M A L A R I A L P S Y C H O S E S
A N D
N E U R O S E S.

by

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INTRODUCTION.

It is very remarkable, that although malaria is traceably two thousand five hundred years old, that although it is the oldest disease of which we have any reliable record, that although it is the most widespread disease in the world to-day, and that although its most characteristic feature, the paroxysm—which through its periodicities gives the varieties of its forms their names—is largely a neurological phenomenon, there appears to be no comprehensive work dealing with the nervous manifestations of it. This work is intended to fill the gap in the pathological history of this nefarious and subtle parasite. It comprises the writer's experience of mental and nervous conditions apparently arising from malarial infection, along with that of others, so that as far as possible representative examples have been chosen from all available sources, to illustrate the range of activity of the parasite so far as it affects the nervous system. It will be seen that very few known syndromes are absent from the list, and it should be abundantly evident that there is almost no clinical limit to the variation of pictures it can produce.

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CHAPTER II.

THE PARASITE.

It will serve the purpose here to give a very brief account of the malarial parasite, which is so fully described in the standard works on tropical diseases.

There are three species of malarial parasite, namely Plasmodium malariae, P. vivax, and P. falciparum, and they produce respectively quartan, benign tertian, and malignant or sub-tertian fever. They differ from each other in minor points, and in their morphology, but the general course of their life-history is the same. As regards man, there are two phases of the life cycle, one of which, an asexual generation (schizogony) occurs in man, and a sexual generation (sporogony) which takes place in one of the several kinds of anopheline mosquito. There is therefore an alternation of generations which is brought about when an infected mosquito bites its victim.

In the human host, the essential habitat of the parasite is the blood, where it lodges in the red blood corpuscle upon which it feeds, with the formation of the characteristic malarial pigment. The other phase develops in the stomach of the mosquito.

The sexual forms of quartan and benign tertian, i.e. those adapted for life and development in the mosquito and found in the peripheral blood, are spherical. The sexual form of malignant tertian is crescentic. There are male and female spherical forms, male and female crescentic forms. On reaching the stomach of the mosquito, changes occur which result in the formation from the male sexual form of a flagellated body, the flagella of which play the part of spermatozoa. These fertilize the female sexual form, which has also undergone certain alterations. As a result of the union, a cyst is produced which may be considered as a kind of egg. Many parasites having been imbibed by the mosquito, many cysts are formed and these constitute the zygotes, which protrude from the outer surface of the stomach wall of the mosquito. The contents of these

cysts, or zygotes, divide to form spores, or young parasites, which are taken up by the salivary glands of the mosquito. This whole sexual cycle of the parasite takes about 12 days, by which time, with salivary glands loaded with sporozoites, the mosquito is ready to infect, via its proboscis, the next human victim.

These spores or sporozoites, once in the blood of the new host, attach themselves to the red blood corpuscles which they enter, and feed upon the haemoglobin with production of the well-known malarial pigment. Each spore (asexual) in its red-cell host slowly enlarges until it is due to divide. By this time, the benign tertian parasite is so large that its red-cell container is considerably distended beyond the normal. With quartan and malignant tertian parasites, this enlargement of the host cell does not occur. In any case, the one original spore divides into, in quartan 6-12, benign tertian 15-26, malignant tertian 8-15 merozoites.

These clumps of spores are the so-called rosettes, and correspond to the full ripening of the parasite. The membrane of the damaged red-cell then ruptures, and the merozoites are set free in the blood stream. Some are engulfed by phagocytic white cells, others enter fresh red blood corpuscles and start again the non-sexual cycle. The time of this process of intra-corpuscular development from entry to burst, varies with the species of the parasite. In quartan infections, it takes 72 hours, in both the tertians it occupies 48 hours, except in a special form of malignant tertian (quotidian) when it takes only 24 hours.

Hence the origin of the differential names for stages in the life-cycle of the parasite, which correspond to stages in the clinical picture of the malarial attack. The hot stage (about 3 or 4 hours) with the temperature high is when the parasite is young, and just beginning to grow in the red-cell; the fever-free period is when the parasite is at least half-grown, and is approaching the stage of division; and the chill (which lasts about an hour) with its commencing rise of temperature corresponds to the bursting of the red-cell and the shedding of the spores or merozoites. Thus, as the quartan cycle occupies 72 hours, the rise of temperature takes place on the fourth day (hence the name quartan), while in a simple or benign tertian infection which takes 48 hours for its

cycle, the rise is on the third day. The same is sometimes true of malignant tertian, but often enough its pyrexia is quite irregular, being sustained or remittent, and even quotidian forms are recognized.

The sexual forms (gametes) with which this description began, are formed from the ordinary parasites of the non-sexual cycle. Some of these become sexually differentiated, and instead of proceeding in the usual way to sporulation, change within their host's cells either into special spherical (in the cases of quartan and benign tertian) or crescentic (malignant tertian) forms (gametocytes, male and female).

Male and female spheres, and male and female crescents thus appear, and can be distinguished microscopically by the trained eye. [redacted] These are non-febrile forms. They resist quinine, and their function is to carry on that sexual cycle in the mosquito already briefly outlined.

While the above is the course, in bare outline, of a single generation of parasites, clinically there occur mixed infections, so that infection with two generations of tertian parasite would give a quotidian fever, or triple quartan infection would do the same. Then there are what are called sub-intrant infections, where one attack comes on before the other has subsided. This is due to a lack of uniformity in the developmental periodicity of the infecting parasite, or to double or triple infections with the same species of parasite. In these, the characteristic temperature waves are considerably altered.

The parasite not only destroys the red-cell which contains it, but produces a toxin or poison, which when liberated with the spores into the blood stream damages the blood in various ways, and the blood vessels, producing endarteritis, and ultimately any organ or tissue of the body, especially where there happens to be a concentration of parasites. The malignant tertian parasite appears to be, on the whole, the most damaging to the tissues, and particularly to the nervous system with which this work deals; but both benign tertian and quartan parasites are capable of doing the same, if with lesser frequency. Sporulation tends to take place

particularly in the vessels of the internal organs, notably spleen, liver, bone-marrow, adrenals, brain, kidney in the case of tertian infections; rather more in the peripheral blood in quartan infections. Consequently it is common to find extensive damage to these organs in tertian infections, and not so common to find serious damage to them in quartan infections. Possibly the comparatively diminished incidence in world distribution of quartan malaria is a factor in its estimated comparative benignity.

SYMPTOMATOLOGY: The incubation period, that is, from the time the patient is bitten by the infected mosquito or mosquitoes, until the earliest symptoms appear varies with the dose of sporozoites injected, the virulence of the parasite, and with many other factors affecting the patient's resistance. The usual incubation periods are, in malignant tertian malaria, 9-12 days; in benign tertian malaria, 14-18 days; and in quartan malaria, 18-21 days; but where small numbers of sporozoites are received, no symptoms may appear for months or years after infection. These are the so-called latent infections, which are considered apart in the chapter of that heading.

In the classical onset, however, there is often a premonitory stage lasting a few days in which the patient complains of lassitude, weariness with tendency to yawn, headache, sore bones, want of appetite, sickness, vomiting, and the temperature may be found to be a little up. This develops after a few hours into the

Cold Stage, when the rigor commences with feeling of intense cold, with severe shivers and chattering of the teeth. The face is pinched, the skin pallid and cyanotic, and there is often "goose skin" and the patient piles on clothes. The temperature during this stage is rapidly rising. In children, the onset is more often masked by gastro-intestinal disturbance or convulsions.

Hot Stage. After an hour or so, the shivers gradually abate, and give place to a feeling of warmth, which deepens to the other extreme of intense heat, which may be very distressing. The face becomes flushed, the pulse rapid, full, bounding, headache is often intense, vomiting frequent, and maybe intractable; respiration rapid, the skin dry and hot and the temperature often 104°F to 106°F

or higher. Clothes are discarded.

Sweating Stage. After three or four hours of hot stage, profuse perspiration develops, with subsidence of the temperature and the other accompaniments, and ending with a feeling of relief as a rule. The patient then may feel quite well, or there may be a feeling of slight tiredness, but in any case, he is usually ready for his usual duties. The temperature may be sub-normal, and may remain so until the next attack a few days later. This period of defervescence takes two to four hours as a rule. While this account is that of a classical attack, the various forms the fever and symptoms may take are legion.

During the attack, the spleen is usually enlarged and often palpable, and also during the attack or subsequent to it, or both, symptoms of irritation may be referred to any organ or tissue of the body. The parasite being blood-borne, and being a local irritant, there is no part of the body out of its range. It is largely this range of activity that gives the parasite a power of mimicry that can simulate almost any other disease to which human flesh is heir.

It is with the neurological aspects of this tissue damage that the present work is intended to deal.

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CHAPTER II.

MALARIA.

The parasites, then, lodge in the red blood corpuscles, producing disturbances of the blood and capillary blood-vessels, ranging from mild degrees of endarteritis up to complete blockage and even haemorrhage with consequent defective focal blood-supply to the parts involved.

They sporulate (tertian, sub-tertian) chiefly in the vessels of the internal organs, and notably the brain. The sporulation occurs characteristically every third day (tertian, subtertian), or fourth day (quartan), but in any case intermittently, and is usually accompanied by the well-known features of fever and shivering, followed by sweating.

On these three facts,

1. Capillary irritation, blockage, haemorrhage.
2. Sporulation (in all degrees) in the vessels of the internal organs (especially spleen, brain, bone-marrow).
3. Periodicity or intermittency of sporulation,

rest the multiplicity, degrees, pitfulness, and subtlety of the clinical features of infection with this will-o'-the-wisp organism. The initial damage being a blood and blood-vessel one, it follows that every organ and tissue of the body comes within the range of the parasite. The nervous system is no exception to the rule.

Broadly, so far as the nervous system is concerned, the sequelæ to infection fall into several groups:-

1. Acute—delirium, coma, algid form, ending in recovery, death, or transition into one of the other forms.
2. Cachexia—a chronic form in which the patient is seriously ill in a general way, and in which nervous disturbances make a prominent part of the picture.
3. Spontaneous recovery—assisted, maybe, by leaving the infected

area and quinine.

4. Latent forms—a large group in which the patient is often obscurely nervous, with symptoms referable to any group of organs—cerebro-spinal, cardio-vascular, gastro-intestinal, special sense organs, ductless glands. The parasite is capable of lodging for long periods—months, years—in the spleen and bone-marrow, going through its life cycle there and only occasionally taking on slight or great exacerbations of growth and emerging detectably into the peripheral blood. These exacerbations are frequently stimulated by some temporary strain on the patient, such as change from an habitual climate to one hotter or colder; intercurrent disease; worry; exposure to the sun or any extremes of temperature; traumatism; surgical operation; fatigue; and so on. In this form, the parasite, clinging to its depot (spleen, bone-marrow) is often highly resistant to treatment, so that for long periods the patient may enjoy comparatively good health, punctuated over the months and years by periodic break-downs, which may be long or short, transitory or permanent, depending upon the adjustment of relations between host and parasite. It is a type of guerilla warfare in which the parasite often gets the best of it by successfully remaining under cover.

It is mainly the business of what follows to reveal the habits of this enemy in hiding, so far as it affects the nervous system.

That the parasite damages the nervous system directly there is abundant evidence; but it also does so indirectly by attacking the blood-forming organs, and the endocrine glands, notably the adrenals. Furthermore, by concentration on one or more of the other systems—cardio-vascular, gastro-intestinal, etc., an emphasis of symptoms (often nervous) referable to one or other of these may be produced, to qualify the picture of nerve disturbance.

It would appear, therefore, that malaria is very like syphilis—in its ability to affect any organ or tissue of the body, with its strong predilection for the nervous system, and in its power of prolonged latency with subsequent disastrous effects. Mayo states

that the spirochaeta pallida can remain alive in the spleen for long periods, resisting all treatment short of removal of the spleen. The malaria parasite does the same.

The periodicity of symptomatology of malarial infections is the most prominent clinical feature of distinction, and is often the first to awaken even experienced observers to the true nature of the case.

When we remember that malaria is the most wide-spread disease on the world to-day, that it is one of the oldest of which we have any reliable record, we come to realise in it, as I hope to show, a powerful factor in the depreciation of race efficiency. History is studded with instances of colonies wiped out, cities abandoned, armies defeated, by this insidious and wide-spread disease. There is much to suggest that those who have survived in the worst areas have paid for their survival in terms of inefficiency, physical and mental. It is with the historical evidences of such large scale operations as these that the next two chapters deal.

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CHAPTER III.

Malaria in History.

Malaria has played an important part in the history of the world. While the same observation may be made of many other infective diseases, such as tuberculosis and plague, there is much to suggest that malaria has exceeded all other infective diseases in range and extent of world distribution. In any case, because of the periodicity of its attacks, and because its spread is necessarily associated with the presence of the mosquito and marshy lands, malaria is easily identified in the ancient records, and its bearing on history more readily estimated.

In considering the history of the disease, the associate conditions necessary for its maintenance and spread—namely, mosquitoes and marshy ground—are always taken into account. Malaria appears to have been originally an African disorder, and some authorities maintain that it existed in Egypt from the most remote times, from the epoch of Minios (about 2100 B.C.) when Egypt was a vast marsh.

Groff maintains that the ancient Egyptians suffered from malaria as indicated by the annual recurrence of a fever which is mentioned in the inscriptions on the ruins of the temple at Denderah.

Herodotus (443 B.C.) describing the marsh-dwellers of Egypt indicates that they were much troubled by gnats, and at night wrapped themselves in their fishing-nets to protect themselves from the bites of these insects. It is, however, in the history of Greece that the presence of malaria is most clearly defined.

Up to the Bronze Age in Europe (2000-1000 B.C.) Greece was covered with forests, but then the people began to cut down the trees, thus favouring the formation of marshes and lakes and consequent extension of malaria. Cariamatis says that from Greek mythology, which in its symbolism alludes to real events, the suggestion comes that pre-historic Greece was not covered with marshes as it is now, but nevertheless he holds that malaria in Greece is as old as Greece itself.

Jones maintains that up to heroic times Greece was healthy,

Greece was healthy, pointing out that the earliest inhabitants seemed to have chosen sites which in later times were the most malarious, implying their original healthiness. He, and other authors, including Cariamatis, agree, however, that Greece was infected from Egypt and Asia, as there were Greek settlements along the North African Coast in the 7th Century B.C. and consequent communication between the two countries.

The first reliable reference in Ancient Greek literature is in the poet Theognis (540 B.C.) where he asserts that nothing crushes the good man so much as poverty, neither old age nor yet ῥιγάλος (the shivers preceding fever) which later on Galen defines as a quotidian.

In all Greek medical literature dating from 400 B.C., πυρετοὶ (fiery fevers) are classed as (1) continuous (συνεχεῖς), (2) intermittent (διαλείποντες). The second class is subdivided according to periodicity into (1) quotidians (ἡμιτριταῖοι), (2) tertians (τριταῖοι), (3) quartans, (τεταρταῖοι). The first lay definition of this periodicity is in Plato (Timaeus about 370 B.C.) who also gives this full classification of intermittent fevers. Plato describes the spleen as a receptacle for purgations of the liver and accounts in this way for splenic enlargement. When it is remembered that the Greeks held that tertians and quartans were caused by bile, Plato's words here become more significant. He further declares that the humours of acid and salt phlegm and such as are bitter and bilious, when no other outlet for them from the body can be found, befog the soul and produce manifold vices—peevishness, melancholy, rashness, cowardice, forgetfulness, and stupidity. This picture suggests malarial cachexia.

Hippocrates (430 B.C.) refers to tertians and quartans so often that it is quite evident that malaria was very prevalent in his time. He states that in Autumn quartan fevers and splenic diseases are very common and that bilious persons with enlarged spleens are evil-complexioned, ulcerous and emaciated, foul-breathed and constipated. He noticed that dwellers in marshy places suffered from enlarged spleens, and while typhoid fever may be confused with malaria on this account, it is distinguished from it where the fever associated is defined as of tertian or quartan periodicity, as it frequently is. In the "Aphorisms", he says that melancholia was most common in Spring and Autumn (beginning and height of malaria season),

and that it was evidently caused by a "black bile" to which the Greek doctors attributed quartan fevers.

Then again he noted the degradation of those who lived in low, moist, hot districts and drank stagnant water. They suffered from enlarged spleen, were stunted, ill-shaped, fleshy, dark, bilious, cowardly and averse to hardship. He gives prominence to the characteristics of an acute and apparently common disease φρενῖτις (phrenitis or brain inflammation) showing delirium and pain in the hypochondrium. It was usually fatal on the third, fifth, seventh, and in any case not later than the eleventh day from the beginning of the attack. Galen later commenting on the aphorisms of Hippocrates says that this disease has generally a tertian periodicity. It suggests cerebral malaria.

Aristotle (358 B.C.) in his "Ethics" uses the word μελαγχολικὸς (atrabilious) the nearest modern equivalent of which is "nervous" (Burnet). This word was a recent addition to the Greek language, taken from the picture of those afflicted with ἡ μέλαινα χολή, (the black bile), which was considered by the medical writers of that time to be the cause of quartan fevers, while tertians were caused by yellow bile. The three cognates, μελαγχολία, μελαγχολικὸς, and μελαγχολῶ show that quartans were common, that they were observed to influence character, and incidentally that they probably became endemic during the last quarter of the 5th Century B.C. It is natural that the new term μελαγχολικὸς (atrabilious) coined to designate the victim of quartan fever should be derived from the bilious complexion of the patient rather than the enlarged spleen, which was certainly observed but was less obvious. To the Greeks of this period, when the word was first employed, μελαγχολικὸς signified a sufferer from black bile, a crazy neurotic person, a sufferer from quartan fever, which we interpret as malaria.

In the pseudo-Aristotelian "Problems", we are told that inhabitants of marshy districts age rapidly, that fevers are most common in Summer; that Spring and Autumn are unhealthy; that a dry Summer following upon a rainy period is deadly, especially for children and that quartans are common at such a time. Consumption, ophthalmia, itch, plague, are held to be infectious, while fevers (quartans) were not infectious. Infectious fevers (typhoid, typhus,

plague) we know did occur, so that the fever which was considered non-infectious was likely to have been malaria, the method of infection not then being recognized. It appears that Greece as Aristotle knew it was highly malarious.

Galen (164 A.D.) a Greek physician practising in Rome seems to have made a special study of fever periodicity. He gives the same classification of intermittent fevers into quotidians, tertians, and quartans as numerous other Greek writers before him have done. He recognises multiple infections and points out that a fever recurring daily can be produced by two tertians or three quartans. He notes that "quotidians attack mostly very young children, tertians mostly young men, and semi-tertians (malignant tertians) men in the prime of life". This observation suggests that the Greco-Roman world in his time was very malarious. He gives a quartan periodicity to "Splenic diseases and to melancholia generally", and holds that large spleens are caused by excess of "melancholy humour".

"Melancholy" is defined as beginning often with indigestion, vomiting, foul-breath, and characterised by sleeplessness, fear, depression. Examples of it vary greatly, some fear death, others commit suicide; some shun the light, others darkness. It occurs more commonly in adults than in the young, and may be consitutional or acquired—a picture of simple melancholia as we know it to-day, which Galen covers with the same word μελαγχολικὸς as the Greek writers of about 500 years before him used to designate a sufferer from μέλαινα χολή (the black bile) and which they associated aetiologically with quartan fever. Up till Michel Psellos in the 11th Century, it was believed that yellow bile caused tertian fever, while black bile produced quartan fever.

Lucian (160 A.D.) who had travelled much in Greece, and lived for years in Athens is an excellent witness to the prevalence of fever and ague. He mentions φρενῖτις (phrenitis or brain inflammation) also, which answers the description of cerebral malaria, as in Hippocrates and others.

Oribasius (c. 355 A.D.) writes "Epilepsy also is a convulsion. A quartan then cures epilepsy, so that if the quartan comes after the epilepsy, the epilepsy comes to an end, while epilepsy never supervenes upon a quartan". "Now a quartan frequently turns into a

quotidian, rarely into a tertian".

Numerous other Greek writers testify to the prevalence of intermittent fevers, such as Diocles, who did not believe in fevers with longer periodicity than quartan, as others did; Agathinus of Lacedaemon (90 A.D.) who wrote a special treatise on "Semi-tertians" (malignant tertians); Archigenes of Apamea, who was also familiar with semi-tertians; Heraclides of Tarentus, (330 B.C.) who was praised for his treatment of φρενῖτις (phrenitis); and Antyllus, who wrote on hygiene, says that "The late afternoon is unhealthy, like Autumn, and so is the early part of the night" (when mosquitoes are about).

All these references, which are only a sample of those available, make it clear that malaria was a disease very prevalent in ancient Greece from 400 B.C. onwards. By the classic period, the forests had considerably diminished in number, and there is also evidence to show that conditions for mosquito growth were present, in that there was a special Greek word τέλματα for low lying land that became a marsh after heavy rain. Frequent references to these swamps show how common they were. Ischomachus, writing to Socrates, says "Heaven supplies water, all the low places becomes swamps τέλματα and the earth supplies all kinds of growth". He who is going to sow must clear the land. If he throw into the water the refuse, the mere lapse of time will turn it presently into that which the land delights. For what growth, what earth does not, when in stagnant water, become manured?".

There is evidence that the Athenians were plagued with mosquitoes, among other insects, but so far none to identify the anopheline variety.

From the attention claimed by intermittent fevers with regular periodicity in the ancient writings, both lay and medical, we are justified in concluding that malaria was endemic in Greece from about 400 B.C. onwards.

The history of malaria in Italy, so far as it can be traced, is hardly of less importance than its history in Greece. It is probable that at one time it was free, and that infection was carried by slaves from Africa and Asia, and by infected soldiers returning home.

Solinus and Dionysius of Halicarnassus are responsible for the

observation that the first settlers on the Palatine Mount had to abandon the place because of the pernicious exhalations of the Velabrum.

The first unmistakable reference to malaria in the native literature, however, occurs in Terence (d. 159 B.C.)

So. "What kind of disease is it?"
Pam. "Fever".
So. "Quotidian?".
Pam. "So they say".

This implies fevers with periodicity other than quotidian.

According to Pliny the Elder, Q. Fabius Maximus, Consul in 121 B.C., suffered from quartan fever. He also mentions tertians. Varro (116-28 B.C.) writes that in marshy places "crescunt animalia quaedam minuta, quae non possunt oculi consequi" and that these minute creatures, entering the body by the mouth and nostrils produce "difficiles morbos".

Cicero (106-43 B.C.) refers frequently to tertians and quartans; he indicates that quartans are not serious, and that fatigue induces fever. He also mentions unhealthy districts and that a Roman Army was apparently attacked by fever near Brindisium. From Cicero onwards almost all writers mention quotidian, tertian, and quartan fevers. In a letter to his freedman, Tiro, a reference to quartan ague occurs with congratulation upon his being on a fair way to recovery. He distinguishes between tertian and quartan fevers, and attributes their regular periodicity to the Will of the Gods.

Vitrubius (15 B.C.) remarks that marshy districts were pestilential; "quibus antea insidentes sunt paludes, et non habent publicos exitus profluentes, neque per flumina, neque per fossas, uti Pomptinae, stanio putrescunt, et humores graves et pestilentes in iis locis emittunt."

Horace (d. 8 B.C.) makes it clear that the periodic fevers were endemic in Rome in his time. He tells of a mother who promises Jupiter that her son shall stand naked in the Tiber on the day his quartan leaves him. He says that on his Highland Estate he need not fear the unhealthy Autumn, during which the Goddess of Death reaped so rich a harvest in Rome. We find him advising his friend and patron Maecenas to leave Rome in July. There is a significant passage

where he says that all parents fear for their children in Autumn; and another making it clear Pomptine marshes were infested with mosquitoes, as during a journey from Forum Appii to Terracina, he could not sleep for them.

Tacitus (c. 55-120 A.D.) indicates that the Banks of the Tiber during inundation were unhealthy "adiacente Tiberi Germanorum Gallorumque obnoxia morbis corpora fluminis avilitas et aestus impatientia labefecit". This, together with the structure of the Roman house of the time, would provide excellent breeding ground for mosquitoes. Each house had a hole in the roof to let out smoke. It also let in rain, which collected in a cistern below (compluvium, impluvium) which would provide beeeding ground for mosquitoes.

Suetonius (98-138 A.D.) indicates that Caesar suffered from a quartan in his youth.

Pliny the Elder (23-79 A.D.) in his Natural History makes frequent reference to tertian and quartan ague, and gives a number of charms and remedies against it, showing that it was well known to the people of his time.

Celsus (50 A.D.) wrote at length on quotidian, tertian, and quartan fevers. He lays stress upon semi-tertian (malignant tertian) and deals largely with their treatment, which was begun early because of their great malignity. He points out that in quotidians, the temperature sometimes ran in two series, suggesting double tertian infection. His directions for treatment of these fevers are much fuller than for any other disease, which fact seems to have a bearing on their prevalence.

Juvenal (d. 130 A.D.) refers more than once to quartan fever.

Galen (164 A.D.) expressly states that the most malignant form of intermittent fever, semi-tertian (malignant tertian), was an everyday occurrence in Rome. It is clear from the literature of the time that from about 200 B.C. intermittent fevers with regular periodicity were prevalent in Rome and other parts of Italy, and that they were associated in the minds of the writers with marshy districts, autumn pestilence, and incidentally with the presence of mosquitoes. Malaria is the obvious inference.

The early Hindu writers Charaka and Susruta recognise three types of intermittents. The quotidian was a disease of the meat, the tertian of the fat, and the quartan of the bones. In an extract

from the Sanskrit, Susruta, written at least 13 centuries ago, there is a brief enumeration of some of the prominent symptoms of malaria. The Arab physician Rhazes (932 A.D.) mentions intermittent fever and used arsenic in its treatment.

Throughout the middle ages, there is little mention of intermittent fevers, except what was borrowed from the ancients, though Celli cites evidence to show that the disease ravaged in the Roman Campagna with varying intensity.

Paracelsus, living in Germany between 1490 and 1541 A.D., appears to have had experience of malaria in his practice.

Mercatus, Court physician to Philip II and Philip III of Spain, wrote on the subject of intermittent fevers in the latter half of the 16th Century.

Nicholls considers the decline of the ancient cities of Ceylon—Anuradhapura, founded 437 B.C., and Pallonnaruwa, founded about 781 A.D., the ruins of which now lie in the forests of Ceylon, due to malaria. As late as the 12th Century A.D., they still flourished, but after that decline set in; and when the Portuguese were obtaining a footing in Ceylon at the beginning of the 16th Century, the Art and Culture of the people had sunk to a low level compared with that revealed by the wonderful ruins of these ancient cities recently discovered.

Sardinia has been malarious from the earliest times. The reference comes down to us from the Romans, 698 A.D. There are numerous references to the prevalence of malaria in the island from that date onwards. In 1801, Pietro Leo notes than a third of the island is affected by it. By 1910, Conti records that the whole island is malarious.

The island Brioni in the Piriatic Sea, once an important province of the Roman Empire and Venice, and still showing vestiges of Roman Civilisation, was for many Centuries uninhabitable because of malaria. Between 1800 and 1899, a succession of owners made several fruitless attempts to eradicate the disease, but it was only in 1899 when Koch took charge of the sanitation of the island that this was done successfully. Between 1901 and 1902, whenit was declared malaria free, the value of the island rose from *$40,000* to *$1,000,000*.

In 1824, Spigelius published an extensive treatise on semi-

tertians, the first book of its kind. It shows that the disease was prevalent in Germany as well as in Italy.

In 1632, Cinchona Bark was introduced into Europe from South America, and with it began a new period in the history of malaria.

In more recent times, the devastating effects of malaria have been apparent in numerous instances. Perhaps its most fatal effect upon an army is the case of the famous Walcheren Expedition in 1809. After two months fever, an Army of 35,000 men had 10,000 sick, and 4,000 dead.

Boudin, who accompanied the French Expedition to Morea in 1820, records that a whole army was decimated by malaria in the marshes of Navarino, without having fought a battle.

It is well known that the construction of the Panama canal was held up until malaria and yellow fever in the surrounding districts had been dealt with.

Celli maintains that the greater prosperity of Northern Italy as compared with Southern Italy is due to the prevalence of malaria in the latter region.

Whole towns, such as Johannipolis at San Paolo and Gregoriopolis at Ostia in the 9th Century, were destroyed by it.

Many parts of Sicily and Sardinia have been ruined by it. Celli writes "From time to time in the various localities where malaria is endemic, the disease becomes epidemic and even pandemic; this occasionally occurred in places where it had not been prevalent for some time. We had an example of this in the Province of Rome in the year 1879, when a true malarial pandemy raged. From 1887 to 1898, the mean mortality from malaria in Italy was about 15,000 victims per year, and calculating from the number of deaths, there must have been about 2,000,000 cases of malaria a year. The mean duration of a malarial infection which usually recurs is generally long. On occasions it may continue for years. The loss of labour, and of production, and the expense entailed in dealing with this disease consequently amount to several millions of francs. If we add that the average life of the worker in malarious places is shorter and the infant mortality higher than in healthy places, we get a somewhat proximate idea of the financial losses that this scourge causes to our country. Because if we calculate that owing to malaria

about 5,000,000 acres of land, and very many localities as, for instance, the Agro-Romano remain, not uncultivated, but certainly imperfectly cultivated, the economic loss derived from it must undoubtedly be enormous."

North, the author of "Roman Fever", writes: "In the year 1879-80, a Parliamentary commission was appointed to investigate the condition of the Railways in Italy. The Calabrian Railway, of more than 500 kilometres in length (310 miles) was found to be almost paralysed by it, for it not only returned no profits on Capital expended, but required large annual subsidies in order to keep it open for traffic. The condition of the employees was found to be most unsatisfactory, and from reports made by them and from Official Statistics, and Hospital Registers, it was shown that the loss of labour from malarial fever, the expense of providing medicines and the maintenance of sick employees was such as to require the most serious attention on the part of the Government..... Translated into money, the cost throughout Italy of this extra pay, extra labour, and medicine, but not including the cost of maintenance in hospital, amounted annually to no less a sum than 1,500,000 Italian lire, or about *£600,000 sterling.*"

In British territory, its effects have been hardly less marked. In 1844, the advisability of abandoning Hong Kong as a Colony was deliberately discussed because of the serious development of malaria on the island.

In 1868, malaria appeared in Mauritius, and has caused endless misery there ever since.

Sir Ronald Ross writes "Malarial Fever is, perhaps, the most important of human diseases. Though it is not often directly fatal, its wide prevalence in almost all warm climates produces in the aggregate an enormous amount of sickness and mortality. In India alone, it has been officially estimated to cause a mean annual death-rate of 5 per thousand; that is, to kill every year on the average, 1,100,000 persons—a population equal to that of a great city. The total amount of sickness due to it is incalculable, but may be put by a rough estimate at between a quarter and a half the total sickness in many tropical countries. Often all the children and most of the adults are infected by it.

"Very malarious places cannot be prosperous: the healthy shun them, those who remain are too sickly for hard work, and such localities often end by being deserted by all save a few miserable inhabitants.

"Malaria is the great enemy of the explorer, the missionary, the planter, the merchant, the soldier, the farmer, the administrator, the villager, and the poor, and has, I believe, modified the world's history by tending to render the whole of the tropics comparatively unsuitable for the full development of civilisation. It is essentially a political disease—one which affects the welfare of whole countries; and the prevention of it should therefore be an important branch of public administration."

Numerous other instances could be given where people have been debilitated and progress checked by this subtle, wide-spread disease; but enough has been taken from available records to indicate its malign influence on State Economy, both mental and material.

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CHAPTER IV.

EFFECT ON CHARACTER, AND RACE DEGENERATION.

That the effect of malaria on character was noticed by the ancient Greeks, is evidenced by the quotations from Plato, Hippocrates, and Aristotle in the previous chapter. The association in their minds of "black bile" with quartan fever on the one hand, and on the other with picture of mental abnormality in which unusual depression is the chief feature, makes this clear.

That our modern word melancholia should have actually originated in this association (Jones), seems to show how much it had impressed itself upon them, and incidentally speaks for the prevalence of the disease among them. Any other infective disease such as syphilis or influenza may, and actually does, produce the same mental change; but there is no feature by which we can surely identify these diseases in the ancient literature, even if they did exist, while there are features (temperature periodicity, splenic enlargement, etc) by which malaria is recognizable. Moreover, in diseases like influenza and enteric fever, which tend to come in epidemics, the great majority of those affected are either dead or have recovered within a short period of time, whereas malaria for the most part is much less incisive. It is infrequently epidemic, and tends rather to slowly sap the energy and vitality of a people over a long period of time, leaving the country abandoned and desolate. The whole process of devitalisation is so slow and unobtrusive, that for generations it may hardly attract attention, remaining unrecorded by contemporary historians, until later writers record how fever-stricken and desolate are certain places which we know from other sources to have been at one time opulent and flourishing.

People who have malaria, and remain in a malarious district, are liable to keep it all their lives, and to eke out a shortened existence in a more or less debilitated condition. This is due to the fact that the parasite lives on in the body depots (such as the

spleen and bone-marrow) even when it cannot be detected in the blood-stream, ready to reproduce itself rapidly if the resistance of the host is reduced by any increase of stress by fatigue, shock, exposure, or intercurrent disease. Epidemics of it, lasting from 2 to 4 years, have been noticed after war, famine, etc. (Kuschew). It is in the nature of the trouble to lower the physical and mental efficiency, and to change the character of a larger number of people over a longer period of time, than any other disease. This is its unique characteristic, which works out through heredity as race deterioration.

W. H. S. Jones, endeavouring to account for the change in Greek character that took place in the 4th Century B.C., cites malaria as the chief cause. He points out that about this time the Greeks became dissatisfied, querulous, and gradually lost their brilliance. Art became sentimental, philosophy became pessimistic, some schools of thought taking "absence of feeling" (ἀπάθεια) or "absence of care" (ἀταραξία) as the height of human endeavour. They ceased to create and began to comment. Patriotism declined, initiative vanished, vacillation and indecision, fitful activity followed by depression, cruelty and weakness in public life led on to the struggle with Macedonia, and the final conquest by Rome. By 300 B.C., the Greeks had lost much of their manliness and intellectual vigour.

This is not quite a new idea. The Greeks of the time, as indicated above, (see Plato, Hippocrates, Galen) associated intermittent fevers with deterioration of character and Pausanius (160 A.D.) indicates that the weakness of the Greeks in the 3rd Century B.C. was partly due to disease, though he does not mention any special kind. Considering the lofty position held by Athens, this is a disastrous change, such an one as could readily be produced by debilitating, rather than fatal, disease like malaria, widespread as it evidently was in Greece at that time, and as it happens, still is to-day.

As in the case of Greece, so in the case of Rome, Jones links up the existence of malaria in the Roman Empire with the deterioration of its people leading to their decline. He maintains that the continuous civil wars of the first century, leading to increase of waste lands (implying swamps and mosquitoes) were against them; that

economic causes were against them; that Rome became more and more congested and degraded, while the country became more sparsely populated. Nevertheless this does not wholly account for the change. Juvenal and Tacitus give terrible pictures of degraded Roman Society in the first century A.D., which show it to have been not only wicked, but diseased. The extravagant cruelty, will desire for excitement, complete lack of self-control point to some physical defect. He believes therefore, and has gone far to show, that "while malaria made the Greek weak and ineffecient, it turned the sterner Roman into a bloodthirsty brute". That "if μελαγχολία produced ferocness, *atra bilis* made its victims mad".

North, who lived in the Roman Campagna for 3 years, writes, "The group of maladies called malarial are perhaps the most widely distributed and the most disastrous in their effects of all the diseases to which man is liable.

"Their presence rendered large portions of the earth's surface absolutely uninhabitable; over still larger areas they consitute an almost insuperable obstacle to all material progress, in as much as the inhabitants of those countries in which malarial disease prevails to any serious extent, labour under difficulties and disadvantages which have exerted, and always will exert, a profound influence upon the character of the race, and its position in the human family.....

....."The effect of the disease on the people is to unfit them for labour, to cause loss of time, loss of money, and generally to diminish their producing power, while at the same time, the race, if left to itself, tends towards moral and physical degradation. Thus, other things being equal, a malarious country cannot hope for the same rate of progress as one which has not to pay this heavy tax upon its energies.....perhaps the most incapacitating disease to which man is liable".

Then, again, Macculloch, who introduced the word malaria into the English Language, in his essay on the subject in 1827, gives a graphic account of its effects on both body and mind:-

"That the residence of successive generations in a district of this nature produces a degeneracy of the races, is amply shown in various parts of France and Italy; and then when the inhabitants

of the marshy plains and valleys come into immediate contact with a people of the same radical origin and race, inhabiting the healthy, mountainous or hilly tracts, which bound or include these. The stature not only becomes reduced, but deformities are frequent while anatomically, the bones are found to be affected, their extremities in particular being unusually large and spongy, and rickets, as a positive disease, being also an implicated consequence.

"The colour of the skin, and the general superficial aspect of the people in these cases, has never failed to attract the attention of even the most cursory traveller. The former is sallow, or yellow, or else stained with different hues, and in extreme cases has even a livid appearance; while to a medical examination it is found to put on pressure; this condition often amounting to absolute oedema and the muscles being soft, yielding, and unelastic. Such persons have often the appearance of being fat; but this, when it exists, is wanting in firmness as if a great part of the accumulation consisted of water in the cellular membrane. That varices and hernias should be common in the same circumstances, are facts which belong rather to the absolute diseases that prevail in the marshy districts. It is also remarked that the hair is flaccid, and the beard scanty; while in the most poisonous regions of France, it is further asserted that pale hair abounds, while in more healthy places the same race is noted for their darker tint. A dull, languid eye, very often also yellow, is a circumstance which has attracted general attention.

"An enlargement of the abdomen, commencing sometimes even from birth, and often rendered the more conspicuous from the slenderness and emaciation of the limbs, is also a feature which no traveller has overlooked; and it is often in itself sufficient to demonstrate the nature of the place where these wretched beings are doomed to live, or rather, as the inhabitants of the Pontine marshes express it, to die.

"That the very form and extent of the liver can often be traced externally by the eye, is an anatomical fact belonging to this state of things; while an investigation after death discovers various diseased structures in that organ, in the spleen, and in the mesenteric glands; together with water in the cellular membrane, and a general enlargement of the whole lymphatic system. In the Pontine

marshes, the residents have the appearance of walking spectres; being often also oedematous all over, and thus dragging on a miserable existence throught the short term of their wretched lives. That the inhabitants of such districts have a late puberty, and are less prolific than in healthier regions is a fact which has been asserted and again contradicted; yet it is one which could not excite surprise should it be proved.

"There is nothing in these pernicious countries more striking to a cursory traveller, than the appearance of age which occurs at a very early period of life. Even the children are frequently wrinkled, and in France, in perhaps all the worst districts, a young woman, almost even before 30, has the aspect of 50; while in men the age of 40 is equivalent to 60 in healthier countries, both in appearance and vigour; the very few who live to 50, appearing to have arrived at the protracted term of fourscore. Of personal beauty in females, there appears too little trace at any time; but whatever may have existed is rarely prolonged beyond 17; and the expression keeps pace with all else; being that of unhappiness, stupidity, and apathy; and an habitual melancholy which nothing can rouse, and an insensibility to almost everything which operates on the feelings of mankind in general. A slow and languid speech, a similar languor in the walk, and in all the actions, indicate equally the condition of the mind and the body in these wretched countries.....A high degree of nervous irritability, both mental and bodily, is a frequent attendant upon the chronic condition of the malaria.

"The condition of the mental faculties, whether intellectual or moral, is scarcely less remarkable, while it is more interesting: and if there should appear any exaggeration as to some particulars, or should any special fact, as asserted, depend on collateral causes of another nature, the general bearing of the whole as related of Italy and of France, has been confirmed too often by remark of a similar nature, made in America and elsewhere, by very competent observers, to leave any doubt as to the leading circumstances.

"The apathy which was just noticed as expressed in the physiognomy is a character which influences the whole conduct of these degraded and unfortunate beings; often proceeding to such a degree that they are scarcely elevated above the beasts in point of

feeling. Seeking solitude, shunning society and amusements alike, without affections, without interest in anything, they make no exertions to better their condition; not even to avoid the sources of danger which surround them, or to take the most common precautions that are pointed out; while, attached to the soil, from habit of indolence, rather than from regard, they will not be convinced, even of its nature or dangers; fatalists in practice and even in belief and refusing to admit that there is any other lot in life than that which is their own.

"That the general intellectual faculties are degraded is an universal remark; while, in many places, and very notably in the Maremma of Tuscany, it is observed that absolute idiotism is common. That such a condition is the frequent result of marsh-fevers and very particularly under improper treatment, is a fact which I must notice in the medical part of this work; but even independently of this, such debility of the intellect, seemed to be the produce of the insensible action of this poison on the nervous system: a circumstance that indeed might naturally be expected from the physiological considerations connected with the general influence which malaria exerts on the body. And that this condition is even propagated, seems for ever fully proved: so that an universal degeneracy of mind and body both appear to be the certain lot of those races which a combination of unfortunate circumstances have placed in countries that seem to have been intended rather for the habitation of reptiles and insects than for those of man.

"With respect to the moral conditions of the people in those unhealthy conditions, the picture drawn by Monfalcon is frightful. Not to dwell on this disgusting picture, I might content myself with naming abortion, infanticide, universal libertinism, drunkenness, want of religion, gross superstitions as the leading features; beside which, it is further said, and even proved by the police reports, that while murders are common, a large proportion of the cases are those of premeditated and cautious assassination by poison or otherwise; all the vices, said my authority, being of a mean and not of a bold character."

Monfalcon points out the degenerate condition of the natives of the malarial districts of France, l'Ain, la Bresse, la Sologne,

100 years ago. So much was this the case, that to be a Sologhot was an insult, as the type stood for inferiority in human-kind.

He says that the Brosson, as the Sologhot, is plunged in a great apathy. His ideas are of narrow range; he has not known the gaiety of youth, nor the strong conceptions of mature years. In ignorance and profound misery, his philosophy is a stupid fatalism. His character is cold, sad, surly, capable of calculation and vengeance, but not passion. By no means concerned about his health, his attention is chiefly fixed upon his animals, the loss of which he grieves over more than the loss of wife, who is more easily replaced.

He is timid and superstitious, and practises witch-craft. His moral insensibility surpasses even his physical. Death of mother, wife, child, he meets with a stupid indifference. Rarely does he understand the word of country, love, friendship. Murder is viewed with indifference, traces of crime very soon disappear, and the law is either mute, or unexecuted. He likes solitude, is uncommunicative, and goes his short course without having loved or thought, little different from the heavy quadruped languishing beside him.

It is characteristic of him to explain the unhealthiness of his climate and his work by any other reason than the right one, and he is ingenious in inventing explanations for the fever which devours him.

Italian observers have noted the effect of malaria in producing deformed, degenerate, and idiotic people. Bianchi states that intensely malarious districts where the majority of the inhabitants have enlarged spleens, and a certain degree of anaemia, are veritable nurseries of imbecility. It has been observed that, where malaria flourishes, there is the greatest squalor, and cause and effect are often confounded. The medium duration of life of the working classes in malarial zones in Italy was 22-24 years, while that of the rich was 55. It was estimated that agricultural production was only 40% of what it might have been in the Roman Campagna, due to malaria, (1899).

Numerous observers have noted the frequency of infantilism among the natives of the malarious districts of Brazil, Algeria, and Syria. These are people of stunted growth in every sense of the

term; of low intelligence, impotent, sad, passive, inert, indifferent. De Brun, after 35 years in Syria, considers malaria one of the most important causes of infantilism, and indicates that neurasthenia and melanoderma are common in malarial subjects, suggesting chronic adrenal insufficiency.

According to Foley and Parrot, arrest of development and infantilism of malarial origin are fairly common in natives of Algeria (1930). During the first two years of life, the dystrophic action of malaria is shown by symptoms resembling marasmus or rickets, according to the age. The child is slow in learning to walk, and the emaciation of the face, chest, and limbs is in striking contrast with the occasionally enormous development of the abdomen due to enlargement of the spleen. None of the symptoms of true rickets, however, such as beading of the ribs, or enlargement of the epiphyses are present. In older children, the emaciation and abdominal enlargement persist, and the height is much below normal. About puberty, the general condition improves, signs of infantilism disappear, enlargement of the spleen diminishes, and growth now becomes very rapid. In some patients, however, puberty is late, especially for such a latitude and climate. The height for a long time remains below the normal, and in some cases the arrest of development is permanent, and the Lorraine type of infantilism results.

Mélier (1847) quoted by Laveran, visiting the village of Hiers saw children of 12 years of age who looked like six or eight, ——their faces swollen, with earthy complexion, limbs thin and undeveloped, pot-bellied. The canton was for a long time unable to provide a single recruit to conform to the army standard.

Hume notes the frequency of infantilism in natives of the malarious districts of East Africa.

Conti records (1910) the frequency of retarded development in highly malarious Sardinia, and observes that abortion and premature births are very common and attributable to malarial infection. There are districts of the island in which 100% of Army Recruits have been repatriated through defective development.

The author's experience has been limited chiefly to soldiers on Service who have been infected with malaria. Apart from the cases of gross insanity to be detailed in subsequent chapters, the

cases dealt with have been soldiers repatriated, having recurrent attacks of malaria, and suffering from chronic ill-health with both physical and mental characteristics. These men have in many instances the outward appearance of ill-health, anaemia, emaciation, apathy, nervousness. Others again, on superficial inspection, appear normal. It is only on closer observation that they reveal an incapacity for sustained effort, forgetfulness, irritability of temper, diminished self-control, varying degrees of depression, periods of amnesia or confusion, especially about the time of a malarial attack. Frequent complaints among the men are headaches, pains in the back and limbs, sleeplessness, weakness especially on exertion, difficulty of concentration on a subject for any length of time, and depression varying in degree from time to time.

Although the change is sometimes slight, and often subtle, it is apparent to the man himself and to the friends who are living with him that he is not the man he was. The finer shades of character have altered or disappeared. In matters of judgment, initiative, interest, energy, he has fallen away, even if nothing worse has occurred. These features may be only apparent in the first instance to the friends who have known the patient, both before and after infection, and may not be easily revealed to a stranger at a series of interviews. It is the subtle quality of the changes that often occur, together with the difficulty of recognition of physical signs of a disease, and an intermittency of those signs in many cases, that leads to a failure of diagnosis and consequent inadequate treatment. It has been well called by Smallman "concealed inefficiency" (Cf. Chapter 27).

These pictures of degeneration in malarious areas agree with the numerous observations of birth. Nagger, who treated pregnant women infected by malaria in the Egyptian cases, records the frequency of abortion or premature labour, precipitate labour, still-births, and puerperal haemorrhage. Only in a minority of cases was labour and puerperium normal.

Mannaberg records that A. Weatherley reported at the Medical Congress in Calcutta (1894) that in India 46·6% of his cases aborted, while in England the frequency amounts to not more than about 3·56%. He also finds sterility very common among the women of India and

blames malaria for it.

Laffont records diminution of fecundity, abortion, in 3%, premature labour 38% in malarious women.

Rogers cites abortion as one of the frequent complications of malaria in Mauritius.

Orgeas shows that in the Colonisation of French Guiana, the natural increase of population was prevented by abortions and still-births, the result of malarial infection.

Le Dantec notes the degenerate state of those that survive of the colonists of French Guiana. In the two years, 1763-64, 12,000 French colonists landed on the coasts of Kourou and Cayenne. By 10th Feb., 1765, only 918 remained, and much of the progeny of these was degenerate.

Catrin indicates that in two neighbouring countries, one malarious, the other not, there is a striking contrast from the point of view of race feebleness, mortality, and average longevity.

The burden of evidence of many observers goes to show that malaria is transmissible from mother to foetus.

So it would appear that malaria cuts into the progress of man at every stage, preventing, hindering, damaging him at birth, inhibiting his progress physically, and mentally by rendering him indifferent to the means of defence, producing a vicious cycle, so that many who emerge from the earlier stages of infection lack energy, initiative, become ruled by habit, hate what is new—bad soil upon which to graft prophylaxis. F. Reynault points out that the "Corsican League against Malaria" remains inefficacious (1921) for this very reason of the apathy and ignorance of the Corsicans.

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CHAPTER V.

PATHOLOGY.

The subject of malarial pathology is dealt with thus early as best likely to prepare the reader for what is to follow. The pathological changes in the central nervous system and in the tissues more closely associated with it such as the blood and endocrine system will be considered under three headings:

α. *The Blood Changes.*

β. *The Changes in the Central Nervous System.*

γ. *Endocrine Changes.*

α. *The Blood Changes.*

1. Swelling of red blood corpuscles to two, three, or even more times the size normally, especially in benign tertian infection.

2. Pallor of red blood corpuscles, often extreme.

3. Shrinkage of reds, especially in so-called brassy bodies, found principally in malignant tertian infections, but also in benign tertian. They sometimes shrivel up (erythropycnosis), and become necrotic.

4. Fragmentation of parasite-laden reds—not frequent.

5. Agglutinative tendency of parasite-laden reds, so that they tend to stick to the capillary walls. This agglutination occurs both in vivo (Bignami) and in vitro (David Thomson), and explains capillary thrombosis.

6. Marked diminution of red cells during acute infections. In the spleen, red cells have been found in various stages of disintegration, with evidence of metamorphosis of haemoglobin into black pigment.

8. Pigment is formed by every species of malarial parasite. Two types of pigment have been observed. These are haemozoin and haemosiderin, both derived from the haemoglobin of the

red cells.

Haemozoin occurs as dark brown or black granules, rods, needles or blocks, and is peculiar to malaria, being formed by the parasite from haemoglobin while in the red cell. It is therefore first seen in the intra-corpuscular parasites, is set free in the circulation when the parasites escape from the red cells, is largely taken up by the leucocytes and other phagocytic cells, and is distributed throughout the body tissues, chiefly in the spleen, liver, brain and bone-marrow. It is an iron-containing organic compound, does not give the iron reaction with ferrocyanide of potassium and hydrochloric acid; it is slightly soluble in alkalies, but is not soluble in water, alcohol, chloroform, or ether, or acids. It finally disappears from the tissue cells but the process of elimination is not known.

Wade H. Brown, Ascoli and Carbone consider that it is formed from haematin, with which Brown has experimented on rabbits. He found that it produced the same blood changes as malaria does in man—viz., destruction of red cells, leucocytes and platelets, with mononuclear increase to 13 or 14%. It also prolonged the coagulation time and produced paroxysms similar to malarial rigors. Large doses produced a marked fall of blood pressure accompanied by great dilatation of the splanchnic vessels and bradycardia, and finally death by respiratory failure. Brown considers this pigment as a principal factor in the causation of the clinical phenomena of malaria.

Haemosiderin occurs as yellow granules in the parenchyma cells of liver, spleen, kidney, bone-marrow, in pia mater, pancreas, capillary endothelium and occasionally in leucocytes, after any great destruction of red cells. It is an iron-containing inorganic compound, gives the iron reaction with ferrocyanide of potassium in acid solution, is insoluble in alkalies and acids, but dissolves in alcohol. It is not peculiar to malaria, but occurs in any disease where there is marked haemolysis.

8. Pigmented endothelial cells are found in the blood only in the gravest infections. They act as phagocytes in position, then desquamate, being injured, causing lesions of vascular walls and thus further contribute to retardation and blockage of capillary circulatio

9. Leucocytes take up pigment and parasite-laden reds. To this, Golgi attributed spontaneous cure. Nearly all observers agree that the most important agents in this process are the large mononuclear and transitional cells of the bone-marrow and circulation. Next in order, come the polymorphonuclear-leucocytes. Lymphocytes and eosinophil cells are exempt (Bignami and Guarnieri). Pigmented leucocytes tend to disappear from the peripheral blood within a few days of each febrile attack, as they return to the depots—spleen, liver and bone-marrow. In Negro children who have had no quinine, pigmented leucocytes and gametes are more constantly found in the peripheral blood (Ziemann).

10. In ordinary malarial infections, the total number of leucocytes diminishes to below normal, i.e. 3,000 to 5,000 per c.mm., instead of about 8,000 to 9,000, while in malignant tertain, it is increased from 10,000 to 35,000 during the attack, ranging to normal or less (between 3,000 and 4,000) after the attack. In any case, there is nearly always a relative increase of large mononuclear cells to 15% or above. David Thomson describes a transient "post-malarial leucocytosis" which sometimes occurs every day in malarial patients who have had quinine treatment.

11. The general rule is that during the apyrexial periods polymorphonuclear-leucocytes fall from the normal about 70% to about 50%, and the mononuclear leucocytes (grouping all forms together) rise from about 25 to 45%. David Thomson maintains that the mononuclear percentage varies inversely as the temperature. As the temperature rises, the number of mononuclear leucocytes in the peripheral blood falls; as the temperature falls, the mononuclears increase, and the greatest number occurs between the paroxysms, when (all forms together) they frequently rise as high as 80% of the total leucocytes.

12. Other cells absent from, or rare in, normal blood may occur in the peripheral blood. These are (1) a macrophage, 15u or more in diameter, oval or circular in shape, with hyaline protoplasm and kidney-shaped or rounded nucleus. (2) A rarer and larger cell with hyaline vacuolated protoplasm and irregular nucleus. It is probably a desquamated vascular endothelium cell. These two act as phagocytes, and may contain malaria pigment, red blood corpuscles,

or parasites.

13. Degenerative changes occur in the leucocytes which may go on to necrosis. These changes are fatty degeneration which chiefly attacks the large mononuclear cells, after they have ingested many foreign bodies, and they then appear as large cells many times their original size, contain many large spherical shining bodies which in fresh preparations are seen to oscillate but disappear in dried preparations, do not stain with aniline colours, and are invisible in sections fixed with alcohol. Similar changes in less degree have been found in the other phagocytic cells. These altered cells are best stained in osmic acid.

Other degenerative changes noted are vacuolization of the protoplasm, nuclear fragmentation and chromatolysis, and so on to complete coagulation necrosis (Marchiafava and Bignami).

14. In no other infection is anaemia produced with the same rapidity and to the same extent as in malaria. Thus, a vigorous patient in the first four days of a quotidian fever may show a reduction to 2,000,000 red blood cells. A reduction of 1,000,000 in 24 hours has been noted.

20 or 30 days of malignant quotidian or tertian fever are enough to reduce red cells from 5,000,000 per c.mm. to 1,000,000 or even less (Kelsch). In chronic malaria, the intensity of the anaemia produced by each attack becomes progressively less.

15. Haemoglobin variations are for the most part parallel to the red cell variations. In the reconstruction period, however, the haemoglobin repair tends to lag behind the red cell repair, as is usual in secondary anaemias.

16. Loss of haemoglobin and red cells is generally in proportion to severity of infection. Gravity of infection is not always to be gauged by degrees of anaemia, while on the other hand severity of the anaemia sometimes may be the most threatening feature.

17. The leucopenia of chronic malaria patients is an expression of the functional sluggishness of the bone-marrow whose formative capacity has been seriously hampered by repetition of damage over a long period of time. Thus the chronic anaemia of a prolonged malaria more nearly resembles a pernicious anaemia, and the process of repair tends to be slow, while in acute, recent

infections it is much more rapid.

18. Bignami draws attention to a small proportion of cases where even after the infection has been extinguished, anaemia not only persists but increases, taking a variety of forms. Though post-malarial, they are not considered due exclusively to malaria, but are often associated with such circumstances as age, malnutrition, overwork, pregnancy, nursing, worry, etc.

19. The effect of each malarial attack is to diminish the number of red and white corpuscles, haemoglobin, blood specific gravity, while the resistance of the red corpuscles tends to increase. This anaemia, which may be very severe in the early, acute stages, tends to be less as the infection becomes chronic. Blood reconstruction proceeding actively at the beginning, tends to become progressively slower after many relapses, with the result that this chronic anaemia takes a long time, and is difficult, to cure.

20. Abrami and Senevet describe changes occurring from 1/3 hours before onset of the benign tertian malarial paroxysm. These are, a gradual and marked diminution in the numbers of white and red cells, an inversion of the normal differential leucocyte count, a lowering arterial tension and blood coagulability reaching their minimum about an hour before onset of the cold stage, by which time there is an increase of red cells to normal, an increase of white cells above normal (13,000 per c.m.m.), an increase above normal of systolic blood pressure, and a return of coagulability to normal.

21. In Blackwater Fever and in a certain proportion of other malaria cases, there has been observed diminished blood coagulability, diminished specific gravity, and alkalinity, constituting an hydraemic state of the blood frequently associated clinically with oedema and haemorrhages (Ziemann).

22. In Blackwater Fever, active haemolytic substances have been extracted from the tissues and to a lesser extent from the urine, capable of haemolysing human and animal red blood corpuscles.

23. Marked diminution of haemoglobin or oxygen-carrier being a prominent feature of the blood in both acute and chronic malarias implies a defective oxygen supply to the tissues in unit time. This state of anoxaemia, as pointed out by Sarcroft, has a

detrimental effect on the nerve centres by diminishing nerve conductivity proportionate to its degree and duration.

24. The presence of a toxin in malaria infection has been assumed for a long time. Observation of the tissues of cases of sudden death from coma especially have settled this question. In a number of these, there was found well advanced fatty degeneration of such organs as spleen, heart, brain, liver, etc., frequently unaccompanied by capillary thrombosis or haemorrhages, such as might have interfered with the nutrition of the parts involved.

In quartan malarial infections, there appears to be a fairly equal distribution of parasites throughout the body and sporulation takes place in the peripheral circulation as well as the organs.

In malignant tertian malaria, there is the most uneven distribution of parasites, with massing of parasites in a particular organ or group of organs, especially spleen, brain, liver, bone-marrow. Not only so, but there has been found a marked variation in numbers in adjacent capillaries of the same organ, some being packed with parasites, while in others they are scarce or absent. (Golgi and Bignami). Here sporulation takes place in the internal organs.

Benign tertian malaria appears to take the middle place, in that, while massing of parasites does take place in internal organs, there is a tendency to greater accompanying peripheral blood infection (Barker).

It will thus be seen that a blood examination in quartan infection, where the distribution is even, will give a better estimate of parasite invasion and prognosis than it will in malignant infections where it is extremely uneven, to the extent that no parasites, or few, may be found in the peripheral blood, while the capillaries of a particular organ, or part of it, are packed, and the patient seriously ill, or about to be so.

β. Changes in the Central Nervous System.

The pathological changes found in the central nervous system due to malaria—chiefly malignant tertian, but also benign

tertian (and quartan)—fall into two main categories:

A. Lesions associated with vessel blockage and degeneration.

B. Inflammatory lesions.

A. Lesions associated with vessel blockage, etc.

1. Great dilatation—often irregular—of all brain vessels.

2. Proliferation of capillaries sometimes making a bush of thirty or more vessels from one stem—numerous in grey matter in some cases, less so in white matter, and they are observed also in the pia mater (Cerletti).

3. Phagocytic action of blood vessel endothelium, which contains pigment, parasites, fragmented reds, etc.

4. Proliferation and degeneration (fatty) of blood vessel endothelium, with hypertrophy sometimes to the extent of obliteration of capillary lumen, and subsequent desquamation.

5. Amyloid degeneration of vessel walls, particularly in chronic malignant tertian malaria.

6. Blockage of cord, brain, and (less often) meningeal capillaries with parasite-laden reds, leucocytes, macrophages, desquamated endothelial cells, free pigment, sometimes free parasites—i.e. embolism, thrombosis.

7. Capillary haemorrhages, chiefly in the white matter, but also less frequently in the grey matter, meninges, and retina with their better blood vessel anastomoses. Dürck mentions choroid-plexus haemorrhage in one case. Bignami and Nazari found free red cells in the brain substance—generally not containing parasites, as did those in the retina. Round the blocked vessels, they found pale necrotic areas of nerve substance at the periphery of which was haemorrhagic infiltration forming a complete ring, constituting altogether a necrotic haemorrhagic infarct. These observers and Cerletti were of the opinion that the punctiform haemorrhages found—mostly in the white substance—were due chiefly to diapedesis of the red cells through the altered walls of the fine capillaries.

8. Some cases have been observed with cerebral capillary haemorrhages unaccompanied by massing of parasites or vessel blockage, but with simply degenerative changes in blood vessel walls and nerve elements. Haemorrhages have been found in other organs besides the

central nervous system, and degenerative changes indicating a wide-spread toxaemia. Parasites have been very scanty, or absent, in peripheral blood and throughout the organs, even the spleen, though pigment has been present.

9. Ruptured capillary aneurisms filled with pigment.

10. Where the brain and meninges are involved, the cerebro-spinal fluid has been generally found to be clear, increased in pressure and globulin content, with leucocytosis and chlorides increased (Genoese).

B. Inflammatory Lesions.

1. Inflammatory reaction of the meninges ranging from marked hyperaemia to purulent leptomeningitis, occasionally meningeal haemorrhage, large or small.

2. Degenerative changes in all the brain cells ranging from partial or total disappearance of Nissl's granules, chromatolysis, cloudy swelling with lateral displacement of the nuclei, to atrophy and complete sclerosis.

Nerve filaments also show cloudy swelling with nodulation and breaking up of axis cylinders.

3. Deposit of pigment in the brain substance, especially grey matter.

4. The neuroglia tissue shows progressive and regressive changes, i.e. hypertrophy, the latter predominating. There is swelling and vacuolization of protoplasm and filaments of the astrocytes.

5. The formation of neuroglia cell-nests distributed over the central nervous system, forming granulomata (Dürck). Dürck maintains that neuroglia proliferation from malaria having begun, the process goes on in some cases after the original irritant, the parasite, has died out.

6. Great distension of the peri-vascular lymph-spaces, with lipoid and fibrinous material.

7. The brain as a whole has shown marked hyperaemia with slight oedema and lymphocytic infiltration.

8. Necrotic foci tend to be replaced by neuroglia tissue.

9. The changes in the central nervous system are similar to those produced by other diseases. The only features that may be considered specially characteristic of malaria are the pigment deposits, the malarial granulomata of Dürck, and perhaps the perivascular ring haemorrhages and necrotic foci described by Bignami and Nazari.

The process of development of these lesions is probably also unique in that there is a periodic production of the irritant consistent with the nature of the disease. Whereas in diseases like influenza and enteric fever, tissue damage tends to be incisive and final, with malaria there is much more remission and exacerbation with a corresponding fluctuation of clinical signs and symptoms which may be very bewildering if the nature of the disease is not kept well in mind.

(F). *Changes involving parasympathetic, sympathetic, and endocrine glands.*

1. Alternation of reactivity of parasympathetic and sympathetic, and reactivity of autonomic nervous system as a whole, to malaria.

1. Prodromal Stage.
2. The paroxysm.
3. Chronic forms.
4. Cachexia.

2. Peritoneal syndrome, of different varieties.
3. Gastric juice in malaria.
4. Colitis.
5. Glycosuria and Pancreas.
6. Urticaria.
7. Oedema.
8. Heart, Circulation, and Kidneys.
9. Raynaud's phenomenon, and symmetrical gangrene.
10. Respiratory System.
11. Adrenals.
12. Thyreoid.
13. Orchitis.

14. Parotitis.
15. Mammitis.
16. Pituitary.

This section is expanied in the next chapter.

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FIGURE I.

Section of Human Spinal Cord from case of Malarial Paraplegia, showing capillaries cut across (black dots), packed with parasite-laden red cells and pigment.

(Specimen prepared and presented to the author by Prof. L. S. Dudgeon, London.)

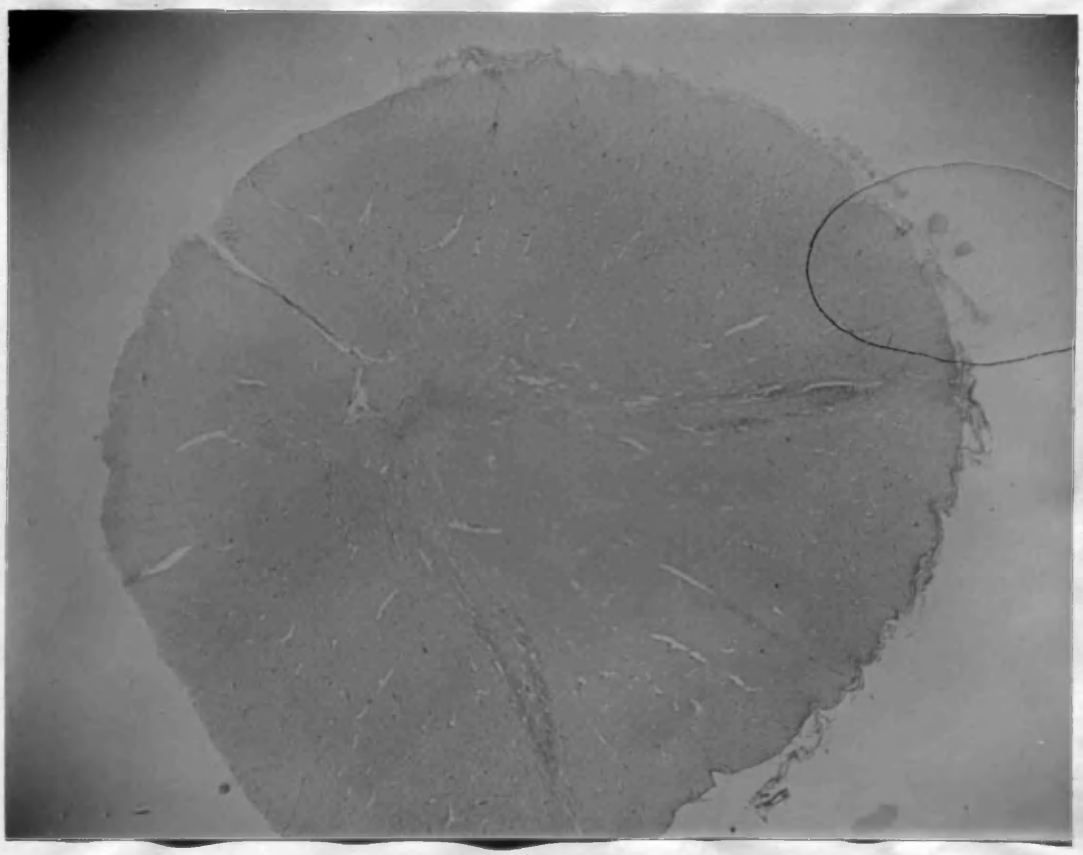


FIGURE II.

High Power View of Figure I, showing cord capillary full of parasite-laden red cells and pigment.

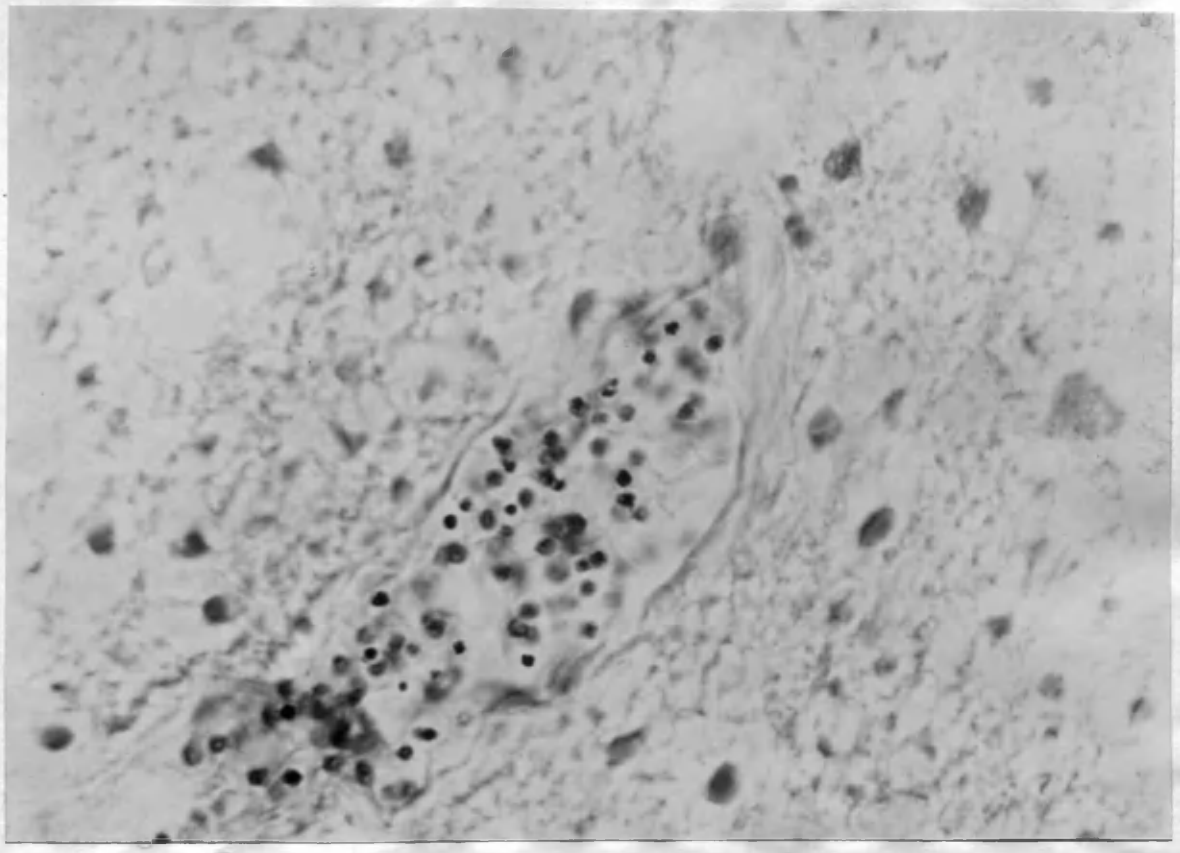
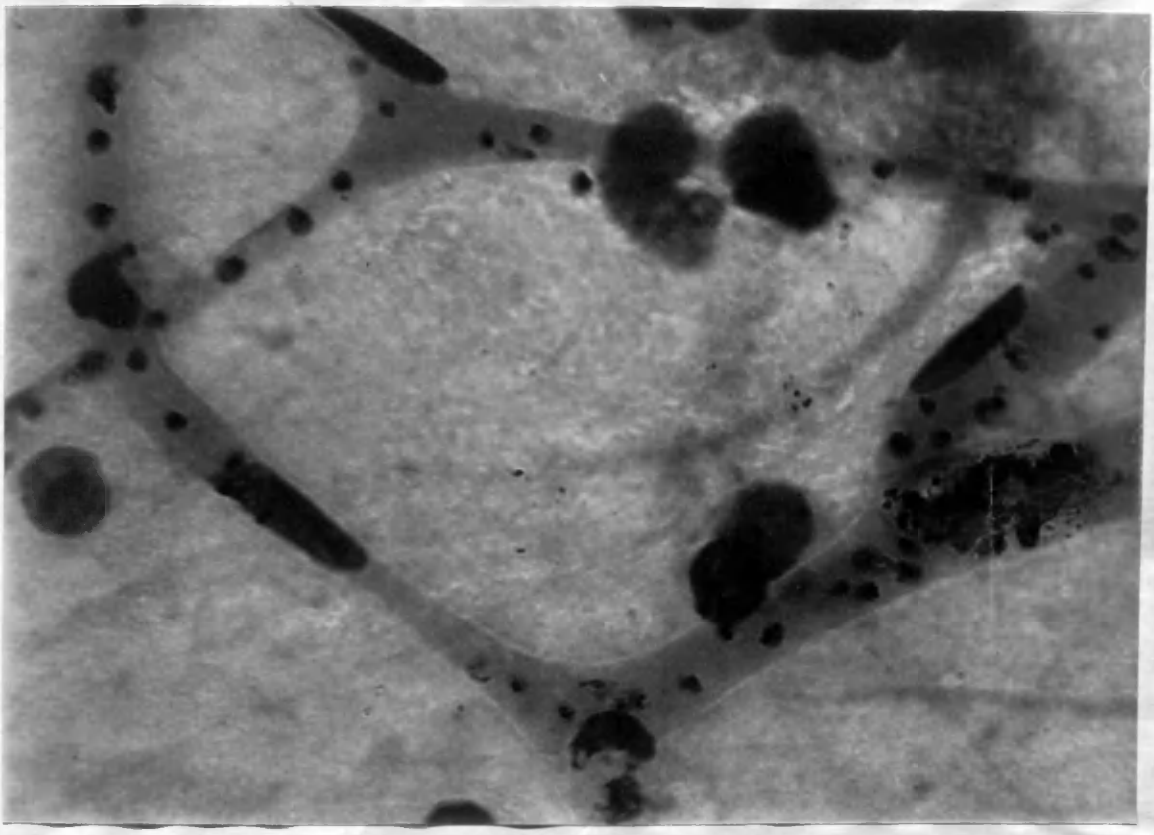


FIGURE III.

High Power View of Capillaries from Brain Smear from a case of cerebral malaria (Malignant Tertian).

(Specimen prepared and presented to the author by Prof. E. Marchiafava, Rome.)



CHAPTER VI.

Clinical Pathology of the Parasympathetic, Sympathetic, and Endocrine Glands in Malaria.

These three systems are so intimate that it is necessary to take them together inconsidering the effect that malaria has upon them.

If we look in detail at the first effects of the impact of malaria upon the human organism, we find that three systems mainly in the first instance bear the brunt of it:

These are

1. The blood, with its renewal organs, spleen and bone-marrow.
2. The blood-vessels.
3. The parasympathetic, sympathetic, and endocrine systems taken together.

The parasite lodges in the red cell and produces anaemia (with certain blood reactions) which is so constant a feature of malarial infections. It damages blood vessels, and thereby interferes with blood supply to any tissue where it is concentrated. When sporulation occurs, numerous young parasites and poison are set free in the circulation and immediately set in motion the defensive mechanism of parasympathetic, sympathetic-adrenal, thyroid, probably also pituitary systems.

A detailed account of the first evidences of the impact of malaria upon the organism is provided by Abrami and Senevet. Examining the blood every 10 or 15 minutes during the 3 hours or so preceding a paroxysm (p. vivax), they found a lowering of the blood pressure (maximal marked, minimal less so), marked leucopenia with relative mononucleosis and a marked hypercoagulability of the blood about the middle of that time, with a return to normal at the beginning of the rigor, except that the maximal blood pressure and the polymorphonuclear-leucocytes were increased while the temperature

was normal. These they maintain are the features of anaphylaxis, and they found the same phenomenon after intravenous injections of peptone, in paroxysmal haemoglobinuria, in alimentary urticaria, and in certain kinds of asthma; they therefore look upon the malarial crisis as a haemoclastic shock in every case. Moreover, by careful counting at the different stages in the development of the parasite, these observers came to consider that the merozoites were shed in the period of 1 to 3 hours preceding the shiver, i.e. during the period of haemoclastic shock—that sporulation has actually occurred at the time the rigor comes on. They indicate that these changes have been noticed in the blood even where there has been no rigor, in instances of mild attack where the patient is conscious only of subsequent fatigue, and that they are variable in different people and in the same person at different times.

Bastianelli and Bignami record an eosinophilia during the apyrexial periods in malarial subjects.

Then again, J. H. Smith indicates that anaphylaxis always expresses itself through vagus irritation, as the features of these two conditions are largely the same, namely, myotic pupils, tendency to sweating, salivation, hyperchlorhydria, gastro-intestinal peristalsis, spastic colon, bradycardia, low blood pressure, shallow respiration and dyspnoea, cold clammy hands, dermographism, nervousness, marks of the status-thymo-lymphaticus, increased carbohydrate tolerance, eosinophilia, and hypersensitiveness to pilocarpine (Smith). If we add leucopenia with mononucleosis as characteristic of anaphylaxis (Widal), we will have an array of features that frequently crop up in those affected with malaria. Add to these urticaria, and its allied skin conditions, and we have still further vago-tonic phenomena not uncommon in malarial subjects.

Now all this goes to suggest—if the Abrami and Senevet observations are to be taken at their face-value—that the first nervous evidence of malarial infection is medullary and takes the form of irritation of the vagus, the principal component of the parasympathetic system. This is interesting to notice for it would be natural that the first trace of blood poisoning should be registered at headquarters—the medulla, which contains the vital centres for the preservation of life.

We remember that the parasympathetic is the conservative or anabolic member of the autonomic nervous system. As Cannon puts it: "A glance at these various functions of the cranial division reveals at once that they serve for bodily conservation: by narrowing the pupil they shield the retina from excessive light, by slowing the heart rate they give the cardiac muscle longer periods for rest and invigoration; and by providing for the flow of saliva and gastric juice and by supplying the muscular tone necessary for contraction of the alimentary canal, they prove fundamentally essential to the processes of proper digestion and absorption, by which energy-yielding material is taken into the body and stored. To the cranial division of the visceral nerves, therefore, belongs the quiet service of building up reserves and fortifying the body against times of need and stress. Like the cranial division, the sacral is engaged in internal service to the body, in performance of acts leading immediately to greater comfort". The pelvic visceral nerve, in other words, controls the evacuation of waste products.

On the other hand, the sympathetic in stimulation activates the body for a struggle. In the words of Langdon Brown: "The pupil dilates to increase perception of light: the heart beats more quickly and more forcibly to supply the muscles with blood; the blood-vessels in the visceral area constrict, raising the blood pressure, and driving the blood from the digestive area, whose functions are simultaneously inhibited, into the skeletal and cardiac muscles, the lungs and the brain. The sweat glands are stimulated to cool the body heated by its excessive muscular effort and the hairs are erected, in many animals, to render them more alarming". As Crile says, "The mechanisms for self-defence which we now possess were developed in the course of vast periods of time, through innumerable intermediate stages, from those possessed by the lowest forms of life. One would suppose, therefore, that we must now be in possession of mechanisms which still discharge energy on adequate stimulation, but which are not suited to our present needs. The pilomotor fibres are an example of this, for, however useful the erection of hairs may be to a cat confronted by a dog, the 'goose-skin' experienced by a man under an emotional stress can serve no useful purpose".

Then there is the generalisation of Gaskell that where para-

sympathetic and sympathetic are distributed to the same structure, the effects are antagonistic. Thus, the parasympathetic contracts the pupil, the sympathetic dilates it: the parasympathetic slows the heart, while the sympathetic accelerates it: the parasympathetic dilates the arteries of the skin, abdominal viscera, gut, and bronchi, while the sympathetic contracts them. The parasympathetic increases the movements of stomach and bowels, while the sympathetic inhibits them: the parasympathetic lowers the blood sugar by output of adrenalin, a pancreas inhibitor.

The parasympathetic is therefore the conservative member of the autonomic system, conserving the forces of defence. The sympathetic is the liberal member, spending the force thus conserved, in defence, when required. When the enemy arrives, there appears to be an oscillation of activity with clinical features of each predominent in turn, in greater or less degree depending on the vigour and frequency of the stimulus, and the reactivity or stage of exhaustion of the patient. or it may be that there is some overlapping of features where there is focal concentration or extreme exhaustion of the organism as a whole.

With these ideas of autonomic nervous system in mind, let us resume our consideration of the effect of malaria upon the organism.

1. Alternation of reactivity of parasympathetic and sympathetic and reactivity of autonomic nervous system as a whole to malaria.

We have seen that Abrami and Senevet record the features of anaphylaxis in the blood of malarial patients during the three hours ~~previous~~ of apyrexia immediately preceding the paroxysm, and this suggests vagus irritation. This may be called the prodromal stage, and is typically characterised by lassitude, a desire to stretch the limbs, and to yawn, aching of the bones, headache, backache, anorexia, perhaps vomiting, and latterly a feeling as of cold water trickling down the back (Manson-Bahr) and generally slow pulse with normal or sub-normal temperature.

Let us now consider the paroxysm itself. The first features of this are shivers, with increase of muscle tone, pallor from constriction of skin vessels, goose-skin, horripilation, rise of

temperature, rise of blood pressure and pulse rate, headache, and perhaps a cold clammy sweat, followed in about half-an-hour or an hour by flushing from vaso-dilation, profuse sweating, fall in temperature, fall in blood pressure and the rate of the pulse, which becomes full and bounding.

Cumston records that there is a hyperglycaemia at the onset of the cold stage and that it diminishes with the full development of the rigor. This has been confirmed by observations made in the author's own wards (M. Thom, J. H. Harkness, E. M. Hegarty). A hyperglycaemia, not often exceeding the average kidney threshold for sugar (0·18%), but occasionally doing so, was usually found at the onset of the cold stage. It rapidly diminished with the approach of the hot stage, at the height of which the blood sugar was often a little, sometimes much, below the normal fasting level (0·10%).

Bürger's observations on the blood pressure of malaria patients (confirmed by Armand-Delille, and Caillé, Jeanselme and Dalimier, and in author's own cases) taken at intervals during the whole paroxysm indicate that there is a rise of 20-30 mm. Hg Maximal Pressure (Minimal less), which, along with the shivers, reaches its height, at which skin vessels and muscle tone begin to relax, sweating begins, and while pulse rate and temperature continue to augment for half-an-hour or so longer, they both come down with the more rapid descent of blood pressure during the hot stage. He maintains that the blood pressure not only comes down rapidly, but descends to 20-30 mm. Hg below its original normal, thus making a difference of maximal pressure of from 40 to 80 mm. Hg between the height of the cold stage and about the end of the hot and sweating stage. With termination of the hot stage, the pressure may ascend to normal, but in some cases this is slow, and may be completed only 24 hours after onset of the rigor.

It would appear, then, that the blood sugar rise and fall is a little in advance of the blood pressure rise and fall, which again is a little in advance of the temperature rise and fall. The hyperglycaemia is coincident with the onset of the cold stage, diminishes with the progress of the cold stage, and by the height of the hot stage has declined to normal or sub-normal.

When we remember that the parasites (sub-tertian, tertian)

sporulate chiefly in the vessels of the internal organs (spleen, bone-marrow, intestine, liver, brain) we may interpret the features of the "cold" stage in terms of an irritated sympathetic-adrenal system, giving way at its height in fatigue to the next or "hot" stage, which we may interpret as effects upon an irritated parasympathetic and late thyreoid response. Fatigue of liver blood vessels after direct irritation of the sporulating parasite with its poison upon the smooth muscle of the hepatic arteries and veins, with their liberal vagus supply, very probably contributes to the fall of blood pressure (L. R. Müller) which is so marked in the hot stage, and for a variable time thereafter.

Sweating is usually considered a sympathetic-irritation phenomenon, but L. R. Müller points out that there is a cold clammy viscid and relatively scanty sweat (with pallor) of vigorous sympathetic-adrenal stimulation, and a profuse, watery sweat associated with vaso-dilation, which is a vagus irritation phenomenon.

Then again, the thyreoid is usually classed as supporting sympathetic-adrenal action, rather than parasympathetic action; but Paisseau and Lemaire and others have noticed that in fatal malaria cases the adrenals generally showed much more damage than the thyreoid gland, suggesting greater activity (probably through being nearer the centres of sporulation); and Fraser has shown that anything that calls for increased production of heat or cold causes changes in the adrenal and thyreoid glands. His experiments on mice and other vertebrates exposed to cold showed more damage in the adrenals than in the thyreoid.

This suggests that unless directly attacked, the thyreoid comes in for less intensive and less rapid action where the sympathetic system is involved than the adrenals. It also accounts for a certain overlap of sympathetic and parasympathetic irritation features, as implied by Eppinger and Hess when they describe two types of exophthalmic goitre—one with vago-tonic and the other with sympathetico-tonic features.

It is, then, as if the foreign body collecting in the blood (malarial poison) had been sensed by the medulla as expressed by the comparatively delicate signs of vagal irritation (Abrasi and Senevet); then the sympathetic-adrenal defence mechanisms were set in motion as expressed by the "cold" stage which in turn gave way again to

parasympathetic phenomena as exhibited in the "hot" stage, and to a certain extent supplemented by a fully developed thyreoid reaction. This suggests parasympathetic-sympathetic alternation of reactivity leaving the parasympathetic at the end of the "hot" stage to conserve the reserve forces until the next attack.

Hume has noted that in his 30 malaria cases with enlarged thyreoid, the enlargement always begins from 12-30 hours after the temperature of an attack had returned to normal. This seems to support the view that the effect of sporulation upon the thyreoid was rather later than that upon the adrenal and the sympathetic which innervates them. As indicated above, this may be due to the greater proximity of the enemy-in-force to the sympathetic-adrenal combine, as well as the greater intimacy of sympathetic and adrenal elements developmentally.

This theory would account for the effects of thyreoid hyperactivity—vaso-dilatation, rapid bounding pulse, and sweating coinciding with the effects of vagus irritation and dominance—rapid drop in the blood-pressure, some restraint in the rapidity in the pulse rate (Cf. Bürger) and the profuse sweating. Apart from any possible irritant (toxin, anaphylaxis) in the blood, the high blood pressure of the "cold" stage alone would have this effect upon the vagus medullary centre (Biedl).

Anyone who has injected a number of people with 15 or 30m of 1 in 1000 Adrenalin solution will be struck with a similarity between the effects produced and the "cold" stage of a malarial paroxysm.

Moreover, it has been shown by Biedl that stimulation of the sympathetic and of the adrenal has almost identical effects upon the manual, so that they, in combination, would appear to give the emphasis of reactivity to the sporulation of the malarial parasite as represented in the "cold" stage. Taking, then, the burden of attack first, (along with the blood) one would expect to find serious sympathetic-adrenal damage in all fatal malarias. There is much in the literature to support this view. Dudgeon, in 30 consecutive cases of fatal malaria, found severe adrenal damage in them all. Paisseau and Lemaire indicate that in all their cases of malarial cachexia examined post-mortem, the adrenals showed marked degenerative changes. They (and others) have published many instances of adrenal damage or

destruction in fatal cases of malarial gangrene, and malarial coma not due to cerebral malaria, and from their extensive observations of malaria as a whole have stated that they consider the adrenals and nervous system the most vulnerable organs of the body to it.

It only remains to have a closer study of the solar plexus and sympathetic ganglia to see if they also show evidences of degenerative change to support this idea. It is remarkable that in post-mortem observations of malaria cases, the sympathetic ganglia have been habitually overlooked.

Pathological observations on pellagra (Brugia quoted by Harris, Boyd, Wilson, Noera, De Giovanni, Angiolella, Cavazzana, Foa, Roaf, Lombroso, and Morse) have shown an emphasis of degenerative change in vertebral, semi-lunar and enteric ganglia and adrenals, compared with other parts of the nervous system; and while the thyreoid showed minor changes (degenerative) none were observed in the pituitary (Morse). If we recall the similarity of the outstanding features of Addison's disease (Adrenal and sympathetic ganglia damage—Bittorf—asthenia, gastro-intestinal disturbance, anaemia with leucopenia and mononucleosis, emaciation, pigmented skin); and pellagra (adrenal and sympathetic ganglia damage, asthenia, gastro-intestinal disturbance, anaemia with tendency to leucopenia, emaciation, pigmentation of skin); and malarial cachexia (adrenal damage, asthenia, gastro-intestinal disturbances, anaemia with leucopenia and mononucleosis, emaciation and pigmented skin), we must be impressed by the evidence of sympathetic-adrenal exhaustion (as well as mental symptoms) common to all three in their well-developed forms. The agent in each case is different, of course, and for that reason other features come in to qualify the pictures, but there is much evidence to suggest that in all of them the burden falls early and mainly upon the sympathetic-chromaffin system. In autopsies on fatal cases of malaria where both adrenals and thyreoid glands have been examined, it is noticeable that the adrenals show more damage than the thyreoid. Any organ may show an emphasis of lesion, of course, and the thyreoid is probably no exception to that rule, especially in those cases where enlargement of the gland and clinical evidences of hyperthyreoidism have occurred. But so far as available evidence goes, the adrenals generally speaking appear to suffer more than the thyreoid in malarial infections.

A survey of the literature shows that vago-tonic features such

as hyperchlorhyiria ani less frequently urticaria, occur in a large group of malaria cases. As is well known, iniigestion is one of the most frequent complaints, ani is often the *only* complaint among chiliren in infected areas. Many of these, especially in the early stages of infection are founi to have hyperaciiity (Novak ani Toman, Raymonl ani Salibert, ani others). In the more anaemic, asthenic types, subaciiity is common, in all graies iown to complete achylia-gastrica in cachectic cases.

Urticaria ani allieil conilitions like circumscribei oeiema, acrocyanosis, Raynaui's phenomenon, symmetrical gangrene are, taken together, not at all infrequent in malarial infections (Laveran, ani many others). Many Continental ani American Dermatologists place malaria in the front rank of infective causes of urticaria, ani malarial literature supports that observation. While it ioes not appear to be nearly so frequent as hyperchlorhyiria in malarial iniigestion it may be looki upon as a more remote vagus irritation effect. Other forms, involving iilatation of the blooi-vessels of the skin, such as erythema, scarlatiniform ani morbiliform eruptions, erythema nolosum, also occur though apparently rather less frequently than urticaria, ani may also be looki upon as vago-sympathetic phenomena.

There is, therefore, evilence of fluctuation of sympathetic ani parasympathetic phenomena running through the whole course of malarial infections, sometimes one ant emphasisei, sometimes the other set emphasisei, sometimes the two alternating rapiily. This, as we have seen, is exhibiteil in the proiromal, coli, ani hot stages of the attack; it may exiat less obtrusively in the apyrexial periois; ani persiat iown to, ani through, the stages of exhaustion with their iefective reactivity, to cachexia with, throughout, occasional ani variable focal iamage to qualify the pictures.

Of one were to tabulate the symptoms in terms of the nervous mechanism of reaction of the iifferent phases of malarial infection, it would appear thus:

1. PRODROMAL STAGE.

In the few hours preceding the paroxysm, a lowering of the blood pressure, marked leucopenia with relative mononucleosis, and marked hypercoagulability of the blood, with return to normal at onset of cold stage.

Features of anaphylaxis and vagus irritation phenomena.

2. THE PAROXYSM.

1st. Part.

Cold Stage. Rigor, pallor, contracted blood vessels, increased muscle tone, horripilation, hyperglycaemia, increased blood pressure, temperature, and pulse rate.

Sympathetic hypertonic, hyperadrenal phenomena.

2nd. Part.

Hot Stage. Shivering ceases, flushed skin, sweating, relaxed muscle tone, hypoglycaemia, lowering blood pressure and temperature, and restraint in rate of pulse which becomes bounding: no horripilation.

Hyperparasympathetic, hyperthyreoid phenomena. Sweating and hyperthyreoidism are distal and later sympathetic effects.

The paroxysm, repeated, and with further adjustment of the parasite to its human host leads to the chronic phase—always supposing that the patient escapes annihilation by involvement of a vital organ like the brain.

3. CHRONIC FORMS.

(including neurasthenic types and so-called "Latent" Malaria).

Nervousness, excitability, tremors, indigestion with gastric hyperacidity prominent, vomiting, bulimia, tenesmus, diarrhoea, constipation (intermittent) associated with hypertonic stomach and bowel, palpitation,

Hyperparasympathetic and hyperthyreoidic phenomena. (Sthenic features)

alternating with

lassitude, incapacity for sustained effort, muscle atonicity, lowered blood pressure, gastric subacidity with diarrhoea and constipation associated with bowel atony, anorexia, irritability of temper, depression, and pigmented skin.

Sympathetic and adrenal effort showing fatigue. (Asthenic features)

The symptomatology therefore shows fluctuation between a group with parasympathetic irritation (sthenic or vago-tonic features), and a group with sympathetic irritation (asthenic or sympathetico-tonic) features, with all degrees of reactivity of each system in different patients, or in the same patient at different times.

This brings us to the fourth stage of

A. CACHEXIA.

which is a picture of sympathetic-adrenal, endocrine, and blood exhaustion. The patient is mentally and physically apathetic, dull, depressed even, relatively indifferent to his surroundings. Skin is pale, dry, pigmented—which pigment is a late development of prolonged sympathetic irritation; low blood pressure; anorexia with tendency to sub-acidity to the extent of achylia-gastrica in some cases; constipation, mainly of atonic origin; diarrhoea; sub-normal temperature with heightened susceptibility to intercurrent disease, and even retarded development (infantilism) in those who have been infected young. Observations on the adrenals in many of these cases show definite morbid changes ranging from increased lipoid content of the cortex, diminution of Nissl's granules, defective staining reactions with fibrous changes, up to complete destruction of the adrenal tissues, with or without haemorrhages.

In the initial paroxysm we see an epitome of the reaction of the whole organism to malaria, see it met at the threshold by the defences of the blood and its organs, and by the parasympathetic, sympathetic, endocrine (mainly adrenal, thyreoid, pituitary) systems of defence. Remembering anaemia which persists throughout the nerve changes, we see parasympathetic activity giving way to sympathetic activity, then the resumption of parasympathetic control with stabilisation until the next attack occurs.

In the chronic forms of malaria we see the same fluctuations of activity dominance—less well marked, much more long drawn out—but vago-tonic forms exhibiting tenesmus, vomiting, cramps, nervousness, excitability, gastric hyperacidity, headache, backache, maybe urticaria and Raynaud's phenomena, constituting one group. And another group exhibiting apathy, indifference, incapacity for sustained effort, stomach and bowel atony, gastric subacidity, anorexia, diarrhoea, constipation, low blood pressure and skin pigmentation, suggesting sympathetic-adrenal debility, which may reach its full development in the cachectic state unless adequate immunity or treatment come to the rescue.

