THESIS for M.D.

MALARIA IN THE BALKANS

1916 to 1920

with illustrative Cases.

Submitted by

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INTRODUCTION.

In the accompanying thesis I discuss Malaria as I found it from the time of my landing in Salonika in August 1916 until my departure in January 1920.

My experience extends over work first in a Base Hospital, then in a Field Ambulance, then as a Regimental Medical Officer, next in the Mental Division of the British Salonika Force, and finally, in the summer and winter of 1919, at the only remaining hospital in Salonika.

STATISTICS.

In "The Lancet" of July 10th, 1920, Phear gives the following statistics. The total number of admissions to hospitals for Malaria during 1916, 1917 and 1918 amount to 161,560, which is equivalent to a ratio of 1053 per 1000: the ratios for the respective years being, 331 per 1000 for 1916; 353 per 1000 for 1917; and 369 per 1000 for 1918. These statistics do not include cases treated at Field Ambulance, but only at General Hospitals, Stationary Hospitals, and Casualty Clearing Stations.

I first landed in Salonika towards the end of August 1916. As there was a shortage of hospital accommodation, we were only given about a week in order to unpack equipment &c. and arrange accommodation in the building that was placed at our disposal, and then along came our first convoy of 200 to 300 patients - at that time we had no Sisters, so the duty of taking and recording temperatures devolved upon the individual officers.

Owing to the difficulties and rush in the Field Ambulances and Casualty Clearing Stations, these patients arrived without any clinical notes and without, in many cases, even an attempt at a provisional diagnosis having been made.

On questioning, I ascertained that in two or three days these patients had travelled a distance of about 50 or 60 miles from the Struma Valley, having passed through their own Field Ambulance and two or three Casualty Clearing Stations, spending not always as much as twelve hours in one medical unit. They reached the Base looking very ill, and simply smothered in dust from this long journey, which had been accomplished, in the first place, from Regimental Aid Post to Field Ambulance by mule litter or travois, or some such improvised /

improvised transport, and then by motor ambulance down the Seres Road.

To see them coming like this, getting out of the Ambulances, many as stretcher cases, and those who could stand unable to walk without assistance, was a pitiable sight, and an hour later the same men, having been bathed, given clean fresh clothes and put into a comfortable hospital bed with clean sheets, could not be recognised. Their whole outlook had been changed - they again felt they were human beings with someone to care for them, and this was a factor of no mean therapeutic value.

On examination I found that most of these men had a sub-normal temperature, and I was unable to obtain much from their histories, as with a total lack of knowledge of the conditions they had been in, and a failure to understand and elucidate the important points, I could come to no definite conclusion. It was appreciated that there was Malaria prevalent more particularly in the Field Ambulances and C.C.S's where these patients had been given some quinine - but there were no confirmatory physical signs, such as enlarged spleen or liver, as practically the whole of these cases were primary attacks.

At first I tried to believe that these patients did not all have malaria, but I only treated as malaria those /

those in whom I could feel an enlarged spleen, and the others I took to be influenza. This belief died a very sudden death on a few days' experience.

I did not have opportunity of studying my patients for any length of time as, if a man came in with a normal temperature but some history of fever, he was put on Quinine gr.10 t.d.s., if his temperature remained normal he was got out of bed in two or three days, given a few more days about the ward, and then after a week or ten days in hospital was sent to Convalescent Camp, probably only to be admitted to another hospital before two weeks were up, but of this fact I remained in delightful ignorance for a long time. If during this short time in hospital a patient took another rigor, he was marked for Hospital Ship and so packed off to Malta. In spite of this rapid turn-over of patients the work increased and increased, i.e. the numbers of patients steadily increased, the numbers of Medical Officers steadily decreased as they either went sick themselves or were posted to other units up country.

After I had been a month in Salonika I was looking after about 100 of these patients, and yet so far as I can remember, I only had one death. He was an oldish man who had been ill about a week before his admission to hospital. On admission he had a high temperature, looked very ill - was jaundiced and had a palpable liver and /

and spleen. He had been treated with quinine so no parasites were to be found in his blood, but he was treated as Malaria. Oral quinine was vomited, he was given intra-muscular quinine (with a hypodermic syringe and needle into the Deltoid) but did not respond, and Jaundice deepened. Intra venous quinine was thought of, I remember, but before this line of treatment could materialise he died. Ever after that I looked on jaundice when occurring in a case of malaria as a complication of grave prognostic importance, and in my three and a half years I never had cause to alter that opinion.

Intra muscular quinine was given thus early in my experience, and very quickly at that time I adopted the routine of giving all patients who had temperatures in the evening of 102 to 104 or 105 intra-muscular quinine as detailed above. In justice to myself I will say that I gave <u>all</u> my own injections, but others who were busier or less enthusiastic allowed the Sisters and others to give them. These, in the summer of 1916, were practically all given into the deltoids, and in many cases our asepsis was much of a makeshift, with the result that many abscesses developed and not a few musculo-spinal paralyses. As will be seen later, these unfortunate effects were blamed upon the poor Regt.M.O. and M.O. at Field Ambulances, when in the summer of 1917 an /

an attempt was made to refuse to allow these people to give intra-musculars.

After about six weeks of this work in a Base Hospital I was at a few hours' notice posted to a Field Ambulance in the Struma Valley, and a day and a half later I found myself 70 kilometres up the Seres Road and only a mile or so from the Struma river.

The first battle on the Struma had been two days in progress and many wounded had passed down the line. The Field Ambulance had suffered casualties, with the result that there were only two M.O. left, both of whom were well nigh exhausted with over-work and lack of sleep &c. Immediately after dusk I rode down to the Advance Dressing Station which had been established just on the left bank of the river, and here I remained on duty for over sixty hours alone, during which time the wounded continued to pass through, but in decreasing numbers. It was most interesting to observe that so long as the actual fighting continued, the number of cases of malaria that passed through the Dressing Station was practically nil, and I was able to obtain from the Regt.M.O's that this too was their experience. The troops I was with were regular soldiers who had come from France to Salonika in December 1915, and then after nine months in the country were having their first real fighting. The cause of this I am unable to state - excitement was no /

no doubt an appreciable factor in keeping the men going, and at those times for a man to "go sick" was regarded as more or less a slur on his character. Once the fighting subsided, the patients with temperatures of anything up to 105 or 6 or 7 began to roll in at the rate of ten to a dozen or more daily - many were very ill and no doubt had been carrying on for several days with the Malaria on them. Of course it was impossible to use mosquito nets or have anything like a complete parade for prophylactic quinine.

In the middle of November 1916 I got my second move. This time I was posted to a pioneer battalion - 26th Service Battalion of the Middlesex Regiment, which was destined to be my home for the next sixteen months.

Here it was, though so late in the summer, I first came into contact with the men returned from the Base whither they had been sent with Malaria. I vividly remember a few days after I had joined this Battalion being called at 10 o'clock one evening to see a man with a temperature of 105, who that very afternoon had returned to his battalion after having been several months away ill with malaria. He was promptly sent back to Field Ambulance next morning, and I saw him no more.

During the winter of 1916-17 I continued to see patients with relapses of malaria, but in the majority of /

of cases two or three days' quinine treatment sufficed, and it was not necessary to send them on to a Field Ambulance. This Battalion had only landed in the Balkans in August 1916, and though it was composed of many old men with low physical efficiency - one of my men had 50 years' service - yet their work, provided it was not drills or route marches &c. was wonderfully satisfactory. Their privations - considering their ages and disabilities - were severe, but they were able to march two or three miles to work, dig &c. all day and return again in the evening, often wet through, yet my sick parade rarely exceeded 2% or 3%.

Early in April 1917 began the pamphlets and circular memoranda of advice and instructions to Regt.M.O's in particular, which was destined to continue in increasing number and volume as the summer advanced.

First of all was the formation of parties for anti-malarial work. Surveys had to be made of so many miles round each camp in order to detect the likely breeding places for mosquitoes, and measures had to be taken to destroy these as far as possible. Next we were informed that no Regt. M.O. was to be allowed to administer intra-muscular quinine - which was later modified so that we Regt. M.O's had to proceed to the nearest Field Ambulance and there spend a couple of days watching someone who was supposed to be more experienced, and receive /

receive advice and instruction as to the correct procedure to adopt.

Then the dose of quinine per diem I first gave was gr.30, which later I increased to gr. 45, then to gr. 60, and finally my largest dose was gr. 80 a day.

So far as possible all troops were moved back from the Struma Valley for two or three miles away from the swamps and on to the foot-hills.

Mosquito nets were issued, and the daily administration of prophylactic quinine commenced. How much good was derived from this prophylactic method it is impossible to state as it was given to all troops, and so there were no facilities for control experiments.

Quickly after this came my first cases of malaria. A man would report sick in the morning, feeling not up to the mark and complaining of headache. As a rule there was no temperature, but he was given gr. 15 of quinine, put on "light duty" and told to report again in the evening, when the temperature was found to be elevated. I very soon had to stop this sympathetic treatment as I found that my sick parade began to get larger and larger. On going into this point I discovered that it had been found out by the men that if they reported sick and told the M.O. that they were feeling out of sorts and had a headache, he would give them "light duty". I was compelled to change my routine /

routine, with the result that these cases of headache &c. were marked Medicine and Duty and had to carry on with their full duty. My sick parade again came down to a reasonable number - it was very hard luck on the men who were genuinely ill and it was pathetic to see men who had been at work all morning come up with a temperature of 105 or thereabouts, but it was his comrades he had to blame and not his Regt. Medical Officer.

It was about this time that instructions were issued that in the more or less permanent summer camps - as mine was - a Regimental Aid Post had to be constructed capable of holding eight stretcher patients.

I started about May 1920 with a small Regt. Aid Post for eight patients, but as the summer advanced my accommodation increased until in August the approximate daily number of patients I had detained in the Aid Post was about 20. By this method I was able to treat 400 to 500 cases of malaria - most of them Primary - and it was only found necessary to evacuate to hospital 2% to 4% of these patients. The rough working rule that I adopted was that, apart from any outstanding or urgent symptoms, no man was evacuated unless his temperature remained elevated for 48 hours. For treatment all these patients whenever they reported sick and were found to have an elevation of temperature were given Calomel gr. 4, Quinine gr. 15, and detained. Quinine in /

in doses of gr. 45 per diem was continued. If I was in camp and saw a patient before he had had quinine I took a blood film which was sent to the nearest mobile laboratory, and in this way it was possible to confirm the diagnosis. In June, July and August, all the patients were found to be suffering from a benign tertian infection, and it was only towards the end of August that I got my first cases of malignant malaria.

