Authors are alone responsible for the statements made and the opinions expressed in their papers.

Journal of the Royal Army Medical Corps.

Original Communications.

MALARIAL EPISODES.

A Clinical Study of Atypical, Pernicious and Lethal Cases Selected from among 10,000 Malarial Patients Admitted to Military Hospitals in Ceylon.

BY

Ceylon Medical Corps; Medical Specialist, Ceylon Army Command (1942-1946).

The common malarial episodes, when presented with an appropriate antecedent history, rarely escape clinical recognition. When persons who have been residents or transients in malarious zones, or those who have previously suffered from the disease, develop a paroxysmal fever, initiated by chills and rigors, accompanied by splenic symptoms and indications of anemia, malaria obviously suggests itself as the cause of the illness. Previous experience of the disease may teach a patient to recognize the symptoms that occasionally signalize an impending attack—malaise, lassitude, anorexia, headache, myalgic discomfort—sometimes showing a perceptible periodicity in incidence or intensity. Such a prodromal phase is generally inconspicuous or entirely lacking, and the patient is usually taken unawares by the fever, which is soon accompanied by constitutional disturbance of varying degree.

Although definitive diagnosis demands the demonstration of malarial plasmodia in the patient’s blood, the disease so often presents its dominant clinical features in typical form so as to render clinical diagnosis easy and reliable. Malaria is the only disease with a fever of tertian or quartan periodicity; even in the subtertian and quotidian forms its typical three-stage paroxysm distinguishes it from other fevers; the clinical triad of fever, splenomegaly, and anemia provides inferential evidence of plasmodial activity; and, finally, the response of the disease to anti-malarial therapy (particularly striking in subtertian infections) substantiates clinical diagnosis.

When, however, malaria presents its various atypical, and sometimes baffling, episodes, it may quite easily lead to erroneous clinical diagnosis. Such anomalous and variable behaviour of the malarial parasites is usually due to their tendency to recede from the peripheral to the visceral circulation, provoking symptoms referable to the particular viscus in which they may sporulate. Consequently, these atypical malarial manifestations may be as widely divergent in nature as, for example, psychotic disturbance and...
pulmonary embarrassment, or nephrotic insufficiency and pseudo-cholera, or algid collapse and haemoglobinuria. Furthermore, the diagnostic difficulties are enhanced by the occasional failure to detect malarial parasites in the blood in some of these cases, and precious time may be lost in futile therapeutic effort directed against some other pathogenic agent, the effects of which may have been simulated by the malarial plasmodium which has escaped suspicion.

When we include the various sequelæ and complications that follow in the wake of this disease, the atypical episodes that may be attributed to malaria are truly protean in character. Though, fortunately, relatively infrequent in incidence, these episodes may be responsible for a significant contribution towards the morbidity and mortality of malaria through their malignant and pernicious effects. To illustrate the diversity of these unusual malarial episodes, and to emphasize the clinical interest they afford, a few selected cases are here presented. Some of the reports are, admittedly, incomplete as a result of the widespread local prejudice against necropsy, and this must be the apology for the unfortunate lack of post-mortem study of some of the fatal cases here recorded. With the exception of one case (Case 6), all patients in this series were soldiers admitted to two military hospitals where no less than 10,000 cases of malaria were treated between January, 1942, and February, 1946, the majority being Ceylonese of various races.

**Apyrexial Episodes.**

Although fever is the most conspicuous manifestation of clinical activity in malaria, afebrile episodes occasionally occur, as in cases of ambulant malaria, latent or dormant malaria, incompletely suppressed malaria, masked malaria, chronic malaria, myalgic types of malaria (Hughes and Bomford, 1944), subclinical malaria (Ferriman, 1945), etc. Despite the absence or insignificance of fever in these cases, malarial parasites may lurk in the blood of such patients for long periods without seriously impairing health. Attention is usually drawn to the condition by recurrent complaints of malaise, accompanied by headache, backache, myalgic discomfort in the neck, chest, trunk, or limbs. The disability may progress to acute tenderness, spasm, and limitation of movement of the affected part. Constitutional symptoms are absent or inconspicuous, anaemia is rarely obvious, except in chronic cases, but tenderness or enlargement of the spleen, and discoloration of the urine by urobilin should direct suspicion towards a malarial pathology. In contrast to the inefficacy of the common anti-rheumatic remedies, the prompt response to anti-malarial therapy is striking in these cases. The importance of careful search for evidence of malaria is illustrated by the following case:

**Case 1. Apyrexial Malaria.**—A Gurkha rifleman, aged 20, was referred for investigation as a suspected psychoneurotic. 'He had reported sick frequently with complaints of aching in his head, spine, and limbs, during the preceding two months or more. Observation in hospital on two previous occasions had shown no evidence of fever or other symptom, apart from stiffness and tenderness of the muscles of the back and limbs. Examination in various specialist departments had revealed no obvious cause for the symptoms. Laboratory investigation had disclosed no pathological abnormality of significance. Blood: W.B.C. 6,700 per c.mm.; D.C.—P. 60 per cent, L. 36 per cent, M. 3 per cent, E. 1 per cent; R.B.C.
3½ million per c.mm.; Hb. 75 per cent; malarial parasites nil. Urine: Albumin, sugar, bile, nil. Fæces: Amœbic, ova, cysts, nil. Symptomatic treatment with salicylates and sedatives had produced no effective response apart from temporary relief. The patient's mental outlook was influenced by an excusable degree of anxiety about his physical symptoms, which he feared might interfere with his Army career; but this anxiety seemed more likely effect rather than cause in relation to his disability. As this soldier had served in malarious jungles where he had experienced mild feverish attacks, for which he had not reported sick, and as a perceptible periodicity was detected in the recurrence of his present symptoms, a careful search for evidence of malaria was recommended. The spleen was not enlarged, but was definitely tender to deep palpation; the urine was dark in colour, and was found to contain urobilin; after repeated examination of the blood, a few benign tertian rings were ultimately found in a smear. The patient was put on a full course of anti-malarial therapy and responded with a quick and lasting recovery.

**Hyperpyrexial Episodes.**

At the other end of the temperature scale, malaria produces some of the highest temperatures recorded in febrile diseases, the thermometer rising to 110° F., or even higher. The possibility of this disease should be kept foremost in mind in dealing with any case of hyperpyrexia, whether of insidious or sudden onset, in persons who have been in malarious districts. The hyperpyrexial episodes of malaria rank among its most pernicious forms, sometimes defying the most energetic treatment, and occurring both in malignant and benign infections, as illustrated in Cases 2 and 4, respectively.