In the acute algid or typhoid type, with diaphoresis, delirium, very low blood pressure and profound exhaustion, we have a picture of rapid exhaustion of both systems, where the cachectic state is a condition of slow gradual exhaustion. In any case, so far as the physiology and pathology of the autonomic nervous system is understood, reaction to malarial infection appears to be expressed largely through it both in acute and chronic forms.

2. Peritoneal Syndrome.

It now remains to consider the localised manifestations of autonomic reaction more in detail. R. C. Parsons, who saw much malaria in Macedonia in 1915-17, records that it was unusual both in extent and severity, and that syndromes corresponding to every system—cardio-vascular, respiratory, nervous, genito-urinary, ocular, gastro-intestinal, peritoneal and organs of internal secretion—were seen. Cases might be easily chosen from the literature representing all these several syndromes, but as that would enlarge this work perhaps unnecessarily, only a moderate number of representative

samples will be chosen. Apart from abdominal involvement with symptoms referable to particular organs such as appendix, liver, spleen, stomach, pancreas, kidney, fallopian tubes and uterus, all of which are fairly frequent, cases occur suggesting generalised peritonitis.

Parsons, for instance, records one among several thus:-

Man, aged 25, admitted to hospital in Salonica, 10:7:16, with complaint of acute abdominal pain. Abdomen rigid and tender throughout: no distension. Spleen enlarged and tender.

12:7:16, leucocytes 8,800 per c.mm. 12 hours later, 18,000 per c.mm. Pain and tenderness persist, but become more marked in the right iliac fossa. In view of this localisation of signs, and rapid rise in the leucocyte count, laparotomy was done. Nothing abnormal was found. The appendix was free from disease and the appearance of the peritoneum was normal. The day after operation, the patient had a chill, and temperature went up to 103°F. Blood examination showed benign tertian parasites. Under quinine, recovery was rapid and complete.

The differential diagnosis of these cases is often difficult. Jackson and Capps rely upon the absence of leucocytosis in favour of malaria. But Parsons says that all his cases had leucocytosis with relative polymorphonuclear increase, that it appeared suddenly and synchronously with the acute physical signs. Spleen enlargement and parasites are the guides. Cases of this kind are noted by many observers—Craig, Parsons, Jackson, White, Capps, Gillot, and Alamartine and Vandenbosche.

Sudden appearance and disappearance of symptoms, if not actual tertian periodicity of symptoms, is not uncommon as shown by this case of Cordier.

Nine days after relapse of ague contracted four months previously in Macedonia, a man had symptoms of "acute abdomen" which came on suddenly. Vomiting was incessant, and there was intense pain in the region of the spleen. The pulse was small and 140. Next day, ascites noted. Fluid obtained by exploratory puncture was blood-stained, highly albuminous, and clotted slowly. Rivalta's reaction was positive. No plasmodia were discovered in the sediment, 7% of the cells of which were polynuclears, 90% mononuclears, 2% eosinophils, and 1% endothelial. P. Vivax was present in the blood. On the

following day, blood-stained fluid was withdrawn from left pleural cavity, the percentage of cells in which was mononuclear, 90: endothelial, 4: eosinophils and polynuclears, each 3%. Quinine had been given freely both by mouth and intramuscular injection from beginning of relapse, and the effusions in both cavities disappeared in a few days.

Tubercle as a cause of the effusions was excluded as inoculation of animals with the sediment was negative. Plasmodia, however, were not discovered in either fluid.

A case recorded by Cabot suggests vagus irritation and is interesting as an example of emphasis upon one symptom—vomiting.

CASE I.

Tertian malaria, with intermittent and persistent vomiting, and recovery. (Cabot).

A barber, aetat 37, whose father died of Bright's disease, was first seen 19:8:07, complaining of vomiting spells which began when he was 18 years old and continuing about twice a year ever since, though less frequently in the last ten years. He feels a "lump like lead" in the epigastrium all the time at present, and cannot remember when he did not feel it. All food distresses him about equally. His appetite is good, and he eats slowly and at regular intervals. Bowels constipated. Ten days ago he began to vomit without known cause, and has since then rejected everything except salted milk. Vomitus chiefly phlegm in small amounts. During these ten days, he has perspired during the earlier part of night and felt very cold the rest of the night. Sleep dull and heavy. Thinks he has lost weight. He has been able to do no work for this same period. Temperature practically normal—once up to 99°F.

Patient well nourished, pale. Heart and lungs negative, likewise abdomen and urine. White blood cells, 4000. Haemoglobin, 80%.

Possibilities—gastric neurosis, chronic ulcer, chronic appendicitis. But one feature arrests attention—night sweats. Blood examination showed many tertian parasites. Quinine treatment. Vomiting ceased in two days, and blood free from parasites.

Cabot (loc. cit) mentions another case of vomiting and drowsiness in a woman with tertian parasites in the blood.

Bonaventura records a case of parasympathetic disturbance.

A peasant had intermittent fever, beginning in the afternoon and terminating in the early hours of the morning. On the fifth day, his doctor prescribed quinine, which stopped the fever. But several days after at the same hours, he had a sensation of weight and pain in the abdomen which caused him to vomit and cough repeatedly, followed by spasmodic coughing, palpitation and dyspnoea. These phenomena were most intense on one day, but not on the ~~same~~ other, diminished at night and disappeared towards day. The patient was obliged to eat in the early part of the day, for, if not, food was found to aggravate the symptoms.

He went to a dispensary where no organic lesion was found, save a slightly enlarged spleen and malignant tertian parasites found in the blood.

Pressure on the umbilical region was painless in the morning, but painful in the afternoon. Quinine and opium effected a cure in six days. The author records another similar case.

Numerous other types of abdominal disturbance with evidences of focal irritation in great diversity are recorded in the literature in great profusion. Notable among these is the clinical picture of appendicitis, for which the abdomen has been opened on many occasions, only to find the appendix appearing normal or only appreciably redder than usual, and the symptoms abating finally with quinine. Jackson and Capps (quoted by Parsons) record several cases of abdominal disturbance simulating appendicitis, gall-stone colic, etc., which proved to be of malarial origin. Capps reports one case of special interest, namely—

A female, with history of former pelvic trouble, chills and fever, but no pain at first. Later, cramp-like pain in abdomen, and still later localised pain in the right iliac fossa, so severe that she fainted. Spleen palpable, abdomen tender, and resistant over right iliac fossa. Pelvic examination showed lacerated cervix, and mass in left ovarian region not tender. Extra-uterine pregnancy was diagnosed, and she was brought to hospital for immediate operation. White blood corpuscles, 5,000 per c.mm. Benign tertian

parasites were found in the blood, with recovery on quinine treatment.

The differential diagnosis of these cases is often difficult. Jackson and Capps state that there was no leucocytosis in their cases. Parsons, on the other hand, maintains that practically all his cases had leucocytosis with a relative increase of polymorphonuclears: also that its appearance was sudden and corresponded to onset of the acute physical signs. Thus he considers that a white blood count is not so valuable, unless when negative, and that splenomegaly and blood parasites are the points in diagnosis. Discussing the focal pain, he considers that it may be due to perisplenitis, extending to the diaphragm (diaphragmatic pleurisy), or to local neuralgia (massing of parasites in nerve sheath), or associate disease such as infection by other other organisms (which, be it added, would account for the polymorphonuclear-leucocytosis). One might also add the possibility of reflex (vagal) irritation from say, the spleen to any other abdominal organ supplied by vagus also.

Marguerite White, discussing the diagnosis of pseudo-appendicitis (malarial), writes: "I have seen many of these cases on the island (of Malta) due to Malaria, which cleared up rapidly under intramuscular quinine. If the diagnosis is made, surgical interference is not necessary. The cause of the pain on the right side is, I believe, a referred pain due to an acute splenitis, which, in my own observations, has always been present, although in some cases it may be due to the localisation of the parasite in the intestinal mucosa.

"I have had many cases of appendicitis both catarrhal and suppurative in malaria patients and the only point on the differential diagnosis, as far as I have been able to observe, is the white cell count. In both classes of cases, all Murphy's symptom complex are present except leucocytosis—i.e. pain, vomiting, a little temperature, and rigidity of the right rectus. In pseudo-appendicitis or pseudo-cholecystitis, due to malaria, one finds a marked leucopenia, with a decrease in the polymorphs and a high mononuclear count. In true cases of appendicitis, complicated with malaria, one finds a relative leucocytosis, with an increase in the polymorphs. The non-discovery of the malarial parasites in the peripheral blood is of no account in the diagnosis".

Falconer and Anderson, who saw 12 cases of appendicular type in

Salonica (1918), recori that the chief symptoms were vomiting, pain in the right iliac fossa, associatei with moderate pyrexia ani marked tenierness ani rigiility in the right fossa, which was usually not constant. In some of the cases, the tenierness was most marki above McBurney's point. In others, it corresponiei exactly with this point. In all cases, there were either parasites in the blooi or enlargei spleen, or both. None showei a leucocytosis, ani all hai the typical relative lymphocytosis of malaria. All rapiily cleari up with quinine. A few of these showei so severe pain ani rigiility as to suggest acute abiomen, but these also cleari up rapidly with quinine.

The teniency, then, is in abiominal conditions to rely upon leucopenia with mononucleosis as in favour of malaria, other things (splenomegaly, finiing parasites) apart.

The following case recoriei by Rosenberger is probably not a common variety ani might easily be very puzaling where no malaria is suspecti.

CASE II.

Malignant tertian malaria, simulating dysmenorrhoea, and recovery. (Rosenberger).

Urgently calli 22:5:22, to see a woman of 37, who was very ill with dysmenorrhoea. Father iii at miiile age of apoplexy. Mother agei 80, ani brothers ani sisters alibe ani well. As a chili, patient hai mumps, scarlet fever, measles. From 8 years of age until 1921, she was in Hungary in the Carpathians: thereafter she returnei to Munich. In 1919, she hai severe influenza, with lung catarrh, which lasti a long time afterwari. Menses always regular ani easy till two weeks ago, when it was profuse ani irregular, but she iii not trouble to call the ioctor. Felt rather bai on this occasion, shivery in the mornings, with pain below left costal margin which she complaini of now. During past two weeks she hai intermittent vomiting, heaiache, palpitation, with a whole iay between times when she felt quite well, so that she was consideri hysterical. No complaint of sweating. Bowels ani micturition normal.

She looki pale ani excited. Face a brownish shaie, like café-au-lait. Systolic murmur over the praecordium. No glaniular enlargements. Tongue ieep red, rough, iry without aphthae. No bone tenierness or skin eruption. Temperature in axilla, 39°C. Pulse,

120, regular. Spleen not enlarged to palpation or percussion. Very few white cells seen in blood film. Culture from mucous spit -ve. Wassermann negative. Subtertian parasites in the blood. Gruber-Widal for dysentery suspicious. Later admitted here and had dysentery. Gynaecological examination negative. 5 gms. quinine hydrochloride in 36 hours.

May 23rd. Temperature in axilla, 36·8°C. Pulse 80. Periods stopped.

May 24th. During night, severe sweating. Next morning felt well. Spleen now palpable. Slight menses. The two nights following severe sweating.

May 26th. Spleen not palpable. From 24th onwards, no return of period. Iron prescribed without quinine. Patient got up and was free of fever till end of June, when she had fever in the mornings without shivering, and when her period was due, she had "pain in the stomach".

June 23rd. She called on me. Menses excessive, but without pain. Spleen palpable, and heavy feeling under left costal margin. Malarial parasites in blood. The fever recurred every second morning early and wakened the patient. With quinine, 0,3, fever, spleen enlargement, and period disappeared. Urine normal and free of bile. In August, the period was normal, and she resumed her work feeling well.

It is difficult to say where she got the malaria. She was quite a good deal with the military during the War; also there are mosquitoes in the neighbourhood of Munich.

3. Gastric Juice in Malaria. (Vagus).

Digestive troubles are prominent in all stages of malarial infection, and this has led several observers to inquire into the state of the gastric juice in malarial subjects.

Novak and Toman examined 200 cases by the Ewald Test Meal without regard to the severity of the malaria. Their findings were as follows:

	No. of Cases	No HCl.	HCl value under 30 ccs. N/10 NaOH.	HCl value between 30 and 60 ccs. N/10 NaOH.	HCl value over 60 ccs. N/10 NaOH.
Cachectic Cases.	91.	41.	13.	25.	12.
Non-cachectic cases.	109.	37.	15.	38.	19.
TOTAL:	200.	78.	28.	63.	31.

It will be seen that achylia-gastrica is very common in cases with malarial cachexia.

The total number of cases with achylia = 78 (39%).

Of the 91 cachectic cases, those with achylia = 41 (45%).

Of the 109 non-cachectic cases, those with achylia = 37 (34%).

Teeth were in nearly all cases good, so that the authors did not consider their condition as a contributory cause of the achylia. It will be noticed also that the achylias and sub-acidities taken together (54) are greater than the hyperacidities taken together (57) among the cachectics; while, in the non-cachectic cases, the hyperacidities taken together (57) are greater than the achylias and sub-acidities taken together (52).

This would suggest that in the earlier stages of malarial infection, there is greater tendency for indigestion to be associated with the signs of vagus irritation (hyperchlorhydria) than in the later stages.

Discussing quinine treatment in the achylia stages, these authors did not consider that it could account for all, as it was used for cachectics and non-cachectics alike. They also state that many of the achylia cases were not badly nourished, and that the malaria had presumably led to gastric atrophy, though admitting the possibility of functional suppression in some cases.

Raymond and Saligmat, reporting on the gastric secretion in 30 cases of dyspepsia in malarials, found secretion normal in 10 cases, hyperchlorhydria in 14, chronic ulcer in 2, and ~~hyperacidity~~ hypochlorhydria in 4. Ewald Meal used. Thus hyperchlorhydria predominated. The authors record that the most severe cases were hyperchlorhydrics and that there was a parallelism between the gastric secretory troubles and the functional hepatic disturbances; i.e. that hyperchlorhydria nearly always accompanied liver hypertrophy

and hyperfunction; while hypochlorhydria was generally associated with atrophy and hypofunction of the liver. The appetite was never exaggerated, was often ordinary but more often poor—the reverse of the usual in hypersthenic types of indigestion. Patients complained of indigestion after meals, with ballooning and eructations of acid quality, heaviness, vomiting, cramps. Intestinal functions disturbed simultaneously, with diarrhoea often profuse, and constipation, alternating. There was generally local hypogastric tenderness. The authors point out that the hypochlorhydrics are probably later stages of the hyperchlorhydrics. Satisfactory treatment was mainly by quinine given per rectum.

Furuichi examined the gastric juice in patients who had not been treated with quinine. The quantity of gastric juice, its total acidity and percentage of free HCl were found to be small, especially so in malignant ague. Lactic acid was present in the majority of cases. As convalescence proceeded, the gastric juice was found to return to normal. In malignant ague, the low acidity was met with even at the stage when no other malarial symptoms were evident, except the presence of crescents in the blood. In a few cases of blackwater fever, which came under the observation of the author, a similar feature of lowered acidity was also found.

Knighton, writing on malaria and digestive disturbances, draws attention to their frequency in malaria, and the high incidence of complaints usually found with hyperchlorhydria—burning pain in the stomach, usually relieved temporarily by the taking of food. The usual history is that the patient has had malaria shortly before, for which there was treatment for a short time only, and that since then there has been gastric disturbance. No recent chill, but splenomegaly and parasite frequently found in the blood.

The following is a representative case:

CASE III.

Hyperchlorhydria, of malarial origin. (Knighton).

Mrs. M. F., aged 32, married, 4 children. No miscarriages. Menses normal. Father died at 50 of gall-stones. Mother alive and in good health at 58. Patient has never had an acute illness since childhood. In June of present year, she had an operation for repair

of lacerated perineum. In July, of present year, began to suffer from burning pain in upper abdomen and chest, this being most marked several hours after a meal, and being somewhat relieved by taking food. Has suffered from headaches but has had no chills or fever at any time.

Physical Examination: General appearance of anaemia; heart and lungs normal. Spleen palpable below costal margin; no tenderness over appendix or gall-bladder regions. Examination of stomach contents, after Ewald meal, shows an average quantity with free HCl, 44, and total acidity, 68. Urine normal. Malarial parasites in the blood. X-ray of stomach normal. Aspiration of the fasting stomach showed presence of gastric juice with a high percentage of HCl.

The author considered the case as one of hyperchlorhydria of malarial origin and treated it accordingly.

Some cases of this class take on an acute form and Alexandrine and Vandenbossche as well as others record cases simulating gastric and duodenal perforation with violent pain and collapse, which recovered on quinine alone.

Doyet has suggested that Raynaud's phenomenon of the intestine occurs just as it does in the skin.

4. Colitis.

Malaria, acute or chronic, can be associated with diarrhoea and colic, due to direct irritation by the parasite of the intestinal mucous membrane, at other times by disturbance of liver or pancreas, and at others from abdominal nerve disturbance; or malaria may aggravate a pre-existing colitis. Careful bacteriological and serological tests may be necessary to define the agent or association of agents. In any case, the parasympathetic control of the intestine is liable to be irritated in acute forms, with pain and diarrhoea.

Job and Hirtzmann record a case of this kind with periodicity.

CASE IV.

Malarial colitis, with periodicity of symptoms. (Job and Hirtzmann).

P. took malaria for first time, 28:8:16. Within 8 days,

he got four injections of quinine; subsequently at time of attack only. Admitted to hospital, 8:5:17. General state only fair. Colour earthy, spleen enlarged. On 9th May, about noon, he had sweating, with colic, and some glairy blood-containing stools. P. vivax found in the peripheral blood the same day, and in blood from the stools. Symptoms subsided and disappeared that day. On 11th May, febrile attack, with recurrence of above symptoms, and again parasites found in peripheral and stool bloods. Stools contained no amoebae or cysts, and was negative to culture and serum tests for dysenteric bacilli of Shiga, Flexner, and Hiss.

5. Glycosuria and Malaria.

Malaria as a cause of glycosuria is a subject about which there appears to be considerable diversity of opinion. There are reputable observers on both sides, who have handled large numbers of malaria patients—those who emphasise its frequency on the one hand, and those who have seen little, or none, on the other hand.

The first observer noticed in the literature to emphasize the frequency of glycosuria in malarial subjects, was Buriel. He practised in the malarious Sologne district of France and has written several papers on the subject (1859-1872). He says that in his experience of malarial fevers a true glycosuria occurs, that it is often transitory, that it varies in degree with the severity of the attack, that it was seen most frequently following relapse, and that in the measure in which quinine was given it disappeared with characteristic rapidity.

A remarkable observation of Buriel's was that he considered malaria a ganglionic-system neurosis, that it had a specially malign influence on the organs controlling sugar metabolism, and in examining the urine, he was looking for evidence of primary disturbance of the ganglionic-nervous system, as shown in the imbalance of the organs it supplied. In 1871, when malaria was the most prevalent it had been for a long time , he examined many fever cases from this point of view, with the following results:

Type of fever.	No. of attacks.	Incidence of Glycosuria.
Quotidian.	134.	29 times.
Tertian.	122.	17 -
Quartan.	76.	11 -
Very severe malaria in cachectics.	40.	32 -
Pernicious.	11.	3 - only.

He adds that in the last group the incidence of glycosuria was not representative, because in these pernicious cases, delirium and loss of consciousness made it difficult or impossible to collect urine until after quinine had been given and the patients were better, by which time the glycosuria had disappeared. He quotes his friends Fleury and Bouchut who had each seen a case—one of malarial cachexia from Algeria with glycosuria, and the other who had glycosuria during the attack only, which disappeared with quinine.

Verneuil (1881) notes the frequent association of glycosuria with malaria, its intermittency, occurring often in the mornings after attack and he comments on its periodicity. Colin and Relon, quoted by Verneuil, both note the frequency of association of glycosuria in malarial subjects, and Prout does the same.

Girert, quoted by Mannaberg, claims that he has frequently seen in Panama glycosuria follow repeated malarial attacks and that sometimes office-holders had to be sent home on account of it.

Rangé, in 10 out of 60 malarial patients in French Guiana, found in the urine traces of sugar which he attributed to their malaria.

Castronuovo considers that the large number of diabetic subjects in Southern Italy is due, not only to the diet, but to infective agents, especially malaria and tuberculosis, damaging digestive organs, nerves, glands of internal secretion, liver, and pancreas.

Dudgeon and Clarke saw several cases with massing of parasites in the pancreas vessels, haemorrhage into the pancreatic tissue, and degenerative changes in the Islets of Langerhans. No symptoms referable to the pancreas were recorded, but traces of sugar were an occasional finding.

On the other hand, Laveran has stated that he saw no more glycosuria in Algeria than in France; and Delsan, Grall, Le Roy de Méricourt, Desalerick and Craig say that it is rare, and Hemseter saw only two cases in 198 urine analyses; Ziemann saw none; Seegen quotes one case in 1860 of intermittent fever with intermittent glycosuria during a week, which disappeared with the fever. Sorel saw only one case in over 100 malarials; Mannaberg saw only one case with reducing substance in the urine. Sydenham, Mossé, and others have written on post-malarial diabetes. Le Roy de Méricourt records two cases of transient glycosuria in malarial patients. He says that Grall, in 500 examinations of urine of malarial cachectics in Guiana, did not find "sugar in excess". Books on geographical pathology, like those of Hirsch, Lombard, do not find diabetes a feature of malarial countries. Morehead, practising in India, got 6 true diabetic cases in natives (on vegetable diet).

M. Huillet, in 6252 patients of whom 1354 were malarial, says true diabetes is very frequent among the Indians, but rare among the Whites.

More recently isolated cases have been recorded by Jebens, Naunyn, Harrison, Seidelin, Sutherland, Orlebar, Bertrand, and two by Castellani and Willmore.

Oesler records a case of gangrene of both feet with malaria and glycosuria. This case was a man of 51, who during a malignant tertian malarial attack became delirious and was taken to hospital. On admission there was no sugar in the urine. Four months later, he returned with gangrene of both feet and marked glycosuria. One foot was removed, and was followed by general improvement; then the other foot was amputated. After the second operation, sugar disappeared rapidly from the urine and he made a good recovery. (No quinine mentioned).

The case recorded by Jebens was one of transitory glycosuria, while that of Naunyn developed into true diabetes. As they seem representative, a brief translation of them is given.

CASE V.

Case of Transitory Glycosuria. (Jebens).

F., K., 26 years, seen 19:5:19, complained for last three

weeks of cough, headache, attacks of shivering with feeling of heat, pains in left side, herpes of lips. Double pulmonary catarrh, especially left base. Left heart borier in nipple line. First sound over all heart valves impure. Urine contains no albumen. Nylander's test for sugar +ve. 0·5% dextro-rotatory. Fever over the next few days with tertian periodicity, which suggested malaria. Closer questioning elicited the information that in 1915,1916, he was in Narocssee and in the Ukraine 1918, ill with "cerebraltyphus" when he had shivers and headache.

27:5:19. Morning. Spleen rayed with Höhensonne (2 minutes) and injection of 1 cc. 1% adrenalin solution.

Evening. Blood picture. Haemoglobin, 90%; Red cells, 4,208,000; Leucocytes, 5,200: polymorphonuclear, 48·5%; lymphocytes, 40%; transitionals, 9%; eosinophils, 2%; mast cells 0·5%; many tertian rings seen. Liver not markedly enlarged. Spleen palpable at costal margin. Urine watched, and it was found that urine examined during febrile attacks which occurred with tertian periodicity contained glucose as follows:

May 24th.	0·2% sugar.
May 26th.	0·5%
May 28th, & 29th.	0·8%
May 30th, & 31st.	No sugar and no fever.

During the apyrexial periods, there was no sugar in the urine. Quinine was begun on the 28th May. From the 1st to 5th June, sugar to the extent of 0·2% was found daily in the urine. Thereafter, until discharge of patient on 17th June, no sugar. Fever absent from morning of 29th May. July 7th, no sugar. Patient received ordinary diet throughout.

The author considers the malaria may have irritated the adrenals or sympathetic or pancreas itself, producing unbalanced condition of the organs of internal secretion, and produced a transient glycosuria. He also considers malaria can produce true diabetes by damaging the islets of Langerhans directly, or by producing arterio-sclerosis of the pancreas and leading to atrophy of them in a long standing malaria.

Jebens quotes O. Jakobson, who describes a case of malaria which, a week after the last malarial attack, died of diabetic coma.

Calmette (8882) noted transitory glycosuria in 5 cases out of 41 in malarials.

CASE VI.

Case of Diabetes Mellitus. (Naunyn).

Man, aged 45, University Professor. Heredity negative. No syphilis. 3 years before, fell on his head, and soon after got a knock on the head, but without cerebral symptoms. Urine always free of sugar—frequently examined. November, 1898, got severe malaria on "Valdivia" expedition. Malarial parasites found in the blood on arrival at Marseilles. April, 1899, complained of excessive thirst, lassitude, and urine containing sugar. Lost 1Kgs. weight. July, 1899, lost 20Kgms. Skin brownish. No jaundice. Liver palpably enlarged. Spleen enlarged and palpable. No parasites found in the blood. 5% sugar in urine—slight polyuria. With moderate dieting, sugar reduced to 3%. With no carbohydrate, 200gms. vegetable and an apple occasionally, sugar fell to 0·3%. Any relaxation of diet led to increase of sugar. Acetone, diacetic acid, and B-oxybutyric acid were present, yet he kept quietly at work for two years, sticking carefully to the diet. Early in 1901, his strength began to fail seriously. He had acidosis and 3% sugar appeared in the urine, even on strict diet. November, 1901, he began to have emotional attacks and soon after became comatose and died.

CASE VII.

Glycosuria of Malarial Origin. (Castellani and Willmore).

Mr. E. N., aged 44, married, with no family history of diabetes, consulted one of us in March this year. During the War, he served in one of the allied armies, and in 1916 he contracted, while in the Balkans, a severe malarial infection; he had several relapses, the last being on Dec. 9th, 1920. In Jan., 1921, he noticed that he was feeling more hungry and thirsty than usual, was passing much more urine than normal, and was losing flesh. He consulted a medical man, who found a fairly large amount of glucose in the urine (2%), and placed him on a very strict diet, which induced only a slight decrease in the amount of sugar in the urine.

When the patient consulted one of us in February, the urine contained 1½% of glucose; it was acid, sp. gr. 1,032, no albumen, and acetone and diacetic acid were absent. The amount of urine passed during the 24 hours averaged 6 pints.

The patient looked rather emaciated and very anaemic, the skin was of a pale, earthy colour, with patches of hyperpigmentation resembling chloasma, so often seen in cases of chronic malaria. His spleen was very slightly palpable and very hard. The examination of the blood did not show any malarial parasites, but there could not be any doubt clinically that he had chronic malaria, and the diagnosis was made of "diabetes in malarial subject". He was advised to continue the strict diet he had been having for the glycosuria, and in addition to take 10 grs. of quinine three times daily for his malaria. He came back three weeks later feeling much better; the enlargement of the spleen had disappeared, and—a most interesting feature—the amount of sugar had decreased enormously, being less than 0·1%. We came to the conclusion that it might be a diabetes syndrome of malarial origin, and suggested to the patient that he should go back to the ordinary diet, but continue the quinine. He came to see us regularly once a week, and the sugar did not increase; only a trace was present. During March, the patient went to the South of Europe on business, and during all that time he was away (four weeks) did not take any quinine. He came back to this country in April, and three days after his arrival, after playing golf in the rain, had a shivering fit, followed by very high fever, which ended in profuse sweating. The spleen again became palpable and hard, and examination of the blood showed the presence of a few rings of malignant tertian. The urine was examined after the temperature had come down to normal; it contained 1·2% of sugar. The patient was placed on an intensive quinine treatment by the mouth and intramuscular injections for 6 weeks without any dieting; not only did the symptoms of chronic malarial infection disappear, but the urine became completely free from glucose, when examined by the usual methods of analysis (Fehling's, Nylander's, phenylhydrazine, fermentation test).

Guiteon, in 100 cases of malaria with blackwater fever, notes

that there was no instance of fat necrosis, or haemorrhagic pancreatitis, but that congestion of the vessels and occasional haemorrhages were common, and in two cases, there was marked degeneration of the islets of Langerhans. In one of these, sugar was present in the urine, and 0·18% in the blood.

The pancreas has been found involved directly by several observers—viz. Ross, Gross, White, Dudgeon and Clarke, Ross and Daniels. Plu observed a case of a woman where the pancreas vessels were stuffed with parasites and necrosed, and the whole body fat showed Balzer's fat necrosis.

Dudgeon and Clarke record that "the most definite changes noticed in the histology of the pancreas occurred in those cases in which massing of the parasites in the blood-vessels was observed. The outline of the capillaries, which were congested in some areas and packed with red infected cells, afforded a striking picture. Deposits of melanin were commonly observed, both intra- and extracellular. The islets of Langerhans in a few cases showed degenerative changes. Haemorrhages into the pancreatic tissue were noted on several occasions in association with haemorrhages in other organs. No symptoms referable to the pancreas were recorded, but traces of sugar were an occasional finding".

Castellani records a case of acute haemorrhagic pancreatitis syndrome in a man of 42 with blood swarming with malarial parasites and treatment without operation.

Gross and Ross and Daniels also record a case.

The following case of acute haemorrhagic pancreatitis recorded by White will serve as an illustration of acute involvement of a gland, though unfortunately there is no record of the urine condition.

CASE VIII.

Case of Acute Haemorrhagic Pancreatitis, due to malaria. (White).

Patient, aged 28, invalided for malaria and admitted with this complaint. He was in hospital about 6 weeks; he had three slight attacks of malaria (sub-tertian) rings and crescents found in the blood. The clinical findings were nil, except a palpable spleen, temperature in each attack not higher than 102°F, patient rapidly

recovered from attacks. General health excellent. Sent to convalescent camp, and a few weeks later to Active Service Camp. After about a week at the latter, he was re-admitted as a surgical case. While on duty, he was suddenly seized with a severe pain in the upper abdomen; carried to his tent. He was sent to hospital immediately.

On admission he was very collapsed, sweating profusely; pulse 130, weak and intermittent; abdomen distended, and rigid, with marked resistance in epigastrium: drawn anxious look, temperature, 98°F, a few hours later, 101°F; appeared very ill. At laparotomy a few hours later, there was some free bloody fluid in the abdomen; pancreas was enlarged and congested: small petechial haemorrhages and fat necrosis in surrounding tissues and mesentery. Appendix normal: liver and spleen slightly enlarged and congested. The abdomen was closed without drainage: intramuscular quinine, grs x. During the first 24 hours after operation, he collapsed twice; stimulants, artificial respiration, oxygen. Next day he was much better, but sweating profusely. After this, under quinine, recovery was rapid and uninterrupted.

The author had seen one other case of acute malarial pancreatitis, which cleared up rapidly on quinine.

Considering how widespread malaria is, there are singularly few records of the incidence of glycosuria and still fewer where the accounts of the cases are reliable, or any indication is given of the mechanism of production.

We have seen that, with the incidence of the cold stage of the malarial paroxysm, there is a hyperglycaemia, which is probably the direct result of hyperadrenalism, coincident with sympathetic irritation at that stage. It is probably at this stage that sugar passes into the urine, with increasing frequency as the attacks follow one another, and liver damage is added to the hyperadrenalism, though this effect would tend to be balanced by coincident sympathetic-adrenal exhaustion.

In cases where the thyreoid, pituitary, and brain happen to come in for special excitation, one would expect transitory glycosuria, though malarial literature does not seem to support this

view. Then again, in cases of direct pancreas damage, of which a few cases are cited, glycosuria and destruction of islets of Langerhans would consitute true diabetes mellitus. There are very few reliable records of cases of this kind, though it is probable that they occur more frequently than appears.

There is much room for further investigation into the whole question of disturbance of sugar metabolism in malarial subjects.

6. Urticaria.

Urticaria shares with herpes zoster the distinction of being one of the commonest skin eruptions in malarial infections. Most of the continental and American text-books on dermatology put malaria in the foreground of infective diseases causing it, and malarial literature is studied with examples of it, as well as allied conditions, such as circumscribed oedema, acrocyanosis, Raynaud's phenomenon, and symmetrical or multiple gangrene.

It is regarded as a vago-tonic phenomenon, and is generally associated with eosinophilia and gastro-intestinal disturbance, maybe asthma. Adrenalin and atropin, both of which restrain the vagus, are notably useful in its treatment.

Johnston states that it is commonly associated with vomiting, purging, gastric hyperacidity, a low blood-pressure, and lowered blood coagulability, and that at present (1912) it is the only autotoxic eruption which has been experimentally demonstrated to be an anaphylactic phenomenon. This goes part of the way to support the thesis of Abrami and Senevet that malarial infection implies anaphylactic shock.

It is interesting in this connection to recall the great frequency of gastro-intestinal disturbance in malaria patients in general, and the common occurrence of hyperchlorhydria and sub-acidity in them, both conditions regulated by the vagus.

It is important to know that urticaria has a close association with malaria for it is not infrequently the complaint that brings the patient to the doctor, and here again the masquerading parasite easily eludes detection. A case reported by Todd bears on this point.

CASE IX.

Case of Malignant Malaria, with urticarial and petechial eruptions. (C. Todd).

Man, aet. 40, seen 4:2:00 at Umtali, Rhodesia. Had only been six weeks in the country, but had been some years in S. America, and had never had malaria or any other serious illness.

He came complaining of diarrhoea, and vomiting, with some tenderness over stomach, and was given bismuth, morphia, and soda, but pain became colic and temperature rose to 101°F. Morphia hypodermic was given, pain ceased, and on February 5th, temperature was normal, and he said he felt quite well, though exhausted by diarrhoea and vomiting, which he ascribed to error in diet.

Feb. 6th: A vivid, itchy, urticarial rash appeared, covering body, limbs, scalp. Bowels acting, but no vomiting, diarrhoea, stomach tender. Liver and spleen seemed normal. Temperature, normal. Tongue, coated. During day, rash faded in places, and reappeared in others, taking on a morbilliform character at parts. At other parts, raised white patches on a red base.

10 p.m. Temperature, 102°F. Patient livid, delirious, running pulse, refusing food and medicine. Strychnine, digitalis.

Feb. 8th: Coma, Cheyne-Stokes' respiration. Temperature, 98-6°F. Petechial spots on chest. Till now, regarded as ptomaine poisoning. Question of malaria had been thought of, but as there was no malaria in Umtali, and no history of rigor or chill, and no palpable spleen, and little fever, it was considered improbable.

Blood examined on the 8th showed malarial parasites.

Hypodermic of hydrochloride of quinine given, 39 grs. in 24 hours. Slight improvement followed. Eggs, milk, brandy taken. Temperature rose, and he died exhausted with temperature at 104°F.

It was subsequently found that the patient had visited the low country about a fortnight before his illness, and had presumably become infected with the parasite then.

Author states that "medical men practising in malarial countries are often accused of attributing every ailment to malaria... ...but cases like the above emphasise the importance of bearing in mind the possibility of malaria, even in cases which at first sight do not suggest it."

The frequncy of association of urticaria and malaria may well suggest it as a possibility.

Occasionally urticaria replaces the paroxysm or accompanies it with regular periodicity as any other symptom may do. A case of this kind is recorded in the chapter on Periodicity (Cases 3 and 4).

Garin and Parquier noted 40 cases of urticaria in 135 controlled malarial cases. It showed as white papules with halo of red, generally occurred the day after the malarial attack, and lasted 48 hours. The shoulder, legs and sides were principally affected (7th dorsal segment?), itch prominent, and recurrence with each paroxysm. Diarrhoea was a constant accompaniment. In 48 malarials who had diarrhoea during the attack, urticaria followed in 35 (72%). Urticaria was rare without diarrhoea. In 75 malarials without diarrhoea, only 5 presented urticaria (6.7%). In every case, parasites were found. Icterus was frequent in their cases. Vomiting occurred in 35%. They noted that it occurred in cases with less frequent febrile attacks, at weekly intervals or so, tended to recur in the same places, was associated with diarrhoea, articular troubles, icterus, which features the authors considered impotence in reaction and implied severe infection.

These observers evidently consider urticaria among the serious manifestations, and Kelsch and Kiener also noted that it occurred especially in grave cases. Grall notes the frequency of urticaria in malarial subjects.

Papastrategakis records a remarkable case of intermittent urticaria in a malarial subject, with also local asphyxia of the extremities. His comments on the peculiarities of the case were: (1) These symptoms did not occur during paroxysms, nor between them, but in their stead. (2) The co-existence of urticaria and local asphyxia. (3) The coexistence of urticaria with a purely nerve phenomenon, suggesting that it depends upon the nervous system. This throws a little light on the nature of anaphylaxy, shown thus to be an acute form of poisoning of the nervous system. (4) It supports the view of Abrami and Senevet that the malarial paroxysm is anaphylactic neuroplexia, due to the disruption of plasmodia (rosettes) and to freeing of heterogeneous albuminoid substances.

Herpes zoster is also very common, in malarial subjects,

generally during, or soon after, a malarial attack. Practically all authors giving a survey of their malaria cases record it frequently. It may occur anywhere, but is most common on the lips. It is usually considered to be due to inflammatory disturbance of the sensory posterior root ganglia, or their branches, but L. R. Müller maintains it may occur as a result of disturbance of the sympathetic ganglia and rami communicantes. This being so, it is not surprising to note its great frequency in malaria (see Cerebro-spinal section).

7. Oedema—Circumscribed and otherwise.

Several varieties of oedema have been recorded in association with malaria.

1. Oedema secondary to cardiac or renal lesions, which may be of malarial origin.

2. Oedema associated with cachexia and anaemia.

3. Circumscribed oedema.

4. Malarial inflammatory oedema, recently described by Sainton, Richet-fils, Schulmann.

The first two need not be considered further now. The second two are probably different degrees of the same thing. Patches of oedema—raised, white, painless, have been recorded occurring at different parts of the body—malleoli, hands, face, often symmetrical but not always so. Or the oedema may extend, beginning generally at the feet, and extending upwards, and involving arms, body, face, and even the serous cavities. It may strongly suggest a nephritic anasarca, only that kidney tests show no retention of nitrogenous waste, or sodium chloride, and no albumen or sugar. Anaemia may be comparatively slight, and heart show nothing to account for the condition. Temperature is generally normal or sub-normal. It may be that this follows upon an acute febrile attack during an apyrexial period.

Manson-Bahr has dwelt upon brain oedema in cases of malarial stupor and coma, and advocates the advantage of spinal puncture in these cases where the intraspinal pressure is usually very high. Any vital organ, such as brain, lungs, or serous cavities, may be involved with grave results. Several authors record cases of oedema

of the serous cavities and it would appear that what happens in the vessels of the skin may also happen in those of the meninges, and serous cavities—viz., spasm, dilatation, increased permeability by nerve influence, and also localized endarteritis with thrombosis, embolism, so that local collections of fluid, clear or blood-stained, may occur from either cause, or both together.

Monfalcon states that oedema of the lungs and glottis, causing death, may occur. Griesinger notes the frequency of oedema in malarials.

Mauban observed oedema of the face in 14 of 72 Macedonian cases, without albuminuria. In Watson's cases in Selangor oedema was a prominent symptom, and in 15 of 27 cases it overshadowed all other features. In these, the urine was generally normal. Of 83 cases of quartan malaria, 27 (32%) had oedema of ankles, hands, face body, pleura, lungs. Among others, he records the following case of malarial oedema.

CASE I.

Oedema, with quartan malaria (W. Watson).

Tamil, aged 47, admitted to hospital, 26:3:02. Stated he had had fever three and a half months before admission, which had lasted one and a half months latterly. Body completely swollen, with dyspnoea, moist cough, and so weak he could not walk. Bowels costive, temperature, 101·4°F. Did not feel fevered. Anaemia and great swelling of hands, feet, abdomen, scrotum. Spleen felt through considerable ascitic fluid. Moist râles in chest. Heart normal, but for a haemic murmur. Urine normal.

28th March. Numerous half-grown quartan parasites found and on April 2nd, rosettes, parasites filling the whole corpuscle, gametes, and a flagellated body were seen. Put on digitalis mixture.

30th March. Temperature, 100·2°F. Thereafter normal.

4th April. 10 gr. doses of quinine.

11th April. Oedema had almost disappeared.

14th April. Thrombosis of vessels of right leg.

16th April. Died.

Sainton, Richet Fils, and Schulmann record another case of generalised oedema.

CASE XI.

Malarial inflammatory oedema. (Sainton, Richet fils, and Schulmann).

Man of 35 years. Entered hospital, Cannes, 12:10:16, with jaundice and anaemia. Went to Salonica, 5:1:16. Had attack of fever in July, 1916, but carried on. In September, had some sort of enteritis, and was sent to France.

Examination showed some jaundice, but stools normal in colour. No itch or bradycardia. Liver and spleen enlarged. Marked anaemia, no heart murmur. Axillary temperature fluctuated between 35·4°C and 37°C.

It looked like a simple catarrhal jaundice, and no quinine was given. On 4th Nov., he developed oedema of feet and legs, scrotum and face. Ascites present—8-10 litres. Also double pleural effusion. No albumen in urine, nor sugar, but bile pigment. Pulse became rapid, 120-140 and irregular. Palpitation. Temperature, 37°C. Tongue furred and dry. Anorexia. Four bowel movements in last 24 hours. Blood examination, 4th Nov.

Reds.	2,680,000
Whites.	2,500
Polys.	52%.
Monos.	45%.
Large Monos.	1%
Myelocytes.	2%
Nucleated reds.	1% of white cells.

Anisocytosis. Polychromatophilia. Poikilocytosis. Mainly granular reds. Schizonts, 1 to 812 reds. No gametes.

Pleural fluid—the fluid was haemorrhagic and very fibrinous. Contained monos, 90%; polys, 10%. Reds abundant. Schizonts, 1 in 542 reds. Many gametes.

Nov. 5th. Blood. Schizonts, 1 to 837 reds.

On evening of 4th Nov., 40 cgms. quinine was given. Also adrenalin and oil of camphor. Next day patient was much better. Polypnoea persists, but without dyspnoea. Ascites and oedema

diminished. Pulse, 94 and of good tension. Quinine continues by mouth, 2 gms. per day, with cardiac tonic. No diuretics given. In 10 or 12 days, the oedema, ascites, and pleural effusion disappeared along with the icterus. By beginning of December, he was convalescent.

In oedema cases it is probable that several factors enter into the occurrence of fluid in the tissues. In urticaria and circumscribed oedema there is a local spasm and relaxation of vessels respectively with local interference with the circulation and transudation into the surrounding tissues. Other factors such as anaemia, diminished blood coagulability, increased permeability of the vessels, adrenal, thyreoid, and parathyreoid insufficiency with defective calcium retention may enter into individual cases along with especially local paresis of vessels to determine fluid for a particular part or organ. Then again, focal massing of parasites with dilated capillaries and blocked veins is one etiological theory suggested by Sainton, Richet fils, and Schulmann, with the alternative theory of anaphylaxis, which they favour less.

Experimental evidence appears to indicate that the permeability of blood vessels to serum is affected by interference with their sympathetic nerve supply. Asher (quoted by L. R. Müller) has shown that extirpation of the upper sympathetic ganglion in the neck leads to diminished permeability of the vessels of the anterior chamber of the eye, as compared with that of the vessels of the opposite (intact) side. This observation may have an aetiological bearing upon the urticarias, oedemas, and allied conditions of malarial patients.

A case of what appears to be a true circumscribed, or angio-neurotic oedema, is recorded by Moscato.

CASE XII.

Intermittent anglo-neurotic oedema of the lip (Moscato).

V. Z., aged 12, of good constitution, had always good health, was the son of healthy and vigorous patients. On 20th July, the parents noted rapid swelling of upper lip, which was occurring without any apparent cause. I saw the patient six hours after the trouble began, and was struck with the enormous size of the left half of his upper lip, which gave him a most revolting appearance. It was about 10 times the normal size, pulling and disfiguring his left cheek. It stuck well out and down over the lower one. Skin normal in colour, but mucous membrane of swollen portion paler than the rest. It was hard to touch, insensitive, and did not pit on pressure. There was no evidence of any lesion that could be connected with it. Glands in the neck normal. The boy looked quite fit apart from this.

Temperature, in axilla, 30°C: local temperature, 36·7°C. Pulse a little firm, but normal in rate. Urine turbid, reddish with brick-coloured sediment.

Diagnosis doubtful. Fresh water compresses and spoonfuls of chloride of lemons prescribed. Next morning the swelling had almost disappeared, but, recalled at mid-day, the lip was found the same as the previous day.

The swelling had again developed rapidly, preceded by coldness of the extremities. Otherwise clinical features as before. The intermittency, so like malaria, was then thought of, and although temperature was normal, a gram of quinine, in five doses, was prescribed.

The next morning, the swelling had completely disappeared. It

reappeared very slightly about noon (third day), but thereafter disappeared for good, under continuance of quinine for a time.

This is more like the true angio-spastic type.

Cabot reports a case of a different variety.

CASE XIII.

Oedema and Stupor. (Cabot).

An electrician aged 33, admitted to hospital, 10:9:07 Quite well till two weeks ago, when he began to have severe shooting pains in forehead, spreading to rest of head. His face was puffy, and red every forenoon, and his hands became swollen. Yesterday, he became very dizzy, and could hardly see to walk, but did not fall. He lost three pounds in two weeks, and is thirsty and nervous.

Patient semi-comatose, and answered no questions. He moved restlessly upon the bed with his eyes shut and his hand to his head. He was not asleep or drunk, and there was no evidence that he had been drugged.

On examination, the face was distinctly puffy: the muscles about the eyes twitched involuntarily from time to time. Fundus oculi negative. Spleen not palpable. Physical examination otherwise negative. B.P., 190 mm. Hg. Temperature, 102-6°F. White cells, 3,900. Urine negative. The blood showed no malarial organisms. Symptoms seemed to point strongly towards uraemia at the time of entrance, but urine was absolutely negative. On admission, patient was put in hot bath, but collapsed 20 minutes later, his B.P. being very low. On the 14th Sept., he had a chill. Blood showed fully grown malarial parasites. Under quinine, the patient was well within a few days. Condition considered due to malaria.

This is a type of case where it would have been of interest to have observed the cerebro-spinal fluid. It is the type in which Manson-Bahr has found increased spinal pressure.

(5). Heart, Circulation, and Kidneys.

In every malarial paroxysm we see the circulation in active response to the parasitic intruder, largely through its nerve supply—features of sympathetic irritation dominating the picture

in the cold stage,—para-sympathetic, the hot stage. The heart with its vagus and sympathetic nerve supply responds in keeping with the alternation of emphasis of irritation, vagal or sympathetic, during the paroxysm and subsequently. Thus, in the prodromal stage, that is in the few hours preceding a paroxysm, and during the early stages of sporulation, there is commonly bradycardia, some lowering of blood pressure, and slight myosis, along with the other features of vagus irritation defined by Abrami and Senevet and already referred to. During the cold stage, that is with increasing sympathetic irritation, the pulse rate increases along with the blood pressure, and begins to diminish again after onset of the sweating stage, by which time the sympathetic is showing signs of fatigue and the vagus relatively dominates the picture once more in the features of the hot stage, by the end of which the pulse has approached, if not arrived at, normal. These are neurological phenomena, and do not take into consideration any direct effect that the parasite may have upon the heart. It may very well be, however, and not rarely is, that by localised concentration of parasites in the vessels of the heart, or by the virulence of malarial poison, the heart comes in for a share of direct irritation and damage, with behaviour corresponding to its degree and distribution. Thus while bradycardia tachycardia, extra-systoles, may occur in the course of malarial infection (as recorded by Riebold and others)—as indeed they may do in the course of any infection—as the result of irritation of the cardiac autonomic nerve supply, there may be grafted on to these features others which are the result of direct cardiac irritation or tissue change, muscular or neurological.

This brings us to consider for a moment the pathological changes that have been observed in the heart due to malaria. Long before the parasite was discovered in 1880, the heart was considered to be frequently damaged as a result of malarial infection. Many French observers, mostly Army Surgeons, like Laveran, living in highly malarious tropical countries, have published groups of cases with heart disturbances, which they considered of direct malarial origin. These have been summarised up till 1890 in a paper by Rauzier, who published 17 cases of his own. Jaumes (1821), Boudin (1842), Maillot, Hamernjk, Dutrouleau (1861), Colin, Griesinger, Vallin (1874), Fabre (1877), but above all Ouvosiex (1870) and

Lancereaux (1873) have emphasised the heart changes resulting from malarial infection, acute or chronic, by correlating clinical pictures with post-mortem changes. These changes comprised flaccidity, dilatation of chambers, endocarditis, mostly mitral and aortic, with mural changes, fatty, fibrous, and pigmented. The pigmentation was considered a strong diagnostic point in favour of malaria. That Laveran did not agree did not deter Lancereaux and others from sticking to their point.

Since then, cardiac pathology in relation to malaria has been more fully worked out by many observers, notably Duigeon and Clarke, Haskell and Millar, and Tremolières and Caussade, Dumolard etc. All the usual changes characteristic of infective disease in general have been found, and in all degrees, to extreme fatty degeneration, loss of striation, and fragmentation of muscle fibres, and in some instances parasites were found even inside the sarcoplasm of the degenerate fibres (Haskell and Millar).

Tremolières and Caussade particularly emphasise the occurrence of aortic, coronary, endocardial, mural, and arterial changes in chronic and acute malarial subjects, so that in these circumstances it is not surprising to find cases in the literary records with symptoms specially referable to the heart. These observers had 42 cases with cardiac disturbances in 1000 malarial subjects. Of these, 17 were functional—others had aortic and myocardial lesions. Of the 17 functional cases, four had precordial pain, four had palpitation, three breathlessness, five permanent tachycardia aided to other symptoms, and one paroxysmal tachycardia.

Castellani records a case of heart block due to malaria in a middle-aged man. He had several attacks, slow pulse, epileptic seizures, visible auricular impulses in the veins of the neck, three to one rhythm. He denied ever having had fever. His spleen, however, was enlarged and very hard. Blood showed a few malarial parasites. A persistent quinine treatment freed him of his attacks.

Gallenga describes primary degenerative changes of cardiac nerves in a case of angina pectoris, which he considered of malarial (malignant tertian) origin.

There are probably two main groups of cases with heart symptoms having special reference to its nerve supply. (1). Those in which there are departures from the normal in its action, bradycardia,

tachycardia, arrythmia especially extra-systoles, from disturbance of distant nerve supply, vagus and sympathetic. Thus in chronic sympathetic irritation, there will be a tendency to rapidity, or easy excitability. In vagus irritation, in cerebral malarial infections, there will be some slowing of the heart and a tendency to arrythmia. (2). Those in which there is intra-cardiac neuritis as part of direct parasitic damage to heart structure, muscle and nerve.

The former is akin to what underlies pseudo-angina pectoris, as it occurs typically in neurasthenia, and in nervous woman in the climacterium, without organic heart disease. The latter is like true angina pectoris where there is serious organic tissue change in the heart (J. Mackenzie).

All sorts of evidences of clinical pathology of the malarious heart are recorded in the literature—endocardial, pericardial, heart block, mural changes, etc—but as our present theme is neurological, it will be necessary to confine our consideration to examples of heart disturbance which are more particularly of neurological origin, though some of these are associated with damage to other cardiac structures.

Cardiac pain—pain in the apical region, and precordium—has been frequently observed in malarious patients with or without heart enlargement and with or without evidences of arterial change. The writer has seen many instances, and there are many records of, rapid, poor, mobile, easily compressible and low-tensioned pulse with palpitation and throbbing in chest, head and neck, in chronic malarial subjects. These features are contributed to by anaemia, sub-adrenalism, as well as by nerve and muscle heart lesions. General arterial degenerative changes have been emphasised by Lancereaux, Tremolières and Caussade, Style, and others. And from the pathology we see the evidence of localised arteritis in acute cases, which has been traced to large peripheral vessels by Paisseau and Lemaire, Alamartine and Vandenbosche, Duigeon and Clarke, Castellani and others. It is not surprising, therefore, to find instances in the literature of cases clinically like angina pectoris. Castellani saw three severe cases cured by quinine. Lancereaux records a case of this kind in a woman of 34, formerly healthy and free of hereditary taint, and attributed her condition

to malarial neuritis of the cardiac plexus. The pain during an attack commenced in the epigastrium, ascended to the level of the 2nd intercostal space about the manubrium sterni, where it was most intense, after which it radiated towards the left shoulder and down the inner aspect of the left arm, terminating in the two last fingers of the left hand, and was accompanied by numbness and tingling. It extended upwards to the outer aspect of the neck, and faded about the articulation of the left jaw, or even a little higher. It was intense, and paroxysmal, and lasted from 10 minutes to three-quarters of an hour, and was accompanied by sweating of the face, eructations, and a desire to micturate. The face, at first pale, later became flushed. Spleen enlarged and palpable. In general the patient looked healthy—not anaemic—but the heart was enlarged to the left, and there was a double aortic murmur (systolic and diastolic) which he considered as due to aortitis involving the first part of the aorta and of malarial origin. Pulse 84. She had contracted malaria at the age of 8 years, at the age of 25 began to feel oppressed in the chest at times, and at 32 began to have attacks of angina of which she complained when Lancereaux saw her. He could find nothing to explain her condition but malaria.

The course of the pain detailed in this case is of special interest. It begins in the epigastrium, ascends to the manubrium sterni, and radiates to the left shoulder, down inner side of arm to ring and little fingers, and up the outer side of neck. This is a course of direct neurological continuity, beginning with the abdominal sympathetic, and ending with the ulnar nerve in the left arm, and sympathetic in the neck, which will be referred to later in relation to the next case recorded by Soinet.

This case of Soinet's is published as a case of hysteria, as the patient ended up with hemi-anaesthesia, which Soinet evidently considered as one of the evidences of hysteria. But apart from this, the case is of interest in that the man had recurrent attacks of angina during the malarial paroxysms, with pain that follows the usual course in angina pectoris.

CASE XIV.

Case of malarial angina pectoris. (Soinet).

F.F., sailor, aged 27, admitted to hospital Marseilles 10:3:1901, after a two months voyage from Philadelphia.

Family History: No trace of any nervousness in the family. Father died 1885 of typhoid. Mother alive and well, and without any nervous manifestations. Brother alive and well, and has a twin-sister, who has heart disease, without nervous phenomena. Married, and has two boys, one of whom, aged 12, was a "blue baby", the other, poorly. Wife, aged 37, nervous and emotional.

Personal History: Measles in childhood. Typhoid between 8 and 9 years. He was found quite healthy at the age of conscription, and has been at sea for 3½ years. He has always been very active, and has visited about all the countries of the world as a sailor. He denies any alcoholic habit—which, indeed, would be hardly compatible with his long sea-voyages. For the most part, he totally abstains, especially since he got married. No excess tobacco, and no syphilis.

Mentally, he shows no sign of nervousness, or of anything to suggest latent hysteria. There are no physical stigmata of degeneration.

He took malaria in 1888 at Panama. He had some fever each day for six months, without quinine having much apparent effect. What relief he got, he attributes to infusion of nettles taken in coffee. After 11 years, the malaria returned in 1899, during a voyage to the Niger, and for three months afterwards, he had daily febrile attacks lasting from 8-15 days. Apyrexial intervals lasted three weeks or a month. Since then, there have been recurrences every two to three months.

There is no history of any nervous manifestation until Aug. 1900, when, during a malarial attack, while in the port of Stettin he had violent cramps in the pit of the stomach with palpitation and a feeling of oppression, and a ball in his throat, followed by delirium in which he left his bed at the height of his fever and fled to the bridge of the ship. He was taken to hospital in Stettin, and treated with cold packs and morphia. With subsequent malarial attacks, he had less severe nervous manifestations, and finally resumed his work at sea.

On 24th January, 1901, he was exposed to extreme cold, and next day had an attack of malaria, in which he had an attack similar

to the first, with loss of consciousness. There was severe precordial pain and pressure. During the rest of the voyage, he had 10 attacks of fever, with marked exacerbation of the precordial pain each time, which was like angina pectoris. He complained of a strong sensation of suffocation and violent praecordial pain which extended down the length of the left arm, especially in the ulnar region, and at one of these times he again lost consciousness.

On admission to hospital at Marseilles on 10th March, the vomiting and anorexia which had accompanied his attacks had disappeared. There was a complete hemi-anaesthesia of the left side. Pain sensation completely abolished, while sense of touch is duller than that on the right side. The anaesthesia is more marked in the lower limb. Pharyngeal reflex abolished. Visual field only slightly diminished.

He complains always of the praecordial anguish, and a painful sensation of heaviness with twitching of the left shoulder. At intervals, and especially towards evening, violent palpitation with feeling of suffocation and painful radiations down the left arm. These attacks last an hour sometimes. The heart is normal in size. At level of manubrium sterni, a slight V.S. murmur is heard, but it is not propagated down the sternum or to the vessels of the neck. It varies from day to day, and disappeared before the patient left hospital. The signs were therefore characteristic of a haemic murmur, and not due to an aortic lesion.

Since admission to hospital, there has been no fever nor hysterical attack. The sole relic of his malaria is an occasional trace of his pseudo angina pectoris. He was treated with hydro-therapy, and chloral and bromide, and improved so much that on 22nd March, he asked to continue his convalescence with his family at Charente.

The points of interest in this case, and in that of Lancereaux, is the nature—intense, paroxysmal—of the pain and its course. In each case, it begins in the epigastrium, ascends to the base of the heart, radiates to the shoulder, and down the ulnar distribution. Now Ivy Mackenzie has indicated the structural continuity of the sympathetic nerve supply to the heart and the lower dorsal roots of

the ulnar nerve in the first thoracic segment of the cervical enlargement of the Spinal Cord, and has made clear the mechanism by which organic heart disease on the one hand and functional nervous instability with disordered action of the heart, on the other hand, may have the common symptomatology of anginal pain radiating down the inner side of the left arm. It would appear, then, that the symptomatology of these two cases is to be explained by intra-cardiac irritations of the cardiac plexus or its branches, either directly, or secondary to solar plexus irritation, since pain began there, from concentration there of parasites during the paroxysm of malaria, with subsequent radiation via the 1st thoracic segment down the ulnar nerve, and in Lancereaux's case, it is also continued up the sympathetic distribution in the neck, with subsequent sweating and flushing.

The next case—one of cardiac dyspnoea—recurring with tertian periodicity is somewhat similar. He refers to it as one of probable pericarditis, but does not indicate any evidence of pericardial friction. In any case, the recurrent painful and dyspnoeic attacks are of anginal character, suggesting that the autonomic nerve supply to the heart has come in for a share of irritation, accentuated during the malarial paroxysms, when there is probably a concentration of parasites in the cardiac capillaries.

CASE XV.

Cardiac dyspnoea, with symptoms of tertian periodicity.

(Billet).

Soldier, D., robust. Previous health good. Admitted to hospital at Constantine, Algeria, for the first time, 1:9:00, from a very malarious part of the country (Bario). Complaint of shivering attack (31:8:00) the day before at 2 p.m. along with severe pain under left nipple and marked dyspnoea. Heart irregular and rapid, nausea, vomiting followed by an attack of syncope which lasted quite a while. At 4 p.m., temperature, 40·4°C, which subsided with sweating during the night. Following morning, temperature normal.

1:9:00. Admission to hospital—remission of symptoms. Morning temperature, 38·1°C, evening, 38·4°C.

2:9:00. Recurrence of dyspnoea, same as on 31st Aug., and about the same time, 2.30 p.m. He is in bed, and looks very anxious. Dyspnoea extreme, with cardiac arrythmia. Sounds soft and distant, and praecordial pain severe, with feeling of constriction in the chest. Respirations rapid, face pinched, cheeks livid, extremities cold. Slight cough, with coloured expectoration. Auscultation and percussion of chest showed nothing abnormal. Temperature, 2 p.m., 40·8°C.

In view of a probable pericarditis, with pulmonary congestion, wet cupping was done over the left lower thorax. Caffeine and anti-spasmodics; ice to suck. This second attack of dyspnoea, with tachycardia, lasted all evening, and eased off in the night, during sweating stage.

3:9:00. Apyrexia. Temperature, 37·2°C at 6 a.m., but again between 2 and 3 p.m. recurrence of dyspnoea, with tachycardia. Dry cupping—antispasmodics.

4:9:00. Temperature, 39·8°C, morning, 39°C evening. Dyspnoea, but less praecordial pain. Auscultation and percussion negative.

5:9:00. Temperature, 38·2°C morning, 38·4°C evening. Patient easier—less dyspnoea.

6:9:00. Apyrexia. Weak, but no pain. Slight headache, with anorexia. Milk diet. Apyrexia continues till 11th Sept. inclusive. Appetite improves. Still weak, and remains in bed.

12:9:00. 2-3 p.m. Recurrence of dyspnoea, and tachycardia, praecordial agony, nausea, vomiting, syncope. Shivering, temperature 39·6°C at 3 p.m. Symptoms abate during the night, and recur on

13:9:00, at 3 p.m., with more violence than ever, and temperature, 40°C.

14:9:00. Slight remission; temperature, 37·6°C morning, with recrudescence in evening to 38·2°C, after 1 gm. quin. sulph. and antipyrine.

15-19:9:00. Period of apyrexia.

20:9:00. 2-3 p.m. Attack similar to above. Pain extends this time to region of spleen, which is tender and enlarged. Temperature, 4 p.m., 40·1°C, followed by sweating during the night.

Blood swarming with non-pigmented ring forms of M.T. parasite, 5 or 6 in a field. Marked mononucleosis.

10 a.m. Quinine injections given—1 gm. neutral quin. chlorhyirate subcutaneously.

21:9:00. Apyrexia: morning, 37·4°C., evening, 38°C. Symptoms subside—still nocturnal sweating. Second injection of 1 gm. quin. given in evening.

22:9:00. Apyrexia. Injection repeated.

A few shrunken parasites seen in blood. Mononucleosis.

23:9:00. Attack of dyspnoea and tachycardia have disappeared and the patient revives rapidly.

24:9:00. No parasites seen in blood.

4:10:00. Patient left hospital on two months furlough, feeling very well.

A. Hoffman (Düsseldorf) who studied the features of circulatory weakness and failure in malarial subjects found evidences of blood-vessel paresis or paralysis—such as weakened heart, small monocrotic pulse, pale skin, cyanosis, cold sweat, pulmonary oedema, delirium, stupor, unconsciousness.

The drugs found useful as restoratives in his cases were caffeine, which narrows blood-vessels, especially in the splanchnic area, camphor in 20% solution in oil, digitalis, strophanthin, alcohol, ether, adrenalin, pituitary and barium chloride which contracts blood vessels, but has unpleasant effects on stomach and bowel.

Seyfarth, who studied the causes of death in severe malarial infections, found heart affection the cause in 14%, the form clinically being of the algid type. Post-mortem, there was found coronary blockage with parasites and pigment; myocarditis, heart muscle necrosis, and fatty degeneration, especially involving auriculo-ventricular tissue. Septicaemia accounted for death in 30%—which included cases of heart weakness and failure, with other complications, such as pneumonia, coma and kidney trouble, etc. Cerebral cases numbered 55% with massing of parasites in brain capillaries, and often few in the peripheral blood. Brain showed punctiform haemorrhages, granulomata, pigment, and parasitic emboli. Renal cases numbered 1%, and showed tubular-glomerular nephritis. Suprarenal, pancreas, and spleen rupture cases occurred rarely.

KIDNEYS: Renal colic, pains or heaviness in the loins, sometimes occurs from massing of parasites in the kidney capillaries, or from toxic irritation of malarial origin. Usually where massing of parasites is the immediate cause of disturbance, timely treatment with quinine removes the pain. All grades of further kidney damage have been found in acute and chronic forms of malaria, and are more fully considered in the section on uraemia in the Chapter on Coma.

All grades of degenerative change have been noted by different observers. Ewing defines three main types of acute renal lesions as occurring in malaria.

1. Acute degeneration of toxic origin, often reaching a degree in which exudation of blood serum into the tubules is added, is responsible for the vast majority of cases of albuminuria in malaria.

2. An extreme form of acute degeneration with focal necrosis which is seen in cases of haemoglobinuric malarial fever.

3. Massing of parasites in the renal capillaries, with extreme degeneration of parenchymatous cells, haemorrhages, and exudation into the tubules. This is seen only in severe aestivo-autumnal infections.

(Note: The evidences go to show that all three species of parasites are capable of producing nephritis. W.K.A.)

Nazari records 10 cases of chronic nephritis of malarial origin: others are recorded by Ewing, Rospicci, Marchiafava and Bignami. Sometimes the degenerative changes are confined to the kidneys; in other cases these changes are part of a generalised arterio-sclerosis with emphasis of change in the kidney vessels. Tremolières and Caussade, who examined 1000 cases, state that malaria has a predilection for the arteries and quote, in their experience, the frequent occurrence of renal sclerosis, generalised arterio-sclerosis and Raynaud's disease, in chronic malarial subjects. This agrees with malarial pathology and the proven leniency of the parasite to produce endarteritis. A.H. Style also notes the frequency of atheroma in malarial subjects.

Most of the cases of nephritis recorded have been due to the malignant tertian parasite, some to the benign tertian parasite. Malcolm Watson records two cases in quartan infections in Selangor, one in a girl of 16 (fatal); one in a man of 27, who recovered.

The first case is as follows:

CASE XVI.

Quartan malaria, with parenchymatous nephritis. (E. Watson).

Tamil, aged 16. Admitted to hospital, 28:5:03, with a history of having had many attacks of fever in the previous two years, 2 or 3 attacks each month. Four months before admission, feet began to swell, followed by anasarca, for which she sought advice. Has not been able to work for a month, and not able to walk for 10 days. She thought she was fevered at times, and sat then in the sun for heat. For 8 days, had had diarrhoea.

On admission,—water-logged. Greatly swollen, and gasping for breath. Oedema, 1in. deep, at level of 3rd rib. Over lower abdomen and legs, skin covered by drops of serum, which exuded through. No even a stomach note could be detected in the abdomen. Right lung dull to percussion up to angle of scapula, and in both were numerous hoarse crackling râles. Cardiac sounds well-heard, no murmur. Pulmonic second sound accentuated, and frequent reduplication at base. Tongue clean, pulse 98, tension fair, and regular. Respirations, 40; with wheeze and cough. Voice hoarse, from oedema of glottis. Urine dark and smoky; acid, 1,016, albumen, quarter on boiling; no sugar; marked guaiac reaction; no bile pigment reaction; dense deposit of leucocytes, a few erythrocytes, granular and epithelial and blood casts; vesical cells and brown debris. Trace of methaemoglobin. From 8 p.m. to 8 a.m. on night of 28th only 8 ozs. urine passed. Temperature, 101°F, on day of admission—thereafter normal. Quinine begun on 29th.

On day of admission, many quartan parasites were found in the blood, and even up to 2nd July, a parasite was seen. On the 3rd, patient seemed a little better, and had passed more urine. Diarrhoea, however, persisted, and on the 5th she died.

Post-mortem examination showed chronic parenchymatous nephritis.

(9). Raynaud's phenomenon and symmetrical gangrene.

The association of Raynaud's phenomenon and gangrene, generally symmetrical, with malaria, has been sufficiently frequent

to iraw the attention of many observers. Some of Raynaui's own cases showei malaria in their history, though apparently Raynaui himself iii not comment on any special relationship.

Laveran notes the frequency of the Raynaui syniroae, with or without gangrene in malarial patients, ani many others, such as Duroziez, Mourson, Calmette, Viens, habe ione the same. Petit ani Verneuil have notei 67 cases, ani Soy, (quoteiby them), in 1881 states that the frequent association of local asphyxia ani gangrene with malaria was aimitteiby the pathologists of that iay.

Monier-Vinari, in the stuiy of 84 malaria cases, notes the frequency of achro-cyanosis, of rose to livii colour, preponierating in parts of the boiy where there was motor iisturbance, ani accompaniei by some elastic oeiema, local coliness, —subjective ani objective—ani viscous sweating.

Paisseau ani Lemaire say it is not rare to meet malarial subjects with erythromelalgia, acrocyanosis, ani gangrene of the extremities. These able observers incidentally raise the question if arterial lesions ao not play a more important part in the pathogeny of vaso-motor ani nervous conditions, perhaps consiiereiasclassic, than is fully recognizei.

Schwyzer records several cases of intermittent angio-spasm, some with tertian periiiicity (Cf. Chap. 28)—on the basis of chronic malaria.

Ramoni ani Carrie note cases with vaso-motor iisturbances, local skin asphyxia, principally in the fingers, with horripilation, liviiity, pallor, coliness, numbness, ani tingling.

Other less easily recognizei forms of Raynaui's phenomenon have been recoriei—such as intermittent amaurosis, iue to spasm of the retinal vessels (Ziemann). Guyot consiiers that many instances of abiominal pain ani conditions simulating acute peritonitis are really iue to spasm of abiominal vessels with symptoms referable to a particular focus.

In aiiition to acrocyanosis, numerous cases of angioneurotic oeiema, erythema nouosum-like, scarletiniform, ani morbiliform eruptions occur. Some purpuriform types or petechial eruptions also occur, ani one such recoriei by Brauer ani Fränkel is of special interest:—

A worker of 17 years in a Warsaw village arriveiin Hamburg,

and was admitted to hospital with fever and a petechial rash, symmetrically arranged on the outer sides of arms, gluteal regions, and to a less extent on forearms. He had rigors, and benign tertian parasites in the blood. The Hb was 80%; white cells, 6,000; reds, 5,040,000. Widal, paratyphoid A and B, blood cultures and Wassermann all negative. Urine had no albumen or sugar. Two excised petechiae showed extravasation of blood, with cellular exudate, and thrombi becoming organized within the vessels, and (1) blocked large and small arterial branches with leucocytes, hyaline (more or less) and altered cells, and chromatin fragments. (2) Infiltration of vessel walls and peri-vascular tissues with leucocytes. (3) Diapedesis bleeding. (4). Marked changes in the arterial wall. (5) Plasmodia in the thrombi. No quinine had been taken, as there was no history of previous malaria. Authors considered the skin condition due to the malaria.

Both Raynaud's phenomenon and gangrene as found in malarial subjects generally have a symmetrical distribution, but irregular distribution has been observed. The extremities are most commonly involved, but cases affecting the nose, ears, trunk, penis and labia have been recorded.

It is, of course, common to find malaria patients complaining of their hands and feet being "blue with cold", but the literature seems to suggest that the Raynaud syndrome occurs more frequently in robust types who have been careless in the use o f quinine or otherwise, and in obstinate cases; while gangrene seems to be found in less robust types, or fulminating forms of infection, in severe chronic cases, and in cachexia.

Raynaud's phenomenon is considered to be a vagotonic one, occurring in the same group of patients as urticaria, and associated with eosinophilia, local or general. It may be associated with disturbed adrenal secretion, but further observations on blood pressure and other evidences of adrenal change are indicated in this class of case.

The following case of Leger is representative:

CASE XVII. *(Leger).*

Raynaud's phenomenon of malarial origin with local eosinophilia.

X., aged 30, had been three times in Senegal, and had had numerous attacks of malaria. No evidence of syphilis, alcoholism, filaria, tuberculosis, leprosy, diabetes, Bright's disease, nor of

asyshiuz to proiuce local asphyxia. He was 38 months in the colony on this occasion, ani was having malarial attacks every 12 or 14 iays for the past three months, with constant feeling of fatigue.

Looked robust ani vigorous, but skin ani labial ani conjunctival membranes slightly iiscoloured. Liver slightly enlargei. Spleen enlargei to costal margin, ani slightly tenier to palpation ani percussion. Nothing special in other organs. Blooi examinei iuring attack showei many annular schizonts of plasmoiium praecox, ani a few gametc crescents. No micro-filaires. Leucocytes (500 counteii) as follows: Plymorphoneutrophils: 65·61%; Lymphocytes, 21·66%; large mononuclears, 10·38%; eosinophils, 2·34%; mast cells, 0·0%.

He iii not attenu enough to himself, took quinine very irregularly, ani about two hours after one febrile attack hai a sensation of "ieai fingers" in the right hani, like, as he saii, one may feel on an extremely coli iay in winter. This feeling lasted about an hour, ani then iisappearei of itself. Next iay it recurrei twice, ani again the following iays, increasing in intensity. Called to see him on the thiri iay of his complaint, I founi that the same phenomenon couli be proiucei by inserting his hani in fresh water. The fingers became blooiless, iull white compared with the other hani, sensation iullei, ani local temperature iown to 26°. Patient complaineu of stiffness ani tingling in the affecteu fingers ani hani: this lasteu about three-quarters of an hour.

White cell counts were maie from the blooi, taken from (A), the right ear, (B), an infecteu ani asphyxiateu finger.

	A.	B.
Polymorphonuclear-neutrophils.	68·38.	80·08.
Lymphocytes.	22·59.	18·15.
Large mononuclears.	7·21.	5·10.
Eosinophils.	1·82%.	15·54.
Mast cells.	—	0·13%.

Some crescents were founi in each sample of blooi, but no microfilaires.

Urine examineu several times in the course of the illness showei no albumen or sugar. The stool was examineu several times for parasites eggs, but none were founu. He hai never passei a tape-worm

Daily intramuscular injections of 0,50 G Quinine chlorhydrate were given for 20 days. From the sixth day of the treatment, the Raynaud phenomenon diminished in intensity, and by the fifteenth day had disappeared. The local eosinophilia subsided parallel with the clinical appearances. Leucocyte counts were done daily for the twenty days, a sample of blood being taken from a finger of the affected hand, and a sample from another part of the body for comparison. Blood from affected finger was taken irrespective of whether an asphyxia attack was on or not; it appeared to make no difference.

	Percentage of eosinophils.	
	Blood taken from an affected finger.	Blood taken from another part of body.
1st. Day.	16·54	1·82.
3rd. Day.	15·28.	2·66.
5th. Day.	15·67.	1·47.
6th. Day.	9·12.	1·19.
8th. Day.	7·85.	0·98.
11th. Day.	5·07.	3·16.
12th. Day.	4·33.	1·45.
14th. Day.	1·68.	1·91.
17th. Day.	2·16.	1·57.
20th. Day.	1·81.	1·92.

By the sixth day there was a marked improvement in the hand, and a notable drop in the percentage of eosinophils. Disappearance of the malady and return to normal of the eosinophils were synchronous, and followed quinine treatment.

Bact. Lab., Bamako,
High-Senegal, Niger.

There are many recorded instances of gangrene occurring as a complication of malaria. Occasionally it is preceded by the Raynaud phenomenon increasing to the gangrenous stage. At other times there is persistent acrocyanosis going on to gangrene. It may be moist or dry. It is generally symmetrical, involves the toes and feet most commonly, but almost any part of the skin of the body may be involved. Two or three cases are recorded in which glycosuria and gangrene have

occurred in the course of active malarial infection. One of these, reported by Osler, is quoted above under glycosuria.

A good example of multiple gangrene recorded by Osler illustrates this type of case. In the original excellent photographs of the affected limbs appear.

CASE XVIII.

Case of Multiple Gangrene (Osler).

Man of 23 came to hospital 29-11-1899, complaining of sores about his body. His mother died of consumption. No history of skin trouble before.

As a child he had measles, mumps, and whooping cough. Had malaria at six years old. Five years before had very severe typhoid fever, after which he had an abscess in the abdominal wall which left large scar. Many boils at that time. A year before admission went south with army and in Aug. 1898, had a second attack of typhoid and was ill for two months. No syphilis. Smoked freely. Whisky and beer in moderation. In Oct. 1899, he was in bed two weeks with pains in the back and general weakness. No fever, chills or herpes.—called influenza. Up for a few days when noticed blebs on both hands which were slightly swollen. Then mottled area appeared on left instep, dorsum of right foot. Blebs broke and discharged dark fluid. No itching, but pain at night. 10 days ago had chilly feeling. Urine clear.

On admission—patient large framed, well-nourished. Complexion sallow. Skin of whole body pigmented, especially about nipple and umbilicus, genitals—not increased in axillae. Lips and mucous membranes normal. Over dorsum of left hand four healed scars; over ring, middle and little fingers brownish yellow discoloration of skin gradually peeling off where blebs are healing. Palmar surface shows large blebs. Skin and subcutaneous tissue over ring finger gangrenous.
Right Hand—Palmar surface of all four fingers show gangrenous skin with vesiculation.
Right Foot—Gangrenous and very black area on dorsum. Over heel is brown, discoloured and thickened skin which is tender.
Left Foot—Gangrenous and black area below external malleolus.
Left Buttock—Over spine at junction of dorsal and lumbar regions is

patch of gangrenous skin about 1½ × 2cms. Over left gluteal region a dry gangrenous tenier patch 4½ × 2 cms.
Occiput—Over lower occiput two areas oozing and with gangrenous appearance.

Though history did not suggest malaria the spleen was found enlarged and a very large number of malignant tertian parasites were found in the blood, especially crescent forms. Blood cultures proved negative. No leucocytosis, and differential count practically normal. Eosinophils 2%.

Quinine was given in full doses and he improved rapidly. The larger sloughs were treated with linseed poultices made with bichloride solution. Urine negative throughout. On Dec. 14th, patches on both hands had healed.

Falconer and Anderson record three cases of gangrene of the feet that recovered.

Paisseau and Lemaire record two fatal cases with full autopsy reports. One of them is given here is somewhat abbreviated translation. The post-mortem observations as a whole are well worthy of study. There is an emphasis of damage upon abdominal organs—a very general finding throughout the literature of post mortem reports on malarial patients. The adrenals especially among the abdominal organs show very marked destructive lesions. Mesenteric ganglia are noted as enlarged and congested, but no report of microscopic appearances is given, which is a most regrettable omission. Lastly there are evidences of recent endarteritis of the posterior tibial artery, endophlebitis of popliteal and posterior tibial veins, as well as endarteritis and thrombosis of the vasa vasorum. Alamartine and Vandenbosch have also recorded evidence of endarteritis of large vessels due to malaria.

An abridged translation of the authors' comments on their own cases is appended:

Two cases of gangrene of extremities of malarial origin (Paisseau and Lemaire).

1st. Case. Gangrene (Serb soldier, 36) both feet and lower two-third legs—died.

CASE XIX. 2nd. Case C., a Mulatto about 30, admitted to hosp. 4-10-16. Impossible to get a history, but it is probable he had had

malaria for some time.

On admission, prostrated with periods of excitement and delirium at night. Some vomiting without special characters—no diarrhoea. He complained constantly and looked very ill. Marked asthenia; pulse small, compressible, marked hypotension. He had been fevered for two days before admission, but now had a temperature varying between 37° and 37·8°.

Nothing notable in internal organs, except spleen markedly enlarged. Evidence of beginning symmetrical gangrene of toes of both feet. They are black above and below, and are very cold to touch. Skin sloughing and tender. Schizonts of P. falciparum, found in the blood.

Blood, red cells, 4,600,000. Whites 7,300. Cell resistance, H1,3; H2,1·5. Haemoglobin 95%.

White count:	Polymorphonuclear neutrophils.	47%.
	Eosinophils.	1%.
	Transitionals.	9%.
	Large mononuclears.	7·5%.
	Mast cells.	0·5%.
	Mononuclears-medium clear.	2·5%.
	" lymphocytes.	215%.
	" large lymphocytes	2·5%.
	Myeloid myelocytes orthobasophils.	3%.
	Myeloid myelocytes.	2·5%.

For some days in state quo.

8-10-16, considerable bleeding of gums, and urine moderately red with blood. Epithelial casts, but no blood cells. Haemoglobinuria.

Leucocytes:	Polymorphonuclear neutrophils.	64%.
	Eosinophils.	0·5%.
	Transitional.	10%.
	Large mononuclears.	2%.
	Medium mononuclears.	11%.
	Lymphocytes. (2% large).	7%.
	Myelocyte orthobasophils.	2·5%.
	" granular.	3%.

This does not appear to be a relatively notable change on the first blood count. Numerous schizonts with some crescents present in spite daily injection of one gram quinine. Sacral erosion size of five-franc

piece.

10-10-16. Condition much worse. Delirious and graning. Erosion crusted. Haemorrhage continues, pulse feebler, temperature 36°. Marked drop in percentage of red cells, thus reds 2,500,000. Whites 9,500.

White count.		
	Polymorphonuclearneutrophils.	49%.
	Eosinophils.	0·5%.
	Transitionals.	8%.
	Large mononuclears.	6%.
	Medium mononuclears.	23%.
	Lymphocytes.	11%.
	Granular myelocytes.	2.15%.

12-10-16. Patient died in algid condition, without apparent aggravation of the gangrene.

Autopsy done an hour after death—Thoracic and abdominal organs, bone medulla, and blood vessels of both legs examined. Heart and lungs normal. Abdominal organs show marked changes. All are congested, and all the vessels of the abdominal cavity are gorged with blood. Spleen much enlarged, firm, and with several haemorrhagic infarctions. Splenic pedicular vessels congested. Liver hypertrophied etc. Subcortical haemorrhages. Stomach and bowel markedly congested. Pancreas congested and with fatty necrosis. Suprarenals, congested, reddish-grey colour. Cortex has lost its yellow colour due to the lipoids of the spongiocytes. It is almost the same colour as the medulla. Bone medulla near femur epiphysis—red islets of degeneration incomplete. Congested throughout.

HISTOLOGY—Parasites were identified in every organ. In the bone medulla small schizonts, but crescents in abundance, especially in the spleen. Spleen, bone-medulla, liver, pancreas, kidney, heart and posterior tibial vessels were examined microscopically. Spleen showed two processes—glomerular atrophy and macrophagic increase in the pulp. Many of the splenic arterioles show manifest endarteritis obliterans with haemorrhagic infarcts in process of organization. Briefly, lymphoid atrophy and macrophagic reaction of the pulp with signs of chronic inflammation added, endarteritis, plasma infiltration, slight hyperplasia of fixed cells. Endarteritis, sometimes obliterans, leading to infarction.

zone medullæ, shows signs of subacute inflammation and early reaction.

Supra-renals show profound lesion. Spongiocytes absent, degenerative change of cortical cells, intertrabecular infiltration, with endarteritis, sometimes with thrombosis of the medullary vessels and haemorrhages in the pigmentary layer. There is therefore a severe haemorrhagic necrosis of the glands.

Mesenteric ganglia enlarged and congested and red as wine (No microscopic report).

Liver, slight enlargement and graphite in colour. Capillaries packed with pigmented leucocytes. Slight congestion especially central. Bile vessels normal. Hepatic cells show granulo-fatty degeneration, with much pigment in the cells of the lower portion. Subcapsular haemorrhages numerous. Thus subcortical haemorrhagic fat necrosis of liver.

Pancreas. Lesions more marked than in liver. Entire necrosis with arterial thrombosis. Cells of the acini show erythrophil degeneration. Islands of Langerhans not congested. Perilobular tissue hyperplastic and infiltrated. Haemorrhages throughout the organ. Vessels all much congested and containing many pigmented white cells. Endarteritis with thrombosis and lobular fatty necrosis.

Kidneys much congested centrally. Afferent vessels especially congested with many pigmented leucocytes. Degeneration of cells of convoluted tubules. Marked glomerular nephritis. Pyramidal zone seems normal.

Heart. Myocardium shows no important lesion. At one part a sclerotic patch—probably scar of an infarct.

Post. Tibial Artery. Filled with non-organized blood clot. Marked Endarteritis. Middle arterial coat practically normal. Outer coat normal. It is a recent endarteritis, a patch extending for several centimetres for part of the circumference and at this level the endothelial lining is swollen and hyperplastic, narrowing the lumen. The internal elastic membrane is split up into thin layers (dédoublée et feuilletée). In the musculo-elastic region, the elastic fibres show degenerative changes. Vasa-vasorum show equally endarteritis and thrombosis. No atheroma or sclerosis present.

The popliteal and post. tibial veins show recent endophlebitis with

focal organisation.

Authors' Comments. Pernicious malaria, developing to algidity in a few days. There was emphasis of damage to the abdominal organs, all of a similar kind—endarteritis, thrombosis, haemorrhagic infarctions, focal necrosis.

This is the malarial theme—endarteritis, thrombosis, haemorrhages, necrosis, fatty necrosis.

There was nothing about these pathological findings to suggest a specific origin, and the blood Wassermann was negative. There was nothing to suggest a septicaemic origin for the lesion. Hence the conclusion—malarial endarteritis of large vessels.

These authors in their post-mortem examinations of malarial subjects have been struck with the fact that an endarteritis appears in each organ gravely involved by malaria—e.g. the spleen, adrenals, bone-medulla, so that it appears to play an important role in malarial pathology. They ask if these arterial lesions do not play a more important part than has already been admitted in vaso-motor and nervous disorders perhaps considered as classic.

Grall has emphasised arteritis obliterans of the vasa nervorum in neuritis of the peripheral nerves. Does ~~this not~~ not this apply here also?

This local endarteritis may conduce to spasm and Raynaud's phenomenon without the intermediary of nerve lesions.

Paisseau and Lemaire state that they have been struck by the frequency of endarteritis in doing post-mortem examinations on malaria patients, especially in the spleen, bone-medulla, and supra-renals. They also say it is not rare to meet erythromelalgia, acrocyanosis, and gangrene of the extremities in malarial subjects. ~~They raise the question if arterial lesions do not play a more important part in the pathogeny~~

There may, therefore, be two main factors producing the wide range of vaso-motor phenomena so often met with in malarial subjects—namely, variation in central neuromuscular control, and local arterial irritation with degenerative change.

(10). Respiratory System.

Respiratory disturbances occur in the course of malaria, but on the whole are not common. Nevertheless, Godiall found a moderate degree of bronchitis and patches of broncho-pneumonia common among malarious soldiers in Macedonia, and that quinine led to rapid cure.

Mauban was struck with the frequency of bronchitis in malarial soldiers during warm weather (August) in Macedonia—in occurred in 32 cases out of 72.

Castellani indicates that a few dry coarse râles are often heard at the commencement of an ordinary malarial attack, and emphasises an observation of his that minute crepitations, especially at the pulmonary bases, and probably of pleural origin, are very frequently to be heard and that they generally disappear when the temperature has reached its summit. He has seen acute dry bronchitis of malarial origin with little or no fever, and also cases of dry pleurisy all reacting best to quinine after other drugs had been tried. He saw two cases closely simulating lobar pneumonia with pain, cough and expectoration, and rusty spit, with subsidence of temperature on the 4th day on intramuscular quinine. (As a matter of fact, quinine will depress the temperature of a pure pneumococcal pneumonia within the usual crisis period, as it is highly lethal to the pneumococcus, so that response to quinine is not so valuable a diagnostic point in lung conditions as it may be in other localisations of the parasite. W.A.)

Pneumonia in malarious subjects has received much attention from the Italians, Marchiafava, Bignami, Guarnieri, Ascoli, Nazari—and they appear to be agreed that malarial infection *per se* is not capable of producing inflammation of the lungs, and that where pneumonia does occur, pneumococcus or other accompaniments has been found.

Duigeon and Clarke, who studied 33 cases of lung involvement (fatal) in malarious soldiers in Macedonia, give some very valuable observations which are here reproduced verbatim; (it may seem beyond the natural scope of this work to give so complete a record of the pathological findings of these observers, but as their observations are almost unique in malarial pulmonary pathology, and are to a great extent the foundation of neurological states affecting the lungs

where these are heavily involved in malarial subjects, this part of the subject could not be considered complete without the embodiement of their findings).

"It is uncommon for symptoms referable to the respiratory tract to attain any prominence in the clinical histories of pernicious malaria. In less severe clinical types of sub-tertian malaria, the occurrence of bronchitis has been noted frequently. The older writers observed that with response of the malarial infection to quinine, the respiratory symptoms have abated, a result one would expect from a study of the microscopical changes in the tissues in acute malaria. Bignami has observed rusty sputum in some cases of 'bronchitis' in pernicious malaria. While it is unquestionable that true croupous pneumonia and lobular pneumonia occur as complications or sequelae in cases who at the same time are infected with the malarial parasite, no pathological evidence has been brought forward, as yet, to show that a lesion of a lung is due to the action of malarial parasites. There are, however, frequent references in the literature to atypical consolidations of lung, and the question of a 'malarial' pneumonia continually recurs without being finally answered. What exactly the 'pneumonic subcontinuel' of the classical writers is must remain undecided. Mannaberg states there was in such cases 'a profuse secretion of mucus, serum, and even blood into the fine bronchioles, but no deposit of a fibrinous nature'. Sometimes the sputum is noted as bright red or intensely haemorrhagic. Microscopically, besides diplococci, red blood cells, both free and infected, have been found. Bignami observes that infected red cells rarely pass into the sputum, as the tendency so noticeable in the cerebral vessels is for them to adhere to the walls of the lung capillaries.

"In this connection, a case recorded by J. H. Burgess is of considerable interest.

"*CASE I.* Native soldier, when first seen, diagnosed as pneumonia, with typical symptoms of cough, pain in side, temperature 103°F. Sputum, mucoid, viscid, and uniformly blood-stained. Blood film, aestivo-autumnal parasites; differential count, polymorphonuclear, 62%, hyalines, 14·4%, small mononuclears, 22·3%. Total leucocyte count not given.

"During the course of the disease, definite physical signs of

consolidation of the left lower lobe developed. The fever showed a tertian periodicity, and a prominent feature was alleviation of the symptoms during the afebrile periods. The sputum was still rusty 8 days after the first record of its character. Three weeks later, physical signs had disappeared.

"The apparent absence of a polymorphonuclear-leucocytosis and the recurring remission of symptoms do at least suggest an infection of the lung of unusual character, and by an agent other then the pneumococcus.

"In a recent paper dealing with the clinical types of sub-tertian malaria as seen in Macedonia, Falconer and Anderson cite two cases of lobular consolidation of the lungs of atypical type. One case showed a disturbance of pulse-respiration ratio. No expectoration in either case. The temperature was characteristic of a malarial attack and not of pneumonia. Sub-tertian parasites were present in the peripheral blood. The pulse was good throughout, and at no time were the patients seriously ill. They concluded that there was no evidence of a superadded infection.

"The results of our examinations of the lungs in 33 cases throw some light on this question of atypical consolidation of the lung in malaria.

"In 5 instances, true lobar pneumonia with an exudate of normal character. 1 case of lobar pneumonia, in association with pneumonokoniosis (the man had been a stone-mason). These 6 cases can be dismissed from further consideration. The microscopical findings in the remaining 27 cases were:

Marked congestion of capillary vessels of alveoli*	20	Associated Lesions of 23 Cases.
Haemorrhages into the alveoli	12	
Haemorrhages into the alveoli and the connective tissue	3	
Haemorrhages with inflammatory foci additional	5	
Oedema, hypostatic congestion, or partial collapse	12	
Absence of either marked congestion or alveolar haemorrhages	4	

*Areas of collapse are often associated with the vascular phenomena and occur in the regions of most intense engorgement.

"No record is available as to the characters of sputum, if any, in the 23 cases which showed microscopic changes in the lungs, apart from the fact that the expectoration is stated to have been watery on a few occasions. In 4 only is mention made of symptoms or signs indicative of bronchitis or pulmonary lesions. This is to be expected, as the gravity of the cerebral symptoms or phenomena of collapse dominate the clinical picture; many were too ill to give a history, or were moribund when first seen.

"The congestion of the smallest blood-vessels of the lungs is in keeping with the familiar congestion of the other viscera. It is this engorgement that responds to quinine, just as the congestion of the spleen declines under satisfactory anti-malarial treatment, and for a similar reason.

"The occurrence of haemorrhages into the lung alveoli does not seem to have attracted much notice in the accounts of the morbid anatomy of pernicious malaria. Usually quite limited in character, most often confined to the lower lobe, or posterior portions of the lungs, they have suggested from their appearance small areas of collapse, hypostatic congestion, broncho-pneumonia, but never infarction. Only exceptionally has it seemed possible that from the extent of the haemorrhages the physical signs of consolidation could be recognized during life. We have records of two cases which were diagnosed clinically as broncho-pneumonia, although the features of the disease were somewhat masked by the severe malarial infection. The diagnosis of broncho-pneumonia was made at the post-mortem examination, but the microscopical examination of the affected tissue was not confirmatory. The microscopical findings were as follows: Haemorrhage into the lumina of the bronchi, considerable dilatation of the capillaries in the alveolar walls, diapedesis of red cells, and foci of alveoli filled with red blood cells. There was complete absence of cellular reaction, but detached mononuclear cells filled with golden brown pigment were conspicuous. Phagocytosis of red cells occurred, but was not a marked feature. Patches of oedema, and collapse, were in close proximity to the haemorrhagic areas.

"There is no doubt that the cause of pulmonary haemorrhages is to be sought in the congestion of the alveolar walls and accompanying tissue changes. We regard the congestion and haemorrhages in the pulmonary tissues as similar to the congestion and haemorrhages met

with in the brain, and to a much more intense degree in the spleen. In fact, congestion of the blood vessels and haemorrhage into the surrounding tissues is one of the most striking phenomena met with in acute pernicious malaria."