By this method of detention in the unit with subsequent return to duty, the statistics of the cases of malaria were much altered, as these patients, including even those in whom had been found malarial parasites, were not reported as cases of malaria. During the summer the accommodation in Field Ambulances and in Casualty Clearing Stations in Corps Area was markedly increased, so that only the severest malarial cases were sent to to Base Hospital.

This camouflage of the cases of malaria was a very short sighted policy, as was shown at a later day as a result of these men receiving inadequate treatment, though under orders existing at that time they were supposed to receive Quinine gr.45 for three months after the attack was over. Personally I found it impossible to ensure that this was efficiently carried out as the men of the battalion were continually being despatched here and there throughout Macedonia, often in small parties /

parties and so with no reliable person to supervise the correct administration. Poor men in many cases who had for months to continue with this quinine treatment - more often than not it was the powdered quinine in scoop-fuls that they had to take and try to wash down with some water. If happened to be placed near a Field Ambulance quinine in liquid solution could be obtained, but tablets were practically unavailable and not recommended by the authorities. What few tables could be obtained were kept for the more serious patients who were inclined to vomit, and later on a small supply of quinine bihydrochlor tablets became available which were of very great benefit for the treatment of these more serious cases.

Cases of malaria combined with diarrhoea were always serious, and I never lost time in sending these patients to the Field Ambulance.

Early in this summer "Malarial Cards" were brought into circulation. I attach a copy of one of these cards from which it will be seen that the idea was that they might contain the whole of a man's malarial history, but in practice I found that this did not work out, as each Medical Officer had more or less a particular method of writing up the card which did not always give the necessary information to the next. Added to this was the fact that the men were continually losing their cards /

Copy of "Cards" issued to Patients.

FRONT.

MALARIAL DETAIL SHEET belonging to ..
(Name).....
Fever ceased..... Where treated.....
Blood Examination.....
Is infection primary?..... No. of relapses.....

Inclusive dates	Daily dose of quinine	No. of days given	Signature of M.O. & Where treated.

You must report again:- ....
You must report again:- ....

BACK.

INSTRUCTIONS TO THE MALARIAL SOLDIER.

1. This card must be kept in your pay-book.
2. Report to the Medical Officer as ordered on the other side of this card
3. On transference during treatment from one camp to another you must report the next morning to your new Medical Officer.
4. Failure to continue treatment with quinine for at least 3 months means that the fever will in many cases return.
5. Relapses are favoured by chill, wet, alcoholic excess or too early stoppage of quinine.

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cards.

So the summer continued, but in September my difficulties increased as the unit I was with was split up into four different parties, each several miles distant from the other, so that it became impossible to keep in close touch with the patients, and an increased number had to be sent to Field Ambulance.

A point that was continually brought home to me was the many different symptoms complained of by patients at the commencement of an attack of malaria - one man would be brought up obviously looking ill, hardly able to stand, and yet his temperature would be found to be only 100° or thereabouts, and a few hours later another man would come to the Aid Post complaining of feeling hot and rather light-headed - would be obviously flushed with temperature anything up to 105°.

During this summer the highest malarial temperature that I recorded was 106·8.

Early in the summer I was very careful of the first batch of patients that I treated myself - I had no precedent as to how soon they would be fit to resume full duty, but as the numbers increased it was not possible for me to give much individual attention to a man once he was sufficiently recovered to be discharged from my Aid Post. At first I did not mark them as fit for full duty until at least a week had elapsed since the last recorded /

recorded elevation of temperature, but quickly found that in the average case two to three days was quite sufficient. It was an undoubted fact that provided these patients could be got to a certain pitch of convalescence without having to be sent from the unit, thereafter the recovery to full health was very, very much more rapid than at any convalescent or rest camp.

Towards the autumn of 1917 when the cases of malaria were more often relapses than primary attacks, the routine that I adopted was some such as this - a man reported one evening with a temperature of say 102 - he was given Calomel gr. 4 and Quinine gr. 20 - he received instructions to report sick the next morning when the temperature would usually be found to be normal. He was marked excused duty - given Quinine gr. 20 and told to report himself again in the evening. Usually there was still a normal temperature in the evening, and another dose of Quinine gr.20 would be given. He appeared again on sick parade the second morning - was given Quinine gr.20 - marked light duty - another dose of Quinine gr.20 was given that night. He was seen on sick parade the third morning - given a sixth and final dose of Quinine gr.20 and marked Medicine and duty. This system I found to work quite satisfactorily and the man received in all 120 grains of Quinine for each relapse.

Later /

Later I still further increased my Quinine dosage and gave it in 40 gr. doses as follows:- 1st evening, Calomel gr.4, Quinine gr. 40, Liq. Strych. Hydrochlor, m.4 - following morning a second Quinine gr. 40 with the Strych. and again in the evening, i.e. in 24 hours a patient received 120 grs. of Quinine. The Strychnine was given on the belief that had been expressed to me that it prevented the occurrence of Quinine amblyopia. I believe the idea was that the amblyopia was due to an acute dilatation of the vessels of the eyeball and the action of the strychnine was to keep up the tone of the vascular system. I have never been able to ascertain if there is any ground-work for proof of this. All I can say is that during the few weeks I tried this method of treatment I did not have any amblyopia develop in my patients. This is of interest in that Phear in Lancet of July 10th 1920, quotes the case of a man who developed severe quinine amblyopia after quinine gr. 55 one day, quinine gr. 40 the second day and quinine gr. 20 the third day. I was unable to continue the treatment as I at this time left the battalion to go to a General Hospital at the Base.

About February 1918 the "Y" Scheme was first brought into action. This was an arrangement whereby men who were riddled with malaria, were unable to continue at their full duties, but without being sufficiently ill to warrant /

warrant continued hospital treatment, could be brought before the A.D.M.S. of the division, and if passed by him sent down the line in order to be evacuated to England by the ordinary routes and not as patients from hospital. This scheme was very welcome in that it allowed me to get rid of chronic cases of relapsing malaria who showed no signs of improvement and would have certainly crocked up probably for life if allowed to remain for another summer in Macedonia. Of course the man's physical condition had to bear our the history as he had to be passed for inclusion in the "Y" Scheme by senior R.A.M.C. officers who could not have the individual knowledge that the man's own Regimental M.O. had. To cite an example, I can clearly remember one of my patients who was the Battalion Goal-keeper. Football was a recreation of much enthusiasm and the competition amongst the different units was of the keenest. Well, this goal-keeper I treated during practically the whole of the winter of 1917-18 for relapsing malaria of fortnightly occurrence. Much pressure was being continually brought to bear on me not to send this man away, to which I gave way. The surprising thing was that this man's physical condition remained extra-ordinarily high. He never became anaemic even to a slight degree, but remained full blooded and healthy looking, and I have seen him play one of his best games only a day or two after a relapse /

relapse. In fact during the whole of this winter I do not believe he missed more than three or four games though there was a match practically every week.

At the end of March 1918, just as precautions &c. were being commenced for another summer's malaria, I got a move and was sent down to a Base Hospital to work in the Mental Division of the Salonika Army.

The Mental Division, under the administration of Maxwell Ross was a self contained place for the accommodation of approximately 150 patients. Until the time of the Armistice when the number of troops was reduced our average admission rate was one patient per day. Practically all the patients were sooner or later evacuated to England - those who exhibited any symptoms of Mental Disease as mental patients and others not exhibiting mental symptoms after careful observation, and at the same time not malingering, were evacuated as ordinary medical cases. The feeling being that if a man had been sufficiently ill to warrant his being sent for observation as to his mental state, then Macedonia was no country for him to remain in. It gave us an immense advantage in treatment to be able to give full assurance to a patient, in whom early signs of mental disease had been detected, that he would be sent to England. This we were able to do as mental patients had not to come before a general invaliding board /

board and so there was no danger of our decision being reversed by a senior officer as was liable to occur with the ordinary medical and surgical cases. It is most gratifying to be able to state that an improvement was observed in something like 90% of our patients as a result of the 2 or 3 mos. treatment they had prior to their embarkment for Malta and thence to England. Malaria as a factor of either predisposing or exciting character in the mental diseases was very obvious in a high proportion of cases but Maxwell Ross made detailed observations which are yet to be published.

During the summer of 1918 I can remember having at one time 4 patients with more or less severe self-inflicted wounds of the neck, not one of which was a genuine case of Melancholia but every one was a Malarial psychosis of one or another variety.

As evidence of the Malarial factor in mental disease I give short notes of a few of my own patients:-

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C A S E 1.

Pte. J.S. Age - 23. Service - 2 yrs. Macedonia - 1½ yr.

Admitted - 18-7-18

History prior to Admission:- Admitted from 21st Stat. Hosp. as N.Y.D. Mental and Malaria recurrent.. His R.M.O. states that patient appeared to suffer from a fixed delusion that his comrades wish his death, also that his conduct for some days has been strange. This patient had had previous symptoms of unstable mental equilibrium about 18 mos. ago and a second attack about 3 mos ago..

On Admission:- Quiet and oriented. Answers questions quickly and readily. Denies all above delusions and simply says that the heat is too much for him..

Physical Examination:- Slight anaemia. Spleen palpable on deep respiration. Coarse tremors of hands..

20-7-18 - Eating and sleeping well. No active signs of insanity.

6-8-18 - Tooth extracted this a.m. - under local anaesthesia. At noon suddenly became hallucinated and then depressed and thought he was to die. Temperature at 5.0 p.m. rose to 101·6. Blood Film showed presence of B.T. parasites.

9-8-18 - Improved - now as before relapse.

Personal History:- /

Personal History:- Working in hat factory before the War.

Family History:- Nil. Habits:- Moderate.

Previous Health:- Nil in civil life. Malaria Sept. 1917 in hospital. Since then about 10 relapses, and several times in Fd. Amb.

Present Illness:- Admitted 83rd Fd. Amb. in 15-7-18 with recurrent Malaria and then to 21st Stat. Hosp. where he was for three days. Denies above quoted delusions but admits having "shivers" almost daily at this time. General intellectual faculties weak - unable to read or write. Oriented as to time and place.