*Case 2. Malarial Hyperpyrexia.*—A Sinhalese Lance/Sergeant, aged 25, with no previous malarial history, was found to have a malignant tertian parasitaemia on the fourth day of a remittent fever, two previous smears having been negative. Quinine therapy was initiated orally, but as the fever rose to 105° F. an intravenous injection of 6 grains of the biphosphate was also administered. The temperature remained elevated for about four hours, and for the first time the patient complained of a slight, dull headache. His pulse-rate was 108 per minute, blood-pressure 100/70, and no neurological signs were present. Intravenous quinine was repeated, after a preliminary subcutaneous injection of adrenalin 1/10, ice compresses continuously applied to the head and neck, and frequent cold sponging of the body carried out. After midnight, the temperature remitted to 101° F. and the patient was free from headache by next morning. Thereafter, the fever began to mount, with remissions, and intravenous quinine was resumed, but with no effect. As the fever continued to rise, mepron 0·3 gramme was given intramuscularly with oral quinine grains 10 t.d.s., but with no response. Signs of cardio-respiratory failure appeared as the fever continued unabated, but cerebral disturbance, such as restlessness, confusion, delirium, or unconsciousness, were conspicuously absent until the temperature had risen past 107° F. Persistent treatment with quinine and mepron, with stimulants (digitalin, strychnine, nikethamide), oxygen inhalations, ice applications to the head and body as well as ice water enemata, failed to arrest the rapidly deteriorating condition of the patient. Lumbar puncture produced a clear cerebrospinal fluid, which was under slight tension; withdrawal of 13 c.c. was followed by no beneficial effect. As the temperature rose to 108° F. at midnight on the seventh day of the illness, death supervened from acute cardiac collapse, without the patient's temperature having once returned to normal since the onset of the fever.

**Algic Episodes.**

Occasionally one meets grave malarial infections where the patients do not complain subjectively of fever, but exhibit a cold, clammy skin, cyanosis, and symptoms of profound cardiovascular asthenia, with a tendency to
collapse and fatal syncope. Despite the extreme coldness of the body surface in algid malaria, the temperature may be found elevated in the mouth or rectum. A factor of grave prognostic import in these cases is the presence of a heavy parasitaemia in the peripheral blood. Algid manifestations often co-exist with the gastro-intestinal episodes of malaria, in which circumstances the symptoms have a frequent tendency to appear during the cold stage of the fever. When occurring independently, algidity sometimes follows the termination of a malarial paroxysm, especially when rapid defervescence has taken place with excessive diaphoresis. Prompt treatment directed towards both control of the infection and a stimulation of the circulation will often avert disaster, as in the following instance:

Case 3. Algid Malaria.—A Sinhalese Serjeant-Major, aged 40, in hospital with his first attack of malaria, showed a very heavy infection of his blood with malignant tertian parasites. His temperature showed quotidian rises between 103° F. and 105° F. with relative bradycardia, but no rigors or chills. Treatment comprised oral and intramuscular quinine for the first two days, followed by oral and intramuscular mepacrine for the next three days. On the fifth evening, during defervescence in a profuse sweat, signs of cardiac weakness and drowsiness appeared, and adrenaline \( n \) 7 was given by injection. When referred for examination the next morning, the patient was in a state of extreme prostration as in a condition of shock, conscious but apathetic, silent and immobile, barely able to answer questions in a whisper. His skin was cold and clammy, his muscles flaccid, his temperature subnormal, and his pulse-rate 70 per minute with a poor volume and tension. Reduplication of the second cardiac sound was audible at the apex, and the blood-pressure was low (98/68). Laboratory reports: Blood: W.B.C. 8,800 per c.mm.; D.C.—P. 60 per cent, L. 40 per cent; R.B.C. 33% million per c.mm.; Hb. 84 per cent; B.S.R. 8 mm. per hour; W.R. and K.R. negative. Urine: Albumin, sugar, deposits, nil. Faeces: Amoeba; ova, cysts, cells nil. Energetic stimulant treatment for restoring cardiovascular activity (caffeine, strychnine, camphor, brandy, glucose, etc.), with continuation of antimalarial therapy, produced a satisfactory response within forty-eight hours, followed by uninterrupted recovery.

Nervous Episodes.