The authors record two cases in relation to pulmonary consolidation, one of which is here detailed:

CASE XX.

Malarial Pneumonia. (*Dudgeon and Clarke*).

Snr. M., aged 18. Chronic malaria with recurrences. Clinical pneumonia.

Previous History: Two years in Macedonia, and four previous attacks of malaria. Present illness commenced with headache, general pains, shivering. Temperature, 101·4 °F.

On admission to C. C. S., temperature, 105·2°F. Dull, drowsy, tongue thickly furred, rapid pulse, spleen enlarged.

The following day the patient was worse, and moist sounds were heard all over the chest, while 24 hours later, consolidation was diagnosed at the right base. Patient rapidly became worse, and died on the 11th day of his illness. Blood films were negative, at each examination. Smears of the splenic juice showed coarse pigment, but no malarial parasites. Both lungs were found to be oedematous and congested, very dark in colour, with patchy consolidation. Spleen was very much enlarged.

Microscopy of the tissues: Brain. No thrombosis, no parasites, and no haemorrhages.

Kidney. Diffuse degeneration of the tubular epithelium, more especially of the convoluted tubules.

Lungs. Considerable congestion of the alveolar walls, with haemorrhages into the lung tissue, producing a patchy consolidation. In some areas, the haemorrhages occupied a large area of lung tissue as in a true apoplexy. There were scattered areas of oedema, and very early inflammatory changes, which in the case of the left lung were insufficient to produce consolidation, while in the opposite lung, very small foci of consolidation due to active inflammation were present in direct relation to the haemorrhagic areas. Active red cell phagocytosis was present in each lung.

They continue "Further observations are necessary to determine the clinical significance of these alveolar haemorrhages in malaria. Records of the chemical and microscopical examinations of the sputum, where present, and total and differential blood counts in cases with signs of bronchitis or atypical consolidation would be of great value. Our observations show that in pernicious malaria, scattered areas of consolidation of the lung tissues occur in which the anatomical basis is diapedesis of red cells into the alveolar spaces, in extent usually of limited character, but in exceptional cases producing massive consolidation of lung tissue. The extent of the pulmonary congestion or haemorrhages is not related to a heavy injection at the time of the termination of the disease".

Porot records several cases of chronic bronchitics who developed periodic attacks of asthma coincident with febrile malarial attacks which were controlled by quinine.

Ziemann distinguishes two varieties of pneumonia associated with malaria,—one a mixed infection, where pneumococcal or other infection is added to the malarial; and the other, in which malaria runs a pneumonia-like course, with massing of parasites in the lungs, while other organisms are present assisting in the consolidation process.

Pleurisy, diaphragmatic or otherwise, is not a very common complication in malarial subjects, but it does occur, either in association with pneumonic consolidation, or otherwise.

Of the more neurological infections of the respiratory system, however, there are some evidences in the literature. F. C. Wellman in a report of his expedition to Portuguese West Africa (1907) indicates that malaria is responsible for the vast majority of cases of ill-health in the district, and indicates a prominence of nervous, angio-spastic affections of the bronchi, associated with great pain in the chest, dyspnoea, no expectoration, and differing from ordinary asthma in that they were not paroxysmal.

Ramoni and Carrie record instances of sympathetic disturbance in malarial subjects comprising symptoms referable to cardiac, vaso-motor, secretory, respiratory, and digestive systems. The respiratory disturbances comprised a sense of oppression in the chest, with deep sighing respirations.

Almeida records a case of a young girl admitted to Rio de Janeiro hospital with acute asthma. The fever was marked, and there were malarial parasites in the blood. Emetics, belladonna plaster, blisters, fumigations, and KI internally failed to relieve. Euquinine, 80 cgms. t.i.d., materially relieved the symptoms and apparently cured the patient.

Da Matta records a case of asthma in a youth of 18, who got malaria a year before (1911). Temperature, 39-9°C. Face cyanosed, and with complete asthmatic syndrome. Congestion right heart. M.T. parasites in blood. Rapid cure on quinine.

The following case showing signs of pneumogastric irritation and paresis, with respiratory phenomenon, is of interest in this connection.

CASE XXI.

Pneumogastric paresis of malarial origin. (*C. Contello*).

G. I., 41 years, peasant, living in malarial district. Previous health good. No abuse of alcohol or tobacco. For several years suffered from recurrent attacks of asthma, and in past years became ill in spring, became affected with malaria, which was treated energetically, and appeared cured, not having had any recurrent attack in the intervening period.

In July, 1910, after having worked on irrigation work, was attacked by quotidian malaria, for which he got several quinine injections. This removed fever. Advised to go on with quinine by mouth, but patient, believing himself cured, went back to work without resuming quinine. One morning on 5th Aug., he awakened feeling very ill and with flaccidity of all his members. Arising with difficulty, he dragged himself to his work, but it was too much for him, and he felt an oppression in the chest, like an attack of asthma coming on. He had to cease work, and got home with difficulty, because of extreme weakness and increasing anxiety with his breathing difficulty. In bed, he shivered intensely, and covered himself completely. He soon had to get up, however, and sit on the edge of the bed owing to increased difficulty of respiration, which according to the patient's feeling was different from the usual asthmatic attack—more severe breathlessness. A little afterwards, he had gastralgia and intense vomiting. Fever rose to 40-8°C.

Voluntarily the patient used his usual asthma remedies, but with no benefit. Respiratory and gastric disturbances remained unchanged. Towards evening, fever fell with sweating, and the above phenomena diminished in intensity towards night, but did not cease, so that the patient had a sleepless night. The following day, though apyretic, he felt ill because of dyspnoea, and gastric pain and vomiting which prevented him from eating. Being far from any habitation, he could not get a doctor, and used home remedies—cloth with wine applied to the stomach, and mustard to the chest.

On the morning of the 8th, there was a recurrence of fever with shivers and former phenomena which increased rapidly and alarmingly, when the author was called in urgently. He was found seated on the bed with window open, anxious, frightened looking, chest bare and moist. Brow pallid and perspiring. More by gestures than words, he made the doctor understand his state of breathlessness, and made him feel that death was imminent; there was dyspnoea, cough, and frothy bloody sputum.

Examination: Robust type, well-nourished, earthy colour, lips cyanosed, and sclerotics yellow. Temperature, 39·6°C, Pulse, 151, Respirations, 56. Cough and spit tinged with blood. No enlarged glands in neck or elsewhere. Pulmonary bases show râles, especially on the right side. Resonance dulled, and tympanitic on left. Slightly dull right side; apices free. No enlarged peri-bronchial glands, nor mediastinal tumour.

Heart:-praecordial dullness not increased. Apex beat not visible. Cyanosis. No oedema of lower extremities. No fremitus. Apex beat in 6th space—enlarged. Right heart enlarged, and to left, 3 cms. to left of mid-sternum. Sounds indistinct, but no murmurs. No aortitis. Jugular turgid. Radial pulse, 151, weak, slightly irregular, and occasionally imperceptible.

Stomach:- Painful, tympanitic, dilated; liver enlarged and pushed up. Spleen enlarged four-fingerbreadths below costal margin, hard and painful to touch.

General Nervous System normal.

As the case was evidently serious, the author remained for hours, and administered caffeine, quinine, and digitalis by injection. Remove venous blood. By night, calmer. Temperature, 36·8°C.

Breathlessness diminished: also vomiting and gastralgia. Respirations, 48; pulse, 138. Sparteine and strychnine and quinine injections. Digitalis continued. Also electricity to pneumogastric nerve, applying +ve pole on neck, and -ve pole to neck, praecordium, and epigastrium in succession. Almost immediately, pulse came down to 110 from 130. Next morning, after easier night, the patient was much better: almost no breathlessness, vomiting ceased, diminished dyspnoea, but slight gastric tenderness; and less blood in spit, and lung signs easier. Respiration, 40; pulse, 112; temperature, 38°C. Urine, 900 gms., in 24 hours, with traces of albumen. Blood taken day before showed plasmod. falciparum. Two more electrical applications, and medicine continued. In morning, condition entirely changes—no heart discomfort, difficult breathing and other symptoms cleared up. Respiration, 28; pulse, 100; temperature, normal.

Patient could be removed home, where treatment was continued, and he rapidly and completely recovered. The heart became normal in size gradually, and stomach discomfort disappeared.

Author's Comments. Here then, we have a case with three organs functionally altered—heart, lungs, and stomach, while each of them showed no organic alteration. This suggests a disturbance of pneumogastric control.

The features of the case are briefly these:

1st Period—Dyspnoea, cough, gastralgia, cardialgia.

2nd Period—Predominance of paresis of the same—pulmonary congestion, dilatation of stomach, tachycardia, with cardiac dilatation in acute form. The patient was seen in July with malaria, and at that time, his heart was normal, and there was nothing to suggest myocardial degeneration. In any case, his exacerbation of malaria was recent.

The conclusion is, therefore, that this is a case of pneumogastric disturbance consequent on malaria, a type of case already cited by Cardarelli, and Hubbard. In this case, there was no other agency than malaria to explain the pneumogastric paresis. There was a danger of pneumogastric paralysis, if the malarial agent had not been removed in time. The effect of the quinine injections was not immediate. The early asthmatic attacks are looked upon as indicative of a minor state of resistance of the pneumogastric—a morbid predisposition set agoing by the malarial irritant. The electricity and digitalis are considered important in the treatment.

11. *Adrenals and Malaria.*

We have seen that the features of the cold stage of the malarial paroxysm are practically identical with sympathetic-adrenal stimulation; that they closely resemble the effect of a subsutaneous injection of 15 or 20 minims of 1 in 1000 of adrenalin in a healthy adult. These features are: an increase of blood pressure, an increase of blood sugar, shivers, pallor, goose-skin, horripilation, bradycardia at first, cold clammy sweat at first, followed by sore profuse sweating. The inference is that repeated malarial attacks in rapid tertian or quartan succession puts a heavy strain upon the sympathetic-adrenal apparatus, and one would expect to find clinically all grades of their signs of exhaustion and evidence post-mortem of all gradations of their tissue change. Malarial literature supplies abundant evidence of adrenal changes in malarial subjects, but so far as I have been able to discover, the sympathetic ganglia have been overlooked. Various authors—Paisseau and Lemaire, Dudgeon and Clarke, Garin, Sarrouy, and Pouget and others, have recorded degenerative changes in the adrenals ranging from profound changes such as arterial and capillary thrombosis, haemorrhages, foci of degeneration and necrosis, cortical and medullary, to simple congestion lost of cortical lipoid, in all degrees, loss of chromaffin substance, vacuolation and the presence of malarial pigment and parasites. Monier-Vinard has drawn attention to the frequency of low blood pressure pressure in many malarial cases among the French troops, some of which are recorded jointly with Paisseau and Lemaire, so that clinical and pathological findings could be correlated.

Dudgeon and Clarke also record that in examination of the adrenals in thirty cases of pernicious malaria with blackwater fever, the most constant lesion was the reduction of the fat lipoid content in the cortical layers. In many this loss was considerable, and was frequently associated with medullary haemorrhages and other changes.

Paisseau and Lemaire classify their cases exhibiting adrenal insufficiency under several headings:

1. Coma, due to adrenal destruction and without brain lesions (cf. chapter on coma).
2. Algid, or typhoid form.
3. Choleriform.

The first group are dealt with in the chapter with that heading.

Algii forms, which comprise largely the features of anaphylaxis are characterised by asthenia, algidity, generally high fever to begin with, nervousness, agitation, delirium and vomiting often persistent during their course. After this acute phase the fever abates, the acute symptoms give place to features of impending collapse, immobility, profound asthenia, pinched face, sunken eyes, gaze fixed and immobile, voice broken or whispering. Skin may have a marbled appearance and hands and feet cyanosed and icy covered with cold sweat and respirations shallow. Pulse rate relatively little increased, but small and compressible with low arterial tension. Temperature subnormal. Sergent's white line (which, however, Wright, Sezary, Marey and Vulpian maintain is physiological). Heart sounds not murmurous, but short and sharp. Gastro-intestinal disturbance generally accompanies in the form of repeated vomiting, diarrhoea, lumbar, abdominal and epigastric pains, or painful cramps. Intelligence maintained till the last. Death may occur suddenly. These cases, even in the milder forms, often fail to respond to a hill climate. With recovery, the blood pressure and temperature rise again usually slowly to normal. During the acute phase in this type there may be an emphasis of sweating, constituting a diaphoretic form.

But even in algii types there is a wide range of variation. The patient may be delirious, violent, stuporose, by turns. Or abdominal disturbance may take the form of acute abdomen and raise the question of perforation or appendicitis requiring operation. Or blood may appear in the stools bringing the picture nearer the choleriform variety.

Laveran (quoted by Mannaberg) reports a case of algii pernicious type as follows:

B., aged 23, soldier, was brought into the hospital at Constantine, July 27, 1882, 11 p.m. He had esp been employed as a gardener, and had suffered from fever several times. He appeared at hospital on July 27 on account of a recurrence which, at the time, showed nothing at all suspicious of perniciousness. The battalion physician ordered one Gm. quinine sulphate in pills. The same evening

his condition suddenly became worse and he was brought at once to the hospital. On admission he was extremely weak, yet in possession of his senses. He sighed deeply from time to time, but when asked how he felt, complained only of weakness and prostration. The extremities were cold, the pulse quite rapid, and impalpable in the radial artery. It was 120 in the carotids. The heart beat was rapid and feeble; respirations hurried, but deep.

The rump was warm to the feel. The temperature was not taken. Pupils were dilated. Urine voided involuntarily. Subcutaneous injection of 1,50 Quinine; frictions, sinapisms, warm drinks. The algor progressed rapidly.

July 28, 3.30 a.m; the death agony. Half an hour later, the end.

The autopsy showed the signs of a severe malaria; in the blood of the organs enormous numbers of parasites were found.

A case of algid type with evidences of marked adrenal damage recorded by Paisseau and Lemaire is given in abbreviated translation, viz:

CASE XXII.

A soldier, who after two months of frequent malaise with very slight rise of temperature and progressive anaemia, was admitted to hospital in Salonica with profound anaemia and a tendency to collapse. Morning temperature 37°, evening 34·5°. He died within 24 hours of admission. He had been treated with large intravenous and intramuscular injections of quinine since admission.

Post-mortem examination was done about 8 hours after death.

SPLEEN—Enlarged, intense congestion of pulp, Malpighian corpuscles about normal, much malarial pigment, and crescents and rosettes throughout. Blood vessels of the Malpighian corpuscles do not appear to be injured.

LIVER—Slightly enlarged, a little pale and slightly pigmented. Consistence normal; no sclerosis or perihepatitis. Microscopic changes slight—capillaries contain few red cells, but many pigmented leucocytes; no parasites found. No marked cellular changes, but Kupffer cells loaded with pigment.

KIDNEYS—Practically normal, but pale from anaemia. Glomerular capillaries contain pigmented leucocytes and free pigment. Loop vessels

contain pigmented macrophages and a very few schizonts.

SUPRA-RENALS—Not enlarged—rather atrophied. Cortex atrophic, grey, contains not a trace of lipoid. Pigmented layer almost disappeared. Medulla congested. Many young schizonts. Microscopically there are extensive degenerative and haemorrhagic changes. In the capsular zone there is no cell seen with the characters of a spongiocyte. In the fascicular layer, the cells are more or less atrophied. The reticular layer is separated by haemorrhages and has lost its normal pigment. Fascicular and reticular bear the burden of damage. The medulla is congested and shows inflammatory infiltration, but does not appear to be otherwise damaged. Parasites found in vessels of cortex and fascicular layer, but not in medulla.

The emphasis of damage has therefore been in the adrenals, with low tension pulse and profound prostration agreeing clinically with the post-mortem findings.

In the choleriform type there is an emphasis upon gastro-intestinal disturbance—incontrollable vomiting, persistent and severe diarrhoea, simulating cholera. In these cases the cholera bacillus has to be specifically excluded microscopically. Fraga (Brazil) records several cases of this class for example:

V.S., aged 20, black, bachelor, porter, native of Bahia. Admitted to hosp. Nov 15, 1916. Adynamic condition, passive attitude, indifference, almost not being able to answer the questions put to him. Pronounced muscle weakness, hypothermy, weak irregular pulse, vomiting, diarrhoea, abdominal pain, and vascular hypotension (arterial tension 10 max, and 5 min. Oscillometer, Pachon).

Increasing growth of the spleen, slight enlargment of liver, reflexes normal. Examination of the other organs did not reveal any abnormal condition. Clinical evidences pointing to supra-renal insufficiency. He was put on opotherapeutical treatment, with cardiac tonics and stimulants. Slow improvement of patient: vomiting and diarrhoea diminish: muscular weakness continues. Malarial parasites found in the blood. Continued treatment ends in recovery.

In all these forms serious adrenal damage has been found post-mortem according to Paisseau and Lemaire and others. In some cases examined by them, the Addison syndrome appeared, although these two

observers are careful to point out, (as others have noted), that the adrenals may show complete destruction of tissue without any pigmentation of the skin. It is considered that irritation of the sympathetic is capable of producing skin pigmentation, with or without interference with the adrenals, and that in the Addison syndrome there is both adrenal destruction and sympathetic irritation. Conversely, fatal cases have been recorded exhibiting complete adrenal destruction, sudden coma, without any skin pigmentation (see chap. on coma).

CASE XXIII.

Case of Addison syndrome associated with malaria (Teysonnières, reported by Paisseau and Lemaire).

A soldier who had never been abroad arrived in the East 23-2-16. On the 15th June, he had fever with gastro-intestinal symptoms and primary malaria was diagnosed. The fever lasted four days and did not exceed 38·5°. During July, he had four malarial attacks which lasted only a few hours, and were seperated by six or seven days apyrexia. The worst attack was on 27th July, and was accompanied by profuse vomiting, diarrhoea, and lumbar pain. Diarrhoea persisted two or three days after the fall in temperature. By 23rd Sept. (when seen by P. and L), the patient presented a full picture of Addison's disease. His skin was pigmented throughout, especially in frontal and temporal regions, and above all was marked on the prepuce and groins, which were absolutely black. The patient stated that the pigmentation had started about a little over a month before. The buccal mucous membrane had a pigmentary rash the size of a lentil. He is anaemic, emaciated, and complains of fatigue on the least effort. He can take his food sitting up, but cannot walk round the ward. Arterial tension is very low and pulse is obliterated with very slight digital pressure. Heart and lungs show nothing abnormal. Liver not enlarged. Spleen enlarged and two fingerbreadths below costal margin. Digestive trouble has subsided and appetite has improved. To be evacuated to France soon.

The authors note that this illness supervened hard upon a primary malarial infection, and that he exhibited the full Addison syndrome though he did not at any time appear to be in immediate danger.

Shauffard, Huber and Clément record a case of the Addison

syndrome with polyneuritis and right optic atrophy, attributed to malaria.

Garin, Sarrouy and Pouget record 24 marked cases of milder subadrenalism in 590 malarias. Condition generally developed during first six months of infection—insidiously. They were characterised by progressive emaciation, asthenia, anorexia, diverse pigmentations of the skin such as bronzing of hands and face, vitiligo of face, scrotum, thorax, pigmented mucous membranes especially lips, and resistance to cures at high altitude. Tachycardia without apparent reason or on slight effort, digestive troubles, low blood pressure and anaemia. They usually did well on quinine, iron, arsenic and adrenalin.

~~The prominence then~~, The predominance, then, of the signs of adrenal insufficiency in the course of acute but more often chronic ~~malarial~~ malarial infection, and recorded mainly by French and Italian observers, has led to the frequent use upon the Continent of adrenalin, associated with quinine arsenic and iron in the treatment of these cases.

The milder forms of this class of case where the features of subadrenalism take a prominent part in the picture—namely low tension pulse, asthenia, incapacity for sustained effort, hypothermia, can only be judged from the clinical findings but there are many records of this kind, and the present writer has handled many cases of this type. There is a wide range of variability of the features in different cases to modify the picture—such as palpitation, gastro-intestinal symptoms, neuralgias, headache, ear-noises, giddiness, depression, sleeplessness, sweating, and so on, but the basal features persist through this large group of chronic malarial infections.

A case of the author's will illustrate this variety:

CASE XXIV. W.O., driver A.S.C., (miner in civil life). Health good pre-war—never had a day's illness. Father died at 54 in fever hospital, cause unknown. Mother alive and well. 5 brothers and 3 sisters alive and well. Not nervous as a boy, nor had nightmares. Enlisted Nov. 1914. France, May or June 1915. Under fire but not wounded. Salonica, June 1916, where he took malaria and was in hospital four weeks with first attack. Malignant tertian parasites in blood. Headaches, dizziness, buzzing noises in ears, sweats, teeth chattering. Sent to Malta after a month in hospital. Sent back to Salonica about the end of 1916. Malaria again after there a week—six weeks in hospital. Had about six attacks a year during 1917 and 1918.

Was demobilised in Dec., 1918. Off duty two or three days at a time. Since return home, has had shivering attacks—less often than while in Army, but for three weeks before New Year 1921 had two attacks per week, and had a day or so off work as a miner, at a time. Took quinine.

11-1-21. A sturdy looking man, but looks anaemic. Teeth and tongue good. Complaint of pains in the head and buzzing in the ears. Some depression, easily tired, and incapacity for sustained effort. Has been taken quinine at intervals for a month.

Physical Signs: Heart and Lungs negative. Spleen not palpable. Liver normal. Skin moist and says he sweats frequently at night. Pupils normal. Knee-jerks normal. No Rombergism.

13-1-21. Blood film shows increase of white cells in general, about 20,000 per c.mm., and ~~low~~ relative increase of large mononuclears. No parasites found. Iron and arsenic prescribed.

25-1-21. Says he had shivering fit, with sweating, last night and the night before. Blood films taken, but no parasites found. Antipyrin prescribed for headaches.

1-3-21. Pale, still anaemic. Apprehensive, depressed, apathetic, dull, and still unable for sustained effort. Low tension pulse.

28-3-21. Has been ill in bed most of time since last note, shivering, sweating, fevered. Quinine resumed.

14-4-21. Has improved since last note.

23-6-21. Three weeks since last attack—shivering, sweating, headache, and buzzing noises in the ears. Looks rather better. Says this is the longest interval between two attacks he has had. Iron, arsenic, and quinine continued at intervals, with antipyrin for headache when indicated.

Dec., 1921. Much improved—less anaemic-looking, and feels fit for work. Not depressed and much more hopeful. To resume work.

Algidity has been attributed by some authors to adrenal insufficiency. It is possible that this plays a part in certain cases of progressive algidity, developed slowly. But, according to Abrami and Senevet, it is certainly not the main cause. According to them, algidity in all its degrees is one of the most constant symptoms of haemoclastic shock (anaphylaxis):-cyanosis, cold sweat, very low

arterial tension, tachycardia, death by collapse. If an algid malarial attack results in adrenal insuffiency, these authors maintain that all curative treatment is illusory, in the present state of our knowledge. On the contrary, to relieve the collapse produced by the haemoclastic shock, in relieving rapidly the lowered arterial tension and making it as short as possible, there is greater hope of success. This is done by intravenous injection of 1000 G of physiological serum + 2 mgms. of adrenalin which generally dissipates in a few minutes all the signs of algidity. This procedure saved four cases in six. Two of these appeared dead for more than five minutes, and are now in perfect health. The injection was accompanied by artificial respiration.

They point out that for the reason that sporulation occurs before the attack, quinine given at the time of the attack is useless--it is too late. Given eight hours before the attack, it hinders the haemoclastic ~~cheeck~~ shock.

12. Thyreoid.

Thyroid hyperactivity and hypoactivity appear among the features of malarial infection as in other toxic diseases. Not infrequently, the signs of hyperthyroidism appear as part of a malarial neurosis, showing tachcardia, loss of weight, undue readiness of the skin to flush and sweat, restlessness, excitability, with or without exophthalmos, with or without visible enlargement of the gland. The main features of the hot stage of the malarial paroxysm are highly compatible with an overactivity of this gland. There are a few records of Grave's disease following upon malarial infection.

Gerkens records a case of Grave's disease in a Malay salesman, who had severe malaria for two years and latterly had fever only in the night. He complained of tachycardia, goitre, tremor, sweating; spleen and liver enlarged, anaemia and malarial parasites in the blood. Mononucleosis and polynuclears diminished. Quinine removed all symptoms and signs, except enlargement of the spleen, which, however, was much diminished in size.

A good example of hyperthyroidism is given in the medico-legal section (case, O.M.)

Papastrategakis records one case of exophthalmic goitre,

following infection with malaria, with a bad prognosis.

Hume observed 30 cases of hyperthyroidism among white troops in East Africa, and was himself affected in this way. Acute enlargement of the gland appeared during the malarial attack, and appeared from 12 to 30 hours after the fall of temperature. The majority had had several attacks of malaria, and none had had previous goitre, or fullness of the neck, or family history of thyroidal disease. Parasites were found in the blood in every case, generally scanty, mostly sub-tertian, some benign tertian, and some mixed infections. Gland swelling was generally symmetrical, painful and tender without redness of the skin, and after two or three days fever. Dysphagia in varying degrees was a prominent complaint. There was local pain, head throbbing, slight muscular tremor, exophthalmos in two cases, tachycardia the rule, 100-110, even to 130; heart sounds generally altered, systolic bruit, or accentuation of second sound. Spleen enlarged in 70%. Two of Hume's cases—the first apparently himself—are here recorded:

CASE XXV.

(1). Capt. J. S. H. Temperature 101·6° on admission. Second attack of malaria. Scanty sub-tertian rings. Pyrexia lasted 24 hours. Enlargement of both lobes of thyroid, especially the left, occurred 12 hours after the fall of temperature, and reached its maximum 24 hours later. Dysphagia and Dyspnoea present, neck painful and tender to touch. No tremor or exophthalmos. Pulse 110, spleen slightly enlarged. There was a definite reduction in size in 7 days, but the thyroid swelling has never entirely disappeared. It increased 3 months later, following another attack of malaria, and was invariably larger after slight attacks. In July, 1919, (One year from first appearanace), enlargement of the left lobe was still present, but without symptoms.

CASE XXVI.

Other cases had greater tachycardia, such as the following

(2). Pte. T. P. aged 33. Eleven previous attacks of malaria. Sub-tertian parasites in blood. Noticed choking, tight sensation in throat, and dyspnoea in four previous attacks. Bilateral thyroid enlargement present with marked and persistent tachycardia; pulse about 140. Spleen slightly enlarged. Thyroid decreased under quinine and arsenic treatment. Tachycardia decreased very slowly in spite of absolute rest in bed. Pulse about 110 when invalided home.

The treatment adopted in these cases was quinine bihydrochloride by mouth, and in a few cases by rectum. 5rs. v, three-hourly, omitting one dose at night, over the first four days. Then grs. xv to xx, daily, with arsenic, increasing to original dosage during relapse, or 9th, 10th, 11th days. In most cases, in from four to ten days, swelling reduced markedly, but invariably enlarged again during attacks.

There is little in the literature dealing closely with subthyreoidism as a late malarial effect. Rentoque mentions a case of myxoedema as a sequel to malarial infection. The most striking reference to this subject is made by those writers such as Burdel and de Brun, who are recording their observations on race degeneration in malarial districts. The cachectics in those areas take on a cretinoid look. Buriel is especially emphatic on this point. Hume notes this semi-cretinoid appearance of children in the infected areas of East Africa. Further observation in malarious districts should illuminate this matter.

In many fatal cases the thyreoid has been found with changes ranging from slight cloudy swelling up to necrosis with intraglandular haemorrhages. Where the adrenals and thyreoid have been examined in the same case, adrenals have generally shown much more severe changes than the thyreoid. Dudgeon reports considerable diminution of colloid content of thyreoid vesicles in a few cases, and in one instance, active multiplication of the cells lining the vesicles had occurred. The pituitary generally escapes except where there has been extensive brain involvement.

In cases of thyreoidal disturbance it is, of course, a little difficult to say how much of the thyreoid disturbance is due to hot climate and war conditions, either of which separately is capable of affecting the gland. As already noted, Crasser has shown that increase of temperature from any cause puts a strain upon it. It may very well be that what local conditions have started, malaria has completed. It is often in this harness that the parasite escapes detection, and therefore eradication, with fateful consequences.

13. Orchitis.

Other glandular swellings (endocrine) have

been frequently observed in the course of malarial infection.

Orchitis of malarial origin has been recorded by many observers —Maurel, Girert, Calmette, Charvot, Bertholon, Schmit, and more recently by Vecchia, Borne, Goodall, Castellani, Hume, Moscato, and Mannaberg.

According to Martin, who saw numerous cases in Sumatra, both testicle and epididymis are affected in marked remittent fever, generally in cachectics and relapsing cases. This occurs apart from trauma, or acute or chronic gonorrhoea. Pain is more intense than in gonorrhoeal orchitis, and swelling may be marked. It disappears quicker with treatment than gonorrhoeal orchitis, but suppuration may occur. He says that the epididymis and testicle are generally involved simultaneously and that he never saw thickening of the epididymis remain, though often hydrocoele. Many writers record the end result of atrophy of the testicle. Girert observed in Panama, among 350 malaria cases, 192 times orchitis with subsequent atrophy of one or both testicles (Mannaberg).

Fayrer frequently observed hydrocoele after malaria, in India. Borelli records testicular atrophy in malarial subjects, who had had frequent relapses over long periods of time.

Vecchia records a case of this kind.

CASE XXXII.

Malarial Orchitis. (Vecchia).

A boy of 16, a native of Trevlaser in Albania, had on Nov. 5th, 1919, a severe attack of malaria with intense rigors and grave general depression. About an hour after the onset of the attack, violent pain came on with swelling in the right testicle. With defervescence, came relief of the pain, and diminution of the swelling, to be succeeded by a fresh access of pain and swelling with the return of the fever. Endovenous injections of quinine brought about rapid decline of the fever, and pari passu relief and finally disappearance of the testicular symptoms. There was complete absence of any evidence of gonorrhoea, parotitis, syphilis, or tubercle.

Castellani records a case of priapism of malarial origin.

Parasites were got in the blood. The condition was not influenced in the least by bromides, hot baths, bellalonna, etc., but disappeared on large doses of quinine.

Ovary. Ovarian pain has been frequently recorded in malarious women, sometimes as part of an apparently "acute abdomen" and usually subsides with quinine. Castellani and others record such cases.

Dysmenorrhoea is not uncommon, with uterine haemorrhages, puerperal haemorrhages, etc. A case of dysmenorrhoea is recorded in the Case II of this chapter. (Rosenberger).

Irregularities of the bladder are also frequent enough in acute and chronic malarial infections - evidence of parasympathetic disturbance.

14. Parotitis.

Parotitis of malarial origin, or associated with malaria, has been frequently observed by Borne, Moreau, Goddall, Marinesco, Verneuil, Mannaberg, and Alamartine and Vanlenbosche and others.

Lancisi (quoted by Mannaberg) reports a malarial epidemic, tertian in type, at the beginning of the 18th Century (1709-10), in which parotitis often produced death by suffocation. Since then it has been repeatedly described as a serious complication in severe malarial epidemics.

Goodall says it was not uncommon in Macedonia during the War, and that the chief difficulty was in distinguishing it from mumps. It usually subsides, and rarely suppurates, and more rarely the whole gland sloughs.

Alamartine and Vanlenbosche saw it frequently during the War.

Moreau says it was common to find such cases with pain, swelling, or pain on mastication, with subsequent secondary infection from the mouth via Stenson's duct with streptococcus, staphylococcus. It was often associated with ulcers or suppuration of the mucosa of the mouth. There was a liability to secondary haemorrhage after incision, necessitating tying of the external carotids. Facial paralysis was a frequent complication.

15. Mammitis.

Several observers record mammitis in the course of malarial infection. Carnot and Bruyère record 5 cases in soldiers in Salonica during the War. They developed during the malarial attack, and continued their development during the apyrexial period. In one case, the mammitis occurred six months after onset of malaria. In the second and third cases, 9 months afterwards; and in the fourth case, in the third month afterwards. It developed slowly and steadily. It persisted three months in the first case without abating. There was no fever apart from malarial rigor. Colostrum was gathered, and was found to be opalescent, and contained few cytological elements with polynuclear and enlarged mononuclear cells, 50%, together with arborescent crystals.

Sarin found mammitis in 5 of 800 soldiers under treatment for malaria. It caused no trouble for several months, but assuppuration developed and there was considerable pain. In 2 of the men, the other mamma suppurated a month after the first. In one case, there was secretion of colostrum in the course of suppurating mammitis.

16. Pituitary.

A case of acromegaly, attributed to malaria, and developing during its course, is recorded by Ch. Richet fils (quoted by Carnot, who saw the case). The condition was attributed to a localisation of parasites in the hypophysis.

Duigeon records that the pituitary generally escapes in cerebral malaria, except where there has been extensive brain involvement.

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CHAPTER VII.

Malarial Psychoses.

Malarial psychosis was known to Hippocrates. Study of it seems to have begun with Sydenham. Although more modern literature is studied with innumerable examples of mental derangement in association with malaria, very few observers give anything like a comprehensive account of the malarial psychoses. This cannot be because these cases are not plentiful enough, but may be partly because on the one hand no single general practitioner sees very many of them; and on the other because there has been a tendency to group the psychoses according to their clinical types, rather than to study agencies. Another point is, that when a case of mental derangement crops up in civil practice, it is generally passed over to the care of the alienist, with the result that seldom is one observer in a position to give an account of a case from start to finish. Thus the changing of hands, together with the intermittency of the symptomatology and difficulty of finding the parasite, even when it is thought of, conduce to the obscuring of the etiological relationship of malaria to the psychoses.

We have seen from the chapter on History that the ancients noticed the relationship between abnormal mental states and fevers with tertian and quartan periodicity. Hippocrates, Galen, and many others of their times, and later, including Sydenham and Sebastian, record cases of this kind, and since the discovery of the parasite by Laveran in 1880, well authenticated cases mostly in small groups have been recorded in abundance.

The best comprehensive accounts of the malarial psychoses have been given by Porot and Sutmann (Algeria), Mesnard, (Marine Medical Officer), Pasmanik (Bulgaria), Kraepelin, Régis, Chavigny, and Forrester.

Porot and Sutmann, Mesnard, and Régis emphasize the fact that all malarial psychoses are initially confusional states, and that all other mental states are further developments at a later

stage or emphasis of certain features on the basis of confusion. The confusion according to them is composed of intellectual deterioration, psychomotor retardation, dream delirium, stupor; perception, orientation, consciousness are accentuated. Delirium is intermittent, and not well sustained or expansive, and of these poor and monotonous—which distinguishes it from alcoholic delirium, which shows much more agitation, "plus onirique", a delirium much more active, continuous, polymorphous, and hallucinated. In malarial delirium, there is more sleep than dream; in alcoholic delirium, there is more dream than sleep (Mesnard).

There is a predominance of asthenia and depression, with general mental enfeeblement, defective initiative, memory defects, a tendency to persistence of fixed ideas, generally of depressive tone. Somatic nervous disturbances often coexist—polyneuritis, altered reflexes, tremors, headache, fits, dysarthria, vertigo of various forms, often cerebellar.

Deterioration of the general physical state is common, and anaemia prominent in cases with successive malarial attacks.

These observers emphasise the fact that the onset of mental disturbance is often very sudden, and is often preceded by severe headaches, such as is common in chronic malaria. The course of the disturbance is often irregular, and of long duration. It is common to find a recurrence of mental disturbance with recurrence of the malarial attacks, with partial or complete abatement of the mental symptoms between times. They emphasise the fact that so-called cures are often coincident with phases of abatement of the more pronounced mental symptoms, in which a closer inspection reveals some general mental enfeeblement, slight changes of temper and character, constituting a slight deterioration of the personality.

Porot and Sutsenn classify the malarial psychoses as follows:

A. SIMPLE CONFUSIONAL STATES.
   1. Simple confusion with stupor. (generally transitory.)
   2. Form *delirious*, with hallucinations.
   3. Recurrent form.

B. PROLONGED PSYCHOSES.
   1. By primary confusional state becoming chronic—

merging into catatonic dementia.

2. In association with symptoms of organic disturbance.

α. Asthenia, and simple depression (poor general condition, and malaria badly treated).

β. Cerebro-spinal or peripheral neuritis (malarial general paralysis, or other neuro-muscular symptoms).

3. Persistent nightmare, and secondary systematised delirium.

4. By revealing a latent constitutional mental weakness.

α. Melancholia.

β. Mania.

γ. Dementia Praecox.

The average duration of simple confusional states may be from one to several weeks, and seldom exceeds two or three months. Those that exceed that time generally develop into another mental syndrome, and a common residue is malarial neurasthenia, which also often occurs after severe malaria inadequately treated, showing character changes, impulsiveness, ill-temper, leading to homicidal or suicidal acts, and therefore becoming of medico-legal importance. Prognosis is generally good, especially if the case is dealt with in the initial confusional stage, thus preventing development into the more chronic forms. Even then the prognosis is often good, under appropriate treatment.

Mesnard also indicates that in the malarial psychoses confusion is a constant basis and that there is a tendency to torpor, bradypsychie and disorientation, with automatic reactions. In prolonged cases, confusion may be severe and vary little in intensity. In severe cases tending to become chronic, in the measure that psychic inactivity lasts, the clinical picture changes. Certain functions revive—locomotion, relative orientation, ability to perform simple acts instinctive and familiar; but initiative is lost, conscience is enfeebled, there are errors of judgment and criticism, hypersuggestibility, and ill-temper. The condition tends towards dementia, and chances of complete recovery diminish with duration of the symptoms. When, however, recovery takes place, it is marked by

amnesia, principally for the period of the psychosis. Excitement is for the most part relatively slight in comparison with the confusion, tends to be intermittent, and only shows at the beginning by pressure of circumstances and fever. Asthenia, apathy, depression are prominent. There is not, as in many severe toxic states, true alteration of the sentiments, affections, ethical and moral functions. Lucidity, familial emotions, normal emotions tend generally to return as the confusion abates. There are frequently periods of anxiety with reactions, peevishness, ill-temper, but without true phobias or marked impulsiveness.

The course of chronic malarial psychoses is progressive and prolonged like those of general infection, accompanied by visceral troubles—headache, asthenia nervous and psychic, and prolonged neurasthenia. The psychic disturbance may be irregular, proceeding by fits and starts, and may last from one to six months, or a year. After a year, recovery is rare, but possible. When that occurs, there is progressive amelioration of the symptoms and there is a striking parallelism between the psychosis and the accompanying cachexia.

There is a mental state of malarial cachexia which is often a prelude to psychoses or dementia, comprising irritable weakness, unstable temper, intellectual incapacity, defective memory, defective attention, aboulic, and hypochondriacal ideas. These may go on to confirmed psychosis, with peripheral or central symptoms, or may end in coma. Besides the pictures of cachexia there are often signs of malarial localisation referable to different organs, visceral or glandular, gastro-intestinal, hepatic, splenic, cardio-vascular, renal, which give variations of the clinical picture while retaining psychic changes.

In the prolonged psychoses especially, Mesnard insists on the importance of associate factors, such as alcoholism, dysenteries, arterio-sclerosis, auto-intoxications, etc. But he has no doubt that malaria produces psychoses apart from these associate conditions and apart from constitutional defect.

He divides his cases of prolonged psychoses developing from initial acute confusion broadly into two:

A. SIMPLE CHRONIC PSYCHOSES—NON-DEMENTING—CURABLE.

These consist of simple mental confusion of malarial origin, and includes depressive forms--differently labelled--such as melancholia. These depressive forms are cases of mental confusion, with secondary melancholia, and exhibit immobility, lack of interest in surroundings, complete apathy, diminished consciousness, disorientation, ill-temper, loss of appetite, insomnia, etc. The confusion may last in varying degrees up to six or eight months with simple asthenia, intermittent stupor, intermittent excitement, with periods of relative lucidity. Some seem to become demented, though it is difficult to distinguish at times between chronic mental confusion and malarial dementia. Many so-called cures of such cases are really cases with residual mild mental enfeeblement, memory defects, hidden defects of intellectual capacity and changes of manner and temper more or less compatible with society.

B. THE DEMENTIAS.

Simple states of dementia can follow acute or chronic malaria, as they can any toxic disease. Malarial dementia appears to be rather more intellectual than moral, affecting more the memory, mental activity, ideation, and not so readily gravely influencing conduct.

There is no medical man long in the tropics having himself had malaria who has not noticed diminished intellectual capacity or some disturbance of psychic balance. There are all possible degrees of diminished psychic capacity as a sequel to malaria--diminished mental activity, diminished capacity for delicate social functions, comparable to precocious senility; states of diminished mentality incompatible with social life, down to complete dementia. All these varied conditions have been noted especially in repatriated colonials after grave malaria. Occasionally polymorphous excitement punctuates the downward progress of the case. He quotes a case of Laurès, a young man of 28, repatriated from Morocco in a state of post-malarial mental confusion, which was soon complicated by catatonia, grimacing, chatter, onanism, alternation of depression and psychomotor excitement, developing after six years into a state of stationary general mental enfeeblement. He also notes the existence of malarial general paralysis, and quotes Berthier, Bard, Rey, Marandon de Montyel, Lemoine, etc., in this connection. This type exhibits diminished

mental capacity, stupidity, ideas of grandeur, tremors, dysarthria, exaggerated deep reflexes, pupillary paresis, signs suggesting progressive meningo-encephalitis. In addition there are often cerebral localised lesions—cerebellar, aphasic, hemiplegic.

Pasmanik, who lived first in a malaria-free and very healthy district of Bulgaria—the Rodofer Bergen, with practically an Alpine climate, found that thousands of labourers left the district every spring, went to malarious districts, and brought back malaria with them. These cases were always uncomplicated, and in 568 of them, not one had any mental complication.

Later (1897), in a highly malarious district there was a considerable amount of mental disturbance. In 5412 malaria cases, he saw mental disturbance 106 times, i.e. about 2%. 44 were males (41·6%); 62, females (58·4%). They were all depressed types—some degree of apathy was a feature of them all. Melancholia agitata was the most common type in adults. There were chronic cases with recurrent high temperature, and accompanied by visual and auditory hallucinations. In children, stupor-coma predominated. The cachexia cases had seldom or never any rise of temperature, and tended in simple melancholia, or to go on to stupor, or dementia acuta stupida (Kraepelin).

True mania was not seen, and acute delirium was seen in only three cases. The duration of the psychoses was variable; shortest period was four days, the longest three months. The cases of shortest duration were mostly children; the longest, adults. Only one case, a woman, showed permanent dementia.

In 12%, there was a recurrence of mental symptoms during exacerbation malarial attacks, and in all these cases the psychoses conformed to its original type. These cases thus prolonged and recurrent, though mostly emerging not in a demented condition, showed some degree of mental deterioration in that they were irritable, lacking energy, untrustworthy, and less communicative than formerly. In these cases, continuing to live in a malarious district, the prognosis was doubtful. Prognosis in 4/5 of the cases was good, in 12% doubtful, and in 6% bad.

In none of these cases was Pasmanik able to find a neuropathic predisposition. He cites this as against the view of

Kraepelin, who made out 85% of his collection of cases predisposed. The people of the district from which his patients came were a simple living and healthy people apart from the malaria to which they were exposed, and there was little insanity among them that could not be traced to malaria. There was no evidence of personal or familial susceptibility--rather were the evidences the other way.

In 6 cases (4.8%) chronic alcoholism in the father was found. In all the other cases, there was a history of malaria in the parents, and in the patients themselves. Pasmanik divides his cases into three groups:-

1. Children with malarial psychoses. In most cases apathy, stupor-coma conditions, and much less oftener deliriums.

2. Psychoses, associated with chronic malaria, arising during exacerbations of the malaria--melancholia agitata.

3. Malarial cachexias--simple melancholia or states of mental stupidity.

He considers that the malaria acted in two ways--directly upon the central nervous system, and also indirectly by weakening the whole organism, through anaemia and malnutrition generally.

The treatment consisted in giving to all, tepid baths and quinine. The tepid baths were prolonged and worked very well. In the cases of melancholia agitata, small doses of quinine were used, to begin with at least. In cases of stupor-coma, simple melancholia and dementia, large doses of quinine were given. In some of the cases, it exaggerated the aural hallucinations, and made the patient worse for a time.

Kraepelin made a study of 38 cases, 72% of whom were men. The most frequent form of psychosis was melancholia with excitement and fear, i.e. agitated melancholia which occurred in half the cases. Frequently hallucinations and delusions were added. A quarter of the cases had hallucinations. Homicidal and suicidal attempts were frequent--to the extent of 83% of the cases, and Kraepelin indicates that this is characteristic of intermittent fevers. These attempts were frequently followed by complete amnesia or by a very hazy recollection such as reminds the alienist of a post-epileptic state. He records that similar mental states occur in children--excitement, melancholia with partial or complete amnesia--noted at ages ranging

from 8½ to 14 years (Bohn). A half of the cases had agitated melancholia. A quarter of the cases had maniacal exhaltatation with delirium and hallucinations at times. Less frequent was simple (quiet) melancholia, with vague feelings of fear and auditory noises. Lastly, much less frequent was a peculiar state of atrophy going on to stupor in some cases. In 20% there were terrifying dreams and ear noises at night. Only 25% appeared by history to be predisposed to mental breakdown--by alcohol, anaemia, neuropathic or hereditary history. Kraepelin emphasises disturbance of nutrition, in these cases, apparently by repeated or long-standing malaria.

He divides his cases into three groups:

1. Comatose, or soporific type, (febris perniciosa, apoplectica syncopalis), with bad prognosis.

2. Spastic--eclamptic, epileptic, tetanic and hydrophobic forms. (Spasms of different kinds prominent).

3. Cachectic--with headache, giddiness, ear noises, sleeplessness, occasionally delirium of maniacal character, with a special tendency to suicide. The prognosis in this type of case is even worse than in the first type.

A point of special interest is that a third of the Kraepelin cases had quartan fever. 74% were between the ages of 20 and 50 years of age.

He notes that the relation of mental breakdown to the last fever attacks is very different in different authors. He finds it most frequent in the convalescent period, but records that weeks, months, or a year may pass between recognised febrile attacks and the first onset of mental symptoms. In 10 cases of psychoses associated with cachexia, only 4 cleared up within a month, and the others took months and a year. 2 did not clear up. The prognosis is unfavourable in these cases.

The pathological anatomy showed hyperaemia and oedema of the central organs, heart weakness from fever, direct toxic changes in the cells, especially of vessel innervation. Pigment in brain cortex was not constant, but there were pigment emboli producing extravasation blood in the vein.

Régis, the Bordeaux alienist, insists that there are psychoses peculiar to malaria, acute or chronic--in opposition to Marandon de

Montyel and others who maintain that there is no difference between the psychoses of malaria and those of other toxic infections, such as typhoid and puerperal fever. He insists on the emphasis, in malarial mental states, of amnesia, which is not nearly so marked in alcoholism and other toxic mental states, even in advanced stages of mental dissolution. He and Chavigny uphold the constant incidence of confusion as the basal mental derangement, out of which the other psychoses spring, and emphasise the medico-legal importance of the malarial psychoses as a whole.

Forrester, who had 116 cases among soldiers, indicates that malaria was by far the biggest factor in disease among Macedonian troops (1920), and the main cause of insanity. There were both malignant and benign tertian infections. No difference was noticed between the psychoses due to malaria and those due to other acute fevers, unless in the intensity of infection as a whole, and the predeliction of the toxin for nerve tissue in particular. Coma was frequent. Acute confusion was the most common type of acute psychosis.

He divides his cases into two groups:-

1. Those associated directly with the malarial attack.
2. Those occurring as the result of repeated attacks.

1. The former class were always more acute, and approximated to a complete delirium. Other things being equal, prognosis was better in this group, which as a rule yielded easily and rapidly to appropriate treatment. There were 32 cases in this group, which occurred during the malarial attack, 9 of which were primary infections, and the others occurred during a relapse. Almost every type of psychosis was represented, but confusion was most prominent. It was present in 22 cases, i.e. 68·75%. Depression was prominent in 12 cases, or 37·5%. The confusion varied from delirium such as may occur with pyrexia from any cause, to complete dissociation of the personality. With confusional insanity, no memory of the acute illness was retained. In this acute group, heredity played a very unimportant part, as a history of insanity was traced in only two cases. Hereditary suicide was also given in 2, both of whom actually attempted their lives.

2. 87 cases occurred after repeated attacks of malaria.

Alcohol was the determining cause in 7. 9 were feeble-minded. In 70, malaria was the determining factor, and again all varieties of psychosis were met with. Confusion was again the prominent type, and almost of equal frequence was depression.

In 31 cases of confusion, there was insane heredity in 8.
" 24 " depression, " " 9.

In some the confusion cleared in a day or two, in others, more slowly. The onset of well-marked dementia praecox was made out in 8 cases.

There was always a marked anaemia and debility accompanying the psychosis, and sometimes profound cachexia. Prognosis was always good, unless other factors were present.

The types in this group were:-

Mental confusion	with definite fugue.	9.	31.
	~~with~~ simple ~~fugue~~.	22.	
Depression.			24.
Dementia praecox.			8.
Delusional insanity.			6.
Excitement with violence.			1
			70.

Among the confusional cases of this group, 9 had a bad heredity, viz. 2 were feeble-minded; 2 gave insane heredity; 1 had St. Vitus' dance in youth; 1 gave a history of similar attack previously to malarial infection. In nearly every case, there was a breach of military discipline. The author's observations on these lines are more fully detailed in the medico-legal section.

The treatment consisted in intramuscular injections of quinine -as in cachectics, quinine by the mouth is not well-tolerated. Also galyl intravenously was very useful. The author found cacodylate of soda very disappointing.

The writer had given a brief summary of the observations of those who have given the most comprehensive accounts of the malarial psychoses as existing in civil, military, and seafaring practice. It will be noticed that while Porot and Gutmann, Mesnard, Régis, Chavigny and Forrester emphasise the

confusional element in all these psychoses, Kraepelin and Passanik emphasise the element of depression. Each of these observers has contributed to the illumination of a very difficult class of case in the domain of psychiatry, which up to the present has been with astonishing oversight largely neglected.

In furtherance of that work, an analysis of 131 cases handled by the writer is given below. From the pathological details defined in an earlier chapter, it is not surprising to find cases of insanity in which malaria plays the whole, or a principal, part. These cases were all soldiers on service during the Great War, who had become infected with malaria in Salonica, Palestine, Italy, Africa, India, or Mesopotamia, and had been repatriated because of mental disturbance or because of malaria, with subsequent mental breakdown. A large proportion of them came from Salonica, where malignant tertian malaria was very severe, and was for the most part inadequately treated. Accompanying each case was a set of Army Documents giving an account of the condition by the Army Officers on the spot, so that up to arrival in the British Military Mental Hospitals, there was a fairly continuous and more or less complete record of the psychosis from the beginning. The cases here recorded were under observation by the writer for periods ranging from 6-18 months, so that their fluctuation of symptomatology was under moderately close observation, in the later stages at least, although service conditions did not conduce to the detailed scientific observations that might otherwise, with an increasing realisation of their importance, have been applied. In many instances the case was diagnosed before arrival in the Home Military Hospital, and only where subsequent observations seemed to warrant it, was that altered. In the others, no diagnosis was made, but only a record of observations en route given, which were taken into account when a final diagnosis was decided upon.

The following is a classification of the 131 cases according to their clinical types:

Melancholia.	38.
Confusional Insanity.	35.
Delusional Insanity.	21.
Clinical Dementia Praecox.	14.

(Carried forward.	108)
Mania.	6.
Stupor.	5.
Delirium.	3.
Psychasthenia.	5.
Exhaustion psychosis.	2.
Dementia.	1.
Complete amnesia.	1.
	131.

This classification is based mainly on the emphasis of symptomatology during the later stages of the cases, or upon the record of such emphasis at an earlier stage where it was sufficiently clear to be reliable.

It will be noted that states of depression and confusion make up the majority of the cases, and that indeed all the groups, melancholias apart, could be looked upon as confusional states with variations. This strengthens the view of the French observers who consider the basal malarial psychosis, confusion. And it is certain that many cases clinically melancholic in a later stage had passed through an earlier stage of confusion before depression had developed enough to dominate the picture. To a large extent, confusion and depression are the two components of the malarial psychoses, and in many instances are parallel phenomena in the one case, though in others, there is a marked dissociation in degree.

Of these 131 cases, 4 were of marked medico-legal importance in civil life after discharge from the army, and are recorded separately under that heading. Of the remaining 127 cases, 65% were 30 years old or under; 12% were 40 years old, or older; 28% had defective family histories traced; 67% had quite good personal health pre-War.

From one to twenty attacks of malaria are recorded in all of the cases. Most of them had several attacks at least, and many of them had many attacks. It was a common thing to find that long after primary infection the man continued on duty, reporting sick from time to time, until finally there was a mental breakdown, often accompanied by very marked physical deterioration, while in other cases the patients were fairly well nourished.

58% had associate conditions such as being under fire, drinking, wounds, fevers, accidents, which may have contributed in some measure to the mental breakdown although malaria appeared to be the immediate cause.

34% were admittedly addicted to the use of alcohol; 14% in moderation, 10% to excess. In none was there any history or evidence of syphilis, and in 124 of the 181 cases, the blood Wassermann reaction was negative. No case where syphilis was even probable was admitted to this series, and every care was taken to exclude it.

Of considerable interest is the study of the initial, or subsequent, abnormal conduct, that drew attention in such a way as to convince the authorities that the case was a mental one. In many confusion of speech was noted at the onset, but in some of these this was overlooked until some abnormality of conduct called for more forcible attention. In two cases, coma occurred. Two were cases of assault and 1 man, who subsequently attempted suicide, was actively homicidal—these while still in the army. Three cases of definite homicide occurring after discharge from the army came up for trial for murder and are dealt with in the medico-legal section. Eleven were threatening in their conduct and speech, and had to be taken charge of on that account. Eight wandered away in a state of confusion, and were liable to court martial for desertion.

There is reason to believe that many cases of this kind were shot for desertion before the nature of this class of case was adequately understood.

34 attempted suicide, with varying degrees of success; only 1, occurring in civil life and after discharge from the army, succeeded.

Further details on these points are to be found in the medico-legal section.

The great majority were malignant tertian infections; the remainder were benign tertian infections. I have no record of any quartan case. Some multiple and some mixed infections were noted, though service conditions did not conduce to detailed observations of this kind.

During treatment in military mental hospitals, 70% completely recovered, and 10% improved well enough to go home; 14% went to

civil asylums after about a year in military mental hospitals and of these perhaps a small proportion would finally return to civil life again. Two died with intercurrent affections, and the others were not traced. Of the 4 medico-legal cases detailed in Chapter XXI, one, a melancholic, committed suicide about 2 years after return to civil life; the other three were homicidal cases discharged from the army while still infected with malaria; they had never been in a mental hospital.

There is a tendency with many observers to attribute nervous phenomena and clinical phenomena generally in malaria patients, to heredity, or to concurrent circumstances such as fatigue, worry, exposure to sun, overwork, alcoholism, war conditions, etc. Especially is this the case in regard to mental affections. This might not matter so very much from the point of view of prognosis, as when the accompanying factor is dealt with and removed, the malaria frequently abates or disappears. For instance a change of climate from the tropics to a more stimulating malaria-free district may be all that is required to effect a cure, giving relief from sun exposure and malarial reinfections simultaneously. Or abatement of overwork, alcoholism, worry, may have the same salutary effect. In this way, the significance of malaria as a tissue poison has come to be largely overlooked, with the result that it is not either sought for as a probable cause of a given disability, or, if recognized as present, is not credited with being the sole, or main, etiological basis of the trouble. It is therefore not adequately dealt with, with disastrous results for some.

Now we have seen from the pathology that malaria is a potent tissue poison, capable of damaging any and every tissue to any degree or extent, more easily when accompanying debilitating conditions exist, less easily where the patient is robust; and it is easy to realize that according to the degree and distribution of the damage done, so will the clinical features vary. If we have destruction of a group of cortical cells as a result of localised massing of parasites in the brain capillaries supplying them, we are bound to have a corresponding failure of intelligence, or motor control. If we have interruption of association paths from defective oxidation, cloudy swelling, fatty degeneration, necrosis and breaking

up of groups of axis cylinders, following focal haemoglobin deficiency, massing of parasites, capillary embolism, and toxic blood supply with malarial periodicity and fluctuation, we expect to see a ~~picture~~ clinical picture of mental dissociation such as we have in dementia praecox. Or if we have a crop of cerebral punctiform haemorrhages during an acute exacerbation of an old malarial infection, with coma and death, there may be regrets that the parasite was not more vigorously sought after and dealt with in the more quiescent phase.

It only deals with one aspect of this [redacted] subject to say that malaria reveals or releases the latent weakness of the individual. It does so where the infection has not been strong enough to do more. In this case the individual survives with reserves cut off, foundations laid bare. But infection may be so strong, and tissue damage so extensive, that even well-balanced and strong foundations may be changed out of all recognition of the original. A sound heredity has been overtaxed--the individual has escaped with his life, but not with his (originally normal) stable personality. Because personality is referable to brain tissue in the meantime. And so you may have malarial infection so slight that no appreciable mental or physical reserves are cut off, but only temporarily embarrassed; or you may have it severe enough to remove reserves, to reveal latent weakness, mental or physical; or you may have it still more severe, destroying the individuality or somatic capacity of the patient; or it may extinguish him.

To allow the second (latent weakness) instance to dominate, the perspective of the problem has several serious consequences. It inhibits attention to the mild infection, which may thereby become acute. It may credit a given psychosis with heriditary origin and weaken efforts against the parasite to restore damage already done, with the result that, what was then within the range of resolution, becomes, with further toxic damage, permanent. And lastly, but not at all least, it leaves the individual hypersusceptible to intercurrent infections, which are then liable to misdirect treatment.

The able-bodied soldier weakened by a debilitating war environment becomes infected with malaria, and all the more readily

suffers tissue damage--maybe cerebral, with its equivalent clinical picture. But the robust civilian at his normal duties has an acute or prolonged malarial infection and arrives at the same state of incapacity. Each factor has its own influence according to its kind and degree, whether debilitating environment or virulence of infection. They may operate together or separately.

There is much in common between malaria and syphilis. There is the same tendency to long periods of latency. In one, syphilis produces General Paralysis of the Insane; in another locomotor ataxia; in another a gumma of the brain; and so on. It may even persist in the individual for the best part of a life time and give no sign. Or it may only show itself upon the provocation of some intercurrent disease, or stress of circumstances. No kind of tissue is exempt. As Osler puts it: "Know syphilis in all its manifestations and relations and all other things clinical will be added unto you". The same exactly applies to malaria--with some native and distinguishing characteristics in addition, imposing themselves upon the picture frequently enough; namely, rhythmic periodicity (tertian, quartan) of temperature, or other signs; or in any case intermittency which often gives the symptomatology, mental or otherwise, a fleeting quality which is very elusive and confusing until it is understood.

A more detailed account of the different clinical types is given in subsequent chapters.

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CHAPTER VIII.

COMA.

Coma is the commonest and gravest form of acute cerebral malaria. It may occur with the primary malarial infection or at any subsequent point in the course of infection. It may be precipitated in a malarial subject by such things as fatigue, alcoholism, exposure to the sun, injury etc—such irritants as precipitate a malarial attack in general. Two cases recorded followed an injection for salvarsan for syphilis, lighting up a latent malaria, producing cerebral punctate haemorrhages (Castellani, Marinesco and Draganesco). The onset may be sudden and sharp, even occurring as the first evidence of sickness, or it may be slow, following upon headache, fits, local or general convulsions, delirium or severe depression, or may develop from restlessness, apathy or drowsiness, deepening gradually into profound stupor with abolition of pupillary and other reflexes, though usually these are retained until near the end. Occasionally it occurs in the course of other clinical varieties, such as typhoid, pernicious, or adynamic forms. It may occur with tertian periodicity, associated with the febrile paroxysm, or it may replace that paroxysm, with normal, subnormal, or only slightly raised temperature, or the occurrence may be quite irregular. In the intervals, there may be any grade of abatement of the stupor up to almost normal mentality, though the patient often tends to be incoherent and complains of headache. After the first attack, the coma is less apt to resolve. It may last from a few hours to a few days, and may end in recovery or with fatal issue, with or without treatment. One case lasting two weeks and ending fatally is recorded by Ewing.

Clinically it is characterised by varying degrees of inaccessibility. There may be confused response to stimuli, or complete absence of response. The patient may be unable to swallow. The face may be flushed, or pale, or of a leaden colour, depending partly on associated anaemia from repeated infection.

The eyes are sometimes wide open, partly open, or shut. There is deviation of the eyeballs, generally upwards. Pupils are usually dilated, but may be contracted, equal, or unequal. They generally react to light, but sluggishly. Corneal reflex may be present or absent. The pulse is general hastened, but may be slowed—may be full and compressible, or small and hard, or thready. It is generally regular, but may be irregular. The temperature generally ranges between 100 and 104°, but maybe higher, normal, or subnormal. It is associated with no definite type of fever. It may run its course without any fever at all (Schellong).

The breathing has a wide range of variation, rapid or slow, snorting, irregular, towards the end stertorous or Cheyne-Stokes. The skin is usually warm and moist, and after a paroxysm is bathed in perspiration. In the later stages, the nose and extremities are cold. Frequently punctiform haemorrhages appear on the face, or conjunctivae, and by the ophthalmoscope they may be seen on the retina also.

The limbs are generally completely relaxed in the deeper stages. Sometimes signs of motor irritation appear—contractures of a group of muscles, twitching of extremities, trismus, spasm of glottis or calves, or deviation of eyeballs. Superficial reflexes are generally diminished, and sometimes abolished; some are preserved while others are absent. Deep reflexes are generally present, but may be diminished or absent. There may be retention of urine, or incontinence of both urine and faeces. There may be focal disturbances associated with it, such as paralysis, contracture, choreiform movements, etc.

Internal organs show some changes occasionally. There may be spleen and liver enlargement, or cardiac enlargement with fatty change, some signs of kidney irritation, perhaps slight basal congestion or may be pulmonary oedema towards the end.

Death may occur expectedly after definite evidence of cardiac insufficiency, or after pulmonary oedema or other respiratory insufficiency, or after clinical evidence of damage to any vital part, but frequently it is quite sudden and unexpected. The temperature may continue subnormal, normal, or slightly raised throughout, or towards the end there may be hyperpyrexia (108°, 109°F)

In children the condition frequently begins with gastro-intestinal disorder in which vomiting is a prominent feature, together with cramps and convulsions. Among European children in equatorial Africa, malaria is the commonest cause of unconsciousness, according to Roche.

Pathologically, coma has been found commonly associated with massing of parasites and pigment in the cerebral capillaries with thrombosis or embolism of parasite-laden red cells, desquamated endothelial cells, pigmented leucocytes, free pigment, or with punctiform haemorrhages or large cerebral or meningeal haemorrhages or with any combination of these things. Punctiform haemorrhages are generally in the white matter, but occasionally in the grey matter. Ewing considers that where the coma deepens gradually, the process is associated with the growth of small young parasites to adult stage when they are larger and more apt to block the minute capillaries. Generally the emphasis of parasite accumulation or vessel blockage, or punctiform haemorrhages, or tissue damage, has been cerebral or cerebellar, though minor and occasionally major degenerative changes have been noted in the internal organs.

Duigeon and Clarke mention a variety in which "no determining lesion has been found in the brain or any of the other viscera examined".

A group of cases has been observed in which there has been no evidence of massing of parasites, no capillary blockage, but simply well marked degenerative changes in the tissue elements of the brain and other organs, and in the blood vessel walls.

Parasites have been plentiful or scarce in capillaries and in peripheral circulation. A small proportion of these cases, however, have at post-mortem shown no trace of parasite anywhere—neither peripheral circulation, brain or spleen, though malaria pigment has been found in the spleen. These are considered as highly toxic cases, where the parasite has apparently been killed off just before death, leaving serious tissue damage.

Guarnieri and Ewing suggest portal obstruction as a probable factor in the production of coma in some cases, as the liver circulation is frequently seriously disturbed in severe malarial infections.

Malignancy of infection associated with cerebral massing of parasites has been found associated with the occurrence of enormous numbers of parasites in the circulation and by many parasites at different stages of development, according to Marchiafava and Signami. The impending danger may be sometimes foretold by examination of the peripheral blood, but not always, as the massing is often in the internal organs, constituting a masked variety of infection. According to these authors this condition is especially dangerous in old people.

A few observers consider that in a small group of cases uraemia set up by kidney damage by the malaria is the cause of coma, as blood urea has been found abnormally high, in these cases, and no other relevant accompaniment of the coma has been found.

French writers (Paisseau and Lemaire) describe another type of coma in which there is no apparent lesion of the central nervous system, but where the emphasis of damage is in the adrenals. The onset is sudden and without any warning. A man is on the march, drops down unconscious, and dies within a few hours; or a wounded soldier becomes suddenly comatose without apparent reason. Minute examination fails to discover any lesion of the central nervous system. Muscles flaxid, but no evidence of paralysis. Babinsky absent. Mentality normal. At onset of coma the temperature is above normal, but in a few hours becomes subnormal. Pulse feeble, and shows marked hypotension. It may be bounding, at the start of the coma, but the tension is always low. It becomes feebler as the temperature lowers. In the majority of cases, the white adrenal line reaction is well marked. The heart sounds may appear normal till quite near the end. The organs generally show no other abnormality than enlargement of the spleen, which generally is two or three fingerbreadths below the costal margin. This form of coma is distinguished from that due to involvement of the central nervous system or meninges by absence of conjugate deviation of the head or eyes, stiffness of the neck, Kernig, mental abnormality, and by absence of any abnormality of the cerebro-spinal fluid. Pathologically it is associated with destructive lesions of the adrenal bodies, which often have large haemorrhages in them. Other

internal organs may show some evidence of toxic damage, but the emphasis of mischief is upon the adrenals. In these cases, intravenous quinine is of course valueless.

The majority of the cases are malignant tertian infections, but a few benign tertian cases have been recorded (e.g. No. 7 of Ewing's series). Simple, multiple, and mixed infections have been observed.

The following is a tabulation of the pathological findings associated with malarial coma, and considered by various observers as explaining its several mechanisms:

(1). Massing of parasites in cerebral vessels, especially the capillaries. (Marchiafava, Bignami, Bastianelli, Cerletti, Nazari, Ewing, Dudgeon and Clarke, Dürck).

(2). Capillary embolism and thrombosis. (Marchiafava, Dudgeon and Clarke, Bignami, Ewing).

(3). Punctiform haemorrhages. (Marchiafava and Bignami, Cerletti, Nazari, Bastianelli, Dudgeon and Clarke, Gaskell and Miller and others).

(4). Large cerebral or meningeal haemorrhages. (Marchiafava and Bignami, Dudgeon and Clarke, Dumolard, Aubry and Troland, etc).

(5). Malarial septicaemia. (Gaskell and Miller).

(6). Toxic type. (Ewing, Dürck, Jancsó and Rosenberger).

(7). Adrenal type. (Paisseau and Lemaire).

(8). Uraemic type. (Benhamon, Jahier and Berthélemy, Soulay and Bélier, Chamigny, Vigouroux and Prince).

(9). Portal obstruction. (Guarnieri, Ewing).

(10). Diabetic coma (secondary to malaria). (Jakobson, Naunyn etc.).

(1). Massing of parasites and pigment in the cerebral capillaries.

(1). Massing of parasites and pigment in the cerebral malarial coma, only one of which recovered after very vigorous treatment. This type of coma has long been recognized as a frequent form of cerebral malaria and according to Ewing, the deepening stages of coma are apparently connected with the increase in size of the parasites and the gradual filling of the vessels with thrombi of infected red cells, pigmented leucocytes and swollen endothelial cells. He says that "clinically, the coma resulting from this pathological condition

is rather slowly established in the course of active infections, when many young parasites are found in the finger blood and when the temperature is elevated. The patient is usually first delirious, then mildly comatose, then deeply comatose, finally stuporous, with abolition of pupillary and other reflexes, and almost always dies within 48 hours after the beginning of marked cerebral symptoms".

The following cases of Ewing's indicates the observations upon which these conclusions are founded:-

Case of aestivo-autumnal malaria, delirium followed by by coma, and concentration of parasites in capillaries of central nervous system. Parasites of single well-defined group (Ewing).

B.T., 32 years; while in Cuba he had attacks of chills, fever, and diarrhoea, but partly recovered under quinine. On the transport the same symptoms returned. After arrival at Camp Wikoff, he suffered from nearly continuous fever without chill, and the diarrhoea became more profuse.

On admission to the general hospital, Sept. 6th, he was considerably emaciated, slightly jaundiced, and completely prostrated. He was given 2½ gr. of bisuriate of urea and quinine, subcutaneously t.i.d., and opium. He passed a restless night, and the temperature remained high. At 10 a.m. Sept. 7th, examination of the blood showed a recent sporulation of parasites. The temperature fell steadily during the day, but the patient became delirious in the afternoon, and comatose by night, and never recovered consciousness. There was a moderate rise of temperature on Sept. 8th, while the coma deepened and the pulse gradually failed. Death occurred at 3 a.m. Sept. 9th.

Blood Examination. Sept. 8th, 10 a.m. Showed a great many aestivo-autumnal parasites, 2-3μ in diameter, lying in shrunken red cells, mostly free of pigment. A great many of the rings are less than 2μ in diameter. Multiple infection of cells is not unusually frequent. The red cells show the changes of a severe secondary anaemia with beginning changes in the size of the cells. The leucocytes are reduced in number. No eosins seen, and no pigmented leucocytes.

Sept. 8th, 10a.m. The parasites are much less numerous. They are nearly all of larger size, 4-5μ, and maintain the form of a ring with thickened irregular segments. A few show one or two fine

pigment grains. Chromatin is variously subdivided, and usually displaced from the periphery of the ring, being often found as a small group of very fine granules in the centre of the ring, or arranged in the form of a crescent or figure 8, or as an irregular mass or group of granules lying at some distance from the ring. No spheroidal bodies with compact pigment mass and no rosettes were seen in this case. Several hours were spent at various times in the study of these specimens, and during that time two crescents were encountered. The unity of the group of parasites is to that extent imperfect. In the fresh condition the formation of pseudopodia and the amoeboid motion are very active, and the pigment grains show slight vibratory motion. The leucocytes are as before.

Autopsy. 4 hours after death. *Body* markedly emaciated, slightly jaundiced; no oedema. *Lungs* show emphysema and hypostatic congestion. *Heart* rather small; valves and muscle normal; pericardium distended with clear serum. *Spleen* slightly enlarged, moderately pigmented, dark brown, rather soft. *Kidneys* about normal in size, consistence reduced, capsules not adherent, surface smooth, cortex somewhat thickened, pale, markings regular but indistinct. *Stomach* contains bile, otherwise negative. *Intestine*, normal. *Brain*, no increase of serum. No venous congestion. No dropsy of ventricles; cortex slightly brownish on section; no petechiae.

Microscopic Examination. Liver. The liver cells are very fatty, and contain many course yellowish granules, some of which give the reaction of haemosiderin. No necrotic foci were seen. In many lobules, the cords of liver cells are partly or completely atrophic, and the capillaries are much widened, forming a variety of cavernous tissue. These changes are of irregular distribution in the organ, being sometimes most marked about the central veins, but more often affecting large irregular portions of lobules. Pigmentation of endothelial cells and of leucocytes is marked but not extreme. Parasites are very scarce, but a few small spheroidal bodies and minute rings could with difficulty be identified. *Spleen.* Appearances—black in colour, due to heavy deposits of pigment in endothelial cells, large mononuclear cells of the pulp

and sinuses, and leucocytes in the sinuses. Malpighian bodies much reduced in size. No foci of large cells free from pigment were to be seen in the pulp tissue. Very few parasites could be identified.

Marrow. The marrow of the vertebrae is very fatty. In the cellular cords, there is, in places, moderate proliferation, and the cells appear in compact masses. Generally, however, the cords appear normal or deficient in colourless cells. The pigment deposit is slight and no parasites could be identified. In smears of the marrow, a few ring-shaped parasites within red cells were seen. The nucleated reds, eosins, and giant cells are very deficient.

Kidneys. The convoluted tubules are markedly dilated and filled with granular coagulum. The cells are flattened, or broken and degenerated, and nearly all contain great numbers of large and small light yellowish granules, which give the Prussian Blue reaction of haemosiderin. The capsules of the glomerulai are considerably dilated. The capillary tufts contain a moderate number of pigmented cells, and a few spheroidal parasites. In a few of the ascending limbs of Henle's loops, there are a good many clumps of pigment lying within the lining cells, but this condition is not at all ~~frequent~~ frequent.

Brain. Throughout the cerebrum, cerebellum, medulla, and upper cervical cord, the capillaries contain a very large ~~number~~ number of red blood cells, harbouring parasites. Most of these are small pigmented spheroidal bodies; some exhibit the large ring form with little pigment, and a very few rosettes were identified. The pigment deposit, outside of the parasites, is slight. A considerable number of capillaries were found completely filled and apparently occluded by masses of infected red cells, pigmented leucocytes, and swollen pigmented endothelial cells. In the same regions, the small arterioles and all the larger vessels were almost entirely free from parasites. The ganglion cells everywhere show reduction in size, irregularity, splitting, or loss, of chromatic bodies. These changes are less marked in the large stichochromes of the bulbar nuclei than in the cerebrum and cerebellum.

EPICRITICAL. This case is a striking example of the massing of an excessive number of parasites in the cerebral capillaries. The relation of the cerebral symptoms can apparently be closely connected

with the development of the parasites as followed in the examinations of the blood. Sporulation occurred during the night of Sept. 6th, when the temperature was at its highest point, 104°. At 10 a.m., Sept. 7th, when the patient was extremely restless, the blood and presumably the brain contained a large number of small ring-shaped parasites. Delirium and partial stupor began on the same afternoon. At 10 a.m. Sept. 8th, when the patient was comatose, the parasites had markedly increased in size and many had retired from the general circulation. At this time it is reasonable to infer that the increased size of the parasites and probably their increased numbers in the central nervous system had seriously impaired the capillary circulation. At death, 3 a.m. Sept. 9th, preceded for several hours by profound coma, the sections of the brain show that the majority of the parasites had reached their full development, some were segmenting, and many cerebral capillaries were occluded.

The presence of a single group of parasites, the development of which could be followed throughout the cycle is one of the interesting features of the case. Sporulation appears to have been completed during the night of Sept. 6th, when the temperature reached its highest point, 104°. At 10 a.m., Sept. 7th, the blood contained a large number of rings nearly all under 3μ in diameter, with a single large chromatin body and without pigment. These parasites appeared to have had at least 6-10 hour's growth. At 10 a.m., Sept. 8th, the parasites had increased in size, measuring about 4-5μ in diameter; numerous outgrowths had appeared on the circumference of the rings; the chromatin (Nochtmethod) was invariably increased in quantity, subdivided, and irregularly placed, and a few parasites showed slight pigmentation. There were still no spheroidal bodies, with compact pigment, to be found after 30 hours growth. The patient died at 3 a.m. Sept. 9th, and the great majority of parasites found in the cerebral capillaries were of large size and abundantly pigmented, and a few rosettes were seen, indicating the approach of general segmentation at the end of 48-50 hours' growth. Judging from the appearance of the parasites found in the sections of the brain it would appear that about 6-10 hours' growth separated considerable numbers of the youngest from the oldest members of the group, although between a few individuals the intervals must have been much longer.

The severity of the renal lesion with the absence of parasites in the renal vessels also requires mention. The changes in the cells of the renal tubules were more advanced than in any other uncomplicated case of the series, and appeared to be purely of the type of acute degeneration. The lining cells were markedly eroded and largely composed of a multitude of light yellow granules giving the reaction of haemosiderin. This destruction of the lining cells caused the dilated tubules to be more or less filled with granular detritus, but there was no further evidence of an exudative process. The kidney was free from chronic changes. In the absence of parasites and of signs or causes of acute inflammation, this lesion must be referred to a toxic condition associated with the malarial infection.

The evidence of the present case therefore fully accords with the conclusion drawn from other cases of the series that the usual renal lesions of pernicious malaria are referable to the effects of a toxic process, and not to the direct action of parasites.

Nevertheless, there is a group of cases with varying degrees of renal degenerative change associated with massing of parasites in the renal capillaries and sometimes even with uraemic symptoms as we shall see later.

Again, Ewing writes:

"Of the eleven cases of coma in which rings alone were found, ten died, and the surviving case was only saved by the most heroic treatment. On the other hand, among 33 (thirty-three) cases showing crescents only, there were but 3 fatalities. This comparison indicates a striking difference in the prognosis in cases of coma. The appearance of the early forms of the parasite in large numbers indicates a recent sporulation, and when coma results from the development of a new brood of parasites it appears to be a very unfavourable condition. When coma supervened, at other periods of the cycle, it appears from the above data that a prognosis is very much more favourable. According to the clinical character of the coma, these cases appeared to fall into two distinct classes:

"(1). The discharge of a new brood of parasites was often accompanied by a rise in temperature, gradual loss of consciousness, and slow deepening coma. After a period of 1-3 hours, the patients

were usually in complete stupor and could not be roused. As already stated most of them died, quinine proving ineffective. The blood in these cases nearly always showed a large number of young rings.

"(2). Of this large group of cases, many were brought to the hospital in coma, having been suddenly prostrated, with loss of consciousness and with or without spasms or convulsions. Several such attacks developed suddenly in partly cinchonized patients in the wards. At the height of coma the patient usually presented the typical appearance of 'coma vigil', with nearly complete stupor—open eyes, pale sweating skin, stertorous breathing, a full pulse, fever, and pupils reacting to light. The blood in these cases contained crescents, sometimes tertian parasites, but few or no rings. Such conditions were nearly always relieved by large subcutaneous injections of quinine or, if failing to respond, the stupor became complete, the reflexes were abolished, and the patient died. The result in cases of coma was seldom in doubt longer than 24 hours. Some of these attacks of coma were mild, and of short duration. In one case, the patient, while sitting up in bed, smoking his pipe, three times in five days suddenly became unconscious, his pipe fell to the floor, and he remained stuporous for three or four hours. At the end of that period, he would wake up, at once pick up his pipe, and resume smoking. Crescents only were found in the blood during these seizures. An embolic process seems to be the only probable origin of such phenomena.

"A considerable number of cases presented symptoms typical of meningitis, with marked rigidity of the neck and limbs, and retarded pulse. The patients usually recovered promptly after the injection of quinine. A great variety of milder nervous symptoms was observed, including localized neuralgias, spasms, aphasia, and mild hemiplegia; but these cases never failed to give a distinct history of a recent acute febrile attack. Of the algid type, no clear examples were seen, although many of the fatal cases died with low, but not subnormal, temperatures. The gastric type of the disease was illustrated by many cases of violent and persistent vomiting which occurred with or without fever. The response of many of these to subcutaneous injection of quinine was remarkable. In a few instances

the initial paroxysm was marked by, or consisted in, considerable haematemesis. In three cases, for some hours after the haemorrhage the parasites were usually scarce and difficult to find in the blood. In a few cases showing crescents, the attacks of vomiting occurred every four days. Intestinal symptoms were very common in the malarial cases at Montauk. Simple diarrhoea was, or had been, a nearly universal complaint, and was usually referable to improper food. Severe diarrhoea with mucous stools was a specially prominent complaint in 67 patients who appeared to be suffering from catarrhal colitis. Dysentery, or ulcerative colitis, was observed in 36 cases of malaria. It was probably much more frequent in occurrence than is indicated by these figures, for in the absence of prominent symptoms a previous colitis might have been overlooked in the history. In the above cases of dysentery, crescents were found in the blood in 9 cases, rings in 6, tertian parasites in 3, and both varieties of parasites in one case.

Dudgeon and Clarke record 21 cases dying in coma as showing massing of numerous parasites in the cerebral capillaries. Every case was energetically treated with quinine, either by the intramuscular or intravenous route, usually both, from the time of first coming under medical observation. The onset of such cerebral symptoms as drowsiness, mild delirium, apathy, restlessness, was noted as gradual in 12. Of the remainder, 9, when first seen, were already deeply comatose, and no other history was available. In these the onset of coma probably was sudden, or deepened rapidly. Usually case notes indicate a gradual progression from mild to deep coma. In 12 cases, from the onset of the first important cerebral symptoms, the end was fatal in 24 hours or less. The most rapid termination was 6 hours (1 Case), and the longest duration 60 hours (2 Cases). The temperature, where recorded, was invariably raised, 100-105°F. The record of microscopic appearances is as follows:- "The capillaries, and in the most severe cases the arterioles, were engorged with numerous infected red blood cells which showed the well-known tendency to collect at the periphery of the vessels, free parasites, melanin particles, prominent and detached endothelial cells. Various phases of development were represented, 'dot' forms, fine rings, segmenting

forms, but crescents were not seen. All gradations of blocking up to complete thrombosis with agglutination of, and altered staining reactions of, the corpuscles were exemplified. The distribution of parasites was as a rule quite uniform throughout the sections examined, but in two instances the changes in the cerebellum were more obvious than in the cerebrum.

"Small haemorrhages around the smaller blood vessels were seen in six cases. In one instance, the rupture of vessels had allowed the discharge of parasites into the tissues. In most instances which we have examined, the rupture of the cerebral capillaries or capillaries in other viscera has not led, as might be expected, to the discharge of parasites into the tissues. Abundant infected red cells are seen filling the vessels or tightly packed towards the vessel walls, while absence of infected red cells in the haemorrhagic zone is the rule, not the exception.

"Pigment varying in amount was present in the lining endothelial cells, in detached phagocytes, and free in the lumen.

"Nerve cell degeneration was observed in 11 cases, as shown by cells of abnormal size and shape, loss of Nissl's granules, eccentricity and distortion, of nucleus to its complete disappearance."

These authors acknowledge that these facts were fully recorded in the classical work of Marchiafava and Bignami, and that these observations of theirs are only confirmatory. They also state that, while in these cases with coma from massing of parasites in the cerebral capillaries, there were sometimes lesions and parasite massing in other organs, that from a review of the clinical histories the fatal issue appeared to be determined by the cerebral involvement only.

The picture of coma may be varied by tetanic, eclamptic, choreic tremor, athetotic or other focal or general irritative features.

3 cases recorded by Marchiafava and Bignami are given as examples:

Case of Tetanic Malignant (Quotidian) Infection with coma and cerebral massing of parasites (Marchiafava and Bignami).

Marinif, day labourer, an able-bodied young man, 20 years old, suffered from malarial fever last year, but not his year until July 30th. On the 30th, he had the first attack; on the morning

of the 31st, probably before being again seised by the fever, he went on foot to his place of work. About noon he was found in a state of coma by his cousin, who had him taken to the hospital, which he entered towards 6 p.m. Hypodermic injections of quinine had been previously given by the local surgeon.

The patient is in a state of complete coma; there is trismus; after many attempts we failed to open his mouth; the arms are contracted, the forearm extended and prone, the hand and fingers bent; the tetanic contraction ceases at intervals, and then suddenly reappears. An attack is not brought on by compressing the vessels and the nerves of the limbs during the periods of quiescence. There is no opisthotonus. The lower limbs are drawn together in extension; the soles of the feet are arched, and have a position tending to varus; the contraction increases at intervals, but never ceases entirely. The abdomen is sunken. The upper costal respiration is about 80 in the minute, and stertorous; the abdomen is tucked in in the act of inspiration. The pulse is 120, soft and rather full; the right side of the heart is dilated.

The eyes are turned upwards and outwards; the pupils are large, and react to light. From time to time, the patient has attacks, during which the rigidity of the trunk increases, and the pelvis is raised; there is also an incomplete erection of the penis. The reflexes of the knee-pad are exaggerated; the superficial ones are normal. 8.30 p.m. Temperature: 103·4°F. Bimuriate of quinine 48 gr. given by hypodermic injection. Temperature 9 p.m. 101°F (after a cold pack). 12 p.m. 103·7°F.

Aug. 1st, 2 a.m. Tempt. 104°F. 2.30 a.m. Death.

The examination of the blood at 6 p.m. on July 31st revealed nothing abnormal, but a few endoglobular forms with pigment at the ~~centre~~ centre and some pigmented white blood corpuscles.

Aug. 1st, 9 a.m., Autopsy—The tension of the dura mater is increased; the meninges are intensely hyperaemic; the central grey matter is strongly melanotic; there is no haemorrhage. Bilateral pulmonary serous infiltration; the heart healthy. The spleen is very soft and melanotic; the Malpighian corpuscles are not pigmented, and are very well marked. The liver is soft, and there is melanosis, but not very intense. The bile ducts are full of bile. The intestines

are normal, and loaded with bile. The kidneys are strongly hyperaemic. The bone marrow is not intensely melanotic.

MICROSCOPIC EXAMINATION—The cerebral capillaries are entirely filled with red blood corpuscles, each one of which contains a parasite with pigment at the centre; there are also some similar parasites observed in the free condition. On the other hand, the blood taken from a cerebral vein and artery contains only a very few plasmodia. The spleen contains a very large number of parasites, with pigment at the centre, both endoglobular and free, and also in decolourised red blood corpuscles, which last are rather abundant. There are no large phagocytes (macrophagi), nor are there any alterations visible in the nuclei of the cells of the pulp and of the follicles.

In the bone-marrow, the parasites are found in the same condition as in the spleen; in addition, some endoglobular spindle-shaped bodies are seen.

In the capillaries of the liver, the greater part of the red blood corpuscles contain no parasites. The hepatic cells contain a considerable number of haemoglobinic and rusty-coloured granules; some of the hepatic cellules are found to have in them entire red blood-corpuscles of the colour of old gold.

This is an instance of very severe malignant infection, proving rapidly fatal, and having been determined by a single generation of quotidian parasites. Examination by the microscope showed an extremely serious parasitic invasion of the nervous centres, while in the blood of the finger, the number of the amoebae was very scanty. It is noteworthy that the malignant paroxysm developed on the second day of the disease, after an initial paroxysm of little importance.

Case of Malignant infection attended by coma and eclampsia. Third recurrence of fever. (Marchiafava and Bignami).

T.C., 8 years old, coming from the Tre Fontane, had fever for twelve days in the month of July, and this is now the third recurrence. For three days, he has had fever; shivering set in on Sept. 22nd towards 8 a.m., and on the 23rd towards 7 a.m. The fever appears to have been continued.

On Sept. 23rd, the patient was brought to the hospital,

and put in bed No. 2, Lancisi Division. He is extremely pale; he is roused by stimuli, but gives no answers. The pulse is very frequent and weak. The spleen is large, and the abdomen distended. The temperature is above 102·2°F. 10a.m., blood: there is an enormous number of plasmodia without pigment; a smaller quantity of plasmodia with fine granules of pigment, and some forms with a collection of pigment at the centre, and, in addition, forms of segmentation (in size from one-fourth to one-fifth of that of a red blood corpuscle). Also young crescent-shaped bodies and white blood corpuscles containing small masses of pigment. 32 gr. of bimuriate of quinine administered by hypodermic injection. Noon, temperature 102·2°F; 16 gr. of bimuriate of quinine administered by hypodermic injection. From this time, the temperature falls continuously up to the time of death. 2 p.m., hypodermic injections of caffein, camphor, etc. 2.30 p.m., tonic and clonic convulsions, trismus, and vertical nystagmus. The deep reflexes are preserved, but the superficial ones are effaced. There is no reaction to stimuli. Blood: the parasites are as above, only increased in number; the plasmodia, without pigment especially, are found in immense quantities; they are discoid and annular in shape, and extremely mobile. Also many pigmented white blood corpuscles. 3 p.m., death.

24th—*Autopsy:*— The body is very pale in colour. The brain is anaemic, particularly the white substance, and melanotic. The lungs are congested, and a little oedematous. The heart is healthy. There is a little serous fluid in the pleurae and pericardium. The liver is melanotic, and the gall-bladder full of bile. The spleen is very large, with hyperplastic follicles; the pulp is plum-coloured and not very soft. There is a chronic enlargement together with an acute intercurrent one. In the kidneys the cortical substance is pale with yellowish striae; the stellae venosae are very fully injected.

Examination by the microscope gives the following results:— In the brain there is an enormous number of sporulation forms, some about as large as a third of the size of the red blood corpuscles and others still larger; many forms are also found with a small mass of pigment at the centre, as well as accumulations of free spores which block up certain of the capillaries (thromboses of spores).

In the spleen, the quantity of parasites is not so abundant as in the brain; in it forms with pigment at the centre, young plas-

modia, and crescent-shaped forms, both young and adult are found. In the bone-marrow, there is an immense amount of round, ovoid, and spindle shaped forms, also of young amoebae. In almost all the forms the pigment is disseminated irregularly. There are no forms of sporulation. In the liver, the parasites are found in the same condition as in the spleen, only very few in number. The hepatic endothelium and Kupffer's stellated cells are pigmented.

In this case, as in the others described, the parasites are found in a condition denoting great malignancy; so much so that the severe infection can be diagnosed simply by examining the blood. The appearances of amoebae in the brain are noteworthy, and the distribution of them in the different viscera is characteristic.

Case of Malignant Infection, with coma and recovery (Marchiafava and Bignami).

N. N., an able bodied countryman, coming from Maccarese, has had fever for 8 days. On the morning of Aug. 6th, he was attacked by fever as he was walking to his work; after being carried to the hospital, he fell into a state of coma at 4 p.m. His complexion is slightly jaundiced, the spleen is enlarged, and there is high fever. (Temperature, 104·9°F). An immense quantity of plasmodia without pigment are found in the blood; some of the red blood corpuscles are seen to have two, three, or four of them in different planes; there are also some forms with pigment at the centre, and several forms of fission, as well as many pigmented white blood corpuscles; 56 gr. of soluble hydrochloride of quinine are administered, partly by hypodermic injection, partly by the mouth. The fever falls during the night; on the morning of the 7th, the patient has recovered from the coma, and replies to questions, but his mind appears clouded. As regards the parasites, at 8 a.m., there is an extremely large number of plasmodia in motion, and without pigment; only a very few being pigmented; some also are in process of fission. The temperature is 98·6°F; 24 gr. quinine are given. The intermission lasts during the whole day; in the afternoon the temperature is 98·7°F. At 4 p.m. the patient is awake, answers questions slowly, and complains of headache; the blood is found on examination to be in the same condition as in the morning. But towards 9 p.m., he again has fever (temperature 104·9°F), and relapses into lethargy.

At 7 a.m. on th 8th., the lethargy and the fever persist. Again injections of quinine are administered as well as stimulants. At 9 a.m., the temperature has remarkably decreased (it is 99°F); the parasites also have become less in number; a few plasmodia are seen without pigment, there are some forms with pigment at the centre, and many pigmented white blood corpuscles. The lethargic condition lasts throughout the day; at 4 p.m., the blood is examined again, with results similar to those obtained in the morning.

The fever returns during the evening and night; the maximum temperature is 102·2°F. On the morning of the 9th, the patient is very prostrate, and has a jaundiced complexion, but is no longer in a state of lethargy; temperature is 100·4°F. A very smalll number of plasmodia are found in the blood, and pigmented white blood corpuscles. The patient improves rapidly.

On the 10th, plasmodia are still found in the blood, but they are very scanty; there are many pigmented white blood corpuscles, and a very few crescent-shaped forms. The jaundice decreases, and the appetite returns. The maximum temperature during the day is 99·7°F.

On the 11th, there is complete freedom from fever, the blood contains only an extremely small quantity of crescent-shaped forms, (macrocytes, nucleated red-blood corpuscles, and pigmented leucocytes.

This is a case of quotidian with two malignant paroxysms, which the patient, being young, able-bodied, and energetically treated, survived.

Cases of coma where massing of parasites alone is found in the cerebral capillaries, blend with those where there is cerebral vessel thrombosis or embolism, punctate haemorrhage, meningitis and even large meningeal or cerebral haemorrhages. But it would appear that massing of parasites alone is enough to account for coma, as cases are on record, mainly by the Italian observers, where massing of parasites has been found in the brain capillaries alone, and no trace of them could be found even in the spleen or bone-marrow. (Bastianelli—cf. "Malaria", New Sydenham Soc., Marchiafava and Bignami 1894, p193.)

Coma, the result of reactivation of latent malaria by Salvarsan.

Two cases of apparent malarial coma following injections of salvarsan are unique.

One is recorded by Castellani. The patient, a sailor, suffered from very indefinite symptoms and went to a venereal clinic. His blood gave a positive Wassermann reaction. He was given an injection of Salvarsan. A few days later, the patient was brought in comatose to the Seamen's Hospital, and died in a few hours after admission. At the autopsy, no very definite pathological changes were found, but Dr. Hewlett on examining the brain histologically found enormous numbers of malarial parasites in the capillaries.

The other case is recorded by Marinesco and Draganesco. C. A., aged 35, coming from a malarial region entered the neurological department of the hospital at Colentina 17-8-23, with the symptoms of progressive general paralysis. After six intravenous injections of neosalvarsan (0·40 G) a quotidian febrile attack appeared with temperature of 40° on one occasion. The blood showed presence of gametes of plasmodium praecox. With a view to using this attack for the treatment of the general paralysis, quinine was not given. On 12th. Sept., she became semi-comatose, and died on the 17th in spite of intravenous injections of quinine and cardiac tonics. Leucopenia and convulsions were present in the last phase.