31-8-18 - Evacuated to Hosp. Ship as "Confusional Insanity and Malaria" having not had any further relapses.

C A S E 11.

Pte. T.C. Age - 34. Service - 4 yrs. Macedonia - 2 $\frac{9}{12}$ yr.

Admitted - 14-8-18

History prior to Admission:- Admitted from 25th C.C.S. with a history of attacking others with a stick during the night - tearing his mosquito net and coming on parade without puttees. Has had several malarial attacks. At 25 C.C.S. was quiet and normal in behaviour and only complained of feeling run down.

State on Admission:- Complains of being "run down". He has had about 12 malarial relapses and also dysentery: in 10-8-18 was classified 'B1' as "Post-Malarial Debility". He is clearly oriented and quite open and frank in conversation. He appears worried and looks more than his age.

Physical Examination:- Some anaemia. Spleen - enlarged and palpable 2 finger breadths below costal margin, hard and tender.

21-8-18 - Patient has temp. of 102·4 this evening and tells me that he feels as he usually does when he has a malarial relapse. Spleen is enlarged and in respiration comes down to umbilicus. He is mildly confused and slightly excited.

Blood Film - B.T.parasites.

31-8-18 - Evacuated to Hosp. Ship as "Confusional Insanity and Malaria".

C A S E 111.

Spr. W.D. Age - 42 Service 3 yrs. Macedonia 1½ yr.

Admitted - 11-9-18

History prior to Admission:- At present under a charge of (1) Absent from duty. (2) Drunk in camp. Sent to Hosp. for observation as he appeared to be surrering mentally and might have done himself further harm. He had shell shock in France in Nov. 1916. At Fd. Amb. he was confused and melancholic and unable to account for cuts on his arms.

State on Admission:- Tells me that he has been much troubled over some home affairs. At times has had headaches when he could not carry on with his work, and 2 or 3 times has lost control of himself. Says cuts on arms were done by barbed wire.

Physical Examination:- Several superficial cuts and scratches on fore-arms. Not anaemic. Spleen enlarged but not tender. Mouth septic and tongue deeply fissured.

12-9-18 - At 4.0 p.m. temp 101·4 . Spleen now tender. Slight mental confusion and nervous with a tendency to ramble. Intra-muscular Quinine gr.20

15 - 9-18 - Temp. remains elevated. Mental condition slightly more advanced than on 12th.

19-9-18 /

19-9-18 - Benign tertian malarial parasites in blood. Still has mental confusion..

26-10-18 -

Personal History:- General labourer. Enlisted Aug. 1914. Invalided from France in April 1916 with "shattered nerves".

Family History:- Negative.

Present Illness:- He is unable to tell me anything. Does not remember leaving his unit, but remembers having been 3 weeks in hosp. with Malaria. Only a very hazy recollection of what happened during his malarial attack last month.

8-11-18 - Evacuated by Hosp. Ship under a diagnosis of "Confusional Insanity - Malaria" having been free from attacks since September.

C A S E IV.

Pte. J.E.M. Age - 30. Service 3 ½ yr.
Macedonia 2 ½ yr.

Admitted - 18-5-18

History prior to Admission:- Came from 28th C.C.S. with an incised wound of the neck. He was admitted there on 8-5-18 with recurrent Malaria and no mental symptoms were noted. Patient was reported missing from his ward at 22.20 hours on the same evening. At 15.36 hrs. on 15-5-18 patient reported to the police Corpl. saying "I am M— look what I have done to my neck". He had an incised wound across the front of his neck and was unable to give any account of his actions whilst away.

On admission:- Pat. appears haggard, worried, tired and depressed. Is oriented and does not appear confused. Says that he cannot remember any details of what he did during the week he was away from the C.C.S.

Physical Examination:- Emaciated and anaemic. He has an incised wound of the front of the neck about 1½ inches long across the front of the thyroid cartilege. There is a small puncture wound with discolouration around in the left axilla and two similar ones in the right iliac region. The spleen is palpable 1½ inches below /

below the costal margin.

1 - 6 - 18.

Personal History:- Labourer. Single.

Family History:- Maternal aunt insane.

Previous Illnesses:-Seven attacks of Malaria and only once in Hospital.

Present Illness:- Went to hosp. feeling "queer" and with shiverings and sweatings. Remembers leaving his ward at 28th C.C.S. in order to go the latrines, as he felt he was going to vomit. He vomited and really can tell nothing from then - he does not even remember leaving the latrines. He recollects nothing he did during the seven days he was away, but so far as he can remember saw no Britisher and had nothing to eat.
He has no recollection of any such previous attack.

6-6-18 - Temp. elevated. Blood film - B.T. parasites. Slight mental confusion.

18-7-18 - Still feels nervous and depressed. Memory poor and concentration bad. Admits that in his previous malarial attacks his headaches were almost more than he could endure.

15-8-18 - Admits feeling muddled in the head during the attack last month. He remains listless and apathetic.

17-8-18. Evacuated to Hosp. Ship under a diagnosis of "Confusional Insanity assoc. with Malaria".

C A S E V.

Lieut. R.B.M. Age - 36. Service 3 $\frac{6}{12}$ yr. Macedonia $\frac{6}{12}$ yr.

Admitted - 12-10-18

History prior to Admission:- Transferred from 50th General Hospital under a diagnosis of Malaria and N.Y.D.. Mental.

State on Admission:- Mildly confused and excitable: Rambling in speech from topic to topic.. Illness started with shivering and sweating &c. on 4th and he was sent to C.C.S. on 12th inst.

Now he tells me that the world has entirely changed with reference to the atmosphere. This occurred about 3 nights ago and took only the smallest fraction of a second in time. The world's scientists realised about 3 days before this happened that it was to occur and consider patient as the medium and responsible for it all and for saving the world from destruction. He describes himself as the axle of the whole business. He informs me that Portsmouth was blown to bits last night. He has no insight into his condition.

Physical Examination:- Temperature 101·4. No Anaemia. Spleen 1 inch below costal margin.

13-10-18 - After I left him yesterday he became hallucinated /

hallucinated - was talking to his wife and told the orderly he could hear church bells ringing. Mental condition unchanged this a.m., but his temp. is normal.

18-10-18 - After his first two days in here this officer rapidly picked up. He is now convalescent from his mental symptoms; has a thorough insight into his condition and realises the absurdity of what he told me. Still his mental equilibrium is not fully regained and he will need further treatment.

Boarded for evacuation by Hosp. Ship as a mental case.

24-10-18 - Evacuated.

C A S E V1.

Pte. J.P. Age - 25. Service 5 yrs. Macedonia $2\frac{8}{12}$ yr.

Admitted - 22-6-18

History prior to Admission:- Found wandering about Infantry Base Depot at night and it was unable to obtain any information from him. Sent to 64th Gen.Hosp. the same day (21-6-18) Temp. 100·2 and could give no account of himself - believed he was in Canada. Was "nervy" and did not know where he had been living.

On admission:- Although not able to remember anything but a few sketchy details in his history, he knew how much money he had in his possession down to a drachma and corrected the orderly who at first had checked it wrongly.

Physical Examination:- Well developed. Anaemic and rather jaundiced. Spleen to 8th rib in anterior axillary line and palpable 2 inches below costal margin.

Blood Film - Banign tertian parasites present.

31-7-18 - Isolation &c. revived his memory almost completely in a week.

Personal History:- Was in Canada before the War. Wounded and gassed in France in May 1915.

Family History:- Mother died in an Asylum.

Previous Health :- /

Previous Health:- Pneumonia - May 1916. Dysentery in June 1916 and sent to Malta. First attack of Malaria in August 1916. Has had 15 relapses within the last six months.

Present Illness:- Patient remembers being with his battalion on June 16th. He had had a malarial attack on June 13th when he had been given 3 days excused duty. He cannot remember more until he found himself in bed in the Mental Division here.

In July 1917 just after an attack of Malaria patient put in an application to revert from rank of Corporal (which he then held) to Private. He did not remember doing so and was very surprised to hear of it a few days later. He had no reason to desire to revert so far as he knows.

Since he had had all this Malaria, patient admits that he has become moody and it requires an effort to keep his spirits up. He has worried a good deal about his stripes.

Previous to all this his memory was excellent, but during relapses of malaria his memory has been very hazy. Now he can remember better what happened a year or so ago than he can of what occurred a week ago. Concentration is fairly good. His self-confidence is somewhat lacking. He sleeps well but suffers from frontal /

frontal headaches.

8-8-18 - Patient had a rigor this a.m. but temperature did not go up; he was very confused, restless and hallucinated.

9-8-18 - Fairly rational again today.

15-8-18 - Between his malarial relapses patient is quite free from mental symptoms. To be sent home as a "mental case."

17-8-18 - Evacuated by Hosp. Ship.

The first six cases have been chosen more or less at random from a collection I have but they illustrate in a striking manner the general types of case met with in association with Malaria. In all of these cases it will be noticed that mental confusion was present. Confusion was the form of mental disorder to be observed in a very high proportion of these Malarial patients. As an additional symptom depression will be noticed to have been present in Case 1., Case 111. and Case 1V. Wandering was a symptom which caused not a few patients to be sent for mental observation and Case 1V and Case V1 exemplify this. In no case could a patient after recovery from an attack of malarial confusional insanity remember what had happened. I cite in Case 1V a patient who was a week away wandering and afterwards was unable to give any account of his doings during that time.

Forrester in an article in "The Lancet" of Jan.3rd 1920 divides his cases of Insanity of Malaria into two groups - those associated with an actual attack of Malaria and those as the result of repeated attacks - but his differentiation is not always very clear. According to his division the cases I have quoted will fall into the first group.

C A S E V11.

Pte. L.T. Age - 35. Service 3 $\frac{10}{12}$ yrs. Macedonia $\frac{6}{12}$ yr..

Admitted - 25-7-18.