Various phenomena of nervous disturbance are frequently manifested in both benign and malignant malaria. Headache is one of the commonest of these symptoms, being an especially prominent feature during the hot stage of the fever. Mental confusion is not uncommon in the high fever of benign infections, while malignant cases show a distinct tendency towards restlessness and delirium. The association of hyperpyrexia with these symptoms, particularly in malignant infections, may be the prelude to cerebral malaria, the most pernicious and dangerous of the nervous episodes of malaria, which culminates in coma and severe depression of the vital functions, only too often ending fatally despite the most energetic treatment. Regional sporulation of malarial parasites in the neuraxis may cause a diversity of focal lesions, both paralytic and irritative, resulting in aphasic, apoplectiform, hemiplegic, bulbar, cerebellar, choreiform, tetaniform, epileptiform, Parkinsonian, and other neurological episodes that may lead to considerable diagnostic perplexities. The following case presents the features of an exceptionally interesting cerebral episode, with four hyperpyrexial crises of 109°, 105°, 107°, and 108° F., focal symptoms, prolonged coma, and the interesting observation that benign, and not malignant, parasites were detected in the patient's blood:
Case 4. Cerebral Malaria.—A Dutch Burgher sapper, aged 22, with no previous history of malaria, was sent to hospital from a malarious station on the sixth day of an intermittent fever, complaining of headache, anorexia, and constipation. He had a temperature of 103° F., and a pulse-rate of 110 per minute, with no other clinical abnormality and a negative blood smear for malaria. Symptomatic treatment with sodium salicylate, aspirin, phenacetin, and a soap enema was followed by a drop of the temperature and pulse to subnormal on the next morning. The fever reappeared during that afternoon and rose steadily throughout the night and the following morning. The blood was again negative for malaria, but as the fever continued to rise, with increasing headache, irritability, and restlessness, an intramuscular injection of quinine grains 15 was given. By noon, the temperature had risen to 105° F., with a pulse-rate of 116 per minute, apha, dysphagia, and increasing restlessness, which was soon followed by severe delirium. An injection of morphia grain $\frac{1}{4}$ allayed the cerebral symptoms, but the fever continued unabated, until it reached 109·6° F. in the axilla within about two hours. The patient was now deeply comatose, incontinent of urine and feces, with Cheyne-Stokes respiration, flaccid muscles, extinct reflexes, and fixed, dilated pupils; his pulse was weak and running at about 140 per minute, his blood pressure had dropped to 88/58; a blood smear taken at this stage revealed benign tertian rings, amoeboid forms, and schizonts, but no malignant forms could be found. No enlargement of the spleen or liver was palpable. Quinine grains 15 was promptly repeated by intramuscular injection, the intravenous route being considered too dangerous owing to the extreme hypotension. About 3 c.c. of hot, clear, cerebrospinal fluid, which was under normal tension, were withdrawn by lumbar puncture. Energetic cooling measures were applied—ice bags to the head and neck, ice massage and cold sponging of the body and limbs, iced saline by proctoclysis, fanning—while half-hourly records of the temperature and pulse were kept. Within one and a half hours the temperature had dropped over 7°, reaching 102° F., the lowest level for the day, but the pulse-rate remained at 140 per minute, with a poor volume and tension, and the patient continued in a comatose state. Within the next two hours, the temperature began to mount again, and this was accompanied by two epileptiform seizures, for which potassium bromide grains 60 and chloral hydrate grains 20 were administered rectally. The next febrile peak occurred a little past midnight, when the patient became restless and delirious with a temperature of 105° F., a weak, low-tensioned pulse of 130 per minute, and muscular twitchings in his limbs. Another blood smear taken at this stage again showed only benign and no malignant parasites. After another intramuscular injection of quinine and ice applications, the fever commenced to decline, and, with further quinine treatment, subsided to 99·8° F. during the afternoon. Despite defervescence, the pulse did not come down below 120 per minute and continued poor in volume and tension; injections of digitalin, strychnine, adrenalin, and nikethamide retarded the pulse-rate to 100 per minute. The patient was quiet, but still unconscious, his breathing was regular and easier, a perceptible return of his reflexes was observed, but his pupils remained dilated and immobile. With nightfall, the temperature and pulse-rate began to rise again till a third hyperpyrexial crisis was reached at 107° F., with a pulse-rate of 130 per minute, when intramuscular quinine, lumbar puncture, and intensive cooling measures were resumed. The response to this treatment was a short-lived subsidence of the fever to 104° F., after which it rose sharply, accompanied by a failing pulse and respiration. Cardiac stimulants, oxygen inhalation, glucose-saline by proctoclysis were added to the treatment, but with no response. The temperature continued to climb, reaching its fourth and final peak at 108° F., when fatal cardiac collapse supervened (fig. 1).

The profound degree of cerebral disturbance caused by the patient's first hyperpyrexial crisis was reflected by the persistent coma, pupillary paralysis, continuous hypotension, and the vagaries of the temperature-pulse relation, that were so prominent thereafter. At no stage of the fever, after that first crisis, was the blood-pressure adequate to justify intravenous quinine medication, while even intravenous saline infusions were rarely possible owing to the collapsed state of the superficial veins of the limbs.

If this patient had survived his illness he would, most probably, have
suffered from life-long cerebral disability through the effects of the high temperatures to which his brain had been exposed. Recovery from cerebral malaria is sometimes rendered incomplete by irreversible changes in the brain due to factors other than hyperpyrexia pure and simple, e.g. as a result of capillary haemorrhages or embolic lesions. Chronic encephalopathic states may, thus, present themselves as sequelae of malaria, even despite prompt and efficient treatment, as the following case illustrates:

**Case 5. Malarial Encephalopathy.**—A Tamil sapper, aged 24, while under treatment for his first attack of malaria, a malignant tertian infection, suddenly developed premonitory symptoms of cerebral involvement on the eighth day of his fever—headache, dysarthria, mental dullness and confusion. He rapidly passed into a state of coma lasting three days, during which his temperature remained elevated between 102° F. and 103° F., with his pulse-rate ranging between 100 and 130 per minute. The blood-pressure being low at first (90/75), quinine grains 20 was injected intramuscularly, with adrenalin η 15 and nikethamide 1 c.c. subcutaneously. As the blood-pressure rose to 100/80, intravenous quinine grains 6 in 20 c.c. of normal saline, was administered twice. During the comatose phase, the patient was fed by nasal tube and a continuous glucose-saline drip maintained rectally. After recovery of consciousness, he was treated with mepacrine orally, and remained apyrexial after the fifteenth day. But residual signs of cerebral dysfunction
persisted—aphasia, dysphagia, spastic paresis of the left lower limb, with mental dullness, lethargy, amnesia, and emotional incontinence (uncontrollable weeping and laughter). Blood examination showed a negative response to the Wassermann and Kahn reactions; the blood-pressure remained stationary at 108/80; the optic discs and fundi showed no abnormality. The patient was kept in hospital for a further period of two months, but as his encephalopathy showed no signs of improvement, he was invalided out of the Army.

The mental changes observed in the foregoing case reflect yet another aspect of the clinical activity of malaria. Mild, transient psychical disturbance, such as mind wandering, failure of concentration, confusion, amnesia, or apathy, is not uncommon in malaria. More rarely, cerebral malaria may introduce itself in the guise of some psychotic episode, such as manic delirium, severe melancholic or paranoid states, etc. Diagnostic errors are likely to arise when some familiar condition is stimulated, e.g. the alternation of confusion and memory loss, with delirious episodes, may be mistaken for alcoholic psychosis, especially in the presence of dysarthria, or of myalgic or neuritic symptoms; listlessness, drowsiness, or lethargy, occurring in a case of continuous or remittent malarial fever, with bradycardia, leucopenia, and a dry tongue, may readily suggest typhoid fever in the absence of serological tests.

It may not be out of place to refer, in passing, to the possibility of the reverse error, namely, ascribing to malaria a psychopathic state resulting from mepacrine toxicosis in susceptible persons. About 18 such cases have come under my observation among soldiers concerned in the present study, and 2 cases among private patients. The majority of these patients exhibited symptoms of a transient hypomania-psychomotor hyperactivity, exhilaration, euphoria, lack of inhibition and intolerance of restraint, with frequent insomnia. A few patients were rambling and loquacious in conversation, with signs of disorientation, amnesia, and confusion. Two patients progressed to a state of acute mania, and had to be invalided out of the Army. All the rest recovered from their psychotic disorder within one to five weeks. In one of the private cases, the psychotic episode provoked by mepacrine appeared to have precipitated a schizophrenic reaction. Many of the patients who recovered were able to recall the salient features of their behaviour during the psychotic phase. Treatment consisted of immediate withdrawal of mepacrine where it was still being administered, and, at first, of diuretics, and laxatives to promote elimination of the drug through the urine and feces, and sedatives and hypnotics as indicated. On the advice of Brigadier T. F. Rodger, Consulting Psychiatrist, ALFSEA, alkalis were withheld in the later cases owing to the risk of lowering (instead of increasing) the excretion of mepacrine, and ammonium chloride was administered instead. The change of treatment appeared to shorten the course of the psychosis in general, several patients becoming free of symptoms within a week of the onset. In one case, the resumption of mepacrine after subsidence of psychotic disturbance, resulted in recurrence of the symptoms, but in milder form, and of shorter duration, than in the original episode. The incidence of mepacrine encephalopathy as a complication of malaria has been extremely small in my experience—18 cases among about 10,000 soldiers...
treated with mepllarine—and the condition may be considered as a very rare and relatively benign therapeutic accident which can easily be remedied.

