follows :—

" One of the commoner psychiatric disabilities found in the Eastern Army at present, even in the absence of large scale operations, is the anxiety state.

Under the label " Anxiety State " I am including all cases where the disability is a preoccupation on the part of the individual with a continued increased emotivity, the physical expression of which is an adreno-sympathetic reaction. The nature of anxiety may be understood if it is thought of as the correlative of fear. Fear is the emotional reaction produced as a result of some danger threatening the organism from without the instinctive response to which is either flight or attack. If these instinctive responses are inhibited the condition of anxiety results. It might be called the emotional reaction to the continued perception of an external danger. This may be called a normal anxiety. When however anxiety is present in the absence of any perceptible cause it is pathological and some other mechanism must be formulated for its production. We will touch on this later.

The official term ' Anxiety Neurosis ' defined in the nomenclature of diseases as a psychoneurotic anxiety state, includes two conditions which, though similar in their clinical presentation are of a different etiology. They are " True Anxiety Neurosis " and " Anxiety Hysteria ".

Strictly speaking in an *Anxiety Neurosis* although the main symptom is anxiety and although this is expressed at the psychic level it is not of psychic but of somatic origin. It does not lend itself to being analysed into psychic components and its cause can only be found at the physiological level. This anxiety which originates from physiological causes manifests itself in the psychic sphere either on the one hand as what is called a free-floating anxiety or on the other hand it may be given ideational content and appear superficially as an anxiety of psychological origin of the type we shall discuss next. The differential diagnosis depends on a study of the personality and the development of the condition. True anxiety neurosis is found in war-time following periods of exhausting exertion, after prolonged mental stress and after debilitating illnesses. The number of cases of this nature have up to date been few.

Anxiety Hysteria is of an entirely different aetiology and depends on the psychological constitution of the individual. Its somatic manifestation is through the adrenosympathetic system, just as in anxiety neurosis, with the addition in many cases of such psychological phenomena as phobias. In its production physiological stress plays no discernible part. An explanation of its mechanism will throw some light on the type of individual and on the circumstances in which it can be expected to be found. In so-called normal individuals a certain equilibrium has been achieved between their basic instinctive individual tendencies and those requirements which in virtue of their social development they conceive that society demands from them. These two psychic factors may conveniently be referred to as the egoistic instinctive impulses and the social ideal. The degree of stability which exists in different people can only be determined by a careful assessment of the unbalancing factors to which they have been subjected and by consideration of the adaptations they have made. Failure to attain an equilibrium leaves free a certain amount of psychic energy which is the seed of an anxiety hysteria.

An individual who has lived successfully in civilian life where ample opportunity exists for altering circumstances tending to upset his equilibrium and for sublimating any free psychic energy resulting from any partially resolved conflict may, under conditions of life in the army and especially in the unfamiliar surroundings of a foreign country, find himself unable to make a satisfactory adjustment.

The sequence of events is this : In certain circumstances from which he cannot escape a conflict arises between the egoistic tendencies and the social ideal. No opportunity exists for an acceptable sublimation of the psychic energy attached to the egoistic impulse. The individual will then endeavour to make use of the mechanism of suppression—trying to put the impulse right out of consciousness, into that realm of the mind to which pure primary instinctive reactions are relegated where it is beyond conscious recall by the ordinary associations of waking life. If he is successful then he reestablishes his equilibrium. If however he does not succeed and the impulse is not suppressed, the unwanted energy remains merely repressed, bottled-up, unattached, dissociated from the personality and awaits as a constant mental irritation an opportunity to express itself. The subjective sensations of the patient to repression or the continued attempt to banish from consciousness part of itself, are irritability, loss of concentrative power, an anxious expectation, and finally a reduction to the somatic level with the production of tremor, palpitation, giddiness, sensations of choking, etc. Some retionalisation may take place and the individual will attribute his condition to various circumstances of his environment. Once this sequence is established the energy of his unresolved, unsuppressed conflict acts like a grain of sand in an oyster and the pearl of anxiety grows by the accretion of smaller amounts of psychic energy derived from even smaller conflicts which the patient is now less able to solve. The palpitating, trembling, choking state we see represents the best the patient has been able to do to achieve psychological equilibrium. In such a patient any stimulus associated with his conflict sets off an enhanced adreno-sympathetic reaction, a patient who has lost his symptoms say in a hospital environment will thus manifest them again during interviews, medical boards, etc.

A phenomenon seen often in anxiety hysteria is the development of various phobias. This may be taken as being a mechanism, parallel to what is called 'conversion hysteria' where the conflict is reduced to the purely physical level. In the production of a phobia the free psychic energy becomes circumscribed in the mind and attached to definite objects and situations, and the intensity of the emotion attached to such phobias is indicative of the degree of the anxiety which has been transformed. The majority of cases seen by me up to date come into this category of anxiety hysteria. Investigation of a number of these cases has shown clearly the existence of a psychopathic tendency in their lives prior to coming into the services, tendencies which however they were able to deal with successfully. These people were found to have required for their psychological equilibrium certain 'aids to living'. Some showed an over-dependence on another member of the family, some were unduly devoted to their wives and children, some to public duties, some to religion, and in several equilibrium was maintained by frequent changes of occupation and environment. In others the anxiety reaction had been conditioned by their upbringing. Few of them had attained any measure of economic or intellectual success.

Consider how such people fare under conditions of Army Service. Some break down because they have been uprooted from a settled environment, an environment they may have taken many years to find. Some break down because in the army they are deprived of their normal outlets for excessive emotivity—their children, their hobbies, sports or social activities; others because the inflexibility of army life deprives them of the opportunity for varied employments and environmental changes through which they evaded their conflicts.

Few cases have been seen where the anxiety has been of sudden onset; its development has been gradual and progressive, often to the point of total incapacity.

If and when the war enters a more active phase in this area there will be a corresponding change in the type of individual afflicted by anxiety hysteria. In addition to the group of men with a definite psychopathic predisposition such as are seen at the moment, others whose predisposition is not sufficiently severe to cause them any upset under existing circumstances will exhibit anxiety states under the more exacting conditions of active war. In many the breakdown will be more acute and the present slow development with its gradually increasing anxiety will be replaced by a rapid onset, the production of amnesias and a higher incidence of conversion hysteria.