History prior to Admission:- Transferred from 63rd.. General Hospital as "Confusional Insanity". Patient was admitted to 63rd Gen. Hosp. from 21st Stationary Hospital on 9-7-18 - diagnosis "Malaria Primary".. He had a temperature of 99·4 on the evening of 9-7-18: was in wards of 63rd for 7 days (until 16-7-18) and complained of weakness. Improvement occurred and he was transferred to the Convalescent Lines on 16-7-18. On 24-7-18 patient looked flushed: temperature 100·8 and he appeared dazed, confused and apathetic.. On being asked how he was, he stated he was being insulted but was unable to say in what way.. In evening given intramuscular quinine. During night of 24th - 25th he was very restless, at times wild and did not get any sleep. On 25-7-18 was still dazed and confused. His eyes were more bulging, pupils equal and reactions slow. Face smooth with absence of naso- labial furrow. Oscillatory movements of eyeballs were noticed and lips and tongue tremulous.. He had forgotten his age and was quite apathetic to his surroundings.

A /

A blood film taken on 8-7-18 was reported as "no parasites found".

Atate on Admission:- Admitted to Mental Division at 6.0 p.m. with above notes in an unconscious condition with stertorous breathing &c.: was wet and had incontinence of urine during journey in motor ambulance.

Physical Examination:- Patient lies on his back profoundly unconscious, eyes half open, deviated upwards. Pupils moderately dilated, equal and irresponsive to light. Breathing rapid: stertorous in time with rattling of mucus in throat. Face and eyes deeply congested. Well marked cyanosis of ears, lips &c. Pulse very rapid, regular and easily compressed. Heart sounds inaudible being masked by low rhonchi and rales all over chest. The liver appears normal and spleen is not palpable. Patient incontinent. Both K.J. are present - left more active than right. Both ankle jerks present. Plantar responses flexor. On deep pressure with pin patient withdraws his legs slightly. On stimulation of his conjunctivae he moves his left hand and left leg, but his right hand and right leg remain immobile. The right arm is completely flaccid but not the left.

Patient appears practically moribund.

Blood /

Blood film to laboratory.

Treatment - Camphor - gr.1ii statim.

Intra-venous quinine delayed for blood film on account of patient's extremely critical condition. Lumbar puncture impossible without an anaesthetic, and at the moment the administration of any anaesthetic is out of the question.

7.15 p.m. - When given the hypodermic of camphor the patient forcibly moved both arms and both legs and required quite a degree of restraint. Bowels moved in bed.

Bacteriologist reports that no malarial parasites are to be seen in blood film.

9.0 p.m. - Temp. risen to 102·8 - ether anaesthetic - about 30 c.c. of cerebro-spinal fluid withdrawn by lumbar puncture. Fluid clear but under a definite increase of pressure. Cells 30 per c.m.m. - no organisms.

Given intravenous quinine - gr. 15 in saline and also 2 c.c. of camphor in oil.

Patient stood lumbar puncture and intra-venous quinine well.

Urine contains albumen and reduces atypically Fehling's Solution.

26-7-18 - Patient had a fairly good night: slept at /

at intervals for about 4 hours - appeared much better at 1 a.m. when he suddenly started to talk quite rationally. He was given a small quantity of milk and water which he took freely and during the night consumed about ℥ xii of this. At 3.0 a.m. he complained of pain in stomach - he was tried with the bed-pan which he was unable to use and repeatedly asked for the stool. This was brought to his bed-side, and he was assisted to sit on it. He had a good motion which gave him much relief, and he also had three large black fluid motions in bed.

At 10.0 a.m. - He is quite clear mentally today. Congestion of face completely gone. Tongue dirty: Pulse accelerated with regular movement, volume and tension. He complains of pain round pericardium and aching in his head in coughing. Speech deliberate, rational, toneless; face expressionless and and relatively immobile. No paralysis or paresis. K.J. and A.J. active and equal. Plantars flexor - No anaesthesia or analgesia. Lungs - clear. Liver - normal. Spleen - not palpable. Heart - within normal limits: slight systolic bruit at mitral area.

Treatment - Champagne - 4 hourly.

Intra /

Intra muscular quinine - gr. 20 twice..

Second blood film - negative.

Polymorphs - 77·6%. Large lymphocytes 2·0%

Small lymphocytes 12·8%. Large mononuclears 7·6%.

Evening - Patient has had a fairly good day and has taken nourishment well but vomited a little at 12.40

Urine - Acid Sp. Gr.. 1018. Albumen + no sugar &c.. Mucus deposit.

27-7-18 - Comfortable night - 7 hours sleep. This morning patient looks brighter. No confusion.

Intramuscular quinine - gr. 20 and to have quinine gr. 10 t.d.s. per oram..

He has had a good day and is making progress.. He vomited slightly about mid-day. This evening there is definite splenic enlargement to be made out for the first time and the spleen is palpable two finger breadths below the costal margin in deep respiration.

11.00 p.m. - Not so well. Temp.. 100 and though he has no definite complaint he admits he does not feel so well.. Pulse only fair but he is quite clear mentally.

Intramuscular quinine - gr. 20.

Blood Film. - No parasites seen - Polymorphs - 64·3%

Large Mononuclears - 19·6%. Small Lymphocytes - 8·6%

Large Lymphocytes 7·0% and Eosinophiles -·5%

28-7-18 /

28-7-18 - Temperature fell after intramuscular injection and he had a good night sleeping 7 hours. This morning his mental condition is quite clear and physically he is about the same as he was last night. He complains of pain across the back and in the region of the spleen. Intramuscular quinine - gr. 20 and to continue oral quinine.

Evening - Some mental symptoms have asserted themselves during the day: slight confusion with disorientation in space. Intramuscular quinine gr. 20.

29-7-18 - Patient had a good night and slept well. Temp. normal. To have 01. Ricini with Tinct. Opii m.10. His spleen is large and he still complains of pain in that region. Mental symptoms not so marked but there is some slight confusion.

To have quinine - gr. 10 t.d.s.per oram.

Laboratory Report on Urine - Hyaline, granular and epithelial casts present. No R.B.C's. observed.

30-7-18 - Patient took oral quinine gr. 30 yesterday he vomited his dose at mid-day but was given another dose an hour later which he retained. He had 8 hours sleep last night and today shows further improvement. His spleen extends from 7th rib to 3 f.b.below costal margin in mid-axillary line and on palpation is slightly tender. /

tender.

1-8-18 - Improvement continues. No mental symptoms for 2 days. Spleen as before. Having quinine gr. 30 daily by mouth.

4-8-18 - Patient not quite so well yesterday. He complained of headache. Quinine administration stopped - given Asperin gr. 10 at night which relieved pain. This morning he is better again.

5-8-18 - Albumen in urine too small to estimate by Esbach's method.

6.0 p.m. - Temperature 100° Patient complains of headache &c. but is perfectly clear mentally. Given Calomel gr. 3 and Quinine gr. 20.

Blood - Film - no parasites seen.

6-8-18 - Vomited twice after quinine last night but this a.m. temperature down and patient somewhat better. He complains of slight headache.

10-8-18 - Patient continues to improve satisfactorily. Yesterday no albumen could be detected with the cold nitric acid test and microscopic examination showed a very few hyaline casts and no blood.

17-8-18 - Progress satisfactory. Urine remains free from albumen. He is now on chicken diet. There are no mental symptoms. Spleen is still palpable and

at/

at times he complains of dull pain in that region.
The spleen is soft and only very slightly tender.

21-8-18 - Improvement continues. Patient has been up for a short time for the last two days.
Put on week-end Quinine - i.e. gr.20 t.d.s. Sat. & Sundays.

27-8-18 - Slow steady improvement. Now spending most of his days out of bed and his strength is gradually returning.
He gives the following history-

Personal History - Belongs Cheshire. Iron packer in civil life. Married with six children. Salonika - Jan. 1918. Not served on any other front.

Family History - No insanity.

Habits - Moderate. Denies venereal disease.

Previous Illness - No serious illness but states that he has never been strong.

Present Illness - He was sent to Field Ambulance from his unit after he had been three days ill. This was his first attack of Malaria. He came down to 63rd. General Hospital. He remembered going to their Convalescent lines and reported to the Sister that he felt queer, as if the Malaria was coming on again.

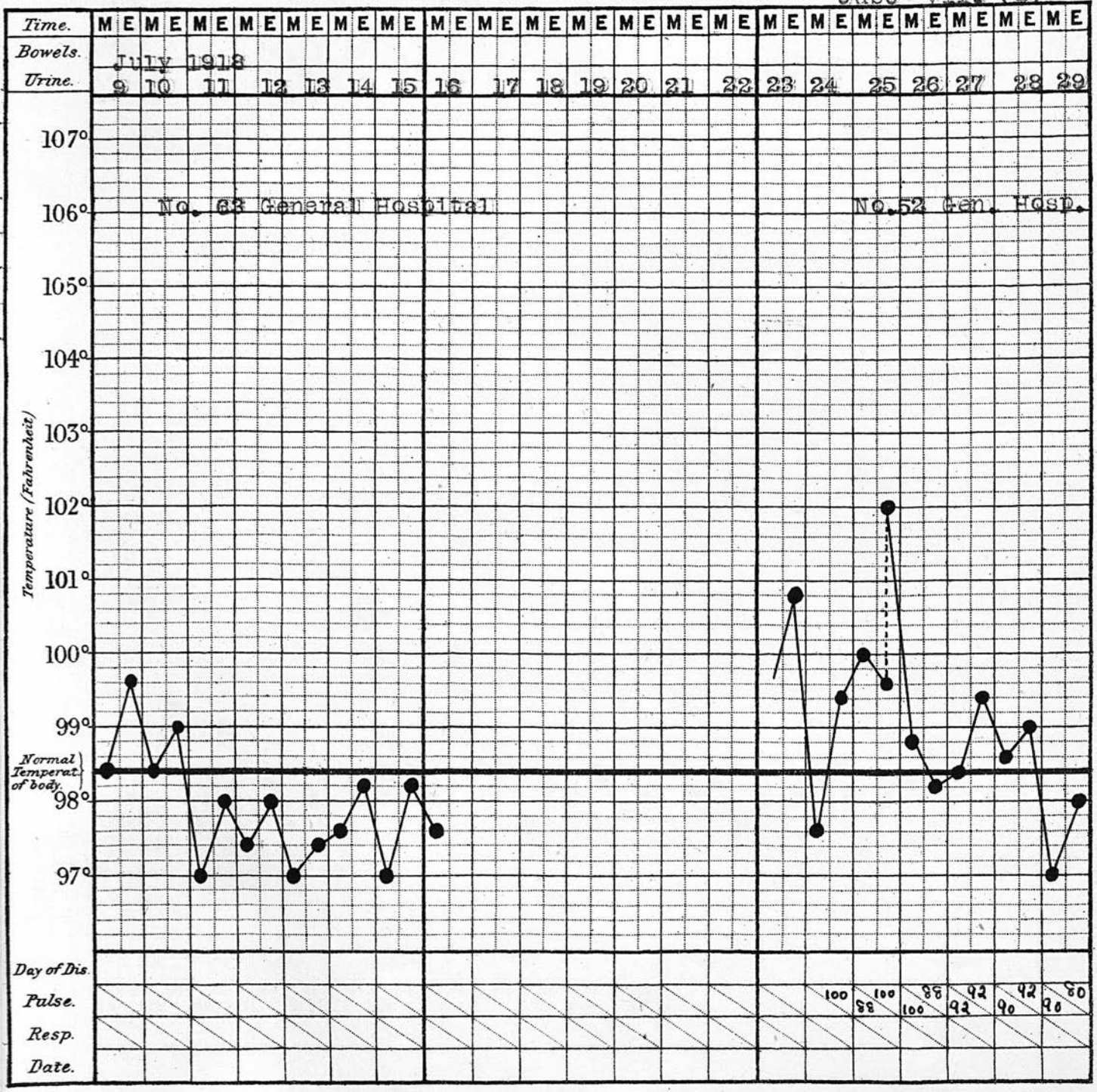
He /

He does not remember any more and does not remember the first day after he came in here.