While malarial episodes referred to the central nervous system are well recognized, peripheral nervous manifestations are conspicuously rare. Transient neuralgia is, perhaps, the commonest of such nervous symptoms, and is often associated with myalgia. There seems to be considerable difference of opinion as to whether malaria causes true peripheral neuritis. The neuritis that is sometimes a feature of malarial cachexia may bear explanation in terms of nutritional deficiency and avitaminosis. But the hyperesthesia and parasthesic sensations, as well as the paretic and myatrophic weakness, that occasionally supervenes for some time after malignant malaria may be expressions of a toxic neuritis. Such episodes most commonly affect the lower limbs, while brachial and facial neuritis, oculomotor and laryngeal palsies, and optic neuritis have been recorded. Malarial amblyopia can be distinguished from quinine amblyopia by the colour of the optic discs, which are bright pink in the former, and white in the latter. Though malarial neuritis is usually transient, it may be persistent or recurrent in an incompletely suppressed infection, as was the probable explanation in the following case, which occurred in a civilian patient who had suffered from several attacks (probably relapses) of malaria contracted during the great Ceylon epidemic of 1934:—

Case 6. Malarial Neuritis.—A Sinhalese schoolmaster, aged about 35, was referred to me about ten years ago, with a history of recurrent unilateral sciatica of several months' duration. The condition having proved intractable to diverse forms of treatment, both medicinal and physical, according to allopathic as well as ayurvedic advice, the question of paravertebral injection of the sciatic nerve roots had come up for consideration. From the patient's point of view, the disability affected him through recurrent interference with his vocation, rather than through its severity.

Examination showed the usual symptoms of subacute sciatic neuritis: abolition of the ankle-jerk, hyperesthesia, and wasting and flabbiness of the muscles of the leg. No evidence of focal sepsis, toxemia, alcoholism, or avitaminosis could be established. Laboratory studies showed no evidence of abnormality in the urine or feces, a mild degree of secondary anemia with no leucocytic abnormality in the blood, and a negative Wassermann reaction. The spleen was palpably enlarged, but not markedly so.

Close inquiry into the history of the case disclosed the fact that the patient had experienced transient tingling and pain after one of his numerous attacks of malaria, the symptoms having affected the opposite upper limb, and that his first attack of sciatic had come on a short time after this episode. It also seemed evident that anti-malarial treatment had been inadequate and haphazard. In view of these facts, a careful search was recommended for evidence of latent malaria, and the blood, after several negative smears, showed the presence of quartan parasites.

An intensive course of quinine treatment orally and by intramuscular injection was advised. About three or four months later the patient's doctor reported that the sciatic symptoms had steadily subsided and completely disappeared, that the patient had improved considerably in general health, and that he was quite free from his disability.

**Alimentary Episodes.**

Anorexia, nausea, and vomiting are common concomitants of malarial paroxysms, and ordinarily call for no special attention. But, occasionally, these symptoms may assume a degree of severity that constitutes a pernicious episode. Vomiting may be profuse and distressing, accompanied by epigastric tenderness.
and pain, and severe aching of the abdominal wall, but high fever is rare in these cases. Gastric episodes of this nature may be intermittent or continuous. Incessant hyperemesis, if uncontrolled, may produce haematemesis, dehydration, acidosis, exhaustion, and prostration, terminating in an algid episode. The only effective control of these gastric episodes is, of course, antimalarial therapy, which should be initiated parenterally. The gastric distress may be relieved by repeated lavage with iced alkaline solutions, followed by the oral administration of cerium oxalate grains 3, cocaine hydrochloride grain 1/8, in pill or cachet; adrenalin hydrochloride m 10 to 20, or creosote m 1/8, or chlorojetone grains 5 to 10, in crushed ice. After the gastric irritability has been controlled, quinine and mepacrine will, usually, be satisfactorily tolerated by the stomach.

Bilious vomiting with slight jaundice may occur in malignant malaria without producing much constitutional upset. Sometimes these symptoms may assume an intensity that produces the condition known as bilious remittent malaria. This episode usually comes on with severe nausea and increasing vomiting which rapidly becomes bile-stained, and may even become sanguineous. Epigastric tenderness becomes marked, and within a day or two jaundice is well established. The urine is frothy, dark, and contains bile pigment; the faeces show a heavy bile content, and bilious diarrhœa may occur; the blood shows the presence of bilirubin. If the liver becomes enlarged and tender, the patient begins to experience a sensation of discomfort and heaviness under his ribs. Although malarial jaundice is one of the pernicious episodes of malaria, it is not dangerous in itself, but through its pronounced tendency to produce rapid anaemia, asthenia, and toxæmia, it may predispose to fatal complications, as in the following case:

Case 7. Malarial Jaundice.—A Malay Lance/Corporal, aged 30, with no previous history of malaria or jaundice, was admitted to hospital with quotidian fever and chills of nine days' duration. On admission, his sclerotics were icteric, his liver tender but not enlarged, and his spleen was not palpable; his blood was negative for malaria, and no evidence of bile was present in his urine. On the third day, severe nausea and hiccup caused much distress, for which intravenous glucose-saline, and subcutaneous morphia were given. The blood now showed a malignant tertian parasitaemia, and oral quinine was initiated. By the next morning, the patient was drowsy and vomiting profusely; his urine became scanty and showed the presence of bile pigment, bile salts, leucine and tyrosine; jaundice was increasing in intensity. Vomiting was allayed by repeated sips of adrenalin in iced water. Calcium gluconate in glucose-saline was given intravenously. By evening, bilious vomiting set in and oliguria became more evident. The blood showed a biphasic direct van den Bergh reaction with a positive indirect reaction. The urine was so dark as to suggest haemoglobinuria, but spectroscopic and chemical analysis revealed that the coloration was due, not to haemoglobin, but to a massive excretion of urobilin. Meanwhile, the general condition of the patient was rapidly deteriorating although the temperature did not reach 103° F. and quinine medication by intramuscular injection was maintained apart from the other treatment. Vomiting was becoming persistent and hiccup almost incessant, with rapidly deepening jaundice, progressive asthenia, and exhaustion. Finally, signs of cardio-respiratory failure heralded the onset of acute pulmonary edema which terminated fatally within six hours. Malignant tertian parasites were present in the patient's blood almost up to the end.