In conditions such as obtain on the battle-field an individual finds himself in circumstances far removed from anything akin to what he has had to adapt himself to in his peace-time existence. The egoistic instinctive impulses concerned with self-preservation which are suppressed in peace-time conditions emerge and are present in consciousness. These have to be either suppressed or sublimated in a way acceptable to the social ideal. Failing this they have to be *repressed*. It is in this state of repression that there is present a large amount of free psychic energy which, depending on the personality of the individual, may produce either an anxiety hysteria or a conversion hysteria. Contributory factors in preventing the individual from sublimating this free psychic energy are enforced inactivity, physical exhaustion and ill health. Many cases who attribute the lesion which brings them to the psychiatrist to such incidents as being blown up or being buried will on investigation show the existence of an acute anxiety present before the precipitating incident.

I have previously stated that the condition of a patient in an anxiety state represents the best he can do to produce a psychological equilibrium. People in whom the social ideal is not well developed seem to have less in the way of free anxiety and more in the way of physical manifestations. In anxiety states while the Social Ideal remains unaltered and the circumstances of his breakdown are still in view, the intensity of the anxiety remains the same. The patient however who is suffering unconsciously looks for some avenue of escape from his anxiety and if he can find an acceptable way of relieving his distress by the production of physical symptoms he will do so. This point is particularly important when the patient is in hospital. If only some disability could be diagnosed which would lead to his removal from the circumstances of his breakdown all would be well. When the doctor doing his round of the ward places his stethoscope on the precordium of each patient and then gravely moves on, he has focussed the attention of his patients on one organ and a particularly dangerous one which reacts normally to emotional stimuli. If he repeats the procedure daily the patient unconsciously

looking for some avenue of escape sees one which is likely to meet with medical approval. His Social Ideal becomes lowered and part at least of his anxiety is relieved by the production of a functional tachycardia. Information circulating in a ward to the effect that patients whose pulses are over a certain figure remain in bed offers a similar acceptable avenue to patients with even a small amount of free anxiety and if such conditions obtained, it is probable that there would be a general rise of the average pulse-rate. It should be remembered that few men in conditions of war are free from some measure of anxiety and as few opportunities as possible for an acceptable lowering of the Social Ideal should be given.

This lowering of compromising with the Social Ideal is a particularly dangerous source of psychiatric disabilities in a protracted war. It is seen in men who have gone on for a long time with some mild degree of anxiety and who then experience some psychical or physical trauma. In the early states of a war they would probably not have become psychiatric casualties but taking advantage of the avenue of escape—" I have done my bit "—they convert their anxiety either at the adreno-sympathetic level or as an added functional element to any physical disability.

In assessing the severity of an anxiety state the most important point to be observed is how the patient sleeps. This should be studied and recorded by every M. O. in charge of such case. In a normal individual at night when he composes himself for sleep the threshold of consciousness is lowered, active repression ceases with the onset of sleep, and ideas in the foreground of the unconscious are free to appear in dreams. In conditions of anxiety the peace and quiet of the night instead of heralding a restful sleep compel the sufferer to give his undivided attention to his anxiety and its physical attributes. He cannot get to sleep because of his preoccupation with his anxiety, the beating of his heart and his inability to sleep. When at last he does fall asleep and, the last remnants of voluntary control being removed, dreams appear, to the subject of these is attached all the free psychic energy of his unresolved mental conflict. The intensity of emotion in the dreams of such patients is often far greater than anything experienced in the waking state and a fear of this contributes to the patient's anxiety. Often they awake displaying the predominating emotion of the dream, perhaps in terror—sweating and palpitating, or, if the emotion was one of grief, sobbing and in tears. Instead of being refreshed in the morning the patient is tired and exhausted. The vicious circle thus established accelerates the general deterioration., If the psychical trauma producing the anxiety state was isolated and severe as occurs in battle conditions, actual scenes may be relieved again in dreams.

The importance of ensuring sleep in anxiety states cannot be over-emphasised ; failure to do so results in a rapid deterioration in the patient's physical condition and a perpetuation of his anxiety.

The first indication of improvement in anxiety states if often the return of normal sleep. It indicates that the individual is making a successful readaptation to at least the modified environment which he is in.

The *treatment* and *disposal* of such cases as are occurring at present depend largely on an assessment of their previous psychological history and of the conditions contributing to their breakdown. No rigid procedure is applicable to them all. The question resolves itself into making a decision as to whether or not an occupation can be found in the army for these psychologically inferior types which is within their capacity, and which will not involve them in circumstances likely to produce a mental conflict which they cannot resolve. A man whose anxiety state develops under conditions merely of army training and routine is unlikely to be worth retaining. If however his condition is the result of a severe mental stress and his previous adaptation good he is likely to be successful in a slightly more restricted capacity. When once an adreno-sympathetic reaction is established in these psychologically inferior types its eradication is a matter of considerable difficulty and requires rather more in the way of therapeutic resources than are available at present.

Prevention of the occurrence of anxiety states is the ideal remedy. This can be done to a large extent by a psychological investigation and classification of the patient before he is drafted into any unit. Grossly inferior types could be weeded out and others less so given selected employment suited to their reduced adaptive capacity.

Adequate military training and the development of a good morale are important in helping those potentially liable to develop anxiety states under conditions of moderate

battle stress. Morale is based on the various sentiments of unity, loyalty, etc., acquired during training and may be defined as collective courage. The potential anxiety hysteric, if in a unit whose morale is good, tends to think collectively and thus by having his egoistic tendencies blunted is relieved of individual responsibilities and decisions and relies on the leadership of a stronger personality.

No discussion of current anxiety states would be complete without mentioning mental deficiency. Many mental defectives of the category "Dull and backward" have unfortunately been recruited to the army. These individuals who were able in civilian life to find some simple stereotyped employment are not capable of assimilating military training of the standard required for modern war. Their lives, if their condition is not recognised, become progressively more difficult until their breaking point is reached. The symptom of their breakdown is commonly an emotional reaction which bears a superficial resemblance to an anxiety state. They complain of not being able to go on, of having lost their confidence, of going off their food, of getting headaches or attacks of giddiness, etc. If they have been near the scene of any action they complain of their 'nerves' being shattered as a result. Their anxiety is not of the intense variety found in people with a well developed social ideal, their condition might be described as one of pseudo-anxiety. The true nature of their condition is seldom recognised and many of these cases have been kept in hospitals and nursed as anxiety states.

In conclusion I would like to emphasise the importance of obtaining as much information about the patient as possible before either coming to any decision oneself or before sending him on to someone else. The label NYDN is hardly enough to enable the psychiatrist to form a fair assessment."

DISCUSSION.