Now he expresses himself as feeling alright except for his general weakness.

Transferred to Medical Division in order that he may be evacuated to England as an ordinary medical case.

THE MEDICAL SUPPLY ASSOCIATION. Case VII. (a)



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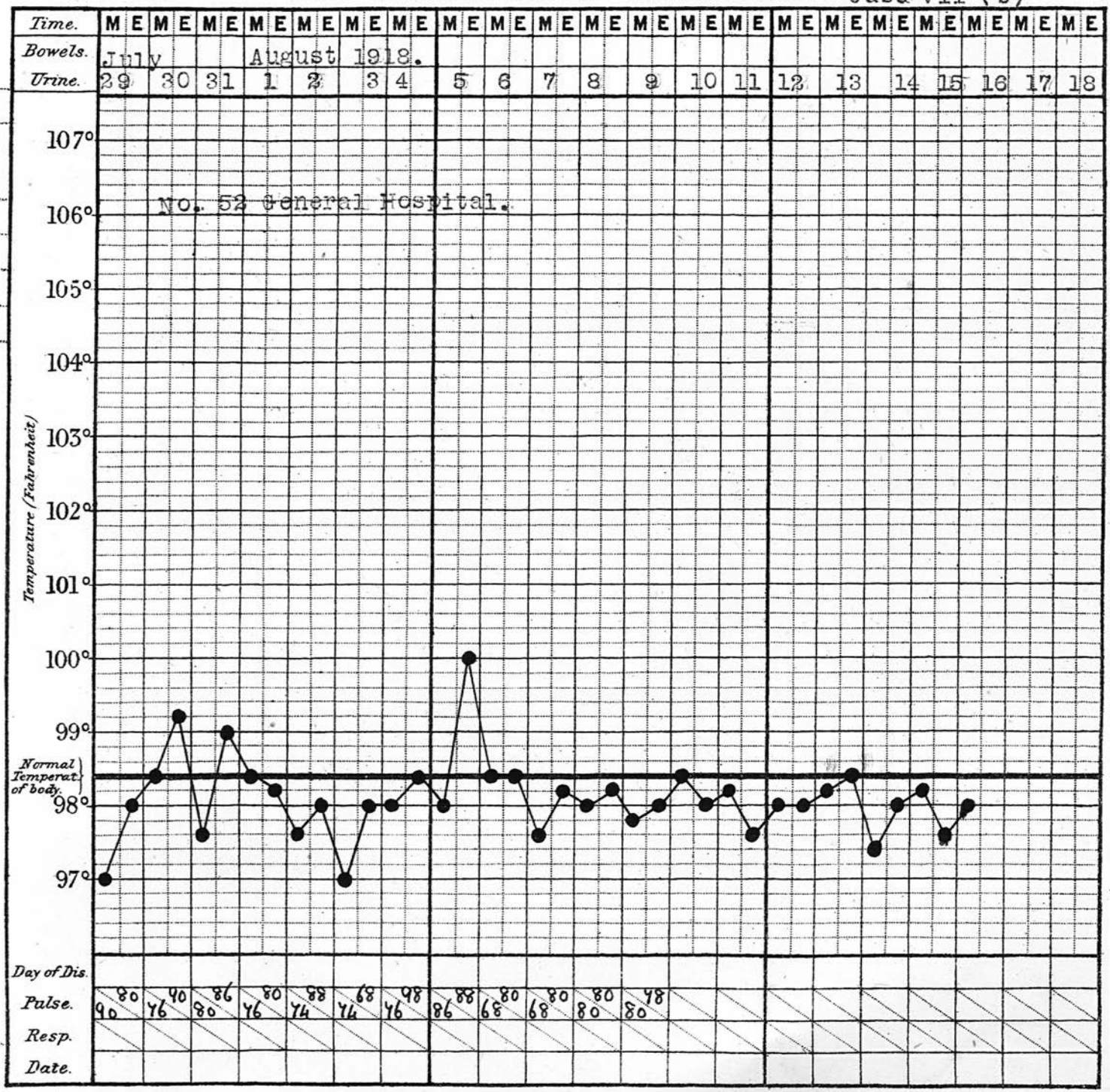
THE MEDICAL SUPPLY ASSOCIATION. Case V11 (b)



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This case even though it was at one time looked upon as a mental case and sent to the mental division can hardly be classified as such, but I record it in full as it illustrates several unusual points difficult to explain.

In the first place in reading the case through it will be noted that at no time were malarial parasites found in the circulating blood. This I am unable to explain unless it be due to the large dose and heroic quinine treatment the patient received, as all the films were examined by a bacteriologist of good experience and knowledge of malarial parasites.

Secondly, splenic enlargement was only observed after the patient had been in hospital for two days. This, no doubt, was due to the spleen being too soft and too deep to be made out on any of the previous clinical examinations.

Another interesting point is brought out in connection with the differential leucocyte counts on 25-7-18 and on 27-7-18. The first of these shows 22·6% mononuclear leucocytes (including 7·6% large mononuclears) and the second count a total of 35·2% mononuclear leucocytes. The Medical Annual for 1920 quotes V. Schilling /

Schilling (Deut. Med. Woch. 1918 XLIV. 1184) as finding a well marked mononuclear leucocyte increase so characteristic of malaria as to enable all cases to be detected by a blood examination in the absence of parasites due to quinine treatment.. One is entitled to say that, in the second count, at any rate, there was a definite increase of mononuclear leucocytes..

The vague ill defined symptoms pointing to a lesion of the nervous system, which were often to be observed in intense and chronic malarial infections are instructive and these were undoubtedly relieved by the lumbar puncture which, though of negative diagnostic value was of very definite therapeutic value in that it relieved the increased intracranial pressure.

The immense value of the intravenous injection of quinine is obvious but this method of treatment I shall discuss later.

It will be observed that with the exception of Case VII there is practically no record of the treatment of these cases of Malaria. This I have not inserted as my treatment was so much a matter of a broad routine basis that it does not warrant note in individual cases..

A patient with a simple Malarial relapse was put on Quinine gr. 15 t.d.s. By a simple Malarial relapse I mean a sudden elevation of temperature accompanied by the usual signs of shivering and sweating in the evening which temp. dropping in the morning not to rise again.. To continue - this 45 grs. of Quinine daily was given to the patient for a matter of 2 weeks and then he was put on an Arsenic and Iron mixture and "week-end Quinine" By "week-end Quinine" is meant Quinine gr. 15 t.d.s. every Saturday and Sunday, which is referred to by Phear in an article in "The Lancet" of January 24th 1920.

This "week-end" method of treatment, amongst many other methods, had been tried in the hospital to which I was attached in research into the treatment of Malaria and prevention of relapses i.e.. total cure.. The giving of Quinine on Saturdays and Sundays to chronic cases had been found to be as effectual as any other method and was certainly better tolerated by patients than /

than giving a daily dose even though it were a small one (see article by Gunson and others "The Lancet" June 22nd 1918)

If a patient did not respond to oral Quinine in 24 to 36 hours then an intra-muscular injection was given into one or other buttock. The point of Quinine abscess still featured and I among others came to the conclusion that this might be due to a descending infection along the puncture caused by the needle. To prevent this it became my routine to seal each puncture with a crop of collodium and then put on a small sterile dressing which was held in place by a strip of adhesive plaster. Of what benefit this was I do not know, all I can state is that so far as I know I never had an abscess develop after an injection given by myself.

Other cases which called for intramuscular injections were patients who vomited oral quinine, or who showed signs of developing delirium or acute mental symptoms.

Patients not presenting any of these definite symptoms, but at the same time obviously not responding to oral quinine were also treated with intramuscular injections /

injections - Vide, Gunson, Winning, Johnstone, Porter and Scott, "Lancet" June 22nd 1918. ~~+~~ Wiltshire in the R.A.M.C.Journal of September 1919 sums up the effects of intramuscular quinine as (a) It improves prognosis of life - (b) It is more certain in action during acute stage of disease - (c) It adds greatly to the chance of effecting a true cure of the disease.

Another line of treatment that was found distinctly beneficial in some cachectic cases who frequently ran a very low temp.. chart rarely rising about 99° was "Galyl" in intravenous injection. (see also article by Falconer and Anderson in "The Lancet" of September 29th 1917.)