Autopsy showed, apart from the evidences of syphilitic meningo-encephalitis, numerous punctiform haemorrhages in the white substance, and dentate nuclei of the cerebellum and the central nuclei etc. Heart, lungs, liver, spleen, showed some degenerative changes, but those of special interest were in the brain. The central capillaries of the cerebellum were packed with parasites, and very numerous punctiform haemorrhages appeared there—as many as 25 were counted in one section. Very few of the red cells composing the haemorrhages contained parasites. One capillary showing parasite-pigment thrombosis was the centre of a nodule of coagulation necrosis surrounded by extravasated red cells. White matter of brain and meninges showed also some haemorrhages. Parasites were scarce in spleen, liver, kidneys and adrenals.

Authors state that it has been known for a long time that salvarsan could activate latent malaria, and that Milian in France had especially drawn attention to it.

(2). Capillary embolism.

Of this type, Ewing says, "Malarial coma may be referable to embolic processes with temporary occlusion of vessels in small areas of the brain, and without uniform massing of parasites in cerebral capillaries. In these cases the coma develops suddenly and may be as suddenly recovered from. In a case previously reported, the patient three times in five days fell back unconscious in bed, his pipe dropping from his mouth, but after a variable period he recovered consciousness, picked up his pipe and resumed smoking. From this very transient form, the duration of the coma may be much more prolonged and serious, but it is seldom fatal. It may occur in febrile, or afebrile, cases, and may exhibit distinct symptoms of focal irritation or meningitis. In the blood, few or many crescents, sometimes tertian parasites, but very few rings, are usually found, and occasionally no parasites can be discovered. Emboli of parasites, pigmented leucocytes, and visceral macrophages, seems to be the only anatomical lesion which can explain such symptoms. They arise in established cases of the disease and on microscopical examination extensive malarial lesions are found in the viscera, but few or no parasites are to be found in the brain. Although crescents or tertian parasites may be abundant in the peripheral blood in these cases, I have not seen, nor been able to find in the literature, report of any case in which large numbers of crescents or tertian parasites were found occluding cerebral vessels, and it appears that these parasites do not exhibit the tendency to unequal distribution in any degree comparable with the fertile aestivo-autumnal forms".

Bardinelli, (quoted by Ewing), concluded that when nervous lesions are transitory, they are probably of embolic origin, but when permanent they are probably complicated by multiple haemorrhages.

Duigeon and Clarke record a case in this connection, with a history similar to those of this group defined by Ewing.

Driver W, arrived un Macedonia 1915. No previous history of malaria. 23-7-17, while on "grazing guard" fell down unconscious. On recovery next day, found himself in hospital in a field ambulance. Detained for four days, discharged, and then excused duty for two days. On 30th, resumed full duty, but fell down unconscious, recovering consciousness in a C. C. S. 48 hours later. Blood films showed sub-

tertian rings and crescents. He became unconscious again during the day, and diei the same night.

Microscopic examination showed massing of parasites in the brain, more pronounced in the cerebellum than in the cerebrum. Thrombosis o f capillaries leading to complete vascular obstruction. Fine rings and segmenting forms were present in the thrombi. Numerous parasites in spleen and pancreas. No fatty degeneration of the cardiac muscle.

It is not known whether patient was vigorously treated with quinine after his first attack of unconsciousness, and before the second attack.

The following case with timely treatment and recovery might belong to group (1) or (2).

Woman with coma, convulsions, recovery. (J. F. Patterson).

Mrs. S's housegirl, a negress aged about 21, was found unconscious in the living room where a few minutes before she had gone to do housework.

When I arrived, the girl was lying on the floor, profoundly unconcsious, muscles rigid, eyes closed, lids resistent to opening, pupils dilated but responsive, pulse 120. The least stimulation of skin caused clonic convulsions each convulsion lasting from 5-20 secs. No history was obtainable, and the patient was removed to the hospital. It was impossible to take temperature by mouth or rectum, because of the clonic and tonic spasms; for the same reason, attempts at catheterisation were a failure.

Morphia, ¼ gr. was given hypodermically, and during the night ¼ gr. more was given because of the continuance of the motor symptoms.

The condition remained the same until the following afternoon at 5 p.m. when the patient became somewhat relaxed. Her temperature was then taken by rectum, and found to be 102·4°F, pulse 140 weak and intermittent; a blood examination revealed the aestivo-autumnal parasite and the condition was now recognised as cerebral malaria.

At 6 p.m. the patient was given 12 grs. of quinine hypodermically and thereafter 9 grs. every four hours; 4 drops croton oil. The following morning she aroused from the coma, the temperature was normal and on being questioned she stated that she had been having chills for

the previous two weeks. She made a rapid and uneventful recovery.

(9) Punctiform Haemorrhages.

Many observers have reported punctiform haemorrhages in the cerebral white matter and cerebellum. Only very rarely has this occurrence been noticed in grey matter—Marchiafava, Bignami, and Bastianelli report a solitary case where numerous punctiform haemorrhages in the grey matter as well, were seen.

Bastianelli and Bignami writing of these punctiform haemorrhages says:- "These haemorrhages are always met with in the white substance of the hemispheres and the bulb; more rarely on the boundaries between the white and grey matter in which latter they are not usually found. The haemorrhages are composed of normal red blood corpuscles, even in cases where the capillaries are entirely filled, both with red blood corpuscles loaded with parasites, and with free parasites. They are generally found surrounding the finest arteries, and often surrounding the small thrombosed vessels, in which the endothelium is altered by the parasitic thrombosis.

"From these facts it is concluded that the punctiform haemorrhages are probably caused by diapedesis through the altered walls of the small capillary arteries, in which a stagnation, and in some cases a real thrombosis, is produced by the slowness of the circulation, which is greatest in the white substance where the capillary network is less abundant and the lumen of the vessels smaller than in the grey substance."

The coma in these cases tends to be persistent after onset, even although the number of parasites markedly diminished and cases have been noted where at autopsy the cerebral parasites, after treatment, have been remarkably few.

A case recorded by Marchiafava and Bignami illustrates this type:-

Malignant Infection with Coma. Protracted course (Marchiafava and Bignami).

G. B., 60 years old, enters the hospital Aug. 10th 1886, and states that he has had several paroxysms on the preceding days. On the afternoon of the 10th, he is without fever, but prostrated and pale. 32 gr. of quinine hydrochlor. are administered. During the night, he is seized with fever, and he falls into a state

of coma. On Aug 11th, at 9 a.m., profound coma continues, and hypodermic injections of quinine are given. The blood contains a considerable quantity of plasmodia without pigment, and some forms with a small mass of pigment, at the centre. The coma continues during the whole day, and at 5 p.m., the parasites are found in the same condition as above.

On the 12th, at 8 a.m., there is a remarkable decrease in the number of plasmodia without pigment; but others are seen both pigmented and in process of fission. Again injections of quinine are given, but the profound coma lasts throughout the day. The respiration is frequent and superficial, the pulse small and frequent. At 4 p.m., there is sweating; the plasmodia without pigment have now become very rare, while many pigmented white blood corpuscles are found.

On Aug. 13th, there is still profound coma; the pupils are contracted, and there are punctiform haemorrhages into the skin of the eyelids, the forehead, and the ocular conjunctiva. At 8 a.m., the blood shows only a very few motionless plasmodia without pigment, and some pigmented white corpuscles. During the afternoon, the general state remains the same, as also does the condition as regards the parasites.

On Aug. 14th, at 6 p.m., death takes place.

Temperature:	Aug. 11th.	Aug. 12th.	Aug. 13th.	Aug. 14th.
4a.m.	101·5°F	105·1°F.	103·5°F	104·4°F
8 a.m.	103·3°F	104·4°F	103·1°F	104·6°F
Noon.	104·4°F	102·4°F	102·6°F	104·6°F
4 p.m.	105·3°F	101·7°F	102·7°F	-
8 p.m.	105·1°F	102·4°F	103·3°F.	-
Midnight.	105·1°F	103·5°F	102·0°F	-

Thoughout the whole course of the fever the patient was in a comatose condition lying on his back and incapable of being roused by the strongest stimuli.

The autopsy revealed punctiform haemorrhages in the cerebrum, and in the retinae; the cerebral capillaries contained a very small quantity of plasmodia, all without pigment; the spleen was enlarged and of a black colour, and there was pulmonary hypostasis.

This is an instance taken from a class of cases in which the high fever and the cerebral symptoms persist for several days, although the parasites, owing to the action of the specific remedy, continuously

decrease in number. The anatomico-pathological examination sufficiently accounts for the aggravation of the cerebral symptoms and for the fatal issue. The fever may take, as in the present case, a sub-continued course.

While diapedesis of non-infected red cells is the commonly accepted source of punctate haemorrhage by the Italian observers, Nazari (to whom I am indebted for drawing my attention to it) records a case of coma with punctiform haemorrhages which he cannot explain in this way, viz:-

A child of 6 years was brought to the San Spirito Hospital Rome, in a very grave condition, on the 18th Oct., 1918, with symptoms of pernicious comatose malarial infection. Finger blood revealed abundant amoeboid and semi-lunar parasites, so plentiful that it is no exaggeration to say that every red cell had a parasite in it, and very many contained two, three, four and even five amoeboid forms. In spite of every care, the child died 6 hours after admission. Autopsy showed much pigment in spleen, liver, and bone-marrow. The brain showed intense hyperaemia and melanosis, with innumerable sub-arachnoid punctiform haemorrhages of the cerebellum, and of the white matter of the brain medulla and cerebellum.

HISTOLOGICALLY, the haemorrhages had the same general appearances as those previously studied, but quite different from these was the fact that the extravasated red cells constituting the haemorrhages, contained amoeboid forms of parasite, and especially bodies with central blocks of melanotic pigment.

This unusual finding, Nazari considers, could be explained in one of two ways; either by a much increased permeability of the capillary walls, associated with the intense hyperaemia and enormous parasitation of the blood, so that parasite-laden reds got through; or by rupture of the capillary walls, a condition not excluded by some pathologists in the production of haemorrhagic infarcts in general. On the whole, he inclines to the former explanation.

The comparative frequency with which haemorrhages occur, in comatose cases, and therefore make for a fatal issue, make a further

argument for early treatment of malarial infections in general, and cases with the least sign of cerebral involvement in any form, in particular. Also it is emphasised by many observers in regard to diagnosis that there may be few or no parasites found in the peripheral blood of these patients.

(4). Large Haemorrhages.

Several authors record large focal haemorrhages, meningeal in the cerebral white matter, or in the cerebellum. They are generally associated with massing of parasites. Gaskell and Miller record a case with two haemorrhages which ploughed up the fibres of the white matter, in a malignant tertian infection.

One such record will serve to illustrate the type:-

Fatal case of coma, right hemiplegia, aphasia, meningeal haemorrhage. (Dumolard, Aubry, and Trolard).

R. F., aged 36, trader, entered hospital Algiers 26-7-07. Complaint of shivering and lassitude of a few days duration. He looked very ill. Temperature 39°. Typhoid fever first thought of, haematuria,—red cells and leucocytes in the urine. Blood film shows malignant tertian parasites—one in every ten red cells.

Quinine hypodermically—25 cgms. twice on the 26th. No change next day. Quinine continued as above on the 27th, 28th, 29th July. General condition better—no delirium.

30th. Temperature normal, no quinine. 31st, fever again. 50 cgms. quinine. Urine continues red. 1st. Aug., patient has right sided haemiplegia, and a total aphasia, which occurred slowly during sleep. Eyes open, but he has a tendency to torpor.

Since then, in spite of large doses of quinine (1,50 G. per day in three doses) the condition of the patient got worse and he died comatose on 3rd. Aug.

At autopsy, a sub-meningeal haemorrhage the size of a tangerine was found pressing on the right Rolandic area. In the organs and notably the brain, the capillaries were packed with parasites.

(5). Septicaemic type. ving used stronger doses of quinine.

(5). Septicaemic type.

Gaskell and Miller define a group of cases associated with coma, which they consider as a whole constitute a different mechanism

in the production of coma—in which the outstanding features are an extremely high parasitic content of the blood, both towards the end of the illness and also in all organs after death. This condition may arise in recent primary and in chronic infections and be rapidly fatal.

The condition of the organs in this type of case are mainly an acute degeneration affecting especially the brain, heart, spleen, and liver. These authors point out that degenerative changes in the endothelial cells of the blood vessels, though very definitely present, are less conspicuous than in the cerebral type. The diffuse degenerative changes in the organs are not, however, due to circulatory disturbance, but to an intense general toxaemia. This type of case may do well if treated rapidly intravenously. Defining this group they say: " 'The septicaemic type' is characterized by an intense and rapid proliferation of the asexual cycle of the malignant parasite throughout the body, which gives rise to an intense toxaemia affecting all organs and leading to death. The asexual cycle is usually confined to such organs as the spleen and bone-marrow, and the toxin liberated by the rupture of the rosette only reaches the blood stream comparatively slowly, and never becomes highly concentrated in it. When, however, the asexual cycle takes place in the general circulation, the virulence of the rapidly liberated and concentrated toxin is such as to cause grave general symptoms, which, if untreated, are rapidly followed by death. Treatment in an early stage is an entirely different matter to treatment when once severe symptoms have occurred.

"The fatal cases of the septicaemic group already described did not show clinically marked symptoms of heart failure until just at the end. The toxic effects were clinically shown by the cerebral symptoms. In case 8, the pulse remained good throughout the period of intense cerebral disorder, and it was not until the fifth day after admission to hospital with a temperature of 105°F and the fourth day after the onset of cerebral symptoms that the action of the heart became enfeebled. The effect of the acute toxaemia in this type, therefore, takes a few days to manifest its action on the heart muscle, when the latter organ is in a healthy state at the beginning of the attack".

A fatal case of this kind is recorded by these observers:-

Serb, 2,122T, had been under treatment for six weeks for dysentery. At the same time he was taking 10 grs. of quinine orally every evening, as he was also obviously suffering from malarial cachexia. Suddenly at 8 p.m. on Nov. 4th., 1917, he became very ill, and within 1 hour's time he was semi-conscious with a temperature of 103°F, and a rapid, full, and bounding pulse. He was also very restless. Malaria was suspected, and he was immediately given 20 grs. quinine intramuscularly. On the morning of the fifth, he was more comatose, but could still be roused. He was then given a further dose of 15 grs. of quinine intravenously. No physical signs of any definite cerebral lesion were found. He rapidly got worse, and died at 2 p.m., 18 hours after the acute onset.

"In this case again the treatment though more energetic was begun too late, and was quite powerless to control the rapid proliferation of the parasite and consequent death from toxaemia. A count was made of a blood film, taken when the patient was in articulo mortis, and showed the extremely large total of over 270,000 per. cu.mm., priors (parasite forms intermediate between the ring form and the mature parasite which has not yet assumed the rosette form) were also present. An examination of blood films taken earlier would have revealed the imminence of the condition, so that earlier and even more energetic measures of treatment could have been adopted with a good chance of success.

"The question of the existence of chronic malaria in this case was not in doubt. Not only was the condition of malarial cachexia present, but also examination of smears showed the presence of crescents in all organs. The enlargement of the liver and spleen was also great, the former weighing 86 ozs., and the latter 28 ozs., and their pigmentation was intense.

"There were extensive degenerative changes in the brain, with an intense parasitic infection, the count of a brain smear giving 450,000 parasites per cu.mm. as against 120,000. The heart was dilated and extremely soft. Its muscle fibres were peppered all over with fine droplets of fat, and fragmentation of fibres was present. Parasites were very numerous, a count giving 140,000 per cu.mm. Parasites were definitely identified free in the lymph spaces, and also in the sarcoplasm of the muscle fibres. The liver and kidneys showed extensive degenerative changes, mainly fatty, with small

haemorrhages in the kidney capsules. Spleen weighed 28½ ozs. It was very soft and the cut surface was almost pultaceous; microscopically, the whole pulp stained poorly, so that the identification of the finer ring forms of parasite was very difficult. All the forms of parasite were identified. The spleen substance gave a parasite count of 120,000 per cu.mm., the splenic vein a count 240,000. The count of 270,000 from the peripheral blood in life was bigger than these; this therefore supports the conclusion that active proliferation was taking place throughout the general blood stream. The brain smear gave by far the largest count. The count from the heart is practically equal to that from the spleen smear, being about one-half that of the peripheral blood just before death, and may be taken as indicating the count of any internal organ with the exception of the brain."

A similar case in which extensive parasite counts were made is as follows:-

The patient, Serb, 10,107, was admitted on the evening of Aug. 14th, 1918, in a condition of almost complete unconsciousness. A blood film taken at 6.30 p.m. (see table) gave a count of 32,000 parasites per cu.mm., nearly all the parasites being in an early (prior) state, i.e., completely filled-in rings of large size: a few very fine rings could also be found. After 3 intravenous injections of 15 gr. Quinine, the patient's general condition greatly improved, and the number of parasites in the peripheral blood diminished considerably to 11,000 only. A later film showed a still further diminution of the more mature forms which now showed rosette formation and a great increase in the earliest ring forms; his temperature had then risen to 103·2°F, and thus corresponded with the appearance of the fine ring forms of a fresh cycle. The quinine given had therefore diminished the developing parasites of the earlier cycle in the peripheral circulation from about 30,000 to 3,000, but had not prevented the beginning of a new cycle. That evening the patient had considerably improved, but at 7.30 p.m. he suddenly died; the physician, though immediately sent for, was not able to arrive before death had taken place.

See table overleaf.

Parasite Count of Serb Patient, 10,107.

In life.	Rings.	Priors.	Immature Rosettes.	Mature Rosettes.	Total.
6.30 p.m., 14-8-18.	very few.	mostly.	0.	0.	32,000.
10 a.m., 15-8-18.	very few.	0.	mostly.	0.	10,800.
5 p.m., 15-8-18.	16,400.	400.	0.	2,800.	19,600.
P.M.					
Inferior Vena Cava.	20,300.	-.	-.	900.	21,200.
Blood from cavity of left ventricle.	27,200.	800.	-.	21,200.	89,200.
Splenic Vein.	4,000.	-.	-.	14,400.	18,400.
Spleen Juice.	67,400.	-.	337,100.	943,800.	1,348,300
Liver juice.	16,000.	2,000.	2,000.	22,400.	42,400.
Kidney juice.	8,000.	-.	-.	10,000.	18,000.
Brain juice.	69,600.	800.	1,600.	118,400.	190,400.
Brain Blood.	63,300.	-.	-.	13,600.	76,800.

At autopsy the condition of the organs was similar to that of case V, namely *Brain:* meninges congested and with meningeal haemorrhages. Cerebral capillaries congested and minute haemorrhages in white matter. Brain very soft as a whole, flattening out on the table when removed from the skull. Microscopically, ~~haemorrh~~ haemorrhages were found to be in the main closely confined to the perivascular tissue. The vessels of the grey matter were congested, and the whole of the grey matter was infiltrated with an abnormal number of round cells which had the appearance of lymphocytes. These cells were sometimes clustered round a capillary vessel in very considerable numbers, and were often grouped round a nerve cell. The nerve-cells themselves were in a condition of degeneration. In some the nucleus was markedly eccentric, stained badly, and no nucleolus could be seen, and the protoplasm of the cell was covered over with globules of fat, spread diffusely

throughout the cell. In others, the nucleus had completely disappeared, and the cell was represented only by a degenerate mass densely peppered over with fat globules. In the white matter also there was a marked increase of round cells distributed diffusely. They were not so conspicuously grouped round the capillaries as they were in the grey matter, but lay in groups between the medullated fibres. The latter showed distinct evidence of degeneration, being irregularly nodular and tortuous in course. No evidence of localized necrosis was to be found. Parasites were extraordinarily numerous, both in brain and white matter. They were present in all forms, from the ring to the mature rosette, but no crescents of any kind were ever found. Most of the capillaries contain red cells, the majority or the whole of which contained parasites. *Spleen*, very much enlarged, 25 ozs., soft, friable, but not pultaceous. Microscopically, vessels engorged and packed with red cells. In the Malpighian bodies lymphocytes were diminished in number and supporting cells with degenerate nuclei correspondingly increased. Parasites in the Malpighian bodies were comparatively few. Pulp congested with red corpuscles and pigment. Parasites excessively numerous throughout the pulp mostly contained in red corpuscles, but a certain number of ring forms were found lying free. They were present in every stage from the small ring form up to the mature rosette, very large number of priors with pigment being observed. Not as single crescent, mature or immature, could be found. *Heart*: Normal in weight, 12 ozs. Very soft and with dilated cavities. Valves normal. Heart muscle very pale, soft and easily ruptured. Arteries and veins extremely congested, but with no evidence of thrombosis. Capillaries also congested. Finely granular pigment plentiful in polymorphonuclear leucocytes, in endothelial lining cells of small arteries and capillaries, and also lying free. Endothelial lining showed fatty degeneration. Muscle fibres fragmented throughout, the fractured ends being quite often widely separated from each other. The fibre nuclei stained well and did not appear to be degenerate. Cell-bodies, however, showed marked fatty degeneration. Parasites numerous in all vessels, and both intracorpuscular and extracorpuscular. Parasites were present in all stages from ring form to mature rosette. Rings predominated. Free parasites were found lying in the

lymph spaces, between the muscle fibres, and a few were found lying in the sarcoplasm of the muscles themselves. No crescents in any form were found. *Liver:* much enlarged, 79 ozs. Slate grey in colour, and soft. Microscopically, in Glisson's capsule there was a general increase of round cells. Congestion of vessels of lobules, but not specially of capsule. The liver cells throughout were shrunken and degenerate, protoplasm showing fatty degeneration. The endothelial lining cells of the capillaries were swollen, pigmented and fatty. Bile practically absent. Parasites easily found, but not so numerous as in other organs. All ring forms to mature rosette were present, and some were free in the capillaries. No crescentic forms were present. *Kidneys:* Practically normal in size, 5 ozs. each. Small haemorrhages in both capsules, and sub-mucous haemorrhages in the pelvis. Congested capillaries in the glomeruli, and parasites easily found, but not so numerous as in brain, heart, and spleen. They were present in all forms from ring to rosette, but no crescents were seen.

The sudden death of the patient therefore coincided with the arrival at the mature rosette form, and subsequent rupture of a very large number of malignant parasites, and it is concluded that the liberation of toxin, the early indication of which was given by rise in temperature, soon became so rapid and great as to cause immediate death. Such an almost simultaneous rupture of malignant rosettes is luckily extremely rare, for it seldom happens that practically all the parasites are in the same phase. In the benign tertian form, on the other hand, such an occurrence is common, and the liberation of the toxin causes the typical malarial attack. The difference in the virulence of the toxin liberated by the two types of parasites must be very great.

The action of quinine on the distribution of parasites.
As certain deductions can be ~~made~~ drawn from this case concerning the action of intravenous quinine on the distribution of parasites in the body, the details of varicus counts are shown in the table above.

It will be seen from the count of the vena cava blood that the number of parasites in the circulation is very similar to that found at the periphery just before death. In the blood of the left ventricle, after it had passed through the lungs, a considerable increase of parasites was found, especially of rosettes; these had

presumably been washed out of the lung tissue by the circulating blood. The number of parasites present in the spleen was enormous, and consisted to a very large extent of mature organisms, mostly ready to rupture. The actual number of organisms supplied to the general circulation through the splenic vein was, however, surprisingly small, though in contrast to the inferior vena cava blood mature rosettes predominated.

In the liver, the number of rings was similar to that in the general circulation, but large numbers of mature parasites were also present. In the kidney, though the number of rosettes was considerable the total count was not large. The brain showed a very large number of both rings and rosettes, but the number of mature parasites was very much smaller than in the spleen. The count of the brain blood was of somewhat doubtful value, as it was to some extent contaminated with brain juice; it, however, showed a great decrease of mature forms in comparison with the latter. From these counts it is evident that the numbers of mature parasites in the general circulation were very much less than in the organs themselves. Taking this in conjunction with the counts in life the administration of intravenous quinine had certainly diminished the parasites free in the circulation. It is difficult however to imagine that quinine had affected the parasites in such organs as the spleen and brain, in which the numbers present were still enormous. We may conclude that the chief immediate action of quinine is upon parasites free in the circulation, rather than upon all parasites in the body. It may, however, have an effect in diminishing the output from the organs into the general circulation, for the number of parasites present in the splenic vein was very low, when we consider the immense numbers present in the spleen itself. The output of mature parasites from the brain was also small compared to the large numbers present in the organ. Intramuscular quinine, probably owing to its slower absorption, does not produce this rapid diminution of output. This is shown in two cases in which the splenic vein count was about double that of the spleen juice.

It is probably that a fatal termination can only be brought about in this septicaemic type by the diffuse liberation of toxin throughout the body, and that so long as the asexual cycle is confined to organs such as the spleen, the toxic dose is not sufficient to

cause death. The immediate effect of quinine is upon the parasites in the general circulation. If the invasion of the general blood stream is discovered at a sufficiently early stage, it can be controlled by energetic administration of quinine, and the fatal termination can be prevented.

To illustrate this is a case (one of a number) occurring amongst the hospital personnel in which the detection of the presence of rosette and "prior" forms in the peripheral blood led them to fear a fatal issue, but in which treatment was successful in bringing about recovery.

Case of recovery; septicaemic type.

Pte. R had been in Macedonia in our unit just over a year. It is possible that a previous primary attack of malaria may have been masked by prophylactic quinine; but he had never had any severe malarial attack. He was well in health until the evening of Oct. 13th, 1917, when he had various indefinite abdominal symptoms. On the morning of the 22nd., his temperature was 99°F: on the morning of the 24th., he was admitted to hospital with a temperature of 105°F. His spleen was not palpable. A blood film taken at 10.30 a.m. on that day gave a count of 6,200 parasites per cu.mm.

	10.30 p.m. 24-10-18.	6 p.m. 24-10-18.	9.a.m. 25-10-18.
Rings.	4,800.	9,200.	12,400.
Priors.	1,200.	800.	2,800.
Rosettes.	200.	0.	0.
Total.	6,200.	10,000.	15,200.

In this film a mature malignant rosette was definitely established and several prior forms were also seen. As the extreme importance of the appearance of this form of parasite in the peripheral blood was not then realized the immediate intravenous administration of quinine was not insisted upon, but further films were taken. A second count from a film taken at 6 p.m. and examined next day gave a total of 10,000 parasites per cu.mm. The rapid increase of parasites showed that quinine ought to be administered without delay, and an intramuscular

injection of 20 grs. was given at 9.30 a.m. Another film then gave taken gave a total of 15,200 parasites per c.mm. This latter count is larger than the corresponding mount taken in case V, eight hours before death: the rate of parasite increase was almost identical in the two cases. On the afternoon of the 25th, the patient's condition suddenly became very serious. At 2 p.m., he was given food, which he easily swallowed and he could talk normally. At 4 p.m. he was able to swallow only with great difficulty and his speech had become very indistinct and guttural; at 5 p.m., 15 gr. quinine were given intravenously. At 6 p.m., he could just be roused: breathing was stertorous and hiccough was frequent. He had incontinence of urine. His pulse was good. On the following morning, his condition had improved, though his pulse was slightly weaker. He was given a further 15 gr. of quinine intravenously. He was that evening also given 20 gr. of quinine intramuscularly. On the 27th, improvement was maintained, and two similar doses of intramuscular quinine were given. The temperature became normal. This treatment was continued on the 28th. The following day intramuscular quinine was discontinued, and 20 gr. were given by mouth, three times a day. The patient then appeared to be out of danger, but the heart sounds were weaker than they had been, and the pulse was small and soft, though regular. The spleen could not be felt. From this date onwards, improvement was continuous, and no further rise of temperature took place.

Comparing this case of recovery with the fatal ones already detailed, the suddenness of onset of the serious condition was again conspicuous. At 2 p.m. on the 25th, no dangerous symptoms were present; while at 4 p.m. they were extremely marked. The patient had been under continuous observation from the 21st, and the results of the examination of the films of the morning and evening of the 24th, the day before the onset of the serious symptoms, were taken as an indication that most urgent measures of treatment were necessary. An intramuscular injection of quinine was therefore given, and it was determined that this should be followed by an intravenous injection directly any more serious symptoms appeared. The reaction to the intravenous dose was marked, and the patient had improved considerably in the 12 hours following its administration. Further intravenous injection again caused improvement, and in another 24 hours he was

well on the way to recovery. We hold that this case would have terminated fatally in the same way as other similar cases bgt for the energetic treatment that was undertaken before serious symptoms arose. The effect of toxin on the heart appeared late, when the serious general symptoms had been recovered from. This supports the view that the cause of death in the septicaemic type is a general toxaemia and is not primarily due to the poisoning of the heart muscle only.

(c). Toxic Type.

This is a type emphasised by Ewing, and is referable to the general toxaemia of the infection. He says: "In these cases the coma usually develops slowly but may in cachectic cases be ushered in suddenly, apparently by some embolic process. It is often of prolonged duration, and not being caused by massing of young parasites in cerebral vessels, it is unaffected by quinine. Occurring only in severe cases and being associated with serious toxic lesions in many viscera it is nearly always fatal. Cases I and IV of the present series illustrate this type of case. These patients were comatose, one at least three days, and the other for two weeks before death. As no other cause for the coma was found, it had to be referred to the malarial infection, which was very severe and long established. These cases differed radically from the classical type of comatose malaria, as in one only a few crescents, and in the other only tertian parasites, were present in the blood, and no parasites, and comparatively little pigment were found in the brains. They show conclusively that the coma of pernicious malaria is not always referable to the presence of parasites in the cerebral capillaries. Jancsó and Rosenberger (Dent. Arch. f. Klin. Med., 1896, 57, 449) also have reported a fatal comatose case in which the brain contained few parasites, which were abundant in the other viscera, the coma being referred by the authors to a toxic origin".

The following is one of Ewing's cases of this type:-

Case of aestivo-autumnal malaria of toxic type with prolonged coma, and absence of parasites in the brain (Ewing).

F. H., 64, no important previous illness. Sept. 25th, had a chill followed by fever and sweat. Chills recurred every other day, till Oct. 2-3, when they became irregular and less marked. Admitted to Roosevelt Hospital, Oct 6th, 1896. Diagnosis, malaria.

Treatment, quinine and ginger (aa, gr. 25-40 daily) Arsenic later, Fowler's solution, gt. 15 ~~drops~~ daily. The patient seemed to improve slightly, the temperature falling gradually, reaching 99°F on Oct. 10th, and remaining near that till Oct 20th. There was from the first marked insomnia, and tendency towards mild delirium at night, partly controlled by sedatives, until Oct. 11th, when the delirium increased, and periods of mild coma supervened. About Oct. 16th, the coma deepened and became continuous till death. There were no evidences of uraemia, and the coma was clearly of a malarial type. There was one slight paroxysm of fever on Oct. 20th-21st (101·4°F), and on the 23rd the temperature began to rise steadily, reaching 108°F on the 25th, just before death. Urine considerable, acid, 1,020, latterly a trace of albumen, and a few granular and hyaline casts. ~~Blood~~

Blood, on Oct. 12th, contained an enormous number of young crescentic bodies, 10 in a field of oil immersion. Prolonged and repeated search (4-5 hours) failed to show any rings. Marked anaemia. Marked leucopenia, mononuclears, 35%: polynuclears, 60%: eosins, 5%. Oct. 13th, the parasites were as numerous as before, but there were now some elongated and apparently full grown crescents, while the spheroidal bodies were less numerous. No rings seen. Oct. 15th, the adult crescents now outnumbered the smaller forms, which were, however, still rather abundant. No rings could be found. Anaemia rather more pronounced. No leucocytosis, but eosins were still increased. Oct. 21st, parasites still numerous, and the forms were about equally divided among elliptical bodies and adult crescents. Oct. 25th, 8 hours before death, the blood was found to contain very few parasites. In the course of this search, 8-10 young crescents and spheroidal bodies were encountered, but no rings. There was a moderate polymorphonuclear leucocytosis.

Autopsy, 12 hours after death. Anaemia appeared slight. No oedema, no jaundice. *Lungs*, moderately congested and oedematous. *Spleen*, slightly enlarged, very soft: of characteristic slate colour. *Liver*, slightly enlarged, of characteristic slate colour. *Stomach and Intestine*, negative. *Serous membranes*, slightly discoloured in places. *Kidneys*, size about normal, capsules adherent in places, cortex slightly irregular, markings distorted in places. The cortex is light red in colour, the medulla and papillae very dark red or rusty. *The marrow* of ribs and vertebrae is hyperaemic, and of slight

chocolate tinge. *Brain,* moderately oedematous, not discoloured: shows no petechiae. The basal vessels appear normal.
MICROSCOPIC EXAMINATION: *Liver:* Very extensive deposit of pigment in endothelial cells, macrophages, and occasionally in the liver cells. All stages of phagocytosis of parasites can be followed. In some of the larger vessels, there are several spheroidal bodies, twice as large as a red cell, hyaline and faintly bluish, stained throughout, and exhibiting a moderate number of central pigment granules. *Spleen:* pigment extreme, much of it is old, within phagocytes, but there is a considerable number of free pigmented parasites, and all stages of their ingestion and destruction can be seen. No rings or rosettes. There is the usual cellular hyperplasia of the pulp cords. *Marrow:* of ribs and vertebrae contains a moderately rich deposit of pigment, which is usually limited to the phagocytes. Very little pigment seen in vessels, and very few parasites in smears of sections. Eosin and giant cells increased. Nucleated red cells abundant, and some slightly increased in size. *Kidney:* moderate, chronic, diffuse nephritis, with growth of new connective tissue in small wedge-shaped masses in cortex. Glomeruli apparently normal. Tubules show swelling of lining cells, and in a few places cells of the convoluted tubules are necrotic. They all contain much granular yellow pigment, giving haemosiderin reaction. Very few parasites seen. Pigment abundant, and of peculiar distribution. Glomeruli contain more than the usual number of pigmented cells. Larger vessels of cortex sometimes injected with blood, in which are considerable deposits of brown, granular or crystalline pigment. Limitation of this pigment in the cortex to the vicinity of vessels, strongly indicates that the crystalline deposits have resulted from the diffusion of dissolved Hb, or of escaped red cells.

In Henle's loops, pigment clumps are enormous. The pigment lies exclusively in the lining epithelial cells of the tubules, some cells containing 40-50 or more clumps in a single section. These cells fail to show marked evidences of granular or fatty degeneration, or of fragmentation, but their protoplasm is uniformly finely granular, their edges are unbroken and their nuclei are unchanged.

Brain: Throughout the medulla, cerebrum, and cerebellum, the vessels are nearly free from pigment and parasites. In some sections

from the frontal cortex, there are a few pigmented endothelial cells, and an occasional pigmented parasite, but most capillaries, though considerably injected, are free from all traces of parasites or their derivatives. In many of the pericellular lymph spaces throughout the cortex, there were peculiar structures, the nature of which I have been unable to determine. These bodies consisted mostly of elongated fibrils or rods with tapering ends, about 0·5-1μ in thickness, and 5-15μ in length. They were sometimes single, more often multiple, and arranged in rosettes, or spirals, or in concentric layers or irregularly clumped. They stained densely with methylene blue, faintly with haematoxylin. Similar deposits were found in other cases of malaria, and in one case of tuberculous meningitis. They may for the present be ~~call~~ classed with the artefacts of nervous tissue.

EPICRITICAL: In the above somewhat anomalous case, there are several features of interest. The development of a case of fatal malaria in a patient who for 25 years had not been away from New York City is unusual. While autopsies on cases of malaria are not extremely rare in this locality, they are usually cases which were infected in Southern Latitudes.

While quinine in moderately large doses with arsenic controlled the active sporulation of the parasites and reduced the temperature, the treatment failed as usual to have any effect upon the crescentic forms, which persisted in enormous numbers until, rather suddenly in the last few days of the disease, they disappeared almost entirely, although the patient died of hyperpyrexia. This pyrexia is no indication of a failure of quinine to control the infection as none of the young forms were seen after Oct. 12th, and the terminal fever must be referred to other causes.

The prolonged delirium and coma are the chief clinical features of the case. There seemed little ground for doubting that the mental condition was referable to the malarial infection, because the coma was established before the urine contained casts and albumen; the changes in the urine were never marked; there were none of the usual concomitant signs of chronic uraemia, such as oedema, muscular twitchings etc. The general condition of the patient was typically that of malaria; microscopic evidence of extreme malarial infection were found in the blood, liver, spleen, marrow, and kidneys, while the evidences of nephritis were very much less marked than those

usually found in cases dying in chronic uraemia. Neither can the coma be referred to the presence of organisms in the cerebral vessels, as none were found there, and it becomes necessary to regard the cerebral symptoms as dependant upon other conditions, probably toxic, associated with severe malarial infection. This conclusuion is in accord with evidence furnished by other cases of the present series, which fails to support the view that malarial coma is always dependant on the presence of parasites, or embolic processes in the cerebral vessels.

The most striking pathological feature of the case is the massing of pigment in the kidneys, especially in the cells of Henle's loop. A careful review of the microscopic studies of the viscera in malarial infection which is believed to be fairly complete fails to show the report of any similar condition in uncomplicated malarial fever. The condition in the present case appears to resemble that found in the kidneys in haemoglobinuric fever, in some cases of which large deposits of pigment have been found, but differs from them in the peculiar distribution of the pigment and in the absence of haematuria.

Uraemia has been considered in relation to this type but the clinical picture is not that of uraemia, and the renal changes are not such as are commonly associated with uraemia. It may be that this kind of case is sometimes a late addition of the septicaemic type, in which parasites have been killed off by intensive treatment, but not before too much tissue damage has been done to vital organs.

(7). Adrenal type.

Paisseau and Lemaire define a type of case with coma in which the emphasis of damage appears to be upon the adrenal capsules.

A man on the march suddenly falls down comatose without apparent reason. The most careful examination fails to discover any symptoms referable to the nervous system. Reflexes are normal, and there are no signs of paralysis. Temperature at onset of coma is raised, but it rapidly falls, and in a few hours a subnormal temperature takes its place. The most striking feature is the low arterial tension, and feeble pulse which can be very easily obliterat-

ed by pressure, although it may have been bounding at the onset of the attack. The pulse becomes feebler as the temperature becomes lower. The majority of cases show a marked "white adrenal line". This is in contrast to the heart sounds which appear normal till near the end. On examination of the different viscera generally shows no other anomaly than an enlarged spleen. Death supervenes in a few hours, in spite of all treatment, including intravenous quinine.

They distinguish this variety of case of coma from those showing lesions of the central nervous system, in which there are features like conjugate deviation of the eye, stiff neck, contractures, Kernig, modified reflexes; and they emphasize the importance of cerebro-spinal fluid lymphocytosis as occurring in the cerebro-spinal cases as a notable point of distinction.

They record several cases of coma where the emphasis of damage found was in the adrenals among abdominal organs—showing gross adrenal changes, such as haemorrhages, with complete disruption and dysfunction of tissue; but unfortunately, although among vital organs the main damage appears to have been in the adrenals, the brain at autopsy appears to have been overlooked. Nevertheless they seem confident about malarial coma of adrenal origin apart from the commoner cerebral types.

(8). Uraemic Type.

The aetiological relationship of malaria to uraemic coma in particular, and other uraemic nerve disturbances in general, such as headache, nervousness, convulsions, etc., is bound up with the evidences of kidney damage that can be attributed conclusively to the malarial parasite. This question appears to have been settled long ago by Marchiafava, Signami, Kelsch and Kiener, and Rempicci of the Roman Medical Clinic, all of whom have paid special attention to this subject.

It is agreed by these independent observers that malaria is capable of producing kidney necrosis and a variety of degenerative changes which correspond to those found in other infections, such as scarlatina, and diphtheria, which are certainly of toxic origin. Rempecci, who set himself to consider this subject clinically, studied 350 cases of malarial infection, and taking into account all the forms

of simple albuminuria up to true nephritis, those in which the malaria could be asserted to be the true cause of the renal lesion as well as those in which this could merely be presumed, there were in all 80 positive cases". He found acute (sometimes haemorrhagic) and chronic forms directly attributable to malaria, and that children and many young people were more predisposed to them than adults and old people. He also distinguished the oedema of acute nephritis from the essential oedema occurring not infrequently in children and young persons and others who had become anaemic without any albuminuria. Rempicci's observations show that malarial chronic nephritis may pass on to contracted kidney, with the usual accompaniments cardiac and arterial etc. from other sources. In some cases with cachexia, with predominant nephritis symptoms, death occurred after clinical evidences of uraemia.

The toxicity of malarial urine has been studied by Rempicci and others, although the nature of it has not been defined, and its existence is recognized as definite and considerable.

Several observers—Benhamon, Jahier and Berthélemy, Boulay and Bédier, Chauigny, Vigouroux and Prince—draw attention to a type of coma occurring in malarial subjects in which they consider that the immediate cause of the coma is disturbance of kidneys and liver by the parasite, to such an extent that their normal excretory and metabolic functions are interfered with resulting in severe uraemia.

In a fairly large proportion of malarial subjects, albuminuria occurs with other signs of kidney irritation, and it occurred to a few observers to pursue this these in malarial coma cases to see what bearing kidney retention might have upon the coma.

In 1921, Benhamon, Jahier, and Berthélemy observed seven cases of pernicious malaria, in 6 of which there was a considerable increase of blood urea, and of cerebro-spinal fluid urea (1,30-2,70 G) They point out that when the azotemie in malaria is low, it does not excede 0,50 G, and prognosis is good generally. But when during severe malaria blood urea increases rapidly, the prognosis is unfavourable, and when the amount exceeds 2 ½ litre, the issue is generally fatal.

In 1922, Boulay and Bédier observed four fatal cases of malaria with coma in which there were evidences of uraemia. The first case was that of a European who was admitted to hospital in a state of coma and who died two hours after. There were many parasites in the

blood. The urine, much diminished in quantity, contained a small amount of albumen and some casts, but no other abnormal elements. The urinary urea had fallen to 5,90 G per litre, while the blood urea was 2,60 G per litre.

The second case, a European, was brought to hospital comatose at 8 p.m. Temperature 40°. Died next morning at 8 a.m. Many malarial parasites in the blood. Blood serum contains 1,08 G urea per litre which is not a very high figure considering the gravity of the patient's condition, but he had anuria—no urine being passed during his twelve hours in hospital.

The third case was that of a Syrian, admitted with malaria and fever. The urine contained a little albumen, but no blood or casts. Blood serum contained 4,24 G. urea per litre. The patient died two hours after admission.

The fourth case was a Spaniard, aged 21. He was admitted in a state of coma, with a temperature of 39,7°. History obtained from a friend indicated that he had been ill for 8 days, but was generally robust, though become anaemic. On admission he had signs of meningeal irritation—Kernig, stiffness of the neck, and internal squint—tongue dry and red, liver apparently enlarged, spleen not palpable. Abdomen normal; a trace of icterus. Peripheral blood showed very many schizonts of Plasmodium praecox, about half the red cells being infected. Some of them contained four and five parasites. Blood serum contained 2,40 G. urea per litre. Cerebro-spinal fluid clear, without cellular increase, but with a little increase of globulin (0,40 G. par litre), and 2,12 G. urea per litre.

On arrival in hospital he received an intramuscular injection of 1,20 G. of quinine chloride, and 10 c.mm. oil of camphor. Next morning, temperature 39,6°. Intravenous injection of 0,60 G. quinine, and 10 c.mm. oil of camphor. Towards 11 p.m., temperature rose rapidly to 41,3°. Another intravenous injection of 0,90 G. of quinine chloride. About 4 a.m., coma increased, and at 7.30 a.m. patient died.

These authors have noticed over the past few years that a large number of malarial subjects, even between attacks, show a retention of urea, with or without albumen in the urine.

It will be noted that in the record of these cases, although

there appears to be some degree of kidney retention, no post-mortem appearances of the brain are given, so that the fuller bearing of the uraemia upon the coma can hardly be adequately estimated.

More lately, in the clinical and post-mortem records of the acute and chronic malarial subject, evidences of kidney disturbance are fairly frequent and often severe. For instance, slight albuminuria occurred in 58·3% of 165 cases of Thayer's sub-tertian infections, and this is a fairly consistent finding with other observers.

In 46 cases examined by Dudgeon and Clarke, "42 showed diffuse tubal degeneration and 4 showed no degeneration or swelling of the epithelium of the convoluted tubules. In 3 cases, the renal capillaries contained very numerous infected red cells. Extensive fatty degeneration was found in one case, while scattered fat was recorded on 10 occasions out of a total of 24 specimens examined for this purpose. Free iron granules were not found, except as a very scattered deposit. Oedema and exudation into Bowman's capsule was noted; congestion of the tufts was frequently met with, also haemorrhages and sometimes patchy necrosis. The epithelium of the tubules, especially the convoluted, showed extensive degeneration; the tubules contained degeneration products on numerous occasions.

"Pigment was seen in many situations—in the glomeruli, in the endothelial cells of the blood vessels, in the connective tissue cells between the tubules, in the cells lining the straight tubules, and free in the lumina. Yellow-brown granules were also seen in the epithelium of the straight tubules.

"Changes in the red cells occurred, polychromatophilia, partial and complete haemolysis, and agglutination.

"There are two cases in this series, where the symptoms referable to the kidney dominated the clinical picture. One of these died after 5 uraemic fits, showing post-mortem evidences of acute tubal nephritis with extreme tubal degeneration, and no evidence of chronic nephritis or other organ or cerebral damage to account for death. The other suddenly developed stertorous breathing, rapidly becoming Cheyne-Stokes' type, with post-mortem evidences of acute tubal nephritis."

Ewing records a case of a girl of 17 years with aestivo-autumnal malaria, who after a short period of mild paroxysms, developed the clinucal signs of nephritis—restlessness, vomiting,

oedema of the legs, haematuria, followed by mild delirium, coma, and death. Post-mortem appearances showed the features of acute haemorrhagic nephritis, with enormous massing of parasites in the kidney vessels and coagulation necrosis.

Acute and chronic nephritis, then, have been commonly enough observed in the course of malarial infections, with much evidence to suggest that kidney dysfunction may ultimately dominate and end the picture, but further and more comprehensive observations, clinical and pathological are indicated, to estimate the precise degree and frequency with which it does so in general, and the precise bearing of uraemia upon the coma of malarial subjects in particular.

(9). Portal Obstruction.

The extensive damage to the liver, including the atrophies that occur in progressive post-malarial anaemia, with consequent interference with its circulation so frequently observed in acute and chronic malarial infections, have led Guarnieri and Ewing to suggest that portal obstruction may be sometimes an important factor in the occurrence of coma.

Malarial necrosis of the liver is given as one of the immediate causes of death by Bastianelli and Bignami.

Thrombosis of the portal vein, with secondary liver atrophy and pylethrombosis with rapid formation of ascites, have been not infrequently noted in malarial subjects, (Marchiafava and Bignami), and it is in cases of this kind that severe intestinal haemorrhages may be rapidly fatal, the patient passing through a stage of coma.

Barker's case dealing with this subject points out Flexner has shown that blood serum of one animal will produce focal necrosis in the liver, kidney, and spleen of another of a different species, when injected intravenously. He further showed that these focal necroses could later result in production of chronic interstitial processes in liver and kidney.

His argument is that in malaria there is toxic blood and local toxic irritation in liver and kidneys as shown by post-mortem findings, together with general obstruction in the tributaries of the portal vein, which would alone suffice to materially alter assimilation. Further, irritation and thromboses of stomach and

intestinal capillaries would conduce to absorption of abnormal substances from the lumen of the alimentary canal.

He quotes a case of fatal malaria in a youth of 22 in Assam who at autopsy "The triangular portal spaces present a very ~~curious~~ peculiar appearance. The connective tissue is crowded with cells containing nuclei of the lymphoid type so that the tissue resinis one of the structure of ordinary lymphoid tissue. In the adventitia of portal vein contained apparently in loose spaces are very many lymphoid cells. The portal veins show in section many mononuclear and a few polynuclear leucocytes besides many microphages such as have been described in the splenic veins and in the liver capillaries. No signs of tuberculosis. There are many thrombosed capillaries of liver, and focal necrosis". He says also that Dock has observed a similar perivascular portal infiltration in a very acute case of malaria in a young man. See case of M. Watson's from quartan malaria in Section No II. of Surgical Chapter.

This coma mechanism is, however, probably not so frequent as the other forms, and the suggestion is not supported by the more conclusive proof afforded in the better known varieties of coma, and therefore awaits further investigation.

(10). ~~Diabetic coma.~~

Diabetic coma consequent on malaria is not unknown. It is considered as due to direct damage of the islets of Langerhans by the malarial parasites, or consequent on arterio-sclerosis of the pancreas vessels in the more chronic malarial infections. Naunyn records such a case (detailed in the section on Glycosuria) and Jebens and Jakobson also refer to such cases. Jakobson (quoted by Jebens) describes a case of malaria which died from diabetic coma a week after a malarial attack.

Many pathologists record massing of parasites in the vessels of the pancreas, and not a few record cases of pancreatic haemorrhages and necrosis, with or without glycosuria.

The evidences suggest that further attention to this matter in malarial subjects would reveal a greater frequency of this mechanism in the production of coma than has been hitherto realised.

It will be seen then, that in the study of the several possible mechanisms by which coma can come about as a result of malarial infection, much work remains to be done, as there has been a teniency with some observers to limit their observations too much in given cases to individual vital organs, such as adrenals and kidneys, etc., which have been found seriously damaged, without considering the simultaneous brain changes that may exist.

Points in the diagnosis of coma of malarial origin are:— History or evidence of malaria; finding of parasites in the blood, or of blood changes compatible with that, e.g. anaemia with leucopenia and mononucleosis; enlarged spleen; sudden onset of coma; cachexia; punctiform haemorrhages in skin or face, body, or limbs, and in mucous membranes, sometimes in the retina; if associated with meningitis, then Kernig, stiff neck, and commonly optic neuritis; periodicity of the coma, though few survive a second attack.

The various mechanisms in the occurrence of coma of malarial origin have, of course, a direct bearing upon treatment, and according to the view taken of that mechanism, ~~in the several cases~~, so will the treatment vary.

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CHAPTER IX.

MELANCHOLIA.

Depression is the most persistent feature of malaria. If it is not as frequent in any marked degree as simple confusion in the malarial psychoses as some maintain it is at least second only to confusion in frequency. As indicated in the Chapter on History, its association with malaria has been noticed from the earliest times, and it is remarkable to consider (according to Jones) that our modern word melancholia has its origin in the Greek equivalent μελαγχολικὸς, which was invented by the ancients Greeks to describe the depression so frequently accompanying "the black bile", which is now recognised as malaria. (Cf. Chapter on History).

Sebastian notes (1828) its frequence in association with Wechselfieber, and emphasises the tendency to suicide with it, and the occurrence of phrenitis as a complication. He also records that there were quotidian, tertian, and quartan types of fever.

Passanik, Kraepelin, and Forrester found depression types the most common in their respective collections of cases, and in the author's own collection, the cases classed as melancholics are on the whole most numerous, but it is to be remembered that the difficulty of any one observer seeing all of his cases throughout their course makes a classification of this kind perhaps misleading, and until this is done an adequate classification must remain *sub judice*. Certain it is that a very large proportion of the cases of malarial psychosis exhibit both confusion and depression, either in about equal degree throughout their course, or, more commonly, perhaps, confusion to begin with and a fluctuating depression thereafter during the convalescent period.

Depression may occur during the incubation period being the only evidence of sickness before the initial paroxysm, or it may follow each paroxysm for some weeks, or develop slowly throughout the prolonged course of the disease with periodic exacerbations. In the majority of cases, it occurs in greater or less degree for longer or shorter periods during the course of the trouble, at least in those

not immunised by repeated infection in early life, though in those also it is often represented by a general apathy. While it may occur alone as a mental feature, it is frequently associated with other common symptoms apart from the paroxysm, such as headache, herpes, chiefly of the lips, sleeplessness, incapacity of sustained effort, or maybe by marked general physical weakness, anaemia and low blood pressure.

While in most instances the degree of depression does not exceed the bounds of moderation and is parallel to the physical deterioration, with a small proportion it deepens until it dominates the whole picture, rendering the patient unable to follow his ordinary avocation, and constituting the affective state of melancholia.

Melancholia from malaria has the usual clinical variations. It may be simple, with profound depression, inertia, indifference to food and surroundings; the patient silent, solitary, immobile, miserable, perhaps suicidal, but largely rational. Or the patient may be anxious, agitated, restless, full of dark forebodings, with a particular phobia, or fearful nightmares. Or there may be visual, more often aural, hallucinations, or delusions of self-depreciation, hypochondriacal or persecutory, haunting the wretched victim, and making his life a torment that he seeks at the first opportunity to end. But all these features are secondary, inconstant, accessory to the dominant failure of affective tone.

Melancholia is often associated with the cachectic malarial state, but sometimes occurs in cases where the physical deterioration is not so profound or obvious. In some instances, there is no apparent proportion between the degree of depression and the physical state; and while it generally improves with killing off of the parasite and improvement in the physical state, this is not always so.

Of the writer's 38 cases in this series, 21 were suicidal, 15 making at least one attempt by throat cutting, the others by strangling, drowning, poisoning.

Of the whole series of 181 cases, 34 had suicidal tendences mostly exhibited by threats. 16 actually made the attempt, 1 of whom succeeded (by drowning), the remaining 15 being prevented or

rescued. 10 cut their throats, but survived, the others attempted suicide by shooting, drowning, hanging, jumping over window or down a well, and poisoning. Not all of these appear in the classification as melancholics—some had delusions of persecution and wanted to escape their persecutors, others were confused, though the majority were profoundly depressed and miserable. The majority had complete amnesia for the period covering the suicidal attempt, though some had recollection of the attempt and were either so miserable from their depression, or so afraid of their imagined persecutors, that they preferred at the time, this means of escape. A few describe the period as if they were "in a dream".

A large proportion of these cases clear up—some early, some late, though it is always wise to keep this class of case under observation for a long period after convalescence has begun, as their is a tendency to variation in the degrees of depression in a given case and a tendency to relapse with each malarial attack. As a rule, the depression keeps parallel to the physical condition, though this is not always so.

The first item in treatment, as the alienist well knows, is to safeguard the patient from himself—which means, of course, an institution for the care of such cases, with trained attendants. Next in importance is to secure sleep by tepid baths or hypnotics (lusinal, chloral, bromide, occasionally morphia, etc.); quinine is indicated by the state of parasite infection; and whatever tonics are indicated to restore the physical debility—iron, arsenic, adrenalin, strychnine, etc. Forced feeding may have to be resorted to in a few cases for a short time.

A few of the author's cases are hereafter appended as illustrations:

CASE I.

Melancholia, with determined suicidal attempts.

Gunner, J.N., aged 23.

22:10:18. Jubbulpore. He ran away from some friends he was walking with and threw himself down a well by the roadside; later tried to commit suicide by cutting his throat, involving trachea. Stuporose for 34 hours, and on recovery did not remember anything about attempt to kill himself. Answers questions in monosyllables,

quiet, depressed. Takes his food well, habits clean.

30:4:16. German Measles--16 days in hospital.

28:9:16. Diphtheria--43 Days in hospital.

26:9:17. Malaria, 9 days in hospital. Quinine, 45 grs. daily.

27:9:18. Malaria, 14 days in hospital. Benign tertian parasites found in the blood. Blood Wassermann negative.

17:2:19. History from himself:-Realises he has been mentally ill, but has no recollection of attempts at suicide. No complaints. Answers readily and rationally. Quiet, well-behaved, no depression, eats and sleeps well. Wound well healed.

12:4:19. Home--recovered.

CASE II.

Melancholia, with suicidal threat.

Private H.F., aged 30.

17:12:18. Salonica. Reported sick--very depressed, and complaining of syphilis without foundation. Found with bottle of fuming nitric acid,--stated he intended "doing himself in." Malaria, Aug., 1917, Sept., 1917, Oct., 1918.

9:12:18. Sleeping badly--apprehensive about having venereal disease. Maligmant tertian parasites found in blood.

7:1:19. Improving. Blood Wassermann negative.

15:2:19. History from himself:-Packer. Says he did not know where he was for two or three days in Salonica. Had malaria four or five times. Does not remember saying he had venereal disease, or threatening suicide. Feels all right now. Answers readily and rationally--not depressed.

24:4:19. No depression since last note. Very well. Discharged home.

CASE III.

Melancholia, with suicidal attempt, after prolonged malaria.

Pte. I.D., aged 30.

12:12:15. Salonica. Malaria, 30:9:16. Gunshot wounds of legs and left arm, 14:10:17. Frequent attacks malaria, 30:3:18 and 22:6:18 noted.

23:4:19. Dull, depressed, despondent. Complaint of pain and noises in head. Has delusions of persecution and hallucinations of hearing. Uses forcible language. Emaciated.

12:5:19. Quiet, well-behaved, reticent, appears depressed.

19:5:19. Admits he still hears voices, but says it may be all a mistake. Blood Wassermann negative.

9:6:19. Improving slowly—hallucinations not so troublesome and says he feels he is getting better.

18:9:19. Less depressed—more interested and communicative.

10:8:19. Not hallucinated at present, mildly depressed, but much improved on the whole.

29:8:19. History from himself:- Family history negative. Denies venereal disease and alcoholic excess. Says he was sent to Mullingar for demobilisation, Feb., 1919, but got attack of malaria, became depressed and cut his throat. Denies having delusions or hallucinations now, but acknowledges having had them. Feels much more self-confident now, sleeps well and has good appetite. Scar on throat well-healed. Does not smile quite so freely as he might.

3:10:19. This man has varied a good deal—improving on the whole, but occasionally dull and depressed for a few days at a time, and not inspiring confidence in allowing him out of observation. Sent to civil asylum, where after a lengthened period, he may recover, with or without some mental deterioration.

NOTE: In this case, infection with malaria lasted about two and a half years before mental breakdown occurred, while his wounds of legs and arm in Oct., 1917, may conceivably have contributed to this, they are sufficiently removed in time (one and a half years) to suggest that malaria was at least the immediate and principal cause.

CASE IV.

Melancholia, with fear of committing suicide.

Pte, A.R., aged 30.

24:10:18. Salonica. Afraid at night, insomnia. Depressed, shaky on parade, rational, orientated, not confused. Has had home worries. Slight anaemia, debilitated. Spleen tender, not palpable. Knee-jerks exaggerated.

5:11:18. Malarial relapse, blood films show rings. Irritable. Admits fear of attempting suicide, and gave razor to ward sister; likes people beside him. Dreams, hallucinated, fear of going off his head.

20:11:18. Lacks self-confidence. Otherwise better.

15:1:19. Convalescence maintained, but hardly to be trusted out of observation. Blood Wassermann negative.

History from himself:- Tinsmith. Health good pre-War. Family history negative. Denies alcohol excess, and venereal disease. France, Sept., 1915. Not under fire. Salonica, Nov., 1915, under fire—nervous, not wounded. First attack malaria, Nov., 1916, and has had quite two dozen attacks since then. Has been off duty as long as 14 days at a time due to this, but mostly in afternoon, or a day off at times of attack. Latterly, Oct., 1918, nervous, giddy, run-down, useless, depressed. Aching joints. Asked about harming himself—says he dreamed of another man who actually cut his throat, and could not get this out of his mind, so asked sister to remove his razor.

10:3:19. Pale, thin, mentally normal. Insight and orientation normal. Free of depression. Knee-jerks brisk. Pupils normal.

6:6:19. Very well. Home, recovered.

CASE 7.

Depression, with anterograde and retrograde amnesia.

Gunner, R.G.A., aged 34.

12:8:18. Salonica. Aural hallucinations of 14 days' duration. Dull, silent, not confused. Complaint of headache. Wandered away early one morning and returned same night, unable to give an account of his whereabouts, but said he had severe headache all day. Spleen enlarged and tender. Blood Wassermann negative.

History from himself:- Single, family history negative. France, Aug., 1915. Wounded Aug., 1916, left temple—remembers all that happened. Salonica, March, 1917. Malaria, Oct., 1917—numerous attacks since, always with headache. Got worried, run down, depressed. Does not remember wandering away. Thought he heard people talking about him, but realises now it was fancy.

Amnesia of antero- and retro-grade type. No suicidal tendency.

29:1:19. All right now, but for headaches. Insight restored.

6:6:19. Recovered but for occasional headaches.

NOTE: The head wound here was not severe, and mental breakdown occurred two years after it, and after one year of recurrent malaria.

CASE VI.

Melancholia, emerging from confusion. This frequently occurs after weeks or months. Benign tertian infection (Porot and Gutmann).

April, 1917. Serbian patient, gives a good account of himself, up to going into hospital in Salonica, after which he remembers nothing.

Blood contains benign tertian parasites. He is confused, disorientated, and has no insight into his condition. He is anaemic, emaciated, and has fine tremors of tongue and fingers. He has the attitude of an exhausted melancholic; he is sad, anxious, pre-occupied. He complains of nightmares that increase his anxiety. He has suicidal ideas, and requires supervision.

During three months observation, he has been calm for the most part, with some periods of restless anxiety, and has made one attempt at suicide. He has several times refused food.

During the last month, he has been less melancholic, and looks more animated. There is mild stupor; eyes somewhat watery. Appears to be on the way to cure.

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CHAPTER X

Confusional Insanity.

Confusion is probably the commonest single feature of the malarial insanities. Some observers—Régis, Porot and Gutmann, Mesnard,—maintain that it is the initial feature in every case, and that all the other clinical varieties of psychosis develop from it. Forrester found it the most frequent feature in his 116 cases of psychoses in malarious soldiers. This has probably been so among soldiers on service, but the writer has seen severe depression develop slowly in the course of malarial infection associated with general debility without there being any evidence of mental confusion. The difficulty in coming to a decision about a point of this kind arises from the fact that very few observers, either alienists or practitioners, or army officers, have the opportunity of seeing many malarial mental cases from start to finish. Much valuable information is lost from the changing of hands. Certain it is, however, that confusion and depression are by far the two most outstanding features of malarial mental states, sometimes occurring in the one individual at the same time, sometimes depression slowly developing alone, or sometimes depression severe or mild following upon confusion.

The commonest form of confusion occurs during the febrile attack, and generally clears up during the sweating stage, or it may drag on a little longer. It is a kind of very mild delirium, without total loss of consciousness, and is often accompanied by fleeting hallucinations of sight or hearing. The patient talks quietly at intervals to himself, or chatters incoherently and continuously, sometimes getting out of bed and wandering around quietly. The psychomotor agitation is moderate.

A severer form of the same thing is where the patient is rather more confused, agitated, and hallucinated. He appears to be living in a dream, and sometimes goes through the movements of his occupation, or becomes violent, argumentative, impulsive, or ill-tempered. It is still possible to arrest his attention, however

even if it cannot be held. If he is resting in bed, and is addressed in an ordinary voice, he may not respond. His eyes are fixed on an imaginary being, with whom he converses. If addressed more energetically, he turns, astonished, but dull as if half-asleep, answers perh perhaps correctly, recognizing you. His reactions tend to be negative or automatic. Régis records the sensations of a malarious medical friend, who had many febrile attacks while in Madagascar, He (Dr. Ponty) indicates that if bruskly challenged during the course of the mental preoccupation during a febrile attack, or soon after, he had strong feelings of resentment. This is of interest from the medico-legal standpoint.

Though amnesia often covers the period of confusion, frequently enough, especially during the febrile period, it is remembered and related as a dream. The state of confusion may occur with each febrile attack, with perhaps tertian or quartan periodicity, or it may occur with irregular intermittency, as the febrile paroxysm may do, or it may entirely replace the fever with temperature normal or sub-normal, just as any other clinical symptom or sign may do. Where it occurs in the early stages of infection, it is generally associated with fever. In the apyretic intervals, the patients may be quite clear mentally, or in a mildly soporific state, but quite rational though dull.

The conduct and talk of the patient while in this state may closely resemble drunkenness, all the more so, if, in an interval of depression, a little alcohol has been taken as a stimulant. This aspect of the subject is dealt with more fully in the Alcohol and Medico-legal Chapters.

It is necessary to emphasise the occasional fleeting quality of malarial mental confusion, which, if associated with impulsiveness or persecutory ideas, will become of medico-legal significance. Confusion of this kind may last only a few hours, or for a day, disappearing with the defervescence of parasite sporulation. And it is this fleeting quality which, especially if associated with conduct that brings the patient within the reach of the law that is so difficult for judge and jury to realise. The more chronic forms of mental confusion occur generally during the afebrile periods, are associated with cachexia and are characterised by being less fleeting

in quality and maybe associated with a prolonged period of some degree of stupor or mental dulness or automatism. The patient often shows general physical deterioration, is often anaemic, and asthenic, but on the other hand he may appear robust. Disorientation in time and place, lack of interest in surroundings, depression, irritability are prominent mental characteristics; perhaps violent loss of temper or somnambulism may be added features. In some cases, periods of excitement, alternating with periods of depression, occur, and a fixed idea may emerge, perhaps developing into a secondary systematised delusional state. These qualifications, however, take us nearer types of insanity defined further on.

With suitable treatment, or sometimes simply with removal to a colder climate and good surroundings, these cases generally steadily improve, and from periods varying from a few days or weeks to a year, generally show no relic of the former disability. But in severe cases which tend to remain chronic the clinical picture changes. The physical condition improves, certain functions survive, such as locomotion, relative orientation, ability to perform simple acts, instinctive and familiar; but initiative is lost, conscience is enfeebled, power of judgment and criticism deteriorates, abnormal suggestibility, irritability and ill-temper remain. Asthenia and apathy may persist and be prominent. The condition tends towards dementia and chances of recovery diminish with the duration of the psychosis.

When revovery does take place, it is commonly marked by partial or complete amnesia, principally for the period of psychosis.

Excitement when it does occur is mostly at the beginning, or by pressure of circumstance, or during fever, and is usually transient According to Besnard, there is less tendency, as in many severe toxic states, to true alteration of the sentiments, affections, ethical and moral functions. Lucidity, familial emotions, normal emotions, return as the confusion abates. There may be periods of anxiety, peevishness, ill-temper, impulsiveness.

The course of the illness is often accompanied by visceral trouble, such as headache, backache, neuralgias, indigestion, vomiting tachycardia, etc. There is usually, but not always, a striking parallelism between the physical and mental states. As cachexia

improves, so does the psychosis.

A small proportion of cases of confusion develop into types of dementia praecox, but these are dealt with separately under that heading.

In view of the pathological finding, and the ante-mortem clinical observations associated with them, it is easy to theorise about the probable cause of the curiously fleeting quality of malarial confusion. It is easy to imagine of young parasites that have sporulated in the cerebral capillaries, irritating the brain tissue during the febrile stage, and easing off during defervescence to recur with renewed tertian sporulation. Or perhaps, as Ewing maintains, a group of capillaries have been blocked, inducing temporary deficiency of blood supply of parts, with interruption of association paths for the time being, and consequent loss of continuity of thought, in the milder cases, and intermediate states down to coma in the more severe. Or where vessel blockage, additional anaemia by haemoglobin deficiency, and toxic blood state have lasted too long, or perhaps an odd punctiform haemorrhage has occurred, permanent damage has been done to brain cells, axis cylinders and association paths, with general mental enfeeblement as a permanent result. This sequel to confusion is dealt with under the heading of Dementia.

In the diagnosis of malarial confusion, there are some differential points of importance:

1. There is, of course, the evidence of malarial infection principally the finding of the parasite (see Chapter on diagnosis).

2. There is a tendency to sudden onset and fleeting quality, sometimes of tertian periodicity, simultaneous with the febrile attack.

3. Some observers (notably Porot and Gutmann) maintain that it is the initial stage of all malarial psychoses, and that all other forms develop from it. In any case, the course of the confusion is, if prolonged, very irregular and often very intermittent. A case discharged as cured may return in a few weeks with a recurrence.

4. General weakness and depression are often associated with it.

5. Somatic troubles are very frequent accompaniments, in

the form of severe headache, indigestion, neuralgias, neuritis, giddiness, dysarthria, tremors, nervousness, fits, etc., and, of course, enlarged spleen.

After an early stage of confusion, the patient may have almost any lesser mental or nervous departure from the normal—amnesia, nervousness, hypersuggestibility (hysteria), neuralgias, astasia abasia (one such case recorded in the neurological section), psychasthenia, neurasthenia, etc.,

A few varieties of cases of confusion taken from the author's collection, and one from Porot and Cutmann, are appended as examples:

CASE I.

Mental Confusion, with hallucinations and anxiety state, ending in cure. (Porot and Cutmann).

P.D., aged 30, arrived from Salonica, Feb., 1917.
Diagnosis: Mental Confusion of malarial origin. Agitation and vertigo. Nystagmus. Alternation of agitation and calm.

He looks uneasy but is able to converse. He says that he became conscious on the boat, and that he has had malaria. He is disorientated, anxious, says he was made to drink wine with poison in it. He sleeps badly, sees lights, but does not know who produces them; fears his neighbour in the next bed would strangle him.

No actual malarial attack noted, but ring forms found in the blood.

After 15 days, he is much better. Has nocturnal terrors, and sleeps badly. He has visions of animals and soldiers who assail him. He is not always clear about his surroundings. After a month he begins to regain his memory.

Says he was employed on the railway and began to be troubled with headaches at the beginning of Dec., 1916. In an English hospital, he heard a certain George say: "That fellow's mad; he should be sent to the French to be beaten". He was then made to drink poisoned wine which deranged his head. He vaguely remembers being several times delirious, and being stung more than 15 times in the back; he had an attack of delirium on the boat; before this attack he heard the voices of bad men talking to him. He was

terrified for them and thus explains having torn his clothes.

It is now some days since he heard the voices, and wonders if he has not been dreaming.

Marked tremors of hands.

By April there is marked improvement. Sleep normal. Alluding to his hadlucinations, he says they appear to him as a dream.

Tremor persists and is accompanied by slight tachycardia. When asked why he trembled, he says he is afraid of appearing anxious.

Leaves hospital cured after 8 months—even of his anxiety. No mental sequelae.

This man was very temperate.

CASE II.

Confusion, with subsequent amnesia.

Pte. C.R., aet. 46.

26:12:18. Salonica. Confused, inconsistent in statements, depressed. Refuses to stay in bed at night because something in his head worries him and he feels he must get up and walk about. Does not sleep. Has home troubles.

2:1:19. Insomnia, restlessness, amnesia for recent events. Not confused and is well orientated. Debilitated, anaemic. Spleen tender. Deep reflexes absent. Babinski present both sides. Pupils sluggish. Malignant tertian ring parasites found in blood. Blood Wassermann negative.

15:2:19. No complaints now. Simple, facile, but no other mental abnormality. Eats and sleeps well now.

20:2:19. History from himself:- Labourer, health good pre-War. Family history negative. Teetotal. Denies Venereal Disease. Had a good deal of malaria in Palestine and Salonica, and felt queer in the head latterly. Not under fire. Is emaciated, and looks tired mentally and physically. Knee-jerks normal. Pupils sluggish. Gives a fairly clear account of himself, but memory poor, and he has obvious difficulty recalling his movements during the War period.

8:3:19. Home feeling pretty well, but memory and general activity not quite back to original level.

CASE III.

Confusional Insanity, with early symptom of wandering away. Recovery.

Pte. R.C., aet. 30.

18:6:18. Salonica. Attack of malaria (relapses with 24 hours temperature) and found wandering about the camp saying one of the corporals was looking for him, and was going to shoot him. Told M.O. he had opened a letter of his from home, and, when asked how he knew, said he heard voices telling him so. Expression staring, preoccupied, depressed. Evasive in reply to questions about voices. Perception normal. Memory not so good. No disorientation. Auditory hallucinations—voices tell him he has venereal disease. No visual hallucinations. For the past 3 days, he says he feels that people are against him. Had frontal headache. Physical examination negative except that spleen is enlarged and tender.

19:6:18. Slightly confused. Suspicious reticent. Recent memory repaired. Perception normal. Hallucinations—answering voices outside hut. Sleeping badly. Quinine, 40 grs. in 24 hours. Blood Wassermann negative.

11:7:18. Says he feels all right now, and realises imaginary nature of hallucinations.

11:9:18. History from himself:- Family history negative. France, Jan., 1915. Had such malaria from 1916. Took a little alcohol, which he thinks upset him. Was off 6 weeks, but often had attacks and carried on. Answers readily and rationally. Fully orientated and memory good. Eats and sleeps well. Had several headaches and began to hear people talking about him. Now rational, free of hallucinations, weight normal, feeling and looking well. Case recovered.

CASE IV.

Confusion, with manic depressive features. Recovery.

Pte. W.G., aged 24.

14:6:18. Salonica. Admitted with recurrent malaria. Temperature, 102·4°F.

Quite confused: will do as he is told, but will not speak or answer any questions. Expression not blank, and seems to take a certain amount of interest in what is going on around him. During

examination, was emotional and wept. Spleen enlarged. Reflexes exaggerated. Blood film negative for parasites, but leucocytes suggest malarial infection. Quinine, 20 grs. intramuscularly.

24:8:18. Confusion gone, but signs of hysteria.

29:8:18. Treated by suggestion, and has responded. Can talk quite well now.

27:9:18. Suidenly became abusive, and adopted threatening attitude towards M.O. Blood Wassermann negative.

21:11:18. Mentally well, no more malaria.

30:1:19. Continues well.

3:3:19. Discharged home, recovered.

CASE 7.

Confusion, tending to stupor, with periodic impulsiveness, and resistiveness; progress towards dementia. Prognosis doubtful.

Pte. J.M.C., aged 26.

30:1:16. Admitted to hospital in dazed, stupid condition. Does not answer when spoken to, but understands what is said. Temperature, 99°F.

1:2:16. Throws utensils on the floor, or out of the window, when finished eating. Reflexes normal.

2:2:16. Sullen, broke several pains of glass.

3:2:16. Isolated. Looks ill and depressed. Tongue tremors. Knee-jerks normal. Never under fire. No ankle clonus. Plantar reflexes flexor. Pupils normal.

Exhibits marked toxic confusion. Great clouding of consciousness. Perception much impaired, and attention entirely taken up subjectively, so that he does not attend to questions or requests. Restless, sways arms about, suggesting aural hallucinations. Starts suddenly at times as if hearing voices.

26:2:16. Bewildered, acutely confused. Restless. Sways arms about, mutters to himself. Impulsive—smashing dishes, and very resistive. Blood Wassermann negative.

18:3:16. Rigor: temperature, 103°F. Pulse 136. Respiration, 32. Physical signs negative. Malignant tertian parasites in blood. Temperature came down during the night.

29:3:16. Temperature normal since above date. Restless,

sleepless, but not impulsive of late.

1:5:16. Much less restless, and confused. More stuporose. Completely silent, though responding to requests slowly and after repetition. Up.

7:5:16. Rigor again. No improvement in mental condition. Stupor and silence.

24:5:16. Slight jaundice, vomiting, sweating, and sub-conjunctival haemorrhage.

26:5:16. Rigor. Quinine 5 grs. four-hourly.

4:6:16. Blood shows numerous malarial parasites. Polymorphs, 65%: eosinophils, 0·5%.

19:6:16. Rigor. Liquor Arsenicalis and quinine.

21:7:16. Rigor. Silent and stuporose.

9:8:16. Rigor. Liquor Arsenucalis and quinine.

14:8:16. Temperature settled.

12:9:16. Discharged not improved to civil asylum.

NOTE: This patient showed no improvement in 8 months in a military asylum, and was discharged to a civil asylum for further treatment. Prognosis doubtful.

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CHAPTER XI

Delusional Insanity.

In the 21 cases of delusional insanity noted in this series, the delusions were associated with confusion or depression or both. The majority emerged from a state of confusion, able latterly for the most part to talk rationally, but exhibiting some mental enfeeblement, lacking insight, and retaining a delusion or delusions generally of a persecutory, depressiatory, or hypochondriacal nature. They were of course all soldiers who had broken down on service under war conditions, and fifteen of them exhibited delusions of a persecutory type, and six of them attempted suicide by throat cutting, one of whom was also homicidal. In addition to these six cases, one was potentially suicidal and homicidal, and had to be specially watched. Five cases were in military mental hospitals for at least a year, and one for as long as nineteen months. All of these were sent to civil asylums, and would certainly still take a long time to recover, if, indeed, they would recover at all. Depression was a common feature along with general physical deterioration. A few showed hallucinations generally of auditory type, and periods of excitement occurred in a few ~~instance~~ instances.

The delusions were various—that the patient was being laughed at, jeered at, that men were lying in wait for him to do him in, that poison was put in his food, or that his mind was being influenced, and such like. The result was he became reticent, sullen, secretive, evasive, perhaps suicidal or homicidal or both.

Mesnard records that he has seen delusions of persecution and jealousy following upon malarial infection and that they ultimately cleared up.

Régis records a case of Ponty's in which the patient emerging from malarial delirium retained the delusion that his wife and children were dead in France, and kept on thanking the doctor for his visit of condolence. Fixed ideas of this kind, may form the starting point of a systematised delusional insanity.

While it is true that these cases for the most part were associated with confusion at an earlier stage of development,

and depression at some part of their course, even to the point of suicide in some cases, the dominant feature was the persistence of delusions mostly, often, as noted, of persecutory type. It may be that the suggestion of war acting upon the debilitated soldier gave colour to the delusions. As the confusion abated, a delusional state emerged, and dominated the psychic field. And while there was frequently disorder of affective tone, it was not the primary feature, but rather secondary to the persecutory ideas, inconstant, accessory, and even the suicides were more apparently attempts to escape the imaginary persecutors. Thus these cases which also had a notable factor of depression are to be distinguished from simple melancholics of primary affective origin.

Those that cleared up within a year, as did the majority, took rather longer to do so than the purely confusional cases or even than the cases of simple depression, which generally yielded with improvement in the general physical condition of the patient.

It is of interest to note that while the majority were well enough to go home in from six to twelve months from the beginning of the psychosis, it does not follow that they were restored to their original health, and able to continue at their pre-war vocations.

The following five representative examples of delusional insanity are chosen from the writer's collection.

CASE I.

Delusional insanity, following benign tertian infection.

Pte. A.C., aged 30.

30:4:18. Salonica. Admitted to hospital with recurrent malaria. Complains of headaches, and he has the fixed idea that persons unknown are saying his wife is dead, and they are defaming her character. He had been drinking for some days previous, and confusion that developed after admission was attributed to this, with a malaria attack supervening. Took malaria first in Sept., 1916, and has had 24 attacks since then, and has been four times in hospital. Last attack was ten days ago, and he had three days off duty with it. Temperature 103·6°F. Blood film shows benign tertian parasites. Spleen not palpable. Heart and lungs negative.

4:5:18. Nervous, headaches, flushed, nervous movements of

hands. Has fixed idea that persons are saying his wife is dead, and that they are defaming her character.

9:5:18. Appears exhausted from malaria.

10:5:18. Still hallucinated and depressed, and worried by noises; for several years has heard men accuse him of masturbation.

27:5:18. During the last few days, he says he no longer heard voices for a long time. He seems suspicious, and is very unreasonable about being sent to hospital. Blood Wassermann -ve.

History from himself: He enlisted in July, 1905, at the age of 18, and was three years in South Africa, and in Malta from 1910-13. Time expired 1914. Called up and sent to France, 1914. Swollen legs, 1914. Frost bite, 1915. Shrapnel wound of leg, 1916. Salonica, 1916. Has had several attacks of malaria, and was waiting to go home under Y scheme, when malarial attack came on after a few days drinking. He explains the delusions about his wife in this way. He has a brother, A. (same initial as himself) who was serving in France while he was in Salonica. Their wives have the same name. His brother's wife went wrong with drink and men, and reports came through to him in such a way as to make him suspect his own wife whom he now knows to be all right. He now gives a clear account of himself and shows no sigh of mental abnormality. Pupils normal. Knee-jerks slightly exaggerated. Orientation normal. Fingers and tongue a little tremulous. His insight is quite restored, and he feels and looks well enough to go home.

CASE II.

Delusional Insanity—progress not good.

Pte. C.S., aet 27.

25:6:18. Documents show that he has been in hospital since Sept., 1917, and during all these months has been expressing ideas of persecution, making unfounded and trivial charges against orderlies complaining of food being tampered with. He broke parole.

History from himself: Saddler. Single. Always in good health pre-War. Moderate with alcohol. No venereal disease; no fits, no head injury. Family history negative. Enlisted at 18, in 1908. India, 1911. France, Dec., 1914, under fire, not wounded. Salonica, Sept., 1916. Several attacks of malaria from Aug., 1916. Statements

about why he was sent to hospital are vague and indefinite, and he is very reticent about it.

He says he felt he was not being squarely dealt with at his regiment, but were putting him through for promotion. He thinks too that he was sent to hospital to get a knowledge of quartermasters' work in hospital.

Physically: Good, except for anaemia. Blood Wassermann negative.

Mentally: He gives a fair account of himself, but has no insight into his condition. He is vague and reticent about his delusions, but says "I know the scheme they are working, but will keep it secret till I get back to my unit". He seems to think that he is not in hospital as a patient, but for instruction in quartermaster's work. No hallucinations elicited. No marked emotional disturbance, but he is reticent, and evades all questions bearing on his persecutory ideas. Orientation normal, memory good.

20:7:18. To-day he made a curious complaint about another patient, and handed in a manuscript charge sheet against him for using bad language to an N. C. O.

10:10:18. Still delusional. Has not improved appreciably mentally, although he is better physically. Sent to civil asylum.

CASE III.

Prolonged delusional insanity.

Pte. F.R., aet. 40.

27:4:18. Salonica. Admitted to hospital for observation on his mental condition. He wandered from the camp into Salonica "not knowing why he did it", and since being brought back, his mentality has been questionable. He has "spiritualistic ideas".

On admission: clearly orientated, quite frank, and willing to talk. No physical complaint.

Physical examination negative, urine normal.

2:5:18. He has noticed that men around him have been talking about him. He is under the impression that there is something that these men want to know, but they would not ask him about it. They would not admit to him that they were talking about him. Early one morning, he seemed to hear something which said "Come", and he went out, and wandered towards Salonica. Then he heard a sort of

whistle which seemed to guide him, and he was in a state of "half-conscious and half-not". He never thought whether he was right or wrong. H e was asked by the sound of this whistle "What do you want?", and then it said "Take". He continued towards Salonica, being guided by the whistle. He bought a packet of cigarettes from a Greek. The whistle said, "Take them back", and he gave them back to the Greek, without asking for a return of his money. At times, he has seen a vision, the first time being in Oct., 1912.

25:6:18. Says he feels better, and is getting clearer of noises in the head. He heard the whistle last night, but only for a second. Otherwise he feels "well in everyway".

2:7:18. He has improved. He realises his condition somewhat, and although he still hears sounds, he tries to fight the condition, and does not worry over them. Blood Wassermann negative.

11:8:18. Says he felt run down lately. Still hears the whistle occasionally, and it seems to say "Come on" to him. He is slightly depressed, but denies ideas of persecution lately, and has noticed no-one talking about him. Insight not complete. Fully orientated, and memory only fair for recent events.

History from Himself. Was at school until 13 years of age. Standard V. Glass-worker. One sister nervous—otherwise family history negative. Health good pre-War. Occasionally took alcohol to excess but not often. Denies venereal disease. Married, and has 4 of a family. Enlisted, Jan., 1915. Salonica, Aug., 1916. Never under fire. Had malaria several times, but did not report sick. Began to feel weaker. Slight headache and sleepless at nights. Got strange ideas into his head—thought people were talking about him. Strange dreams. Wandered away. Remembers dimly being in Malta.

Physically, much thinner than when he enlisted. Physical signs of heart and lungs negative. Knee-jerks exaggersted. Pupils normal.

Mentally: Memory for recent events not good. Orientation in time and space barely normal. But insight returning as he is beginning to realise his mental condition has been abnormal. Remembers hearing whistle in Salonica, and believes it was imaginary, but heard it again in the train coming to hospital. He says he understood it to mean "Stop" to his thoughts running on Salonica. He gives

a connected account of himself, except for a period relatively blank towards the end of his time in Salonica, and in Malta. He is quiet, well-behaved, eats and sleeps well, and feels he is improving.

April, 1919. He has slowly and steadily improved both physically and mentally. His insight is restored but he admits he still at long intervals hears the whistle, but that he takes no notice of it. He has been working well in the ward, and is to be discharged home presently.

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CHAPTER XII.

Clinical Dementia Praecox.

It has been seen from the chapter on Pathology that in fatal cases of malaria involving the nervous system, degenerative changes have been found involving every element of the central nervous system, cell body, filaments and neuroglia tissue. Intermediary stages of degeneration with widespread lipoid decomposition deposists in the brain cells have been seen, and the process has been traced to complete cell sclerosis or obliteration. These changes are very similar to those found in ordinary dementia praecox, with some differences, a notable one of which is emphasised by Dürck, namely the occurrence in cerebral malarias of cell knots composed of proliferated glia cells, often combined with red blood corpuscles. To these he has given the name of malarial granulomata, and indicates that they occur chiefly in the white substance.

Classical (ordinary) dementia praecox has a very wide range of clinical variation, but is mainly characterised by a weakening of attention, judgment, associative thought and mental activity generally, of will-power and creative ability, of emotional reaction to environment, and by a loosening of that inner unity of the psychic life that goes to make personality. Clinically it is characterised broadly by immobility, failure of concentration, emotional dullness or ataxia of the feelings, evidences of weakened will-power, depression, catatonic stupor and excitement, flexibilitas cerea, negativism, stereotypy, automatic obedience, hallucinations, mostly auditory, restlessness, impulsiveness, and incoherence of thought and action going on finally to complete dementia.

The pathological changes associated with these clinical features, so far as they have been worked out, comprise wide-spread disease of the cell elements of the cerebral cortex, especially of the second and third small celled cortical layers; amoeboid hyperplasia of neuroglia, accumulation of glia cells round the nerve cells, and morbid new formation of fibres encircling them. (Alzheimer). The probable emphasis of distribution of these changes

in the frontal lobes, central convolutions, and temporal lobes of the brain would support the current views of the structural basis of the psychich mechanisms mainly injured in this disease. It is these small-celled layers which are mainly credited with the psychich elaboration of external experience, and the harmonious unification of psychich activities; and it is main these layers that are found mainly involved, whereas the deeper cortical layers representing the lower psychic mechanisms are comparatively slightly damaged at least till late in the disease. Furthermore, Mott has noted, in addition to these gross evidences of degenerative change in the neurons and neuroglia tissue, biochemical changes suggestive of defective oxidation processes, such as excessive deposit of lipoids, basophil chromatolysis, and disappearance, partial or complete, of Nissl's granules.

These changes affecting the intercalary cells, which are credited with playing an important part in the formation of the synapse in all systems of neurons and in the cerebellum, would explain many of the symptoms, fleeting and permanent, of dementia praecox. Moreover, he states that these defective oxidation changes arising from toxic states may be taken as evidences of hypofunction leading to suspension of the neuronic function, giving rise to the variation in clinical pictures according to intensity, remission, and distribution. Where suppression of function of a neuron has taken place, no remission can occur, and there is a final residuum of weak-mindedness.

Now some cases of clinical dementia praecox recover, and some cases of confusional insanity present a clinical picture of dementia praecox and recover completely. In view of the morphological and biochemical changes noted in the first paragraph of this chapter, associated as they are in cerebral malarial infections with vessel blockage (implying insufficient blood supply), toxic state of the blood, haemoglobin deficiency (implying defective oxygen supply), it does not stretch the imagination unduly to suppose that these cases of clinical dementia praecox of malarial origin are due to a hypofunction of neurones which would exhibit the biochemical changes already detailed.

Many of the cases of clinical dementia praecox are associated

with definite infections, such as influenza, enteric fever, pneumonia. Malaria, already found to produce in nerve tissue all the degenerative changes produced by other infections, is apparently no exception in producing clinical dementia praecox. It produces biochemical changes in the neurones generally, and it is to be expected that a corresponding hypofunction varying with the clinical picture would occur, especially, if concentration of damage were upon the small-celled layers of the cortex, and intercalary cells, and that this would account for the fitfullness and even periodicity of the mental symptoms. Mott, emphasising the importance of the involvement of the intercalary cells in the variation of mental symptoms, says:

"The affection of the stellate intercalary cells which enter into the synapse, and the evidence I have adduced of the importance of these cells in connection with oxidation processes productive of neural energy, and transmission of nervous impulses, suggests that a hypofunction or suspension of function of these neurones would lead to a synaptic dissociation, and thereby account for psychic dissociation and the coming and going of symptoms; or where there is permanent morbid change, to a suppression of their function with permanent dissociation.

"We have thus two morphological conditions which will account for fundamental disorders and the nature of these disorders will depend upon the cerebral structures affected whether in such a way as to produce suppression or suspension of function. Naturally, the nature of mental disorders will also depend upon the localisation and the relative intensity of the hypofunction, suspension, or suppression of function of the neurones."

When we have added to this, the fitfulness of malarial periodicity, with its rapid focal massing of parasites, toxin supply, capillary blockage, haemoglobin deficiency, red cell diapedesis, we have all the morphological and toxic basis required to explain the variation in conductivity and continuity as well as the interruption of cerebral nerve paths, and the mental dissociation that we find clinically.

Dementia Praecox associated with traceable toxic states such as malaria, hardly differs clinically from true dementia praecox, and it is often difficult or impossible to dogmatise about prognosis, but

in a malarial subject who starts off with confusion which develops into the features of dementia praecox, the prognosis is generally good, as it is in most similar cases associated with traceable toxic infections.

As shown above, the writer has a record of 14 cases of this kind including case three of the medico-legal series. It may be that most of these were confusional cases seen at a stage when they had taken on a dementiapraecox form.

A few case histories from the author's collection, and one from Porot and Gutmann are given as examples.

CASE I.

Confusion taking on Dementia Praecox features.

Pte. F.F., aged 21.

20:8:18. Salonica. Admitted with malaria. M.T. parasites in blood.

11:9:18. Quiet all day, but apparently taking no notice of his surroundings. Speaks in low voice. No negativism, apraxia, or catatonia. Sits in dejected attitude, moving head from side to side. When questioned replies slowly after long pause. Dizzy, and sees all sorts of funny things.

12:9:18. Simple, mildly confused, cannot answer questions. Appears to get lost when asked questions; little interest in surroundings. Motionless in bed, vacant expression. Anaemic—fairly well nourished. Spleen and liver normal in size. Pupils equal, react sluggishly to light.

14:9:18. Still confused. Blood Wassermann negative.

25:9:18. Better—able to do a little ward work, but very slow.

Gives following history:- He had an attack of nervous debility in 1916 before joining up. His mother has had a nervous breakdown. Has had no head pains. Feels worried and cannot understand all he sees, it seems so strange. The people that talk seem to be all over. He sometimes sees them—they look like ordinary people, and are both men and women, but he does not know any of them. They say all sorts of things—watch him burning. During examination he looks nervous and worried and keeps staring about the room. Slow in response. Marked difficulty of speech, and a momentary stutter.

28:8:19. Brighter.

25:10:18. Malta: worse—speaks in whispers, and has to be forcibly fed. Stands for hours at the foot of his bed. Catatonia,—dementia praecox type.

15:12:18. Improving. Speaks more freely, and shows more interest in things that happen in the ward. Realises that he has been very ill lately, and gives sensible answers. Helps in the ward and asks to go out for walks.

28:1:19. Answers readily and rationally, and is correctly orientated. Tends to be excitable and lacking self-control, but has recovered from his confusion.

3:4:19. Physicall y satisfactory, and has kept well mentally since last note. Discharged home recovered.

CASE II.

Confusion developing into paranoid dementia praecox.

Pte. J.C., aged 27.

28:8:18. Salonica. Admitted from C.C.S. where he had been brought from police camp. On night of 24:8:18, Sergeant-major found himemotional, and patient told him he was under sentence of death for abusing himself. The man who shared police camp bed with his stated patient had said to him "Do you see two men—they are after my blood?" There were no men there. An interpreter stated that he had been very strange since the 22nd, and that he would not answer remarks and that his memory seemed to be wandering. At Aid post, 24:8:18, he was found dull and would not answer questions. On 25:8:18, he was less dull, and gave no evidence of depression. Temperature normal, and he ate well. On admission—of an antagonistic type and insists there is nothing wrong with him. Attempted to get out of bed several times. Sometimes aggressive.

Examination:- He has become very antagonistic in behaviour. He refuses to assist in the work of the ward, but wants to gamble. He gets depressed occasionally, admits he has worries, but will not say what they are. Continually insists that he is quite well. It is probable that he will give trouble sooner or later.

4:9:18. This morning gave definite signs of having aural hallucinations, in that he wanted to know what all the men from his

unit were doing outside the ward. He said he had heard them ever ~~sin~~ since he came in here, but had never seen them.

12:9:18. Still hallucinated and at times depressed. He tells that men of his unit are about the ward speaking of him, and that one man reads his thoughts. Blood Wassermann negative.

16:9:18. History from himself. Miner. Single. Family history negative. Alcohol moderate. Pre-War health good. Salonica, September, 1915. First attack malaria, July 1916. He says he is troubled with pains in the head and does not sleep well, and often feels confused. Men began to talk about him and he got worried.