Brig. Marriott in opening the discussion enquired if many cases of anxiety states had been engendered by injudicious examinations and treatment carried out by medical officers. The reply was given that instances of such had occurred. Recent illustrative cases of this nature were quoted by Lt.-Col. Seward from his own experience.

Lt. Col. Shah emphasised the importance of a thorough physical examination in cases of anxiety states to exclude any underlying organic disease.

Lt. Col. Seward advised that the patient be thoroughly examined by a medical specialist, that the heart should never be examined first and, having been found to be organically normal, never examined again.

Any physical illness found should be treated. The medical specialist's findings should be recorded on a A.F.I.-1237 and signed in the usual way before the psychiatrist sees the case.

As soon as it has been decided that the psychiatrist's help will be required, the following *pro forma* might be sent to the patient's C. O.:

CONFIDENTIAL. Ref. H/8/Gen.

Subject:—Interviews—PSYCHIATRIST.

Date.....

Officer Commanding,

.....

No. .....Rank.....Name.....

The a/n patient is about to be referred to our Psychiatrist. It would be of material assistance to us in diagnosis, to have any views, you, your Medical Officer, and the man's company officer may have formed as to his character, intelligence and behaviour.

May this information please be forwarded immediately by confidential letter to me at this Hospital.

Lt.-Col., R.A.M.C.,
Officer i/c Medical Division,
47th British General Hospital.

This was the procedure followed at 47 B.G.H. and Capt. White agreed that it had proved practicable, valuable and time-saving.

Lt. Col. Ransome: "This question of hysteria and malingering, particularly among the I. O. Rs. is a problem which is of great interest to all of us. During the last two years in Malaya before the Japanese invasion, I had the experience of working with

Col. Bennett, consulting physician to the Far Eastern Army, who was both a physician and a psychologist. The neurological clinic in Singapore was used as a diagnostic and treatment centre for many of his more flagrant cases where I had the opportunity of investigating them under his supervision. One of the most important points mentioned by Capt. White was discipline in the unit. In the British Army this is based on mutual respect between the men, N. C. Os. and officers, a point which is extremely important with the new army recruited from civil life. In the Guards Regiment during the last war there were very few cases of " shell shock ". They were far more common among less disciplined units. In Malaya one came across very much the same sort of thing in the State Forces as contrasted with regular Indian Army. The regular Indian Army, apart from the Sikhs, who are experts in the art of malingering when it suits them gave very little trouble. Among the native troops where the discipline was not particularly good, if for some reason or other the N. C. O. did not seem to respect a sepoy, there were many cases. Many of them were quite simple in their origin such as victimisation of a sepoy by an N. C. O. Many of these Indian cases were an escape from reality, hysteria being the means. Very often the reality was quite a small one such as the desire to get out of the situation such as mentioned above. The underlying causes were not so deep as in the corresponding English cases. Another point that needs stressing very strongly is the mind-blindness of M. Os. to hysteria or malingering in their own wards. Perhaps due to the stress of work they are not able to make up their minds about a certain case. They leave it for another day and meanwhile more work—malaria and dysentery come up which give a fairly satisfactory response to ordinary examination and treatment. Meanwhile the unfortunate hysteric is lying in the ward and is not diagnosed. After the lapse of some days or weeks the M. O. feels that he ought to examine the patient and he already approaches that case with a feeling of guilt because he has not been able to make up his mind as to the diagnosis nor has he really given the case a very thorough examination. In other words he himself has become neurotic about it and very frequently may escape from the reality by one or two examinations of the case from day to day until the neurosis becomes even worse. Col. Bennett quite frequently found cases who had been in base hospital upto periods of 3 or 4 months and even longer with hysterical symptoms, diagnosed, usually on very insufficient grounds as organic disease, N. Y. D., hemiplegia, arthritis, etc. It is obvious that these patients are best picked out by an outside person going round the wards. This is the duty of the divisional officer.

The method of treatment adopted in Singapore was quite simple. It depended on two main factors. First of all there had to be a first rate physical examination, backed up, if there was any question of doubt, by the use of laboratory tests or x-rays. It is essential that the examination and the correct diagnosis, if possible, should be arrived at in one day. After this the patient must not be examined at all. Secondly, it was usually desirable to make the cure rather worse than the disease and to allow the patient to be " cured " without loss of face to himself, unless he was a malingerer when it did him good. This was achieved in a number of cases by placing them on a milk diet and telling them that as they got stronger their diet would be increased. After about 3 days of this treatment there was usually some desire for improvement and this could then be effected by preparing the mind for this cure whatever it might be such, as electricity or evipan. It was essential to effect it at one sitting. This is every instance we have done with a little practice. Finally these patients when they were cured they were always amongst one's most grateful patients. This late type of case however is of small moment compared with a number of cases which could be prevented further up the line if proper facilities existed for examination of the patients. Col. Bennett just before the invasion, had an idea of establishing diagnostic centres for somewhat doubtful cases far up the line so that this type of case could be disposed of forward rather than have to make the weary journey undiagnosed back to the base hospital. One can see the corollary of this that one must have some really experienced men well forward who are capable of ruling out organic disease and to do this they must be equipped with modern methods. Otherwise the time factor comes in and the neurosis will often become established."

Lt. Col. Shah " I have to submit that :

1. The causation of this syndrome is still *sub judice*. There are at least half a dozen theories other than the psychological one.

2. The psychiatrists tend to assess the constitutional aspect of these cases only in psychological terms and no attention is paid to its physical aspect.

3. May I suggest that a psycho-therapeutic centre should be set up where such cases could be properly investigated and disposed of under the supervision of a physician ? This centre should have a definite policy of (*a*) evacuating those unfit for service, (*b*) helping to adjust those in need of advice, and (*c*) adjusting the work by suitable categorisation of those who are yet capable of doing useful work.

Capt. White replying to Col. Shah, agreed with his first point, and said that his second point had been dealt with by Lt. Col. Seward in his comments ; his remark about a psycho-therapeutic centre applied to all psychiatric casualties and was what was in fact being carried out.

The conference met again at 9 a.m. on the 18th March 1943 at the Loreto Convent.

Major Mullen read his paper as follows :

PROPHYLACTIC TREATMENT FOR MALARIA IN "V" FORCE.

" I wish to point out that the undermentioned figures have been obtained in the jungles of Assam, Lushai Hills, Tripura State, Arakan, Chittagong Hill tracts, and Chin Hills. This is an immense territory of over 1,000 square miles of country where roads do not exist and transport is almost entirely a matter of marching. In a little less than one year," V " force has collected a certain amount of data which I present for your interest and I do not wish to suggest that the deductions made are in any way final. We have evolved a system of prophylaxis which does work but I have no doubt we shall make many improvements in the months to come.