During my stay in Macedonia I personally only saw one case of haemoglobinuria - Black-water fever.. He was a Russian patient admitted to the Mental Division suffering from Malaria with mental confusion. On examination he was found to have an enlarged spleen, anaemia and other signs of chronic Malaria. He was placed on Quinine - gr. 15 t.d.s.. and made progress for a week or so when his quinine was stopped.. One evening after he had been about a fortnight in hospital he suddenly took a rigor and his temperature shot up to about 105° I was not at all pleased with his general condition /

condition and in order to ensure the action of Quinine an intramuscular injection was given. Next morning his temperature was still elevated and the film taken the the previous evening was reported as containing no malarial parasites. He was passing the typical port wine urine and his condition was critical and another film showed no parasites. The opinion that then held the field was that in a case of black-water fever if there are malarial parasites found in the circulating blood then give Quinine and if no parasites are to be found withhold Quinine. This treatment I adopted, all Quinine was stopped and patient recovered in 3 or 4 days. About a week later he had another rigor with port wine urine - there were no parasites found in the blood - Quinine which had been re-commenced was again stopped and patient recovered. There were two theories in vogue as to the causation of Black-water fever - one was that it was entirely of malarial origin, and the other that it was due to Quinine poisoning, hence the above line of treatment. Parsons and Forbes in "The Lancet" of Sept. 7th 1918 state that quinine is not the cause of haemoglobinuria, but they believe it to be due to Malaria.

In /

In September 1918 came the final fighting of the Salonika Army which was destined to culminate in the surrender of the Bulgarians. Before all the wounded could be collected into hospitals along came our big Influenza epidemic causing an overwhelming number of patients and many deaths. The men were tired out with several days severe fighting in very hot weather - the majority were malarial subjects, and therefore their bodily resistance was markedly lowered. At this time I had many interesting and instructive cases and now regret I have no records but at that time the work was so heavy that it was impossible to give anything like the time one would have wished to individual patients and impossible to records findings of any kind.

At this time, as I have above stated, most of these patients were malarial subjects who had been two , three or even four years in Macedonia. The probability that these patients had had Malaria, in spite of their denial, is obvious and therefore all my patients received Quinine in one form or another unless it was strongly contra-indicated. My contention was that it was impossible to examine all cases thoroughly and therefore I did not have the courage to withhold Quinine therapy.

Now /

Now it was that I first began to have practical experience of intravenous Quinine. I regret to have to record that not a few patients admitted at this time were very obviously suffering from severe Malaria and only questionable from Influenza and that they had received no quinine for several days. This was the type of case that called for intravenous injection.

I will state what I can recall of one of my worst patients which will serve as an example of the line of treatment. This man came into hospital about 11 a.m. one day: diagnosed as Influenza, and had been ill for several days - it subsequently transpired that he had not been treated with any quinine. To me he was at once obviously seriously ill with Malaria, in fact he was almost in a moribund condition. A blood film was taken and showed M.T. parasites in enormous numbers. The Bacteriologist took a small quantity of blood and was able to keep the parasites alive for a few days which I understand is of very rare occurrence and can only be done in cases of a very heavy infection. I gave him a intravenous injection of Quinine gr. 10 in about 20 c.c. of normal saline. Another film taken about 4 hours later showed practically no reduction of the number of parasites. /

parasites.. I gave a second intravenous injection of gr. 10 this about 4 p.m. - a third injection at 10 p.m. and a fourth at 4 a.m.. the following morning. Twenty-four hours after admission his film showed decreased number of parasites and obvious signs of their disintegration. Thereafter he received intra-muscular injections of Quinine gr. 20 twice daily and this was gradually replaced by oral quinine.. In about a week or 10 days he was out of danger and subsequently was evacuated to England. One can honestly say that if this patient had not been attended to at once, and if this strenuous treatment had not been adopted he could not possibly have survived..

It was in cases such as these that I saw the immense advantage to be gained from intra-venous quinine. I always gave it in the above dilution and for preference used a hypodermic needle as by so doing the quinine could not be rapidly thrown into the circulation. The ideal time to take for an intra-venous injection of quinine is at the rate of gr. 1 per minute, but this is not easy in practice..

After this rush many patients were evacuated owing to increased shipping facilities and the work diminished. /

diminished.

In February 1919 I got my first leave home and at the end of March 1919 I returned to Salonika to find only 2 or 3 General Hospitals left in place of 15 that had been there during the summer of 1918. I was sent to the 43rd. General Hospital and destined to remain there until January 1920 when I left again for England.

I found the hospital now contained many chronic malarial patients and the practice we adopted was to do our utmost to get every patient home to England. In this, in view of the slow progress of demobilisation, and the many years some of these men had spent in the Balkans, we were encouraged by the authorities.

Another Malarial season started and from the very commencement the cases were much more serious and the mortality much higher than I had experienced in my previous three summers. This I ascribe as being due to three causes - (1) the discipline of the troops was much slacker and the same rigorous attention was not paid to the correct use of mosquito nets and other prophylactic measures, (2) demobilisation was proceeding at an increased rate and many men would not report sick until they were driven to it as they feared they might /

might be sent into hospital and so miss their turn for demobilisation (3) another fresh severe infection on the top of a chronic one of perhaps two or three years duration.

By way of example I can quote the case of a man who reported sick one day at mid-day: was sent to hospital that evening and died within two hours of his admission.

Another group responsible for the large numbers in hospital and severe cases were the Bulgarian and Turkish prisoners of war. At this time peace with these two countries had not been signed and prisoners could not be repatriated except on medical grounds. We were beginning to feel the shortage of R.A.M.C. Officers with the result that these prisoners of war had to be left to the tender mercies of their own medical officers. To these Malaria was nothing at all and it was impossible for us to teach them otherwise.

Again during this summer of 1919 the immense advantage of intra-venous quinine in the treatment of acute collapsed moribund cases was being continually brought to my notice. But latterly in my opinion I began to find that this line of treatment was being used to excess. Personally I never gave intra-venous /

intra-venour quinine unless malarial parasites could be found in the circulating blood. Many of our worst cases were prisoners of war, they did not know our language - we did not know theirs, and in the rush there was no time to palaver with interpreters &c. but we simply had to take the patients as we found them. When I say that in the latter part of August and in September we were getting an average four to six or eight moribund cases every evening our onerous duties will be appreciated: and for a short time at the end of September we were reduced to 3 M.O's. for 700 to 800 patients.. I always argued that although Malaria was certainly the most likely of diseases, that in a moribund case due to Malaria pure and simply, parasites would be obvious. To me there is an enormous danger in the intra-venous method of giving quinine which was not always appreciated. I well remember one morning a collapsed and obviously dangerously ill prisoner of war was admitted to a ward under the charge of a Greek civil doctor.. This poor Greek had had intravenous quinine dunned into him until he could almost think of nothing else.. He promptly proceeded to get ready the apparatus in order to carry this out.. Fortunately for the patient I was requested to see him before any treatment was /

was commenced and found on examination that he was suffering from pneumothorax of tubercular origin ! Cushny in his Pharmacology tells us that quinine is a protoplasmic poison and that "when a drop of blood is examined under the microscope the white cells are observed undergoing constant changes of form and position exactly similar to those of the amoeba, but minute quantities of quinine salt are sufficient to stop all movements at once and the leucocytes assume a spherical form; become darker in colour and granular and soon break up into debris", and later that "the number of leucocytes in the human blood is diminished by ordinary quantities of quinine".

I found many people to disagree with me in these points, but I still maintain that I do not consider I lost any patient by withholding too long from this line of treatment, and I certainly saw not a few cases of death as a direct result of an intra-venous injection.

I quote cases to show the value of intra-muscular and intra-venous injections of quinine &c. and these three cases also serve to illustrate the intense infections that were occurring during these summer months:-

C A S E V111.

Corpl. A.B. Age - 42. Service - 4 yrs.
Macedonia - 3 6/12 yrs.

Admitted - 28-7-19

On Admission - Patient was very anaemic and debilitated Temperature sub-normal. Denied history of malaria or dysentery.. Tongue - dryish and covered with brown fur. Heart sounds closed but feeble. Spleen - palpable 3 finger breadths below costal margin and tender. Liver enlarged to percussion..

History of having been unwell for 3 days and complaining only of general weakness and no appetite. The only time he has been in hospital before in this country was in 1915 when he was 14 days suffering from jaundice.

28-7-19 - Temperature rose to 99° and patient was put on Quinine Sulphate gr. 15 t.d.s.. in acid solution. He became rather restless that evening and was given Bromide gr. 30 and even then spent a poor night.

30-7-19 - His condition was grave though he exhibited no fresh clinical symptoms. His tongue was still furred and dry and he practically refused all nourishment. A Blood Film showed a very heavy infection with M.T.. rings. Patient was given Intra.muscular Quinine gr.20 and /

and placed on "Dangerously Ill" list. Adrenalin m.10 4 hourly was also administered hypodermically. Patient had been vomiting.

1-8-19 - There was no improvement - parasites were still present in the blood and so he was given Quinine gr. 6 intravenously in almost 20 c.c. of saline. This was repeated on 2nd and again on 3rd with intramuscular Quinine gr. 20 each day. There were no parasites to be seen in the film on August 4th and his condition was rather more satisfactory: his pulse rate too had dropped.

5-8-19 - As patient had not been vomiting for about 2 days he was given Quinine bi-hydrochlor gr. 20 in tablets which he retained. On Aug. 6th film showed malarial pigment, but no actual parasites but that evening patient relapsed - pulse to 88 - refused food, his mouth again became dry. He was given an enema, and intra-muscular quinine was given and repeated for the next 2 days, - then oral quinine gr.30 daily. Patient showed appreciable improvement but even yet took extremely little nourishment, refusing all fluids except albumen water.

12-8-19 - There were no malarial parasites to be found in the blood but again he relapsed with a temp. to 99° - pulse 96 and constipation. Intra-muscular Quinine /

Quinine gr. 20 was given and repeated the following morning. For the next 5 days though his pulse rate kept up patient improved - his diet was increased and for the first time he shewed interest in what was happening around him and was for 2 or 3 days carried in the afternoons outside the ward.