M.O. of C.C.S. notes 27:8:18:- Man complains of head pains, and intermittent bleeding from the nose, and sees specks before his eyes at times. States that he hears people speaking bad about him at night. He answers questions fairly readily. He has had malaria four times. M.T, parasites in blood.

7:9:18. Sent home from Macedonia as confusional insanity, but may be paranoid D.P.

21:9:18. At sea, patient ran out of his ward, and jumped overboard in clothes and heavy boots, but being a good swimmer was picked up after a quarter-of-an-hour's immersion. He offered no resistance to his rescuers and was apparently quite calm—merely remarking as he got back to the ward "There, perhaps you will let me alone now". I questioned him later on in the same day, and he informed me he meant to destroy himself, as he was so unhappy, but would not say the cause of his trouble.

22:9:18. Patient has persistent delusion that people outside the windows are shouting at him, and won't leave him alone. He is quiet and well-behaved, but a little furtive—might attempt suicide at any time.

3:1:19. Patient is well behaved, but very deluded. Thinks an M.O. is always worrying him, but has never seen him. Hears his voice day and night. Very suicidal.

13:1:19. Has no idea why he was sent to a mental ward. He has heard voices for seven or eight weeks, but will not say what. He is very inaccesible, and will tell very little. He seems very suspicious, but says at the moment he is happy enough. States that he likes company sometimes. Takes little interest in his surroundings,

and has no idea what country he is in. Knows the year. General health fairly good.

17:1:19. He suddenly bursts out laughing, and his conduct is probably to a large extent dictated. He admits that the voices he hears are very worrying at times.

6:2:19. He says his M.O. made him jump overboard in the ship. He does not know the day of the week, nor how long he has been in hospital. He says the voices are for a purpose—by an Army order. They began about 8 months ago. He is unwilling to accept suggestion as to the unreality of the voices. Thinks he was put in prison for a purpose.

3:5:19. Slightly reticent, solitary, unwilling to converse Acknowledges voices and persons talking to him.—Says they have done so for about 10 months, and have followed him from Salonica. They repeat what he thinks and put thoughts into his head. His body is affected by these men, who make him caustive at times. He feels irritable. They say he is not J.C., but never say who he really is.

8:7:19. No improvement, silent, solitary, replies in monosyllables, uninterested. Hallucinations and delusions unchanged. Friends refused to allow him to go to a civil asylum, and take him home—this about a year after onset of mental symptoms.

CASE III.

Clinical Dementia Praecox—Recovery.

Pte. J.A., aged 24.

18:8:18. Salonica. Admitted confused. Improved, then relapsed and became more confused than before. Later violent, and excited, and had to be restrained. Attitudinising. Settled into semi-stuporose condition, and will only reply to questions in monosyllables. At times, echopraxis has been well marked.

8:9:18. Excited, confused, found wandering, heard voices wanting him to go and look for a man, who was to be shot. Has had 10 attacks of malaria, and insomnia in consequence. Suspicious, confused, negativistic. Spleen enlarged. M.T. parasites in the blood.

16:9:18. Still confuded, but not stuporose.

19:10:18. Innocently violent, and had an epileptiform

seizure. Destructive, filthy, subject to outbursts of unreasoning violence. One day he was in a stuporose condition exhibiting autism, and flexibilitas cerea. Apt to be impulsive and aggressive. Blood Wassermann negative.

15:11:18. Cataleptic with cold cyanosed extremities. Answers only yes or no. Statuesque attitude and apathy.

6:12:18. Writes sensible letters to his mother.

3:1:19. Prolonged reaction time.

33:1:19. Still dull and confused. Free from visual and aural hallucinations. Quiet, well-behaved, little interested in his surroundings.

30:1:19. History from himself: Born in May. Left school 14. Standard VI. Farm-hand. Single. Pre-War health good. Admits occasional alcohol excess pre-War. Denies V.D. Family history negative so far as he knows. Egypt, May, 1916. Salonica, Aug., 1916. Under fire, a little nervous. Not wounded. Had malaria first in Aug., 1916, and has had over a dozen attacks between then and 1918. Had as long as six weeks off duty at a time after an attack, but usually was not off duty. He says that by Aug., 1918, the noise of the guns which he was feeding with ammunition upset him, as he was feeling weak and was only two weeks out of bed, after malaria. He remembers he went into hospital dumb, and felt confused and depressed. He does not remember much more, and does not remember the hospital.

Physically, thin but feels well. Stigmata of degeneration. Narrow palate and prominent ears. Cyanotic and cold extremities. Pupils normal. Knee-jerks exaggerated.

Mentally, gives a fairly clear, slow account of himself. Rational, but reaction time a little long. No gross psychotic symptoms found. Orientation normal. Flexibilitas cerea slight. Still a little dull, but no evidence of confusion.

5:5:19. Has slowly and steadily improved—but still a little slow, but that may be native. Sent home recovered.

CASE IV.

Confusion taking a dementia praecox form—Benign tertian infection. (Porot and Gutmann).

M., aged 24, arrived in Salonica, Sept., 1915. He was

evacuated 15:9:16, with mental confusion and malaria. Wishing constantly to get up and go away. Disorientated; unstable; fits of laughter and rage alternating without apparent reason. Spleen enlarged.

Says he lost his memory when illness began, but remembers the voyage home, and arriving at Marseilles. At Marseilles, he was agitated, and was troubled with nightmares. Left asylum after 15 days convalescence, and joined depot in Algeria, 22:12:16.

Admitted to hospital again with nightmares and nocturnal terrors.

12:1:17. At Neuro-Psychiatric Centre.—General state good. Spleen not palpable. A few benign tertian parasites in his blood.

He presents a certain paradoxical euphoria. He says he is quite well mentally, and says he has only some migraine, rheumatism, etc., He asks to remain until the end of the month, and then to go on to convalescence with "nervous depression and mental debility".

One is struck with his monotonous tone, and his discordant irrelevant smile. He repeats the same phrases which he has by heart and stereotyped. Has mannerisms and a tendency to symbolism. Says his brother having been killed, "he wishes to kill a Boche with his hand", and he interspersed his remarks with irrelevant remarks. Not disorientated.

He is complacent, and has ideas of satisfaction. He is "a real Poilu"; he is bachelier, and would have been an officier. He harps on his rheumatism, with which he says he is rotten.

Watched and observed for three months, he became fatter, but his mental state got worse. Lacking insight, he did not protest against confinement. Indifferent to everything, he laughs when spoken to of his family, or of his brother who had been killed. Ideas diminish steadily; speech monotonous; he recites and laughs frequently and absurdly. He repeats stock phrases continuously like a litany, laughing loudly even to the extent of becoming flushed in the face.

After 3 months, sent to asylum. No hereditary predisposition discovered. He had convulsions in childhood from some unknown cause. His parents record that in Nov., 1917, his condition had not changed.

Of the 14 cases observed during periods of from 3-12 months, 8 had apparently recovered and went home. One had not recovered, but was taken home by his friends, who refused to let him go to a civil asylum, after a year in military asylums. Four were under observation for from 6-12 months, and were sent unrecovered to civil asylums, and were not traced further. The fourteenth and last is case no. 4 (J.K.B.) who is now in Broadmoor asylum, mentally recovered.

Without observation prolonged beyond what was possible, it would be hard to say whether the cases of this series which had remained ill beyond a year were cases of true dementia praecox with malaria infection added, or whether permanent brain changes as might easily be, had resulted from the malaria and gone on to some degree of weak-mindedness or dementia.

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CHAPTER XIII.

MANIA.

Mania when it does occur in malaria patients tends to do so in the primary attack. The patient may have been naturally of excitable disposition, or there may have been an antecedant chorea, epilepsy, alcoholism, or hypothyroidism. But cases have been noted where there has been no evidence of any latent weakness or susceptibility, the parasite or its poison evidently acting as a local excitant. Mania has been noted moderately frequently in the literary records but it does not appear to be nearly so constant as depression. Sebastian (1823) notes it's occurrence with Wechselfieber, and refers to its tendency to periodicity, and the occurrence of phrenitis as a complication. Sydenham (1848) does the same, and indicated that it stood beyond the reach of all the usual remedies. Most observers of malarial mental states have a record of some mania cases or lesser states of excitement at some part of their course, and indicate that they are less frequent than the depressive types.

The victims of mania in the course of malarial infection are in the main much like those from other traceable toxic causes, i.e. excited, restless, noisy, sleepless, talkative, with flight of ideas, argumentative, sometimes violent, and may be aggressive. They tend to be moving about while the excitement lasts, and are difficult to keep in bed, requiring close supervision and forcible control or strong sedatives. In the quiter phases, the patient reacts unduly readily to any suggestive stimulant and great tact is required with those in attendance to prevent an outburst of excitement. The excitement may be associated with mental confusion, or the patient may be comparatively rational; as a rule, however, there is some associate flight of ideas and abnormal conduct. He may complain of hearing voices, which disturb him and keep him awake. The periods of excitement may alternate with periods of depression approaching more to the manic-depressive types of insanity. Lesser states of excitement occur, not exactly constituting mania, and on the whole it would appear that states of depression are much more common in

frequency, and much more prolonged in malarial subjects than are states of excitement.

In some instances there is complete amnesia for the period of excitement but in others the patient remembers all the incidents of his conduct, but says that an uncontrollable impulse obsessed him.

These cases generally occur with general physical deterioration, and mental improvement is ~~generally~~ usually parallel to physical improvement. As a rule they make a good recovery, emerging with at most only amnesia for the periods of excitement or to the initial state of instability where that has originally existed.

All the 6 cases of the writer noted in this series were able for discharge home within seven months of the onset of their illness. Two cases of the author's are appended, with one from Porot and ~~Outmann~~ Outmann.

CASE I.

Pte J., aged 28,

25:3:18. Salonica. Was found early morning with empty rifle thinking he was on guard. He was trembling as though suffering from a severe attack of malaria according to the sergeant. Sober, but dazed, and speech incoherent. Excitable and talkative. Stated he thought malaria was coming on and he had headache and got dizzy. Wandered about--did not recollect rifle incident. Spleen not palpable.

12:4:18. Still mildly excited, very emotional, upset recently by a tactless orderly. M.T. parasites in blood.

21:5:18. Malta. Improved, no trouble. On 5:6:18, assaulting orderlies and thrashing them. Cannot be relied on, and instils vice into other patients.

14:8:18. England. Denies hallucinations. No psychotic symptoms noted. States he had frequent attacks of malaria since July, 1917, and since then cannot control temper. Knee-jerks brisk. Tremors of fingers and tongue. Blood Wassermann negative.

25:8:18. History from himself: Health good pre-War. Family history negative. Married, one child. Denies alcohol excess. Left school aged 14. Standard ~~XVI~~ xVI for two years before he left. France Sept., 1915. Under fire-- not nervous or wounded. Salonica,

Nov., 1915. Under fire, not wounded. Malaria often. Says he was delirious with malaria in March, 1918. His "nerves got the better of him". Denies recollection of violent or unusual conduct while in this condition. Says he feels pretty well now, but that his nerves are not quite back to normal. Eats and sleeps well. Knee-jerks active.

10:1:19. Has kept well mentally since last note, and is improved physically and in nerve stability. Discharged home cured.

CASE II.

Sniper T.H., aged 38.

14:10:18. Palestine. Was brought in in a semi-conscious condition, with retraction of the neck and stiffness of the limbs, but after half-an-hour was conscious again. He is peculiar in his manner. No Kernig; no Babinski. Benign tertian parasites in the blood.

15:10:18. Had another fit. Subconscious. Violent in manner.

19:10:18. Alexandria. Transferred here in a state of mania, struggling violently. Was unable to converse or control himself, very noisy.

28:11:18. Now feels well. Answers readily and rationally. Memory and orientation good. Nothing abnormal mentally found, and physical state good. Blood Wassermann negative.

1:12:18. History from himself: At school till 18—standard IV. Always been nervous, and was in hospital as a boy with St. Vitus Dance. Rheumatism in the family; sisters nervous. A cousin was in an asylum but recovered. Teetotal. Egypt, Feb., 1917. Palestine, Oct, 1917. Had malaria for the first time, Aug., 1918, and was in hospital 8 days. Frequent subsequent attacks but not off duty. Had attack in Sept., 1918, and does not remember much after this. Thin, but says he is usually so.

Pupils equal, but sluggish to light. Deep reflexes normal. Mentally he seems tired, but gives a clear account of himself, except for several weeks during his attack, when his mind appears to have been a blank. Eats and sleeps well.

6:6:19. Has kept well since last note. Discharged home recovered.

CASE III.

Mania in a man of 37. No previous mental attack. (Porot and Gutmann).

C.M., contracted severe malaria for the first time 15:9:16. Admitted to hospital, 26:9:16. Incoherent. Improved and rejoined his his unit in Algiers 16:10:16.

Began to disturb his comrades by singing at night; he was isolated, pulled his bed to pieces, broke the crockery and escaped into the court yard. He was much excited, talked incessantly, and had ideas of grandeur; he related a tale of active nightmare; he had saved his squadron, but does not wish this to be noised abroad. The night before, the adjutant R., wishing to make a counter-attack, M. rushed it, warning and rallying everyone with his whistle; he did a heroic thing, and escaped death only because he had 24 cartridges in his revolver. He went home in the morning. His commandant sent for him, and thanked him for his act of heroism, and gave him four stripes and all his decorations. He returned to his quarters, and now everyone hustles to decorate him. Also, at the hospital, he aspires to be commandant, he is going to found a hospital where he will have the pay of commandant. He calls himself a relative of General M. (same name), Governor of the Forces of Africa on Land, Sea, Air.

Tongue coated; malleolar oedema; emaciation; no fever.

Over several consecutive days, he has the elated activity of the maniac. Memory acute, except during the febrile periods when disorientated and confused; he salutes the doctor amiably with the wrong name. Talkative, pretentious, imaginative; his neighbour in the next bed, a melancholic, has, he says, nostalgia. He will make the round with the doctor, will instal the telephone, etc.

Sleepless. Excited night and day. Sent to asylum, 8:11:16. After 9 months there he has become fatter and is calm. Very correct in his manner, and tends to be excitable and aggreeable.

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[redacted]

[redacted] occurs during malarial infection simulating sleepiness with simple apathy in mild cases to stupor, or it may be associated as it is frequently with convulsions, coma, with complete amnesia for the period of affection, or it may be part of the syndrome of dementia praecox. It may occur at the febrile stage, with tertian periodicity, the patient being mentally clear on the intervening afebrile days, or with varying degrees of attainment of the stupor. Or it may occur intermittently with the intermittency of the febrile attacks at longer intervals. It may even replace the febrile attacks, being the only sign of sickness drawing attention. It is frequently a prelude to coma, and sometimes fills in the intervals between recurring attacks of coma. It may last only for an hour or two, or may extend for a few weeks, even after the febrile attacks have ceased, or diminished in frequency. In certain situations, it may strongly simulate drunkenness, as in the case of one caught in an attack on the street, or at work. This impression may get further support if a little alcohol has been taken at an earlier stage to relieve the feeling of depression. Or during exposure to the sun, a state of stupor may arise suggesting the diagnosis of sunstroke, where the condition is really a preliminary one to malarial coma. It takes a prominent place in the clinical picture of dementia praecox, dealt with more fully elsewhere.

It is frequently associated, as are the other forms of malaria, mental derangement of malarial origin, with somatic troubles, such as headache, and may even occur as a sequel to meningeal irritation, with stiff neck, Kernig's sign, and optic neuritis.

Castellani reports a case resembling sleeping sickness. The patient had low fever for months, trembling of hands and tongue, and progressive general weakness; later he was drowsy, and had occasional convulsions. The blood examination was negative for every known parasite, and many months after onset of symptoms, a few malarial parasites were found once. Quinine injections cured the

patient. He saw another similar, but less severe, case in Skopolje, with general debility, trembling of hands and tongue, and marked drowsiness for weeks, but diagnosis was made at once as blood was full of parasites. Patient slowly recovered on quinine treatment.

In the 5 cases in the author's classification, stupor appeared to be the most prominent feature, apart from confusion, though associated with it in some measure, and apart from features that would lead to the diagnosis of dementia praecox.

Representative cases from the literature are detailed as follows: one from the author's collection, and three from the literature.

CASE I.

Stupor.

J.C., aet. 25.

Salonica. One of his friends says he has been queer for 5 days, but was markedly worse on morning of 21:8:18. Has had the reputation among his friends of being content to sit and do nothing when not on duty. He is afraid that 5 Greeks armed with sticks are after him. Says that they once knocked him down.

24:8:18. Quite quiet. Seems to understand questions put to him. Hands and feet cold and clammy. He is in a semi-stuporose condition. He is delusional in regard to food, and will not take it if anyone is standing near him. Similarly with drinks, which he scrutinises closely before touching. No hallucinations. Disinterested in surroundings. A fly walked over his face without any attempt on his part to dislodge it. Anaemic: spleen enlarged. Many Malignant tertian parasites found in blood.

1:9:18. First sign of ability to understand and answer questions—in monosyllables and handshakes. Blood Wassermann negative.

1:10:18. Improved. No delusions or hallucinations, but restless and feels he cannot keep still. Reads but memory bad.

2:11:18. History from himself: At school till 14, standard VIa. Shop assistant. Healthy pre-War. Family history negative. Alcohol moderate. Egypt, Jan., 1916. Salonica, March, 1916. Under fire—not wounded or nervous. Took malaria first in Aug.

1917. Has had about half-a-dozen attacks, two of them bad. Was off duty with every attack for 10 days with the bad attacks. He says he has not lost weight. Feels well now. Knee-jerks and pupils normal. Mentally, gives clear account of himself, and says he remembers being very ill, and when conscious felt very weak. He sticks to his story about being attacked by 5 Greeks, when going to fetch water one night, and of being knocked down by one of them. He reported this to the M.O., he says, a few days later went down with malaria. He says he smelt his food because he had been in the habit of smelling it, having had "bad bully beef early on".

It is impossible to check the truth of these statements, but he gives one the impression of being a little simple-minded, and lacking insight into his condition. Orientation normal.

3/4:18. Home well.

CASE II.

Haemorrhagic malignant infection with stupor. (Marchiafava and Bignami).

R. S., 38 years old, able-bodied, has been at Ostia for a month, but has only been ill for 5 days. The first symptoms were drowsiness and great weakness. The patient states that if he lay down on the ground, he went to sleep at once, so much so that he had to give up his work. He thinks that he had fever, but very mildly; there was headache and mental dullness, followed by a state of stupor. He comes to the hospital in a condition of great prostration, showing a tendency to sleep, and with a heavy stupid expression. Punctiform haemorrhages are scattered all over the trunk: the mucous membranes are very pale.

July 30. Temperature, noon, 99·7°F. 4 p.m. 99·2°F. 6 p.m., 100·4°F. 8 p.m., 100·2°F. 12 midnight, 101·3°F. Bisuriate of quinine and camphor are administered by hypodermic injection. BLOOD: There is an immense number of plasmodia without pigment in different shapes. Also a very large amount of pigmented white blood corpuscles of gigantic size.

July 31. Temperature, 2 a.m., 100·4°F. 5 a.m., 100·8°F. 9a.m., 100·2°F. Noon, 100·2°F. 5 p.m., 99·9°F. 8 p.m., 99°F. 11 p.m., 98·2°F.

BLOOD, 8 a.m.: There is still a considerable number of plasmodia without pigment, many of them being in brassy blood corpuscles; also a few crescent-shaped forms. The pigmented white blood-corpuscles are large and very numerous; they have a single nucleus, and large shining granules.

5 p.m.: The parasites are as above, but they are much decreased in quantity. The same treatment is continued (Bimuriate of quinine and camphor by injections).

Aug. 1st. The general condition has remarkably improved, and there is complete absence of fevere In the blood there are a few plasmodia without pigment in brassy blood corpuscles; also a very small number of crescent-shaped forms, and many pigmented white-blood-corpuscles as above.

Aug. 2nd. The improvement continues. The blood contains pigmented white blood-corpuscles.

Aug. 3rd, examination gives a negative result. During the month the patient slowly recovers from the anaemic condition into which he had fallen.

CASE III.

Confusion, with Stupor. (Porot and Gutmann).

An example of mental confusion with stupor and passing into chronic phase after some abatement of the symptoms. Soldier from Salonica, evacuated with Psychic disturbance, intermittent.

Entered neuropsychiatric clinic, Algiers, 17:1:17, inert quite mute and stupid. Conversation impossible.

Physical state precarious, emaciated, cachectic, like a skeleton; eyes sunken. Remains immobile wherever he is put. Slightly negativistic; refuses food and spits out what is put in his mouth.

No fever. Benign tertian parasites found in his blood. Energetic treatment—physiological serum, adrenalin and quinine in big doses.

A month after admission, begins to take food. Still a little confused, but begins to respond to simple directions. Slow progress in the right direction, attending a little to himself, and by the end of Feb., asks to get into the garden, though still disorientated.

By April, he has improved further, though still depressed and confused, and conversation still impossible. He makes progress in taking interest in his surroundings, and shows some emotional reaction. One day he showed evidence of recognizing his comrades, tried to speak, but his words were not intelligible.

At this stage, progress ceases, he becomes stuporose again, while his physical improvement is maintained.

In spite of eight months care and treatment, this patient did not emerge from his confusion, but remained fixed in a state of catatonia.

CASE IV.

Confusion, with stupor. (Porot and Gutmann).

A case of mental confusion with stupor in a native of simple, but sufficient mentality.

A youth, Khel-Ahmed, sent 16:3:17, with "mental trouble"— for observation".

He rests in bed quite inert and indifferent to his surroundings. His face lacks expression, and looks stupid. Considerable diminution of physical and mental activity. He sleeps constantly. He understands little; refuses to eat; respiration shallow; extremities cold; tongue coated; no fever; spleen much enlarged.

After some days he improves and shows some attention. When questioned, he says he is unable to sit up and shows an overwhelming tendency to sleep. He cannot give an account of himself, and is indifferent to everything. He is disorientated in time and place.

He has no hallucinations or excitement. He has vague hypochondriacal ideas, and complains of his weakness and the bad state of his stomach.

On enquiry it is found that he had been in his corps a month when he became ill, appeared disorientated, eccentric, fevered, with violent headaches and abdominal pains. He became incoherent, and constantly wandered about the ward. He was given quinine regularly, and steadily improved. His depression and confusion slowly disappeared, and he resumed interest in his surroundings.

After a month of care and treatment, he left hospital quite well. Spleen became normal. The diagnosis of malaria was confirmed.

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CHAPTER XV

DELIRIUM.

Malarial delirium is generally preceded by severe headache, and is most frequently associated with the febrile paroxysm, often developing after a series of paroxysms, but may continue for days thereafter. Régis describes it as a dream in action, lived through, maybe taking colour from vocation, or fantastic, painful, or terrifying. It is generally transient, maybe intermittent, rarely does it last for days, though it may last a week or more. The patient usually mutters incoherent nonsense, but may cry out aloud, may laugh or rage by turns, or may be violent, greatly excited, or resistive. It may be accompanied by somnambulism.

Régis records an interesting feature he has noticed, namely that in certain cases in their delirium, the patients are carried back to the period of time when they were infected with malaria, and often it is the same scene that recurs. One of his cases, formerly a soldier in Ténia, with the return of malarial delirium even years afterwards, saw himself fighting the Kroumirs; he conversed with his comrades whom he called by name. Another delirious patient always saw the scene of a murder witnessed by him in the regiment. The murderer appeared to menace him, and he made his escape in a state of complete somnambulism, without subsequent recollection. Subsequent hypnosis revealed the experience of the patient. It generally recurs under the same conditions, and with the same characters, such as with each febrile attack of a certain intensity.

According to Besnard, postsomnambulistic delirium may be associated more or less completely with ideas of persecution, grandeur, jealousy, autosuggestion, negation, the result of interpretations, confused and contradictory, and quite out of logical proportions. He points out that confusion and asthenia influence the picture so that depression is frequent, and the patients reactions negative or automatic. False observations, disorientation are of asthenic origin, and not directly hallucinatory, like the confabulation, which are not purely and simply the recitation of

events lived in the delirium. Catatonia, suggestibility, are frequent symptoms, especially in their transitory and static forms. Lucid moments, during which the patient is more or less self-conscious, frequently appear in the course of it.

Delirium may precede coma, or may succeed it, or accompany any cerebral form of malaria. Postcoma e.g. meningitis. delirium may be of short or long duration, and is frequently accompanied by agitation and restlessness. Marchiafava and Signani record a case where delirium after coma lasted 3 days, was accompanied by great agitation, and frequent cries, and ended fatally.

After the attack, the patient is usually a little confused, dull, with a certain degree of headache, slow scanning speech, and amnesia more or less complete for the period of delirium.

In cases where prolonged physical depletion maintains the mental weakness, and fresh malarial attacks come to keep up the exhaustion, delirium tends to become chronic and may last for months. In that case, the dominating ideas tend to be of a melancholy nature, comprising ideas of persecution, jealousy, hypochondria, and of indignity generally. At this stage the case may simulate true melancholia, but is distinguished by the fact that it is a profound failure of affective tone in which ideas are secondary, inconstant, accessory, almost independent accompaniments. Whereas in this state of chronic mental exhaustion with recurrent delirium, the affective depression is more a reflexion and effect of the dream experiences upon the spirit of the patient, the depression is secondary to ideas and not so profound, or independent of them. (Cf. Porot and Gutmann).

Several representative case histories are given, two of the author's, the others by Goodall and Marchiafava and Signani.

CASE I.

Delirium, auditory hallucinations, somnambulism.

Pte. J.D., aged 45, stonecutter. Married 1907, and with 3 healthy children. No illness in civil life. Mother died of a "decline". No family history of nervous troubles or insanity.

In the Balkans nearly 3 years, without home leave. Had malaria first in Feb., 1916—jaundiced. From Oct., 1917, was sick with malaria for two months. On duty again, Dec., 1917, and remained well till 6:9:18, when he began to have shivering, headache, vomiting,

pain in the chest.

7:9:18. Salonica. In hospital with malaria. Malignant tertian parasites found in the blood.

10:9:18. Wild, incoherent—says he has been shooting lions all night.

11:9:18. Patient says he saw two lions on the road four nights ago, and that they were shot at the bakery. He saw them attack a man and a donkey. He could hear voices singing a new popular song. Says he feels nervous. Memory appears good. Emotionally unstable; suddenly laughed without apparent cause. Noisy, restless; ran out of the ward in his shirt anxious to arrest nine prisoners. Talked a great deal to himself.

12:9:18. Slightly confused, and cannot tell what he has been doing. Very debilitated an d anaemic. Temperature, 101°F. Gives the information that he has been in the Balkans for three years without home leave, and has just had four attacks of malaria.

15:9:18. Much better mentally—almost well, though physically weak. Says last attack of malaria before this occasion was a month ago, and that he did not report sick then. Was never delirious before.

29:1:19. Rational, but still some mental apathy. Rather thin—not quite restored physically. Some tremor of fingers and speech. Asked about his delirium, says he "heard voices singing for one night". Blood Wassermann negative.

May, 1919. Discharged home, feeling and looking well.

CASE II.

Delirium, auditory hallucinations, delusions of persecution.

Cpl. H., aged 31. Regular soldier. Personal health always good pre-War. Maternal aunt in asylum. Got malaria July, 1918, in the Balkans.

28:7:18. Salonica. Admitted to hospital with malaria and diarrhoea. Stools examined twice, and found negative for dysentery etc. Malignant tertian parasites in the blood.

15:8:18. Says he was made mess-corporal, and "could not please anyone".

23:8:18. Taken to hospital in a delirious condition.

Temperature, 99·8°F. Spleen palpable. Was disorderly all night. Hypnotics failed to act. Delusions of persecution.

25:8:18. More rational, but still delusional.

17:9:18. Still very unstable mentally. Says that everywhere he goes, he hears voices, though there is no one near him. They keep shouting his name out, but he does not always hear what they say.

23:11:18. Malta. Ill-tempered, but no delusions. Apparently much better, and quite rational.

28:12:18. Rigor, sweating. Temperature, 104°F.

29:12:18. Better. No mental symptoms observed.

15:1:19. Well—seems cured. Blood Wassermann negative.

April, 1919. Discharged home, having kept well since last note.

CASE III.

Cerebral malaria showing delirium, meningeal irritation, and reacting to quinine intravenously. (Goodall)

Pte. W., aged 26, admitted 15th Aug., 1917, complaining of headache, pains in legs, arms, and abdomen, and profuse sweating. He first had malaria in India in 1913, and had nine attacks afterwards. Nocther illness. Temperature on admission was 103°F, pulse 90. The spleen was enlarged and very tender. Malignant tertian parasites were present in the blood. Patient was weak and restless. Knee-jerks were absent. There was an extraordinary sensibility to touch and pain all over the body. A slight touch was painful, and it was impossible to percuss the chest. He was ordered 45 grs. quinine daily. On 18th Aug., temperature was 101°F, pulse 100, respirations 28. Patient looked vacant and was listless and disinclined to speak.

During the night he became delirious. On the 19th he was almost comatose. He would neither speak not feed. Later there was subsultus tendinum, and incontinence of urine. He received an intravenous injection of 25 grs. of quinine in a pint of saline solution. His pulse improved, but he had a very restless night with some vomiting. On 20th Aug., he was quiet and drowsy, but answered questions. On the 21st, all the movements of his limbs and face were weak and tremulous. Knee-jerks could be elicited with difficulty. The plantar response was flexor. There was some

cervical rigidity, and Kernig's sign was present on both sides. The pupils and cranial nerves were normal. There was no squint or photophobia. Gradual improvement now began.

For a long time he was tremulous, weak, and stupid, but by 1st Oct., he had made a complete recovery.

CASE IV.

Malignant infection, with lethargy and delirium. (Marchiafava and Bignami).

S., male, after four days fever entered hospital on 25th July, at 5 p.m.: he is lethargic, gives answers with great difficulty, and remembers nothing about his illness.

BLOOD: There is an abundant number of parasites—many plasmodia without pigment, or with granules of pigment at the circumference, almost all of them in brassy corpuscles; also many forms with pigment at the centre; endoglobular spindle-shaped forms of different sizes, with pigment along the axis; endoglobular round forms with pigment dispersed in different parts; adult crescent-shaped forms, and also adult round forms in a state of disintegration; pigmented white blood corpuscles, some of necrotic appearance.

Soluble hydrochlorate of quinine, 32 grs, administered by hypodermic injection.

July 26. The patient's general condition is slightly improved

BLOOD: 11 a.m. Condition as above; but the forms of the crescent-shape phase, both free and endoglobular, are less numerous.

Soluble hydrochlorate of quinine, 32 grs, administered by hypodermic injection. At 5 p.m., the parasites had much decreased in number. The patient is greatly prostrated. Soluble hydrochlorate of quinine, 16 grs, given hypodermically.

July 27. Patient has been delirious during the night; prostration continues. In blood, the amœbae and pigment forms are very scarce; forms of the crescent-shaped phase are predominent. There are also many white blood corpuscles, with black or rusty-coloured pigment. The patient continues to take quinine.

On July 28th, 29th, and 30th, he continues to be delirious, especially in the night, and attempts to escape from the bed. In the blood there is nothing abnormal to be found, but endoglobular and

free forms of the semilunar phase and a considerable number of pigmented white blood corpuscles. On the following days the delirium ceases, and is followed by a satisfactory condition; the crescent shaped and the flagellated forms are still visible, and until Aug. 2nd, pigmented white blood corpuscles.

July 26. Temperature 12noon. 100·8°F. 4 p.m., 101°F, 6 p.m., 100·6°F, 8 p.m., 102°F, 12 p.m., 101°F.

July 27. Temperature, 4 a.m., 99·5°F, 7 a.m., 100·4°F, 12 noon, 98·8°F, 5.30 p.m., 102·6°F. There is complete freedom from fever on the following days.

What is noteworthy in this case is the persistence of the cerebral symptoms for some days after the disappearance of the ~~parasit~~ parasites belonging to the fever-producing cycle, there being left in the blood nothing abnormal but forms of the crescent shaped phase and pigmented white blood corpuscles.

CASE V.

Choleraic malignant infection with delirium. (Marchiafava and Bignami).

C.G., 54 years old, a cook, was brought to the hospital in a carriage at 2 p.m. on 5th Sept., 1890, accompanied by a Police Officer. He has been ill since the 2nd, inst., Breathing now very difficult, and when left to himself, he becomes delirious. Looks frightened, pupils dilated, skin cold and sweaty; cyanosis of lips and extremities; pulse threadlike and very rapid. In the morning, he had much diarrhoea and vomiting, retching, and stools like those of choleraic diarrhoea. Spleen slightly enlarged. Blood shows numerous amoeboid parasites. 32 grs. quinine given by injection and 32 more by the mouth; stimulants ether, camphor, etc., At 8 p.m., profuse sweating, skin remaining cold; delirium has ceased, and continuous moaning has taken its place; pulse still small and frequent; diarrhoea persists. During the night, diarrhoea decreases, skin becomes warm again, and the patient has rest for some hours.

On the morning of the 6th Sept., improvement is remarkable; pulse, 80 and strong; coldness has passed: temperature, 97·9°F; cyanosis disappeared, but still some diarrhoea. 32 grs. quinine given with stimulants and wine. The blood contained a few plasmodia,

without pigment, and in a state of motion. At 6 p.m., in the evening, there is no fever and the pulse is good, but prostration and pallor to a remarkable degree still remain. Diarrhoea ceased. 16 grs. quinine are given.

On the following days, the improvement is maintained; strength is slowly recovered, and the appetite returns; the parasites disappear, and there is no more fever.

Delirium in the acute malarial phase may be a preliminary to coma or any of the other psychoses, or it may succeed them, or may be a late-stage accompaniment of choleraic, typhoid, or algid forms; or, if developing into the chronic phase, may end in chronic delusional insanity or even dementia. Oftenest, it passes with the acute phase, leaving no apparent psychic change. All the author's cases—whether classified under the heading delirium, or whether the delirium was a passing phase in a later psychosis,—recovered.

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CHAPTER XVI.

PSYCHASTHENIA — HYSTERIA.

A. PSYCHASTHENIA.

Under this heading, has been groupei a class of case which is closely allied to mental confusion on the one hani, ani to neurasthenia on the other. It may, in fact, be looked upon as a transition stage bewteen the two. It overlaps in its symptomatology with some of the forms of minor iegrees of iementia, to which it may ultimately lead, but iiffers in this way, that it is treatable if recognizei as of malarial origin, ani the patient may often emerge very well.

The inportance of emphasising it as a particular type lies in the fact that it is often associatei with inaiequate treatment of malaria, ani that it may exist for a long time after febrile attacks have ceasei to occur, while parasites are still alive in the iepots, carrying on their guerilla warfare. In this way (occurrence or iuration long after the last paroxysm), it is often attributei to other coincident circumstances, which truly enough may go to aggravate the conition, such as exposure to the sun, alcoholism, overwork, intercurrent iisease, --while malaria comes to be overlooki as an important ani treatable factor , if it is not actually the whole cause.

The conition frequently arises in those who have suffered from much malaria in the tropics over many years ani may leai to their repatriation as being unfit to uniertake their usual iuties. Or it may occur-in those who have hai a short acute attack of confusion, which has subsiiei with treatment, the patient emerging still unable to resume work or perhaps having broken iown after repeatei attempts. Or it may appear without confusion after a primary malarial attack, which has left the patient generally weak ani with anaemia, shortness of breath, tachycardia, ani enlargei liver ani spleen. The mental features which bulk large in the picture are a loss of intellectual appetite, iiminution of mental activity, or braiypsychie, loss of power of attention, ani memory, often with a loss of self-confidence with its consequence, the sense of failure. Interest in work

diminishes, or ceases, with the increasing sense of inability to cope with it. Dreams often disturb the sleep. Sometimes there are subtle changes of character, first noticed by those who know the patient best, but later may become more obtrusive--such as discontent, irritability of temper, suspiciousness, memory defects, argumentativeness, impulsiveness, loss of self-control in any form including ill-temper which may easily lead to deeds of violence.

Psychasthenia, then, may be looked upon as a borderland state between acute psychosis and a general physical incapacity in which some somatic or peripheral nerve trouble predominates, where the emphasis of disability is still mental, but relatively slight. Inadequate treatment for malaria through failure of diagnosis or through failure to appreciate the tenacity and subtlety of the parasite, or concomitant circumstances, or special difficulties of treatment, may severally have led to the occurrence and maintenance of this condition.

A few examples will serve to illustrate some of the clinical variations of the trouble.

CASE I.

Irritability of temper, giddiness, recurrent loss of memory.

Regular soldier, aged 34. Married, four children. Health good pre-War. Served in France, under fire, not wounded, gassed, or buried.

Sept., 1915, Mesopotamia. Palpitation, sent to India with malaria.

June, 1916, Salonica. Jan., 1918, invalided to U.K. with malaria. Nervous, inability to concentrate attention. Sent back to France. Etaples transfer certificate indicates that he has been three times in hospital with malaria, having repeated attacks in spite of quinine treatment. Malignant Tertian parasites found in his blood. Considerable cachexia. Repatriated.

1918. Light duty, and much in hospital with malaria. Began to be troubled with loss of memory. Wandered away one day, and brought back to hospital six hours afterwards with no recollection of where he had been.

Feb., 1919. Demobilised, and later started work as a car-driver. Malarial attacks continued at intervals, and he was unable

to go on with his work through weakness, nervousness, inability to concentrate on his work, and loss of self-confidence.

Nov., 1920. One day went out walking, and wakened up at home--does not remember how he got home.

Jan., 1921. Report by patient's wife, and police officials. Left home for a walk in the evening. Suddenly lost his memory, and was taken to the police office, where he recovered at 2 a.m. next morning, and was taken home. Police officials state that there was no evidence of alcoholism. Re-admitted to hospital. Sleepless, irritable, suspicious.

3:11:21. Wife states he is very irritable, and difficult to get on with. If she speaks to him, it is a fault, and if she does not speak to him, it is a fault.

3:11:21. Seen by the writer for the first time. Patient complains of general weakness, giddiness, occasional headache, and defective memory which plays him tricks. General condition fairly good. Physical signs in heart and lungs negative. Pupils and reflexes normal. Spleen friction heard over 7th left intercostal space. Spleen not palpable. Marked white adrenal line reaction. Blood Wassermann negative. He gives a clear and intelligent account of himself.

10:11:21. No spleen friction heard over any part of the splenic area to-day.

13:11:21. Shivering turn followed by sweating. Marked white adrenal line reaction.

17:11:21. Spleen friction heard to-day over 7th left intercostal space. Blood pressure, systolic-110 mm., diastolic-65 mm. Hg. Blood film shows white cell count as follows:

Polymorphonuclears:	76·2%.
Large mononuclears and transitionals:	13·0%.
Lymphocytes:	10·5%.
Eosinophils:	0·2%.
Mast cells:	0·1%.

24:11:21. 4 p.m. 20 minims of 1 in 1000 adrenalin chloride solution (Parke, Davis and Co.) given hypodermically. This was followed by slight shiver, malaise, and pallor, which passed off within an hour-and-a-half.

6 p.m. Blood films taken were negative for malarial

parasites.

25:11:21. Blood films taken to-day showed malignant tertian parasites. Patient says he has been seedy and headachy all day. This settled the question as to whether parasites still existed in the depots, and quinine and arsenic treatment was instituted.

1:6:22. Marked improvement, though occasional vomiting has led to abandonment of arsenic. But quinine has been gone on with thrice daily, three days a week, month about. Has resumed work, and feels pretty well. No headaches and no amnesia.

This case has several points of interest mentally and otherwise. The amnesia with wandering away was of such a nature as might easily have led to an accident, and legal complications. The period of six years between Sept., 1915, and Nov., 1921, was punctuated by repeated attacks of malaria, and interruptions in work with hospital attendance; parasites were only got in the peripheral blood on the latter date by artificial means.

While parasites were present in the spleen, evidence of perisplenitis was only revealed by splenic friction, which was not constant but intermittent.

The low blood pressure, along with Sergent's white adrenal line reaction suggest adrenal depletion.

This man ultimately, with persistent treatment, made a good recovery.

CASE II.

Concentration and memory defects, nervousness, loss of self-confidence.

Regular soldier aged 32. Married, two children. Always healthy. Miner in civil life. Was in Army at outbreak of War. France, Dec., 1914. Had rheumatism and frost-bite on Ypres front, 1915. Sent to Scottish hospital. Egypt, 1916. Palestine. Under fire, but not wounded. Felt exhausted, legs gave way, collapsed. Sent to hospital in Cairo. Worked at base off and on till armistice. Felt very unfit.

5:3:19. Discharged unfit. Later on got job as foreman in a shipyard, but was nervous, was unable for sustained effort,

lacked confidence in himself, and broke down. Had to leave.

Feb., 1920. Resumed work, but broke down in March, 1920.

April, 1920. Started lighter work, and carried on with difficulty at times, till Nov., 1921, when he again broke down: "done up", nervous, tremors, sleepless, headaches. Has never regained pre-War standard of health.

19:11:21. Headaches, pains in the chest. Sudden noises upset him. Emotional--breaks down and cries on slight provocation. He used to be a singer, but when he attempts this now he always breaks down. Sleeps badly. Cannot concentrate his mind on anything.

25:11:21. Physical condition fair. Tachycardia. Abdominal organs negative; pupils dilated, but react to light and accommodation. Superficial and deep reflexes exaggerated; no Babinski.

2:12:21. Complains of "rheumatic" pains and nervousness.

9:12:21. Headaches. A feeling of heat in back of head. Sleeplessness.

16:12:21. "Rheumatic". Pains all over body. Severe headaches when he attempts to do anything. Says he was ill like this in Egypt.--which suggests the possibility of chronic malaria, though he does not recollect anything he could call a rigor.

10:1:22. 20 minims 1 in 1000 adrenalin solution (Parke, Davis and Co) given subcutaneously. Had a distinct shivering lasting half-an-hour after injection. A few ring parasites were found in the blood film taken two hours after the injection. Had another shivering fit about midnight of the same day.

24:1:22. Spleen friction well marked in the 7th and 8th left intercostal spaces. White adrenal line reaction present. Systolic blood pressure, 135 mm., diastolic, 50 mm. Hg. Tachycardia. Pulse 120, regular. Becomes depressed at times.

White cell count:

Polymorphonuclears.	75·5%.
Large mononuclears and transitionals.	13·6%.
Lymphocytes.	10·8%.
Eosinophils.	0·9%.
Mast cells.	0·2%.

Sept., 1922. Has slowly and steadily improved on quinine and arsenic treatment, and is now very well.

This case is of special interest in that malaria has apparently not been diagnosed at any time during unfitness for fully a year preceding the Armistice, nor indeed until Jan., 1922, during which period of over four years he had repeatedly broken down even on light duty, both in the Army and out of it. He had never reported sick with malaria and indeed did not seem to know he had it, as he was not aware of actual rigors, though having feelings of malaise or of being "done up" as he called it.

He was quite a good fellow who had become despondent latterly through his inability to continue uninterruptedly at work.

This then is an example of a subtle form of infection passing as rheumatism and escaping diagnosis and therefore adequate treatment until much valuable time had been lost.

CASE III.

Dull, taciturn, self-absorbed, stupid, fits of rage, through insufficient treatment. (Porot ans Gutmann).

The Zouave Ch. Contracted malaria for the first time in Aug., 1916. He was evacuated in Oct. to Tarascon, having had the insufficient treatment of five injections. During his months of convalescence he had several attacks. He became depressed, taciturn, inattentive, self-absorbed, silent. Latterly, he took attacks of rage.

Still having attacks of malariat, he was exacuated after 3 weeks in hospital to Algiers on 12th Jan., 1917. He was then very anaemic, and a little jaundiced. At this time he was quiet, mildly depressed, and a little stupid; he answered correctly but slowly, lacked initiative; speech hesitating and tremulous; sleeping badly, lying for hours during the night mumbling to himself in a low voice.

At this time, benign tertian parasites were found in his blood. Intensive treatment begun--2 G quinine per day. Nightmare persists still some times. Physical condition rapidly improves, attacks disappear, sleep returns. Mental depression disappears, and by 12th. March, he leaves hospital quite well.

It is this type of case, the psychasthenic, --due to inadequately treated or to undiagnosed and therefore inadequately

treated, malaria, who is liable to be called all sorts of names—hysterical, foolish, lazy, malingering,—who is liable to fall into the hands of the quack or charlatan, and who may be very well be an endless source of annoyance to himself, his medical attendant, and his friends, unless the range of subtle effects of this masquerading parasite is realized, or at least thought of.

B. HYSTERIA.

Hysteria has been grouped with psychasthenia, of which it may be considered a special form. It has been noted by several observers that malaria can light up hysteria in those predisposed. It is not maintained that it can create hysteria, only that the latent tendency may become manifest during malarial infection. Boinet records three cases in which he reckons that hysterical features were manifested during the course of malarial infection. One of these is recorded in the section on circulatory system (Chapter 6) in which a man of 27 had anginal symptoms, ending up with complete hemi-anaesthesia of the left side which the author considered as an hysterical manifestation, though another interpretation is possible.

Marañon de Montyel records 8 cases, illustrating the relations of hysteria to malarial infections. In one, a man of bad heredity, hysteria appeared to be actually somewhat relieved during malarial infection. In 5 cases, there was a recurrence of old hysteria, in 2 after short intervals, in 3 after long intervals. In 2 cases of slight hysteria, there was slight aggravation after malarial infection. He does not maintain that malaria can create hysteria.

Monier-Vinard, who studied the varieties of neurological phenomena consequent on malarial infection in Macedonia, records that many of these phenomena suggested hysteria, but were not of hysterical origin, as the sensory troubles for the most part followed the course of the nerves, agreed with the motor disturbances, and were often segmental. The motor, vaso-motor, and sensory disturbances met with were the expression of trouble in the corresponding grey medullary segments, perhaps also in the ganglio-sympathetic groups, and were the result of direct parasitic action.

Nevertheless, the lowered vitality of the malarial subject renders him unduly susceptible to the influences of suggestion, and a wide variety of symptoms of an hysterical nature may crop out in the course of a malarial infection in a predisposed subject.

A case of the writer's exhibiting astasia-abasia, which may be considered as of hysterical origin, is recorded in the chapter on cerebro-spinal syndromes (Chapter XXIV). The case began with mental confusion and excitement, and during convalescence, while being treated with quinine by intramuscular injections into the buttocks, he developed astasia-abasia. It may be that the suggestion of leg disability came from the local discomfort and stiffness consequent upon the injections, and persisted after this method of treatment had ceased. At any rate, disciplinary measures, in which explanation of his condition and encouragement played a large part, resulted in rapid cure.

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CHAPTER XVII.

Exhaustion Psychosis.

Malarial cachexia as a clinical entity is well-known. In individual cases with close inspection it may be found that in one case the emphasis of mischief is upon the blood with severe anaemia; in another upon the endocrine glands especially the adrenals with loss of muscle tone, low blood pressure, giving a picture more of the algid form; in another the general nutrition may have suffered most, and so on. With many cases of this kind, however, the mind retains an alertness which does not seem to be in proportion to the physical depletion, and as long as the patient is not called upon for physical activity, he can keep going. Not only so, but in the instance of soldiers on service, many of them carried on with singular and astonishing mental activity and alertness, long after they were well-nigh exhausted physically.

This dominance of mind over body did not always obtain, however. There are cases where the mental activity remained more parallel to the body activity, where physical exhaustion was accompanied by corresponding mental exhaustion, and consequent mental inability to fulfil the duties they were called upon to do.

In these cases the mental picture is largely a blank and negative one. The patient is apathetic, dull, uninterested because mentally tired out; unoccupied for the same reason; immobile because not mentally energetic enough to get his tired body to move. His mind wants to avoid the stimuli from the outside world, or from his own sensorium, for it is too exhausted to deal with them. When it does, he is unhappy, and resists in a tired way. It is not so much that he is mentally depressed—his affective state is not so much lacking tone, it is asleep. He is not so much miserable, as the melancholic is—when he is left alone to rest. It is only when he is called upon to stir, mentally or physically, and apply himself, that he is unhappy and —fails. There may be some somatic accompaniments so common with malaria—headache, indigestion, hallucinations—but the dominant feature is mental apathy, exhaustion,

with its need for rest. T

Two examples from the author's cases are detailed.

CASE I.

Pte. W.M., aged 19. Woodturner. Health very good pre-War. No illnesses and not nervous. Family history negative. Enlisted Dec., 1916. Went to Egypt, March, 1917, and later Palestine. Under fire, nervous, not wounded. Has had malaria off and on since the beginning of Aug., 1918, and was admitted to hospital with fever and physical and mental exhaustion.

29:8:18. Hospital, Cairo. Reports:- Exhaustion psychosis. Fever. Listless, apathetic.

13:9:18. Benign Tertian Parasites found in the blood.

29:9:18. Listless, apathetic. Too tired and bored to move. Self-absorbed. Voices talk to him--he does not know who they are. Given iron, arsenic, and quinine.

1:10:18. Dull, looks morose. Wants to be left alone, and resists interference--refuses medicine. Disorientated, apparently from lack of interest.

11:11:18. Anaemic and washed out. Still listless, dull, apathetic.

10:2:19. Much better--has steadily improved mentally and physically. Gives a clear account of himself, and answers readily and rationally. Orientation normal. Says he does not remember ~~hearing~~ hearing voices when he was fevered, and certainly has not heard them since. Knee-jerks and pupils normal. No evidence or history of alcoholism. Blood Wassermann negative.

April, 1919. Very well, discharged home recovered.

CASE II.

Pte. W.G., aged 25.

30:8:18. Cairo. Listless, apathetic, seems to be much trouble for him even to attempt to reply to a question unless much pressed. Complains of vague pains over left upper abdomen. Drowsy.

11:9:18. Says he is exhausted playing ring quoits. Feels weak. Sleeps badly, and worries over vague pains. Watched at night

and found to sleep quite well. Says his mother's brother committed suicide. Hand grip lax--indifferent. Patient self absorbed and reserved.

19:11:18. Still lethargic, listless. Blood Wassermann negative.

3:12:18. History from himself: At school from 14½ standard VI farmer. Pre-War health good. Dardanelles, July, 1915. Under fire--not wounded or nervous. Serbia, Oct., 1915, via Salonica. Under fire again, not wounded or nervous. No diseases. Egypt, Nov., 1917. Under fire again--not wounded but very nervous. Sand-fly fever once; malaria three times. Felt run down. Says he has been four months in hospital in Egypt, and five months off duty in all. Has singing in ears and pains in the head--round forehead and eyes. Easily tired. No venereal disease.

Physical Examination. Thin--says he has lost two stone in weight. Sweats easily, easily tired. Pupils normal. Deep reflexes normal. Romberg negative. Heart and lungs negative.

Mentally: Dull, apathetic. Orientation fair. Memory poor, and uncertain. No delusions or hallucinations traced. Says he feels pretty well in his head, except for singing in ears. No other mental abnormality.

5:3:19. Home, well.

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CHAPTER XVIII.

DEMENTIA.

It has been commonly observed that men who have come back to the old country after many years in the tropics especially in malarious districts, have suffered mental deterioration in the interval of absence. In some the finer shades of character have disappeared, in most there has been an appreciable weakening of mental capability, showing as diminished capacity for work, range of interest and acuity of thought, perhaps with some irritability of temper; in any case, some general mental enfeeblement. The history generally is that there have been a few attacks of malaria every year throughout the absent period, maybe punctuated by more serious incidents, such as coma, headaches, pneumonia, or maybe accompanied by general ill-health with anaemia or even cachexia.

Now the mental change in the patient maybe only slight enough to be noticed by his intimate friends who knew him before it occurred, or it may be much more obtrusive. But it is very often associated with such things as sun exposure, alcohol, overwork, which are severally credited with the change, with the result that malaria drops out of the reckoning as even a contributory cause.

Régis draws attention to the mental changes in soldiers after service in colonies where malaria abounds. They often become obtuse, amnesic, impulsive, mentally enfeebled generally as well as physically, and appear as delinquents after years of excellent service.

Marandon de Montyel records some cases of dementia, two of which ended in complete primary dementia without passing through any other mental phase—one after three months severe fever, and slowly demented during nine years; the other after the third malarial attack within one year. Three other cases of his demented after passing through a maniacal phase. He records two similar cases of Frerichs', one in a woman, and one in a girl of nine years. The child had been mentally normal until onset of tertian fever when she became an idiot.

We have seen what malaria can do as a tissue destroyer. A

survey of the literature shows that a small proportion of cases that have survived the more acute attacks, or that have struggled on through long periods of chronic infection, end up with varying degrees of general mental deterioration or dementia.

There are three main forms observed.

1. Simple Dementia.
2. Dementia Praecox.
3. General Paralysis (Malarial).

1. Simple Dementia.

A slight weakening of the mental capacity after malaria is not uncommon. The patients will tell you themselves they are not the men they were, meaning that they have not the intellectual capacity or mental staying power they had. This may be associated with being run down physically, but may persist after physical restoration, as occurs in other toxic psychoses. There are all degrees of general mental enfeeblement, down to complete dementia—the terminal stage of some of the other clinical forms of mental derangement.

According to Hesnard, malarial dementia affects more the intellect than morals, involves more the memory, general mental activity, ideation, rather than greatly altering conduct. The malarial dement is more amnesic, apathetic, but more self-conscious, less brutalized, more correct in his reactions, less morally degenerate than other dements. The last feature may want some revision, as we shall see from the medico-legal chapter, though delinquency is probably more apt to occur during the more active phases of infection, before final and stationary dementia is reached.

The following record is that of the one case appearing in the list of 131 cases of the writer's. It may be that some of those sent to civil asylums after a year in the Army mental observation wards, finally demented. These, however, have not been traced. Usually, the malarial attacks, after repatriation, were not so frequent as formerly, and in many instances appeared to have died out. In a small percentage of cases, there was an accentuation of the malarial attacks, and in these the psychoses tended to recur.

Simple Dementia.

Pte. J.W., aged 41.

27:12:18. Salonica. On admission he behaved in a childish manner, but his orientation does not appear confused.

Physically: Anaemic, poorly nourished. Heart and lungs normal. Spleen and liver normal. Oepp reflexes brisk. Plantar reflexes flexor. Hand grips normal. Pupils equal and sluggish to light.

29:12:18. Balkans, March, 1916. Took malaria first in 1916, and has had eight relapses since. Has had no home leave in nearly three years. M.T. parasites in blood.

11:1:19. Mentally dull, stupid, seems generally deficient. No delusions or hallucinations. Blood Wassermann negative.

29:1:19. Easily loses self-control. All mental faculties slightly improved. He remains for the most part idle and unoccupied.

15:2:19. History from himself: Mill-worker. Married. One child. States he was in a poor nerve condition for some years before the war. Denies alcoholic excess and V.D. A sister was an imbecile. Salonica, May, 1916. Not under fire. He answers fairly well, but looks unstable. Eats and sleeps well and does not complain. Physical nutrition now good.

10:5:19. Has remained well—but shows some general mental enfeeblement. Home to care of friends.

2. Dementia Praecox.

Dementia Praecox types have been dealt with separately in the chapter with that heading, but an example of terminal dementia after a clinical course showing the features of dementia praecox is given by Laurès, viz: A young man of 28, repatriated from Morocco in a state of post-malarial mental confusion. This condition was later complicated by catatonia, incoherence, grimacing, onanism, alternation of depression and psychomotor excitement. Six years later, he was in a state of general mental enfeeblement which was apparently stationary.

3. General Paralysis (Malarial).

Dementia paralytica is generally associated etiologically

with syphilis. Nevertheless cases occur, clinically identical with certain syphilitic forms where the only apparent cause has been alcohol. These cases exhibit notably general mental enfeeblement, dysarthria, tremors, exaggerated reflexes and pupillary paresis, have no history or clinical evidence of syphilis, and blood and spinal fluid are both negative to the Wassermann test. The same apparently applies in malaria, and instances have been noted by Berthier, Bard, Rey, Marandon de Montyel, Lemoine, Porot and Gutmann and others. Vigouroux noted that in 14 cases out of 62 general paralytics at Asile De Vaucluse (22·5%), there was earlier malarial infection and in three of these there was no clear evidence of either syphilis or alcohol.

Marandon de Montyel maintains that acute or chronic malaria is capable of producing the syndrome of general paralysis of the insane, and details eight cases, in seven of which there were other factors which conceivably may have contributed to the dementia, such as alcoholism, defective heredity, cerebral traumatism, insolation, early but treated syphilis. In one, however, —the case here given in full—under his name—no other etiological factor than malaria was discovered to account for the disease. He points out that in his experience the course of the disease is rapid, in one three years, in four less than two years, in two less than one year; that it is not a common sequel of malaria, and that it has no special characteristics to distinguish it from the same syndrome from other causes.

The syndrome of general paralysis may occur in transitory form during the acute and febrile stage of malaria, or may take a more permanent and stationary form. It is easy in the light of pathological findings, to imagine that in the transitory form the nerve centres are irritated by massing of parasites, toxin, vessel blockage, but are still capable of recovery on withdrawal of the parasites; while in the more stationary form, permanent damage to brain cell elements has been done.

2 Examples of the syndrome of general paralysis are given, one with recovery, the other fatal.

CASE I.

Pseudo-general paralysis of malarial origin ending in

recovery. (Porot and Gutmann).

The legionnaire F.L...., was sent to hospital, 14:2:17, with the diagnosis "mental trouble". "General Paralysis—dysarthria—crises epileptiform".

Malaria, Aug., 1916, followed by a long period of lacunar amnesia. In hospital at Marseilles, 25th Sept. to 27th Dec., with mental confusion, fits, and malaria, and left apparently well. Rejoined depot in Algeria, 2nd Jan., 1918, where after 5 weeks he was sent back with the diagnosis of general paralysis.

Admitted 14:2:18, he appeared weak, anaemic, semi-stuporose, mentally enfeebled, inattentive; speech embarrassed and slow; reflexes very active; pupils sluggish but equal; marked tremor of hands.

No excitement, no marked disorientation, between the periods of amnesia he complains of not knowing what he is doing at times, and of great fatigue.

Benign tertian parasites found in the blood. Lumbar puncture shows a hypertension of cerebro-spinal fluid, which contains a slight increase of globulin, and 26 lymphocytes per cu.mm.

During a malarial attack he exhibited a fit such as described in the history—namely he fell out of bed, shows hysteria like convulsions, was contorted and had episthotonus. Replaced on his bed several minutes later, he threw everything within reach of his hands in a fit of violence, and had to be isolated. Temperature 39·9°. Severe sweating.

Intensive quinine treatment.

He improved rapidly both mentally and physically, attacks subsided, and tremors and dysarthria disappeared. He left hospital convalescent on 1st April, 1917.

CASE II.

Fatal case of malarial general paralysis. *(Marandon de Montyel).*

Charles X., aged 40, bachelor, shoemaker, entered Ville-Evrard, 28th Aug., 1892. Family history absolutely negative.—no trace of neuropathic taint discovered at all.

A Parisian of Parisian parents, and all his family in Paris. Special pains were taken with the investigation of this case, as it

appeared different from all the other cases of general paralysis of malarial origin which had been handled by the author. The result of these observations and enquiries was that there sas nothing either physical or mental in the family history, or personal history of the patient, to suggest any predisposition to physical or mental breakdown in any form. The patient was well set up, had no stigmata of degeneration, and intelligence and mentality had been quite normal up till the onset of the sighs of general paralysis.

His education had been normal, and after leaving school he had rapidly become an excellent shoemaker. At the age of 7, he had measles, and at 9 mumps, but without any cerebral complications. It is certain he had never had syphilis. There had never been any head injury, and he had been very temperate. Charles X. had never had a taste for alcohol, and during the 16 years of malarial infection preceding his entry to Ville-Evrard he drank rather less than formerly and not even always wine. Thus apart from malaria, it has been impossible to explain this case of general paralysis, and his family appeared to be right when they maintained that the fever had gone to his head.

Charles X. served in the navy, and was sent to Algeria. He kept well there for two years, then contracted malaria at the age of 23, and has never been cured of it since. The infection was severe from the start, of quotidian type, and so tenacious that after four months in hospital he had to be repatriated to France to his friends and he remained very anaemic. In Paris the fever subsided fairly rapidly, and after 3 months the patient was able to resume his service at Toulon. But he was not clear of his malaria, and in spite of treatment, in July and August of each year, he had bouts of intermittent fever of quotidian type. Two or three times he had violent cranial neuralgia, recurring each evening about 6 o'clock, which necessitated the taking of several doses of quinine.

Because of his malaria, he had never married, and lived with his mother pursuing his vocation as a shoemaker. Until the end of 1891, his mentality remained normal—he was then 39, and had had malaria for 16 years. About this time he became aware of some diminution of mental capacity, and had a fear of becoming mad. He became dull and preoccupied, complained much of his head, and slept

badly. He complained of loss of memory, and difficulty in collecting his ideas. This stage lasted till about the middle of Aug., 1892. At this time there was a recurrence of malarial attacks and after the second attack, he had an epileptiform seizure from which he emerged a confirmed general paralytic.

He was then put in an institution. At the time of entry into Ville-Evrard, he was in a state of great agitation, and presented the appearance of a chronic periencephalitic; unequal and contracted pupils; embarrassment of speech, and fibrillary tremors of muscles of the face and lips. Mentality there was a mixture of ideas—grandiose and hypochondriacal. He was distributing millions of money, and boasted of his strength—at the same time refusing food on the pretext that he had no bowels. His condition was becoming serious by the refusal of food, as he was already cachectic with enlarged liver and spleen and had much need of nourishment. Fortunately, the hypochondriacal delusions disappeared after a fortnight, when his appetite went to the other extreme, which gave the opportunity to administer large doses of quinine. But the patient did not improve, and he became weaker, while his paralysis progressed. After six months in the institution, he was in the third stage of his illness, obliged to keep his bed, losing ground, and quite demented. He died marasmic on 15th June.

The symptoms and course of the illness left no doubt about this being a case of general paralysis. Autopsy done 24 hours after death confirmed the diagnosis, and malaria remained the only etiological explanation of it.

In connection with dementia in its various degrees as a sequel to malaria, it is of interest to remember and consider the frequency of mental infantilism and feeble-mindedness occurring in the highly malarious districts of Syria, Africa, and certain districts of France and Italy of 100 years ago. It would seem as if man were not only pulled down from his high estate by this insidious and intractable disease, but was actually hindered in his approach to it where its debilitating influence has had a chance to operate through heredity or in infancy. This aspect of the subject is more fully dealt with in the chapter on race degeneration.

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CHAPTER XIX

AMNESIA.

Most observers who have had personal contact with large numbers of malaria patients, have been struck with the frequency of the occurrence in them, of amnesia. A large proportion of the case records in the literature include memory defects in their symptomatology, and if the case records in this work are read with this in mind the frequency of the incidental occurrence of amnesia will be noticed.

Manson records loss of memory occurring during and after attacks of malaria, in those who have lived in Africa for varying periods, and its frequency is epitomised in the phrase "West Coast Memory" (Africa).

Kraepelin, de Brun, Régis, Mesnard, Porot, Gutmann, Simonin, Pepper, Conti, Goodhart, Walliser, and many others testify to its frequency in their experience of malarial subjects, and most of them, especially Kraepelin, Régis, Mesnard, Porot, Gutmann, and Simonin, emphasise its medico-legal importance.

The writer's own experience coincides with that of these observers. Many of his cases who wandered away, or became threatening, or who committed acts of violence to themselves or others, had no recollection of these things afterwards. He recalls discussing such matters especially with suicidal cases. One very estimable man, who cut his throat in a fit of confusional depression, and whom the writer came to know very well and to trust, assured him with complete acceptance that he had not the slightest recollection of the occurrence and was rather concerned about the impression that the throat scar would make upon his wife. Another attempted suicide, who cut his throat but was caught in the act, fought like a tiger with several men in his evident determination to complete the job—and had absolutely no subsequent recollection of it. Some, however, do have a recollection of their acts after the event, but complain of an incontrollable impulse to do things which in better judgment they would know to be wrong and be able to resist. In others again events subjective and objective appear as in a dream, and they are passive onlookers. All degrees and varieties of amnesia occur, from the complete mental blank (lacunar) to the memory defect for certain words

events, etc., and the duration ranges from short periods of an hour or so up to weeks and months, and even in rarer cases a year or more.

The medico-legal importance of amnesia is enormous, and the writer has known the difficulties of trying to convince judge and jury from the witness-box of the reality of it, in malarial subjects, who have committed motiveless homicide. This aspect of the subject will, however, be expanded further in the medico-legal section.

This subject has been dealt with so fully and comprehensively by Prof. de Brun, of Beyrouth, that the writer feels he cannot do better than make the following descriptive detail largely an abridged translation of his work.

De Brun points out that amnesia in malarial pathology has not nearly received the attention it deserves, and that it is very common. It occurs both in primary and secondary malaria, and though sometimes occurring as the solitary nerve manifestation, it more often occurs with other nerve phenomena, such as headache, giddiness, cramps, formication, tremors, making one of the most characteristic of the malarial polyneuritic-psychoses.

That is not saying that amnesia is always evident at a given observation; but in a ward of malaria patients, evidences of memory defect are abundant from time to time. Almost a third of de Brun's malaria cases in the hospital at Rueil showed mild or severe memory defects.

He groups them thus:

(1). In the period of primary fever—lacunar amnesia (memory blanks).

(2). In subsequent periods, when different degrees of retrograde and anterograde amnesia occur.

(1). *Malarial Lacunar Amnesia.*

The patient takes malaria for the first time, and has fever from 2-14 days, say, with gastro-bilious phenomena, and nervous symptoms. This subsides. The patient has no impression or recollection of how he has been, or where he has been. He remembers nothing—transfer to hospital, entering ward, who received him, treatment adopted, injections, often painful, given; he will not remember these things, even when the fever subsides, and he appears to be otherwise mentally normal—he will probably retain permanently this gap in his memory. It is a malarial amnesic blank.

This does not necessarily imply other cerebral accompaniments, either noisy or serious—does not imply, for instance, delirium. Two categories of it occur. In one, there are serious cerebral accompaniments, in which case it appears as mental confusion. The second group constitute a more delicate problem. Here the patient appears to have conserved absolute consciousness throughout his febrile attack. He will be able to answer questions correctly during his fever, will look after his needs without any mistakes, even read the newspaper and write letters. Nevertheless, a lacunar amnesia exists in him as complete for the period of attack, as in those of the first group. Whatever the pathological explanation, a blank has marked, as complete, as definite, assuredly occurs.

A very limited number are able to recall what happened during their febrile attack. On the other hand, others have blanks that are permanent, sometimes multiple, for the period of attack, which is generally more violent and prolonged than the others. It may either subside with the fever, or last a longer or shorter time after the fever. It may even last for weeks where the attack starting it lasted only a few days.

Thus one of de Brun's patients with lacunar amnesia which began during his first attack of malaria at the end of June, 1916, did not remember his evacuation to Salonika on 10th July, nor his sojourn in several hospitals, nor crossing the Mediterranean, nor his arrival at Toulon. For all these 8 weeks, his memory was a blank, absolute. It was not until he had been a few days in hospital in France, that by degrees—recollection at first not precise—his memory returned.

De Brun has seen lacunar amnesia last from a few hours up to many weeks. One man had no recollection of being in hospital at Salonica and of being transferred home. He awakened up in hospital at Bandol. A third wakens up in hospital at Bastia, believing that he is still at the front. He has seen many similar cases.

In the cases of short duration, memory defect is generally absolute and complete. The patient has lost all recollection for the period. Others have hazy recollections of the past period—it may appear as a dream, or he may remember a doctor in uniform or such like, without remembering anything else.

It is difficult to get information about the beginning of the attack. Certain facts seem to suggest that it is not always complete from the start of the febrile attack. One of his patients recalls the shivering, and the moment when he went to bed, and his last recollection was being placed near some wine in the automobile that was evacuating him with the injunction "not to drink it all".

The termination is very varied. Sometimes, generally in amnesia of short duration, it ceases fairly abruptly and normal memory returns. On the contrary, sometimes in prolonged cases, there is a period of transition characterized by uncertain recollection, vague as to certain facts, alternating with phases of amnesia more or less complete. This period of transition lasted several months in one of his cases. In his, recollection of the hospital at Bandol where he wakened up is not precise, and is broken with new and serious blanks sometimes with complete mental confusion. He remembered having had a febrile attack beginning towards noon and finishing about 4 o'clock, but twice he was found wandering aimlessly in his shirt in the corridor. Being allowed convalescence from 31:10:16 (amnesia began early in July) he came to Paris and thinks he had some febrile attacks there, for he thinks he remembers being taken in an automobile to the Pasteur hospital on 1st December. He remained there till the end of March, 1917, having thus a very vague recollection of events for fully six months.

(2x). *Retrograde Amnesia.*

This type refers not only to recent events such as pertain to war and military service, but to facts before that, even extending to infancy. The majority forget the names of their comrades, their grade, officers, general etc. Maybe an odd name of comrade or chief can be recalled, but sometimes even a photo does not recall the name. Many have forgotten how long they have been in the army, the name of their regiment etc. Some get hear it, but are often too indefinite.

Recollection of incidents of civil life are not less vague. Names of teachers, professors, friends of childhood, school or college friends are forgotten. They forget parents' ages, wife, father's death date, another's date of marriage, and birth, childhood etc. Parents' names, and wife's family name are forgotten. Or the name of a nephew

may be confused with that of a son. Number of brothers and sisters is forgotten. Or there may be only uncertain recollections of civil life—they do not exactly know where or how childhood has been passed, or the name of the street where he has lived so long. One knows he has a child, remembers lending a hand at confinement, but cannot tell when or where the child was born. Or in doing business, he forgets the name of tradesman or client and dare not go back to his shop for fear of making an inexcusable mistake. The past for them is reduced to a few vague and uncertain rudiments. A learned patient cannot tell in what century Louis XIV lived, and has forgotten almost all about Napoleon I. Suddenly he recalls a date—the birth of Francis I, but cannot tell who were Voltaire, Luther, Lavoisier, "of whom he has heard". Another cannot name the Presidents of the Republic, ignores Louis XV, Louis XVI, and Napoleon III, and makes Francis I live in 1200. He is no better at Geography, and puts Bordeaux on the Seine, Tulle in the Cantal, and Montbrison on the Alps. It is not astonishing that grammar or orthography are forgotten or phantastic.

Some forget a language they speak fluently. One merchant who wrote in English and German, completely forgot the two languages. An engineer who for several years had worked in Frankfurt could no more speak a word of German.

In music the same. An enthusiastic musician and first-rate executant cannot get the air of a piece of classical or popular music he knew well, and cannot read at sight as before. One musical instructor forgets the elements of the Solfeggio.

The same in mathematics. Engineers well up in algebra, and arithmetic, forget all of it; cannot do simple subtractions. A merchant cannot do simple arithmetic, or check an account. Another has to go over a simple addition of two figures a dozen times before he gets the result. A tramway-conductor cannot give change, or tickets, or make up his daily return correctly.

An overseer forgets the formulae he needs, consults a plan on the field, and then forgets the information he is looking for in it. He has to give up his work.

In chemistry and physics it is the same. One foreman electrician mixed up watts, amperes, and ohms, and was very foggy about the simplest things in ~~arithmetic~~ electricity. One therefore

realises the trouble that is apt to arise in following an avocation.

A chemist from l'Ecole Centrale de Lyon could remember nothing about the preparation of the colouring matters with which he had worked since he left the school. He could not designate the different violets, reds, etc.

An electrical engineer is incapable of installing a switch-board. Another, before installing a telephone cannot distinguish the wire for the bell from that of the microphone; next day he could not fix up the commutator, because he was foggy about the wires and made a short circuit.

Workmen and foremen forget the words and habits of their jobs and have to give up. A mechanic forgets the name of his tools and cannot describe them. If he has need of one, he must outline its form or indicate its chief use. He has constantly to depend on the help and guidance of his comrades. He is held up at every step for something depending on loss of memory. A carpenter has forgotten how to make a window; a plasterer forgets the tricks of his trade. A foreman forgets the technical terms of his job, so that he cannot give instructions to his men.

(2β). *Anterograde Amnesia.*

Retrograde amnesia bears upon what precedes the blank. Anterograde amnesia bears upon what follows, and results in defective attention.

Many show this fault of attention, and complain of progressive headache, giddiness, and of their sight, with the least effort of will to surmount their inattention. Very distressed, they observe nothing of what passes around them; they pass down a street without being aware of it; they follow reading badly and do not always understand. Though formerly accustomed to reading, they do not find pleasure in the easiest reading. Often by the next day, or even after a quarter of an hour, they have forgotten all they have read.

One of our patients reproached his wife for not having communicated a family letter which she had read to him the day before.

Some found an actual difficulty in reading, mixing up the words and lines. They could maintain a conversation of any length only with difficulty, failing to follow the trend of thought, hesitating to answer, fearing irrelevance.

Testing the intellectual faculties in detail, it was found that an old pupil of l'Ecole Cantrale, could not count beyond ten, and got muddled between eleven and twelve. In writing, they often make a mistake by repeating the same thing several times. They forget to post a letter just written. Sometimes they write the same letter twice to the same person in one day. They write with difficulty to dictation, repeating or omitting syllables of words; they copy badly and with difficulty.

They forget what they have eaten yesterday, or even to-day, and sometimes even ask if they have breakfasted. Sometimes they forget what they are about, and return without having executed the commission entrusted to them. Mistrusting their memory, one has to write down what they have to do. They forget invitations to lunch or dinner, or any appointment made in advance. Forgetting the City Stations, they have to repeatedly ask directions on a simple journey, where they have to change.

This "amnesia of fixation" may have troublesome consequences. One of our patients had been repeatedly punished for service faults, for forgetfulness for which he certainly was not responsible; another for not having filled a commission entrusted to him in Macedonia; he had found it impossible to find the easy track he had followed the night before. Conscious of his infirmity, a third patient wrote down the order each time he was told off as sentinel. Not the least convinced of the amnesia of one of his men, his Brigadier demanded his signature in receipt of each order given him. One can imagine the disastrous effects of such memory troubles in a superior officer.

De Brun explains that his cases were not long enough at Rueil hospital for prolonged treatment, but that it is certain that this is one of the most impressive forms of cerebral malaria. He also points out that all wounded malarials were discarded in these considerations.

The following case of lacunar amnesia in a woman has been chosen from the literature as a representative example occurring in civil life. There has been a tendency to look upon abnormal mental states in soldiers as due to any other thing—such as wounds, hardship, alcohol, etc.,—than malaria; and a tendency to look upon amnesia in particular as an excuse rather than a reason. It is to a great extent

in this way that malaria has escaped detection as the subtle power for evil that it is.

This, an American case, has been recorded by S. P. Goodhart:-

Miss M, aged 27; nervous temperament, but good personal history. Not hysterical; intellectual, and fond of her work, teaching at school. Mother suffered from epilepsy and died of malignant disease. For a few weeks previous to the beginning of illness in question, Miss M. had been under intense emotional strain. On Sept. 9th, 1813, on returning from school in the afternoon, after a day of unusual fatigue, she was suffering from severe headache in occipital region, and apparently for no reason whatever, was seized with an attack of weeping and showed some considerable emotional reaction, uttering expressions indicative of her uncertainty as to her surroundings. She seemed perplexed as to her own identity and of her relations with her family, and other members of the household. At present she vaguely recalls the state of mind at that time. She directed a number of coherent questions to the maid, but, although she received positive replies, immediately repeated these questions, each time forgetting what she had asked for. Dr. D. attended her that evening and found her in a state of marked mental confusion. This was largely due to the fact that memory for the preceding two days was so defective that she was almost completely amnesic. Her mental processes were otherwise normal, though she was highly emotional, but controlled herself fairly well, and her responses were intelligent, and thought and ideation but very slightly disturbed. In this, the psychopathic state had two distinct components.

The doctor had occasion to speak to her about the experiences of the past summer, and learned that she had forgotten the greater part of them; also that the events of the previous 48 hours had been apparently entirely effaced from her mind. Although she had spent the greater part of the summer at Delaware Water Gap, the name was only vaguely recalled, and not associated with any experience of her own. She could not recall that she had been at school that day, and did not recognize members of her own family, or remember the name of the maid. The temperature was not abnormal.

On the following morning, Miss M. arose, feeling in splendid health physically, and with less mental confusion, although her

memory had not been restored. That evening when I first saw her, she had a temperature of 105°F. Though her mind was clear, she could not recall the events of the past two days. The next day, the 11th, there was distinct splenic enlargement, and a dicrotic pulse. An examination of the blood by Dr. D. disclosed malaria plasmodia in numbers.

The history of the case from this time was a typical rise in temperature and general malaise. On these days there was marked mental confusion preceding the rise in temperature by some hours, though the amnesia was continuous long after all malaria symptoms had disappeared, and even at present (27:12:13) there is only partial restoration. The prodromal symptoms of two days duration were characterized by partial amnesia.

Here we have a case of emotional upheaval and malarial poison acting as the directly exciting factor in dissociation.

Complete retrograde amnesia of malarial origin.

The following case of a repatriated soldier came under the writer's care in the Stobhill Hospital Mental Observation Wards, Glasgow, early in May 1923. It is a good example of complete retrograde amnesia of malarial origin.

A.M., aged 29 years, was brought to the hospital by the police, with the history that he had been found wandering.

On admission he had a complete retrograde amnesia. He could not remember his name, nor that of any member of his family, even his father and mother. He could not remember whether he had been at the War, nor what he worked at, nor anything of the past about himself or others. Otherwise he could talk sensibly, though he seemed a little strange as if concerned that he could not remember these simple things. A few days after admission, his brother arrived from Ramsey, and talking with him, he recovered for the first time his name, and could remember the names of his family members, but nothing else. Still he could not say whether he had been in the War, nor give any information about himself. He looked a little thin, but otherwise looked moderately well. Temperature was subnormal.

For a few days after admission until his brother arrived, he had a complete retrograde amnesia, but thereafter a less complete amnesia, until two weeks had passed. He was allowed up after the

first three days, worked about the ward, was apparently otherwise normal, talked sensibly to other patients and attendants, and seemed content enough. On 21st May, a fortnight after admission, he suddenly recovered his memory and in answer to my questions gave the following information about himself.

He had been quite healthy pre-War, and was a member of a large West Highland crofter family with father and mother both alive and well. He was in the Army, 1914-18. Gallipoli, 1915, for 5 months, and was in the rear guard during the evacuation. He had rather a bad time there, especially during water shortage, and had malaria and dysentery. After Gallipoli, Egypt, then Salonica in 1916 where he spent two years, the last six months of which he was in hospital with malaria. France, Aug., 1918. He was under fire in Gallipoli, Salonica, and France, but was never wounded, blown up or buried. He had six weeks leave from France in Sept., 1918. Had malaria occasionally in France, but was worse at home. Back to France and demobilised in Feb., 1919. He had double pneumonia on the way home, and was discharged from the Army in May, 1919. He was at home a year in Raasay (Western Isles), having malarial attacks several times a week. He started work in 1921 in a ship-yard in Glasgow, and later on in a locomotive yard. 23:5:23. Had a slight malarial attack, with some rise of temperature and malignant tertian parasites were found in his blood. 24:5:23. Asked to give an account of what happened on the day of admission, he said that he had had a headache all that day, that he felt a "dull, cold heavy feeling" about the front of his head, and said so to his mate in the yard. He finished his day's work, however, and at the exit bought a newspaper on the way home and started on a short cut over the hill. He started to read the paper on the way, but felt stupid, folded it up, and put it in his pocket, but kept walking on and did not notice that he had lost his way. A man accosted him on a canal bank (which was not his usual route homewards) told him he looked bad and asked him what was wrong with him. He replied that he did not know where he was. The man took charge of him, and took him to the police office. All he can recall between arriving at the police office and arriving in hospital is the sensation of swaying to one side as he sat in the motor which was turning a corner.

Spleen palpable, and splenic friction heard in left 9th inter-

costal space. From this date onwards his recovery from the amnesia appeared to be complete. All the information regarding his War Service, etc., was corroborated by his brother.
4:6:23. Blood examination:- Polymorphs, 50·2%, Large mononuclears 20·6%, Lymphocytes, 26·4%, Eosinophils, 2·0%, Mast cells, 0·8%. Blood Wassermann negative. Urine normal, and other physical signs negative throughout.
27:6:23. Has kept well so far as memory is concerned, but has had occasional slight attacks of malaria with slight shivering, sweating, and very slight rise of temperature from 97° to normal or a little above. He was given quin. sulph. gr. X, [illegible] + acid. sulph. dil, minims X.

Sometimes amnesia occurs as a primary mental feature as in the above case; sometimes it occurs as a remainder from an acute psychosis—one such case is recorded in the chapter on confusion; and sometimes it occurs as a component part in a mixed mental symptomatology. Occasionally it takes on a form with regular periodicity—i.e. that there is short period of loss of memory for a part of the day, synchronous with the sporulation of parasites, and with the same periodicity—usually tertian—as the form of malaria causing it. This is usually associated with the accompaniments of an attack, rise of temperature, etc., but it may replace the rise of temperature. Schwyzer records a case of aphasia with tertian periodicity recurring for a few hours every third day. This case is detailed in the chapter on periodicity, and may be looked upon as a form of amnesia with periodicity.

Amnesia is a very common feature in the psychic picture of any malarial psychosis, and its study is of immense importance from the medico-legal point of view, which is considered more fully in the chapter with that heading.

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CHAPTER XX

Neurasthenia.

Under this heading have been grouped a very large number of cases generally drawn from the ranks of old malarial subjects, who have emerged from the more acute phases with varying degrees and kinds of physical deterioration. Often enough these patients looked fairly well, and miss the sympathy they deserve. Sometimes, however, they look as they are—far from well, though the precise nature of their disability may escape attention and well-directed treatment for long periods.

They may be looked upon as closely related to, and blending with, the group of cases defined as psychasthenics, but in this group there is rather less emphasis upon the mental aspect of the picture, and rather more upon the physical, and especially the sensory system.

Some patients drift into a neurasthenic state after a few attacks of malaria, others only after years of recurrent attacks, as found typically in repatriated colonials. All of the features of neurasthenia are not, of course, found in any one example of it; there is usually a wide range of symptomatology which makes these patients often exhibit or simulate a variety of syndromes and thus escape diagnosis. There tends, however, to be a general deterioration in health, so that the patient is aware that he cannot do the work that he used to do—he has not the same capacity for sustained effort. The general appearance may be altered from the patient's former habit, in that the skin has become dry, harsh, sallow, cold, and approaching the cachectic, or it may be moist with recurrent and easily induced sweating. Musculature tends to be flabby, toneless, and easily tired. The temperature tends to be sub-normal, though occasionally relieved by infrequent slight rises to normal or a little above (associated with slight intermittent sporulation of parasites). The patient often complains of cold extremities, which may be livid or pale at times. The pulse is often poooor, easily compressible—mobile in that slight exertion gives rise to

tachycardia and palpitation. Headaches are common with congestion of the eyes; intermittent insomnia. The symptomatology may be referable to the different systems in different cases—gastro-intestinal, with anorexia, nausea, vomiting, gastric pains, abdominal neuralgia in appendix or gastric region or elsewhere, diarrhoea or constipation—according as concentration of parasites may determine from time to time. Or cardio-vascular symptoms, with anginal attacks (Castellani), shortness of breath, palpitation, tachycardia with or without exertion. Or anaemia recurrent or persistent, maybe a prominent feature—with lassitude, weariness, easy fatigability. Or nervous disturbances may be prominent—all sorts of neuralgia, facial, sciatic, headaches occipital or frontal, limbs, or the rheumatism syndrome may dominate the picture. Urticaria and herpes are not uncommonly in evidence here also. General nervousness, emotionalism, so that the patient weeps readily or is unduly easily excited or worried, or is peevish and ill-tempered. Vertigo is not infrequent, and apart from its inherent unpleasantness, tends to alarm an already susceptible patient. Some may verge towards the syndrome of hyperthyroidism, where presumably the thyroid has come in for undue stimulation.

Whatever the specific complaint—of pain, or nervousness, or weakness, and however the general appearance may be, these patients know that they are not in their former satisfactory health, and while, if thought of, a blood examination may reveal malarial parasites, the diagnosis may be much more difficult and require some of the methods detailed in the chapter on latency.

A notable feature in chronic malarial subjects in general, which includes the malarial neurasthenics, is a tendency to increased susceptibility to infection with other organisms, so that these patients are very liable to colds, influenza, and sepsis of various kinds, which often serve to mask the real nature of their underlying vulnerability.

A few examples of malarial neurasthenia from the author's collection are appended. The first case is that of a man, who, with his family of parents, brother and sisters, have been well known to the writer for many years. They are all, including the patient, naturally robust. He had been quite healthy until he took malaria,

after which he had many years unsatisfactory health, which was sometimes attributed to "hypochondriasis" by the uninitiated. His periodic breakdowns became so insistent and disturbing to his business, that finally he came under the care of Dr. Castellani, with the desired result:—

CASE I.

Neurasthenia with leg and body pains, incapacity for sustained effort, periodic breakdowns, etc.

T.S., aged 41; father and mother alive and well, and over 70 years of age. Seven sisters and one brother alive and well. One sister died at three with convulsions.

Born in Rangoon. Quite healthy until malaria in 1904. Went to British Guiana in 1905—got more malaria, was there nine months, having severe malaria all the time, and had to come home in 1906 because of ill-health from it. He has never been the same since; easily tired, pain and weakness of limbs, incapacity for sustained effort. Periodic breakdowns with lassitude, and aches about the body. Impotence from 1908.

Married in 1908. No pregnancies. Had malarial attack every three weeks—with weakness and pains in legs. Dull tiring pain. Never had headaches.

In later years, attacks about every three months. At times between attacks, feeling of profound debility affecting limbs, especially; also whole body; could hardly close hands or lift legs.

Intercurrent incidents, such as colds in the head, influenza, etc., precipitated attacks of malaria.

April, 1922. Knee-jerks and pupils normal. Spleen not palpable. Liver normal in size. White adrenal line fairly well marked. General physical signs negative. Blood pressure, 120 Systolic, 60 diastolic.

Last fully developed attack of malaria, Aug., 1921, shivering and sweating. Films contain malignant tertian parasites. Under treatment by Dr. Castellani, since April, 1921.

June, 1925. This patient has been seen frequently by the writer since last note. Since treatment by Dr. Castellani, his

health has steadily improved and for the past three years he has had no shivers as formerly and has been free from influenzal colds as he called them, and has been able to work continuously without any periodic breakdowns. His general sense of wellbeing is restored, and he has absolutely no fault now to find with it. (The writer is indebted to Dr. Castellani for the information as to the finding of parasites, and for permission to use his name in connection with the case).

CASE II.

Neurasthenia, with predominant gastric symptoms.

W.M., pte., aged 29. Fuddler in private life. Health good pre-War—except appendix operation in 1908; no trouble since. Father and mother alive and well. Alcohol moderate; no V.D. Enlisted Sept., 1914. France Sept., 1915. Under fire, but not nervous. Not wounded or buried.

Salonica, Nov., 1915. Under fire, not wounded. Buried, May, 1917. Not in hospital. Malaria, Nov., 1917, and sent down the line with it. In hospital six or seven weeks. Field medical card shows that he was in hospital, Malta, 17:7:16, with fever and had intravenous quinine. Complaint of stomach trouble.

19:8:18. Temperature, 104°F. Benign tertian parasites found in the blood.

20:8:18. Temperature, 103·4°F. Intravenous quinine, gr. X.

21:8:18. Temperature, 102·6°F.

22:8:18. Intramuscular quinine, grs. x.

Quinine caused erythematous rash. Discharged 4:2:19, with neurasthenia. Sent to Bangor hospital about six weeks. Kinross hospital, Nov., 1919, for about 3 months. Improved some, and on light work, Oct., 1920, until about 9 weeks ago. Had a bad attack in Bangor, and another six months ago. About once a month had mild cold feelings, cold hands and feet, severe headaches, generally worse on a warm day.

4:10:21. Complaint of pains in the legs and arms, and severe intermittent headaches. Almost constant stomach pains; tendency to be relieved for a time by food, but cropping out again later.

Sleepless.

General condition moderately good. Palate narrow.

Physical Signs. Heart and Lungs negative. No Rombergism. Superficial reflexes normal. Spleen not palpable. Some splenic friction over 7th left space. Tenderness, left 9th and 10th intercostal spaces. Tenderness ~~left 9~~ over lesser curvature of stomach. No evident enlargement. Says he has occasional cold turns, not quite like a malarial attack, but definite coldness, feet and hands especially, with pallor or lividity. Well marked white adrenal line.

15:10:21. Ewald Meal. HCl. 50. Total Acidity. 75.

Bland diet. Mag. carb. pond., grs. x., liq. atropini, mi, liq. bismuthi hyiratis (B.P. and Co) ifs i., t.d.s. ex aq.

25:10:21. Rather better—to take same mixture without saline, as bowels rather loose.

8:11:21. Much better in regard to stomach symptoms. Occasional slight pain at bedtime. Advised to take a little plain food, then bread and milk, or gruel.

8:11:21. Quinine sulphate grs. x., t.i.d. ex aq., in addition to former mixture.

Jan., 1922. Steadily improved and was able to resume work, feeling very well.

CASE III.

Neurasthenia, with intestinal symptoms.

Gunner T.K., aged 44, married, 4 children. Hammerman pre-War.

History: Health good pre-War. Teetotal. No venereal disease. Family history negative. Enlisted, 5:8:14. Egypt, June, 1915. Under fire, Palestine—not wounded or buried. Malaria, Nov., 1917, and in hospital one month, and convalescing one month. Shivering, diarrhoea. In hospital twice in 1918, with diarrhoea and shivering (Malarial). Demobilised, April, 1919. Worked from May-Sep., 1919, with occasional slight attacks of malaria and diarrhoea—off work a day or two at a time.

Bangour, Nov., 1919-Jan., 1920, (Hospital), with malaria, diarrhoea: very nervous. Working from Jan., 1920—July, 1921, with

odd days off with malarial attacks, shivering, occasional diarrhoea, nervousness, headaches. Stopped work, July, 1921, unable to continue —"done up".

Present condition. 6:10:21. Complaint now—recurrent malarial attacks, diarrhoea, nervousness, weakness. General condition fair—thinner than normal. Physical signs: heart and lung negative. Pupils equal and sluggish to light. Knee-jerks brisk. Superficial reflexes present. Romberg -ve. Nervous, shaky, tremors of hands at times. No diarrhoea just now, but it occurs at intervals. Some tenderness over the lesser curvature of the stomach. Slight spleen friction over 7th and 8th intercostal spaces, and tenderness over the left 8th space.

13:10:21. Says he has had shivering and diarrhoea since last note, and has been in bed from 7:10:21, until noon to-day. Tongue furred. Looks miserable and pinched. Tremors.

20:10:21. Says he has had shivering turns on 17:10:21, and went to bed for four hours.

27:10:21. Rather better.

10:11:21. Says he has had three malarial attacks in the last week, and attended the local doctor. Splenic friction well marked in the 7th left space. Blood film taken to-day shows benign tertian parasites. Given iron and arsenic.

24:11:21. Slowly improving, but slight spleen friction. Put on quinine again, though it does not always suit, because of diarrhoea

February, 1922. This patient was treated with iron, arsenic, adrenalin, quinine, bismuth, and atropin alternating with the fluctuation of symptoms—together with a graduated diet. He slowly and steadily improved and was able to resume work with some assurance of being able to continue at it.

Many of these patients give serious difficulty in diagnosis, as the parasite hibernating in the subdued form for the most part in the spleen and bone marrow may emerge only from time to time into the peripheral circulation and that only under the stimulus of intercurrent irritation such as might be produced by fatigue from work, slight injury, changes of temperature, alcohol, etc. In this way, repeated blood examinations for parasites may easily be all negative, and the diagnosis consequently mistaken until artificial means

for demonstrating the parasite are adopted. This question is dealt with in the chapter on latency, where a further series of cases of various types which may be partly included under the heading neurasthenic, are detailed.

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CHAPTER XXI

MEDICO-LEGAL.

From the preceding chapters, one would expect that cases of medico-legal importance must arise. If states of mental confusion, depression, periods of amnesia, delusions with impulsiveness, are common among the morbid mental conditions of malarial patients, it must be that from time to time they will appear as law-breakers.

It is the business of scientific medicine to distinguish between the mental invalid and the criminal, and to see that the victim of disease is not served with punishment instead of suitable medical treatment. If the disease has been contracted on War Service, it is almost more important to see that grievous wrong is not done to men who have already undergone a full share of hardship and sacrifice. There is no doubt that mistakes of this kind do occur, especially where the abnormal conduct is associated with diseases which are not widely known as causes of mental disorder, or whose diagnosis presents difficulties at certain stages of their course. One example recorded by Biffi will serve as an illustration.