1. *Splenic rate of personnel at start of " V " force.*

Indian troops	62 per cent.	B.O's.	nil.
Tribesmen	69 per cent.	B.O.R's.	nil.

2. *Average splenic rate of villages.*

(*a*) Below 4,000 ft. 50 per cent.
(*b*) Above 4,000 ft. 25 per cent.
(*c*) Above 4,500 ft. 5 per cent.

NOTE.—Hill tribes plant their rice in the valleys and owing to soil erosion move their terraced fields down lower, while the village stays in its original spot. Where fields are far below the village the tribesmen with their families go to the paddy field and live there for several days. Thus a village above 4,500 ft. might have a fairly high spleen rate owing to children getting malaria when living at the paddy field at a level of 2,000 ft. In our experience we have never had a fresh infection above 4,500 ft.

3. *Villages.*—When we spent nights in villages the average sick was always above 30 per cent. per day. When we slept at least a mile from the villages sick rate was to 28·7 per cent. per day.

Most of our Indian personnel had chronic malaria, and sleeping out meant exposing them to cold and wet, so that pyrexias were frequent. This figure does not show the importance of avoiding villages.

4. *Cold and wet.*—(*a*) After a warm dry night, pyrexia in the morning occurred in about 0·5 per cent.

(*b*) After a cold wet night, pyrexias in the morning occurred in 38 per cent.

NOTE.—Our men have to carry all their equipment and, therefore, travel with a maximum of 40 lbs. We now have overcome this difficulty by sleeping in pairs and issuing one blanket to two tribesmen.

5. *Mosquito nets.*—(*a*) Without nets the sick rate amongst tribesmen averaged 85 per cent. per day.

(*b*) With mosquito nets 10 per cent.

NOTE.—We carry one net per two men. This was equipping whilst the men share their blankets. The cost of equipping our force with mosquito nets was so high that for a long time the suggestion to equip our tribesmen was met by the argument that as they were natives of these parts, there seemed no good reason for their requiring a net now because they were working for us. The sudden increase in malaria rates in tribesmen taken from their village to work for us was due to the lack of accommodation such as they were used to.

For the hillman usually goes indoors before nightfall and starts to cook his evening meal. The smoky atmosphere drives away mosquitoes and, since it is cold, the natives do not stray far from the fire till morning. When the hillman has to cook in the open he huddles round the fire end is fair game for the anopheline. This is borne out by the following malaria rates :

(i) Labour corps without huts Malaria rate . . . . . .87 per cent.
(ii) „ „ with huts „ . . . . . .21 per cent.

6. *Anti-mosquito cream.*—It was found that in troops not using anti-mosquito cream the malaria rate was 9 per cent.; whilst for troops using anti-mosquito cream the malaria rate was 12 per cent.

These figures, I believe to be unfair. I wish to point out that our men hate anti-mosquito cream and they now know that they have to spread it on thickly on all exposed parts and renew hourly to be really successful. It is so unpleasant that the men dodge using it and swear that it attracts mosquitos. Even the B.O.'s now make the same claim.

7. *Clothing.*—This is one of the most valuable points in our experience. Figures taken from all areas show that where mosquito boots, slacks and shirts with long sleeves have been worn every night from before dark the malaria rate is nil.

Unfortunately protective clothing is seldom practicable for "V" force personnel in forward areas.

8. *Prophylactic quinine.*—In a survey of 60 patrols it was found that in 10 patrols without prophylactic quinine only 2 would reach their objective with as much as 5 per cent. of the original strength if they had a badly infected country to go through, marching by night and sleeping by day.

With prophylactic quinine given as recommended in the army pamphlets all our men now reach their objective. This includes a survey of 60 patrols.

9. By following the above routine the malaria rate of our troops during the rains dropped to 0·8 per cent. This, compared with the troops in less badly infected areas, is a good figure, but I would like to point out that our troops are most definitely "malaria conscious" and never take stupid risks. They do not need to be told how dangerous it is to disobey the rules of prophylaxis—they know.

Rum.—In each area, after an exhausting trek or long exposure it has been found that 1½ oz. of rum prevents a recurrence of malaria.

DISCUSSION.

Col. Ainsley. "I should like to congratulate Major Mullen on the high degree of importance with which malaria is regarded in the force in which he acts as D.A.D.M.S. and I would like to reiterate his remark that malaria is as important an enemy as the JAP. If we can reduce the incidence of malaria in our troops on this India-Burma front to a greater extent than the Jap can do it in his troops it may well prove to be the deciding factor in ultimate success.

With regard to the statistics given by Major Mullen I appreciate the difficulty he has under the conditions in which he is working of getting reliable figures. The statistics he has given, however, are, I feel, misleading. There is absolutely no doubt whatever that villages must wherever possible be avoided at night in malarious country during the transmission season. The figures of malarial attacks in personnel sleeping in a village and in personnel sleeping away from villages are really not relevant.

There are no data given to indicate whether the sites were in equally malarious country, and the fact that it was cold and that the warmth of village fires was the attraction suggest very strongly that it was the non-transmission season with a temperature below 60°F., and such cases as occurred were unprotected by anti-mosquito cream. There is no doubt whatever as to its value.

Properly applied it will considerably reduce the number of bites over a period of two hours in a body of men, though it will give less protection to some individuals than to others.

Major B.A. Lamprell then gave his lecture as follows:

"SUPPRESSIVE" AND BLANKET TREATMENT.

Our knowledge on the subject of suppressive treatment and its value to the army is far from complete and such data as are available are somewhat conflicting. Information on the degree of success that may be expected from blanket treatment is still somewhat sketchy but the subject is less controversial than that of suppressive treatment and can be dismissed more briefly.

Suppressive treatment.—This was termed prophylactic treatment by all the earlier writers when it was more fully appreciated that it was *not* prophylactic in the true sense of the word and it was referred to by many writers by the cumbersome phrase "the so called prophylactic treatment" until someone coined the eminently suitable term "suppressive treatment".

In 1916 the prophylactic dose was usually 5-6 grains daily but 10 grs. daily, 10 grs. on two days in the week and 20 and 30 grs. daily were tried.

Wenyon states that the consensus of opinion was that quinine administration had little or no effect in controlling the disease.