Unfortunately, it was not possible to get permission from the patient's relations to make a post-mortem examination of the case, which might have
Malarial Episodes

revealed interesting information about the liver, for correlation with such findings as tenderness of the organ without enlargement, persistent oliguria with the excretion of leucine and tyrosine, apart from bile products, uroblin, etc., which suggest some hepatic catastrophe in the nature of acute yellow atrophy of the liver.

Malaria generally exhibits no significant manifestation of intestinal disorder, and the faeces rarely show any abnormality apart from an increase of bile pigment. Diarrhoeic episodes are, therefore, regarded as pernicious manifestations of malaria. Fortunately, simple malarial diarrhoea is usually readily amenable to antimalarial therapy, but when the condition complicates a debilitated case, it may induce a fatal termination, as in Case 9.

Some of these malarial episodes may closely resemble acute amœbic or bacillary dysentery. The isolation of malarial plasmodia from the faeces and intestinal exudate in such cases, comparable to the demonstration of amœbic, ova, or cysts in amœbiasis, has been found possible by special technique. The dysenteric episode, even in benign tertian malaria, may arise with dramatic suddenness and rapidly cause death despite energetic treatment, as in the following case:

Case 8. Malarial Dysentery.—A Sinhalese Lance-Corporal, aged 21, with no previous history of dysentery or malaria, was sent to hospital with fever and diarrhoea of a day's duration. He had a temperature of 100° F. with a pulse-rate of 80 per minute on admission. His tongue was clean and moist, no clinical abnormality was present in his heart, lungs, liver, or spleen. His stools were watery, but devoid of blood or mucus on inspection. The routine laboratory examinations were ordered and the patient was put to bed on an arrowroot diet. During the subsequent twenty-four hours his temperature rose to 101·2° F., and his pulse-rate to 100 per minute; the diarrhoea became more severe (20 stools a day) with severe griping, but not muco-sanguineous. The abdomen was soft but diffusely tender, and the liver and spleen remained unpalpable. Laboratory reports. Blood: Benign tertian rings and amœbic forms present; W.B.C. 3,400 per c.mm.; D.C.—P. 38 per cent, L. 50 per cent, M. 12 per cent. Faeces: Amœbic, ova, cysts, nil. Urine: Albumin, sugar, deposits, nil. Treatment comprised quinine by intramuscular injection, calcium gluconate in glucose-saline by intravenous infusion, starch-opium enemata, an increased fluid intake, and glucose-brandy by mouth. As the diarrhoea continued unabated, stools being muco-sanguineous and passed half-hourly, tincture of opium and sulphaguanidine by mouth were added to the treatment during the evening of the second day. By the morning of the third day, the patient was severely dehydrated, with subnormal temperature, soft, running pulse, dry, furred tongue, but no abdominal rigidity or distension. Treatment was maintained, but the diarrhoea was uncontrollable. The rapidly failing circulation and respiration were treated with cardiac stimulants and oxygen inhalations, despite, which the patient passed into an algid condition, and died within eighty hours of the onset of his illness.

The most dreaded, and happily the rarest, of all the alimentary infections in malaria are those severe malignant infections of the bowel which produce choleraic or choleraiform phenomena. These episodes are characterized by profuse, almost incessant, diarrhoea, with pale watery, mucoid stools, which may sometimes be sanguineous; severe dehydration, often augmented by vomiting; oliguria, or anuria; agonizing muscular cramps; profound prostration, algidity, and coma. When such a pernicious episode develops independently of fever or other evidence of malaria, and pursues a rapid and virulent course, clinical
differentiation from true cholera may be impracticable; and, if uncontrolled, the patient may collapse and die from heart failure.

### Hæmogenic Episodes.

The diminution of red corpuscles in malaria is only partly due to the direct destructive effects of the parasites. Considerable numbers of erythrocytes, both parasitized and normal cells, undergo disintegration in the spleen. The malarial pigment, hæmozoin, is presumed to play a part in this blood destruction, perhaps by hæmolytic action, and by increasing capillary permeability and facilitating hæmorrhagic loss. This latter possibility would explain the purpuric and other hæmorrhagic episodes occasionally met with in malaria. The youngest red corpuscles and the reticulocytes are, generally, the most vulnerable of the blood cells to the malarial plasmodium, but cells of all ages are parasitized in malignant infections. When oligocythæmia is pronounced, degenerative changes, such as poikilocytosis, anisocytosis, or punctate basophilia, may be exhibited by the erythrocytes. The anæmia of malaria is hypochromic in type, both through loss of hæmoglobin from hæmolyed cells, and through a lowering of the hæmoglobin content of the surviving ones. A further factor in chronic malarial anæmia is a diminution in the blood volume. Erythrocyte counts of two or three million cells per c.mm., with hæmoglobin contents of 40 per cent. or 50 per cent., were commonly encountered among soldiers who had suffered from recurrent attacks of malaria. The following is presented as an example of an exceptionally severe anæmic episode resulting from chronic malaria:

**Case 9. Malarial Anæmia.**—A Moor pioneer, aged 22, was admitted to hospital complaining of breathlessness, precordial discomfort, progressive wasting and asthenia, of two months' duration. He had suffered from numerous attacks of malaria in an endemic locality of North-Western Ceylon before enlistment. Within the preceding year he had undergone treatment for benign tertian malaria and anæmia in two military hospitals; on the last occasion he had been placed on the danger list, and remained in hospital for three months.

The patient was emaciated, weighing 89 lb., and presented obvious indications of severe anæmia—palpitation, dyspnœa, and faintness on mild exertion; an earthy pallor of his skin, pearly white conjunctive, blanched nail-beds, a flabby, pale tongue; a hæmic systolic bruit audible over his precordium; marked enlargement and tenderness of his spleen. Diagnosis was substantiated by laboratory reports: **Blood**: H.R.C. ½ million per c.mm., Hb. 20 per cent; blood picture—anisocytosis, poikilocytosis, polychromasia, pessary forms present; W.B.C. 4,000 per c.mm., D.C.—P. 64 per cent, L. 29 per cent, M. 7 per cent; blood smear showed benign tertian parasites after repeated search. **Urine**: Albumin, sugar, bile, nil, urobilin present. **Fæces**: Amebanœ, ova, cysts, repeatedly nil. **Gastric analysis**: n.a.d.