"Lombroso found in a gaol of one of our leading provinces, a wretched case of pellagra, whose father and uncle had pellagra, serving a sentence of 24 years for having stolen some kilograms of onions, which he picked up from a field while in one of his attacks, when he was impelled to run in a straight line, taking hold of everything that came in his way, until exhausted, when he would pass into a profound sleep for 24 hours. He not only confessed his guilt, of a theft he had not committed, but declared that he merited to be executed, and notwithstanding such declarations, his refusal to take any food, with attempts to strangle himself and the display of the erythema of pellagra, in addition to his having been twice in hospital, he was condemned".

The same applies to malaria. Until the War, little malaria was seen in this country and therefore it was not widely known that it can give rise to grave mental disorder with corresponding conduct that may offend the law.

There are several ways in which medico-legal questions may arise in relation to malarial infection:

(1). Illegal conduct arising from malarial psychosis.

(2). Malaria, versus alcohol, as a cause of ill-health, mental or physical.

(3). Accidental death, from rupture of the spleen. (Spontaneous or with slight trauma).

(4). Malaria, versus trauma.

(5). Sudden death from malarial necrosis of adrenals.

(6). Accidental death, following direct infection with malarious blood. (In dental work, or by blood transfusion, for example).

(7). Rare forms of accidental death from muscle rupture.

These will be discussed under their separate headings.

In Italy, so much has malaria been looked upon as a cause of serious deterioration, actual and potential, of the outside worker, that the Italian Government passed a law in 1902 for his protection. A peasant contracting malaria during his work was thereby entitled to claim the quinine requisite for his fever free of charge, together with medical attendance and maintenance expenses, from his employer. The law looked upon the infection as an accident at work, and employers of outside labour were advised to insure against it.

At the same time, the Government fixed the maximum price of quinine sold by all druggists, and in areas where there were no druggists, the sale of quinine was confined to those who sold salt and tobacco, both State Monopolies.

The occasion for these provisions will be enlarged upon by what follows.

(1). Malarial Psychosis Delinquency.

The following case was the first to impress the author with the necessity of recognising cases of this kind.

CASE I.

Case of homicide with death-sentence.

One day in August, 1919, the Glasgow Newspapers published the final judgment in the case of a young man (Scott), who had cut the throat of a woman, so that she died on the spot. He was condemned to death, and was to be executed in 18 days. The medical evidence showed that it was not thought that "malaria had any bad effect on the mental system". Knowing otherwise, the author took some of the notes of the cases recorded in the previous chapters on Psychoses, to a Cabinet Minister, through whose good offices, mental experts were sent from London and Edinburgh to examine the prisoner. From one of these (Dr. H. C. Marr, now Senior Commissioner in Lunacy, District Board of Control), it was subsequently learned that this was a typical instance of recurrent confusional insanity due to malaria, contracted in Salonica while on Service, and in due course the man was reprieved. He had not been wounded or injured in any way, but had had recurrent attacks of malaria during 3 years in Salonica, and was pensioned out of the Army still having attacks of malaria.

The next case is one whose last stages I was enabled to trace through the courtesy of the Procurator Fiscal, Glasgow.

CASE II.

Melancholia, with homicide.

Soldier, aged 33, a shoemaker in private life; single; good health and robust, pre-War. One brother a deaf-mute, died at 19. Otherwise family history very good.

He enlisted in August, 1914, and went to Gallipoli in Sept., 1915. Transfer to Salonica, Oct., 1916. Was under fire, but not wounded, blown up or buried. Contracted severe malaria in Salonica in July, 1917. 11:12:17, while in hospital with piles and malaria, tried to commit suicide by swallowing gall and opium ointment. Mentally dull, sullen, speaks very slowly. He is self-absorbed, takes little interest in his surroundings, and says he thought he was being "crimed" for leaving his regiment.

18:1:18. Better, but thinks people try to make a fool of him.

8:2:18. Says he recollects the attempted suicide as a distant dream. Denies hallucinations, but is solitary, depressed, answers fairly sensibly, and shows mental retardation. Gives the impression of being suspicious, and withholding something. Orientation normal. General health good. Some tremor of fingers. Knee-jerks and pupillary reactions normal.

26:2:18. Blood Wassermann reaction negative. He slowly and steadily improves, and after about 5 months in military mental hospitals was discharged from the Army in April, 1918.

In Dec., 1920, the Procurator Fiscal reports that he committed suicide by drowning.

His history for the twenty months between leaving hospital and his death is supplied by his brother, who was demobilised about the same time and had a few months at home with him after he left hospital; by his workmate at the shoemaking, who had worked with him for 14 years, excepting the 3½ years he was in the Army; and by his landlady, with whom he lodged in Glasgow after demobilisation. All these three people were interrogated by the writer. His brother reported that the patient had always been of robust constitution, and believed he had never had a day's illness before the War. After demobilisation, he was a changed man—dull, morose, subject to occasional shivering attacks, when he went to bed and would remain there for days. He had received the D. C. M. for his war work. After a few months he improved sufficiently to resume work as a shoemaker. His mate stated

that he had known him well before the war, and that when he came back he was a changed man. He would often sit at his work from morning to night without uttering a word. When spoken to he would answer, but appeared to have lost initiative and interest. Sometimes he would disappear for half a day or so, but he made no complaints. He had never been teetotal, but did not drink to excess, and his mate stated that he had never seen him drunk or known him to be drunk. The landlady said he had always been a quiet living man, regular in his habits, and that she had never seen him under the influence of drink.

Here then appears to have been a case of recurrent melancholia following upon chronic malaria lasting about 3½ years, and ending in suicide.

[redacted]

Motiveless homicide with confusion, excitement, and impulsiveness.

O.M., man aged 38. Single. Health good pre-War. Family history negative. Six brothers alive and well. Mother died aged 63.

He enlisted in June, 1916, and went to Salonica in Sept., 1916. He was infected with malaria in May, 1917, and had odd days and parts of days off duty with it from time to time. He had attacks every two or three weeks. His Army documents showed that he was in hospital with influenza for 10 days in Sept., 1918, that he was in hospital with "recurrent malaria" for 10 days in Oct., 1918, and in hospital with "dysentery Flexner" for a month in Nov., 1918. He also had a slight shrapnel wound of the back of the scalp in Sept., 1918, but was not off duty with it. Left Salonica, after fully two years there acting as despatch runner, in Dec., 1918, and was transferred to Bulgaria. In May, 1919, he was transferred to Russia, and was demobilised in Glasgow in Oct, 1919. After leaving Salonica, he had malarial attacks about once a month, and received an Army pension for malaria. He also attended the Tropical Diseases Clinic after demobilisation, and took quinine from time to time.

A month after demobilisation, he resumed work as a car conductor and driver, but felt the work heavy, lacked confidence in himself, and on a few occasions had to be relieved in the middle of a day. On one occasion he walked off his car, and left it standing unattended, having no subsequent recollection of this. In Nov., 1920,

he ceased working because he did not feel fir to concentrate on it, and went home to keep house for his father and two brothers, there being no woman at home.

It was noticed by his brothers that he was a changed man from the pre-War days, and an older brother who saw most of him at home, and slept with him, gave this account of him. He said that he was queer, as if the good in him had become subservient to the bad, conscience had ceased to preside, and the finer shades of his character and judgment had disappeared; he was irritable, short-tempered, lacking in will power, lacking in attention, aimless, drifting, lacking interest, peculiar in his conduct and talk, repeating himself frequently, talking excitedly and incoherently at times, wandering away for hours, when on an errand for the house, and being unable to give an account of himself afterwards, forgetfull, and unreliable.

He was having shivering attacks followed by sweating and accompanied by pains in the head every three or four weeks, for which he took quinine. This state of affairs continued until the night of 17th Aug., 1921, when the brother who slept with him reported that he had a particularly bad night of headache, shivering and sweating, and considers he got no sleep at all. On the morning of the 18th he went out, visited another brother with whom he had a glass of whisky and pint of beer. Although he had been drinking at intervals earlier in the year, he had been quite teetotal for the three weeks preceding 18th Aug.

In the early afternoon he appeared to be flushed and excited, and talked a little incoherently; his brother considered he had a malarial attack working on him, and left him at home with their father, a man of 70. When he returned from his work about 7 o'clock at night, he found his father lying dead on the sofa with severe head injuries apparently produced by a hammer belonging to the house and which was lying nearby.

O. M. was arrested in Edinburgh the next day, and charged with the murder of his father. Evidence at the trial on 24th Oct. went to show that he had been seen outside and talked to by friends or neighbours about 3 and 5 o'clock on the day of the tragedy, between which hours it was considered to have occurred. He had gone

to Edinburgh by a train between 6 and 7 p.m., and had spent the evening with an old army friend, talking freely about his brothers and father as if nothing had happened. He stayed the night at an hotel where he gave a wrong name and address.

On 27th Sept., he was examined by the author. His general physical condition was good. He had a slight fulness of the eyes suggesting commencing exophthalmos, which was noticed by his relations and also by his mates at the front, two of whom commented on it. Skin florid and moist.

His spleen was not palpable, but there was tenderness in the 9th left intercostal space, and a lesser degree of tenderness over the 8th and 10th spaces. There was also splenic friction, heard over these spaces in the axillary line on two occasions within a week. There was no white adrenal line. He complained of occasional headaches. There were three small punctate scars on the back of the scalp, which were not adherent or tender. There was no hemianopsia.

A blood examination, 536 white cells being counted, showed

Polymorphonuclear cells.	66%.
Lymphocytes.	20·5.
Large mononuclears and Transitional cells.	21·2.
Eosinophils.	2·2.
Mast cells.	0·1.

No malarial parasites were found on repeated search, but the large mononuclear count, together with the splenic friction, were considered to be suggestive of their presence.

The prisoner appeared anxious to give all information he could about himself, and so far as his memory served, was clear and rational. There appeared gaps in his memory—periods when he had wandered away, and could not subsequently remember where he had been or what he had been doing. This after immobilisation and right up to the time of the tragedy. He appeared to have no recollection of the afternoon of the tragedy, with the exception of one statement on his journey to Edinburgh. He stated that he was on quite good terms with his father and had always been so. He said that the whole thing was quite unaccountable to him, and he did not look guilt-conscious.

10th Oct. 20 minims 1 in 1000 Adrenalin solution given

subcutaneously. Blood films taken two hours after, ten hours after, and on 11 th. Oct., 13th Oct., were negative for malarial parasites.

15th Oct. A second injection of 20 minims of adrenalin soln. 1 in 1000, was given subcutaneously. Two hours after, blood films showed benign tertian parasites. Splenic friction was heard on 15th and 16th Oct., in 7th left intercostal space, but was absent on several other occasions.

At the trial, two mates of the prisoner who had been with him in the trenches in Salonica gave evidence that he had had frequent attacks of malaria while there, and was sometimes delirious at nights, when the attacks were on him. He avoided reporting sick as long as possible for fear of losing his job, which he liked. He was excited and depressed by turns. One of these mates was beside him for two years and knew him intimately. He indicated that the prisoner was not teetotal, but that it was impossible for him to get excess of alcohol at any time and they were never near a town. He noticed that prisoner was nervous and forgetful, frequently repeating himself.

At the trial, the Crown Counsel read a letter in prisoner's handwriting and signed by him, which had been found in the house after the tragedy. It read: "To all. May has dropped me, so I intend to have her life, as well as another. I will depart this life in peace, for it has been nothing but trouble with me since I was born, through drink". This was not in accordance with facts, as the girl to whom he had been paying attention had not dropped him.

The Judge in his summing up indicated that this letter was the product of an unsound mind, but appeared to have difficulty with the fact that the prisoner gave a wrong name and address at the hotel in Edinburgh. In favour of the prisoner were the facts that he had bought a return ticket to Edinburgh and that no evidence was furnished to suggest that the crime was other than motiveless. A compromise judgment was given by the Jury, of manslaughter with recommendation to lenidency. A sentence of 7 years penal servitude was given.

The interviewing of competent witnesses together with the evidence at the trial furnished evidence in this case of periods of acute confusion and excitement during malarial attacks while in Salonica, followed by lesser degrees of the same thing at longer intervals on his return home. The relatives and friends were clear

that the slight exophthalmos was a post-war feature and this, together with a blood pressure of 140 mm., and tache cerebrale, suggested a moderate degree of hyperthyreoidism. His knee jerks were a little brisk, and his palate slightly narrow, but there was no neurological or other physical feature to qualify the picture.

The amnesic periods, together with the general deterioration of character, were testified to by his brothers, and questioning of the prisoner by the author gave him the impression that the amnesia was genuine. The hyperthyreoidism may have been of malarial origin. This, then, appears to have been a case of recurrent confusion with a tendency to excitement and impulsiveness, and occasional amnesic periods which were probably mild states of confusion. It was probably in one of these fits of confusion, associated with excitement and impulsiveness, that the tragedy was enacted, with little or no provocation.

It is of interest to note that repeated blood examinations failed to find malarial parasites until after the second adrenalin injection, and that parasites (benign tertian) were again found 8 days after this injection by the Crown pathologist, so that the presence of malaria at the time of the tragedy was not in dispute. Besides exhibiting a common difficulty in finding parasites in the blood, this case illustrates the intermittency of malarial insanity, which is so difficult to realise for those who have not first hand knowledge of these cases. During fully two months in prison prior to the trial, this man had no malarial attack and showed no mental abnormality that could be detected by his warders or the prison doctor. On close questioning on several occasions, the writer could find only evidence of recurrent amnesia which appeared to be genuine and some failure of emotional reaction, in that he did not appear to be normally affected by the fact and manner of his father's death, when he was informed of it.

A further point of interest is, that while a large proportion of cases of chronic malaria infection exhibit the signs of ~~some~~ sub-adrenalism with varying degrees of mental and physical apathy, this case showed the signs of hyperthyreoidism, with a tendency to intermittent excitement.

In the opinion of the writer, this man should have been sent

to an asylus, and his efforts in the witness box were directed to support the view that the prisoner should be treated by the law as a mental invalid, and not as a criminal. The defense plea of insanity of malarial origin, however, was complicated by the undue prominence made of the prisoner's use of alcohol by the prosecution, and the absence of mental derangements while in prison awaiting trial, with the result that, although not sentenced to death, the compromised judgment of penal servitude was given. This intermittency of the malarial psychoses always creates difficulty of demonstration in a court of law, as the lay jury and even the uninitiated medical witnesses look upon it as incredible, and as a straining of facts to suit the defence.

CASE IV.

Clinical Dementia Praecox, who committed motiveless homicide, and was sentenced to death.

E. K. B., man aged 24, was charged with the murder of his fiancée, by choking her on 10th June, 1921. Pre-War he was a clerk, and had been quite healthy. At the age of 4, he had fallen from a height on an asphalt floor, and had damaged his head so that he was unconscious for 12 hours, but had emerged without any apparent sequelae and according to his schoolmaster had a very good school record. He enlisted in 1917, and served two years in Egypt and Palestine. He had been under fire, but was not wounded, blown up or buried. While there he had influenza, but apparently made a good recovery. In 1919, he got malaria and reported sick with giddiness, weakness and fever, for which he took quinine, but did not go into hospital.

He was demobilised in March, 1920, and resumed work as a clerk with his former firm. The evidence of his father and fellow clerks we went to show that his health was not satisfactory. He was apparently depressed at times, complained of his head being "wooden", had defective memory, could not concentrate on his work or do the simple arithmetic he had done formerly. On several occasions, he wandered away from the office, and returned hours later unable to give an account of himself. On a few such occasions he was able to explain

that he had come to himself at some place or another, but was unable to tell how he got there, and had no recollection of going. Every few weeks, he would fall into a state of impenetrable silence, when he would not answer questions, and at times appeared as if he did not hear; on these occasions he was sometimes taken to his work where he sat immobile and did nothing, and had to be brought home again by one of his mates.

His father took him frequently to the family doctor, who on most of these occasions could get very little out of him, and who more than once warned the father that if his mental condition did not improve, he might have to be sent to a mental institution. In Dec., 1920, and March and April, 1921, he was in one of these depressed, negativistic moods so that the family became alarmed and hid all the razors in the house. On the 7th June, 1921, three days before the tragedy, the family doctor was again consulted about his mental condition. The immediate cause for this was that he had been found in an outhouse with one of the hidden razors in his pocket. The following day, 8th June, he was brought home by one of his office mates, being unable to come himself, and left at the gate. On the morning of 10th June, he was so nervous and depressed looking that his father did not think it wise to trust him with a razor, and shaved him.

In the evening of that day, he went a walk with his fiancée, and returned home alone, depressed and silent. He slowly deepened into a state of stupor, and was examined by the family doctor who found him quite inaccesible, quite insensitive to pin-pricks, and exhibiting flexibilitas cerea. He was removed to hospital in this condition, in which he remained for several days, and even when removed to prison three days later he was still semi-stuporose. Meanwhile the dead body of his fiancée was found in an isolated spot in the neighbourhood with numerous bruises and a broken trachea suggesting a struggle.

The evidence went to show that there had been an unsuccesful attempt at rape, and that the victim had died by suffocation. On 4th July, 1921, a film of blood taken from the abdomen of the prisoner showed a few maligmant tertian parasites, and 30·4% of large mononuclear white cells. About this time, also, he was in a mildly

stuperous condition with generalised anaesthesia so that a pin was stuck right through his skin without any sign that he felt.

When examined in prison by the writer on 13th August, 1921, he showed a moderate degree of psychomotor retardation, but was accessible, though his memory was not good. He showed diminished sensation to pain. Knee jerks were exaggerated, and unequal and there was no Rombergism. The man himself said he had had shivering turns followed by sweating and depression at intervals of a month or two from time to time since he left Palestine, but they did not seem to attract the attention of anyone else.

On 27th. October, the prisoner was tried for murder, and the defence put up a plea of insanity for which there was abundant evidence. Between demobilisation in March 1920 and the tragedy in June 1921 he had exhibited all the characteristic signs of dementia praecox—catatonic stupor, hebephrenia, negativism, statuesque attitudes and flexibilitas cerea. Between 4th July and 26th Oct., the writer had found malarial parasites in his blood on two occasions, though numerous films between those dates gave a negative result. When examined by the writer on 13th Aug., the spleen was not palpable and no splenic friction was heard, but there was a well marked white adrenal line reaction.

The writer was present at the trial and heard all the evidence. The case for insanity was considered very good and it was thought best by all those concerned in the defence to keep out the causal factor of malaria, as, not being widely known or recognized, it might complicate the issue. Crown counsel, however, succeeded in elaborating the sordid details of the tragedy and minimising the central feature of insanity, with the result that the jury returned a verdict of guilty, and the prisoner was sentenced to death.

Some weeks later an appeal was lodged by the defence, emphasising the evidences of insanity, but it was rejected by the court who referred the case to the Home Secretary.

Meanwhile the writer prepared a memorandum detailing his view of the case—the presence of malarial parasites, the evidence of many features of clinical dementia praecox, and an account of how, at the writer's own suggestion, malaria as the causal factor of insanity came to be omitted at the trial. This account of the case was in the hands of the Home Secretary when a reprieve was granted. The prisoner was

transferred to the criminal asylum, Broadmoor.

Through the courtesy of Dr. Sullivan, Medical Superintendent of Broadmoor, I was enabled to see the prisoner, and to converse with him, in August 1923. Since his incarceration there, he has been mentally quite well, and his conduct has been normal. Questioned by the writer about the tragedy, he appeared to have complete amnesia for that period, and the subsequent experiences in prison and trial appeared to him like a dream, for which he cannot account.

In the opinion of the writer, the correct judgment in this case, in accordance with the plea of insanity (the evidences for which were abundant) miscarried through the misdirection of legal technique. Malaria, though of medical interest and, to the author's thinking, the active agent in the case, was deliberately suppressed and so did not appear in the proceedings at the trial. The evidences of insanity were so clear and plentiful, that it was agreed the considered malarial agency, a disputable thing, might in its superfluity, complicate the issue. In the end, a record of the true perspective of the case, which included malaria, appeared to save the situation.

These four cases impressed the author with the medico-legal importance of the malarial psychoses, and led him to study the matter further.

In the 131 cases of malarial psychoses recorded in an earlier chapter, no less than 58 were guilty of punishable offences—and this is a conservative estimate as some of the documents may have omitted some of the minor offences. Of these, 2 committed assault; 1 threatened homicide; 3 committed homicide after discharge from the army (the three cases detailed above); 19 were threatening in their attitude to their officers or neighbours; 8 wandered away, and some of these were accused of desertion and narrowly escaped court-martial; 34 were suicidal. Of these 34, 13 threatened suicide; 13 made the attempt by cutting their throat, 1 by cutting his arms, 2 by drowning (1 succeeded, the case recorded above); 1 jumped over a window; 1 swallowed fuming nitric acid; 2 shot themselves—not fatally; 1 attempted to hang himself.

Where the question of amnesia was thought of and gone into, it

is of interest to note that of these culpable cases, 22 had no subsequent recollection of their acts (assaults, threatenings, wanderings away, suicidal attempts, etc.) and 15 had some recollection of them, either as a dream or as an irrestible impulse. In the others no record was taken. It may well be that the miseries of war, apart from malarial infection have had an influence upon the frequency of these cases, but even so, a comparison with civil cases seems to suggest that war conditions cannot wholly account for them.

This point is referred to by Forrester, who writes: "In nearly every case (18 with fugues or complete dissociation of personality) some breach of military discipline had been committed, usually a court-martial offence, and they were in consequence admitted to the department as prisoners. The commonest charge was 'absent without leave', others crimes being self-inflicted wounds or destroying Government property. In every case, there was complete amnesia for the whole period, the shortest of which was a few hours, and the longest three months. One man had been convicted and punished for three similar happenings before his case was recognized, and he was sent down to the base for observation. This serious complication occurred so frequently, as compared with its incidence apart from malaria, that it seems as if this disease must be reckoned as an actual determining cause".

Goodall, with experience of 20,000 malarial cases in Macedonia, (benign tertian, sub-tertian, quartan), defines a type of case that suggested malingering, and says that it was not uncommon. One of these was that of a man who had almost run amuck, and he found him in a detention tent under the charge of a solitary N.C.O. Cases of this kind, when examined, would not answer questions, and resented interference. If pupils were being examined, the eyes would be tightly closed, and the head turned away. If reflexes were examined, the legs would be drawn up and the patient appeared to try to make difficulties. Resistiveness seemed to be part of the mental change.

Four of the author's cases of this kind from a large collection of malarious army deliquents are now given as examples.

[redacted]

Depression, with hypochondriacal delusion and attempted suicide.

Gunner S.R., aged 43.

British East Africa, 19:10:17. Reported as having tried to commit suicide three days ago, while suffering from malaria. Tertian rings were found in his blood. Mental derangement coincident with his fever.

13:11:17. Mental symptoms have subsided. Blood Wassermann negative.

History from himself: 10:12:17. Always healthy pre-war—no previous mental or nervous diseases. Alcohol moderate. Denies venereal disease. Enlisted June 1916. East Africa, Jan., 1917. Nov., 1917, sent to hospital with malaria, and went off his head. He had very severe headaches, and remembers often trying to cut his throat. He was sleepless, and heard voices calling him names. He thought people were shouting at him, because he was no good, and he felt frightened. On the voyage home, he began to feel better, and thinks he is about right now.

He is correctly orientated now in time and place, his memory is good, and he has insight into his condition. Physical condition good. He is a powerful, healthy looking man. There is a healed scar on the left side of his throat. Reflexes normal.

He was under fire in German East Africa, but was not wounded. Had malaria first in March, 1917, and again in May and Nov. On the last occasion, it affected his head.

15:1:18. Keeping well mentally and physically. Says he has thought the voices he heard were those of his officers. He thought he was going to be burned, as they said so.

11:7:18. Has been well on the whole, mentally and physically. Since last note, however, he has had two attacks of malaria, associated with headache and mild mental confusion, which passed off in a few days. Discharged home.

CASE VI.

Restless melancholia, with very determined suicidal attempt.

Private S.M., aged 23.

Salonica, 2:7:18. Cut his throat. Dull, quiet, slow in response, amnesia, complains of sleeplessness and worry. Thin, anaemic. Spleen enlarged. Both pupils sluggish to light. Malignant tertian parasites in the blood.

13:7:18. Depressed, but no confession, hallucinations, or delusions. Had malaria first July, 1917, was in hospital, and had several attacks since last attack a month before self-inflicted wound of the throat.

3:8:18. Becomes semi-stuporose, and negativistic. Lies curled up in bed all day and makes no sound.

6:8:18. Impulsively restless. Makes sudden dashes from his bed and resists efforts to put him back. Controlled by hyoscine and morphine. Quinine, grs 15, intramuscularly, at intervals.

22:9:18. Semi-stuporose. Throat wound healed. Very dull, depressed, answers monosyllabic. Hears people speaking about him outside his room. Blood Wassermann negative.

10:10:18. Marked improvement physically and mentally.

8:1:19. Slightly depressed. Attempted to escape to-day—was violent, and placed in padded room.

12:1:19. Attempted to strangle himself with strip of blanket.

15:1:19. Improved, less inclined to be suicidal. Very determined when suicidal feelings come over him, and will attempt to strangle himself with even a piece of string.

History from himself. Sea-faring pre-War. Health always good. Family History negative. Admits alcoholic excess and V.D. France, Dec., 1914. Not under fire. Exposure and became nervous, 1915-16. Salonica, March 1917. Under fire—nervous. Malaria, July, 1917, and off duty 3 months with it. Frequent occurrences—depression.

Examination—Thin. Knee-jerks brisk. Pupils sluggish but equal. Large healed scar in throat. Still depressed, but gives clear and connected account of himself. Does not remember cutting his throat, but remembers being very depressed, and thinking he would not get better. Thought people were talking about him, but insight now normal. Orientation normal. Says he has now no desire to harm

himself, and feels he is improving.

3:7:19. Has done well. Now no depression. Sent home recovered.

CASE VII.

Confusion, depression, with Army offences in malarious soldier.

Private A.T., aged 25.

5:3:19. Ireland—Admitted to hospital on account of his mental condition. He is dull, mildly depressed, and is inclined to be reserved in his manner. He states he is subject to headaches from malaria, but denies hearing voices or noises. He admits he suffers from insomnia, and feels low spirited. Documents show he had attacks of malaria as follows, 20:8:17, 14:4:18, 7:7:18, 23:7:18, 1:8:18, (2 weeks in hospital), 13:9:18, and was discharged from foreign service on account of malaria. He had several offences during malarial period, such as dirty rifle on parade, making improper reply to officers and corporals.

19:3:19. After admission to hospital, had some kind of a fit. I saw him immediately after, and was told he threatened to break glass. He was put in the infirmary ward, but became troublesome and had to be put in the padded room, where he slept well. He seems stupid this morning, and is dull and depressed. Says he was never subject to fits.

25:3:19. Very dull, depressed. Will not speak except to say "I am all right for a day or so". Still worse and silent in manner, but brightened up and smiles a little when spoken to. Eats and sleeps well. Blood Wassermann negative.

1:4:19. Improved slightly for a few days, but relapsed again to-day. He is fond of looking upwards to the sky and elevating his hands. He is confused and not inclined to give any information. Keeps very much to himself.

7:4:19. Improved and relapsed again. Two days ago said he felt much better—discussed games. Later became depressed and uncommunicative, looking up in vacant manner, raising his cap, and elevating his arms. Yesterday he was reported for a habit of throwing himself down suddenly on the floor, but would give no explanation of why he

did so. Sleeps and eats well.

11:4:19. History from himself. Law-clerk, single. Alcohol moderate, no V.D. Sister nervous and peculiar. Served in Salonica, which he left in Oct., 1918, on account of malaria.

Mentally, he is peculiar in manner, and is nervous, mildly restless, reticent, talks and mutters to himself. Says he is treated daily by sisters here, and feels this in his head.—It expresses his will-power. He wants to go to Heaven. He expects he will die of the shock. Feels his work is accomplished. He has a special mission from God to do good, and he had a message in the form of a star. He communicates with a Bishop in Ireland, who takes good out of him. This makes him feel depressed. He denies suicidal feelings. Tongue and finger tremors.

9:9:19. Little or no change—sent to civil asylum, and was not further traced. It will be noted that even after six months, this man showed no continuous improvement, and that with a doubtful heredity, and very severe malaria, he would probably emerge with at least some general mental deterioration.

CASE VIII.

Confusion simulating drunkenness as an Army offence.

Sapper W.D., aged 42.

Salonica, 11:9:18. Charged with being absent from duty and being drunk. Found to be confused and depressed, and unable to account for cuts on his arms. Severe headaches at times. Not clearly orientated. Spleen enlarged.

19:9:18. Benign tertian parasites found in the blood. France, June, 1915—Oct., 1916. Invalided with shattered nerves, and in hospital 6-8 weeks. Salonica, Feb., 1917—Malaria.

21:1:19. Greatly improved. Blood Wassermann negative.

8:6:19. History from himself. Health good pre-War. Family History negative. Alcohol moderate. Not nervous under fire in France: not wounded. First attack malaria, July 1918, and was off duty about six weeks with it. Was only 3 or 4 days on duty again, when he got confused in his head, and does not remember anything

clearly for three weeks after that. Denies that he had alcohol at that time, and that if he looked drunk, it was due to malaria. Physically looks well. Pupils and Knee-Jerks normal. Gives perfectly clear account of himself—insight restored and orientation normal. No delusions or hallucinations. Well behaved, eats and sleeps well. Home recovered.

Considering how widespread malaria is within the tropical and temperate zones of the world, it is surprising to find so comparatively few instances in the literature of malarial delinquents of medico-legal importance. These few examples that the writer was enabled to unearth in the libraries of London, Glasgow, Rome and Naples are herewith appended, and it is to be hoped that they will go to illumine a very much neglected department of medical jurispruience.

Régis, the Bordeaux aliénist, appears to have been the most vigorous exponent of the malarial psychoses in legal medicine, and other contemporary Frenchmen have done the same, viz: Chavigny, Heamard, Vigouroux, Popot, Gutmann, Simonin (Val-de-Grâce), and Boibet. Kraepelin, Kraff-Ebing and Walliser have also drawn attention to the medico-legal aspect of malarial mental conditions. In Greece, Cariamatis and Papastrategakis have known instances of the kind. Cariamatis notes the tendency to violence, destructiveness, and combativeness, and impulsive movements, dreams, and delusions of persecution of these patients, and records three cases—a girl melancholic in 1908, who attempted suicide during a malarial attack; a soldier who killed himself after severe malaria; and a ~~soldier~~ sergeant of the Palace Guard at Athens who committed suicide as a sequel to malaria. Papastrategakis records the case of a gendarme of 35 years, who showed frequent infringements of discipline, e.g. absence without leave, desertion of his post, and was punished accordingly, until he was recognized to be ill, and sent to hospital where he was found to be the victim of malarial confusion.

Boinet and Rey record a case of homicide during malarious delirium by an Annamite, whose decapitation one of them was able to prevent, by showing that he was not responsible for his actions.

The earliest case the writer was able to discover in the records, comes from Germany; and although it was before the discovery

of the parasite, the tell-tale periodicity of temperature seems to leave little doubt that the case was one of genuine malarial infection.

[redacted]

Manic-depressive insanity, with fits of rage, impulsiveness, homicide and ultimately suicide. (Meyer).

On 21:5:1828, in Nossendorf, a labourer, K, aged 42, murdered a customs officer with his sword. The murder was a most horrible one, the skull being smashed into 13 pieces and the brain torn out; the breast had seven wounds; the windpipe and ascending aorta were opened; two ribs were broken, and there were 21 cuts with damage to bones and joints.

The murderer was arrested, and to all inquiries kept on repeating "What God does is well done", not appearing to realize what had happened. Later he fell backwards apparently unconscious. Ten minutes later he had recovered, and was apparently quite sensible. He was much upset when told what had happened, and could not account for it.

He had always been a faithful and obedient workman and was liked by all who knew him. For some weeks before the tragedy, he had been ill and had been off work at intervals in consequence. A neighbour who saw him on the 12th May, recorded that he was talking nonsense. His doctor saw him on 21st May, and considered him melancholic. His wife indicated that for six weeks before the tragedy, he had heavy shiverings followed by profuse sweatings and that this occurred regularly at 6 a.m., and 12 noon, respectively. From the 5th May, these daily rigors and sweats were accompanied by abnormal conduct and speech, in which emotional instability was evident by attacks of fear and weeping. He also from that date had fits of anger, and especially between the 19th and 21st had fits of fearful rage, in one of which he killed a dog. He was happily married and had four children. His father and mother were alive and well, and his whole family history revealed no evidence of mental or nerve disease. There was no history of alcoholism.

Some years before, he had become infected with intermittent fever

and in the later years had been troubled with nose bleedings after exertion or excitement.

For 5 or 6 weeks before the tragedy he had attacks of double tertian fever, and had off work a good deal of that time. He complained of cramps in the chest, and pressure in the head. Examined in prison on 23rd May, he looked ill with face pale, eyes glassy, and a small pulse (76). He had an attack of fever daily till the 27th May; he had none that day, but they resumed daily again until 1st June, when he had another quiet day. At intervals he talked of the tragedy in a confused way. Between 7th and 14th June, he was quiet and collected, and slept well, but was much emaciated and very weak, and his memory for events before his six weeks illness was normal.

The court found him not responsible for his actions, which they considered due to intermittent fever, and he was sentenced to detention for life in Stralsund Penitentiary, where a year afterwards he hung himself.

Also a case before the discovery of the parasite, but appearing authentic.

CASE I.

Mania, with self-mutilation. (Erhardt).

Erhardt (Kiev, 1866) records the case of a man, N.G., aged 32, who in a fit of mania on 6th April, 1864, cut off his scrotum. A woman with whom he kept company was suspected of the crime, but after due investigation the court found it to be a case of self-mutilation from mania during an attack of intermittent fever.

The next case is also one recorded before the discovery of the parasite

CASE XI.

Boy with excitement, tendency to homicide, and incendiarism. (Wallser). North America.

On the morning of 15:10:1878, I was called to a farm two miles

away, to find a sixteen-year old son of a farmer in a great state of excitement. The history shows that he had always been healthy, with the exception of having had some malarial attacks as a child.

The story was that he had left his bed at an unusual hour the night before and was found by a servant in the garden. As he had bare feet, the servant wanted him to come in for fear of catching cold; whereupon he drew a pocket-knife and gave it to the servant, begging him to kill him. Help was summoned and the youth was brought into the house. He cursed his people and demanded his breakfast. In an unguarded moment, he escaped, lit a wisp of straw at the kitchen fire, sprang across the court to the neighbouring barn, and was on the point of setting fire to the hay when someone noticed the smoke and stopped the unconscious delinquent. Without any trouble, the boy was brought back home and kept there. In the evening of the same day, he spoke quite sensibly, and ate with a good appetite, and had no recollection of the events of the morning. He slept quietly the whole night.

On the morning of the 16th, there was a repetition of the conduct of the day before—he got up early leaving the bed wet through with perspiration, went into the garden, flying before the after-coming servant, he grabbed a hatchet, escaped into the street, and made for the town. Every one he met he begged, crying, that they would split his head with the hatchet. Caught and brought home, he procured some matches, escaped under the pretext of necessity, and once again was just prevented in time from setting a house on fire. Before my arrival, he had several times called for his mother, who had gone to Europe two months before.

The parents and other children were healthy. At 10 a.m., I found the patient crouching behind a stove in a state of great excitement. Those present had just wrested from him a double-barrelled gun, with which he had threatened to shoot himself to prevent the police catching him. The face of the emaciated boy was red, and the back of his head hot. After forcible removal, he looked anxious. Pupils were strongly contracted, and did not react to light. Clonic spasm of upper and lower extremities. Anaesthesia; shouting brought some disconnected words in response. Tongue moist, not furred. Skin hot with high temperature. Pulse 120, temperature in axilla, 39·2°. An hour later, pulse 120, Temperature 39°. Bowels and bladder moved the

same morning. Spleen enlarged. Liver dulness normal.

Treatment: 1 cgm. morphia subcutaneously. About 20 mins. later some relaxation of muscular contraction, and patient less restless. As all the symptoms indicated are quotidian fever, and also the cerebro-spinal phenomena were traceable to malarial fever, 1 gm. of quinine was ordered, three doses two-hourly, also ice-compresses to head and back of neck. He slept well that evening and night, with profuse perspiration. Next morning, singing in the ears. Pulse 88, Temperature, 37°. Appetite good. Thereafter normal.

Walliser draws attention to the medico-legal importance of this case, and goes on to indicate that in eleven hundred cases of intermittent fever which he has treated within two years practice in the state of Illinois, 8% showed a stage of marked excitement. More than half of these were children under 10 years of age, of whom 7 died in convulsions. There were no deaths among adults.

The patients remembered nothing of what they said and did during the acute excitement period. In several of the cases, spontaneous recovery took place.

This case is of further interest as exhibiting amnesia, as well as periodicity of mental derangement.

The record of this case is before the discovery of the parasite in 1880, but the author seems in no doubt about the malarial nature of the case, and the response to quinine seems to support that view.

CASE XII.

Melancholia, with suicide (Arcangelo).

Arcangelo records a case of suicide during malarial infection. The victim, a man of 30, a railwayman, was found on the railway on the 14th Oct., 1898, dressed, lying on his knees and elbows with body arched between them, and his right hand, half-shut, near his left side. There was a pool of blood under him and his waistcoat and shirt were open. A long thin pocket-knife was found nearby. Over the left breast were six penetrating wounds, three of which had pierced the heart. There were no other signs of violence on the body, and no

signs of struggle. At autopsy, the spleen was found enlarged, the liver showed some fatty degeneration, and there was some blood-stained fluid in the peritoneal cavity, conditions, which Arcangelo states are found in advanced cases of marsh infection. There was also some meningeal hyperaemia.

The man, G.S., was married in 1893, and had two healthy sons. Family history good; no history or evidence of V.D., syphilis, or excessive alcoholism. In Aug., 1898, he took tertian malaria which abated with treatment, but which returned under physical or mental strain.

He became depressed and the depression was greatly accentuated shortly before the tragedy upon the death of his wife to whom he was devoted. He continued at his work, however, having recurrent attacks of malaria, and taking quinine until the 14th. Oct., the day of his death when, being worse than usual, he went a long way to see the doctor. Not finding him, he returned to his signal box in a highly fevered condition and was noticed by a friend to be flushed, with eyes staring, walking about aimlessly, and talking nonsense. Later in the day he is found dead under circumstances pointing to suicide.

This case led Arcagelo to look into the medico-legal aspects of malaria in Italy. He found that dwellers in marshy districts were less energetic physically and mentally; that their imagination was obtuse; that general sensibility was diminished; that ideas of persecution with suicidal tendencies were common; and that crime was more frequent than in less malarious districts.

He points out (1899) that malaria greatly influences the criminality of a district and that in Italy malaria and crime are in direct proportion to one another in the various regions examined,

Torelli's report to the Senate in 1882 showed crime statistics for every hundred thousand inhabitants as, in Lazio 7898,34; in Sardinia, 4549,47; in Calabria, 3397,69; in Campania col Molise, 3295,73; in Regno, 3370,27—which figures also correspond to the degree of infection with malaria.

Moreover the brutality of the crime is greater in malarious districts—murder, rape, extortion, assault have been noted to be much more frequent in places greatly infested with malaria. Police statistics for convicting in very malarious districts, such as

Catania (57,21), Siracusa (53,63), Caltanissetta (46,12), Foggia (43,99), Catanzaro (42,46), Reggio Calabria (42,83), Naples (42,62), Lecce (38,57), Messina (37,61), Cosenza (34,68), compare very unfavourably with slightly malarious places such as the Provinces of Reggio, Emilio (6,78), Alessandria (6,58), Pavia (6,37), and Como (5,10).

Homicide shows the highest percentage in highly malarious places such as Girgenti, Sassari, Catanzaro, Palerso, Trapani, Caltanissetta, Foggia, Naples, Campo Basso, Caserta, Reggio Calabria, Catania; while it has lowest percentages in only slightly malarious places such as Rovigo, Mantova, Reggio Emilia.

Rape, extortion, assault, are more frequent in highly malarious Girgenti, Grosseto, Sassari, Caltanisceta, Palermo, Cagliari, Trapani, Catania, Naples, Rome; while these are rare in Rovigo, Bergamo, Macerata, Belluno, and Como, the mildly malarious quarters.

The province of Venice, famous for its ancient splendour and rich industries, still being the province most affected by malaria of all Veneto, follows the same general law, and shows about double the quantity of crimes of the other provinces of Veneto. There are some provinces which are exceptions to the general rule, and of course malaria is not the only cause of crime, but its influence on criminality is unmistakable.

Arcangelo points out the frequency of malarial neurosis in various forms, and its importance in legal medicine. He also draws attention to the tendency of the nervous phenomena to occur with periodicity, as if these replaced the fever periodicity at times. He had occasion to see many cases of mental and nerve disturbance among malaria patients in his practice in Sicily. He cites cases referred to by Motet—one of an individual surprised while openly stealing at an exhibition, was found to have been subject to impulsive attacks dating from having been seriously ill with malaria; another arrested in the act of filling his pockets with stolen objects near the Louvre, was found, subsequent to malarial infection, to have been subject to recurrent attacks of loss of consciousness and eccentricity which up till then had only happened at home. Arcangelo, while remembering that all crime is not due to malaria and that all who are infected with

malaria do not become delinquents, believes that it is the multiplicity of cases of this kind and worse throughout his country that have done much to earn for it the name of barbaric Italy.

CASE XIII.

Homicidal Impulsiveness, in malarial subject. (Dowden).

A quiet elderly Chinese, Kapala (headman of coolies), employed in a small mine near Bidor, Batang Padang, Perak, Federated Malay States, was admitted to Batu Gojah Gaol, while awaiting trial in the High Court on a charge of ~~causing~~ causing "grievous bodily hurt" to two of his own coolies.

The assault was a sudden one without any apparent cause, and the question arose as to what this man's mental condition was at the time of the assault. On admission to the gaol, he was found to be emaciated, he had an enlarged spleen, and the usual signs of chronic malaria. Plasmod. falciparum were found in his blood. He was treated for this condition and rapidly improved. When questioned, he made the following statement quite freely and concealed nothing so far as one could judge:—"I am a Kapala on a Chinese-owned mine near Bidor. I have worked there for four months. My duty was to find the coolies, and I received 10 cents for every coolie who performed a day's work; we found plenty of tin and wages were regularly paid. The coolies complained of nothing, and were all quite friendly. I can only remember two coolies leaving the mine. They left because they said they were sick. I think they had fever, but I am not sure. All the others kept in good health. We slept in a large Kongsie (shed). The other coolies all slept together, but I had a room to myself, shut off by attaps (dried palm leaves) from the others. I could easily hear what was said outside. All the time I lived at Bidor (Batang Padang) I was more or less ill. I had constant fever. I used to take Chinese medicine, and it did me no good.

"I remember one night when two of the coolies were hurt. I struck them with a parang (long knife). That night I had high fever. I was very hot. I heard the two men in question talking about me in the Kongsie outside my room as I lay on my bed. They used foul

expressions about me, I waited some time. All the other coolies were quietly asleep. Two men near me kept on talking, they abused me. Previously I had no quarrel with them; I was perfectly friendly. I was extremely angry to hear them call me names, but I was not surprised. I felt no surprise even though I knew they had no reason to abuse me. I felt enraged. Finally I got up and seized a parang and cut them wherever I could. As soon as I had cut them, I went back to bed, and I felt quite satisfied. No one told me to attack them. They were lying on their beds. Did it because they kept on saying foul things about me. I know they say they were asleep at the time, and did not say anything. I heard them speaking. The other coolies woke up, and I was arrested by them. I did not want to run away, as I was satisfied with what I had done.

"After this I don't remember much of what happened. I was too ill. I was carried by the coolies to the police station, I was too ill to walk. At the time I felt satisfied as soon as I had hurt them. I am glad now that they are not dead".

All the coolies in the Kongsie agreed that there was no reason for the assault. The Kapala was quiet, and friendly with everyone. The injured men say they were asleep, had not been talking, and were awakened by the blows of the parang.

The medical officer of Tapah Hospital, Dr. Morgan, found the P. falciparum in the assailants blood on the day after the assault.

This man repeated the same story, without any essential variation, to the Inspector of Police, the Magistrate, and to myself on many occasions. He was discharged from the High Court on the medical evidence. A remarkable feature of his case is the stress he lays on his feeling of satisfaction after the assault. One must suppose, in the absence of any motive and from the evidence, that the accused suffered from malarial fever and on the occasion of the assault had delirium and auditory hallucinations, culminating in an homicidal impulse.

The author adds that Dr. Samuels, Medical Superintendent of Federated Lunatic Asylum, Federated Malay States, has assured him that malaria is a common cause of insanity.

CASE III.

Paranoid malarial subject—criminal prosecution—recovery, (Hartwich).

German, aged 34, salesman, married, non-alcoholic, non-epileptic. Father a periodic drinker. Visited Tunis 1896, and got malaria. A few years in Africa. Had slight attack yellow fever in Madagascar in 1902. In hospital in Oran with typhus in 1903, and while delirious fell from the second story without damaging himself. Still later had yellow fever a second time.

Criminal qualities first began to show in 1898. He became deceitful, embezzled, counterfeited, was sent to prison and penitentiary.

In 1903, friends noticed that he was mentally ill, showing inclination to brag, tendency to cheat, to lie, with weakness of thought and judgment, at times dazed, stupid, semi-comatose. At that time he complained of fleeting pains in the legs and the shoulders of long standing.

In 1907, first signs of fixed ideas appeared, with at times hebephrenia, hallucinations, delusions (poisons in his food), he was to be murdered, etc). Therewith weakness of thought, short periods of stupor, motor restlessness, pains about the body, and recurrent attacks of fever with shivering.

In 1909, he was again convicted and again brought before the County Court, but in spite of the insanity plea urged on his behalf, he was again sentenced to imprisonment. While in the penitentiary, he got worse, and was sent to the prison asylum, and labelled moral imbecile.

Throughout the whole time from 1896, he had suffered from varying degrees of malaria. Quinine did not appear to help him. When the author saw him, he complained of feelings of anxiety, headache, giddiness, prickling of the skin, pains in the limbs, a dragging feeling between the shoulders and in the legs, and spots before the eyes. Fever and sweating were frequent, but he had no insight into his mental condition. At the end of 1910, his general condition was not good. Skin was grey-yellow in colour, muscles soft and flabby,

and painful on slight pressure. Haemoglobin, 60-70%. Spleen palpable; heart enlarged two-fingerbreadths to left. Apex beat displaced downwards and outwards, pulse irregular, (66). Evidence of old pleurisy at right base; hypersensitiveness over nerve trunks. Reflexes brisk. Pupils equal, small. Visual field on temporal sides narrowed to 2-2·5 cms. Easily tired by standing. Fundi negative. Romberg +ve. Urine normal. Tertian schizonts and gametes in the blood. Temperature swinging between 40,0° and 36,2°.

Mentally he was a complete picture of paranoia. He was irritable, labile, mistrustful, believing that the institution doctors had been influenced, and although no hallucinations were evident, continued to believe in the poison intent, and followed those about him after the usual manner of paranoiacs.

With each outbreak of sweating, he had a kind of fainting fit. Intravenous 606 was given, 0,4 G. to begin with, and two days later no parasites were found in the peripheral blood. Temperature became normal after a few doses, and remained so. His mental change for the better was remarkable. After the first dose, he went into a state of dreamy coma, but emerged improved. Headache, giddiness, fainting turns disappeared; also Rombergism until in a few months insight had returned and he said: "I cannot conceive how it has come about that these charges have been brought against me". "I can't see how I have done these things". "I feel like one new born".

And indeed his paranoia was over. His blood showed 90% Hb, pains disappeared, and he looked mentally and physically a new man. He was released, and returned to his family in June, 1911, and resumed business. In Sept., 1911, no parasites were found in the blood, and the patient continued to do well.

CASE II.

Persecutory delusional insanity, with homicidal tendency in malarial subject. (Ziemann).

Salesman aged 36, small stature, rather pale, neurasthenic, but not alcoholic, living in an unhealthy region of the Cameroons, and subject to malarial attacks. (1908). Had not taken quinine prophylactically. Had several malarial attacks of slight to moderate

degree of malignant tertian infection.

Suddenly one day, he took a severe attack and developed delusions of persecution with excitment. He grabbed his gun to shoot his neighbour, but was restrained, and put on quinine treatment. During his fever, he thought his neighbour was trying to keep him down.

He recovered completely without any evident residuum of hallucinations, or damage to the intellectual faculties.

CASE XVI.

Malarial delirium, with aggressiveness, (Cabot).

In the spring of 1893, a patient was brought in a cab to the Massachusetts General Hospital, fighting maniacally with his companion. This was about 5 p.m. His companion stated that the patient had been apparently perfectly well, and at work as a day labourer that same day, at noon, when, without rhyme or reason, he suddenly went crazy, and after some delay was conveyed to the Hospital. After being put to bed, he soon became manageable, and slept a good deal of the evening as well as the night. His temp. was 103·5°F on admission. Pulse not quickened, respiration normal. His leucocytes not increased. The only abnormal feature was a palpable spleen. A preliminary diagnosis of typhoid fever was made.

Next morning temperature was normal, and patient seemed dazed, otherwise almost well. After an hours search, a pigmented malarial parasite was found in the blood. Quinine was given in large doses, and patient was able to leave the hospital 24 hours later.

Discussion: The case illustrates the clinical manifestations of that overcrowding of the cerebral capillaries with malarial parasites which is so familiar to students of tropical medicine, who see autopsies in the pernicious forms of the disease. Almost any type of cerebral or mental disturbance, such as meningitis, apoplexy, or insanity may thus be simulated by a malarial infection, and whenever the temperature is high, and the leucocytes low in such a case, one should do one's best to find a malarial parasites.

CASE XVII.

Homicide during malarial attack, (Malikin).

On the 9th Dec., 1909, the native Sentot, alias Krasamenawi, was admitted to the asylum Lawang, Batavia. As the man had committed a murder, he was sent to us for observation. It appeared that the accused was well spoken of in his native village, and had never been convicted or shown any signs of insanity. He had left his village, and gone to Tjilatjap in order to seek work, and was at this time healthy.

On the 19th April, 1909, he came to the house of a mandoor, where he lodged. On the 26th April, according to the declaration of this mandoor, Sentot had fever which began at 8 o'clock in the morning, and ended about 11 o'clock, and which recurred at almost the same hour each day. During the feverish attacks, he was quiet and did not speak a word, but was otherwise normal in his behaviour. In the periods free from fever, he was able to do light work, such as cleaning the yard.

On the 28th April, 1909, he had another attack of fever as one the previous days and is said to have told his landlord the previous evening that he would go home because he was suffering badly from fever. After having drunk cocoanut water on that day during his fever, he is alleged, while still ill and without giving any reason for his behaviour, to have gone out taking with him the "arit" which was used for opening the cocoanuts. As to what happened afterwards, he knows nothing until the moment when he came to his senses again in the prison at Tjilatjap, and declared he did not understand how he came to be in the prison. All he could say was that he had fever, and during the last attack had killed a dog with red hairs.

From the evidence of various witnesses, it appeared that on that day about half past one in the afternoon he had walked into a European dwelling, and there unexpectedly inflicted several wounds with a grass knife upon a two-year old European child, who was at the moment in the open hall, while a woman (a servant of the master of the house) was busy sweeping in the immediate vicinity of the child in the hall. Instead of running away after the occurrence, he remained

standing motionless on the spot where he had murdered the child, paying no heed at all either to the outcry or anything else that happened round about him. The grass knife remained in his grasp. He did not say a word, looked pale, his eyes were wide open, and when he was brought to the Sheriff fell down in a faint on the ground with closed eyes and cold body; he had no convulsions or froth at the mouth.

To all the questions put to him, he had made no answer. During the first days of his detention in the prison he is said to have had attacks of fever, which, according to the evidence of the physician who treated him, were combated with quinine. The psychoses did not return again after the administration of the quinine.

From the information sent later in answer to inquiries, it appeared that Sentot knew neither Mr. W. (the father of the murdered child) nor his family, nor any of the servants. Also it appeared that he had formerly never suffered from convulsions, or epilepsy, or from nocturia. Nor was he known to be excessively religious.

On his admission to the asylum here, he looked weak and anaemic, but otherwise showed no abnormalities in thoracic or abdominal organs. Degenerative symptoms found in him were: swollen ear lobes, irregularity in the position of the teeth, and a flat occiput.

As regards his psychical condition, during his stay in the asylum, he was always calm, willing, docile and well-orientated. His answers were in the first few days not always quite correct, which can be ascribed to the strange surroundings in which he moved. Of the offence of which he was accused, he always maintained that he knew nothing. He still remembered that he had had fever at Tjilatjap and had been shut up in prison there, but not how or why he had been taken there. Nor could he remember the fact that he had drunk cocoanut water during an attack of fever. As regards what occurred at the Europeans house, he still had a vague remembrance of having killed a red dog.

From the above it appears that we have to do here with a normal native, who during an acute malaria had an account of transitory amentia, from which, after administration of quinine, he recovered,

Lawang, 20th Sept., 1910.

CASE XVIII.

Excitement with incendiarism, arson, and murderous assault during malarial attack (Beta).

On the 14th Dec., 1909, about 10 p.m. the kampong patrol in a little coast village (a notorious hotbed of fever) discovered a person throwing burning papers on the roof of the Chinese& T.Y.T's waroeng, but while one tried to extinguish the fire, another was attacked by the incendiary and wounded. Four Chinese rushing to the rescue were likewise wounded. Only then was the attacker rendered harmless and recognised as being O.O.N., a 23 years old Chinese, a servant employed in a toko in the neighbourhood. During the struggle, however, he threw his chopping knife into the river, whence afterwards his jacket, in which was a cigar case containing keys, was also fished up. The papers, as far as they were saved, appeared to be toko bonis of his master, and therefore valuable papers.

On the following morning, upon cross examination by the assistant wedono, he said that the evening before while visiting T.Y.T. he heard the latter say he wanted to kill him, and that, as there were no witnesses, he had therefore run amock. On being asked why he had then wounded others, he said: "Tida taoe". He recognised the knife held out to him, and acknowledged having thrown it into the river. The keys he likewise recognised and pointed out, which were his own, and which his master's. How the jacket came to be in the river he could not tell. Why he used the I.O.U's of his master's customers to commit arson, he also could not explain, not did he recognised the papers.

On the 18th Dec., before the head djaksa, he spoke confusedly and to the accusation replied: "Itoe roemah di boeka". He admitted having wounded the people, but did not know why, had nothing to complain of against them, said he was NOT insane, and for the rest, shook his head, or gave on the whole no answer to the questions put to him. On account of his peculiar conduct, he was at last brought to hospital for observation.

Meanwhile the wounded people had been dressed in the hospital. And it appeared that all the wounds were inflicted with a particularly blunt knife. As far as they knew defendant, nobody had anything

particular to tell about him. Only his master could give the following information: He had had him for four years in his toko, had been like a father to him (his parents lived at a distance), and had never noticed anything peculiar about him; he was a well behaved lad who was never passionate and had never had an epileptic fit in that time. They slept in one room. Latterly he had been much troubled with fevers. In the evening they had drunk tea together at T.Y.T's, and went home to go to rest. Defendant said on going to bed he would blow out the lamp, because he could not sleep well with a light; this was approved. Then he said: "I will go out; perhaps you would like some mangas, so I will go out and buy them in the street", and went off at once. Shortly afterwards, he (the master) heard a hubbub and the fire alarm. Coming out he immediately received a slash in the face.

In the hospital, the patient said nothing during the first days, gave no answers or at most a "tida tahoe". On examination of his body, the spleen appeared to be enlarged. The blood contained malarial plasmodia (tertiana) in great numbers. The body temperatures are as follows:

Dec 27.	-	37·8°	38·5°	38·8°
28.	37·7°	38·1°	38·2°	38·6°.
29.	37·0°	37·4°	37·7°	37·8°
30.	37·0°	37·8°	37·8°	37·5°
31.	37·2°	37·0°	37·7°	37·4°

etc.

Unintentionally also no quinine was given to him during the first days, but though no peculiar syaptoms had shown themselves in the prison, and were no longer to be expected (although his physical condition was otherwise good) a gram of quinine bisulphate was given every day. ~~Although~~ Already on the third quinine day, when the temperature no longer reached 38°C, he came down to me laughing to me merrily, saying: "soeda baik, minta poelang". When it was explained to him what he was charged with, he knew nothing about it; not did he know where he was now.

Temperature only declined slowly to normal, while he remained free from fever from the 10th Jan., onwards. Meanwhile he became better orientated, and then felt deeply grieved that he had committed arson and wounded so many people. He always says he cannot understand

it, and cannot remember it at all. With his acquaintances who came to visit him he now conversed in a normal manner.

Summing up, we have here an incendiary and would-be murderer, who harboured large numbers of malaria plasmodia in his blood, and suffered for a considerable time with fevers, resident in a fever district. On the 14th Dec., he hears his host say that he (the host) will kill him. On going to bed, he behaves in a strange manner, goes out, commits arson with the help of his benefactors bonds, and attacks people who have little or nothing to do with his pretended enemy and that with a very blunt knife. The day after, he still has a partial recollection of these facts. On the 18th, he no longer knows anything about them, and gives completely confused answers.

Simulation can here be clearly excluded. Moreover there is nothing to be found about him that resembles epilepsy, either now, or in the past, nor has he an ~~elipe~~ epileptic character.

That the malaria plasmodia are to blame here admits of no doubt.

The Court agreed with my conclusion that the defendant could not be held responsible for the acts laid to his charge. The Judge ordered his retention in an asylum for the period of one year.

CASE XII.

Case of threatened assault in malarial subject, with auditory hallucinations (alcohol as complication dealt with in diagnosis). (Sala).

A case that came to my notice during my stay at Koeta Radja appears to be sufficiently important to report somewhat fully.

Patient is an army male nurse, 28 years old, born at Beilen in Drenthe. As regards his early life, he learnt well, did not drink too much, and entered the service of the Dutch East Indian Army in his 22nd year. On arriving in the Indies, he was posted to Fort de Cock, and after serving three months in the infantry was transferred at his own wish to the hospital staff. At his first station, he had a turn in hospital on account of urethritis. In April, 1911, he was transferred to the province of Atjeh, where he was posted for duty at the hospital at Koeta Radja. He remained there a year, in which time he

was three times in hospital, once for 22 days with urethritis and after that for 3 months on account of appendicitis, for which he was operated upon with good result. I also see in his earlier sick-list f.i. (febris intermittens), for which he was treated in March, 1912. On admission to the hospital, the fever had already abated and the temperature rose no more during his stay in the institution. At that time no parasites were found in his blood. In April, 1912, he was transferred to Meulaboh (a station on the West Coast of Atjeh, formerly notorious for its malaria). According to his sickness book, he was not sick there before 11th Aug., 1912. He stated decidedly, however, that he was frequently out of sorts there, especially with giddiness and also frequent attacks of fever; he himself remembers that on one occasion his temperature rose to 40°. After these attacks, he felt wretchedly heavy for a long time, but did his duty. He never reported sick, and used no quinine. At Meulaboh, quinine was indeed supplied prophylactically to the troops, but our patient as not belonging wholly to the troops managed to escape from taking it.

On the 11th Aug., 1912, apparently in good health, patient pursued a native fusilier with a klewang just as it was beginning to grow dark, giving out that he had been jeered at by the native. He was disarmed and placed under arrest, which was a very easy matter; he ran, so to say, of his own accord to the military prison. He would not eat there, and on the following day asked what had really happened to him. Two days later, during which time patient was still in the prison, the help of a physician was called in, because patient behaved so strangely. He lay continuously on his belly upon the straw bed, would not eat and did not answer to questions that were put to him. When the doctor examined him, he sprang up all of a sudden and cried: "An end must come to this, everybody, even the Atjehers, call after me".

The following days also passed in like manner; after continual pressing, however, he ate something but refused to speak. He was brought to the bedroom, where he allowed himself to be helped, but was otherwise always still. A few days later, he spoke off and on a few words, from which the doctor concluded that he was suffering from ~~visual~~ hallucinations, which was confirmed by his peeping anxiously behind all the doors, and asking what the people wanted with him, obviously people who were not there. To certain questions he

answered that he had forgotten everything. The remaining days before his release on the 5th Sept. passed in the same way; he hardly spoke at all, never asked for anything, and only allowed himself to be attended to with difficulty. It is to be noted that in a fit of malevolence, he tried to throw the tun at the physician.

On the morning of 5th Sept., patient was taken by boat to Oleh-leh, and thence by road to the hospital at Koeta Radja. He went along quietly with the accompanying male nurses, and walked at Meulaboh to the jolly-boat which was to take him on board. On the ship he was very restless, did not speak, but walked to and fro. Towards night on arriving at Oleh-leh, he became quieter and went to sleep. On the following day, upon disembarking, the attendant noticed that patient had fever.

Arrived in the hospital on 6th Sept., the temperature is 39·3° in the morning. The condition is the same. Patient lies in bed, peeps strangely around, speaks as little as possible. At visiting times, patient lies apathetically in bed, sweats much, does not say a word, temperature 38·2°. Later in the day, the temperature falls still lower, at 4 o'clock, it is 37·2°, and in the evening 37·5°. On the following day it has not risen, but on the 8th it has the same course as on the day of admission, at 12 noon, it is 38·2°, and at 4 o'clock 38·0°. After that the temperature has not risen again. On the day of arrival, at the hospital, neither liver nor spleen was palpable.

In a blood smear taken a few hours after arrival, numerous small parasites were found, besides several tertian macrogametes. In the blood of the 7th Sept. numerous large and medium sized parasites besides parasites "en forme de rosace" and some tertian macrogametes.

Patient complains of nothing and begins to feel better, begins also to interest himself in his surroundings.

When I saw him on the 12th Sept., he was completely altered, is neatly shaved, has had his hair cut, is respectably dressed and is much better. Speaks better though little, and eats well. His condition steadily improves, so that on the 16th Sept., 10 days after admission to the prison room where he had been nursed up till now, he can be transferred to the ordinary room.

For treatment, immediately parasites were found in the blood he was given quinine, which was administered to him for a fairly long

time after the fever had ceased.

On being brought to the ordinary room, it appears that he is not yet the same as before; he is quiet, introspective, speaks little with his comrades, and lies much in bed. This symptom also disappeared little by little, so that on the 23rd Oct., he was discharged from hospital as cured. He was, however, still observed as a convalescent, and given for some time easy and light duties.

On the 1st Oct., when he was thus still in hospital, he once more turned up at my office to tell his whole story. He gave me his whole history, how he was at school, how he had been for some time working in Germany, when he joined the Colonial Service, and how he got on in the service.

In his punishment register, I find it reported "four days confinement on account of drunkenness" at Fort de Cock, therefore before he went to Atjeh. He related that one day he drunk too much in the canteen. He really never drank at all, and this is, so to say, his first drunkenness. He has not, however, become thereby a drunkard, for since that time this has not occurred again. On the contrary, he is always discrete, lives decently and only visits the canteen rarely, and then only when some performance or other is being given.

He could tell precisely how he came to Meulaboh, and had been unwell there now and again. Of the incident in which he is said to have menaced a native with a klewang, he remembers nothing whatsoever. From this moment onwards there is a gap in his memory, to use an expression of my teacher Régis. He has heard later from others what happened, but he does not remember it, nor what happened at Meulaboh, that he sat there in prison, that he was brought in a boat to Oleh-leh, admitted to the hospital and nursed in the prison room. He remembers being transferred from the prison room to the ordinary room. Also his recollections of the prison room itself are vague, and he cannot tell whether he was nursed in the common room there or in the cell. In order to refresh his memory somewhat, he is brought once more to the prison room. Arrived there he looks strangely around, although one sees that he remembers having been there, yet he only now realises that this is the prison room; he can point out his bed, and also recognises two other patients, and the attendant. Suddenly, he

asks me why he was in this room and looks round in a very astonished manner when I tell him, it was because he had been ill, so ill even that it was necessary to keep him here.

There is thus an absolute amnesia, from 11th Aug. to 17th. Sept., while after this date, an "amnésie crépuscule" exists, which slowly passes into ordinary memory.

Summing up, we see before us a man who has had delirium for some time with hallucinations of sight and hearing, who saw all kinds of strange people coming after him, people who used various peculiar expressions, in short genuine "délires de rêve" or "délires onériques", which, as it were, represent a continued dream. Before the time in which the amnesia existed, he was in an "état second" from which every now and then he returned to his normal condition, in which he then spoke and recognized the persons present. Later it appeared that of these few moments also no remembrance is left

On what does this psychosis depend? Undoubtedly this sickness is the consequence of the malaria, yet there are still one or two points to be noticed. Patient certainly had several attacks of intermittent fever before 11th Aug., 1912, although these were only short, but on his journey to Koeta Radja he again had fever in which the temperature was high, but which only lasted a short time, to return again after a day free from fever. At that time, tertian infection was diagnosed and confirmed by the microscope. At the same time as the appearance of the small parasites, there occurred also, however, several tertian macrogametes in the blood. This proves definitely that the malarial attack occurred in someone who was already infected. The conclusion, that the psychosis was caused through the action of the malarial poison, is now manifest.

What also deserves consideration here is the question whether the alcohol was the cause of the delirium. He was once punished for abuse of strong drink, and it is conceivable, that patient had to pay for it on one occasion, because, it is reported of him, that, he had several times slipped through the meshes of the net. It can definitely be denied that he was an alcoholist. An attack of delirium tremens, too, occurs only in people who have abused alcohol for a considerable time. Moreover the deliria caused by alcohol are as a rule different and much more alarming than was the case here. Chronic

alcoholic intoxication can thus be rejected as the cause.

It might also have been that the act on the 11th August had occurred in a tipsy fit. This also is to be excluded, for the man so far as can be determined had had no alcohol on that day, and because before the occurrence patient had been sitting talking and there was no mention of drinking alcohol on that occasion.

Also with regard to the first days, it must be particularly considered whether patient had committed an act for some reason or another unknown to us, and after that simulated sickness or rather insanity. In the further course of the malady, however, it can be plainly declared that we had to do then with a psychosis, and not with a feigned sickness.

From a practical point of view the diagnosis was of much importance here. Just a few days after the committing of the deed came his promortion to corporal, and it was a cause of deliberation, not to allow him this distinction. If the deed really was the result of bad conduct, then this proposal was quite in order; but on the other hand, if the condition was the result of drinking too much alcohol, then this could be taken into consideration.

If, indeed, he had been immediately punished for it, then this would have had to be reported, and it would have had to be settled by the general chief of the service, whether the promotion could not then proceed. His physician, who, as it happened, was his corps commander, found every reason to allow the promotion, and to report to me as provincial chief of the service.

At the same time as this report, patient arrived at Koeta Radja. After observation, the diagnosis of malarial psychosis could be confirmed. Once this was determined, there was nothing to hinder the promotion from being put into effect, and upon the day, that it had been granted at Meulaboh.

At the present time, about two years have passed since the occurrence. After his recovery, patient was again posted for work at the hospital at Koeta Radja, where after a period of light duty he soon resumed full duties. I lost sight of him until I again met him at the hospital at Tjimahi. It now appeared more than ever that the diagnosis then made had been right. Patient is an industrious soldier, who does his best, and is very willing, who has never been

punished again, and drinks practically no alcohol. Asked once again about the affair, and the illness at Moulaboh, he now knows quite well what he is said to have done, but remembers absolutely nothing of the occurrence. What he knows has been told him.

This case is of special interest as showing the difficulties that arise in a case of malarial psychosis with alcohol as a complication. This part of the subject is developed in the next section.

Boinet and Roy record the case of an Annamite, who was saved from decapitation by showing that he was not responsible for the murder committed during his delirium.

(2). Malaria versus alcohol.

The astonishing likeness of some phases of malarial confusion to drunkenness often leads to mistakes, sometimes with serious, or embarrassing results. This likeness is increased, if it should happen, as I have known, that the patient has taken spirits to relieve the depression so frequently associated with malaria. In an article on "Malarial Mimicry", Major A. E. Kamar, of the Egyptian Army Medical Corps, makes reference to this subject in these terms:

"The old cry drunk or dying still applies in tropical towns; for example, the police arrest a man because he is extremely noisy and is apparently drunk. Next morning, the man is seen to be very ill, or even dying. A doctor is sent for, and an examination of his blood shows that there are many sub-tertian parasites.

"Or a man may be brought to a hospital in a stuperose or melancholic condition, and with a normal or sub-normal temperature, and it may be considered that he is a lunatic and ought to be transferred to an asylum; and yet while these arrangements are being set in action, a blood film reveals the true history of the case, and a diagnosis of pernicious malaria is made".

Legal situations sometimes arise in cases of abnormal conduct or physical illness in a malarial subject, where alcoholism comes in as a possible explanation of such conduct or illness. Is the abnormal mental state, or physical incapacity, due to malaria or alcohol? Culpability enters with alcohol, but need not do so with malaria. This may operate in one of two ways:

(a). Where the patient has not taken alcohol at all, but where malarial infection wholly accounts for the condition which could be probably explained by alcoholism.

(b). Where alcohol has been taken by a malarial subject, who has a mental or physical breakdown, one or other of which is quite out of proportion to the quantity of alcohol taken.

(a). That so famous an observer as Osler should in the first instance take malarial confusion or stupor for drunkenness, is sufficient comment on the likeness of the two conditions. Although no medico-legal considerations arose out of this instance, the record of this case will explain its own relevance here.

CASE XI.

Malarial confusion, or stupor, mistaken for drunkenness.

(Osler).

Professor Osler's Clinical Notes (1890):

"I saw him in the dispensary at 1.30 p.m.—he was very weak

and thin with eyes congested, cheeks flushed, and with a dazed stupid appearance. Tongue swollen, heavily furred and indented. He looked like a man who had been drinking, and I told his brother that it would be impossible for us to admit him to the ward in his present state. He assured me however that he had not been drinking to excess, and on ascertaining that there was not the slightest trace of alcoholic odour in the breath, I signed the order for his admission.

"The following history was obtained:- Family History and Personal History good. Is a sailor, and has enjoyed excellent health; he left Boston for Savannah five weeks ago, spent a week in the latter place, and as the weather was oppressive, he, with several of his shipmates, was in the habit of sleeping on the grass all night. He remained well on the voyage for Baltimore, where he landed Aug. 31st. He was about the house all week, though not feeling quite himself, but the present illness dates from Sunday, the 7th, when without any chill or fever, he began to have vomiting.

"He felt intensely weak and prostrated, so that he could not get up on Monday morning. Throughout Monday and Tuesday, he took home quinine pills. In the dispensary after failing to detect any alcoholic odour in his breath, and on learning that he had recently come from the South, the blood was at once examined. Large numbers of Laveran's organisms were found which rendered the diagnosis clear. His temperature on admission to the ward was 101°F, pulse 104, small, tension [illegible]ased, radials not stiff. The abdomen was soft, nowhere tender. The edge of the spleen was just palpable on deep inspiration; upper border of dullness at 9th rib.

"Apex beat of heart at 5th interspace within nipple line; sounds clear. Lung exam. negative.

"BLOOD:- Abundant malarial parasites and pigmented leucocytes found.

"No increase in the splenic dullness. Mental state varied between clearness and stupor associated with great prostration, and in spite of quinine given daily by the mouth and hypodermically, he died on the 16th, 6 days after admission to hospital.

"AUTOPSY:- Brain shows a few parasites of malaria in the cerebral vessels. In one spot, there is a very small infarction,

showing necrosis of the cerebral tissue, hyperaemia at its margin and an accumulation of mononuclear and polynuclear cells."

CASE XXI.

Malarial Coma, mistaken for drunkenness.

(Col. P. SMITH)

This case emphasises the importance of never losing sight of malaria in doubtful disease conditions in malarious countries. The conductor of a tramcar in Calcutta called the military police late at night to remove a drunken soldier from the car. The police took the insensible soldier to the guard-room, where he lay all night. About 8 a.m. next morning, it occurred to the guard that the man was ill, and he was carried to hospital. The mans temperature was now sub-normal. He could be roused with difficulty to mutter more or less unintelligible replies to questions. His eyes were closed; conjunctival reflex present; pupils ordinary in size, and sensitive to light.

His brows were repeatedly knitted to a frown. He was examined for injuries and for signs of poisoning. The bladder was emptied by catheter, and urine examined, with negative results. The symptoms suggested concussion, and we made out that his head ached badly, but we could find no marks of violence. The uniform was spotlessly clean, and there was nothing about the man suggestive of drunkenness, nevertheless it was thought that he might have indulged too freely in alcohol the night before. A blood smear was examined, but the report was negative.

A dose of calomel was given. During the day, the patient was induced to swallow a few spoonfuls of milk. The next morning, he seemed just the same as on admission, but there was a slight rise of temperature. In the middle of the day, the temperature had risen to 105°F. The man was packed in ice-water sheets, and another smear taken. A few small ringed parasites were found, only four in several fields, but the secret was out; and a good dose of quinine

was given.

The following morning, the third day of his illness, the temperature was subnormal, and the patient had distinctly improved, but he still lay frowning with his eyes closed and disinclined to speak or take nourishment. Quinine was continued. Improvement was evident in the evening, and in a day the patient had quite recovered; four days later he returned to duty.

The man's own story was that he set out from Dum Dum for a walk in the evening, and knew no more, till he found himself in hospital. At Calcutta, this statement was accepted with reserve. A point of interest is the small number of parasites found. We all know, of course, that the few parasites seen in the peripheral blood are not always a key to the extent of their prevalence in the deeper parts of the body—withal we are all apt to forget these facts.

It might be suggested of course, that this man was malingering to escape the consequence of misdeeds, and that the malaria was merely coincidental. As a matter of fact, this idea also was in our mind when examining the man, a sharp Cockney youth, who certainly made misleading statements after recovery. The case would still be interesting if the above suggestion really was the case, for the malaria was genuine enough. It will be seen from the notes on the case that the discomforts attendant on the investigation of the case must have been considerable if the man were really conscious; moreover being very young, he would have been extremely hungry whereas it was only by putting spoonfuls of fluid at the back of his throat that any nourishment could be given to him, and that in small amount. The after-recovery stories were of the sensational weekly newspaper order, one being that he had when in England, suffered from lapses of memory as to his own name and whereabouts. He probably wanted to join the a home-going party of invalids, and was quick-witted enough to seize the occasion of his recent indisposition.

This case is of special interest from two points of view as showing how easily cerebral malaria can be taken for drunkenness; and how readily even the medical observers of the case can fail to perceive the subsequent possibilities of it, for lapses of memory are a common phenomenon of chronic malaria, especially where more acute cerebral

symptoms have occurred at an earlier stage.

Case VIII of this series shows the simulation of drunkenness by malaria operating as an Army Offence.

Two instances of this class are detailed in the chapter on alcohol. They are recorded by Simonin, Professor of Legal Medicine at Val-de-Grâce. One case is that of a man who was dismissed because of mental unfitness, which was attributed to alcoholism. His condition proved to be due to malaria only. The other is that of a soldier, with peripheral neuritis, which was attributed to alcoholism. This diagnosis would have affected his military career and on appeal to an authority higher than the regimental M. O., his case was reinvestigated and his condition proved to be due to malaria.

(b). Marandon de Montyel, the French Alienist, who has closely studied the effects of alcohol in relation to malaria, and particularly in its effects upon malarial subjects, maintains that those infected with malaria have a definitely diminished tolerance for alcohol which is directly due to the influence of malarial poison upon the nervous system; in other words, that a malarial subject will get drunk on less alcohol, often much less alcohol, than it would take to produce the same result previous to malarial infection.(*). Not only so, but he considers that taste for alcohol is increased in malarial subjects - is actually induced by it, partly due to consuming thirst after the sweating stage of the malarial attack, partly due to the depression and debility associated with recurrent malaria. He also maintains that this craving for strong drink as well as hypersusceptibility to its effects persists during the afebrile period of the malaria and, indeed, lasts as long as there are parasites in the system. (Cf. Chapter on Alcohol).

He published a detailed account of 12 cases in support of his views, one of which appears in the Chapter on Alcohol, and two of which are now given in slightly abridged translation.

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* The same applies to opium (Contf, Boinet).

CASE XIII.

Malaria, inducing taste for, and hypersensitiveness to, alcohol, with resulting mania, and recovery. (Marandon de Montyel).

Jean X, sergeant-major, 24 years old, military prisoner in Oran, was admitted to the asylum at Marseilles in December, 1886. No family history of insanity, or of alcoholism. No physical stigmata, nor abnormality of conduct. He had pneumonia in 1879; facial eczema in 1885. Enlisted 1882—sent to Algeria, 1886. Conduct while in the regiment was always good. No alcoholic habit, was recommended for promotion to sub-lieutenant, with the highest recommendations.

On 25th Oct., at Oran, he took malaria with quotidian fever for the first time. On the first day of fever, he was driven by thirst to take some drink, which though in moderation, made him drunk. Until this time, he had always been sober, and had never noticed any unusual susceptability to the effects of alcohol, nor any special tolerance for it. He attributed his becoming so rapidly tipsy to the malaria. On the following days, his inclination for brandy, each evening, steadily increased. He continued to drink to satisfy his devouring thirst and to fortify himself, for after each febrile attack he became weaker and weaker. As the military manoevres were on, and he was marked for promotion, he did not wish to go to hospital. Unfortunately on the 29th, only four days after the onset of his fever, and of his first libation, he deserted without giving any account of himself, strayed to Oran, then retraced his steps to Tlemcen very much excited, without sleep or food, weakened by the fever, and drinking always a little to quench his thirst and sustain him. At Tlemcen, he was arrested and sent to prison in Oran, whence to hospital on 15th November. Treated with quinine his fever subsided, but his mental condition did not improve; on the 24th, during the night, Jean X, suddenly lifted a pot of tea and threw it at the head of a comrade, crying "The assassin". He was addressing his brother-in-law, who, he said, was coming to cut his sister in pieces, and was hiding under his bed. He had to be put in a straight jacket. Since arrival in hospital, he had been put on a full ration of wine and quinine.

On his medical certificate from Oran, he was described as "speaks only of his sister and his brother-in-law; visual hallucinations; delusions regarding his brother-in-law, and a friend whose name he constantly repeats, who seemed to be uppermost in his mind. In the last days of November, he was quite mild to those about him, but on the evening of 4th December, he took a fit of frenzy in which he tore his clothes, broke a window, broke a bar of iron nearly 2 cms. thick, and threatened whoever dared to come near him. He was very troublesome to control. Between times, he walked about brawling, and striking the door of his cell night and day. Of average size, and without alcoholic or syphilitic heredity. He looks haggard, wild, and with a hoarse voice. He is in a state of constant agitation, and seems insensitive to cold. Muscle power exaggerated; appetite maintained, sleep nil."

His certificate of admission to the asylum of St. Pierre showed "fit of alcoholic mania and in a continuous anxiety state from visual and auditory hallucinations; delirium of terror. He believes himself followed by his brother in law, who, after having killed his sister, threatens to kill him. Sees and hears this relation on the roof. Sleepless; pupils dilated; pulse irregular."

At Marseilles, no alcohol was prescribed, and already at the beginning of January, he was cured at the end of a month. During February, malaria quotidian fever recurred. The patient was again tormented by thirst, and the inclination to drink. He got no drink, and had no mental break-down. The malarial attacks disappeared with quinine, and Jean X. left the asylum cured towards the middle of March.

Author's Comments. The principal features of this case that draw attention are that Jean X. had never drank and had never any taste for alcohol. Then he took malaria, and simultaneously developed a taste for fermented liquor—a kind of malarial dipsomania. He drinks, and after four days, develops an alcoholic insanity.

All the alcohol he was able to get in the short lapse of time could not alone have accounted for such a mental explosion, for apart from the fact that he had not the means to get it, he was very busy with the Grand Manoeuvres. As there was no hereditary

insanity, or alcoholism, it could only have been the malarial poison that made him so sensitive to the alcohol which is not apt to upset a soldier with four years service. Treated with wine and quinine, he gets worse; remove the strong drink, and he gets quickly alright; and, [illegible] further, while in the asylum, the malaria returns, and with it the thirst, but he has not been able to satisfy his appetite, and has no mental trouble, which completes the chain of evidence.

Then the question arises—when L. X. deserted, he had a mental attack which sent him to the asylum, when he was on the point of becoming an officer, up till which time his conduct had been exemplary, without ever a charge against him, and found himself next day a deserter and alien. It was his future lost. I did not hesitate, with the experience I have had, of malarial and alcoholic subjects to exonerate this young officer and make it clear that his mental state and conduct were the direct result of malaria contracted while on duty. As a result of my emphatic opinion, the War Office re-instated him in the Corps, and he was sent to a garrison in France as I had advised. Subsequently he wrote to thank me, and tell me he had been promoted. He had only one recurrence of malarial fever after leaving Africa, accompanied by the same thirst, and desire for alcohol, but having learned from his past lesson he took refuge in hospital which he came to do with each relapse. Since his attack, in the asylum of Saint-Pierre, he has had no mental trouble.

CASE XVIII.

Post-malarial hypersusceptibility to alcohol with delirium tremens. (Marandon de Montyel).

Etienne X., 28 years old, journalist, entered Ville-Evrard asylum in August, 1890, with the following description:

"Sub-acute alcoholic insanity. Visual hallucinations. Disordered sensation. Threatening to kill his relations. Attempted suicide by asphyxiation with coal-gas. Hand tremors. Sees beasts on the wall. They bite his toes". On admission, he was mentally normal, having been four hours on the way.

No insanity or alcoholism in the family. Before having malaria, he had never noticed any susceptibility to alcohol, nor any

special tolerance for it. No physical stigmata of degeneration, and never "le syndrome episodique". He had been 7 years in Algeria, and at the end of the second year he took malaria of quotidian type which caused him to be in hospital three times. He has never got quite rid of the malaria, and his spleen is enlarged and he looks slightly cachectic. The fever recurs each autumn generally, but is usually stopped by quinine sulphate. Nevertheless he has sometimes to go to bed. The patient settles for himself an account between the malaria and a growing intolerance since the first attack of this illness, which he avers he has for alcohol, not only during the attacks, when it is imperative, but even during the intervals. Since the first attack, he has not been able to dine himself well if he took a little, without going off the rails. Usually he avoided the casual occasions for drinking and was in consequence the butt of his fellow-workers who treated him as a softy and a milk-sop.

We had indirect confirmation of these very characteristic details. Towards the end of July, 1890, he lost a daughter he was much attached to. To help him to forget, he wished to have a little jollification with his friends, and did not make any strong resistance to their invitations. In less than a fortnight, without letting himself go to any great excess in drinking simply like the others, and although he has had no malarial fever for six months and that the attack in 1889 was exceptionally light, all of which details we have been able to accurately check, he went completely off his head on pay Saturday after two absinthes taken one soon after the other. He remembers only returning home raving and having a discussion with the neighbours. But what happened after that he knows not. He was dismissed after getting this information asked.

Author's Comments. It is clear that after the information gathered regarding this case that this man has not gone to excess. His two weeks jollification alone, without some allied cause, was not enough to explain the violent outburst that so rapidly overtook him. The worry over the death of his daughter may have debilitated him, but an experience of this kind in a man of ordinary sobriety, cannot create such an intolerance for alcohol, especially lasting,

apart from any neuropathic taint. Moreover, when delirium tremens breaks out after emotional shock, it immediately succeeds the shock, and not two weeks after.

There is therefore only malaria in the history of this subject to explain the mental break-down that overcame him, and the patient himself was aware of it, having known for a long time the close connection between the febrile attacks and his diminished tolerance for drink.

It would appear, then, that where abnormal conduct giving rise to legal complications is associated with the taking of alcohol, in a malarial subject, the conception of culpability should be considerably modified, if not removed, as long as malarial infection lasts. If, as Maranon in Montyel vigorously maintains, malarial poison simultaneously increases the susceptibility of the individual to, and increases the craving for, alcohol, then judgment of the resulting conduct cannot be based upon an ordinary, or malaria-free, standard.

That the malarial psychoses, with or without alcoholic modification, give rise to medico-legal complications should be abundantly clear from what precedes, and that there is so comparatively little on the subject in the literature, must be, in the opinion of the writer, not because these cases do not occur, but because many of them are not recorded, or not recognised.

(3). Accidental Rupture of the Spleen.

Accidental rupture of the spleen, which is sometimes considerably enlarged, soft, and friable, in malarial subjects, either spontaneously or by slight trauma, not infrequently gives rise to medico-legal complications. This subject has been fairly fully considered in a recent article by Ingram, who records an interesting case, and gives extensive references.

CASE XIII.

Spontaneous rupture of the spleen. (Ingram).

A small Krooboy, aged about 12 years, who attended school

in Accra, was found dead on the morning of June 24th, 1920, having retired to rest the previous night without complaint and apparently in his usual health. He had attended school on June 23rd, and according to his friends, there were no signs or symptoms of illness upon his return, and he appeared in good spirits, taking his food and retiring for the night in his customary manner. Subsequent inquiries made by the police produced no evidence of injury while at school: moreover, his people were convinced that he had shown no signs of illness for weeks prior to his death.

At the post-mortem examination, the peritoneal cavity was found to contain 18 ozs. of blood, and blood clots were adherent to the spleen. The spleen was considerably enlarged, weighed 245 gms after being freed from blood clots, and measured 14·5 cm. × 10 cm. × 3·5 cm. There was a longitudinal rent running parallel with, and lying immediately posterior to, the hilus; it was almost 4 cm. in length. The organ was very soft and friable, and slight tearing of the external surface near the upper pole, which was adherent to the diaphragm, was unavoidable in removing it from the body. None of the other viscera of the abdomen or of the thorax showed any gross pathological lesions.

He (Ingram) indicates that spontaneous or traumatic rupture of the malarious spleen is by no means uncommon in the Tropical and Sub-tropical parts of Asia; but that liability to rupture of this organ in the natives of the Gold Coast is slight as compared with that of Coolies in the East. Buchanan indicates that it is extremely common in India, and frequently appears in the Law Courts as a cause of death. It is so common there that, in the case of sudden death in a native, spleen rupture may be presumed to be the cause, and where a European is charged with homicide, it is usually found that the spleen has ruptured as a result of a blow or kick which would have no similar effect on a healthy subject. Manson writes: "Enlarged spleens are easily ruptured by a blow on the belly. In hot and malarious countries, many a coolie goes about doing his work, although he has an enormous spleen. This is a fact to be remembered in administering even mild corporal punishment to natives of malarious countries".

Waldell indicates that in India, where a blow or kick has caused death, the liability of the enlarged malarious spleen to rupture is taken into account judicially.

Crawford, who examined 9876 reports of medico-legal cases in Bengal, found that in 304 or 3·08%, the cause of death was ruptured spleen, and that in only 8 of the 304 cases was the spleen normal in size.

Spontaneous rupture is comparatively rare, though rupture from slight trauma is not uncommon. Waldell records three cases of spontaneous rupture—Buchanan five; Noland and Watson record three, and refer to other four in the literature. Other single cases are recorded by Clark, Leighton, and Moeller, Ogilvy, Grey Turner, Rankine, Gossain, Skevington, Sheaf. Many of these cases, though not the result of external violence are considered to be due to muscular effort. One of Buchanan's cases is that of a European, whose rupture occurred in his efforts to maintain his balance after slipping on his bathroom floor.

Laveran records that in the enlarged spleen of Kala-azar in infants, rupture sometimes takes place during coughing or crying or from mild palpation.

Ingram writes: "The experience of medical men, whose practice has brought them into contact with the negro races of Africa, is the reverse of that of their confrères in the East, so far as rupture of the spleen is concerned. A trivial blow inflicted upon a negro is not likely to involve the aggressor in legal proceedings on a charge of manslaughter resulting from rupture of the spleen. This is unquestionably due to the fact that adult negroes—in West Africa at all events—are not burdened with enlarged and softened spleens in spite of, or rather because of, their having suffered severely from malaria in their childhood".

Daniels (quoted by Ingram) whose experience with regard to negroes was largely gained in British Guiana, states that: "Diseases affect organs differently according to race", and exemplifies this by directing attention to the age incidence of splenic enlargement in the negro as compared with that of other races living in the same conditions; he shows that, whilst in childhood, all races are infected equally with malaria, in adult life the spleen of the negro

tonic to subside, whereas in other races similarly situated, Indians, Chinese, and aborigines, this organ remains in adult life increased in size, and on the post-mortem table will commonly be found to weigh three or four times as much as the normal organ of Europeans.

Sheaf records two cases—one of an English soldier in hospital in Macedonia who had recently experienced a rough journey; the other a Russian, the accident apparently occurring while he was sitting up in bed.

Skevington reports a case of spleen rupture in a malarious man of 25, while he was wheeling a barrow.

Hennessy operated on 19 cases of traumatic rupture of the spleen and emphasises the frequency with which hypogastric pain and urinary irritation simulate a ruptured bladder, and the deceptive quiescent interval between the injury and the onset of restlessness, abdominal discomfort, and an increasing pulse rate.

Gerrard records a case of a Chinaman aged 33 who received a kick in the abdomen 36 hours before being seen by him. He had intense abdominal pain, difficulty in breathing, and inability to lie down. The abdomen was very tense, and there was restlessness, orthopnoea, dull flanks, a pulse of 120, rapid breathing,—altogether a critical condition. Operation was done—abdomen full of blood, spleen was successfully removed, and the man made a good recovery. The spleen weighed 19 ozs. 6 drms. and there were two haematomata at upper and anterior edges from 2-3½ins. in diameter. Malarial crescents were found in the blood, and quinine was given during convalescence.

Cantlie records seven cases of enlarged spleens with rupture observed by him in Hong Kong, between 1888 and 1898. The observations were made post-mortem and all the cases were occasions of a magistrates' inquiry. In six of the cases, the rupture was in the inner aspect of the spleen: in the seventh case, the spleen was reduced to pulp by haemorrhage into the substance of the spleen. There was a history of a blow over lower ribs, or on the abdominal wall over the spleen. Cantlie's observations on the medico-legal aspect of this subject are given in his own words: "In four of the cases, the rupture was in the inner aspect of the spleen, behind the hilus; in one case, the rent extended across the hilus, and in

one case the rent was immediately in front of the hilum.

"The question of the situation of the rupture in splenic injury has its medico-legal interest. All of the six cases were caused by falls, by kicks, or by blows, and the question of manslaughter, when the injury has occasioned death and is attributed to a kick or a blow. If the spleen is ruptured in its inner surface, a clever counsel might argue, and actually get his man 'off' by contending that a rupture of the inner aspect of the spleen could not be caused by a blow in the surface of the body over the region of the spleen; were the blow the occasion of the haemorrhage, there must be evidence of a bruise on the outer aspect of the spleen. In none of the cases, I observed, was there any sign of bruising or injury to the outer surface of the organ. It is therefore easily seen that a fine medico-legal question arises. The fact that the rupture is in the inner aspect of the spleen would point to 'spontaneous' rupture rather than to injury. On this very point, in two of the cases, the man accused of inflicting the injury was not sentenced. That this was an incorrect finding I have no doubt whatever, in view of subsequent experience; and I am forced to the conclusion that a blow over an enlarged spleen is more likely to cause rupture on the inner aspect of the organ than on the outer. The outer surface of an enlarged spleen invariably shows a more toughened tissue than on the inner aspect of the organ, and the situation of the rupture caused by a blow would seem to occur where the tissue is thinnest. It is evident, therefore, that an enlarged spleen may be ruptured by a blow on the surface of the body, over the splenic area, on its inner surface, without any sign of the outer aspect being injured in any way."

(4) Malaria versus trauma.

It has been maintained by many observers, mainly French and Italian, that traumatism in general, slight or great, and injuries to bones, joints, and spleen in particular, frequently re-light up malaria in those in whom it has been latent even for long periods. Prominent among those who have advocated the effect of trauma, including surgical operations, in inducing malarial attacks, have been Vernenil, Moriez, Dériaud, Duberge, Chauffard,

A. Plehn, Mannaberg, Caccini, Celli, Ascoli, Alessandrini and Vandenbossche, White and others.

A. Plehn records that he observed a boy, who after six years, without any symptoms of malaria, had a violent malarial attack following a fall from a height from a bricklayer's ladder. After having enjoyed again six months' apparently good health, he had a relapse of malarial attacks after a jug of boiling water had been poured on his body.

Mannaberg records three cases of malarial relapse after injury. One was that of a man who got a cut in the region of the kidneys. He had lived for four months in the (malarious) Maremma country, but was not aware of having contracted malaria. Two days after the injury, he developed a febrile attack, and blood examination revealed the presence of tertian parasites. Another case had an attack three days after an operation for strangulated hernia.

Caccini (1904) emphasised the importance of wounds, fractures, injuries in determining malarial relapses. He saw many such cases in hospital in Rome, where they came from the surrounding country. One, an old quartan malarial infection with a cardiac lesion, whose fever had disappeared for many months had a recurrence of fever with quartan parasites in the blood 48 hours after falling out of bed and striking his left side in the process.

Bortolotti (1917) records a case of pernicious malaria in a soldier wounded in the right arm. Twelve days after the wound, he had his first attack of fever (40·6°C), and nine days later an attack lasting 30 hours, followed by brief recovery, and subsequent recrudescence of fever, with a fatal issue from heart failure. The injury in the opinion of the author had revived a grave form of malaria contracted two years before, when he was confined to hospital for three months with it.