At one time very large body of men were given 30 grs. quinine daily with iron and arsenic twice, and it is reported by Wenyon that there was at first a fall in the admission rate but it gradually mounted until it was as high as it had been originally.

Mesopotamia.—Malaria in this campaign was described at length by Christophers and Shortt. The Army's total strength was about 400,000. In 1916-17 all units were supposed to be receiving 5 grs. quinine daily and every effort was made to ensure the actual administration.

Christophers in summing up the results says : " In regard to the value of quinine prophylaxis, the only thing that can be said is that, as in Wenyon's experience in Macedonia, the incidence might have been even higher if it had not been carried out ".

I will quote Christophers in his summing up of quinine prophylaxis after renewing malaria in many theatres of war in his presidential address to the Royal Society of Tropical Medicine in November 1939.

It would be unduly optimistic in face of the experience of the last war to regard quinine prophylaxis as a measure which can at any time be relied upon easily to control malaria in an army in the field. In fact in our troops under these conditions quinine prophylaxis, as ordinarily carried out, must be regarded in the light of actual experience as of somewhat doubtful value.

" If anything is to be achieved in this respect for more attention must be given than at present to preparation and organisation. If then the effectiveness of this measure by improved administration is to be increased, and must be by such steps as ensuring recognition of its great importance by the higher command, by previous propaganda amongst officers and men and by clearly thinking out details by which administration is most likely to be facilitated. Obviously all this should be done before the army is in the field and not left for someone to cope with *de novo* on the spot. "

There are various other reports of the use of suppressive treatment by British troops in small and large formations but no conclusive evidence I think of its achieving any great measure of success.

There have been claims made, the most noteworthy perhaps being by the French in Macedonia and by the nations in the Abyssinian campaign. These claims have not however been accepted by all unquestioned.

Wenyon expresses doubts as to the French findings and there has been very considerable doubt on the claims made by Castellani regarding the complete freedom of the Italian forces in Abyssinia. One point however should be made regarding the French and Italians and that is that they both adopted ruthless discipline and the Italians in addition made the fullest use of propaganda. The French are reported to have periodically paraded units and tested the urine of very tenth man. If quinine was not found then the Commanding Officer was broken.

So much for suppressive treatment in armies. In peace a classical research was carried out in Malaya at the invitation of the League of Nations Health Organisation and was planned in accordance with the scheme drawn by the Commission.

The investigation was carried out between August 1935 and October 1936 on two labour forces, one in a tea estate and one on a rubber plantation. Results obtained from the former only will be considered as they are of greater interest. The essential features are as follows :—

The average population was 420 individuals, it was located in an isolated tract of country completely surrounded by jungle, distant from other habitations and difficult of access. The vector was *A. umbrosus*, dissections of which at the commencement of the investigation showed an infective rate of nearly 6 per cent. There was a high morbidity rate in the population. In August there was a case rate of 61 in 142 individuals and a spleen rate of 59 per cent. the majority of cases showing B.T. infection.

The population was largely Tamil, some being resident for a long period and having a considerable degree of tolerance to the local strains and some recently recruited from South India. It was divided into three parts, as equally distributed in all respects as was possible.

I propose firstly to refer briefly to such experience as we have on suppressive treatment in armies and then in a little more detail to suppressive treatment in peace, because it is only under peace conditions that any really sound scientific data have been obtained.

In war the work done in Macedonia has been recorded by Wenyon and by numerous other writers, as is well known and altogether operations covered a period of some three years. In June 1916, there was a move forward into the Struma Valley by both British and French troops. Previously there has been little malaria in this threatre of war but in June there were 90 cases and in the remaining part of the year some 30,000 cases. In 1917 there were some 70,000 cases and still more in 1918. In 1918 some 25,000 of the worst cases were repatriated. It has been estimated 2,000,000 service days were lost.

To group I, 0·4 grms. of atebrin were given weekly (0·2 grms. on two successive days); to group II, 0·4 grms. of quinine dihydrochloride daily, and to group III simple tablets as a control. Routine blood surveys were carried out, anopheline larvae and adults were collected regularly throughout the investigation and *A. umbrosus* was dissected.

The administration of drugs were supervised as closely as possible, checks were instituted and it was reported that there was no reason to doubt the honesty of the administration.

The treatment commenced on 2nd Sept. 1935 and was discontinued on 24th August 1936. The first effect was an abrupt reduction in malaria attacks in the coolies in the atebrin group and less obvious effects in the quinine group. Among the adults of the quinine group there was a rapid decline after the first few weeks, but there was a much slower response amongst the children, from 10 to 20 per cent. being attended monthly for several months.

After six months however in both adults and children in both the quinine and atebrin group, there were only occasional attacks.

On suspending the treatment there was within a week a sudden and considerable reappearance of malaria in the atebrin group and during the eight weeks following the suspending of the treatment the incidence of malaria was nearly twice that of the controls.

In a careful analysis of their findings the writers reported that the effect of the treatment was to prolong the incubation period for a period which might be as long as a year, the infections taking place throughout the period being clinically and in some cases parasitologically hidden.

It is impossible now to deal at greater length with this investigation but two important points should receive mention. One is that calculation shows that the average gametocyte rate in the atebrin group was 1·2 per cent., whereas the rate was 16·6 in the control group. In view of this, as one would anticipate, the sporozoite rate in the vector was found at dissection to have fallen over the period of treatment. It was in effect merely 6 per cent. at commencement and about 0·4 per cent. at the conclusion.

Reference will be made more briefly to one other investigation. It was carried out in Assam on similar lines to the one in Malaya. The population was much higher, originally 2,173. A limiting factor was money and the object was to determine whether a reduced dosage would be economically sound. The atebrin group was first given a blanket treatment consisting of 0·2 gms. daily for 5 days and subsequently 0·2 gms. daily exactly for 17 weeks.

The number of cases occurring during the course of 20 weeks of treatment and the 13 weeks following suspension were as follows :

	Atebrin group.	*Control group.*
During treatment . . .	77	151
After treatment . . .	127	77
TOTAL .	204	228

This investigation was not supported by large scale blood examination and dissection of vector but it is of interest to note the malaria case rate in the control group was the lowest rate recorded over a period of seven years on this estate.

Discussion of apparently conflicting data.—It is believed that the difference that appears to exist in suppressive treatment as applied to an army and to an individual or large body of individuals resident over a long period in a malarious area may be ascribed to a degree of acquired immunity or tolerance.