Treatment comprised iron medication for the anæmia, supplemented with liver extract and arsenicals; a modified course of quinine and mepacrine for the malaria; minerals, vitamins, tonics, and appropriate dieting to improve the nutritional state; and symptomatic treatment as required.

The initial response to treatment was satisfactory—the patient's weight rose to 94½ lb. in the first month, with a rise of his erythrocyte count from ½ million to 2 million cells per c.mm., and of his hæmoglobin content from 20 per cent to 45 per cent. Progress was retarded during the second month by frequent nausea and anæxia, which interfered with medication and feeding. Recurrence of alimentary complications during the third month was followed by a setback, with deterioration of the blood to its original
Malarial Episodes

condition; this was remedied by repeated small blood transfusions. Further progress was dramatically cut short by the unfortunate onset of a severe, intractable diarrhœa, which rapidly induced an algid state with emaciation, dehydration, cardiovascular asthenia, prostration, and fatal collapse.

Patients who do not tolerate oral medication with iron owing to gastric irritability and intestinal upsets, or those who do not appear to absorb iron from medicinal preparations, often readily assimilate iron from vegetable foods. The ayurvedhic physicians of Ceylon depend mainly upon a ferruginous vegetable diet in their treatment of anæmia, and of the herbs and shrubs utilized by them for this purpose, the leaves of Hydrocotyle asiatica and Sesbania grandiflora are two of the richest local sources of iron; the former is a little creeping herb with violet-like foliage, that has enjoyed from time immemorial a reputation for manifold medicinal virtues; the latter is a leguminous shrub whose white succulent flowers are considered a delicacy when lightly cooked. A diet rich in these two vegetables was the principal means of combating the extreme anæmia in another malarial patient, who was so gravey ill that the mere act of turning him on his side was sufficient to induce cardiac distress and dyspnœa. His condition was even worse than that of the last-mentioned patient, for he was quite unable to tolerate quinine or iron by mouth. With intramuscular quinine and a diet rich in the two vegetables, referred to, this patient made a remarkable recovery from what seemed, at first, to be an impending fatal anæmia.

The white blood corpuscles exhibit an interesting numerical oscillation in malaria. During apyrexial intervals there is a relative leucopenia with an increase of large hyaline mononuclear leucocytes. As a paroxysm comes on, more white cells appear in the blood, producing a moderate leucocytosis, while the mononuclears diminish rapidly with the rise of temperature and reappear with defervescence. A leucocytic count of 3,000 to 4,000 cells per c.mm., with a mononucleosis of 10 per cent to 15 per cent during afebrile intervals is considered pathognomonic of malaria. Both the mononuclear and the polynuclear leucocytes sometimes show pigmentation due to phagocytic ingestion of hæmозœin, or malarial pigment derived from disintegration of plasmodia and erythrocytes. The following interesting malarial episode is presented as a reminder that malaria may adopt a guise with a remarkable superficial semblance to typhoid fever:

Case 10. Malarial Leucopenia.—A Sinhalese Lance Corporal, aged 35, who had received his T.A.B. inoculations a few months previously, and who had experienced two attacks of malaria, was in hospital with a remittent fever which continued above 100° F., a slow pulse of 74 to 80 per minute, headache, thirst, a dry, furred tongue, with tenderness and enlargement of the liver and spleen. Blood examination showed no malarial parasites in two successive smears, and the Widal, Wassermann and Kahn reactions were negative. Blood-counts showed: W.B.C. 1,800 per c.mm.; P.C.-P. 19 per cent, L. 63 per cent, M. 11 per cent, E. 7 per cent; R.B.C. 3¾ million per c.mm.; Hb. 75 per cent. A third blood smear was examined and malignant tertian rings were seen. Blood culture reports were all negative, while the urine, feces, and sputum disclosed no abnormality.

The patient was put on a routine course of antimalarial therapy, (quinine grains 30 for two days, mepacrine 0.3 gramme for five days, followed after a two-day interval by pamaquin 0.03 gramme for five days). During the first few days a pleural rub was audible.
over the left lung base, and a catarrhal laryngitis appeared a few days later; these complications responded to treatment without affecting the clinical course of the case to any appreciable extent. By the fourth day of mepacrine treatment the fever was controlled, and the patient began to feel comparatively well.

But, despite attempts to raise the leucocytic content of the blood by protein injections, etc., the leucopenia remained between 1,800 and 2,400 per c.mm., with transient rises to 2,600, 2,800, and 3,600 per c.mm. during febrile paroxysms occurring in the first ten days. After completion of the antimalarial treatment, the leucocytic count showed a steady rise, reaching 7,000 per c.mm. by the nineteenth day (fig. 2), after which the patient was discharged from hospital. Subsequent re-examination of the blood after varying intervals during about a year revealed no abnormality whatever.

**RENA L EPISODES.**

The remarkable upheavals caused by the malarial parasite in the blood of its victims provide a notion of the factors that determine certain renal episodes in malaria. Polyuria is common during the malarial rigor, when the frequent passing of large quantities of pale urine indicate increased renal secretion during this stage. As the fever rises, the urine darkens in colour and diminishes in quantity, while with diaphoresis and defervescence it becomes scanty and high-coloured. During the cold stage there is an increased secretion of urea, chlorides, sulphates, and carbonates; with a diminution of phosphates. With the onset of the hot stage, the output of urea and carbonates progressively declines, while an increased secretion of phosphates occurs during the sweating stage. Transient urobilinuria, usually subsiding with defervescence, is very common in malarial paroxysms. Massive urobilinuria may impart a dark sherry...
Urobilinuria is a reflection of the degree of intravascular haemolysis caused by the malarial plasmodium; the liberated haemoglobin, is transformed in the reticulo-endothelial system into hemosiderin and bilirubin, the latter being excreted as urobilin in the urine, as well as in the bile; the latter phenomenon, when exhibited in excess, accounts for the icteroid and bilious episodes of malaria.

When intravascular haemolysis becomes too rapid and intensive for the reticulo-endothelial tissues to cope with the resulting massive haemoglobinæmia, the excess of haemoglobin over the renal threshold leaks out through the kidneys and appears in the urine as oxyhaemoglobin, methaemoglobin, and acid haematin, producing the phenomenon of blackwater fever. The exact pathogenesis of this form of haemoglobinuria remains obscure, but the condition appears to be some mysterious malarial episode in which, perhaps, a metabolic dyscrasia conditioned by the plasmodium, and probably also related to quinine, releases some haemolysin which disintegrates the erythrocytes and then splits up the liberated haemoglobin. Various theories advanced to explain the causation of blackwater fever have been recently reviewed by Skipper and Haine (1945).