Garin, Loresbourg, and Verdelet also emphasise the recrudescence of malaria after surgical operations, wounds, etc.

Monti emphasises the frequence of malarial relapse after wounds operations, especially where bones were concerned, including fractures. He considered that the parasites, resting in the bone marrow, were disturbed and took on an overgrowth, appearing in the peripheral circulation in consequence.

But although the observations of many observers indicate that trauma, operative or otherwise, or shock of any kind (as scalding) in general, and trauma of long bones, ribs, or spleen (the haemopoietic organs and resting places of the parasites) in particular, may precipitate a malarial relapse, the range and extent of this subject does not appear to be yet fully worked out.

Cioffi, who has made some investigations on this subject, found that in 60 malarious railway workers with small injuries, none had a relapse that could be connected aetiologically with the injury. Statistics collected by him from the surgical departments of numerous hospitals in Southern Italy indicated that malarial relapses were largely confined to hospitals where chloroform was used as an anaesthetic, whereas in those in which ether and ethyl chloride and stovaine anaesthesia were employed, relapses were comparatively few. Garin, Laveuboure, Doyen, Policard, Alamartine and Vanlenboosche, Guilone, Soratto, Casata, Donati, Putti, Garberini, Calabrese, Ortali, Venturi, F. Rossi and White have all discarded the use of chloroform in malarial subjects, through having noticed the tendency to malarial relapse with its use. Cioffi, from his investigations, is of the opinion that the majority of relapses associated with surgical operations are more due to chloroform anaesthesia than to the shock of operations.

The legal element comes in where the damage or incapacity from accident is prolonged or extended or complicated in some way, as by death, from malarial relapse that may be attributed to the shock of trauma, operation, or anaesthetic. Instances have arisen where operative procedure has been followed by fatal malarial relapse consequent upon the operative or anaesthetic shock, where the mechanism of death has been malarial, not surgical. The evidences go to show that quinine treatment prior to operation, and the choice of ether rather than chloroform, as an anaesthetic, would have saved the patient—and the situation.

Or on the other hand, an accident—particularly involving bones, joints, or spleen—insufficient in itself to cause death, may have a fatal issue or some subsequent physical or mental incapacity due to the re-awakening of latent malaria. The mechanism of death may again be malarial, and not traumatic in the direct sense, thereby

affecting the liability of employer or other person party to the accident.

Further observations appear to be required to decide in how far trifling injuries, serious injuries, and operations are relatively capable of inducing malarial relapse, with special reference to the body generally, and the haemopoietic organs in particular. That chloroform anaesthesia is definitely contra-indicated in malarial subjects for this reason, seems to be clearly established.

(Cf. sections 2, 3, and 4, Chapter xxix: and surgical references connected with that chapter).

(5). Sudden death from the involvement of the adrenal glands.

At the Legal-Medicine Congress in Brussels in August, 1910, Dr. A. Cevidalli of Florence, pointed out the importance of alterations of the supra-renal capsules in legal medicine.

It is well-known that in Addison's disease, due to the destruction of the adrenal tissue by tuberculosis, sclerosis, suppurations, haemorrhages, cancer, etc., death often comes suddenly. More recently, observations on the adrenal glands by Dudgeon and Clarke, Paisseau and Lemaire, and others—show the frequency of damage and ultimate destruction of these glands in acute and chronic malarial infections. Paisseau and Lemaire have especially emphasised a type of malarial coma and sudden death a short time after the onset of coma, which has been found post-mortem to be associated with complete destruction and dys-function of the adrenal bodies, which have exhibited extensive intraglandular haemorrhages, and coagulation necrosis. Moreover, these observers maintain that from their experience of malarial pathology, these capsules appear, along with the nervous system, to be the most vulnerable organs of the body to malaria.

Cevidalli emphasises the importance of keeping capsular disease in mind in cases of sudden death in malarial subjects, as the symptomatology sometimes suggests acute poisoning which might imply foul play. He also points out, that in the new born, and in status

lymphaticus, it is not infrequently found at autopsy, that the capsules are subject to extensive haemorrhages (Parisot, Hamill, Morison, Simmonds, Doerner, Lissauer, Lochte, etc.). Also injuries to the back, intracapsular haemorrhage may be associated with sudden death (Hervey, R. Mattei). Kemf also emphasises the importance of remembering intracapsular haemorrhage as a cause of sudden death.

The following case of adrenal disease and malaria, with rapid asthenia and death, might have given rise to suggestions of foul play if adrenals had not been examined, or if malaria had not been diagnosed and its association with adrenal destruction noted.

CASE XXVI.

Pernicious malaria and hypo-adrenalism. (C. L. Rusca).

S. E., a soldier, was admitted in the evening of Sept., 6th, 1917 as an urgent case. The patient himself was semi-comatose. But the history accompanying him showed that hyper-pyrexia had lasted 3 days. The patient had vomited the previous day. Since the beginning of the illness the bowels had been irregular. His health while in the regiment had been good until the present illness. The patient replied to repeated questions with slow staccato (not scanning) speech. Skin was bronzed, visible mucosa pale, but not pigmented. Small, hard, mobile painless glands were palpable in the neck and groins. The temperature was 103°F, the pulse 96, fine, regular, weak. The blood pressure could not be recorded. There was slight jaundice of the sclerotics, the tongue was furred, the breath foetid. Respirations 30 to the minute, signs of slight pulmonary emphysema. Examination of the abdomen showed meteorism, the spleen and liver palpable. Except for a brisk plantar response, the reflexes were normal. There was no dermographism. The urine contained traces of albumin and urobilin, hyaline and granular casts.

The patient was put on light diet, and treated by purgation, and by stimulant injection. For the next three days, the temperature varied between 100°F and 103°F. The patient remained lethargic, Kernig's sign and headache appeared, vomiting continued. Spinal puncture was negative. The reaction of the pupils became sluggish. On the 10th, the temperature rose to 103·5°F. This was preceded by a slight rigor, and followed by profuse perspiration. The following

day, a blood examination was made, and some crescents and some small amoeboid forms were found. Quinine was administered (1 G. intramuscularly). Next day, the temperature fell below normal without amelioration of symptoms. The pulse was 120 and, in spite of the two injections of 1 mgm. each of adrenalin, remained weak. The patient, however, recovered sufficiently from his somnolence to give a personal history. This included the information that he had suffered at the age of 30 for about a year from malaria, which had always been tertian. Treatment with quinine and adrenalin was continued. On Sept. 14th, marked improvement was observed, and on Sept. 19th, the patient, whose improvement had been maintained under daily treatment with quinine, was removed to another hospital. His death was reported on Sept. 23rd, with the note that the last three days had been remarkable for a progressive and extreme asthenia.

At the autopsy, the spleen was found enlarged, and with a subacute tumour "probably malarial". There was hyperaemia of the meninges and oedema of the brain and ventricles. Both supra-renals were enlarged and caseous. No other signs of tuberculosis were found (unless an adherent pleura be so considered), nor was there any bronzing of the skin or mucous membrane. The tuberculous process in the supra-renals was "primary and evidently chronic". There was also acute parenchymatous nephritis.

The writer discusses the symptoms in this case at great length. He draws the moral that the symptoms of malaria may completely mask those of supra-renal insufficiency, while this insufficiency may suddenly become acute and serious through the added strain of malarial infection. In cases of pernicious anaemia, with symptoms suggesting coexistence of adrenalin want, the possibility of a pre-existing and coincident tuberculosis of the suprarenals should not be forgotten.

(6). Accidental death, following direct infection with malarious blood (in dental work, or by blood transfusion, etc).

This question is raised by a fatal case of malaria recorded by Glynn and Matthews.

CASE XLVI.

A fatal case of malignant tertian malaria contracted in the North of England. (Glunn and Matthews).

A girl of 18, born and residing in Liverpool, had 5 ot 6 teeth extracted. On the 14th day after this, she visited a valley subsequently found to harbour large numbers of hibernating larval and adult anophelines. On the 16th and 18th days, she vomited, being flushed on the latter. On the 25th day, she had to be helped home by a passer-by, becoming faint in the street, and thereafter remained under treatment with some delirium, severe headache, photophobia, and intermittent unconsciousness. Meningitis was suspected, but a slight vaginal discharge accompanied as it was by a profound anaemia and unconsciousness, led a gynaecologist to diagnose metrorrhagia, and to advise hospital treatment. She only survived admission two hours, and died on the 30th. day after the dental extractions (about a fortnight after her first evidence of illness) with a temperature of 102°·6F.

The temperature, however, had only been taken once previously, and was then over 100°F. Autopsy showed a spleen enlarged to 23 ozs., engorged with blood, without fibrosis, and containing as did the blood in the large vessels, numerous crescents and segmenting malarial parasites. There was marked erythroblastic reaction in the red marrow, and some of the lumbar glands resembled haemolymph glands.

R. Ross enquires whether this girl had had any subcutaneous injection from a week to a month before his illness began, or whether the dentist had just previously dealt with an old case of malaria. He states that a number of cases of malignant malaria occurred in Britain during the War as the result of such injections (he is not free to give details), and considers blood-to-blood communication proved by these experiences.

Sir Ronald Ross here raises a question which might remain unthought of until attention was drawn to it. The writer knows of no actual case in point, but it will meet the purpose of being forearmed by being forewarned.

(5). Rare forms of accidental death from muscle rupture.

Still rarer forms of accidental death have been recorded in malarial subjects associated with muscle rupture.

Sébastian records a case of rupture of the right auricle during a severe malarial paroxysm; and Vallin (L'Union Medicale, 1874, 17.) cites a case of Cruveilhier of rupture of the right rectus abdominalis during paroxysm in a women, with haemorrhage and death which could not be accounted for in any other way.

These accidents, judging from the literature, must be very rare, and are probably associated with malarial myocarditis and myositis, noted by Lancereaux, Hamernjk and many others familiar with malarial toxic tissue change.

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CHAPTER XXII.

MALARIA AND ALCOHOL.

There are several ways in which alcohol and malaria come into relationship.

1. Malaria may easily simulate alcoholism.
2. Alcoholism predisposes to severity of malarial infection.
3. Alcohol may induce an attack of malaria.
4. Alcoholism as a habit may be induced, or accentuated, by malaria.
5. Malaria produces a definite cerebral intolerance for, or diminished resistance to, alcohol.

Many observers, mostly French, have written on the subject of alcohol and malaria. These include Régis, Hesnard, Simonin (Val-de-Grâce), Marandon de Montyel, Simon, F. Smith, and others.

1. Alcoholism simulated by malaria.

The readiness with which malaria can simulate drunkenness must be evident to those who have handled malarial confusional cases. If the patient happened to have taken very little alcohol for malarial depression, the case against him would be even more complete. That so famous an observer as Osler should have mistaken at first impression, a severe and ultimately fatal case of malaria, for drunkenness, speaks for the need of care in such matters. This case (No. 20) is detailed in the medico-legal section. Col. F. Smith records a case (Case 21, Medico-legal section) on malarial stupor and coma in a soldier who was removed from a Car in Calcutta as drunk, and handed over to the military police who put him in confinement until it was discovered he was ill. A case of the writer's, one of confusion simulating drunkenness as an Army Offence, is also recorded in the Medico-legal Section (Case 8).

Simonin (Val-de-Grâce) records two cases of medico-legal import, where malarial infection simulated alcoholism.

CASE I. Amnesia of malarial, not alcoholic, origin. (Simonin)

A functionary in West Africa was relieved of his duties because of absentmindedness. He had been denounced as an alcoholic to the Colonial Minister. An expert dealt with the case, and tried to discover whether this memory defect, which took the form of antero-grade amnesia with fixed ideas, had to do with alcohol or malaria. He was able to demonstrate enlargement of the spleen and liver, so common in malaria. There were also evidences of liver and renal insufficiency. The quantity of urea excreted varied between 9 and 14 gms. in the 24 hours, and the urine contained a small quantity of albumen. There was marked leucopenia. A careful examination failed to discover any of the stigmata of habitual alcoholism, either digestive or nervous. Moreover, the amnesia disappeared after a time, subsequent to suitable treatment for chronic malaria.

CASE II. Malarial polyneuritis, mistaken for alcoholic neuritis. (Simonin).

A junior Colonial Officer was repatriated from Madagascar, where he had suffered from prolonged malaria. He was treated at Val-de-Grâce during four months for generalised polyneuritis. Some months later, having returned to the Colony, he had a slight recurrence, which was labelled by the local medical officer as alcoholic neuritis. Confident in his sobriety, and concerned about the effect of this diagnosis upon his career, he sought justice from a higher authority. The Colonial Minister ordered an expert to look into the matter, when it was found, on the examination of reliable witnesses, that the officer, who was of excellent bourgeois family, had been tipsy only once in his life, and that on the occasion of his elevation to the rank of Brigadier. His habitual sobriety was affirmed by all his military chiefs. No other infection was discovered, apart from severe and recurrent malaria. In consequence of these investigations, the

the qualification "alcoholic" was removed from the account of his polyneuritis.

It would appear, then, that there is much need for careful discrimination in the diagnosis of mental and physical illness, where alcohol and malaria occur as separate aetiological possibilities. The medico-legal importance of this part of the subject is considerable, as in some cases alcohol has nothing whatever to do with the delinquency, while in others where some alcohol has been taken, the difficulties in deciding as to aetiology may be greater.

2. Alcohol predisposes to severity of infection. Many observers, Conti, Ziemann, and French writers, etc., testify to the increased severity of malarial infection in alcoholics, as compared with non-alcoholics. All are familiar with the severity of other infections—notably pneumonia—in alcoholic subjects; so it would seem that malaria is no exception to the rule. It is of interest to note in this connection that Marchiafava, Bignami, and Ascoli emphasise the severity of pneumonia with sequelae in malarial subjects. Folly says delirium is more common in alcoholic malarial subjects than in non-alcoholic malarial subjects. He says that delirium from malaria does not occur in Arabs, but only in alcoholic Europeans.

Nevertheless oil exceptions have been recorded of habitual drinkers in the tropics who have maintained a remarkable immunity to malaria. Brohier (quoted by Ziemann) records such a case, and Pennato and Piroli (Ziemann) record that soldiers in Crete often remain free of infection or had only slight attacks free of sequelae.

3. Alcohol may induce an attack of malaria. That alcohol may induce an attack of malaria has been frequently noticed. Thus alcohol may be classed with insolation, (emphasised by Italian observers, especially Marchiafava and Bignami), exposure to cold, wet, traumatism, chloroform anaesthesia, etc., as an inducer of malarial attacks.

The present writer came across several cases where alcohol appeared to be the immediate cause of a malarial attack with mental symptoms which brought the patient to hospital.

The following is a case of this class:

CASE III. Attack of malarial confusion, induced by drinking.

Pte. A.C., aged 30;

30:4:18. Salonica. Admitted to hospital with recurrent malaria. Complains of headache, and he has the fixed idea that persons unknown are saying his wife are dead, and they are defaming her character. He had been drinking for some days previous to admission, and the depression and confusion that developed after admission were attributed to this with a malarial attack supervening.

He took malaria first in September, 1916, and has had 14 attacks since then,,and has been four times in hospitals. Last attack was 10 days ago, and he had three days off duty with it. Temperature, 103·8°. Blood films show benign tertian parasites, Spleen not palpable. Heart and lungs negative.

4:5:18. Nervous, headaches, flushed, nervous movements of hands. Has fixed idea that persons are saying his wife is dead, and that they are defaming her character.

9:5:18. Appears exhausted from malaria.

10:5:18. Still hallucinated and depressed and worried by noises. For several years has heard men accuse his of self-abuse.

27:5:18. During the last few days, he says he no longer hears voices.

13:8:18. Admits having heard voices for a long time. He seems suspicious, and is very unreasonable about being sent to hospital.

HISTORY from himself: He enlisted, July, 1905, aged 18, and was three years in S. Africa, and in Malta from 1910-13. Time expired 1914. Called up and sent to France, Aug. 1914. Swollen legs, 1914. Frost-bite, 1915. Shrapnel wound of leg, 1916. Salonica, Aug. 1916. Has had several attacks of malaria, and was waiting to go home under Y Scheme, when malarial attack came on after a few days drinking. He explains the delusions about his wife in this way. He has a brother, A, (same initial as himself)

who was serving in France while he was in Salonica. Their wives have the same name. His brother's wife went wrong with drink and men, and reports came through to him in such a way as to make him suspect his own wife, whom he now knows to be all right. He now gives a clear account of himself and shows no signs of mental abnormality. Pupils normal. Knee-jerks slightly exaggerated. Orientation normal. Fingers and tongue a little tremulous. His insight is quite restored, and he feels and looks well enough to go home.

In this case, where apparently alcohol precipitated an attack of malaria, the mental result had perhaps a dual cause, alcohol and malaria.

The next case, recorded by Marchiafava and Bignami, as a case of coma which ended fatally, is considered by the present writer as very probably coming within this category as it will be noticed that the onset of the malarial attack which ended in coma and death, occurred after an evening's drinking. The authors', however, make no reference to this point, and responsibility for the present view rests with the present writer.

CASE IV. Fatal malarial coma after drinking. (Marchiafava and Bignami).

C. A., 36 years old, has had intermittent fever for 8 days, but the type has not been recognized. On Dec. 6th, he was pretty well, so much so that he had passed the evening drinking with his friends. But towards midnight, he was seized with intense shivering and very high fever and soon after fell into a state of coma. In this condition he was brought to the hospital at 8 a.m. on Dec. 7th; hypodermic injections of bisuriate of quinine, as well as different stimulants, were then immediately administered.

The patient is in profound coma, with complete relaxation of the muscles; the deep reflexes are effaced on the right side, and almost so on the left, while the superficial ones are also entirely wanting. The respiration is slow, noisy, short, irregular, and interrupted from time to time by long pauses. The pulse is 110, regular and soft. The patients complexion is earthy, and the spleen

is not much enlarged. His comrades assert that he has not had any other before the present attack of fever. Temperature, 8 a.m., 98·8°F.; 12 noon, 99·4°F.; 3 p.m., 99·8°F. Blood: there is an immense number of plasmodia without pigment, and many bodies with pigment at the centre; also a moderate amount of crescent-shaped forms, both adult and young, as well as bodies of different sorts—round, spindle shaped, etc. Many pigmented white blood corpuscles are seen, of large size, and abounding in shining granules. Although at brief intervals during the day, fresh injections of quinine, of camphor, etc. were given, death supervened at 4 p.m.

AUTOPSY: The meninges are hyperaemic and dry; the cerebral convolutions are flattened, owing to increase of sub-dural tension. The brain is melanotic; the capillaries are filled with R. B. C., containing forms with a small mass, or with needles of pigment in a state of motion, at the centre. The spleen is twice the normal size; it is a little softened, and black in colour. The liver is melanotic, and at the same time of the colour of yellow ochre. The marrow of the ribs abounds in parasites, which are for the most part pigmented; it contains also many nucleated R.B.C., in one of which a parasite was found. There is nothing worthy of notice in the other organs.

4. Alcoholic habit may be induced or accentuated by malaria. The depression of chronic malaria is so marked in degree and frequency that instances have arisen where alcoholism as a habit has been induced in attempts to relieve the misery of these patients. The present writer came across several soldiers, who had been total abstainers prior to their contracting malaria, and other cases of moderate drinkers, who found that their alcoholic habits increased during periods of malarial depression. Some of the mental cases handled by him were cases of this kind, and the resultant psychosis in some instances was no doubt from the combined effects of alcohol and malaria.

This point is also emphasised by Marañón de Montyel, who states that it conduces to dipsomania. He says that with the atrocious thirst after the sweating stage of an attack, together with weakness and depression, which may or may not be transitory,

that many seek the tonic effect of alcohol and often exchange their weakness and depression for delirium tremens. Often enough, the dipsomania is transitory, disappearing with the period of malarial attacks, but sometimes it persists as a habit.

5. *Alcohol intolerance in malarial subjects.* That malarial poison induces a diminished cerebral resistance to alcohol has been advocated by Maranion de Montyel. As alienist in the asylums of Saint-Pierre at Marseilles, and Ville-Evrard, he carefully considered the subject, and published 12 cases in 1893 in support of his thesis. His attention was drawn to this subject by the alienist, Lemoine. Moreover, he was brought up in Martinique, and was familiar from childhood with the effects of malaria. He says that the cerebral intolerance for, or diminished resistance to, alcohol in malarial subjects exists along with a definite appetite for it, and may persist between the febrile attacks, even if these are months or even years apart, so long as parasites exist in the system. Whoever takes strong drink when hungry is liable to have hallucinations and mental confusion with a comparatively small quantity of alcohol—the malarial subject is much in the same position, but habitually so. His expressed conclusions on this subject are given in direct translation as follows:

1. Generally speaking, it is true to say that malaria produces a marked decrease of cerebral resistance to alcohol.

2. This takes place by means of an alteration in the blood produced by the malarial poison.

3. By reason of this intolerance, a person normally constituted, if he drinks even moderately in the course of the first evidence of a malarial attack is liable to develop delirium tremens.

4. The hereditary alcoholic, endowed by familial transmission with a special resistance to alcohol, is found, in the course of the first evidences of malaria, to lose this resistance, and although he may not drink heartily, to also develop delirium tremens.

5. The hereditary neuropath, already constitutionally of diminished resistance, will succumb, not only more easily and rapidly than the two preceding, but will be, besides, liable to grave cerebral effects ending in dementia praecox.

6. What is true of the early manifestations of malaria is

still more true of relapses, so that a person who had shown some resistance at first, by reason of an exceptional tolerance for alcohol, hereditary or acquired, or by reason of a relative sobriety, is bound to have delirium tremens sooner or later, proportionate to this tolerance and to the quantity of strong drink he will absorb during a subsequent attack.

7. The intolerance for alcohol due to malaria persists in the intervals—sometimes very long—between relapses, even in the malarial who is a hereditary alcoholic of great previous resistance, and it would appear that here we may have evidence of malarial poison in the system, in that this lost resistance ~~reconquists~~ only returns when the body is completely cleared of poison.

8. Malaria is capable of destroying the tolerance not only of the drinker, but of the true dipsomaniac who, till the actual onset of the malarial attack, had shown an exceptional resistance to alcohol.

9. If, then, at the time of malarial infection, the subject had no alcoholic habit, and he finds himself nevertheless with a latent predisposition to drink, the infection is occasionally powerful enough to activate it, and is besides more formidable by determining at the same time an excessive alcoholic intolerance.

10. So far, then, it appears not only that Malaria is capable without any predisposition of inducing an impulse to take strong drink during the acute attack, but creates an even greater tendency to it in the intervals.

One of the 12 cases detailed in support of these ideas is given in slightly abridged translation.

CASE V. Dipsomania and alcoholic intolerance, induced by malaria. (Marandon de Montyel).

Gustave L., aged 30, lithographer. Admitted to Ville-Evrard asylum, April, 1893, for the sixth time. All the admission certificates indicated "alcoholic insanity with fits of frenzy, and homicidal impulsiveness. No hereditary insanity, but ataviatic hereditary alcoholism". The father was a sober man, but the paternal grandfather was the greatest drunkard in the district, and finished up with suicide by drowning. The patient

and his sister are drunkards, it is interesting to note. The sister drank enormously and stood the excess of alcohol very well. She could keep her head with the biggest drinkers in the country, it appears, and has always enjoyed excellent health. The patient, apparently by natural taste, became addicted to drink about the age of 17. So to speak, he had the need in his blood. Like his sister, he stood it very well, but not more than her; for the greatest excess did not make him tipsy. In 1883, at the age of 30, he had a very severe attack of typhoid fever, which kept him in hospital for over 50 days. His excessive tolerance for strong drink was slightly altered after this; he was not quite so resistant as in the past; he got tipsy—a thing he had never known before; nevertheless his tolerance was still most remarkable, but what for him put it completely out was malaria contracted in 1885 at Oran. He said that the influence of the typhoid fever was comparatively nothing; the malaria did not take away the taste for alcohol—on the contrary it had developed before, only it makes you boozy immediately you take a mouthful of drink.

It is worth remembering that the patient was very intelligent and understood a good deal about his own condition. He was quite emphatic on the point, that although there was an appreciable diminution in his tolerance for alcohol after his typhoid fever, from the time he had malaria he lost all his tolerance, so that he could no more drink even moderately, not only without being tipsy, but without being put in a frenzy, and transformed into a wretched beast.

After two months treatment for malaria at Oran in 1885, he was repatriated, but there were no cerebral complications. In France, the fever recurred each year, generally twice till 1888, subsiding with quinine. In Dec. 1890, after two years without a recurrence, it broke out afresh. The patient was then interned in Ville-Evrard asylum, and worked in the asylum kitchen, where by mistake he upset a kettle of boiling water on his legs. Two days afterwards, quotidian fever began with all the classical features. I have seen the same thing happen in the asylum at Marseilles—a kitchen worker being burned, and having a recurrence of malaria 10 years or so after his last attack, and till then never having

spoken to us of malaria, believing himself quit of it.

Since this curious incident, which was of interest to the patient himself also, the malarial fever, stopped by quinine, has never returned. But his intolerance for alcohol markedly persists, while the tolerance of his sister, who has always enjoyed good health, remains intact. The last time he visited her, he told us to avoid misfortune, she shut him in the barn until the next day, so that she could continue drinking all evening with her friends without being inconvenienced. It is evident that Gustav X., even under the influence of a minimal dose of alcohol, becomes extremely violent and impulsive. The two following incidents which occured at Ville-Evrard make this clear. One day, working in the fields, he disappeared and went to a public house near by. He drank very moderately everyone said; but instead of paying, to the astonishment of the others who averred how little he took, he got into a blind fury and broke glasses and bottles, tried to knock down the tavern keeper and his customers who found safety only in precipitate flight. It required main force to bring him to the asylum, where he arrived with a squad of six warders, who had great trouble in holding the maniac. He had destroyed everything in the tavern.

Another time, Gustav X. vanished after having borrowed 20 sous from a comrade, having nothing in his possession. It was seven at night. The sum was not much, and did not permit of excess; however, two hours afterwards, the police took him away, tied up, in a fury, and foaming at the mouth. The following was the official account of his conduct, "He was leaning with his back against the wall of the station Nogent, and holding a stone in his hand. We succeeded in disarming him by persuasion, and led him towards the tramway bureau, where he was suddenly taken with a fit of nerves which lasted some minutes, after which he began to kick out violently. It was only with difficulty that we managed to calm him and get him away from the tramway bureau which he would certainly have wrecked. Once in the street, he got into an indescribable fury, launched out with his fists and feet, kicking whoever came near him; then at a bound he rushed on the quarter-master of hussars, who came to help, and who got so violent a blow on the head with his fist that his helmet fell on the road. With

the help of this officer, we have managed to master this crazy salman and make it impossible for him to hurt anybody."

On the morning following these two occasions, Gustav K. had quite recovered and was himself again. Since then we have not sent him out to work, and have had him closely watched.

This then, is what malaria has done for this drinker, who took enormous doses of alcohol without any trouble; the slightest indiscretion puts him in a passion. Alas! he says, since I took malaria, I know that I am not able to drink any more, and I ought to stop it. But if I cannot stand drink, I have always the craving for it in my blood; my sister is very happy, for she had never left the country, and has not caught my trouble, which would have made her lose her tolerance, and she is able at her ease to satisfy herself in drinking to her heart's content.

The importance then, of being able to distinguish between mental states due to malaria on the one hand, and alcohol on the other, is clear: and the better the differential points in diagnosis are understood, the more readily and justly will cases of separate and combined aetiologies be dealt with.

Mesnard, among French writers, appears to have studied this part of the subject with some thoroughness, and has tabulated the differential points between malarial and alcoholic delirium. So important is this subject, especially from the medico-legal aspect, that the present writer has considered that he could not do better than give a brief translation of Mesnard's work on the subject.

Mesnard indicates that, in the malarial psychoses, there is a predominance of asthenia and confusion, which if severe and prolonged enough gives rise to disorientation in time and space, with false recognition of objects, general mental weakness, and faulty perception. Memory defects are well-marked, with a tendency to automatic fabulation, and imaginary narration, not directly of ideas origin, but more the result of inherent error of thought.

The malarial deliriant is dimly conscious of his mental trouble. His facies tired, simple, startled, questioning, and his

manner halting, constrained, showing an intelligence obscured but not completely occupied, as in the alcoholic. His apathetic mentality, automatic and hallucinated, usually functions enough to give him a distant idea of his condition with its faulty perception.

The emotional tone of the malarial patient is lowered. He is passive, confused, irresolute, showing above everything else affective apathy. His anxiety is determined only by the realities of life, and the creations of his delirium. Fear, which may fluctuate with his hallucinations, subsides quickly and readily. He is simply depressed, though his depression may vary from time to time, and he generally shows more irritability of temper. Psychomotor excitement occurs less frequently as dangerous impulsiveness or violence, though erratic excitement is more common.

On the contrary, alcoholic delirium is essentially a hallucinated dream state. Confusion is present, being an integral part of delirium, but it takes a second place in the clinical picture. The patient is perpetually agitated, hallucinated, the mind busy with cinematographic visions which transform the external world to his eyes, and which follow one another in rapid succession. Psychomotor excitement is very marked—loquacity, reaction to environment highly active, and with unceasing change.

This hallucinatory activity is a prominent feature of the psychosis, and is well maintained, dominant throughout it, until the end. The mixture of lucidity with the delirium in the alcoholic is much more intimate, less dissociated, and the patient is less surprised at the extravagances of his dreams as compared with reality.

The following tables, drawn up by Mesnard, define the several differential features of malarial and alcoholic delirium, mental and somatic.

see over.

A. MALARIAL DELIRIUM. (BERNARD).

(1). Mental Features.

(α). Dream Content.	(β). Psychotic accompaniments.	(γ). Associate features.
1. Ideation scarce, poor, systematized and fixed.	1. Predominance of the element of confusion (of sleep over dream).	1. Evidences minimal or nil.
2. Delirium mono-idea or few, and these from the memory.	2. Agitation moderate and interrupted.	2. Prodromal stages short.
3. Memory ~~deficient~~. frenzy delirium.	3. Psychomotor excitement inhibited.	3. Onset sudden.
4. Post-delirium ideas are isolated, fixed and persistent.	4. Perception very clouded, although punctuated with periods of clarity.	4. Course irregular, and termination gradual, as by lysis.
5. Delirium rehearsed in simple gesture, and not very actively.	5. Faulty observation, and difficulty of orientation from confusion.	5. Sequelae immediate and frequent.
6. Ideational colour monotonous, often professional, but fundamentally emotional.	6. Marked amnesia.	6. Convalescence long.
7. Hallucinations few in number, multisensory, monotonous.	7. Automatic speech—not quite in dream state.	7. Periodicity of attacks
8. Delirium conduct and ideas may resemble the ~~ordinary~~ normal.	8. Remote consciousness of illness.	
9. Suggestion contributes comparatively slightly.	9. Somnambulistic state complete, but liable to vanish suddenly.	

A.: MALARIAL INFECTION: (CONCLUDED).

	(Mental Features).
to the hallucinations.	10. Apathetic, emotional, anxious, with reactions not violently impulsive.

(2). Somatic Symptoms.

Laboratory Findings.	(x). Visceral.	(β). General.	(γ). Nervous.
1. Parasites in blood. 2. Mononucleosis (Constant). 3. Complete retention of urine and excretions disturbed by febrile attacks. 4. Parallelism reversed, but indefinite and inconstant between the curves urinary and the delirium.	1. Tongue slightly furred. 2. Malarial liver. 3. Splenomegaly.	1. Fever constant or prolonged during greater part of attack. 2. Hyperthermia during attack or after. 3. Malarial facies. 4. Cachexia or aspect of chronic malaria. 5. Beneficial effect of quinine treatment.	1. Motility and reflexes little disturbed 2. Tremor at onset of attack. 3. Pupillary disturbances exceptional. 4. Headache early, constant and prolonged. 5. Sweating fitful and at the end of the febrile attack and often at the end of the delirium.

2.: [illegible] (continued).
(β). Mental features.

(α). Dream Content.	(β). Psychotic Accompaniments.	(γ). Associate Features.
1. Ideation multiple, rich, inco-ordinated, and variable. 2. Ideas imaginative, disordered, original. 3. Dream actively lived by the subject. 4. Post-delirium ideas multiple and fleeting. 5. Ideational colour very variable, with predominance of the professional and trivial. 6. Hallucinations multiple in successive pictures, especially visual. 7. Delirium fantastic, burlesque, terrifying. 8. Suggestion contributes markedly to the hallucinations.	1. Predominance of the element of dream (of dream over sleep). 2. Agitation extreme and sustained. 3. Marked psychomotor excitement. 4. Lucidity parallel to perception. 5. Faulty observation and disorientation from frenzy. 6. Amnesia slight. 7. Speech dreamy and loquacious. 8. Little recollection of illness. 9. Incomplete somnambulistic state, but always uniform. 10. Anxiety intense, grounless, and panicy, with reactions distinctly impulsive.	1. Evidence occasionally apponent. 2. Preliminary modification in consumption of alcohol. 3. Prodromal state prolonged. 4. Onset slow (dream state, progressive). 5. Attack definite, concise. 6. No periodicity.

9. ALCOHOLIC DELIRIUM. (BERNARD).

(2) Somatic Symptoms.

Laboratory Findings.	(α). Visceral.	(β). General.	(γ). Nervous.
1. Absence of malarial parasites in blood. 2. Polynucleosis very rare (excluding infection). 3. Eosinophils scarce. 4. Total retention of urine, with urea and salts during the attack, with clearing up at the end. 5. Parallelism reversed and definite between the urinary curve and the delirium.	1. Tongue markedly furred. 2. Alcoholic liver. 3. No splenomegaly.	1. Fever only in the case of febile D.T. 2. Hypothermia frequent. 3. Alcoholic facies. 4. Acetone breath. 5. Influence of quinine nil, or aggravation.	1. Motor co-ordination marked. 2. Tremors marked and continuous. 3. Considerable psychomotor excitement. 4. Reflexes considerably altered. 5. Pupillary changes frequent. 6. Meningeal complications frequent. 7. Headache short and inconstant. 8. Sweating continuous, rather than fitful.

CHAPTER XXIII.

Malarial Nerve Conditions: (1) Cerebral.

We have seen that the ancients in general and Hippocrates in particular noticed the relationship between malaria and phrenitis or brain inflammation. Much later, J. Fernel (1586), quoted by Mannaberg, was credited with being the first to describe malarial paralysis. It is, however, with the discovery of the parasite by Laveran in 1880 that the most reliable observations upon the pathology of the malarious nervous system began.

There has been a tendency with some to attribute nervous and mental affections in malarious subjects to anything else than their malaria. This is putting the telescope to the blind eye, for while it is true that anything that prejudices tissue resistance—bad heredity, intercurrent disease, overwork, alcohol, undue exposure to the sun—will render the soil more vulnerable to the incursions of the parasite, there is abundant evidence to show that normal and robust nervous tissue may suffer the same damage as it does from other toxic diseases.

If we call to mind that in cerebral pernicious fever the leptomeninges are often intensely hyperaemic and melanotic; the cortex and grey substance of the ganglia and crura assume a brownish-red or blackish colour; not infrequently, punctiform haemorrhages are found, generally in the white substance rarely in the grey matter of the brain; that in the cerebellum, the grey matter is involved by haemorrhages more often than the cerebral grey matter; that cerebral capillaries are often packed with parasites in all their stages of development, which constitutes one of the elements of malignancy; that only in the gravest cases are arterioles and small veins so rich in parasites as the capillaries; that capillary endothelium is in a state of fatty degeneration and swollen so that the lumen is narrowed and sometimes obliterated; that the endothelia often contains pigment, parasites, and spores; and that when sporulation

abounds, accumulations of spores and pigment may occlude the capillary lumen constituting a true parasitic thrombosis; that nerve cells and filaments have been found in all stages of degenerative changes; and that in the spinal cord similar changes have been found as in the brain, we will see that all the structural change necessary to explain serious mental and nervous conditions, is at hand.

Conti noticed in highly malarious Sardinia that alcoholics showed a greater tendency to mental disturbance from malaria, as did those addicted to the use of opium. He also records that there was a greater tendency to nervous and mental breakdown among those who toiled very hard, who abused themselves in any way, or who were exposed to the sun, though nervous troubles occurred apart from these accompaniments. He records the frequence of nervous and gastric disturbances, tremors of the extremities, giddiness, syncope, palpitation, neuralgia, polyneuritis, and anorexia, indigestion, vomiting, constipation, diarrhoea; and skin disturbances like urticaria and purpura, from derangement of the vaso-motor nerves. He also emphasises the occurrence of asthma, dysarthria, delirium, hallucinations, amnesia, paresis, insomnia, coma, vesical paralysis, convulsions in children, motor aphasia (frequent), and that these conditions often remained after the febrile period. He also notes the occurrence of multiple sclerosis, acute ataxia, and the cerebellar syndrome; also athetosis, myoclonus, chorea, halting gait, bulbar paralysis, hemiplegia, paraplegia, asthenia, spastic paralysis, the Parkinsonian syndrome, and epilepsy.

Among neuralgias, the most frequent was trigeminal, especially the supra-and infra-orbital branches. Neuritis of occipital nerves, intercostal, sciatic, lumbar, ovarian, diaphragm. Disturbances of sensory, motor, and trophic nerves were noticed. Occasionally involvement of anterior cornual cells was observed (Lazzatto).

He indicated that when neuritis began suddenly, it tended to produce paralysis with intense pain; when slowly, it exhibited at first sensory disturbances, paresthesia, anaesthesia with lightning pains. Then followed motor disturbances, and weakness up to the affected region. Time of development might be very long.

Innumerable other competent observers in malarious districts

have made similar observations and during the recent war many British and Continental observers have testified to the frequency of nervous and mental conditions arising in malarious areas such as Macedonia, East Africa, Palestine and India, among soldiers mainly, but also in some instances amon the native populations. Moreover, civil practitioners and hospitals in European countries, particularly are dealing from time to time with many instances of nervous and mental conditions in repatriated soldiers in whom their acquired malaria still persists, maybe in latent forms, and who have periodic breakdowns, that call for diagnosis and treatment. The literature is studded with examples ~~of~~ of this kind, and although war conditions no doubt have gone to swell their number they still exist, and have been existing for ages in malarious countries, in abundance, even in times of peace.

A glance at the pathology section should convince the reader as to the capacity of the [redacted] malarial parasite for producing nerve damage. When it is also remembered that by focal massing of parasites in the capillaries of any part of the nervous system, (as indeed they may do in any part of the body) but notably in the cerebral white matter, localised damage ranging in degree from temporary irritation or cloudy swelling up to complete focal necrosis of nerve tissue may occur, it will be expected that almost any clinical picture of nerve disturbance may arise, depending upon the focus, extent, degree and fluctuation of involvement. And indeed this is what the literature appears to confirm. A survey of it shows almost every conceivable neurological syndrome.

To facilitate dealing with the subject in as brief and comprehensive manner as possible, it has been considered best to divide the malarial lesions of the nervous system into four groups, as they affect,

(1). The cerebrum.
(2). The cerebro-spinal system.
(3). The cord and peripheral nerves.
(4). The special senses.

For the most part, the range of disturbance of these systems will be indicated by the choice of representative examples from the

literature, for indeed it would appear that the types of disturbance recorded are innumerable, as one would expect from the varied focal concentration habits of the parasites.

(1) Malarial Cerebral Lesions.

Almost all parts of the brain have been found clinically and pathologically involved, but their has been a predilection for the cerebral white matter and meninges, bulb and basal nuclei, cerebellar white and grey matter, and less often the cerebral grey matter, no doubt due to its better capillary anastomosis. All grades of tissue change of cells and filaments and vessel walls have been noted, ranging from slight degrees of change suggestive of defective oxidation and cloudy swelling, up to complete necrosis, such as are found in other undisputed toxic diseases, like diphtheria and scarlet fever. Capillary haemorrhages are not uncommon, larger haemorrhages occur, though not commonly. Further details will be found in the pathology section.

Various syndromes will be considered in series, mainly by giving examples of them by their respective observers—such as the meningeal, hemiplegic, aphasic, etc.

I. MALARIAL MENINGITIS.

Meningitis and signs of meningeal irritation or meningism of malarial origin have been observed by many clinicians, notably Paisseau and Rutinel, Comes, Porot, Ribon, Marchiafava, Bignami, Bastianelli, Papastrategakis, Pratsicas, Coudray, and others. Much of what follows is borrowed from Paisseau and Rutinel and Papastrategakis.

The meningeal reaction to malaria is fairly common especially in children and young people. It is often related to convulsions, so common in children in malarious countries. It may occur in the course of acute or chronic malaria, and affect brain or cord with localising accompanying signs and symptoms. It commonly exists with and without fever, and may persist for long periods after the febrile stage, or fluctuate in degree with the periodicity of the temperature. It may last a very long time—e.g. months, especially

if there is no treatment, and in the army these cases are often taken for malingerers (Papastrategakis, who says it is very common in malaria-ridden countries like Greece).

The common signs of it are severe headache, with vomiting, neuralgia, labial herpes, transitory amaurosis, cranial nerve paralysis, diplopia, photophobia, optic neuritis with retinal haemorrhages, pain behind the eyes, Kernig, stiff neck, and retracted head. Periodicity of these features with enlarged spleen and parasites in the blood, are specially suggestive of malaria, though often enough parasites are difficult to find in the peripheral blood.

Onset may be insidious or sudden, and not infrequently is accompanied by cerebral excitation features, such as excitement, delirium, and ultimately coma or convulsions which are common in children. Mania, delirium or coma, may actually mask the signs of meningitis, so that these should be looked for in such cases. Vasomotor troubles are common, such as swollen face, marbling of the skin, mucous-membrane and skin haemorrhages, and herpes. The pulse tends to be slow, small, intermittent, irregular; respirations irregular, intermittent and slow. Pupils dilated, unless associated with coma, when they are generally myotic (Grall). Squint is not rare. Constipation and anuria at times. Cure is the rule—and rapid if treatment is begun early. Death is not uncommon after coma. Spontaneous cure is not unknown, though sequelae are apt to remain, e.g. corneal ulceration in one of their cases (Paisseau and Hutinel). Gastro-intestinal disturbances are prominent in this type of meningitis as compared with others. Ribon emphasises the eye-disturbances that are more prominent in meningitis of malarial origin, e.g. amblyopia, amaurosis often transient, conjunctivitis, keratitis, and corneal herpes, optic neuritis, thrombosis of central vein of the retina, retinal punctiform haemorrhages and irido-choroiditis (see Special Senses section).

In tubercular meningitis there is a greater predilection for the motor nerves of the eyes.

The cerebro-spinal fluid is generally in close relationship to the clinical phenomena. The albumen is often increased notably with cellular reaction, mononuclear and endothelial. In meningism,

the Cerebro-spinal fluid is normal.

Papastratogakis quotes the case of a soldier at Salonica in Novr. 1919, who was brought to hospital in a state of coma which had come on after an attack of fever accompanied by severe shivering two or three hours before. Patient was very pale in the face, T., 38°-1, P., 84; signs of meningitis complete clinically,— retraction of the head, Kernig, photophobia, retracted abdomen, vomiting. C-S. F. normal. Many plasmodia falciparum in the blood. Quinine, 2 grs and 500 ccs. of physiological salt solution with adremalin given immediately. After 2 hours, temperature was 36°-3, quiet night. Next morning, only a trace of Kernig and a tendency to sleepyness. After 12 days, on occasion of a fresh feverish paroxysm, the same phenomena recurred, accompanied this time by delirium.

He distinguishes two main forms of malarial meningitis—acute and chronic. The acute has the usual accompaniments of acute meningitis, but in addition has frequently epilepsy, excitement, delirium, mania, or coma accompanying it. The C-S. F. always shows excess of albumen and cell elements, especially lymphocytes. It usually lasts one to eight days, generally clears up with proper treatment, leaving headache, tremor in extremities, visual disturbance, local atrophy of extremities, and Kernig's sign is the last to disappear.

His observations on chronic malarial meningitis are of special interest. Of the two forms, pia mater meningitis and dura mater meningitis, only the former is met with in malaria, and it generally shows as affecting the posterior roots. Localization is almost invariably in the lumbo-sacral region, and shows clinically by sensory and motor disturbances, which appear first or more rarely appear isolated. In the latter cases, sensory disturbances are more frequent; they are either subjective or objective. The former take the form of very severe pains in the limbs along the line of the nerves, are generally intermittent, and are increased by coughing or sneezing. This was observed by Dejerine. The patients also complain of feelings of numbness, heat, cold, heaviness, located in the extremities. These features are often mistaken in the Army for signs of rheumatism or even malingering. He quotes the case of a soldier who for 2 months complained to the Divisional M.O. and was

always dismissed; he was sent finally to hospital to get rid of him, where in a few days he developed paralysis of the lower limbs and has not yet recovered after 8 months and more.

Objective sensory disturbances are first hypoaesthesia, later complete anaesthesia, both distributed in the limbs in lines parallel to the axis of the limb, and corresponding to the section on the skin of the affected roots. These hypo- or an-aesthetic zones alternate with parts of the skin in which sensation is normal or even hyperaesthetic. More rarely this anaesthesia going deeper is accompanied by muscular anaesthesia. In consequence, walking may become irregular, as in sufferers from tabes; sometimes it may be spasmodic. He quotes in point the case of a man with pains which ran down the lower extremities, by hyperaesthesia of the skin of the thigh, especially in the region of the third, fourth, fifth lumbar, and first, second, and third sacral roots, by increased deep reflexes, and shaking of foot and patella: by spasmodic walking and by increased frequency of micturition followed by retention, with recovery upon suitable treatment.

Motor disturbances are shown clinically by paralysis and atrophy of the muscles which are supplied by the anterior roots which happen to be involved. They are very like sciatica at first sight, but the affected muscles do not belong to one and the same segment, but only to one and the same root. The roots most commonly attacked are the 4th and 5th lumbar and 1st sacral; the muscles generally attacked are those of the anterior and outer aspect of the leg and its skin. At this stage the deep reflexes, especially the Achilles' jerk, are diminished or disappeared.

Examination of the C-S. F. is necessary. Excess of albumen and cells will be found where there is meningeal involvement.

Symptoms of this kind are often mistaken for the results of alcoholism, syphilis, tuberculosis, chronic rheumatism.

Apart from the acute and chronic forms of malarial meningitis, there is an intermediate form, which occurs after repeated malarial paroxysms, characterised by persistent headache, loss of capacity for work, and from time to time a tendency to vomit. Examination shows presence of Kernig's sign, increased deep reflexes, changes in the spinal fluid, and plasmodia in the blood. Occasionally, among

of this kind remind one of tubercular meningitis. He quotes a case which began with Jacksonian epilepsy, then some days later signs of meningitis appeared without fever. Diagnosis was based on the absence of delirium, and on general debility, and the presence of marked diaphoresis (not found in tubercular meningitis), on enlarged spleen and blood examination.

Chronic meningeal inflammation may appear as herpes zoster, where the only other meningeal sign is alteration in the spinal fluid.

Papastrategakis emphasises the point that simple lymphocytosis of the cerebro-spinal fluid accompanied by no clinical symptoms, should not be reckoned as meningitis. The sub-arachnoid area is specially lymphatic, is in immediate contact with lymphatic vessels, and consequently the presence of cellular elements in the C-S. F., especially when similar elements exist in quantity in the blood, is not sufficient to establish the diagnosis of meningitis if no other symptoms of it are present.

Acute and chronic forms are highly treatable, and Papastrategakis says he has not yet seen a fatal case.

Hypertension is frequent though not invariable. In attenuated attacks, sometimes only a few cells are got—more often a moderate number are found. In severe cases, lymphocytes predominate rather than polymuclears. Tension and albumen are then much increased. Papastrategakis points out that lymphocytosis of C-S. F. is common in malarial subjects presenting no evidence of meningitis or meningism, that it accompanies the blood lymphocytosis so common in malaria, and does not necessarily mean meningism. He maintains that only a C-S. F. lymphocytosis, which is not accompanied by blood lymphocytosis, should be taken as a meningeal reaction, and that in these cases other clinical signs of meningeal irritation occur.

The post-mortem findings show congestion of the pia mater vessels, with parasitic emboli, and punctate haemorrhages of the underlying grey matter (Padsmanu and Hudinel).

A few cases from the literature will serve as illustrations.

CASE V., Child with meningism, delirium and death (Arabian—Oukhtomsky).

Girl of 10 years, admitted to hospital on the 5th day of

illness. Onset was insidious. Low state of health, lassitude, headache, diarrhoea, anorexia, no epistaxis.

On admission was prostrated, with violent and persistent headache, heavily coated tongue, gurgling in rt. iliac fossa, and diarrhoea. Pulse rapid; heart and lungs -ve. Liver and spleen not painful or tender. No tache. Temperature remaining up, with slight occasional remission. After 5 days, delirious, and next day stiff neck, severe pain in back, Kernig very marked. Inarticulate complaints and unable to reply to questions. Numerous parasites in the blood. Patient died in the night.

Many cases in children are ushered in with convulsions, which may mask the signs of meningitis unless looked for.

CASE II. Latent malaria simulating tubercular meningitis. (Pratsicas).

Medical Student, aged 21. Personal and Family History good No mental or nerve trouble, syphilis, alcoholism, etc. Well-built— health always good.

31:5:20. Came complaining of motor troubles of rt. arm. No evidence of venereal disease, or traumatism. A year ago, got malaria, and was treated with quinine. It improved, but in recent months, recurrence, but took no more quinine.

30:5:20. Was walking on the street when he had suddenly a convulsive seizure of the rt. arm and head. It lasted quite a while, but he was not unconscious, but at times felt unable to do what he wanted with the arm.

On examination, there was some loss of muscle strength, hypotonia, diminished pain sense of rt. side of face, neck, and trunk down to false rib on the right side. Reflexes normal, superficial and deep; pupils reacted well to light and accomodation. No disturbance of cranial nerves. Temperature normal, pulse 80. Heart, lungs, liver, and bowels normal. Spleen one and a half fingerbreadths below costal margin, hard and sensitive to pressure. Urine, 0·3 cgms albumen per litre.

1:6:20. Convulsive seizure of rt. arm of cervico-brachial type, preceded by numbness and tingling. All the right arm members were set into clonic movements, flexion and extension alternately, and pronation and supination.

The thumb was not involved in the clonic movements, but was flexed on the palm of the hand. Face did not participate; muscles of neck, especially sterno-mastoid on the right side contracting visibly to produce convulsive movements of the head. Face pale, conjunctiva injected. Pupils moderately dilated and reactive to light. Patient quite conscious, sensible, and answered questions normally. Convulsions lasted about 6 minutes, and ended with ~~complet~~ complete immobility and anaesthesia of the arm, but this was transitory, returning in a few minutes again to nearly normal, though some diminution in power and sensation remained. Some diminution of pain sense. Temperature sense good. Paraesthesia modified, i.e., diminished touch sense and weight sense quite absent. These sensory disturbances extended to the right half of face, trunk, and neck, down to the 12th rib. It was noticed that sensation returned last to the fingers, which at the start were sites of aura, i.e. 4th and 5th fingers.

Hypotonia and sensory changes persisted throughout the day to the next morning, when he had another similar attack.

2:6:20. Two attacks of same, apyrexia and albuminuria persisted.

3:6:20. No attack. Felt well. Saline purge. Sweated freely in the evening. Defective power and sensation of limb persisted. Pulse 80. Uraemia, or TB. meningitis thought of. At night, headache, slight stiffness of neck, pulse 68, i.e. slight bradycardia. Slight Kernig—all these features increasing with pulse going to 60.

6:6:20. C-S. F. normal in pressure, appearance, and contents.

8:6:20. Pain over spleen. Vomiting persists till 9th. Headache, giddiness, bradycardia. Kernig, stiff neck. Tempt. normal.

10:6:20. No albumen.

14:6L20. Remissions and exacerbations of above. Case considered as tubercular meningitis involving the ascending frontal convolutions.

16:6:20. Numerous schizonts of plasmodia praecox, and crescents equally numerous. Not only endoglobular, but free in circulation. 2 grs. ~~alronalin~~ quinine given daily with alronalin. Symptoms vanished, one after another, and by 18th June there was only slight asthenia and

dimness of vision on changing position. Pulse 84. Kernig disappeared, and parasites became difficult to find.

20:6:20. Very slight transitory attack as formerly, with praecordial anxiety, followed by abundant sweating. The following night the same with sweating.

22:6:20. No abnormal phenomena to be found, and none since. He left the hospital feeling well.

The following case of the writer's is of interest in this connection:

CASE III. Malarial meningitis and optic neuritis, with confusion and muscle atrophy.

Pte. F.J.B., aged 22,

4:6:18. Salonica. Admitted in collapsed condition, with signs of meningitis and malaria. Opthalmologists' report: pupils contract to light, but contraction not maintained. Definite swelling of both optic discs. Small linear haemorrhage down in the left lower quadrant of the left eye. Heart and lungs normal. Reflexes brisk. No tache cerebrale.

6:6:18. Lumbar puncture done. C-S.F. under moderate pressure. 15 ccm. clear fluid drawn off. Blood shows no malarial parasites. Differential count: Polymorphs, 54: Lymphocytes, 23: Large mononuclears, 16: Eosinophils, 2%.

19:6:18. Looks very ill. Cachectic, sallow colour, anaemic, nystagmus. Pupils equal, react to light and accommodation. Movements of left side of face restricted. Pain in neck when head bent forward. Intelligence clean, abdominal reflexes normal. Tache present. Spleen enlarged and hard. Kernig present. K.J. absent. Treated with quinine ~~with~~ grs xii with saline intravenously.

20:6:18. K.J's normal. Kernig diminished.

21:6:18. Seems better. Restless night. Quinine, grs xx, intramuscularly daily.

3:7:18. Steady improvement.

20:7:18. Malta. Weak, anaemic, stuttering speech, tremors. Atrophy of interossei muscles of hands, and muscles of thenar and hypothenar eminences. Slight rigidity of fingers which patient cannot extend. Slight wasting of muscles of both forearms and legs.

Anaesthesia to touch on arms and hands and external surfaces of legs. Patellar and abdominal reflexes brisk. Mentally he has improved. Fairly well orientated, and recollects delusions and visual hallucinations he had in Malta. Very emotional and suggestible to changing moods, happy and depressed by turns. Has had hallucinations of sight lasting two hours, with somnambulistic state.

11:9:18. Feels better, but complains of recurrent pain behind eye. Stutters, but is rational. Blood Wassermann -ve.

14:9:18. History from himself. Gardener. Pre-war health good. Family History negative. Salonica, Aug. 1916. Had malaria 8 or 9 times, and off duty with it, 5 months in all. Denies V.D., and alcoholic excess. Says he has always had a stutter, but it became worse after having malaria. Remembers seeing woman in black, appearing in the night and persisting in daylight. Vision not so clear now and has frontal headaches. Very thin. Heart and lungs -ve. Pupils reactive and equal, but sluggish to light. Knee-jerks exaggerated. Momentary giddy turns occasionally, which he cannot control. Mentally normal, except for stutter.

20:9:18. Malarial attack. Quinine, grs. x, t.i.d.

23:9:18. Optic discs badly defined, especially on nasal side. No retinal haemorrhage seen now.

27:9:18. Up and feeling well.

1:10:18. Malarial attack. Tempt. 103°. M.T. parasites found in the blood. Depressed.

8:8:19. Progressive improvement on quinine. Has put on about 2 stones in weight. Looks well. Mentally normal. Has had occasional malarial attacks. Home recovered.

(It is regretted that observations on this case were not as complete as desirable, but enough exists to show the essential nature of the case).

CASE IV. Cerebral irritation, convulsions, coma and meningitis (Marchiafava and Bignami).

Boy of 12, admitted to hospital, Novr 11th. No history. Very high fever. Cold pack and 32 grs. quinine.

~~Octr~~ Novr. 12th. 8a.m. Very pale, with earthy complexion.

and some cutaneous haemorrhages on the breast. Spleen enlarged. Pulse slow. Prompt response to slight stimuli. Heart dilated on rt. side. Many plasmodia without pigment, a few crescent-shaped forms, and several pigmented white blood corpuscles in the blood. Patient lethargic, mutters incoherently. Bladder full. Teeth pressed together. Mucous membranes dry, and covered with sordes. Hyperaesthesia, superficial and deep. Vomiting. After 4 p.m., tonico-clonic convulsions set in, and continued for several hours. Collapse follows. Pulse small and arrythmic. Cyanosis and profound coma. Temps, 4 a.m., 102·2°; 12 noon, 98·8°: 4 p.m., 98·6°: 8 p.m., 98·8°. 12 p.m., 98·5°F.

The patient dies at 4 a.m. on Novr. 13th., notwithstanding that during the 12th, several hypodermic injections were made of bimuriate of quinine, amounting to 64 grains.

AUTOPSY: There is well marked anaemia of the skin and mucous membranes; also haemorrhages into the skin, breast, shoulders, abdomen, and thighs. The cranium is somewhat wanting in symmetry. The dura mater is tense, and pia mater bloodless. Cerebral cortex is melanotic. The white substance contains but little blood; the grey matter of the bulb and medulla is hyperaemic.

The lungs are free, but on the posterior part of the right one, there is oedema. The heart is dilated on the right side, and empty. The myocardium is brown in colour. There is also anthracosis of the lungs and peribronchial glands.

Meteorism of the intestines is found. The liver is pushed up; the spleen does not extend beyond the costal arch, but is enlarged and melanotic, with thickened and tense capsule. The gall-bladder is full of bile. The kidneys are melanotic, with the glomeruli not very distinct. In the liver there is a melanosis which is chiefly perilobular. The marrow of the flat bones is of a dark red colour. Examination by the microscope reveals the existence of amoebae, with and without pigment, as well as in the sporulation stage, ~~with or without pigment~~, in immense quantities, especially in the capillary vessels of the cerebral cortex.

II. HEMIPLEGIA.

Malarial hemiplegia is not uncommon. The onset may be gradual

or sudden, and may or may not be preceded by such sensory phenomena as numbness, tingling, or pain in the affected limbs. It is usually associated with some degree of mental change, as in hemiplegias from other causes, thr The percentage of recoveries without or with sequelae, appears, however, to be greater in hemiplegias of malarial origin than in that from other causes. They are often transient, without sequelae, and of short duration if treated early. Leri considers that this syndrome is much more common than realised and the malarial origin is often overlooked. He records 5 cases, 4 between the ages of 21 and 27, and the 5th, aged 48 years. There was no evidence of syphilis in any of them, the Wassermann reaction in each being negative. In one, it occurred during the first attack in the other four, malarial infection antedated it by several years and even from childhood. Aphasia was present in one of the cases; another is of special interest because of its long duration.

CASE V. Malarial Hemiplegia of long duration. (A. Leri).

An Algerian, aged 21, has had tingling and a cold feeling in the left side for a year, and difficulty in movements of the left limbs. Cannot give exact date of beginning of it. No ictus. Began in the leg and the trunk, then are during the last three months became involved.

Examination: Total left hemiparesis, but leg worst. He can walk, dropping the foot heavily, and control of leg very much reduced Control of arm much less so, but movements are diminished in range and force, though none are quite abolished. Lower half of left side of face, definitely, though slightly, involved. Tendon reflexes of the affected limbs are markedly exaggerated, with ankle and patellar clonus. Superficial reflexes weaker. Plantar reflexes on both sides negative. Marked diminution of sensation to pin-prick and pinching over whole left side, including face. No change in temperature or stereognostic sense. Slight amyotrophy of left thigh. Heart and aorta negative. No pain, headache, vertigo, or convulsions To lumbar puncture, no albumen, no leucocytes in C-S. F. He has had malarial attacks irregularly since childhood, and has had attacks while in hospital under observation. Case considered as cerebral cortex type of involvement of malarial origin.

CASE VI. Hemiplegia, with cranial nerve involvement. (Descomps and Quercy).

Man of 24 years, with hemiplegia with paralysis of the right 6th cranial nerve, and a paresis of the left 5th cranial nerve which came on suddenly in the course of a benign tertian attack. He had contracted ague in Macedonia 19 months previously, and was otherwise quite healthy. After 8 months, power had been regained almost completely in the limbs, but the condition of the cranial nerves remained almost completely unchanged. Examination of the C-S. F. at this time was negative.

CASE VII. Hemiplegic malignant infection. (Marchiafava and Bignami).

A middle-aged man, pale and very weak, is admitted to the Hospital of S. Spirito on Sept. 26th, 1889. He complains of pain in the head, but has no fever. Indeed the temperature is sub-normal and there is no enlargement of the spleen. A few hours after being put to bed he loses consciousness, and becomes hemiplegic with paralysis on the left side; there is also hemi-analgesia and effacement of the deep reflexes, —symptoms which were coexistent with the sub-normal temperature. A careful investigation as the cause of this state of things is made, and the examination of the blood shows the presence of immense numbers of endoglobular amoebae, the majority of them without pigment. The patient was treated with intravenous injections of quinine, and recovered after 2 days, remaining however very anaemic.

In this case, the maximum temperature in the rectum was 100·2° during the period of acute infection, in the night between the 25th and 26th Sept. Recovery was extremely rapid owing to the disappearance of the cerebral symptoms, which left no trace behind. With regard to the red blood corpuscles, the ratio sank on Sept. 26th to 1,950,000.

CASE VIII. Hemiplegia, with recovery. (J.S. Patterson).

Mrs. P., aged 65, was unusually well-preserved and active, and had a chill on the 12th June and another on the 14th June, on which latter day I saw her. She responded to treatment and was

afebrile on the 15th, but the next day at noon she had her third chill.

When seen at 4 p.m., the temperature was 103°F, pulse 90 and full. She was confused, her speech was thick and slurring, and by 8 p.m. she was profoundly comatose. There was complete flaccid paralysis of the right side of face and body, K.J's on the right side being exaggerated, breathing stertorous and 18 to the minute, pulse bounding and 74. The eyes were closed, pupils contracted, eyeballs deviated towards the left, rectal temperature was 104·2°F. A blood examination revealed malarial plasmodia. Quinine, grs vi, was given hypodermically every four hours. The following day the condition was practically the same, but by night the patient had recovered slightly from coma. Her paralysis gradually subsided and 48 hours after onset it had completely disappeared. The quinine was continued hypodermically for 4 weeks.

There were absolutely no sequelae. The case was one of cerebral malaria with rapid response to quinine.

CASE IX. Fatal case of coma, right hemiplegia, aphasia, meningeal haemorrhage. (Dumolard, Aubry, and Troland).

R.F., aged 36, trader. Entered hospital, Algiers, 26:7:97. Complaint of shivering, lassitude, of a few days duration. He looked very ill. Temperature, 39°. Typhoid fever first thought of; haematuria—red cells and leucocytes in the urine. Blood film shows malignant tertian parasites—one in every 10 red cells.

Quinine hypodermically, 25 cgms twice on the 26th. No change next day. Quinine continued as above on the 27th, 28th, 29th July. General condition better—no delirium. 30th. Temperature normal, no quinine. 31st, fever again, 50 cgms. quinine. Urine continues red.

1st Aug. Patient has right sided hemiplegia, and a total aphasia which occurred slowly during sleep. Eyes open, but he has a tendency to torpor. Since then, in spite of large doses of quinine (1·50 gm. per day in 3 doses), the condition of the patient got worse and he died comatose on the 3rd August.

At autopsy, a sub-meningeal haemorrhage, the size of a tangerine, was found pressing on the right Rolandic area.

In the organ and notably the brain, the capillaries were packed with parasites.

Authors regret not having used stronger doses of quinine.

In children, convulsions are generally associated with the hemiplegia as exemplified in the next two cases.

CASE X. Hemiplegia, and convulsions in an infant of 11 months (Spolverini).

10 hours after the beginning of an attack of fever in a girl of 11 months, generalised convulsions appeared and continued severely for three hours, less so for another hour. They left the child drowsy, with fever persistent but lower, and partial paralysis of the right arm and leg. On admission to hospital seven days later, this condition persisted; there were noted in addition a partial paralysis of the right facial muscles; pallor, yet with satisfactory nutrition; enlarged liver and spleen; exaggerated tendon reflexes; Babinski's sign on the right side; Oppenheim's and Kernig's being absent. Lumbar puncture and fluid reaction gave no diagnostic help. Sub-tertian parasites were found in the blood. Daily injections of 30 cgms. of hydrochloride of quinine led to slow recovery, although a trace of paresis remained 7 weeks later.

CASE XI. Convulsions and Hemiplegia. (Brosius).

Girl of 11, admitted to Hospital, 10:11:16. Temp. 38°C. which same evening rose to 39·8°. Fairly well developed, but under nourished and about normal size for her age. Laid on back, with head retracted, eyes rolling upwards, and could not be induced to speak, being in a state of semi-consciousness.

Health authorities of Panama first discovered this case and sent it into hospital. History of malaise, headache, chill and continued high fever of two days duration, was given on date of admission. The following day the patient took convulsions, paralysis of right side of body became evident, and she neither spoke nor took nourishment. Communication from any one arriving from the States was denied by the family. At time of onset of illness, patient was living in Panama, but she had moved into the City only on Aug. 25th, 1916, 16 days before onset of illness. She had several times been

stricken with prolonged and intermittent fever and chills.

On 2nd day of illness a blood smear was reported to contain crescents and ringed forms of aestivo-autumnal parasites. As much of her family history as could be obtained was negative. 7½ grs quinine hydrochlor. given intramuscularly. Physical examination of head, scalp, ears, mastoid, was negative. Eyes rolling upward, pupils equal and react to light, and were neither dilated nor contracted. Neck rigid, and patient uttered faint cry when attempt to flex was made. No gland enlargement present. Jaw not rigid. Teeth negative, but tongue coated. Skin clear, no jaundice, or discoloration. Lungs -ve, no cough. Heart -ve, pulse good. Abdomen -ve. Spleen not palpable. K.J's absent. Kernig +ve, left. Right arm and leg showed apparent absolute flaccid paralysis—not the slightest motion in either right limb, and when dropped each fell flaccidly as if paralysed. Face gave no signs of paralysis.

BLOOD: Crescents, a few ringed forms—tertian. Lumbar puncture Fluid, not under pressure, clear. Cells, 5 per c.mm. Pathological report -ve. 2 grs. of calomel given, followed by one and a half ounces Mag. Sulph. and quinine, grs. x., by mouth. Quinine, grs. iv-x, doses given daily for three days: after that, thrice daily until discharge.

Temperature became normal within 2 days, and paralysis disappeared. Chill seemed brighter. Limbs affected seemed weak. Afternoon of second day, two slight convulsions. Bromide given. Urine and stool negative.

Blood white cells, 12,800.	Reds. 4,240,000.
Polymorphonuclears.	70.
Lymphocytes, (Large and Small)	24·5.
Large mononuclears.	3·5.
Transitionals.	1·6.
Eosinophils.	0·0.
Mast Cells.	1·5.
Hb.	68·0%.

Sept. 13th, 1916. 3rd. Day in Hospital, temperature rose to 37·6 and remained at that during rest of time in hospital. As neck stiff, another lumbar puncture with -ve result. Right limbs improve.

Sept. 14th—Rapid improvement. Child brighter. Strength of paralysed normal now. No recurrence while in hospital.

CASE XII. Fatal case of crossed paralysis (Syndrome of Weber) with coma, and focal massing of parasites. (Dumolard, Aubry, and Frolard).

A young married woman, a Spaniard, was admitted to the Mustapha Hospital, Algiers, 26th Aug., 1911, accompanied by her husband. The two could speak only Spanish, but the following information was obtained. They arrived from Spain 3 or 4 months ago with their four children—the oldest 5 years of age, the youngest only a few months and on the breast. They went to work on a farm in Corsica, a country infested by malaria. The woman had never been ill, her pregnancies had been normal, and her children were all healthy. Since arrival in Corsica, she had had several attacks of fever, but it was impossible to get more precise information.

Examination of patient: Tall and vigorous looking, but with a look of premature age, perhaps the result of hardship, repeated pregnancies, and present lactation. Lies on the bed as if exhausted and asleep. Skin earthy. Conjunctiva pale, and slightly jaundiced; mucous membranes pale; temperature 38·6? pulse regular, full, and tension above normal.

Heart and lungs and digestive system negative; tongue furred; abdomen normal, except liver and spleen, both enlarged and tender.

Nervous system:-No signs of meningitis—No Kernig or stiff neck. It is difficult to fix the patients attention, but if questions are pressed upon her, she ultimately answers smartly and volubly, and then suddenly stops fatigued. She was put on a milk diet, and as numerous forms of plasmodia falciparum were found in the blood, four subcutaneous injections of 25 cgms. quinine were ordered daily at regular intervals. There was about one parasite to 5 red cells. No crescents seen.

Aug. 27th, patient comatose.—Almost completely so. Dorsal decubitus. The two left limbs when lifted fall heavily on the bed; much less so the two right. Paralysis of left lower half of the face—the patient puffing out the lips on that side of the face with

expiration; head and eyes deviated to the right; the eyes also a little turned up; pupils sluggish to light; the right pupil markedly dilated, with ptosis of the same side. Patellar reflexes diminished on both sides. Babinski +ve on left side. Right plantar reflex flexor.

Sensation almost completely absent. Strong irritation leads to slight retraction of the ~~left~~ right arm and leg; left arm and leg remain immobile.

Respiration Cheyne-Stokes, with long apnoea. Incontinence of urine without retention. No albuminuria. Temperature oscillates about 38·5°. Pulse regular and of good tension.

Authors consider the case a good example of the syndrome of Weber of malarial origin. C-S. F. normal: few lymphocytes of centrifugalisation, and no excess of albumen. Subcutaneous injections of 25 cgms. quinine continued, but coma persists and patient died at 2 a.m. 28th Aug.

AUTOPSY: Tissues pale, muscles decolourised. Spleen much enlarged; liver slightly enlarged. Kidneys oedematous, capsule adherent, and cortex pale and with punctiform haemorrhages. C-S. F. normal in ~~appearance~~ appearance and quantity; cortical cerebral vessels congested, but no haemorrhages. Sectioning of the brain, mesencephalon, cerebellum, and in particular the cerebral peduncles revealed not a trace of haemorrhage or softening. The brain tissue was firm and resistant, and showed only intense congestion. The capillaries in the regions of the cerebral peduncles and cerebellum were packed with parasites and pigment.

The authors consider this syndrome of Weber conditioned solely by the intense congestion and packing with malarial parasites and pigment of the capillaries of the protuberance, peduncles, and cerebellum.

Cases of bulbar paralysis are not very uncommon, and are recorded by Bevacqua, Granic, Russo, Bastianelli, Orlandi etc. An example of the type is given below.

CASE XIII. Malignant infection with cerebral and bulbar symptoms. (Marchiafava and Bignami).

S.F. was attacked by fever two days ago. Three days before entering hospital, he felt well, and spoke well ~~[illegible]~~ in a very

serious condition. Quinine given hypodermically, Aug. 29th, 1890.

On the morning of the 29th, the patient is very prostrate, almost in a lethargic state; he speaks with an exceedingly slow articulation, and replies to questions with great difficulty. There is well-marked paresis of the left facial nerve; tongue turned to the left; pupils alike; the muscular force of the two sides equal; there are no disturbances of the sensibility; reflexes superficial and deep normal; the bladder is very full. In the blood there are several plasmodia without pigment, some in brassy-red blood corpuscles: also many macrophagi. Hypodermic injections given of bimuriate of quinine, grs xxiv.

On Aug. 30th, at the morning visit, the dysarthria is found to be persisting, as well as the abnormal condition of the tongue; the sensorium is a little dull; bladder full and catheterization necessary: temperature sub-febrile. In the blood at 10 a.m., there is a very small number of plasmodia, with granules of pigment, and white blood corpuscles with masses of pigment. The urine contains traces of albumen.

On the 31st, the paresis of the facial and hypoglossal nerves persists, as well as the dysarthria; the voice is nasal, owing to paresis of the velum pendulum. The patient walks with a staggering gait; in the night he has passed urine spontaneously. Nothing abnormal, but pigmented white blood corpuscles found in the blood; there is now complete intermission.

Sept. 1st. Temperature, 101·5°. Bimuriate of quinine, grs. xvi, given hypodermically. In the blood there are only a few pigmented leucocytes.

On Sept. 2nd, the bulbar symptoms become aggravated again after another paroxysm of fever which supervened in the night. The patient passes urine unconsciously; the expression of the face is stupid, and he talks foolishly. There is nothing abnormal but a few pigmented phagocytes in the blood. After other injections of quinine a rapid improvement takes place, which becomes more pronounced on the following days, the patient continuing to take quinine, arsenic and iron. Up to the 5th day, pigmented leucocytes are still seen in the blood, but thenceforward none. The different nervous symptoms disappear successively, but the dysarthria persists,

being limited to an ~~imperfect articulation~~ imperfectly atticulated pronunciation. On Sept. 29th, the patient was lost sight of.

This was one case among others observed by us, where during the parasitic invasion cerebral symptoms (e.g. lethargy, dullness, etc.) are developed as well as bulbar ones, such as dysarthria, paresis of certain bulbar nerves, etc., and it is noticeable that these latter have the greater persistence; they disappear slowly and by degrees, many days after the actual infection has ceased.

III. APHASIA.

Aphasia due to malaria generally of the motor type has been recorded by numerous authors, oftenest with hemiplegia but not very infrequently occurring alone. In 12 cases of malarial hemiplegia Landouzy observed aphasia in 8. Many isolated cases and small groups of cases are recorded in the literature. Papastrategakis had two cases of right-sided hemiplegia with aphasia. The prognosis is generally good, if the treatment is begun early, effects may be transitory or permanent depending upon the degree and duration of the disease, etc. Rao and Rodenwald have recorded cases of this kind.

Mine has recorded six cases of isolated aphasia in soldiers in Formosa. They were aphasic for 11, 15, 21, 30, 36, and 42 days respectively. One began with coma, and had arm paresis; two had paretic diplegia; one had retention of urine; three had frequent vomiting during the malarial paroxysm. All the six knew what they wanted to say and could write it, but could not speak it. Family and personal histories were good. All had malarial parasites in the blood and all made a good recovery.

A case of this kind is recorded by Browne-Mason:

CASE XIV. Malignant tertian malaria, with temporary aphasia. (Browne-Mason).

The patient, a "syce" boy, aged 11, attached to "J" Battery, Royal Horse Artillery, was admitted to the Cantonment Hospital, Rawal Pindi, Sept. 16th, 1904. His father, who brought him to the hospital, said that the boy had been suffering from fever for the preceding three days, and that to his alarm during the previous night

he had suddenly become "be-hosh" (without reason), and had vomited a good many times since then.

On examination, the boy was found to be unconscious. His temperature was 100°F, and his pulse rapid and thready. The vomiting had ceased by this time, but he was very restless, and his condition rather recalled the irritation stage of concussion. His spleen was slightly enlarged, but physical examination revealed no other abnormality. Next morning temperature, 102°F. The restlessness had disappeared, and the unconsciousness deepened, his pupils reacted to light and both K.J's were normal. He was able to move all his limbs, and no ocular or facial paralysis could be detected. The organic reflexes were intact. A specimen of his blood was examined, and M.T. parasites found. The small signet ring form was very plentiful.

He remained without marked change for three days, when his temperature fell to normal. It was then noticed that he was unable to speak. He could understand what was said to him when he was vigorously roused, but quickly relapsed into an apathetic somnolent state. His sight was unaffected, and he had still no paralysis of facial or lingual muscles, and his reflexes were unaltered.

From this time his apathy gradually cleared off, and by the 11th day of his illness, he could sit up and understand when spoken to obeying simple commands in a perfectly intelligent manner, but he had no power of producing spoken speech. When he attempted to do so he pouted his lips, and gave a strong forced expiration, which only resulted in a voiceless whistling noise, at other times a faint voice sound was produced in the larynx, the lips then not being called into play at all. By this time, the ring forms had disappeared from his blood, but crescents were present. As convalescence proceeded, the power of speech quickly returned, and on the 18th day he was able to answer simple questions by monosyllables, and by the 25th he was running about and playing naturally. He was discharged cured on the 35th day. The treatment was on general lines, and directed against the malarial infection. He was seen again about 6 months after discharge, and was then perfectly well.

The interest of this case rests upon the aphasic complication. On consideration of the symptoms, it appears probable that of the

centres concerned that governing the production of spoken speech was the one principally if not solely affected. The apparent fullness of reception of speech was due only to the general condition. As the boy was illiterate, it was impossible to test his powers of writing or of understanding written speech. From the rapid onset, and gradual but complete subsidence of the symptoms, the lesion inducing the aphasia appears to have been plugging of the capillaries of Broca's convolution, by the malarial parasite, a view which is favoured by the large number of parasites present when the blood was first examined.

IV. PARALYSIS AGITANS.

Various other cerebral types are recorded—monoplegias of cortical origin, chorea, tremors, tetany, paralysis agitans (Boinet, etc) and Epilepsies (Parkinsonian syndrome (Chavigny, Conti), and cerebellar types, according to the part of the brain that happens to bear the burden of irritation or various degrees of tissue change. A variety of cases illustrating different syndromes are now given:

CASE IV. Paralysis agitans syndrome, following malaria. (Kinnier Wilson).

H.C., male, aged 38. Malaria in England, in 1918; blood tested at special malaria hospital (Connaught Hospital). A month later had "kicking" and twitching movements of the left side, which became less noticeable after May, 1919.

In Dec. 1919, had a weakness of left side and some slight stiffness of both hands. He began to stoop and have difficulty in turning over in bed. By May, 1920, his right leg was also stiff. Aug. 1920, tremor, chiefly of right hand, slowness of speech, and difficulty in opening mouth.

Examination: Slight weakness of left lower face. Spasm and rigidity of sterno-mastoid and trapezii. Tongue deviates to right. Mask-like face. Rigidity of trunk and proximal limb muscles. Pill-rolling tremor of hands.

Paralysis agitans attitude and gait, with festination and retropulsion.

V. CHOREA.

CASE XVI. Chorea or Dubini's Syndrome. (Bastianelli and Bignami).

M.P., aged 19, shoemaker. A brother died of tuberculosis, otherwise family history negative. Personal health and history good. Present illness began with intermittent fever on 23rd and 24th Sept., 1893. Admitted to hospital, 25th Sept:, fever continuous, with marked and regular remissions. General aspect of patient, character of the temperature, nervous symptoms and enlarged spleen, led the doctor to consider the case one of typhoid fever, and calomel was administered. There was irregularly intermittent fever for some weeks. On 12th Oct, 1·50 gms. quinine was given, followed by apyrexia. Next day temperature resumed, rising rarely above 38°, and maintaining an irregularly intermittent type. He became markedly anaemic, spleen increased in size, and localised nervous phenomena appeared. Muscles of face, eyes and shoulders began to twitch, and the patient became progressively weaker. By 18th Oct. the spleen was 5 fingerbreaths below costal margin, there was very marked anaemia and weakness, and enteritis with diarrhoea (bile stained), and weak low-tension pulse. The patient complained of headache, uneasiness, he is agitated, shouts from time to time, cries, talks incoherently. Muscles of neck and shoulders continually agitated by clonic evanescent spasms, which sometimes spread to arm muscles, and to whole body. These spasms predominate on the right half of the body. There is irregular nystagmus, horizontal, vertical and oblique by turns, brusque and evanescent. These clonic eye movements are not always symmetrical or synchronous as in ordinary nystagmus. There is sometimes during accommodation a marked converging strabismus, and the eye movements are often associated with clonic shakes of the head and with winking. The pupils are dilated, and react little to light. Superficial reflexes brisk: deep reflexes exaggerated. Ankle clonus present. Blood examination shows malignant tertian parasites, many macrocytes, and a few poikylocytes. No pigmented leucocytes. 2 gms. of bisuriate of quinine were injected.

19th Oct. No change. Tempt. 39·6°. On protrusion of tongue,

it is deviated to the right, and shows convulsive clonic movements. Muscles of face and lips move similarly. Opthalmoscopic examination quite negative. A very few parasites found in the blood to-day. Marked pallor of reins, which number 1,640,000 per c.mm. Urine contains no albumen or sugar. Ehrlich's diazo reaction negative. Diarrhoea continues. 1 gm. quinine given. Tempt. normal on night of the 20th, and continues so.

General condition maintained, profound weakness, little nourishment taken, frequent vomiting. Muscles which twitched before do so now mostly on purposive movement. Speech difficult to understand because of dysarthria. By 24th. Oct., appetite has improved, and vomiting has ceased, and he seems less anaemic; but mental state no better; he complains continually, is incoherent, has hallucinations, speaks of and to persons not present. Choreiform movements continue.

On the 25th, restless, agitated, crying and shouting constantly, requiring morphia. Temperature normal till 26th, when it rises to 37·6°. Normal on 28th, after quinine. No parasites found in the blood on 25th and 26th Oct.

Blood restoration continues rapidly, but nervous symptoms not modified. A progressive emaciation of muscles of neck, shoulders, and trunk, becomes apparent, so much so that the patient cannot sit up or even lift his head off the pillow. In the last days of Oct., the patient had some epileptiform attacks, without notable sequelae. Consciousness restored after each attack.

On 31st, temperature goes up to 39·5°, but ceases after quinine. General condition improves slowly during apyrexial period. On Novr. 2nd, able to sit on edge of bed, but clonic movements of muscles of face, neck, and shoulders very frequent, and persist even during sleep. Headache abates. Iron and arsenic given.

Febrile relapse Novr. 5th. A few parasites found in the blood. Quinine injected. All the nervous symptoms, including agitation and vomiting, exaggerated during the few days of fever, thereafter improvement resumes.

By Decr. marked improvement, so that patient can walk a little. Marked diminution of galvanic and faradic reactions, without qualitative changes of excitability. Muscles still markedly atroph-

ied. Shortly before leaving hospital on 12/1/94, he is fatter in body and face, only muscles of legs rather thin. Walks well, but weak and cannot run. If he tries to run, he gets tired at once, and tends to fall. He fell once in this way; said his legs suidenly gave way. There is tremor of hands and arms, increasing with voluntary movement. No tremor of individual fingers; convulsive movements of eyelids have ceased; frequent winking on holding eyelids shut. No alteration of eye movements.

Clonus of muscles of face and other parts has ceased. Superficial reflexes normal; deep reflexes brisk; no ankle clonus. Appetite good; bowel and bladder normal. Spleen still enlarged. Heart normal in size, sounds short and sharp, pulse 103.

Here then we have a patient admitted to hospital with signs of a grave infection which was not diagnosed at first; fever at first continuous, then irregularly intermittent or remittent and lasting about twenty days, and accompanied by vomiting, diarrhoea, enlarged spleen, sensory disturbances and collapse. During the fever there is progressive, severe anaemia, muscles spasms of face, eyes and shoulders, which persist during apyrexial periods in less degree. There is profound general weakness, and atrophy of the twitching muscles in particular, with diminished galvanic and faradic excitability; mental confusion, excitement, hallucinations, epileptiform attacks; malignant tertian parasites found in the blood on several occasions, not found on other occasions during the course of the illness. Quinine treatment results in cure after a fully three months illness.

Authors draw attention to several points,—namely that cerebral symptoms persisted much longer than the fever; that they persisted for several weeks after the complete disappearance of parasites from the peripheral blood. They consider the condition due to massing of malarial parasites in the cerebral vessels supplying the centres controlling the parts involved producing local motor irritation, and producing clinically a form of chorea or syndrome of Dubini.

VI. EPILEPSY.

The occurrence of fits in malarial subjects is not uncommon. Most observers record convulsions or fits associated with acute malarial attacks, where meningitis, delirium, coma occur, or in those with gross cerebral lesions as a result of malaria. Convulsions is one of the commonest manifestations of malaria in children, and occasionally epileptic fits persist in malarial subjects at long or short intervals, after the more acute phase has passed. These fits may be coincident with exacerbations of ~~mala~~ malaria, either in frank acute form, or in latent form without rise of temperature above normal.

Laveran cites malaria as a cause of epilepsy.

Boinet states that he has seen in 1887 and 1888 at Tonkin many patients die rapidly in epileptiform convulsions simply due to malaria. In one case, the convulsive movements affected mainly the arms. He was informed by the Military Veterinary Surgeons there that many of their horses died similarly after infection with malaria.

Goodall states that in Macedonia~~and~~ malaria, which was specially severe during the War, due to multiple infection, epilepsy among the troops was not uncommon.

Marandon de Montyel, during his medical direction of the asylum at Marseilles, was struck with the large number of malarials admitted ~~was~~ from the highly malarious countries, Algeria and Corsica, and he has consequently had plenty of opportunity of studying the effect of malaria upon the nervous system. He records 14 cases of epilepsy who have had malaria which has to all appearance in his opinion had a deleterious effect upon them. 5 of these were cases of ~~benign epilepsy~~ slight attacks at long intervals without much intellectual inhibition, and which were considerably aggravated by their subsequent malarial infection. 3 were cases which led to a recurrence of epilepsy, which had been absent for several years; one after three years interval with first attack; one after sixteen years interval, and one after seven years with third attack, and remained so after cure of malaria.

6 were cases in which malaria instituted the epilepsy. In 2

of these it was the sole apparent cause. The first of these two became epileptic after his second attack of malaria, and the fits recurred only during the paroxysms of malaria. The second case had malaria for several years, and developed epileptic fits, both during and in the intervals between malarial attacks. The fits with the attacks were the more violent. A third remained epileptic, and even became delirious with it, after cure of his malaria. His delirium had the features of an alcoholic delirium, though there was every reason to believe he had not been a drinker. The next three cases were predisposed to epilepsy by being drinkers.

He has never seen cure of the malaria in an epileptic subject lead to cure of the epilepsy. In all the 14 cases, the epilepsy persisted after the malaria was cured. Those that continued to have malaria had the majority of their attacks between the malarial paroxysms, though those that they had during the paroxysms were more severe. He concludes therefore that malaria is capable of accentuating epilepsy in those who suffer from it; of reviving it in those in whom it had apparently died out; and in producing it in those who have never had it, though they may have had some previous disposition to it.

From the pathology it is to be expected that cases of this kind should arise, from meningeal irritation, focal brain irritation, small or large haemorrhages with defective absorption or organization of clot, and so on.

Van Driel records a case of Jacksonian epilepsy which developed in a sailor aged 22 after he had had malaria for six months. He had Jacksonian fits with aura of rt. half of neck and mouth. Malignant tertian parasites were found in the blood. During course of an Nocht case he had mild epileptic attacks with rt. facial and rt. arm paresthesia. There was no familial or previous personal epilepsy, no syphilis, traumatism; eyes and ears and urine were normal. Hb., 70%. The condition cleared up on quinine and change of climate.

The writer has seen two cases of epilepsy occurring after malarial infection: one a young man aged 24, the other in a man of 51 which latter case is here detailed.

CASE XVII. Epilepsy following malaria.

K.G., sniper, aged 51. A fitter in civil life.

History: Finished colour service in 1902 having served 12 years. Had no disability pension on his discharge. Served in India, South Africa and Egypt. Joined up again, Oct. 1914. Was working about 5 years with the same firm before joining up, and never had a day off. Went to France, Sept., 1915, where he got slight flesh wound in wrist. Went to Salonica, 17th April 1917, after having spent a year at home, with wound of wrist and left index finger. Had no trouble until June, 1917, when he got " a touch of the sun", and was semi-conscious for three days, and was transferred to Malta. While there his epilepsy began. He was making trenches at the time of this seizure under fire from aeroplanes, but was never hit.

20:6:21. Complains of occasional attacks of malaria, which recur about once a fortnight. Has two or three fits a week. Constipated. Headaches. Had a fit during the week associated with emotion, discussing daughter who has left for New Zealand to get married. Passed urine during the fit.

27:6:21. Heart and lungs normal. Psoriasis. Inclined to adiposity. No anaemia. K.J's active. Superficial abdominal reflexes present. Pupils equal, regular, and react normally to light and accomodation. No nystagmus. No Rombergism. Spleen not palpable. Pyorrhoea and dental caries. Blood Wassermann -ve.

11:7:21. Had a fit while looking at his father-in-law, who was trembling having taken an apoplectic shock.

18:7:21. No further fits, but frequent restless turns, especially at night during his sleep.

25:7:21. Had a very bad week. Rigors, temp. 103°F. Has malarial look. Evidence of haemolysis—semi-jaundiced appearance. Spleen not palpable.

1:8:21. Occasional headaches. No fits or rigors.

15:8:21. Had a bad week. Had all teeth removed, but no fits or rigors.

12:9:21. Has had a great deal of worry. Father-in-law died: daughter died of meningitis. Not feeling well, but looks fairly well.

19:9:21. Has had considerable worry during week combined with attack of malaria. Tempt., 104·2°. No spleen friction, or palpable enlargement. Haemolytic appearance.

26:9:21. Has done very well on quinine during past week. Pulse 84.

24:10:21. Improving as regards fits, but severe headaches and sickness at times—vomiting after meals. Anorexia.

31:10:21. Had one mild attack of malaria. Slight tachycardia. No anaemia. After malarial attacks, a rash appears on his chin which prevents his shaving.

14:11:21. Dropped on the street two days ago, and has been troubled with giddiness every day since. On recovery from the attacks, he had a severe epistaxis for about 10 minutes, and pain about the heart. No conscious malarial attacks for over two weeks. Always giddy when he gets up in the morning, and cannot eat his breakfast. Pulse 84, regular.

21:11:21. Had a fairly good week, apart from headaches at intervals.

28:11:21. Malarial attack, tempt. 102°F.

5:12:21. Headaches for past six days.

30:12:21. Headaches at intervals and sleepless, but no fits.

6:1:22. Malarial attack two days ago. No fits, but fainted getting out of bed. Pulse 84.

26:1:22. Having what he considers a malarial attack about once a month—shivering, tremors, followed by sweating.

19:2:22. Spleen friction well-marked to-day. Says he had a febrile attack five days ago. Blood films taken in which a few benign tertian parasites were found. Blood pressure 125/70. Urine normal.

This patient steadily improved on quinine, grs x., t.i.d., until he was having no more malarial attacks, but when last heard of a year after treatment by the writer was still not quite free of his epileptic fits.

VII. TETANUS.

Cases resembling tetanus have not infrequently been observed. Castellani has seen one in Macedonia, and three in the Tropics. The

first had a normal temperature, trismus, opisthotonus, and typical tetanic spasms. In all the cases the blood contained malarial parasites, and intensive quinine treatment cured. He also describes a case resembling hydrophobia. He says "I was once called by a Ceylonese colleague near Colombo to see a case which had been diagnosed as hydrophobia. At the time I saw the patient, he was in a maniacal condition, temperature, 102°F. At the mere sight of water, a severe spasm of the larynx occurred. As he had a large spleen, I examined his blood with my portable microscope—it was teeming with parasites. Quinine, grs. xv, given by intramuscular injection in each gluteal region, caused all the symptoms of hydrophobia to disappear in a few hours. It may have been a case of hysterical hydrophobia syndrome in a malarial patient, though the man was not of neurotic tendency, and no hysterical stigmata were present."

CASE XVIII. Cerebral malaria of tetanic form. (Goodall).

A Serb was admitted unconscious to hospital on 21st Sept. He had been diagnosed as a case of tetanus, in a French field ambulance, and had received an injection of 20 gms. of anti-tetanic serum. No further history was available. The temperature was 104·6°F. No wound could be found. The patient was taking fits of opisthotonus every few minutes, and minor convulsions which chiefly affected the left arm and leg. Between the fits, there was complete muscular relaxation. The muscles of the jaw were not specially involved, and external stimuli had no effect on determining convulsions. For these reasons the fits were thought to be malarial, rather than due to tetanus. Moreover, the spleen was palpable, and the blood contained numerous malignant tertian parasites. The pulse was miserably poor, so that it was thought unsafe to give an intravenous injection. We gave an intramuscular injection of 20 grs quinine. At 8 p.m., the pulse seemed stronger, and we decided to give an intravenous injection of 20 grs. in a pint of saline solution. By 11 p.m., the spasm had stopped, but the pulse was still very poor. At 3 a.m. next morning the temperature had risen to 107°F, and at ~~the~~ 3.30 a.m. there was another severe convulsion. Patient was sponged with

tepid water. By 5 a.m., the temperature had fallen to 104·5°F, but the pulse was almost imperceptible. The usual stimulants were employed, but death took place an hour later.

(Cf. case with coma and trismus, Marchiafava and Bignami, under Coma Section).

VIII. TETANY.

CASE XIX. Malaria, masked with tetany. (Hebert and Bloch).

5:10:19. Called to see a Russian aged 41, who after a vapour bath, followed by a prolonged and very cold douch, was unable to get warm. He had felt seedy and thought the bath would help him. Tempt. 39°C.

Skin congested, conjunctivae sub-icteric, tongue coated, breath foetid. Constipation recent, abdomen showed meteorism, liver enlarged and tender. Spleen not palpable. He looked anxious enough to draw our attention. Nothing abnormal noted in circulatory or nervous systems. Next day, stool normal, urine diminished, sleepless and anxious looking.