Christophers in his classical investigation at Singbhum showed how in the 1 to 2 age group 100 per cent. had parasites discoverable in their blood at an average of over 12,000 parasites per micro m.m. and almost continuous clinical malaria, and how there was a steady graduation through the age groups to adults in whom only 50 per cent. showed parasites, with only 120 parasites per Mmm., the period of attacks being approximately 6 monthly.

With a high degree of acquired tolerance fever can generally be controlled with a few doses of any anti-malarial drug. The rubber planter, the tea planter in highly malarious tracts like Malaya and Assam, and the teak man in Burma, have found by experience that they can keep themselves fairly free of clinical malaria by suppressive treatment, and excellent results can be obtained by suppressive treatment in coolies long resident in Malaya and Assam or recruited from other malarious areas, but these examples are no criteria of what may be expected from armies recruited from Britain, France or the United Provinces and sent to Macedonia or Burma. Strickland who was malariologist to the Burma army last year is, I understand, of the opinion that suppressive treatment is valueless until a degree of natural immunity is established following a clinical attack.

This may or may not be an exaggeration of the truth but it does appear certain that the greater the degree of acquired tolerance the more readily malaria is suppressed by exhibition of drugs. I will conclude with a few remarks on the procedure laid down for suppressive treatment.

The dose is now 0·6 grms. mepacrine weekly given in three doses of 0·2 grms. on successive days. It is given only on express sanction of G.H.Q. or in certain cases the authority is deputed to administrative malarial officer of lower formations.

The dose is somewhat high and if taken regularly it is possible that some toxic effect may result. Slight toxic symptoms are more likely to occur in the early days and disappear later.

Field states there was no evidence of toxicity in the cases in his investigation using 0·4 grms. Sinton however has raised the point that all large scale experiments so far have been with vegetarians—or people on a diet mainly vegetable and that there may be more toxic effects with meat eaters.

It is recommended that the dose be given after food in the evening. One further point may be mentioned and that is coloration of the conjunctiva. Field found this did not occur till after administration had been continued for three months and then could be found in a large proportion of cases.

Conclusions on suppressive treatment.—It is believed that better results can be expected with mepacrine than were obtained in the last war with quinine but if suppressive treatment is to be of value one cannot stress too strongly the importance of a proper organised distribution and the danger of suspending the administration. If troops who have been on suppressive treatment discontinue taking the drug in the stress of active operations or because supplies fail then casualties from malaria may well be so high as completely to immobilise a force and lead to its destruction.

The details of administration must be carefully worked out and every commanding officer must be made aware of the dangers.

I would urge the French method be adopted, with ruthless disciplinary measures if it is proved that treatment is not being properly taken. The yellow coloration of the conjunctiva may be a useful index, but not till after some weeks of treatment. Periodic examination of urine should afford irrefutable evidence of the degree of efficiency with the treatment is being given.

Blanket treatment.—This subject can be dealt with briefly; there is as yet little data regarding the degree of success that may be expected but if it is properly administered very good results can be anticipated. This treatment is given only on the express sanction of G.H.Q. or as in the case of suppressive treatment, though in certain cases authority is deputed to administrative medical officers of lower formations.

At present it is being given as a rule to units which during the transmission season have had a case rate of over 40 per cent. of their strength.

It is by definition the mass treatment of a body of men who are known to have acquired a high degree of infection.

It is used for units who have had a very high proportion of cases of clinical malaria and also for units who are known to have acquired a high degree of infection, clinical malaria however having been controlled by suppressive treatment.

The procedure adopted is for all men in the unit or formation to be examined by an M.O. Those who show signs of malaria, enlarged spleen, anaemia or debility are admitted to hospital and receive the full course of treatment. Those who show no obvious signs receive a course of 3 tablets mepacrine daily for 5 days no drug for two days, and then 3 tablets pamaquin daily for 3 days.

For the treatment to be properly carried out the full co-operation of commanding officers is essential.

DISCUSSION.

Lt. Col. Dimson: "I was directly concerned with a small experiment in Blanket Treatment which may be of interest although it was carried out outside India.

Some 40 per cent. of the battalion I was looking after went down with M.T. malaria outside Freetown in a space of two months. The epidemic (for such it was) quickly subsided on prophylactic quinine grs. 5 daily. We were recalled home and in the ship, I examined the blood of a whole company selected at random and found 8 per cent. positive. Since we were due to arrive in England in February and had such a large amount of latent infection, I decided to apply blanket treatment. Half of 600 troops were given quinine 10 grs. t.d.s. for 10 days and the other half mepacrine 0·1 gr. t.d.s. for 7 days followed, in the case of 100 men (including all officers), by pamaquin 0·01 grm. b.d. for 5 days. This treatment was preceded by propaganda which included scotching the fallacy that quinine caused impotence. Soon after treatment was started, Tanret's test was applied to a whole company of men and 50 per cent. only were positive. Platoon commanders were put in charge of all parades and there was a great improvement. Except for a few cases occurring in the first 12 days of the voyage, which lasted nearly 5 weeks, not a single case of malaria occurred. On arrival in Glasgow, I was told 300 beds had been made available in the district but we could not fill one with a case of malaria. Major General Manifold issued to everyone a sealed envelope with detailed instructions to general practitioners should a man on leave report sick. Not a single case of proved malaria during the two weeks disembarkation leave of two weeks afterwards occurred.

Posting prevented a follow up.

This experiment may not apply to India, because my cases were nearly all primary, there were very few relapses and the strains of M.T. parasite may well differ from those found in Assam. But since it is, I think, the only instance in this war where a large body of troops who had suffered heavily from malaria in one area returned to England and even possibly the first occasion in this war on which blanket treatment was used, this little experiment is not without interest. Acquired tolerance does seem, as Major Lamprell has said, to be a prerequisite for the success of blanket treatment.

Finally a word about atebrin. I took it myself—4 tablets weekly for five months and noticed a yellow discoloration of the skin after three months but not of the conjunctivae. It took quite two months after stopping taking it before the discoloration disappeared."

Col. Taylor.—"The present army policy of treatment is to abstain from antimalarial treatment between active attacks, as Brig. Covell has stressed.

On the other hand evidence is accumulating that blanket treatment is achieving good results.

This illustrates our ignorance of malarial treatment and stresses the importance of collecting all available data upon it, and for that matter, upon all subjects of medical importance to the army.

Major M.H.P. Sayers then gave a dissertation upon Medical Board procedure.