The only instance of this episode in the present series occurred in a patient under observation in hospital, who had apparently contracted the disease in a hyperendemic locality, made a satisfactory recovery, and later developed permanent renal damage:

**Case 11. Malarial Hæmoglobinuria.**—A Sinhalese pioneer, aged 23, had completed a routine course of treatment for malignant tertian malaria. He had received quinine grains 90, mepacrine 1·5 grammes, and pamaquin 0·15 grammes, remained afebrile throughout the treatment, and was awaiting discharge from hospital.

He was a native of a malarious village in North-Western Ceylon, and during two years' service in hyperendemic jungle districts of North Central Ceylon with the Pioneer Corps, he had suffered from malaria six times. While on pilgrimage to a Buddhist shrine in Southern Ceylon, six weeks before admission to hospital, he had spent a night in a notorious blackwater fever zone.

On the day he was due for discharge from hospital, the patient suddenly fell ill, complaining of malaise, headache, nausea, vomiting, constipation, and aching in his loins. He had a temperature of 99·8° F., a pulse-rate of 100 per minute, with a sallow complexion, icteroid sclerotics, furred tongue, and a soft abdomen with tenderness over both kidneys. The urine revealed no abnormality apart from urobilin, amorphous phosphates, and a few epithelial cells, but by evening it became reddish, turning darker in colour during the night, with dysuria and increasing pain in the loins.

When referred for examination the next morning, the patient complained of exacerbation of all his symptoms, with profuse sweating, bilious vomiting, and severe aching over his renal, splenic, and suprapubic regions, which were extremely tender on palpation. His temperature was 99·4° F., pulse-rate 100 per minute, tongue dry and thickly coated, icterus marked, liver and spleen not palpable though tender. The urine, when freshly passed, appeared opaque and as black as stout, with a brown froth, but, on standing, separated into a clear, blood-red supernatant liquid, and a thick, opaque, blackish-brown sediment; it was neutral to litmus, and had a specific gravity of 1026, a heavy albuminous precipitate, positive reactions to the benzedrine and guaiacum tests for blood, no bile or water-soluble colouring matter; microscopical examination revealed no erythrocytes, but epithelial cells, pus cells, and granular casts were recognized amid a mass of cellular
debris and phosphatic crystals; spectroscopic analysis showed the characteristic bands of methæmoglobin and, after reduction, of oxyhæmoglobin. Blood examination showed a scanty parasitaemia (one malignant tertian ring in every two fields); marked secondary anæmia (R.B.C. 2 ½ million per c.mm., Hb. 50 per cent; a moderate leucytosis (W.B.C. 10,500 per c.mm., D.C.—P. 62 per cent, L. 34 per cent, M. 4 per cent); a negative direct reaction and a biphasic indirect reaction to the van den Bergh test. Records of the blood-urea concentration are, unfortunately, not available.

Treatment was directed towards increasing the secretion and alkalinizing the reaction of the urine, controlling the malarial infection, and giving symptomatic relief. Strict rest in bed was ensured, and a special nursing-orderly detailed for the case. The fluid intake and urine output were charted, the former being maintained at 10 pints per day by oral and intravenous administration: frequent drinks of sweetened citrus juice, small feeds of milk three-hourly, intravenous drip of 3 per cent sodium citrate in a pint of glucose-saline twice daily, etc. A mixture containing grains 30 each of sodium bicarbonate and potassium citrate was given four-hourly. Mepacrine 0·2 grammes was given orally thrice daily. Radiant heat was applied to the loins. Following a rigor with vomiting, dysuria, and oliguria, in the afternoon, the temperature rose to 103·4° F., with a low-tensioned pulse of 130 per minute. The patient became very apprehensive and alarmed about his condition, the gravity of which became evident to him in the light of his previous malarial experiences, which had been relatively uneventful. Injections of nikethamide 1 c.c. subcutaneously, and mepacrine hydrochloride 0·375 grammes intramuscularly produced a satisfactory clinical response, allaying the patient’s anxiety. A similar episode occurred in twenty-four hours. The urine was then alkaline, with a specific gravity of 1020, less darkly coloured, still albuminous, and with the same deposits as before. The liver and spleen showed palpable enlargement for the first time, forty-eight hours after the onset of the blackwater episode. The blood showed a parasite count of one malignant ring in every three fields and an increase in the anæmia (R.B.C. 1 ½ million per c.mm., Hb. 45 per cent). Thereafter, the case showed steady progress in response to the treatment: mepacrine was continued orally for five days, by, when the fever subsided; the urine was kept alkaline for a week, by which time the discoloration and albuminuria had cleared up, and the specific gravity was normal; the anæmia responded to iron, liver, and feeding. The patient was discharged from hospital thirty-six days after admission for malaria, and twenty days after the onset of his blackwater fever.

About two months later, this patient was referred again with asthenia, albuminuria, and oedema of his feet. Rest in bed and treatment for about a month was ineffective in controlling the albuminuria, and the patient was recommended for invaliding out of the Army on account of his renal defect.

Although albuminuria is said to be frequently noted in malaria in quantities exceeding a trace, particularly in quartan infections, the foregoing case was one of the very few instances in the present series where any albumin at all was found in the urine. The association of albuminuria and oedema with a reduction of serum-albumin is generally interpreted in terms of nephrosis rather than nephritis. Such a renal reaction may be induced by the irritative activity of malarial toxins, and, if prolonged, a nephrosis may, apparently, be the starting point of degenerative changes leading to chronic nephritis, either of the parenchymatous type or of the interstitial type. The application of this hypothesis, which postulates such a sequence of pathological reactions in the kidneys, would serve to provide a satisfactory explanation of the ultimate renal damage observed in the last case.

PULMONARY EPISODES.