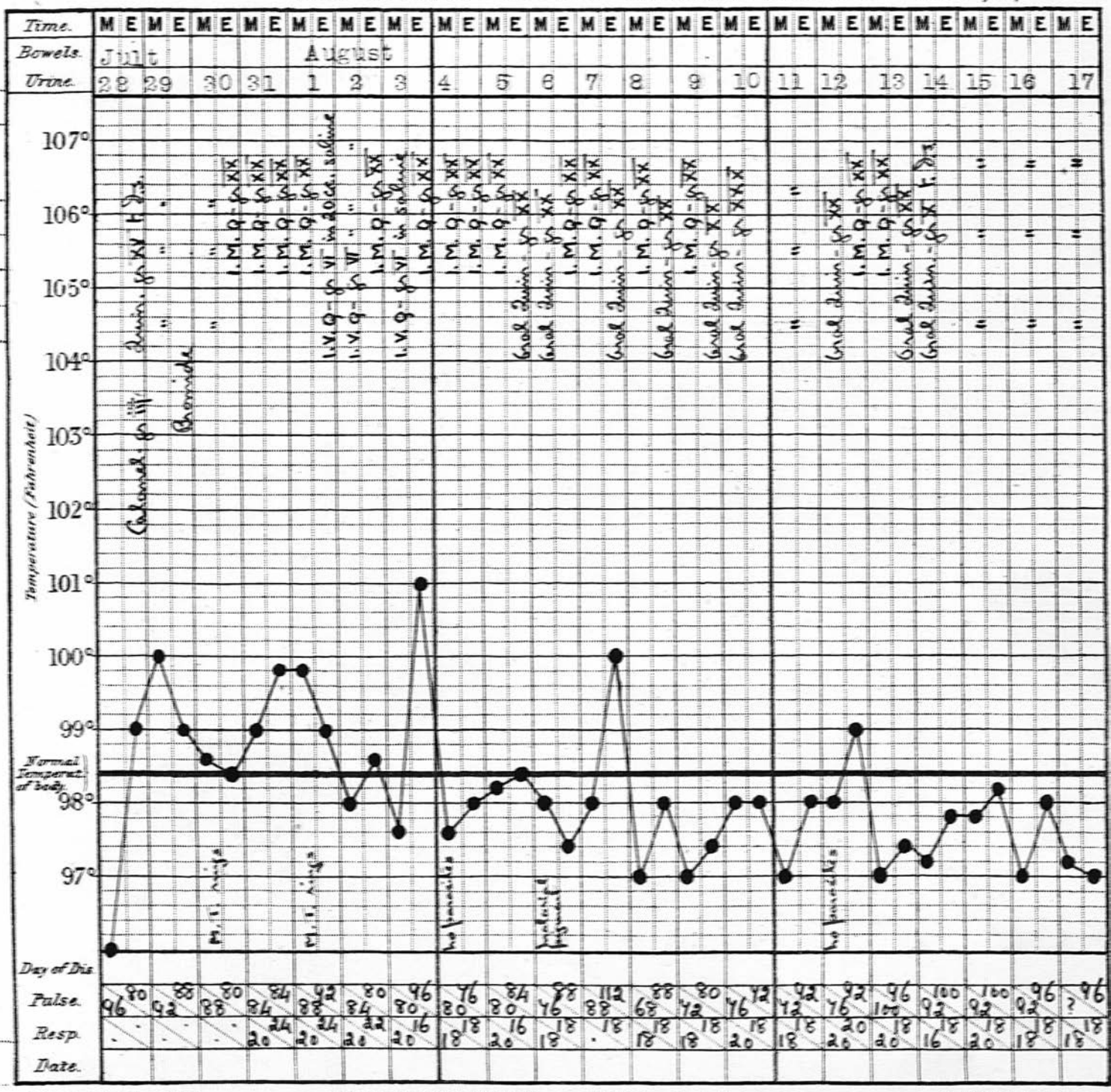
18-8-19 - He was not so well - no parasites in blood, but he was listless: objected to treatment and refused nourishment. Intra-muscular quinine gr. 20 was given twice without improvement. Aug. 20th his condition was worse than when first admitted: he now became restless attempting to get out of bed - mildly delirious and had a dirty dry tongue and pulse rate of 120. There were no further clinical signs. He was given Galyl 20 cgr. intravenously. On Aug. 21st a few M.T. parasites were found in a blood film and he was given intra-venous quinine gr. 10 in 20 c.c. saline and also ½ pint rectal salines every four hours. He did not respond and on 22nd was given ½ pint intravenous saline containing gr. 10 of Quinine which improved him for a few hours, also intra-muscular quinine gr. 20 morning and evening and rectal salines every four hours.

His condition got worse - he became totally confused: temperature rose to 102·8°: pulse to 144 and respirations /

respirations to 36 and he died at 3.25 a.m. on Aug. 23rd. His urine on 18-8-19 contained a few pus cells but nothing more.

Post-Mortem - 24-8-19 - Lung bases congested and slightly oedematous, No pus in tubes and no excess of fluid in pleural cavities. Heart - soft, pale, fat, and flabby with marked atheroma of aorta. Spleen - four times the normal size - very dark in colour - substance soft and friable. Both kidneys small, pale, and fatty. Liver - slightly enlarged - dark in colour and firm. Marked excess of fluid in brain. Membranes adherent to brain at vertex Superficial vessels injected and marked injection of vessels in cross section.

THE MEDICAL SUPPLY ASSOCIATION. Case VIII (a)



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C A S E IX.

Pte. J.W.T. Age - 21 . Service 2 $\frac{10}{12}$ yrs.. Macedonia $2\frac{1}{12}$ yrs..

Admitted - 22-8-19.

On Admission - Patient gave history of having suffered from repeated mild attacks of Malaria. He had been four times in Hospital and had had six attacks this year.

General condition and nutrition good. No anaemia.. Tongue slightly furred, moist. Heart sounds strong,. closed. Spleen not palpable but tender. No hepatic enlargement. Chest clear.

He had been having Quinine for 2 days prior to admission.. Temp.. 99° on admission and he was put on Quinine - gr.. 15 t.d.s..

On morning of 23rd. temperature normal.

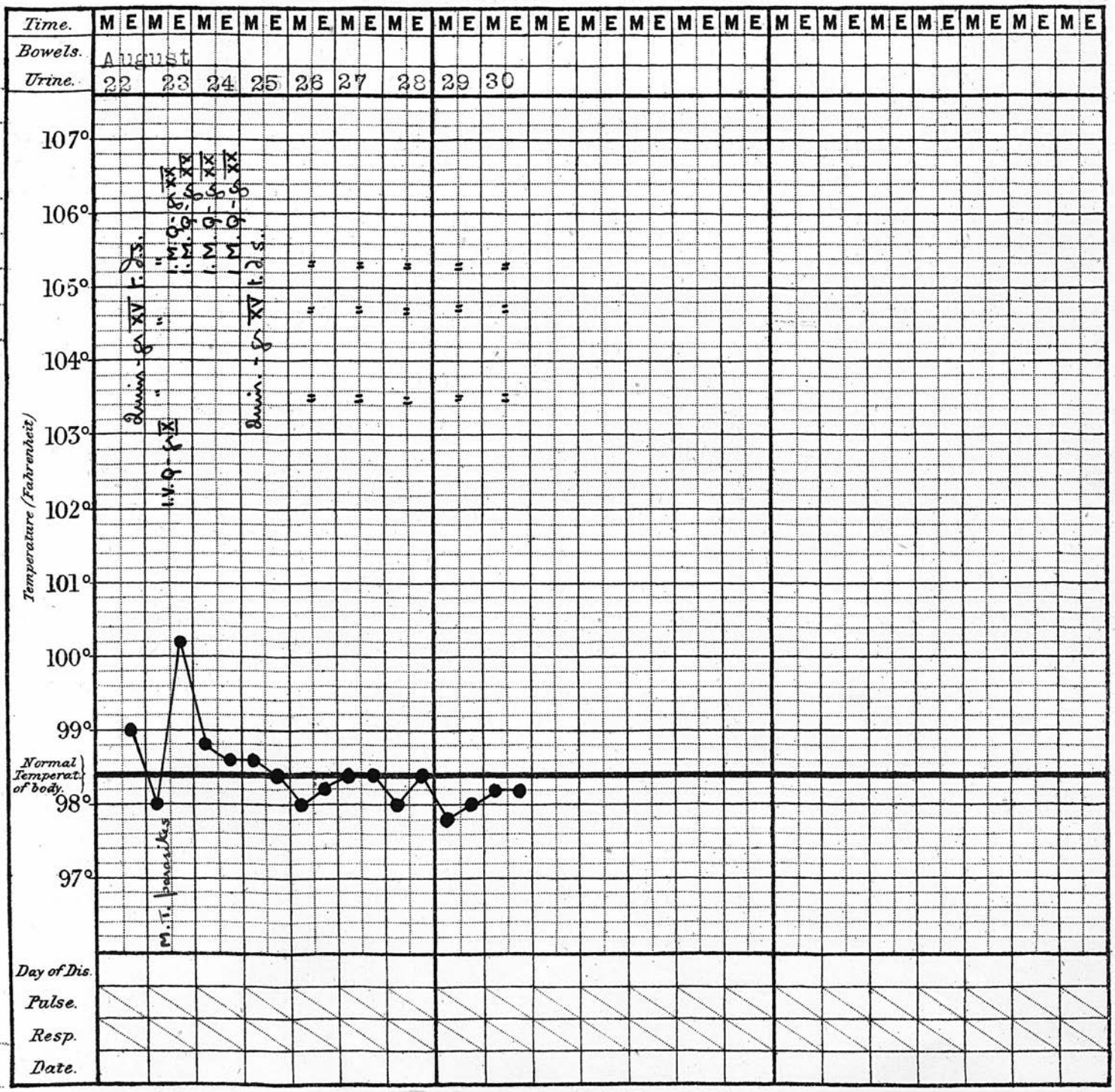
I was suddenly called to see patient about 1.30 p.m.. on this day when I found him very collapsed - extremely cyanosed: pulse at wrist not perceptible: restless and in a mildly delirious condition. He was given brandy, pituitrin &c. as general stimulants and a film taken. This film showed a very heavy infection with M.T.. parasites.. (Temp. 100·2° : pulse 96 and respirations 24) He was immediately given Quinine gr. 10 intra-venously in 20 C.C.. of normal saline and also an /

an intra-muscular injection of Quinine gr. 20 and put on adrenalin m. 10 hypodermically every four hours.. At 6 p.m. pulse was just perceptible at wrist: patient was still very cyanosed, restless and confused. He was given a second intra-muscular injection..

He spent a comfortable night and on the morning of 24th no parasites were to be found in a film. All mental symptoms had disappeared and he could only give a very hazy idea of what he had felt like the previous day. He was given an intra-muscular of Quinine gr. 20 which was repeated in the evening.

On 25th he was put on Quinine gr. 15 t.d.s.. and thereafter made a complete recovery and was at a later date evacuated to England as a walking case.