As G.H.Q. have since intimated that a compendium comprising the latest instructions governing Board procedures is now in the press, it has been decided to withhold the publication of Major Sayers' paper until he has had an opportunity of reviewing it in the light of the bearing these instructions may have upon Board procedure in Eastern Army.

Major M.H.P. Sayers then read his paper on

THE INTERPRETATION OF AGGLUTINATION REACTIONS.

1. The common diseases in which agglutination reactions are used in military practice are :

(*a*) The enteric group.
(*b*) Typhus fever.
(*c*) The Brucella group.

2. The difficulty in deciding criteria in diagnosis is due to lack of uniformity in the technique by which the test is carried out. Thus one worker uses live suspensions, another killed. One uses Dreyer's tubes and another the tubes advocated by Felix.

In an attempt to obtain uniform standards in the army, G.H.Q. published a note outlining technique in performing agglutination reactions, methods of reading, etc. In this way it was hoped it would be possible to obtain data from which definite conclusions could be drawn.

From the available literature and from one's own experiences in this country, fairly reliable standards in the interpretation of agglutination reactions can however be drawn.

3. Up to about eight years ago ' H ' suspensions were used in the routine diagnosis of the Enteric Group for the army in India. The disadvantages of this method were :

(*a*) The response of 'H' agglutinins to T.A.B. inoculation is high and therefore their estimation is of little use in diagnosis in an inoculated population, such as we are dealing with.
(*b*) 'H' agglutinins tend to appear late in the course of disease.
(*c*) Non-specific reactions are common after previous inoculation.
(*d*) The results are not an index of immunity.

In the uninoculated 'H' agglutination is the technique of choice, as the results are clear cut and specific for the type of infection.

4. Nowadays 'O' agglutination is used in all cases where there is a history of inoculation with T.A.B. The advantages of this method are as follows :

(*a*) The response to T.A.B. inoculation is very much lower and less confusing.
(*b*) The agglutinins appear earlier in the infection.
(*c*) Non-specific reactions are not common and only occur as a rule in low titre.
(*d*) The rise in titre is some index of immunity.

The reaction is however a group phenomenon due to the sharing of common somatic antigens with other members of the Salmonella group.

5. Are 'O' agglutinins present in the sera of uninoculated individuals ? In a series of 50 uninoculated individuals examined by Bhatnagar, 32 had a titre of 1:100 against 'T.O' while 1 had a titre of over 1:50 against 'A.O'. He was however using live suspensions which are more sensitive and usually give a reading one tube higher than the killed suspensions we now use in our laboratories.

6. What titres are found in inoculated subjects ? The answer depends on two factors :

(*a*) The time that has elapsed since inoculation.
(*b*) The number of times previous inoculation has been given.

Bhatnagar found that out of 20 people examined 6 months after primary inoculation, only 8 had a titre of over 1: 100 against 'T.O', while in no case was the titre over 1:300. Thus titres had fallen to almost pre-inoculation levels by the end of 6 months. 'A.O' titres were very much lower.

Common findings after primary inoculation are 1:160 ('T.O') and 1:40 (A.O). By the end of 6 months after inoculation, this figure has usually fallen.

Secondary inoculation was found by Bhatnagar to lead to a higher initial response, while the titre of residual agglutinins remained higher for a longer time, falling to pre-inoculation levels at about the 12th month.

Summing up—titres above 160 against 'T.O' and above 40 against 'A.O' except during the first few months after inoculation, are unusual and are an indication for an early repetition of the test.

7. *Response to infection.*—Significant rises are usually present by the end of the first week. Titres vary from say 1:320 to 1:2,500 ('T.O'). A rising titre in the early stages is the diagnostic factor.

'T.O' titres tend to be much higher than 'A.O' titres. This is partly due to the greater sensitivity of the 'T.O' suspension, and partly due to the higher residual titre of the 'T.O' agglutinins as a result of T.A.B. inoculation 'T' fraction of which is more antigenic.

We have seen that 'O' agglutination is a group phenomenon. Thus an attack of paratyphoid fever is often associated with a higher rise of 'T.O' agglutinins, then 'A.O' agglutinins. This may be puzzling at first because there appears to be no antigenic relationship between these two organisms, according to the tables of Kauffmann-White. This shows that the antigenic structure of this complex Salmonella group is not yet altogether fully explained.

8. *Vi and RV.*—These suspensions are essentially the same antigens, but prepared from different strains of *B. typhosum*. These agglutinins are not present in the sera of healthy persons, whether inoculated or not, except in very low titre (1:10) and even then this is exceptional. Nor do they appear to occur in conditions other than the enteric group. A titre of 1:20 is suspicious of enteric group infection and the higher titres say 1:40 or over are strong presumptive evidence of infection. The technique of reading the tests must be scrupulously observed or false positive results will be reported. The suspensions require to be fresh. For these reasons this test does not appear to be employed as often as it should be in military laboratories.

9. *Anamnestic reactions.*—These may occur in low titre in several diseases *e.g.*, pneumonia and sand-fly fever, but quite high titres may occur in typhus. Thus in a recent epidemic of typhus fever a titre of 2,500 against 'T.O' was recorded in one case, while titres of 320 were found on several occasions. Occasionally a bacteriologically proved case of the enteric group will fail to show a rise in agglutinins.

10. Thus the Widal reaction must be considered as only one factor in the diagnosis of the enteric group and it should fit in with the remainder of the clinical picture. The test must not be allowed to minimise the importance of repeated blood cultures in establishing the diagnosis. There can be no argument about a positive blood culture.

11. *The Weil-Felix reaction.*—Apart from typhus fever titres of 1:50 against 'OX2' and 'OX19' may occur, while a titre of 1:250 against 'OXK' is not uncommon. There appears to be no typical reaction to the Indian tick-borne disease. High titres against 'OX2' or 'OX19' are common findings, reaching their maximum in the third week and then tailing off slowly in convalescence. Figures of the order of 1:2,000 are common and much higher figures occur.

As stated above a rise against 'T.O' is not uncommon in typhus fever. Another anomalous finding is that the Brucella group is sometimes agglutinated.

12. *Brucella group.*—High titres against one or other of the Brucella group usually give the clue to diagnosis, but it is not possible to decide the infecting strain, owing to a considerable overlapping of antigens. Titres of 1:80 are suspicious, while titres of 1:1,000 are rarely met with apart from active infection.

Lt. Col. M. H. Shah then read his report on *post mortem* findings as follows:

POST MORTEM FINDINGS.