A mild initial bronchitis associated with coryza is not uncommon in malaria, especially in malignant tertian infections. This may, occasionally, be the pre-
Malarial Episodes

include to a bronchiolitis or a bronchopneumonia, and less frequently to a lobar pneumonia. The diversity of features manifested in the pneumonic episodes of malaria would seem to imply the existence of a variable pathogenesis. Certain cases of malarial bronchiolitis and bronchopneumonia exhibit a perceptible periodicity that is suggestive of a direct relation with plasmodial activity. While some cases of pneumonitis are associated with a marked degree of leucocytosis, little or no leucocytic disturbance can be demonstrated in others. Of practical interest is the observation that, while some cases of malarial pneumonia are readily amenable to chemotherapy with sulpha compounds, there are others that resist control by such treatment but show a remarkable response to quinine and mepracrine medication. Most of the disappointing results in our treatment of the earlier cases of malarial pneumonia in this series, including among them a few fatalities, would appear, in the light of subsequent experience, to have been due to undue reliance on the antipneumonic virtues of sulpha therapy with insufficient antimalarial medication. Pneumonic episodes in malaria, if controlled by effective treatment according to the indications of the individual case, rarely give rise to any morbidity. The same may be said of the average pleural complications in malaria, as is illustrated in Case 10. But a protracted malarial pleurisy with a persistent effusion may lead to indefinitely prolonged ill-health; in a few cases where this happened in the present series, the patients had to be invalided out of the Army, after months of ineffective treatment in hospital, owing to chronic pleural thickening and diminution of respiratory efficiency.

The following case illustrates some of the observations referred to above:

Fig. 3 (Case 12).—Malignant malaria with pneumonia.
Case 12. Malarial Pneumonia.—A Sinhalese gunner, aged 23, who had suffered from malaria five years before, was admitted with fever, chills, rigors, and cough. For the first four days his temperature remained elevated between 102° and 105° F., with the pulse-rate varying between 90 and 120 per minute; but no abnormality was found in the spleen, lungs, or heart, the blood was negative for malaria and showed—W.B.C. 6,200 per c.mm. D.C.—P. 76 per cent, L. 29 per cent, E. 1 per cent; and the sputum was negative for tubercle bacilli. Quinine grains 10 t.d.s. was commenced. On the fifth day, clinical signs of apical pneumonia appeared in the right lung, subsequently confirmed by radiological appearances of uniform consolidation of the entire upper lobe of the lung (fig. 3). The appearance of malignant parasites in the blood at this stage substantiated the clinical diagnosis of malaria. Quinine medication was supplemented with sulphapyridine, vitamin C, antiphlogistine plasters, etc. The patient’s condition became so grave within thirty-six hours with restlessness and other toxic signs, that he was placed on the danger list. It was decided to withhold sulphapyridine and intensify quinine therapy; during the next twenty-four hours the patient was given parenteral quinine in two intravenous doses of grains 6 each and one intramuscular dose of grains 15. This was followed by a dramatic fall of temperature to subnormal, with a marked improvement in the general and pulmonary condition. Continuation of oral quinine, followed by mepacrine, completed the resolution of the pneumonia, and recovery was uninterrupted thereafter.

During the acute phase of this patient’s illness, his blood-pressure varied between 104/74 and 118/80, while the leucocyte count was remarkably constant between 6,000 and 6,800 cells per c.mm., arising to 8,800 per c.mm, when the patient was quite afebrile and his lungs almost clear.

Splenic Episodes.

The spleen being the principal seat of plasmodial activity, signs and symptoms referable to this organ are of special significance in malaria. The absence of splenic enlargement or tenderness cannot, however, be held to exclude the disease at any stage. Rarely does the primary attack of malaria produce clinical signs of splenic involvement until the fever has lasted for about a fortnight. The degree of parasitaemia bears no constant relation to the size of the spleen; though a large spleen may be evident with a moderate parasite count, a heavy parasitaemia need not necessarily be associated with pronounced splenomegaly.

Acute splenitis is an implication of excessive plasmodial activity. The organ becomes congested, tense and painful, and palpation may elicit extreme degrees of tenderness. Prompt therapeutic control of the infection is generally followed by subsidence of the acute splenic episode. But if clinical activity be protracted, or if the infection remains latent, some degree of chronic enlargement may persist in the spleen.

Chronic splenomegaly is the result of fibrotic changes in the organ caused by repeated attacks of malaria. This may be the result of recurrent infections or of relapses due to inadequate treatment. Occasionally, one encounters cases where the most energetic antimalarial therapy fails to control the disease; the only example of such an episode in this series was recorded in a Ceylonese medical orderly who had numerous relapses of malaria, showing both benign and malignant parasites in his blood, despite vigorous treatment with quinine and mepacrine, both orally and by injection, pamaquin, and the Ascoli technique; the case was observed through a period of sixteen months, and the patient was invalided out of the Army with his parasitaemia uncontrolled, though he was physically not severely affected by the prolonged infection.
Malarial Episodes

Although fairly large spleens were frequently seen among Ceylonese soldiers, who had developed chronic malaria, the really striking cases of splenomegaly that came under my observation occurred among East African and Indian troops. Some of these patients gave histories of chronic malaria lasting over periods of from three to six years, and most of them had probably suffered from malignant infections. One specially remarkable case, in an African soldier, presented an unforgettable picture of severe malarial cachexia, with advanced secondary anaemia, marked cardiovascular asthenia, and a huge, hard spleen extending for about three fingerbreadths below the umbilicus and resulting in a protuberant abdomen which contrasted strangely with the extreme emaciation of the rest of his body.

The clinical cameos here described are but reflections of a few facets of the many-sided clinical picture of malaria. They serve to emphasize the polymorphic activity of the malarial plasmodium, which seems to be able to evoke with ease symptoms of almost unlimited range and variety. When we contrast the simplicity of the common malarial paroxysm with the complexity of fulminating episodes associated with grave disturbance of bodily function, sometimes with lethal effect, there seems to be no analogy between this disease and any other. Some of these pernicious episodes, as, for example, hepatitis, pneumonitis, or haemoglobinuria, are as yet imperfectly understood. Are they coincidental complications, or may they be specific malarial phenomena? Until the pathogenesis of these still obscure manifestations is established, it may not seem unjustifiable to include them under the designation of malarial episodes.

This paper is published with the permission of the War Office, and of Brigadier C. A. Slaughter, D.D.M.S., Ceylon Command (1944-1946), to whom the author wishes to express his acknowledgments, as also to Lieutenant-Colonel H. R. Sheppard, R.A.M.C., Lieutenant-Colonel H. G. Alexander, I.M.S., Colonel V. H. L. Anthonisz, O.B.E., E.D., and Lieutenant-Colonel F. G. Smith, C.M.B., O.B.E., E.D., under whose successive commands these observations were carried out during the last four years of the war. The author is also grateful to his colleagues in the medical divisions of the military hospitals where he served as medical specialist for referring all cases of interest to him and for co-operating in their investigation. The views expressed in this article are the author's personal opinions, and not necessarily those of the military authorities.

REFERENCES.