THE MEDICAL SUPPLY ASSOCIATION. Case IX



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C A S E X.

Pte. A.E.M. Age - 23 Service 3 1/2 years. Macedonia 2 1/2 yrs.

Admitted - 21-8-19

On Admission - History of much malaria and four times in hospital.

Had been ill two days complaining of body pains, some shivering and sweating. No vomiting. He had been treated with quinine. Spleen - tender: not palpable. Liver - palpable.

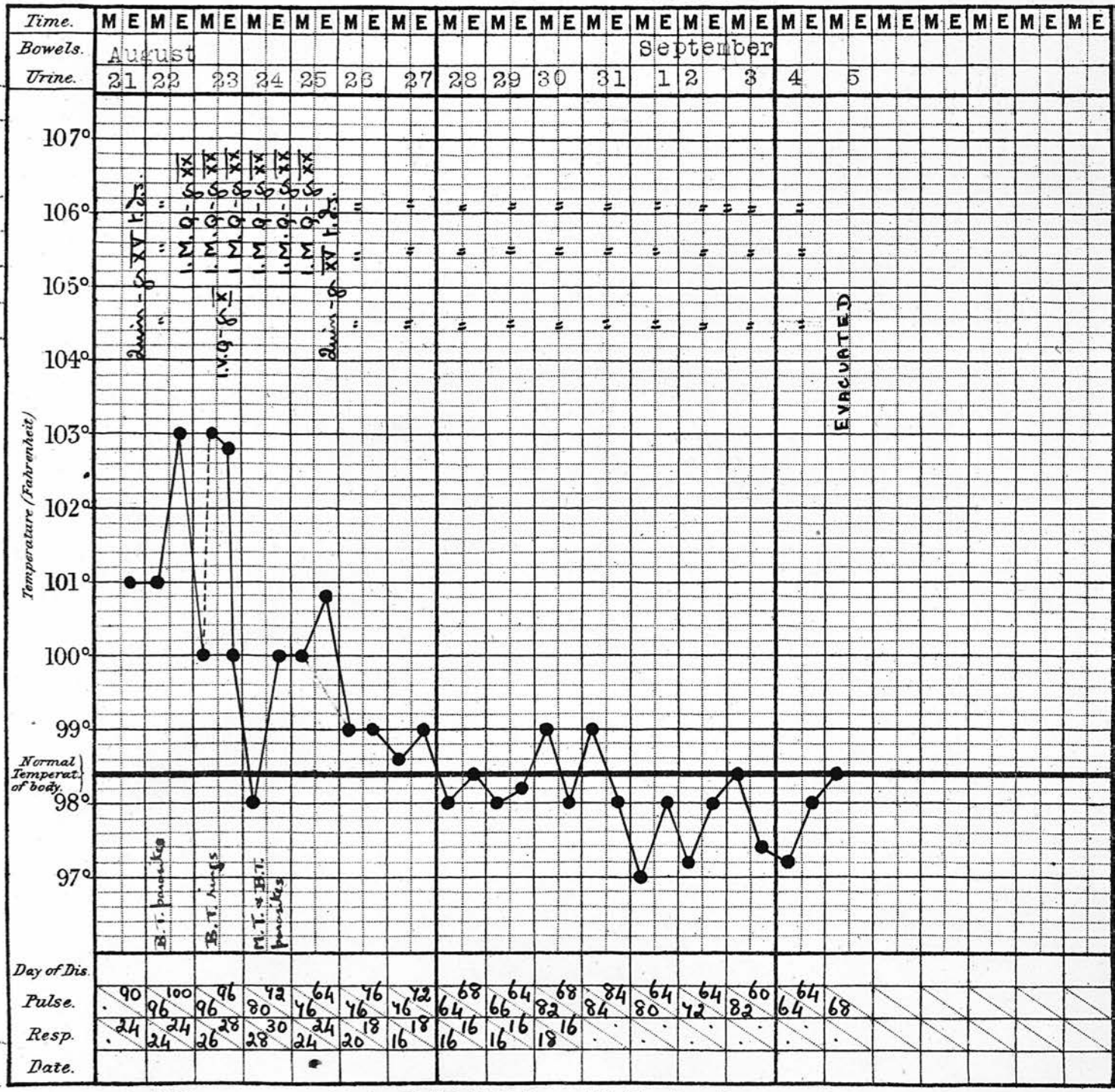
Given Calomel gr. 4 and put on Quinine gr.15 t.d.s.

August 22nd - Blood film reported as B.T. parasites +++ Further elevation of temperature in evening when he was given intra-muscular Quinine gr. 20 and repeated on morning of 23rd when he was slightly improved. He took a rigor at mid-day when B.T. rings were found in blood. His condition appeared critical as patient showed tendency to collapse with a weak pulse and clammy perspiration. He was given intra-venous quinine gr.10 in normal saline and a second intra-muscular injection in the evening. On the 24th though his temperature was normal both B.T. and M.T. parasites were found in a film and he was given two intra-muscular injections. His temperature remained up all 25th, and the intra-muscular /

muscular injections were repeated.

His condition on the 26th was very much more satisfactory: he was placed on oral quinine gr. 15 t.d.s. - continued to improve and on September 5th he was evacuated convalescent.

THE MEDICAL SUPPLY ASSOCIATION. Case X



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Case VIII illustrates very well one of the more severe type of case we were getting at this time. He was a patient the subject of chronic malaria as his general debilitated condition and his enormous spleen showed: he was due for demobilisation and would not report sick until he was compelled to give in: the treatment he received prior to admission must have been irregular and accordingly inadequate.

It is obvious from reading this case over that the patient did not respond to treatment anything like as should have been expected. He tolerated quinine badly and at the time there appeared to me - vividly in this case and to a lesser degree in many others - that there were two methods of treatment open.. One - which I shall call the direct - was to attack the malarial parasites with large doses of quinine and keep up a comparatively high quinine percentage in the blood stream: The second - or indirect method - was to first of all attempt to improve as much as possible the patient's general condition, in order to get the body defensive mechanism into the best possible order, and then deal with the malaria per se. A combination of these two methods was attempted here but without success..

It is interesting to observe that in the space of

26 days this patient received 19 injections of intra-muscular quinine and 5 intra-venous injections and yet the issue was fatal.

The post-mortem findings were those consistent with chronic malaria, but it is unfortunate that no microscopic examinations of the organs could be made.

The last two cases are illustrative of patients who had been subject to mild repeated attacks and were admitted to hospital in what appeared to be a simple relapse. Case X. is particularly interesting in that the acute collapse only came in after the patient had been over 36 hours in hospital and had received two intra-muscular injections - this was very exceptional. Though his urgent symptoms abated after an intravenous injection his temperature remained elevated. His condition on the 5th day was much more satisfactory than would appear from his temperature chart. I wish to draw attention to the intense quinine treatment adopted in these two cases and the happy results.

C O N C L U S I O N.

As will be seen from these last cases the dosage of quinine was much larger and the treatment more intense than in the previous years, yet in spite of this much progress towards the absolute cure of Malaria did not appear to have been made.

During this, my last summer in Macedonia, I at times became very disheartened and disappointed over the results of treatment. I felt that I had spent practically four summers in this intensely malarial country: I must have treated thousands of cases of Malaria, yet, in spite of all my experience, in spite of all the knowledge I had obtained from expert advisors and expert investigators, I was no nearer curing Malaria than I was in 1916. In fact my experience simply made me appreciate that I was further away from the cure than I had thought. In 1916 Malaria to me was more or less a straight forward disease, the cure of which was quinine - now I feel that quinine therapy as at present practiced cannot be claimed as a conclusive cure. I agree that it appears to be the only efficient treatment for relapses, but that is very far from curing the disease in toto.

It /

It is very interesting in reviewing these four years of Malaria to notice how the dosage of quinine kept gradually increasing and increasing. In the summer of 1919 for an acute and moribund case of cerebral malaria quinine gr. 10 intravenously and gr.20 into each buttock - i.e. a total of gr. 50 was recommended. My experience had not taught me that any better results could be expected with these massive doses and I did not give them. I saw them given by others with, I can honestly say, no better results than the smaller doses. If after this the patient did die it was not the want of quinine that was responsible for the fatal issue!!

With regard to the various methods of quinine administration, oral quinine appeared to take 24 hours to act and so it was not until the expiry of that time that response or otherwise on the part of the patient could be expected. With an intramuscular injection response on the part of patient could be expected in about 8 to 12 hours. Wiltshire in the R.A.M.C. Journal states the safety-point is reached after the second dose of intra-muscular quinine has been given, expect in cases already in a critical condition at the time treatment is started. Reference to Case X. will /

will show that of a patient who collapsed into a moribund state 2 or 3 hours after his second intra-muscular injection but this only serves to illustrate what I have previously recorded with regard to the severity of the cases seen during the summer months of 1919. A patient after receiving an intra-venous injection of quinine was expected to give evidence of response to this line of treatment more or less immediately, and if he did not the prognosis was accordingly very grave.

An interesting point I have never been able to decide is what effect does previous prophylactic treatment by quinine have on a patient who develops Malaria. Has he acquired any quinine immunity and are the causal parasites more resistant to quinine therapy? - in other words are larger doses of quinine required in the treatment of a patient who for several months has been having prophylactic treatment, than in a patient who has not been subjected to any such prophylaxis?

The amount of research work that has been accomplish-in connection with this disease is colossal and nowadays hardly any medical journal can be picked up without some reference to Malaria being found therein.

An /

An important point that in my opinion appears to have been overlooked by many observers in this country is the change of the patients from a tropical to a sub-tropical country. My experience in Macedonia made me observe that patients, the subject of chronic Malaria, usually had a relapse in about two weeks in the summer time and in about 3 to 4 or 5 weeks in winter. Take these chronic cases away from a Malarial climate, put them in England, and this relapse period lengthens gradually and progressively. Some of these patients are at a later date collected together and a new line of treatment is undertaken by them. They are kept under observation for perhaps three months and then a new method of treatment with a high percentage of cure is announced. Were these patients actually under observation over more than one relapse period?

I DECLARE THAT THE COMPOSITION OF THIS THESIS IS MY OWN AND THAT I HAVE PERFORMED THE WORK AS RECORDED IN IT.

Jas. M. Smellie

SEPTEMBER 1920.

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