These were begin in November 1942 with the idea of determining the factors responsible for five deaths a day that were commonly occurring in my hospital. Nearly half of these cases came in a moribund condition and with little or no history. Personal contact with commanding officers enabled us to secure permission for making autopsies upon the required basis and this saved much time and trouble. They are now the regular routine and have proved of very great value in checking diagnoses, but they are the findings of physicians rather than of pathologists and serious laboratory work and section cutting have not been possible.

I shall give you the general findings in these autopsies. The period under review was from December 1942 to February 1943 and the figures for deaths and autopsies were as follows:

	Dec.	*Jan.*	*Feb.*	*Grand total.*
Total deaths	87	76	32	195
Total P.Ms.	73	67	32	172
The P. Ms. were upon:	*I.O.R.*	*A.P.C. unit*		*State Labour.*
	10	23		139

Cause of death	*Dec.*	*Jan.*	*Feb.*	*Total.*	*Percentage.*
Lung disease	25	27	12	54	37·2
Dysenteries:	..	..	..	..	22·7
Amoebic	13	4	2	19	
Bacillary	5	11	4	20	
Malaria	16	15	7	38	22·1
Meningitis	9	5	2	16	9·3
Other diseases	5	5	5	15	8·7

Taking the *post mortems* as a whole the following observations were made :—

1. Malaria was directly responsible for death in 22·1 per cent. of cases. Evidence of recent or active malaria was present in 60 per cent. of *post mortems*.

2. Emaciation was found to be present in 18·4 per cent.

3. Hookworms were present in 89 per cent. of a consecutive series of 100 bodies.

4. Round worms were present in 14 per cent.

5. Varying degrees of anaemia were almost universal but these could not be measured in the autopsy room.

Difficulties in diagnosis will be best illustrated by the recounting of a few cases :

1. A labourer from the 10th T.L.F. admitted in moribund condition as pneumonia. At *post mortem* gross emaciation, congestion of lungs, hook and round worm, infestation and active malaria of which he dies.

2. A labourer from the 18th C.S.L.F. diagnosed from exudate as bacillary dysentery. *Post mortem* revealed emaciation, dehydration, hookworm infestation and amoebic dysentery from which death occurred.

3. A case of M.T. malaria was found on *post mortem* to have meningitis.

Conclusions.

1. The majority were dying of diseases which were really terminal in malnourished, anaemic, hookworm infested men who had been suffering also from malaria. These should have been evacuated from the area to avoid overcrowding of hospitals.

2. Because of the high percentage of malaria, the quinine should be commenced in all cases without waiting for the result of the blood slide examinations. Col. Taylor is in agreement with this view.

3. In order to facilitate adequate medical and nursing attention all infectious and acutely ill cases should be collected in one ward.

4. The diagnosis of dysentery should be the responsibility of the medical officer in charge of the dysentery ward, who should have facility for instant examination of the stools as soon as they are passed. The examination of a really freshly passed stool was found frequently to provide the diagnosis at once.

5. Dahi-kichuri diet was found satisfactory and replaces the rice water feeds on an early case in cases of malnutrition. It was much appreciated and greatly benefited the patients.

6. By January it would be observed from the figures the diagnosis of amoebic dysentery had materially improved, but death from bacillary dysentery had considerably increased. It was found that the rigid enforcement of the two hourly saline treatment which had given excellent results elsewhere might have increased the dehydration in these cases. Accordingly castor oil emulsion and treatment with M & B 693 were commenced. Our impressions are that these treatments will be valuable, but dehydration continues to be our main problem.

7. Apart from the dehydration associated with specific diseases, dehydration appears to be chronically associated with malnutrition. In such cases the giving of intravenous salines does not produce the expected results and if intravenous therapy is pursued, oedema of the lungs tends to appear. It is hoped that with a better diet and copious drinks by the mouth checked up by the daily observations on the quantity of urine as has been advised by Brigadier Marriott this problem may be solved.

8. In the early days of our experience a few cases of malaria were found to have died of cerebrospinal fever. With the introduction of lumbar puncture for all cerebral malarias, no such case has escaped recognition.

9. Malnutrition has been said to be very common and some of the Indian labourers have frequently been found to be extremely emaciated. Yet there has been no evidence of beri-beri either in myocardial form or peripheral neuritis.

GENERAL DISCUSSION UPON THE PROCEEDINGS OF THE CONFERENCE.

Lt. Col. Seward read a letter from Col. Gardham regarding sigmoidoscopy which stressed the value of the instrument in diagnosing the carcinoma of the rectum with the skilful use of the instrument.

Brig. Marriott spoke on Col. Gardham's observations. Out of 3 cases of carcinoma of the rectum declared as such by experts two were found to be amoebic granulomas.

Lt. Col. Ransome asked "May I ask were these physicians, Sir, or surgeons who did the sigmoidoscopy ?" (Laughter).

Brig. Marriott. Both.

D.D.M.S. in concluding the proceedings said : "Gentlemen, We have had a most instructive, interesting and pleasant four days. We can, in the first place offer our congratulations to Col. Taylor on having arranged this and brought this meeting to pass. It is very pleasant to see Brig. Marriott here representing G.H.Q. and I hope he will realise what the Eastern Army medical personnel are doing. We have had a very large amount of useful information in these four day's which I hope wont fall on sterile ground. It is definitely our duty to go forth and spread the lessons to all those with whom we come in contact or to those who actively serve under us. I hope everybody will make a point of doing that.

As regards the question of looking at the individual cases and hospitalisation, dont let us get hold of men with whom there is nothing very much the matter. They wander here and there and go from bad to worse. They require severe handling. There is a great deal of actual malingering. Going round recently I saw a great deal of malingering going on. I want you people to sit on it absolutely. Not only medical malingering but surgical malingering also. There were 60 cases of wound of the hand, 20 on the left hand. In the stress of battle fellows get broken like that. There are again the conditions of the eye. There were recently 19 cases who had self inflicted conjunctivitis in one I.M.H. These are for court martial. If you hear of such a case recommend it for court martial.

Remember that we are at war. Our job is to produce men fit for service, whether in the front line or forward. The bulk of the hospital admissions are for trivial cases. The acute or the unusual case may be the most interesting. But let us also deal with the very trivial cases to the best of our ability and see that they are quite rapidly returned to duty. The junior officers who just come from civil practice are very much inclined to take the matter leniently. I would like you to make personal contact not only with such junior officers but also with the medical staff, the fellows who see the trivial cases and the early cases. I hate to preach about it but this is our job.

Last year the medical service did a magnificent job. All those who did it, I thank from the bottom of my heart."

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