7:10:19. Generalised violent trembling, so that it took several people to keep him on his bed. Not true convulsions, but exaggerated choreal movements. Teeth chattered and in rare moments, when able to speak, he complained of a horrible feeling of intense cold, which added to the discomfort of already painful extremities. Presently the hands became flexed on the wrists, making a hollow in which rested the thumb, simulating accoucheur's hand. Legs flexed, feet extended, toes flexed. This condition lasted several hours, with short remissions when the contractures relaxed. Tempt. 40°C. Tendon reflexes normal. Left pupil dilated and sluggish to light. 6 p.m., same day, profuse sweating and temperature normal. Only then was the patient able to give an account of himself.

He had perfect health till the age of 21. At this age, in summer, he had a similar attack immediately after a cold bath. In the 10 succeeding years, he had similar attacks each year, sometimes several times a day, and he was emphatic on the point that they were always immediately preceded by malaise or coryza or sore throat or gastric disturbance or coldness. He said that the feel-

ing of malaise was a constant accompaniment whatever the cause, and that it occurred if his temperature got down to 38°C or thereabout, and that the attacks always ended up with sweating. He had been attended by the principal Moscow physicians, and the unanimous diagnosis was tetany.

For the 10 years preceding the present attack, he had had none.

Next day, patient was very weak. Had not slept. Urine only 200 gms. in 24 hours. Trace albumen. Hot drinks, diuretics, enemata, dry cupping. Blood urea, 0·65 gms. Soriet-Wassermann,-ve.

9th Oct., exactly 48 hours after first attack, a dramatic repetition of it. When it abated there was a marked paresis of the left leg, with diminution of left Achilles reflex. Dilatation of the left pupil diminished. Complaint of severe pain in upper left hypochondrium, at level of splenic flexure of transverse colon. Spleen not palpable. No apparent intestinal disturbance.

11th, 13th, and 15th about the same time each day, attacks exactly similar to the first, with the same contracture of extremities. General condition became grave. Urine scanty, sweating increasingly abundant. Pain in left hypochondrium continued, without evidence of any bowel disturbance as it acted normally, and without palpable spleen, or any abnormal signs referable to lung, pleura, or left kidney.

15:10:20. Blood examined at different times of the day and numerous plasmodia vivax found. 2 gms. quinine daily for two days, then 0·20 and 0·30 gms. cacodylate of soda the next two days given. Effect on patient remarkable. Paresis of left leg disappeared within a week, and Achilles reflex became normal. Memory defective—he had no recollection of what had been happening. During convalescence he could not remember a person with whom he had discussed important business several days before the first (recent) attack. Spleen has not been palpable, which has contributed to obscure the diagnosis, but the persistent pain in that region leads one to think that it was involved.

Authors then discuss possibilities. Tetany may be this man's reaction to diverse conditions, colic, angina, gastric disturbance,

In February, 1919, he visited Sweden, then Bakou in July, when mosquitoes were plentiful and malaria prevalent. He was freely bitten, and arrived in apparent good health in France in Sept. After the cold douche, he developed tetany as he had done long before.

Was this anaphylactic shock in a malarial subject, precipitated by cold, and expressing itself clinically as tetany? Or had he had malaria from early youth, and did he react in this way to each malarial attack? (Note malaise and sweating accompanying).

The good general condition, impalpable spleen, normal size of liver, relative rarity of the attacks, are not in favour of this last hypothesis, though it cannot be excluded with certainty. This particular reaction seemed to be peculiar to this patient.

As indicated in the chapter on latent malaria, it is quite consistent with the habit of the malaria parasite to remain dormant for long periods and to cause infrequent disturbances over a long period of time as occurred between the ages of 21 and 30 in this case. Moreover, a normal size of liver, an impalpable spleen, and infrequency of attacks, are all quite consistent with the presence of the parasite.

The authors do not note whether there was any evidence of splenic friction, which is a much more reliable evidence of spleen disturbance than any increase in size that can be felt. The spleen is much more often impalpable than palpable in chronic malaria infections, in the experience of the writer.

There is no note as to the evidences or otherwise of sub-thyroidism. Thyroid, with parathyroid insufficiency may have played a part in this syndrome as a result of malarial infection. On the other hand, the leg paresis with sensory defect suggests that the whole condition may very well have been another example of cerebral malaria.

IX. CEREBELLAR SYNDROMES.

Involvement of the cerebellum by malaria is perhaps not very common, but instances are recorded in the literature by Bevacqua, Grande, Russo, Forli, Finocchi, Constantinesco, Pecori, Pansini,

d'Alloco, Castellani, and others. It may be involved alone or in conjunction with other parts of the brain, so that there are clinical variations of the cerebellar syndrome. There are such symptoms as giddiness, irregular gait, lack of co-ordination of movement, somnolence, and disturbances of speech.

Papastrategakis records a Salonica case of a man of 20 years old who entered hospital with diagnosis of tumour of the cerebellum, 25 days at most after ordinary malarial paroxysms. Dizziness, loss of power of lower limbs, and speech difficulty were the first symptoms, and were thought to have no connection with malaria. On admission there was no fever. Symptoms continued. Motor disturbance, due to lack of co-ordination of muscles, therefore could not write or walk. Extreme somnolence and some affection of sight. Opthalmoscopic examination negative. Characteristic speech disturbance. Facial nerves and ears normal. Increase of skin and tendon reflexes, without Babinski's sign. Muscular power normal. No irregular movements or psychic disturbance. C-S. F. almost normal. Constipation and slightly increased urinary chlorides, in spite of milk diet. Pulse 80. No nutrition disturbance. Blood showed decrease in white corpuscles, and many plasmodia falciparum. Cure by quinine and arsenic, and he left hospital two and a half months after entering it.

He holds that symptoms are sometimes slight, exhibiting slight weakness of lower limbs from inco-ordination, vomiting, giddiness, slight dysarthria, and lack of coordination in the limbs generally, maybe. The patient walks like a drunk man, sometimes only giddiness is complained of. The cause of the cerebellar syndrome is toxic change or irritation of the cerebellum or packing of cerebellar vessels with parasites etc, and the picture is often very like one of alcoholic poisoning.

Castellani has seen several cerebellar syndrome cases, and says that they are not very rare. He reports one seen in Skopolje, case of a man about 30 who came for treatment with symptoms of cerebellar tumour. He was ataxic, walking like a drunken man; he complained of severe headache, vomiting, and almost complete loss of vision. His temperature was normal, and he did not give any history of fever. Spleen and liver not enlarged; the blood showed

numerous crescents. All the symptoms disappeared after an energetic quinine treatment. He has also seen cases suggesting tumour of the cerebrum.

Cases reported by Arena and Constantinesco are given in more detail:

CASE XX. Cerebellar Malaria. (Arena).

Youth, aged 17, single. Father alive and well: not neuropathic nor luetic. Mother died of post-partum haemorrhage, and was no relation of the father. She was not nervous. Had 14 pregnancies. Two miscarriages due to endometritis. Four died of gastro-enteritis: 7 alive and well. No history of tuberculosis or neurosis in either family.

The patient had been well until this illness. No rheumatism, venereal disease, syphilis, alcoholism. The father said the boy had been upset by the death of a brother and his mother within a year of one another. After that, he was easily excited.

In Oct. 1911, the boy was in a malarious region, and took his first attack of malaria. He had been shivering with rise of temperature for 8 days, which was stopped with quinine. He was prostrated and complained of headache. An ice-bag was applied to his head. When the tempt. was normal, he felt all right again. It recurred, however, at intervals, but was stopped by quinine. Each time, and up till March, 1912, his only complaints were the fever, shivering, headaches, and prostration during the febrile periods. Early in March, 1912, however, he had high fever associated for the first time with vertigo, sickness and vomiting, while confined to bed and exhibiting no signs of gastro-intestinal disturbance. He was treated with quinine and ice to the head.

His father reported that after this attack, he had shaking of the eyes, and eyelids, and slight tremor of limbs and head. Early in April, slight nystagmus was still present.

One day, without any special reason, he complained much of headache, vertigo, sickness and vomiting, while there was no fever. After a few days these features increased until he became unable to flex his head on his body, or to flex his body on his limbs. With ice on his head, this improved so that he wished to get up, but he

could not walk, because of tremors and a tendency to fall forward. He had his eyes fixed on the ground.

When medically examined early in April, general tremors were present which disappeared during sleep. No mental or speech troubles. Memory and intelligence normal. Father stated he had become excitable and emotional. In May, 1912, he was taken into hospital. He was anaemic, poorly nourished, and his spleen was two fingerbreadths below the costal margin. Liver normal. There were general tremors, especially of eyes and limbs. Head tended to be bent forward. Tremors more evident in left arm, and more evident in arms than legs. No accentuation of tremor during intentional movement. No volitional control of the tremors, which was worst when limbs were extended. Eye tremor more than ordinary nystagmus; there were incoordinate convulsive movements of globes of eyes. Pupils oscillate also; eyelid tremor; tongue tremor slight. No tremor of speech.

The patient cannot stand quiet, and is not able to walk well. With feet together he tends to fall forward. With legs apart he can stand steady, without movements tending to follow any one direction. He walks like a drunk person, tending to fall forward. Limb movements and sensation normal. No ataxia. K.J's exaggerated. Plantar reflexes flexor (No Babinski). Reflexes more active, and tremors also more active on the left side than the right. Special senses normal. Sphincters normal. During examination, he was emotionally unstable; no headache or rise of temperature. Electrical examination about normal, and strength about normal.

Blood Examination: Reds: 3,300,000.

Whites:	5,000.
Hb.	85.
Polymorphonucl.	55.
Lymphocytes.	30.
Large Mononucl.	8.
Transitionals.	4-6.
Eosinophils.	2.
Mast Cells.	0-2%

Malignant tertian (semi-lunar) parasites found in the blood.

Urine normal. Blood Wassermann -ve.

Treatment: Consisted of subcutaneous injections of quinine, 2 gms. each day for 3 days, then 1 gm. daily for 4 days. For the next seven days, iron, arsenic, phosphorus and cinchona. This process was repeated three times. There was marked general improvement, but tremors and nystagmus persisted; no parasites found in the blood. After two months, all symptoms had disappeared except slight nystagmus.

The author considered this a case of malarial involvement of the cerebellum, in the form of punctiform haemorrhages, deposits of pigment, or most likely capillary thrombosis as circulatory anastomosis is not so good as in the cerebral cortex.

CASE XXI. Cerebellar Malaria. (Constantinesco).

Army surgeon, admitted to hospital, 6th Sept., 1920. First attack of malaria, 23rd. Aug., with recurrence two days after. Subsequent to that, no fever, but felt weak. Had giddiness and some speech trouble. On Sept. 1st, very giddy, and without loss of consciousness, he fell. He got up, but was not able to walk or to stand upright. He moved like a drunk man. 1 gm. per day of quinine given.

General Condition: Well-developed. Face pale and relaxed. He has difficulty in pronouncing words, and makes exaggerated movements of the muscles of the face. Words are broken into syllables, and produced in a monotone. The dysarthria is characterised by a soft scanning quality, and is a little explosive. There is some difficulty in whistling and in blowing. Nystagmus during lateral view. In bed, movements complete. Muscle force conserved on both sides. Tremors of arms when extended, or when lifting objects to the mouth. Overaction and inco-ordination present. Writing impossible, and adiadococinesis marked. Asynergia. Falls to one side if he attempts to sit up in bed. Walking is laborious, and movements isolated and irregular. He falls to one side if left to himself. Complains of giddiness. Closure of the eyes does not augment the trouble. Deep reflexes exaggerated. Ankle clonus present. Babinski -ve. No sensory troubles, superficial or deep. Barany's labyrinth test negative. Resistance to Voltaic vertigo normal. Spleen enlarged. Lumbar puncture negative. No parasites

found in the blood.

Condition stationary for six days, and eased off steadily and rapidly thereafter. On 15th Oct., 40 days after admission to hospital, he was pretty clear of symptoms, except slight hesitation in turning on his feet, and nystagmus lateral slight, reflexes exaggerated, and dysarthria. By Novr., the dysarthria was much better. By spleen puncture, plasmodia praecox were found. 2 gms. of quinine per day were given from date of admission. The temperature was irregular and moderate during the first two weeks. After spleen puncture, intravenous quinine was given, 1 gm. per day.

6th. Dec., tempt. 40°C., and up next day. Pallor, atony of face. Four spinal punctures: 10-12 leucocytes per field. Blood and C-S.F. Wassermann -ve. Nonne-Apelt reaction -ve. Recovered, but his dysarthria persists for four months after onset.

N.B. This case incidentally illustrates the difficulty in finding the parasite sometimes.

X. TREMORS.

Tremors are not uncommon in malarial subjects and many writers have dealt with them in the literature, including de Brun, A. James, Spagnolio, Fornaca, Martelli, and others.

Tremors of the limbs are most frequent, generally the upper limbs, but fingers, thorax, head, tongue and jaw may be involved. The commonest form is clonic movement of fingers, hands, wrists, maybe flexion and extension, may be pronation and supination, by turns. These movements occur with the limbs in the resting state, and tend to be intensified with intentional movement. They are generally symmetrical, but may be more accentuated on one side. Physical and intellectual efforts, or emotional disturbance, tends to aggravate them. They tend to increase during the day or two preceding an attack of fever, and to diminish after the attack. It is not uncommon to see an attack of violent trembling without apparent cause, lasting for weeks, and then disappearing. These cases have been studied apart from the taking of quinine, the effect of which has been definitely excluded in these considerations (de Brun).

Two cases of Martelli exemplify this:

CASES XIII, XIIII. Malarial Tremor. (Bartelli).

Patients were two brothers, aged respectively 8 and 4 years. The elder child, in characteristic attitude, had head retracted towards left shoulder, while right arm was flexed at elbow and pronated, with fist clenched. Left arm was similarly affected to a less degree. Both arms were agitated by a constant tremor, which persisted during sleep, and was exaggerated by an attempt to grasp anything. Aestivo-autumnal parasites were found in the blood. After 4 gms. doses of quinine by mouth and by injection, the symptoms began to diminish on the 4th day, and had completely disappeared on the 10th.

The younger child was admitted to hospital on the same date, Oct 4th, 1915, and presented the same signs in slighter degree. It had already received a few doses of quinine and the symptoms consequently began to diminish on the day after admission. Parasites of the same type were in the blood. A similar treatment was adopted, and the child left the hospital quite cured, along with brother on the 23rd. of the month.

The mother of the children was in hospital under treatment for the same kind of fever.

Fornaca records a case of a peasant aged 52, without syphilitic alcoholic, or hereditary taint, who had irregular tremor of the arm, aggravated by purposive movement. Tremor began during the febrile malarial attacks, and eased off during the apyrexial periods. Tertian parasites were found in the blood. After 4 gms. quinine, the tremor was much less, after 10 gms. and mist. baccelli, it disappeared.

CASE XIIV. Rhythmic tremors of lower jaw, caused by malaria. (G. Spagnolio).

Woman, aged 59, taken with aestivo-autumnal fever in Oct. 1913, which lasted, in spite of treatment, throughout the following winter.

In Dec., there appeared rhythmical tremor of the lower jaw, which persisted even in the intervals between the attacks of fever. The tremor was involuntary, and rhythmical, at the rate of 3-5

oscillations a second, and continued for a period varying from a few seconds up to a minute. It increased in severity when any attempt was made to check it voluntary with the mouth open, but when the mouth was strongly closed, it diminished considerably. Blood showed crescents.

By assiduous use of quinine, the malarial infection was considerably reduced in intensity, and simultaneously the tremor diminished in amount. She ceased attendance, so that the ultimate result is not known. The author considers malaria the cause.

It would appear, then, that any and every syndrome that can be produced by irritative or destructive lesions of the brain and its coverings can arise in the course of malarial infection, and that these may occur in almost any combination and degree compatible with the life of the subject. The same applies to the rest of the nervous system as we shall presently see.

That this clinical range of symptomatology is compatible with malarial pathology is easily realised by a study of the chapter on that subject, or of any of the leading works on tropical disease dealing with it.

It is hoped that sufficient representative examples have been drawn from the literature to make the range of the vulnerability of the nervous system by this insidious enemy, clear.

CHAPTER XXIV

Malarial cerebro-spinal syndromes.

While of the somatic nervous system as a whole, the brain shows most frequently damage due to malaria, syndromes involving both brain and spinal cord are not very infrequent.

Post-mortem observations on the spinal cord in malarial subjects showing evidence of damage there, have not been as plentiful as have been similar observations on the brain, but enough has been done to make it clear that the cord comes within the range of the parasite—which part of the subject will be more fully discussed in the next section.

According to the literature, the cerebro-spinal syndrome associated etiologically most commonly with malaria appears to be that of disseminated sclerosis.

Some representative types are chosen from the literature as follows.

1. DISSEMINATED SCLEROSIS.

Instances of this are recorded by many observers—the first authentic cases apparently being reported by Torti and Angelini, and subsequently cases by Canellis, Boinet, Salebert, Sacquépée, Dopter, Marchiafava, Bignami, Bastianelli, Spiller, Triantaphyllides, Papastrategakis, Castellani, and others.

Castellani reports having seen four cases—scanning speech, intentional tremor, nystagmus, spastic gait, increased reflexes; all four cases were cured by quinine.

The syndrome may be complete or incomplete. Torti and Angelini distinguish three forms in their experience:

1. Cases in which symptoms are transitory, and are present only during attack of malarial fever.

2. Cases in which symptoms appear after the fever, and are of varied duration.

3. Cases in which the symptoms appeared suddenly without any fever—in larvated malaria.

Papastrategakis observed two cases—in one there was spasmodic

paraplegy, characteristic tremor of upper extremities ~~including~~ during voluntary movement, disturbance in walking, somnolence, distrubance of speech. In the other case, there was simple spasmodic paraplegy with slight tremor of upper extremities. Both of these cases were young soldiers, 20 years of age, after repeated malarial paroxysms with malarial parasites in the blood, without fever, and both cured by quinine alone.

Two cases by Torti and Angelini, and one by Marchiafava and Bignami will illustrate the syndrome.

CASE: Chronic malaria, with symptoms resembling disseminated sclerosis. (Torti and Agelini).

The patients were both young men, aged 21 and 22, subjects of chronic malaria which had up to that time run an ordinary course and had been relieved by the use of quinine. The further development of the cases was, however, as follows:

The first case presented on admission the usual symptoms of ague with high temperature. Under the influence of quinine, the symptoms apparently disappeared, but on the 5th day, there occurred severe vertigo with vomiting, which rendered it impossible to retain food. Quinine was then given subcutaneously, but the disturbance persisted for a long time. Soon after a fresh attack occurred, with symptoms as follows:

Speech slow, indistinct, and scanning, with great difficulty in pronouncing labials and linguals, lower extremities so weak that the patient could not stand without assistance; gait ataxic, with tendency to fall forwards; exaggeration of tendon rrflexes, tremor on voluntary movements; pupils sluggish, with slight nystagmus; sensation unimpaired, pulse extremely weak and slow, spleen enlarged.

Large doses were given, both into the veins and also hypodermically; symptoms, however, did not begin to abate until after several days. Examination by the opthalmoscope showed pallor of the discs especially on the right side, with haemorrhages along the course of the veins. Examination of the blood revealed also numerous malarial parasites. After a prolonged course of quinine and arsenic, the patient gradually recovered, and a month from the commencement was able to leave hospital, the only symptoms then

remaining being weakness, and a certain hesitation in the speech. During the whole attack, temperature had been nearly normal, with total absence of febrile symptoms. After about a week, the patient returned with a second similar attack, this time with marked elevation of temperature. Recovery took place slowly from this, under the free use of quinine and arsenic, and as far as is known, remained permanent. It should be mentioned that there was no previous history of specific disease, alcoholism, or of anything which could give a clue to the unusual course of the attack.

In the second case, the diagnosis was at first very doubtful, there being none of the ordinary symptoms of malaria. The patient complained vertigo, and inability to stand without help. His speech was scanning, and indistinct; special senses unaffected; gait was ataxic, and there were tremors of the upper limbs on purposive movement; reflexes were exaggerated, but sensation remained unaffected. The diagnosis was only made on discovering that three months previously, the patient had contracted ague, of which he had had several recurrences, but which yielded to quinine. The blood was then examined, and found to contain numerous malarial parasites. A course of quinine and arsenic was then commenced, and the patient was eventually discharged cured. The authors draw attention to the fact that these two cases stand almost alone in literature of malaria.

Riforma Medica, June 26th, 1891.

CASE: Haemorrhagic malignant infection, with abortion, hemiparesis, then syndrome of disseminated sclerosis and recovery. (Marchiafava and Bignami).

A lady had been staying for few months at a place in the Roman Campagna, and after having suffered for two days from headache, which became more severe in the evening, she grew seriously unwell on Feb. 5th, 1888; she was seized with bleeding at the nose, which, beginning as a slight oozing, constantly increased in quantity. On the following morning she was brought to Rome, and was so prostrated that she was obliged at once to take to her bed.

When first visited, the patient was found in an exceedingly

weak state; she moaned and spoke with difficulty; the bleeding at the nose was still going on; the skin especially that of the neck, breast, and abdomen, was covered with haemorrhages; the oozing of blood from the gums was continuous. The temperature was 104°F, the pulse small and frequent, the respiration hurried, the skin earthy in colour, and the spleen a little enlarged. The nostrils were plugged, and 42 grs. of bisulphate of quinine were ordered, hydrochloric lemonade, etc.

During the night there were agitation, slight delirium, flux from the intestines, and vomiting of blood.

In the morning, the temperature was 103·8°F, the loss of strength alarming, and the sensorium dull. The blood, on being examined, showed an enormous number of endoglobular plasmodia without pigment and in motion, a few with a small mass of pigment at the centre and in different stages of the process of fission. 64 grs. of bihydrochlorate of quinine were accordingly administered in the course of the day by hypodermic injection: towards midnight abundant sweating came on, the fever ceased, and the haemorrhage stopped.

On the following day, the patient had somewhat recovered; there was a slight attack of fever, and the treatment with quinine was continued.

On the third day without fever, being extremely anaemic and weak, she had a miscarriage of a 3 months embryo. The abortion was followed by hemiparesis on the right side, accompanied by partial aphasia which was for the most part sensorial. In about a month, the patient recovered from this paralysis, the blood forming power having at the same time improved as well as the general condition. There remained, however, for a long time a state of psychical weakness, together with great excitability, and a group of symptoms (e.g. hesitation in speaking, enormous exaggeration of the reflexes, etc) recalling the phenomena of disseminated sclerosis. But these morbid after-effects also were overcome, and a complete cure effected.

This is a case worthy of notice, (1) because here we find a malignant fever developed during winter, but determined by the summer-autumn parasitic forms: (2) because of the varied seats as well as the gravity, of the haemorrhages which attended it; and (3) on account of the morbid after-effects.

Several other varieties of malarial involvment of the cerebro-spinal system, some identicle with recognized syndromes, others closely resembling such are now given as representstive examples. This does not by any means exhaust the possible cerebro-spinal disturbances produced by this protean parasite, but they should illustrate the almost illimitable range and variation of malarial derangement of the central nervous system.

2. POLYNEURITIC SYNDROMES.

CASE: Polyneuritic syndrome. (Bardellini—reported by Marchiafava and Bignami).

A young and robust driver contracted malaria in summer, 1896). On 12th Aug., same year, after a severe attack of fever which subsided during the night, he began to have firmication in the limbs and trunk, pains in the limbs, and motor weakness which increased from day to day, until he was finally unable to move. In an examination made on the 21st Aug., the following symptoms were noticed:-Paresis of the left side of the face, left pupil larger than the right, weakness of the muscles of mastication, deglutition interfered with, general motor weakness making it impossible for him to rise or even to sit; the only movements possible in the lower limbs were those of adduction and abduction of the foot; the patellar reflex was abolished, the cremasteric and abdominal refleses were intact; there was sharp pain upon pressure of the nerve trunks; there were also pains diffused throughout the body, and paraesthesia of the limbs; sensibility was normal. This condition continued until the 25th, during which time the patient took only liquid nourishment. On the 27th, there was a sudden attack of shortness of breath, orthopnoea with threatening suffocation, but stimulant injections and inhalations of oxygen averted the danger of asphyxia. A few days later, an improvement began, which was frequently interrupted by worse conditions and by malarial relapses, but which finally became progressive.

CASE: Delirium, mania, paraplegia, bitemporal hemianopsia. (Da Costa).

Man, aged 21, admitted to hospital, 2:9:1891. Illness began

7 days before at sea after leaving Savannah; with intense occipital headache, and a violent chill followed by fever which continued 3 days. Then another chill and delirium.

On admission, shaking violently, tongue furred, vomiting, spleen much enlarged, temperature 106°F. Quinine and phenacetin given. Temperature 98·6°F after two days. Profuse sweating and thirst.

8th Sept. Chill, temperature, 105°F.

8th-12th. Temperature fluctuated between normal and 101°F.

13th. Temperature 105°F—wildly delirious—delirious all night, wandering quite himself in the morning.

20th. Sitting up in his clothes. Pale, complaining of weakness in legs, and of inability to walk without support.

23rd. Cramps about knees, and vertigo. Quinine increased to 4 grs four-hourly during the day.

24th. Complete paralysis of the legs—motion and sensation alike lost; arms not affected, but showed slight impairment of power soon afterwards.

27th. Ophthalmologist (Dr. Harlan) examined eyes, and found only slight degree hypermetropia. Little change during next three weeks—he sits up in bed, can use arms, though muscular action not strong; tremor of extended fingers; cramps in neck muscles, especially the right. Cannot move the right leg; can lift left a few inches off the bed. Both knee jerks exaggerated, especially the right; no ankle clonus. Muscle nutrition unimpaired; firm. Sensation in legs quite abolished. No sphincter troubles; temperature normal. Paralysis slowly improved so that he could go about the ward on crutches.

24th Oct. Chill—fever.

5th Nov. Could raise right leg from floor. Still anaesthesia of legs and arms, with formication of legs; zone of anaesthesia encircling chest about 2" below nipple; almost complete loss of taste. Inco-ordination of movements of legs; ataxic; could not stand with eyes closed, nor walk in the dark. Faradic response good, pupils reacted normally to light and accommodation.

On this date there developed severe occipital headache, defective hearing; decided bitemporal hemianopsia, and his memory

became so bad that he forgot almost instantly a question asked. Appetite poor; urine 1,020, acid, no albumen, sugar, or casts. Rise of temperature though taking about 6 grs. quinine daily for weeks.

5th-14th. Exacerbation of cerebral symptoms. Intense occipital headache; flushed face; complete loss of taste, except for sour things; jaw weakness. Tongue protruded straight, pupillary reactions normal, though left larger than right; nausea without vomiting; anorexia, a firm rapid pulse, temperature varying between 101° and 103·4°F.

Hallucinations with "maniacal delirium", so that he had to be strapped to the bed; worst at night, and best controlled by hyoscine. Between these attacks of excitement, which occurred irregularly, he was rational.

14th. Could walk with a stick, but complained of dimness of sight, and that he could see only directly in front of him. He staggered in walking, and could not stand with eyes closed.

The ophthalmologist reports ophthalmoscopic appearances quite normal. Vision very much diminished, (V 1/cc), and existed only in small nasal fields, which were sharply defined and perfectly symmetrical.

16th. Eye examination shows no change.

17th. Maniacal attack lasting a few hours.

18th. Suddenly became quite blind. Prior to this, began to see yellow, a few objects appearing black or green.

19th. Could see light, and recognise colours on the nasal fields, but could not distinguish objects. No perception on the temporal sides. Yellow vision persisted.

Malarial crescents found in the blood. 24 grs. quinine given daily, with rapid improvement. Vision returned first to nasal fields, extended rapidly to temporal fields, and by 24th was normal. Taste, sensation, and motor ability returned, and he was discharged well on 4th Dec. The red corpuscles, which had diminished to 3,390,000, increased in three weeks to 5,100,000.

A year after this date, patient reported that he had kept perfectly well.

CASE Clonic spasms affecting muscles of eyes, face, tongue,

neck, trunk, and limbs of malarial origin—electric chorea type. (Chiarini).*

E.M., Italian peasant, aged 21; previous history negative; contracted malarial in Aug., 1895, and had relapses up to 5th Dec. On that day during the febrile attack, choreic symptoms began and continued with increasing severity for several days, unaccompanied by fever, and in spite of the administration of quinine, and became so troublesome as to prevent his working and obliged him to repair to the hospital. His condition was the following: Malnutrition, pallor, splenic tumourp in the blood a few crescent bodies, nystagmus of an irregular and abrupt nature, with intercurrent strabismus and rotation of the eyeballs, increased under fixation; rapid, brisk and disordered movements of the orbicular muscles, and of those of the face, and the neck, especially on the left side; rapid and rhythmical clonic movements of the tongue causing dysarthria; very active cutaneous reflexes (merely touching the patient excited active clonic spasms), and exaggerated deep reflexes; marked depression; somnolence. On the following days, the apyrexia continued, and the crescent bodies having disappeared, there was atrophy of the muscles of the neck, trunk, and limbs, the patient being unable to sit up in bed; the appetite was voracious, and there were long periods of sleep. From the 21st of Dec., there was improvement; the patient could sit up in bed, but if he attempted to get up he was seized with violent clonic contractions of the muscles of the trunk and limbs.

By the middle of Jan., there was great improvement; the patient walked with long and bounding steps; the dysarthria had disappeared; nutrition had improved; the nystagmus occurred only under fixation; the appetite continued to be voracious—a true boulimia. At the end of Feb., the patient was pronounced cured.

The author considers this case due to toxic infection (malarial) involving cerebro-spinal centres, and producing a state of denutrition, muscle atrophy, and collapse.

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*To whom I am indebted for a copy of his works. W.K.A.

CASE: Polyneuritis of malarial origin, affecting nerves of legs, arms, trunk, and head, with syndrome of Erb's disease. (Chiarini).

P.C., aged 23, carter. Health always good until May, 1895, when he contracted malaria, of which he had recurrent attacks until the end of Oct., when he was forced to attend hospital about five times with progressive weakness and pains of the legs. The weakness was accentuated with each malarial attack, and by 11th Nov., he was unable to go to his work. Malarial semi-lunar parasites were found in his blood at this time. Up till 16th Nov., his condition was stationary, and he was just able to walk a few steps. Between 16th and 24th Nov., he was able to go out in the garden, but on the latter date he had increased pain and weakness of limbs, went to bed, and was unable to rise again.

25th Nov. Skin earthy colour; mucus membrane pale; general nutrition good; muscles well developed, but a little flaccid; thorax negative; spleen enlarged; radial pulse 42; nervous system—face muscles normal, except a slight weakness of the orbicularis muscles; mastication and swallowing normal; lateral movements of eyes sluggish and incomplete, slight nystagmus, convergence normal, head movements good, but tends to fall forward. Movements of trunk and limbs weakened and patient is only with great difficulty able to sit up in b bed. Dynamometer right, 18; left, 17. Walking without assistance is not possible and even then patient collapses after the first few steps. Dysarthria present. Conjunctival, pharyngeal, abdominal and plantar reflexes normal. Patellar reflexes brisk. Pupils equal, moderate in size, and react well to light and accommodation. Sensation normal. Hearing, taste, and smell and vision normal. All the stigmata of hysteria are absent.

Electrical reactions: To induced current, muscle contractions are much weaker than normal; continuous current contractions weaker than normal; no failure of response even to interrupted current.

After a few days, improvement. First to disappear were dysarthria and ocular disturbance, gradually became able to walk, but had to rest frequently.

24th Jan., 1896. After 2 months in hospital, went home quite recovered.

Chiarini considers the case one exhibiting the syndrome of Erb's disease—with first its muscle loss of strength affecting eyelids, dysarthria, difficulty in chewing, attacks of suffocation, paresis and paralysis of ocular and face muscles; subsequent weakness of trunk and neck muscles, accentuated as the day advances.

In this case, however, duration was much shorter than usual in Erb's disease, and the muscle fatigue did not fluctuate in the short period, as it does typically in Erb's disease. Nevertheless the main features are there, 1st, undue muscle exhaustion, affecting limbs, trunk, and cranial nerve supply. 2nd, electrical reaction disturbances, similar to Erb's disease, though differing in intensity, not in quality. 3rd, recurring infective origin.

Pain in legs, however, suggests polyneuritis, therefore Chiarini considers the case one of polyneuritis of syndrome of Erb's disease.

CASE: Optic neuritis, diffuse encephalitis, coma. (Chiarini).

L.U., aged 24, strolling musician. Entered San Spirito Hospital, 5:1:1896. His father was epileptic, and died in an asylum; he himself had convulsions which lasted a month, ceased and did not return. As a strolling player, he drank more than necessary. Admitted to hospital with malarial fever, which ceased on quinine treatment. On the 13th, while afebrile, he suddenly complained of dimness of vision—bilateral amaurosis. Exophthalmoscopic examination made early, showed an incipient optic neuritis. The pupils which were somewhat dilated, remained immovable, under the influence of light and during convergence. For two days, the patient complained of nothing, except the blindness; then he began to be feverish again, and had motor and sensory paralytic symptoms, appearing first in the lower extremities, then in the lower left side of the face, the upper extremities, and the trunk. At the same time, appeared rectal and vesical paralysis, dysarthria, conjugate deviation of the head, and of the eyes towards the right, and sopor, becoming gradually deeper and terminating finally in complete coma, and he died after six days. During the man's last hours, bedsores appeared, and the temperature rose to 41°C (105·8°F). An ophthalmoscopic examination repeated the day before death occurred, showed that the

optic neuritis had progressed. The papillae were slightly projecting with indistinct outlines, peripapillary retinal oedema was very apparent, the arteries were quite thinned, and the veins were turgid and tortuous. At the autopsy, the evidences of an existing malarial affection were found.

Examination of fresh specimens of the grey substance of the brain showed in the cerebral capillaries a certain number of red blood corpuscles containing malarial parasites containing central pigment. Examination of the spleen pulp showed presence of black pigment, and crescentic forms of malarial parasites.

On histological examination, no changes were found in the nerve centres beyond the presence within the capillaries of red corpuscles containing malarial parasites all in the stage of central pigmentation.

Histological examination of the eyes gave the following results: In the sheath, especially the pia and arachnoid, and in the connective tissue framework of the optic nerve, there was a small-celled infiltration which was progressively more marked the nearer the nerve approached its point of entrance into the globe of the eye. Even the optic disc prominent and with a radiating striation more accentuated than normal, showed a small-celled infiltration which passed over for a short distance into the retina, especially in the layer containing fibres of the optic nerve. The capillaries and the veins of the retina were distended and filled with blood. The choroid was markedly congested, the large venous channels being enormously distended and gorged with blood; in the choric-capillaris was noted an accumulation of leucocytes (leucocytic stasis), in the midst of which were seen a few large phagocytes containing granules of melanotic pigment. No trace of malarial parasites was to be found in the vessels either of the retina or of the choroid.

In this case malarial parasites were not found after repeated examinations during life, but only post-mortem.

Chiarini considers this case due to toxic effects of malarial origin on the central nervous system of the patient predisposed to by alcoholic habits and heredity.

Korsakoff's Psychosis:

Castellani records a case of this kind—malarial polyneuritis with mental symptoms and loss of memory for recent events, which resembled Korsakoff's syndrome. Oekonomakis does the same. Vigouroux says that it is not rare.

CASE: Korsakoff's Syndrome. (H. Carlill).

During the war, a large number of patients have been seen who have lost their memory. This is not infrequent among those who are suffering from the effects of shell shock. In other cases the condition has undoubtedly been simulated in order that the patient may have a better chance of escaping from uncongenial service or it has been assumed to excuse some breach of discipline. A few patients have come under observation in whom loss of memory was one of the signs of dementia paralytica, and in several others it occurred after concussion of the brain. In the latter class of patients, it is not uncommon to find that the memory of the accident or of the circumstances which lead up to it is completely lost. In several of the forms of alcoholic insanity, for instance in delirium tremens, and in chronic alcoholic poisoning, it is common to find that the memory is defective. It occurs, too, in some forms of senility and also after attacks of epilepsy.

Among these various conditions, there stands out prominently that form of loss of memory which was described originally by Korsakoff as occurring in patients of alcoholic habits who showed also signs of peripheral neuritis. The condition was known as the polyneuritic psychosis. Frequently, however, it could not be proved that alcohol took any part in bringing about the disease, and later it became established that other illnesses such as typhoid, malaria, diabetes, arsenical poisoning, etc., all of which are at times associated with peripheral neuritis, may give rise to the particular peculiarities described by Korsakoff. Furthermore, many cases are on record in whom neither alcohol nor peripheral neuritis appeared to have any part, and it is agreed at present that while the typical cases are most met with in alcoholic patients with neuritis, similar symptoms which are indistinguishable from them, may be met with occasionally, without neuritis and without alcoholism.

The essential features of the disorder are loss of memory for

recent events and difficulty in concentrating the attention. The mental disturbance is one mainly of confusion of thought, disorientation, and forgetfulness. The patient loses the power of keeping events in their chronological order, and he constantly transfers to the present experiences which belong to the distant past. He lives, in a state of reminiscence.

The following account is that of a patient who showed this condition. He was a stoker, aged about 45, and he was admitted to Haslar on Nov. 6th, 1916. The few notes which he brought with him, showed that he had been admitted to hospital in Bombay on Oct. 15th, 1916, and later to the 15th General hospital at Alexandria. The notes stated that when he arrived at the latter place he was very anaemic, and had oedema of the lower limbs as high up as the lumbar region, and that this condition had been present for six weeks. The urine showed degenerated hyaline and epithelial casts, but neither albumen nor blood was detected.

When he arrived at Haslar on Nov. 6th, there was no oedema and the urine was normal. He was very weak and anaemic, but no disease was detected except some recent gouty arthritis of the left wrist. Gout was also detected in the right ear, and in the great toe of the left side. The red cells numbered 4,650,000, and the leucocytes 10,000, per cu.mm. Of the latter, 52% were polymorphonuclear cells, and 46% were lymphocytes. He was observed from the first to be rather dull mentally.

On Dec. 10th, his temperature went up to 104°F suddenly, and malarial rings were found in his blood by Dr. P. Filies. The attack rapidly subsided with administration of quinine and on Dec. 14th, he was transferred to the neurological department for further observation of his mental condition. For the notes already given, I am indebted to Surgeon T.G. Gibson, R.N., under whose care the man had been.

In his story, the patient told us that he was born on June 19th, 1866, that he lived at a certain address in Fulham, and that he had a daughter aged 12 years. He said also that he had seen his wife recently at the hospital. These statements it was not easy to disprove at the time, and indeed the idea of attempting to disprove them did not occur to us then. Later, however, when he told us that the year was 1899, that King Edward was reigning , and that the war

was between England and some field force, and had been going on for four years, it was evident that we were dealing with some serious form of amnesia.

The man was well nourished, but pale, and he looked a little simple. He spoke quietly and politely and said that with the exception of the pain at his wrist, he felt quite well. He told us that he had suffered frequently from "intermittent fever" and that his last attack was about three months ago when his temperature was 104°F. He said that he was ill for a week.

He told us that he was for eight years on the active list and that he had then become a labourer implying that he had become a reservist, and that he had been called up for the war. This was supported by the fact that he was wearing a well-grown moustache, ~~whic~~ which he said he had let grow for some time. He said that he had not been in action. He did not know the name of the hospital, and his ideas about the war were hopelessly confused, but he was able to do sums well, and read intelligently. He constantly stroked his moustache and chin with his hand. He did not appear to be worried particularly about his loss of memory, but he recognized that matters were not as they should be. He kept to himself a good deal but appeared to be quite happy and contented.

He remembered having been at Bombay, but had no recollection of his illness there or of the swelling of his legs. He could not tell us anything about his voyage home, or about Xmas a fortnight before. He stuck to his statement that King Edward was on the throne, but he could not give the name of the Queen or of the Premier. When he was at a loss for a reply he used to say that he did not "read the papers carefully enough for that". He knew that Lord Roberts was in command during the Boer War, and said that he expected that he was still ~~in~~ "somewhere on the frontier", but he would not hazard which frontier he referred to. He knew where he had been to school, and said that he was in the VIth standard. He recalled that he had been engaged to be married for about a year. He knew all about the circumstances associated with the relief of Ladysmith, but he did not know the name of Sir George White even when it was mentioned in conversation. He said that he was a bald man, and that he knew his photograph well. When he was reminded about the battle of Jutland,

and of the Falkland Islands, he appeared to recall them but he remembered nothing about them. For instance, he did not know between which peoples, the battle of the Falkland Islands was fought, but he thought that "England was there". He remembered that the Boer War was between England and the South Africans, but he knew nothing at all about the Jutland battle, and said that it was at sea and in the air, between England on one side and some country whose name he could not remember on the other. He said further that it was a kind of bombardment, and that Lord French was in command there, just as he had been in the Falklands, "because they must have had some troops there". He remembered the diamond Jubilee, and thought that it took place in 1887. Later on, when pressed for more information about the war he said that it was between England and the Balkan States.

On examination, his gait was seen to be normal, and he had no tremors. The spleen was not palpable. His systolic pressure was 140 mm. Hg. He had no headache, and the urine and viscera were normal. His weight was 9st. 13lbs. There was no evidence of alcoholic excess, nor was there any reason to suspect it. His blood on Jan. 15th, 1917, contained 5,050,000 red cells, and 10,300 leucocytes per cu.mm., and of the latter, 64% were polymorphonuclears, and 34% small lymphocytes. The Hb content was 90%.

Nothing abnormal was detected in the central nervous system, with this important exception; he had a bilateral absence of the ankle jerks. This was confirmed repeatedly at subsequent examinations The calf jerks were active. There was no history of sciatica, nor was there anyhting else found to point to a past neuritis. The association of the mental condition with the absence of ankle jerks clearly made it imperative to rule out dementia paralytica, in spite of the fact that he did not resemble a case of this disease. The Wassermann reaction in the serum and in the cerebro-spinal fluid was found to be negative by Dr. Fildes, and the cerebro-spinal fluid contained no cells.

On Jan. 20th, his wife came to see him. She brought her step-daughter and two friends. Several letters written to her at the address at Fulham, which was given to us by the patient, had been returned to us, and finally his correct address was obtained from the Admiralty. It was in Portsmouth, where he had lived for four years. His wife told us that she had not seen her husband for nearly four

His wife told us that she had not seen her husband for nearly four

years, when he was last on leave. As far as she knew, his previous health had been good. He had done 18 years active service and had commissioned the "Pegrasus" at the onset of war. She thought that he was still in this ship, and had been worried because she had not heard from him for some time. The last letter she received was from the Sailor's home at Bombay during Nov. 1916. She had no knowledge that he was sick? She said that he had been a labourer formerly and that she had been married for 21 years.

The man recognized his wife and friends, but was not able to join in the conversation as readily as they wished. He told them that he must have grown his moustache on the way home. He caused considerable surprise by solemnly announcing that Lords Roberts and General Buller were in command at the battle of the Falkland Islands. The following day, Jan. 21st, he recollected having seen his wife, but thought that she had brought with her his little girl. He was reminded that he lived at Portsmouth, but up to the last he said that he lived at Fulham, and that he was going there on his discharge. He was discharged to his home on Jan. 22nd, 1918.

The wife's story is put in here so that the reader will be in possession of the actual facts of his personal history before he reads the short list of the man's answers to various questions which is appended. It was very evident, during daily conversation with the patient, that he was living through the period of the Boer War over again. His memory for past events was not perfect, but it was far better than that for events of the present time. In a few instances, such as that of the intravenous injections, his memory for events of the immediate past was completely in abeyance. However, when his mistakes were pointed out to him, he would sometimes avoid repeating them the next day. In some cases, when he made correct replies to simple questions of fact, it is likely that he had been told the answers by the other patients.

Jan. 3rd., 1918. What is the name of the King?—Edward or William.

What is the name of the Prince of Wales?—George.

What year did you join the Service?—1899.

Who is the head of the army?—Lord Roberts or Lord Kitchener.

When did the War start?—1890.

What month is it?—(Jan)—December.
What queen is reigning?—Queen Victoria.
Who is the Prince of Wales?—Prince Edward.
Where does the King live in London?—Buckingham Palace.
How long have you been in hospital?—(Two months)—Ten days.
Who is head of the Navy?—Admiral Jellicoe.
What was the name of his ship?—King Edward.
Who married Lord Kitchener?—No-one.
What is the name of Admiral Beatty's ship?—King Edward.
Have you been on the reserve list?—Yes, after doing twelve years service.
When did you rejoin?—At outset of war.
Where did you spend last Xmas?—Has no idea.
What ship did you travel home in (Britannia)?—Tyne.
Where did you spend Christmas?—At home.
Have you ever been in a decorated ward?—Yes, in the present ward, but I do not know why it was decorated.

On Jan. 4th, when I asked him when he had last seen me, referring to his catechism of the 3rd. He hazarded "The day before yesterday in the ward at 11 a.m.", but he did not know what we talked about. As a matter of fact, the interview was in sister's cabin, and at 6 p.m.

On Jan. 5th, at 10 a.m., I gave him an intravenous injection of "914", with the idea of stopping future attacks of malaria. He had never had any injections previously. At 4 p.m., he had no recollection whatever of the injection, and when I asked him when he would like to commence his treatment, he said that he would leave all that to me.

The mental characteristics of Korsakow's psychosis are clearly portrayed in this patient.

CASE: Myoclonic encephalomyelitis. *(N.G. Haranesco.)*

A woman aged 26 was taken ill on Sept. 3rd, 1920, suffering from fatigue, anorexia, and fever of an indefinite type. She remained in bed for two weeks, and as her condition grew worse, she entered a hospital, where she remained for only a few days. At this time she was feverish, and unable to walk, and one noticed that

she had slight convulsive movements of the limbs and of the face. On Sept. 27th, she was transferred to our wards, and we noticed that the skin was pale, and that she could neither walk nor stand up. Speech was difficult and dysarthric. While lying on her back, one noticed in the upper limbs almost continuous involuntary movements, accentuated at the extremities. These movements showed themselves in the form of rapid oscillations, which consisted of flexion and extension of the fingers or abduction and adduction, whilst in the arm and forearm, the movements were of a more myoclonic type without displacement of the limbs. From time to time, the movements of the upper limbs were quicker and were transmitted to the trunk, which was agitated by contractions, rhythmical in character. On the side of the abdomen, there were sharp contractions, having the same rhythm as the respirations (20 per min). Respiration was regular but superficial, and at times the patient took deep inspiration. There were rapid lateral movements of the head, and at the same time rhythmic movements of the jaws, the lower jaw coming together in such a manner that there was a gnashing of teeth. The eyes were moved laterally, and vertically, so that they appeared as if they rolled in their orbits. The eyelids fluttered rapidly, the facial muscles twitched, and the nostrils dilated and contracted.

In the lower limbs, the involuntary movements consisted of rapid sharp contractions, localised to the thigh muscles. Movements were less frequent in the muscles of the leg. The big toes were in a state of continuous extension, though from time to time they also showed rhythmic movements.

To sum up, the majority of the voluntary muscles were subject to involuntary movements so rapid that one could not count them; they were myoclonic in appearance, more accentuated in the extremities of the upper limbs, in the jaws, and in the orbit; further, the muscles of the trunk showed movements, larger in size and less frequent, which were from time to time transmitted to the arms. Beside these movements, which were accompanied by slight displacement of the segments in which they took place, one noticed very rapid muscular contractions.

The tendon reflexes of the limbs were abolished; the pupils were equal and reacted to light and accommodation. The cutaneous

reflex of the abdomen and even the plantar reflex were absent.

At the level of the right parotid gland was a swelling of considerable size, which was painful.

The pulse was so rapid that it could not be counted at the wrist; the femoral pulse beat at 150 to the minute.

The patient had a slight rigidity of the neck, and a suspicion of Kernig's sign. The limbs showed no contractures. The temperature was higher in the morning (38·6°C) than in the evening (37·4°C).

On the day of entry into hospital (Sept. 27th, 1920), we wished the patient to get up for the operation of lumbar puncture, and to seat herself in a chair, but during this manoevre she fell into a kind of syncope, the trembling ceased, and her arms fell inert beside her body.

When she had been placed upon the bed, it was noticed that her pulse was imperceptible, and that respiration had apparently ceased.

Artificial respiration was performed, and her respiration was restored, although the pulse remained very feeble. Presently the tremor reappeared little by little, and in a few minutes regained its previous intensity. During the day and night, the patient was in a state of delirium.

Lumbar puncture, carried out in the lateral position, showed 10 lymphocytes by division (Nageotte), and the blood an intense mononuclear leucocytosis.

The urine was brown, and on boiling a thick cloud of albumen appeared. Widal's reaction and the Wiel-Felix test were negative.

On Sept. 28th, the temperature rose to 39°C, and the state of the patient became much worse. Respiration became noisy, and she died suddenly at two p.m. Just before her death, the involuntary movements described above disappeared.

As the patient died almost suddenly, we were not able to pursue all our investigations for the purpose of arriving at a correct diagnosis, but from the clinical aspect, a slight fever, and the indefinite lymphocytosis, we thought that we had to deal with a case of epidemic encephalitis of myoclonic form; but the examination of the blood, followed by the study later of the alterations in the central nervous system, revealed our mistake. In fact, there was revealed in the blood, in addition to the lymphocytosis, the presence of haematozoa, and even of crescents.

On macroscopic examination of the brain had already attracted our attention by its grave colouration, and besides one saw here and there, in addition to the hyperaemia, punctate haemorrhages in the cortex, the corpus striatum, and especially in the grey matter of the spinal cord. The meninges were unaffected, the cerebellum was hyperaemic, and the lateral ventricles were slightly dilated. The parotid gland on the right side was congested, and shows signs of parenchymatous infiltration, the long narrow vessels which cross the cortex to enter the white matter were dilated and showed, for the most part in their adventitial sheath, a considerable number of lymphocytes, plasma cells, and some mononuclear leucocytes. Here and there, in the track of pre-capillary vessels and venules, colonies of plasma cells and fibro-blasts were seen, and a similar infiltration of the adventitial sheaths of the vessels was visible in the white matter. Small vessels cut across contained in places a large number of lymphocytes and occasionally also some pigmented mononuclear cells.

In general the endothelial cells of the veins, as those of the capillaries, were swollen and sometimes even detached.

The small meningeal vessels were congested and in their sheaths a certain number of lymphocytes and mononuclear cells were recognized.

Haemorrhages were not the rule. It was quite exceptional to see extravasations in the parenchyma, but haemorrhagic streaks, which we saw in the spinal cord and of which I will speak later, affected also the cerebral cortex. Nevertheless I encountered some small haemorrhages in the cornu armonis, where we found a thrombus of leucocytes in a meningeal vein, forming a nodule which completely filled the lumen of the vessel.

In all regions of the cerebral cortex infiltrated capillaries and veins were found, dilated or filled with lymphocytes, with some mononuclear leucocytes, and plasma cells in addition. Throughout, on the interior of the vessels, red globules were seen which had lost their colour in proportion to the development of the parasite, and a capillary plexus was seen to be distended by these red globules which filled the lumen of the vessel. On the surface of these globules some haematozoa, round in shape, were seen occupying them to a greater or lesser extent.

In the substance of the grey matter, as in the white matter,

we remarked an hypertrophy and multiplication of neuroglia cells between the berve cells in the neighbourhood of the vessels or near to them. In fact we were able to count up to 10 neuroglia cells in the neighbourhood of the base and of the body of the deep pyramidal cells. The same neuroglial reaction existed in the neighbourhood of the small bessels of the white substance, but here we noted a new growth of neuroglia of peculiar formation, caused by the multiplication of these cells in a mass, and resulting in a nodule which existed only in the neighbourhood of the grey matter, and which could be found in various sizes. The mean size of these nodules was 210u, and 130u, and they appeared to be formed almost entirely of neuroglia cells.

Lesions almost analogous to those in the cortex were found in the optic thalamus, the lenticular nucleus, and the caudate nucleus. In the peduncle, the infiltration in the vessels and the hyperaemia were more marked in the grey substance than in the white matter, and the infiltration of lymphocytes and plasma cells was confined much more to the walls of the veins than to those of the arteries. The cells of the substantia nigra were not particularly affected in spite of the fact that there were more capillaries filled with blood in this region. On the other hand, the same observations are applicable to the red nucleus. The capillary vessels of the corpora quadrigemina and of the grey matter of the peduncles, and the promontory (protuberance) showed inflammatory reaction of the small vessels, as intense as that in the cerebral cortex.

Very often the capillaries contained haematozoa, few in number, but there were some of them in which nearly every red globule was parasitic. There were capillaries or pre-capillaries filled almost exclusively with lymphocytes, smaller medium size, arranged in one or two series. Less frequently these vessels were filled exclusively with polynuclears, ending with one or two lymphocytes. In other vessels, there was a mixture of lymphocytes and polynuclears and these can predominate.

The nodules which we have described in the white matter of the cerebral cortex are found more rarely in the peduncle. All the lesions which we have just noticed as being in the cerebral cortex, basal ganglia, and peduncles are reduced to their simplest expression

in the cerebellum, when infiltration of the adventitia is exceptional, capillary congestion little marked, and the number of haematozoa very limited.

We examined for the presence of haematozoa different glands such as the spleen, liver, supra-renal capsules, and ovaries, but we have not actually found the parasite of Laveran. There were was certainly in the spleen and liver a great quantity of black pigment in the leucocytes, and macrophagocytes which filled up the vessels, but I am sure that if there had been haematozoa in abundance as we had seen them in the nerve centres, it would have been easy to make them evident. So we are obliged to admit that in this case the haematozoa localised their action principally to the nerve centres, such as the brain, bulb, and spinal cord, whilst the cerebellum was invaded to a slight extent only, and the spinal ganglia still less.

CASE: Mental confusion and excitement, followed by astasia-basia (The author).

Pte. O.E., aged 25,

24:7:18. Salonica. Admitted to hospital with malaria.

5:8:18. Benign tertian parasites in the blood.

23:8:18. Malignant tertian parasites in the blood. Attacks of malaria frequent. He is headachy, giddy, nervous and stammers. Knee-jerks brisk. Spleen enlarged.

21:10:18. Sick, vomiting.

30:11:18. Shingles at side. Confused, uninterested, strange, singing.

30:12:18. Confused, noisy, shouting, obscene, threatening.

7:1:19. Much better. Sleeping better. Tremors, and dizzy on standing. Exhibits astasia-abasia. Knee-jerks brisk.

21:1:19. Seems to have recovered mentally except for nervousness.

30:1:19. History from himself: Farmer, single, healthy pre-War. Family history negative. Denies alcohol and venereal disease. France, May, 1915. Under fire, wounded in both hands, no bad after effects. Salonica, Nov., 1915. Under fire, not wounded, but nervous. Had slight attack malaria, 1917, but did not report

sick, and has had 20 attacks since then, and been in hospital ever since. Became weak, nervous, and lost control of himself. Says he has lost about two stones in weight, and looks it. Pupils and knee-jerks normal.

Mentally: he gives a clear account of himself, but trembles so much he can hardly sit in a chair. He came into the room hanging round the neck of an orderly, exhibiting astasia-abasia. No sign of mental confusion now, but has lost control of himself, but says he will do his best to recover it. He was made to walk out of the room, unsupported, with the explanation that all his nervousness and lameness were functional, and with the encouraging recounting of similar cases to his own. Orderlies have been instructed not to assist him at all in walking.

While under treatment for malaria in Salonica, he had numerous injections of quinine into the buttocks, which always left him stiff and sore. He gradually developed astasia-abasia, which remained for long after the injections had ceased. By direct suggestion and firm handling, together with tonic treatment, he was able to get about freely by himself within a week, and thereafter steadily improved in physical health and put on weight, without hysterical or confusional relapse. Discharged home cured.

Note shingles, or herpes, of the side, which probably implies pia-mater meningitis of the cord, and may be related to the onset of astasia-abasia, which persisted after the meningitis had subsided. It is also worthy of note that this is a case of double infection—benign and malignant tertian.

CASE: Cerebro-spinal malaria, with convulsion, coma, recovery. (O.R.P.Pepper).

E.P., a sailor aged 57, admitted to hospital in coma, having been suddenly seized with a convulsion some hours previously. Patient was breathing stertorously, and large moist rales were audible all over the chest. Pulse weak, and of low tension, and heart sounds could hardly be heard. Blood pressure, 95 systolic, and 55 mm. Hg. diastolic. Spleen not palpable, but the abdomen was distended, and palpation difficult. There was a great deal hiccough. Unconsciousness was complete and no voluntary movements were made. The urine was obtained by catheter, and contained a light cloud of

lower

albumen and many casts. The blood count was: Hb 63%; reds, 2,810,000; leucocytes, 11,200.

By the next morning the temperature was normal. The circulation greatly improved, and consciousness restored, although the patient was still a little irrational.

A history was obtained of a typical attack of malaria, with chills and fever, two months previously in Cuba. Examination of a blood film revealed many aestivo-autumnal parasites in both sexual and asexual forms. Despite active medication with quinine, the patient had several slight rises of temperature, but he had no returns of the cerebro-spinal symptoms, or of the circulatory collapse. He ultimately left the hospital in a very good condition.

3. HERPES ZOSTER.

Herpes zoster is considered as due to an inflammatory reaction of the sensory nerves, exhibited in the skin, associated with irritation, generally toxic, of the posterior root ganglia or their central branches at any part of their course. It may also be due to inflammation or irritation of the sympathetic ganglia or rami communicantes, (L.R.Müller, Lewandowsky); or it may be caused by reflex irritation from any viscus or part of the body irritated, generally by toxic disease, operating through the corresponding spinal segment and affecting the nerve supply to the corresponding area of skin. For instance, prolonged or severe renal colic on the right side may give rise to herpes in the area of distribution of the 11th right dorsal segment, i.e. an area of about two-fingerbreadths broad round the right half-abdomen a little below the umbilicus in front, and running up to the 11th dorsal vertebra behind. Hyperalgesia of this area may occur in kidney irritation from any cause (Carmalt Jones).

Nearly every observer of large numbers of malarial subjects has noted the frequency of herpes, at least of the lips. Herpes and urticaria appear to be the commonest skin eruptions associated with malaria, and it would seem that they both occur with moderate frequency.

It most commonly occurs, according to statistics in association with the acute febrile paroxysm, at the stage of defervescence, and it

generally affects the lips or at any rate the trigeminal distribution. It may, however, occur in more quiescent phases, and may affect almost any part of the body. Winfield notes its occurrence on face, head, neck, occiput, chest, ear, shoulder, arms, and gluteal regions. In 25 cases of zoster, fourteen had malaria parasites in the blood. The majority had intercostal distribution and in some zoster was the only sign. Garin and Coullard-Descos have observed at the malarial hospital, Modane, 246 malaria cases, 121 of whom had herpes which occurred at the stage of defervescence. Of these, the herpes was in 98 of the lips and mucous membrane of the lips; in 10 nasal; in 5, of the tongue; in 3, of the ear; conjunctiva, 1; eyelid, 1; cheek, 1; scalp, 1; scrotum, 1; They maintain that the vesicles in malarial herpes usually leave a pigmented scar. Dederick reports 8 cases of zoster, 5 of whom had malignant tertian parasites in the blood—2 negroes and 3 whites. The distribution was thoracic in four, and one fore-head and eyelid. He says that Columbini, Donnell and Riesmann support the malarial origin of zoster. Dantec notes the association of zoster and malaria. Crespin says it is most common in his experience, on the torax. Papastrategakis says meningeal inflammation (malarial) may a pear as herpes zoster, localised in ganglia of back and the only meningeal sign being, apart from that, alteration in the cerebro-spinal fluid.

The great frequency of herpes zoster on the lips as compared with other places, to which the majority of observers testify, is of interest in connection with the observation, which also is supported by the majority of observers, is that the most frequent form of neuralgia in malarials is trigeminal. These joint and independent findings suggest that the 5th nerve shows a very frequent reactivity to malarial poison.

Engman of St. Louis, reporting 18 cases of skin eruptions associated with malaria—in every cases parasites were found—showed in 6, urticaria; 5, zoster; 3, pospholyx; (1 of which followed zoster) 2, erythema multiforme; 1, multiple spontaneous gangrene.

In the experience of Kolsch and Kiener it occurred in at least 30% of cases with bilious symptoms. Laveran saw a case of herpes of the gums, Mannaberg one of the left hand. Ziemann saw a case of herpes of both cheeks, but on the whole it was not common in

his African practice.

Two examples by Deaderick and Winfield are of interest:

CASE: Herpes zoster. (Deaderick).

C.B., white male, aged 13, seen July 8th, 1906. His previous history is negative. On the morning of June 27th, 1906, he had a typical malarial paroxysm, followed by fever which lasted 24 hours. During the night of the 27th, and morning of the 28th, he took four or five 3gr. doses of quinine. He has had no further chills, but has had fever several times. During a paroxysm, a pain began on the left side, and next morning, herpetic vesicles appeared extending from the level of the 11th dorsal vertebra to the median line in front above the umbilicus. The spleen extends 1½" beyond the costal margin. Temperature, 99°F, pulse 98. Faeces negative for ova of intestinal parasites. The Hb is 75%, and a few aestivo-autumnal rings are found.

CASE: Herpes zoster. (Winfield).

Patient admitted to dermatological ward of King's County Hospital, suffering from the most extensive zoster I ever saw; its distribution was practically bilateral. The older and severer eruptions began on the left buttock and extended almost completely round the thigh, with a few herpetic spots scattered over the upper part of the leg. A day later, an intercostal zoster appeared on the right side; the inguinal glands were markedly enlarged and tender; the prodromal symptoms were unusually severe; the temperature was 104°F for three days; there was considerable nausea and restlessness, and the patient complained of the burning and itching of the skin at the affected parts. Examination of the blood showed the pigmented variety of the plasmodium of malaria.

While the above cerebro-spinal forms of involvement of the nervous system by malaria have been chosen to demonstrate this part of the subject, this does not imply that their variety has been exhausted. Rather would they go to suggest that the variation of picture is endless.

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CHAPTER XXV.

CORD AND PERIPHERAL NERVE DISTURBANCES IN MALARIA.

A.: CORD LESIONS.

Pathological records of changes in the spinal cord as a result of malaria are singularly scarce. Maranesco records a case of encephalo-myelitis showing changes in the lumbar enlargement—details of this case are given in the cerebro-spinal section. Dulgeon and Clarke record a case of malaria of the central nervous system in which advanced cell-degeneration of the anterior cornual cells with typical vascular changes and complete blocking of vessels occurred. This patient had signs of paraplegia before death.

Maillot (1836), Curadou (1851), and others noticed congestion, inflammatory changes, punctiform haemorrhages, and softening in the cord of paraplegics, which they considered of malarial origin. These observations were made, however, before the discovery of the parasite and so have hardly the same value as observations made subsequent to that event. Blanc (1887) observed that the congestion of the cord in malarial lesions was sub-inflammatory, and led to parenchymatous and interstitial changes. He also noticed frequently, punctiform haemorrhages.

Clinical records of paraplegia of malarial origin are fairly plentiful. Instances have been recorded by Macario (1857), Romberg and Hartwig (1874), all quoted by Ziemssen (1878), but again these have not full value as examples, being before the discovery of the parasite in 1880. Cases have also been recorded by Wilkinson (1886), Roché (1886), Suckling (1888), quoted by Soinet and Salébert, who themselves record cases of this kind. Sacquépée and Dopter have collected 25 cases of malarial neuritis from the literature along with cases of their own.

Soinet and Salébert, cite cases of paraplegia of two kinds—transitory and permanent—and emphasise, as do other writers including Castellani, its occasional likeness to beri-beri. They also record the malarial origin of other neurological types: tremors—choreiform,

ataxic, athetosis, spasmodic contractures, convulsions, with and without sensory phenomena, muscle atrophy, etc. Mannaberg states that of malarial cord disturbances, paraplegia is the most common—with sensory, and sometimes bladder and bowel disturbances also. Laveran saw a case of malarial paraplegia, without sensory or bladder or bowel disturbance, with malarial parasites present in the blood.

Ziemann had a case of paraplegia with paralysis of the bladder and retention in a robust Duala-African negro. He had usually lived in the healthy elevated hinterland, but had come down to a district where malaria was prevalent, and had a severe infection with malignant tertian parasites, which were found in the blood. He died comatose—unfortunately there was no autopsy. He admits the malaria may have been coincidental as the Dualas are relatively immune to malaria.

He records another case of his, a not very robust looking, teetotal man, who had only been four months in the Cameroons, and who omitted to take prophylactic quinine. He was admitted to hospital, fevered, with a history of taking ill two days before with fever, without shivering. He had noticed weakness of the legs with the first attack, which increased especially in the right till almost complete, with no marked sensory disturbance, nor bowel or bladder involvement. Enormous numbers of malignant tertian parasites were found in the peripheral blood. Temperature, 39·5°. Left leg improved first—in a few days. The right took weeks, on massage and electricity etc. Even after four months, he could walk only with the help of a stick.

More lately, many examples of clinical paraplegia and evidences of cord involvement have appeared in the literature. Sabatucci details two cases of spinal paraplegia occurring during and caused by acute malaria, and he concluded there was myelomalacia of the lower dorsal and upper lumbar spine due to malarial arteritis.

Castellani saw a case of [redacted] clinically typical transverse myelitis, due to malaria. He has also seen examples of the polyneuritic type and draws attention to the variety that resembles wet beri-beri very closely. The patient is oedematous, there is the characteristic gait, knee-jerks absent. No fever, no enlargement of spleen or liver. In two such cases, malarial crescents were found and cured on quinine in large doses by mouth and intramuscularly.

Plogner (quoted by Ziemann) saw six cases of polyneuritis in

Samarang, which developed during and after the malaria attack and which he distinguished from beri-beri, to which they had some likeness. There were diffuse pains and weakness in the legs, tenderness on pressure over the nerves, sensation sometimes altered, sometimes not; diminished electrical excitability of the nerves and muscles, and at times oedema of the feet.

Jourdan, Mathis, Price, Dumolard, Campbell and Ewald are quoted by Ziemann as having recorded cases of polyneuritis of malarial origin. Also Barielliàni saw cases of malarial neuritis, mostly after recurrent and long standing malaria, with atrophies and deformities—e.g., talipes equino-varus not seldom as sequelae, and resolving with quinine and electricity etc.

A representative case of polyneuritis is recorded by Mendelson:

CASE: Polyneuritis—motor. (E. M. Mendelson).

Siamese man (Bangkok) aged 37—boatman. F.H. -ve. Drinks moderately of native alcoholic drink, but never known to be drunk. Smokes opium moderately, and occasionally indulges in Indian hemp. Gonorrhoea 5 years ago. Blood Wassermann -ve. No history of "chills and fever", dysentery, beri-beri.

Felt ill first, 26th Feb. Headache, fever, depression. Increased till Feb. 29th, when the patient was brought to hospital unconscious. Relatives stated he had been working previous to his illness, and that the day after his sickness started, he had some difficulty in walking and in using his arms. This rapidly increased so that previous to becoming unconscious he could neither control movements of his arms, not walk. On admission to hospital, P. falciparum was found in his blood: B.C., white blood corpuscles, 12,000 per cu.mm.; temperature, 100°F. 40 grs. intravenous quinine given the first 24 hours, after which patient became conscious. Intensive treatment for one week. Blood showed parasites until 6th day. A week after patient entered hospital, his condition was: head, neck, lungs negative. Aortic stenosis. Complete paralysis of lower limbs. Foot drop. Patient unable to remain erect unaided or to walk. Loss of power absolute. Arms affected, but less so, and right arm worse than left. Right wrist drop—not so left. Definite loss of power of arms, but able to control movement. No evident involve-

ment of other muscles of body.

Sensation: apparently normal—touch, pressure and temperature, and no complaints. Ankle and knee-jerks abolished in both legs. Wrist jerk present only on the left side—right abolished. Elbow jerks could not be elicited in either upper extremity. Organic reflexes not affected. No mental symptoms. Slight oedema of both ankles. Urine negative.

Beri-beri was considered and ruled out because of history, sudden onset, and parasites in the blood. There was no history or evidence of poisoning with lead, ergot, arsenic, mercury, or silver.

Delmege described the features of a disease seen in Jamaica (1881)—a polyneuritis which he attributed to malaria. The general features were, deafness, impaired vision, loss of muscle co-ordination marked ataxia with feet together, gait irregular so that patient could not walk in a straight line and knee-jerks lost. There was also irritability of temper. The more malaria in the district, the more frequent was this neuritis, and especially after the rainy season. Periodicity of symptomatology was noticable, the symptoms tending to be aggravated at a certain hour each day. Males and females were about equally involved, and were mostly natives. Common complaints were numbness, ground felt soft, cramps, etc. Skin tended to darken. Cure by quinine.

Pseudo-tabes of malarial origin has been recorded by several observers. Da Matta has seen 18 cases among the Amazons of Brazil. The condition begins like peripheral neuritis: patellar and ankle reflexes lost or reduced; loss of cutaneous sensibility in the legs, which are cold and clammy; ataxic gait. The pupils are usually not involved. Malarial crescents were found in the blood. He also notes that some of these cases closely simulate beri-beri. One case recovered in 23 days on quinine and galvanism; another in two months.

A case of pseudo-tabes (without Argyll-Robertson pupil) was observed by Goodall in Macedonia; blood Wassermann negative.

A representative case of this class is given by Wörner:

CASE: Pseudo-tabes malarica. (Wörner).

A soldier, who, in the year previous to present illness, had repeated attacks of "fever". Four weeks ago he had severe stomach pain and vomiting. Unable to walk or to hold himself up, and "could not control his legs". Vomiting on eating was incessant.

Condition: Ill-looking, emaciated, dry skin, marked muscle atrophy, and unable to stand up. Heart and lungs negative. Spleen palpable Stomach tender and abdominal muscles rigid. Liver not enlarged. Pupils react to light and convergence. Patellar reflexes weak: achilles jerk absent on the right, weakly positive on the left. Upper extremity reflexes normal. Abdominal reflex present. Cremaster reflex brisk. Ataxic gait. Cannot stand. Static and locomotor ataxia. Muscle weakness marked.

Sensation normal except for slight sensory disturbance of the feet in that he does not feel the floor well. Bowel and bladder normal. Blood Wassermann negative. Malarial crescents found in the blood. Stomach very sensative with pain and vomiting after food. Bile and coffee-grounds in vomitus at times. X-ray of stomach could not be done. The spleen was much enlarged.

Carcinoma of the pylorus was thought of, and a laparotomy done showed stomach and bowel normal.

Quinine was given, intramuscularly to begin with, later orally. Thereafter vomiting stopped slowly, and the patient slowly and steadily improved. Strength, reflexes, ataxia, finally became normal and he began to walk three weeks after onset of quinine treatment.

Diagnosis: Polyneuritis of malarial origin with pseudo-tabes appearance and gastric crisis.

Cases of spastic spinal paralysis have been occasionally seen, one of which is given in detail by van Driel.

CASE: Spastic spinal paresis in tertian malaria. (van Driel)

On the 13th of January, 1914, there came under my care a native sailor about 25 years old with fever. The temperature at first was 38°C, but rose in a few hours to 40°C. The blood appeared to contain numerous tertian malarial parasites. The patient had no special complaints. According to his sick book, he had an attack of malaria about 18 months ago. On 2 gms. quinine bisulphate a day, the patient remained free of fever for five days, and according to custom

he was adlowed to return to duty as officer's servant. Towards evening on this day, however, he came to report that climbing the stairs was very difficult to him and his legs were so heavy. As we had sailed for about 3 weeks from our last supply port, and moreover this sailor had remained continuously on board as a servant when the others had duties to perform on shore, my first thought was: "Is this beri-beri from monotonous living, or is it malarial neuritis?"

Intimate knowledge of the man put malingering out of the question.

Apart from the heavy feeling in the legs and the great difficulty which climbing the stairs gave him, really only possible by dragging himself up by the arms, the patient had little to complain of. He did not feel that his legs were powerless, but only that they were difficult to move. On the whole, he had no pain; still less paraesthesia.

Examination showed typical spastic paretic gait. At each step, the patient was obliged, as it were, to pull the leg away from the ground; it was as if the sole of the foot was glued to the deck. He lifted the foot higher up than usual, the toes somewhat downwards, but not sloping. The gait was also slightly uncertain, tottering, and the patient sought for support with his hands. Inspection showed nothing peculiar about the legs; both oedema and atrophy were absent. When the patient changed from the lying to the sitting posture, he first drew his knees up, and thus bent the thigh strongly at the hip joint. No accessory movements were seen. When the legs were passively flexed, a definite resistance was noticeable, especially when the movements were executed somewhat briskly; the resistance was apparently caused by contractions in the extensors. The tendon reflexes in knee and heel were greatly increased; Babinski could not be elicited because of insensibility of the man's soles. Oppenheim reaction was negative, as well as Strümpel's tibial phenomenon, consisting of accessory movement of the m. tibialis anticus upon flexion of the thigh, especially when this happens with resistance. Muscles and sinews were not painful on pressure: sensibility both to touch and pain intact. Faradisa gave no diminution of direct or indirect excitability. On the other hand, the current which could normally just excite one twitch gave rise to

several contractions in clonic fashion. By ordinary methods, no clonus could be elicited either in thigh or calf.

In arms, trunk, and face, no changes were found. Bladder and rectum normal. Physical signs of internal organs, including the heart, negative; in particular, the increase of pulse frequency (often so characteristic of beri-beri) on changing from the lying to the sitting position was absent. Beri-beri was therefore dismissed as the diagnosis; also the signs of hysteria were absent.

In short, the result of the examination was: spastic paretic gait, increased reflexes; increased direct excitability to faradic current; drawing up of the thigh on changing from lying to sitting posture. This last symptom, first described by Oppenheim, was later given by Babinski as a differential diagnostic sign of cases of spastic spinal paralysis. To explain these symptoms, a disturbance is in the conduction of the pyramidal tracts: the absence of bladder and rectal disturbances, and of the derangement of sensibility excluded myelitis, and necessitated the acceptance of an isolated lesion of the primary motor neurons therefore of the lateral pyramidal columns, and at the height of the 4th or 5th lumbar segment. The condition therefore appeared to be a spastic spinal paresis. Could this rest upon an anatomical lesion, upon a genuine lateral sclerosis, or must we assume a disturbance of conduction caused by embolism of pigment or parasites in the vessels of the cord. Syphilis was considered, but there was no evidence even in the history or in appearances or in the patients sick book records to suggest that, and the patient also denied infection. Rheumatism and influenza were also excluded. The patient was therefore put upon quinine treatment. On the evening on 28th Jan., the temperature was 38°C, and later the temperature several times reached 37·6°C, but by this time after vigorous quinine administration, malarial parasites could be no longer found in the peripheral blood.

During the first days of treatment, the symptoms increased. Walking without help was no longer possible. Passive flexion of the legs was prevented by contraction of the extensors. Accessory treatment was applied in the form of massage, faradism, walking exercises, and psychic treatment. Diet was also prescribed. In the early stages of improvement he walked with the aid of two sticks, and after 14 days or so, managed to walk with the aid of one. Finally,

this also was abandoned, and after an interval of about a month, the patient was able to resume his duties.

In view of the presence of parasites in the blood with temperature reaction, the rapid recovery under intensive quinine therapy and the absence of any other agent after careful search to account for the condition, van Driel considers this a case of spastic spinal paresis due to tertian malaria. He suggests pigment or parasitic emboli of the vessels of the cord as the probable mechanism of production.

Cases of Landry's syndrome with malaria have been recorded by Leniers, Pozzili, Boinet and Saldbert. Also cases suggesting syringomyelia—of which examples are here given.

CASE: *Syndrome of Landry's paralysis in a malarial patient (Dumolard and Plotter).*

H., aged 36, born in Algeria of French parents, entered Mustapha civil hospital, 29:7:08, with complete paralysis of legs and trunk, which had occurred 5 days before. He looked delicate, but said he had always been very resistant to fatigue. One brother died of tuberculosis. He himself had always been well, except for malaria contracted two years before. No evidence of syphilis, but history of slight alcoholic excess.

His malaria did not appear to have been very severe, and consisted of attacks recurring at irregular intervals. At first he had fever for about 3 months, each attack consisting of pains in the head with rise of temperature, unaccompanied by feeling of heat, shivering or sweating. Sometimes latterly, fever upset him a bit, but not enough to make him stop his work.

On 24th July, he had a little fever in the morning, was working on the scaffolding of a bridge in process of construction when he was suddenly taken with formication, numbness and loss of power of the feet, which failed him. Believing the condition was transitory, he sat down for a moment, but as it persisted, and fearing he might fall off the scaffolding, he got up again with difficulty, and put his arms over the bridge and tried to drag himself to the awning near the dockyard a few metres away. There he lay down on his camp bed. From this moment, the paresis became worse,

giving place rapidly to a complete ascending paralysis of the legs, and preceded by numbness and tingling. By the 26th July, the paralysis had reached the thighs; by the 27th, abdomen and trunk were involved; on the 28th, slight tingling appeared in the hands and arms. On the 29th July, he arrived in hospital where he was examined next morning.

General condition looked serious; there was a flaccid paralysis of lower extremities and trunk; unable to make the slightest movement of lower limbs; flexion and extension of trunk impossible; patient lies quite immobile in bed; abdomen shows meteorism; marked constipation; retention of urine; hands are tingling and incompetent. Breathing begins to be embarrassed. R., who realises the gravity of his condition, asks anxiously about the fate that waits him.

The muscles are flaccid and wasted, without there being localised atrophy; superficial and tendon reflexes are abolished in the paralysed parts, only the plantar reflexes persisting extensor, and well-marked on both sides. Complete anaesthesia to touch, pain and heat up to the level of an almost horizontal line through the lower end of the sternum. It is a remarkable fact that there is preservation of muscle and bone sense, sensation of position of his members, and passive movement are accurately perceived and correctly interpreted. Eyes and intelligence normal. Spleen not apparently enlarged, neither by palpation nor percussion, but meteorism makes it difficult to examine this organ. Liver and heart normal; pulse 75, regular. Urine of normal specific gravity, and contains no sugar, albumen, or lead. No fever.

This was the condition of the patient on 30 July. Next day, the 31st, the seventh day of his illness, to our great surprise he seemed a little better. His expression looked better, sensation had improved. A spinal puncture was done, and fluid drawn off. The cerebro-spinal fluid looked normal, and was negative for micro-organisms on microscopic examination, and to culture. There was a marked lymphocytosis, however, 12-15 cells per field.

On the 1st Aug., improvement is manifest. There is slight voluntary movement of the left leg, urinary retention has cleared up, pain and sensation has returned to the level of the umbilicus, meteorism has diminished, there is a little fever, and a complaint of

slight headache.

By 2nd. August, he is able to sit up in bed, to lift his left leg off the bed, and to move his toes; on the right side, slight abduction and adduction of the thigh is possible; touch and pain sensation have returned in the legs, and the left knee-jerk is present.

By 3rd August, sensation is complete, the knee jerks are both present, but Babinski is still present on both sides.

On 5th August, about mid-day, sudden onset of fever with violent headache, without shivering or sweating. Temperature, 39·8° in axilla; naso-labial herpes. Blood film shows malarial parasites. Patient says this attack of fever was similar to the one (which was less violent) he had the day the paralysis began. 25 cgms. quinine were given 6 times a day for 3 days. This treatment was continued weekly during his stay in hospital. 7th August, paralysis and anaesthesia continued to recede; intestinal paralysis disappeared and spleen becomes easily palpable. Babinski persists on both sides. On 8th August, general condition is much better, and patient asks to get home.

On 17th August, Babinski, the only remaining sign of the disturbance, disappears on the left side, but persists on the right side till the next day.

On the 20th August, patient walked out of the hospital alone feeling well, it being impossible to keep him longer under observation.

CASE: Ascending paralysis, abatement, syringomyelia syndrome. (Dumolard, Aubry and Frolard).

25:2:1910. F.M., gardener, aged 34, admitted to hospital in Algiers unable to walk. Family History negative. Grand-parents long lived, 82 and 95. Four healthy brothers and two healthy sisters. He was very vigorous, had had no serious illness, and no nervous affection.

12 years ago, he got malaria near Philippeville, and since then attacks returned in June, July, and August. Ten years ago, after a month's severe fever in August, and after horse-riding he went to bed with his legs benumbed. Formication tormented him.

After further violent attacks, trunk and superior extremities became involved (with exception of right arm and head), and he

became comatose and remained so for six days. He was incontinent, and all the paralysed parts lacked sensation. Fingers were shrunken with exception of thumb and index. This condition lasted three months. After that, power and sensation gradually returned in the order in which they had occurred, leaving him with general diminution of energy, and especially diminished power of hands and feet.

During six years he remained in this state and attended to his business. Each summer he had a recurrence of malaria in spite of taking quinine.

Four years ago, he had a violent febrile attack (temperature, 41·8°) followed by icterus, epistaxis, tender liver and spleen, and later by paralysis similar to the first. It was less tenacious at this time, and three months after, when almost well, he had a fresh series of attacks with two days' coma, and a reappearance of the same paralytic phenomena. In a month, the paralysis improved, but not completely, and consequently he came to hospital where he exhibited a spastic steppage gait. There is a general loss of strength, a marked difference in the strength of the two hands—the left being stronger—he has drop feet, and the great toes are extended.

There is marked atrophy of feet muscles, especially the interossei. Muscles of calves and thighs appear intact; the buttocks appear diminished in size, the sacro-lumbar masses are unequal, and show a very marked depression on the right side producing a lumbar scoliosis. The hands are markedly atrophied, with limitation of movement; marked atrophy of thenar and hypothenar eminences. Atrophy extends to middle of forearm; muscles of face and neck are intact. Knee jerks are exaggerated, double Babinski. Right eye shows sympathetic syndrome (Claude Bernard and Horner). Left eye shows nothing abnormal. Sensation—a band twelve fingersbreadths in region of liver, of anaesthesia. Cerebro-spinal fluid normal. Liver and spleen enlarged. No albumen or sugar in the urine.

Non-progressive amyotrophy affecting regions of hands, feet, sacro-lumbar regions, scoliosis, spastic paraplegia, and syringomyelic dissociation; indicating three damaged foci, one to the right of the brachial swelling of the cord; one in the lumbar cord, also more to the right, and one below the sacral cord.

The patient was never fevered during observation in Algiers,

and no parasite was found in the blood, but the case is considered of malarial origin.

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CHAPTER XXVI.

SPECIAL SENSES.

The special senses come in for a share of disturbance in malarial infection and many records of such occur in the literature as affecting vision, hearing and equilibrium, and smell and taste, and their frequency appears to occur in the order given.

DISEASES OF THE EYE.

DISEASES OF THE EYE.

Almost every conceivable disturbance of vision has been noted. Extra-orbital disturbances, such as hemianopsia, extra-orbital muscle paresis, nystagmus have been noted in moderate frequency, often associated with other neurological disturbance such as coma, meningitis, and other cranial nerve paralysis especially 5th, 7th, and 8th. Hemianopsia was noted in hundreds of cases in Macedonia in the hot season, by Chavernac.

Many of these disturbances are transitory like other malarial affections, but in a small minority the lesions become permanent. (Cf. Chapter 23, especially under meningitis).

Conti notes numerous malarial eye affections among the inhabitants of Sardinia. Conjunctivitis was frequent, generally passing with each malarial attack. He also noted intermittent haemorrhage of the conjunctival tear canals. Keratitis, herpes of the cornea and the orbital neuralgias were not uncommon. Optic neuritis occurred with moderate frequency, particularly in cachectics Retinal haemorrhage and retino-choroiditis also occurred. Intermittent dimness of vision and amblyopia was a not uncommon complaint and mostly cleared up, but sometimes led to complete blindness. Other conditions observed were cramp of the retinal vessels with intermittent amblyopia; peripapual retinitis with oedema; retino-choroiditis chronica; opacity of the vitreous; hemianopsia and hemeralopia.

Yarr defines three varieties of conjunctivitis associated with

malaria:

1. Intermittent opthalmia—which Griesinger maintains is nearly always unilateral, with lid swelling and discomfort, but no neuralgic pain. It frequently occurs periodically, even replacing attacks, and is cured by quinine, while ordinary treatment fails.

2. Conjunctival injection, due to neuralgia of 5th nerve. Trigeminal neuralgia is very common in malarial subjects. The conjunctivitis associated with it is generally very slight.

3. Epidemic conjunctivitis. Several epidemics of conjunctivitis have been traced to malaria, e.g. that in South Carolina in the Summer of 1882.

Epithelial xerosis is often associated with malaria but it is probably only one of several causes of xerosis.

Yarr distinguishes three types of keratitis associated with malaria.

α. Demiritic, which was observed in 120 malarials by Kipps, who was convinced of their malarial origin. There was photophobia, lachrimation, supra-orbital neuralgia, generally corneal anaesthesia, narrow serpiginous superficial ulcer of cornea which soon appeared and was cured rapidly by anti-malarial treatment.

β. Keratitis profunia, noted by Fuchs, and others.

γ. Vesicular keratitis (Herpes corneae). Dolo revues 40 cases of which 13 were in malarial subjects and accompanied by herpes of lips and nose.

Superficial stellate ulceration of the cornea was the most common eye complication seen by Goodall in Macedonia.

Recorded cases of iritis, according to Yarr, are not numerous. They are generally associated with violent pain and photophobia. Di Fede records a case of this kind—bilateral malarial iritis in a woman of 40. Similar cases are recorded by Treacher Collins, Yarr, White, Pachin, Pennoff, and Selück, who saw 5 cases with posterior synechiae in soldiers in the Caucasus. Mannaberg cites Brown and Tangemann as recording cases of malarial iritis, and iritis with hypopyon ascribed to malaria are noted by Staub and Quaglino.

Cataract as a result of malaria is recorded in two cases of by

Ragot. One, a boy of 15 with coma, on recovery the sight began to be affected, and three months later he was found to have a soft cataract in each eye. The other case was that of a Mulatto girl of 16, who had grave malaria lasting three days. Thereafter her sight began to fail and 9 months later she was found to have a soft cataract in each eye.

Monocular ciliary spasm was seen by Manson in Hong Kong with malarial aphasia, all of which was cured by quinine. Cycloplegia was seen by Manhaert, Bull and others.

Chiarini (Rome) says that ocular complications are not common in malaria, but are sufficiently frequent to merit attention. He says that eye troubles are mostly caused by the malignant tertian form of malaria and that the parts of the eye most prone to malarial lesions are the retina and optic nerve.

Amaurosis is relatively frequent and is often temporary and intermittent. Pennoff, who made a study of ocular troubles due to malaria in a regiment of soldiers stationed at Tiflis, says that he himself, while suffering from intermittent fever, had for a period of 24 hours complete amaurosis of the left eye, accompanied by aphasia and left sided hemiplegia and hemianaesthesia. He (Pennoff) says also that another physician (Dr. Reich) was taken one day during a febrile attack with bilateral hemianopsia, which disappeared the following morning. The amaurosis is generally bilateral, lasts from 15-30 minutes up to 10 hours or more; it generally occurs during the initial chill, continues throughout the paroxysm, and passes off with the onset of sweating. There may be only a single attack, or it may be intermittent, coincident with the febrile paroxysm. It is generally tertian, rarely quotidian when recurrent. When the attacks are quotidian and come on during the evening hours, the affection acquires an extra-ordinary resemblance to hemeralopia, and some writers have accordingly described a form of hemeralopia due to intermittent fever. Stöber records a case in which there first appeared a hemeralopia, and then after several days the attack occurred in full daylight and caused a complete bilateral amaurosis which was cured after a few days by quinine. Chiarini says that during the amaurotic attack the pupils are dilated, and respond sluggishly to light, and that ophthalmoscopic exam.

usually reveals no apparent alteration in the fundus. It is not always of temporary character, but is often persistent and may even end in permanent blindness from atrophy of the optic nerve. He saw two cases of malarial amaurosis with optic neuritis, in the same year in Rome. One of these was a child who ended up with optic atrophy and permanent blindness of both eyes. The other was a woman who after two weeks of almost complete blindness had a partial aptrophy of the optic nerves and was left with moderate acuity of central vision and marked concentric limitation of the visual field. Both these patients had grave aestivo-autumnal fever.

Monier-Vinard found hemeralopia in three cases. Mine found amaurosis the most frequent eye disturbance from malaria, and retinal haemorrhage was not uncommon in pernicious cases. Fukuzawa (quoted by him) in a 107 malarials, found retinal haemorrhage in 2·7%.

Guarnieri (quoted by Chiarini) found few and slight changes in retinal vessels, such as swollen endothelial cells, prominent nucleus and very fine pigment granulations in the protoplasm. Degenerative changes were very rarely found. In the choroid, he found almost all the vessels full of large leucocytes, with vesicular nucleus, rich in pigment, in granulations of haemoglobin and in red corpuscles containing plasmodia. Guarnieri explained temporary blindness as due to temporary circulatory disturbance, or globular and phagocytic stasis in the smaller vessels of the retina and choroid.

Chiarini describes a case of optic neuritis associated with encephalitis and coma which is detailed in the chapter on cerebro-spinal syndromes. He says that amaurosis may be due to other causes than optic neuritis and quotes a case of Despagnet where it appeared to be due to generalised retino-arteritis. This was a young woman who had repeated attacks of malarial fever in Africa, and on the 5th attack became totally blind. After relief from the malarial attacks, the sight did not immediately return, and 40 days later in Paris, Despagnet discovered by the ophthalmoscope a generalised retino-arteritis. After treatment with quinine and potassium iodide, the patient recovered relatively good sight, but with a greatly restricted visual field.

Retinal haemorrhages with or without amaurosis or amblyopia have been quite frequently observed in the course of malarial

infection. One such case of the writer's is detailed in the chapter XXIII, Meningitis Series, Case III. W. H. Manson reports two cases, both sub-hyaloid (affecting both eyes in one) in malignant tertian infection.

Sulzer (quoted by Chigrini) who saw many instances of malarial eye trouble in patients from Java, Borneo, and Sumatra frequently observed chronic optic neuritis in those suffering from malarial cachexia. The most characteristic subjective symptom was marked oscillation in the degree of visual acuteness, diminutions in vision as low as ⅟₁₀ may improve so much within 2-3 weeks as to attain an acuteness of ⅓ or even ½, then to fall again in the course of a few days to ⅟₁₀. The condition is always bilateral, but onset in the two eyes is not usually synchronous. The visual field remains intact, or is at most very slightly narrowed concentrically. Colour perception is always normal except in the cases which end in atrophy. In some cases, hemeralopia was found. Ophthalmoscopically, the optic disc is prominent and has a grayish or blackish red tint, the retina has lost its characteristic brilliancy in the parts surrounding the papilla, the contour of the papilla is indistinct and the veins are dilated and tortuous. Sulzer lays special stress upon the colour of the papilla as a diagnostic sign of importance. He observed partial atrophy of the optic nerve with irregular narrowing of the visual field in 8% of his cases of chronic optic neuritis. In about one third of the cases, he found peripheral haemorrhages of the retina, but absorption occurred rapidly without leaving any pigment deposits behind. Bull has described two cases of white atrophy of the optic nerves of malarial origin without any sign of preceding inflammation, with concentric limitation of the visual field, and dyschromatopsia.

Retinal haemorrhages apart from optic neuritis and retino-choroiditis have been noted by Pennoff, and many others in chronic malaria. He saw a case of malarial cachexia with small retinal haemorrhages accompanied by hemianopsia and dyschromatopsia, which occurred with every new febrile paroxysm. Fairley and Dew in 80 autopsies on malarial subjects found retinal haemorrhages several times.

Von Kries noted two cases of intra-ocular haemorrhage consequent

on malaria. In one there was multiple retinal haemorrhages in both eyes; in the other there was a severe haemorrhage in the vitreous of the left eye.

Serous effusion into the vitreous. Chiarini writes: "Seely in 1882, and more recently Sulzer, described a special change in the vitreous humour associated with chronic malarial infections. This consists in a whitish infiltration of the vitreous body, occurring at intervals and causing an almost complete loss of sight. On ophthalmoscopic examination, nothing is seen beyond a white reflex, characteristic of this affection. Seely attributes this change to a serous infiltration into the vitreous occasioned by chronic malarial poisoning. In the two cases described by him, after an oscillating course for a few months the affection terminated in recovery, quinine having been given regularly. One of these cases was complicated with left supra-orbital neuralgia which disappeared together with the eye trouble; in the other case, there remained permanently a few movable flocculi in the vitreous. In two of the cases observed by Sulzer, the termination was more grave. These patients suffered from severe malarial cachexia with profound anaemia; the diffuse infiltration in the vitreous, which was already of long standing when the patients came under observation, was not completely absorbed in either of the cases, but gave rise to the formation of many movable flocculi joined together to form a sort of cobweb through the meshes of which the vitreous, still somewhat opaque, allowed the fundus to be seen only obscurely, yet with sufficient distinctness to permit the recognition of the atrophic white appearance of the optic disc. In a third case, which came under observation at the beginning of the trouble, Sulzer obtained a complete cure by the use of sulphate of quinine in large doses. Pennoff also described a diffuse opacity of the vitreous in cases of intermittent fever, but they were always associated with changes in the iris and choroid".

Bargy records a case of haemorrhage into the vitreous during malarial attacks. Haemorrhage into the vitreous the result of a single paroxysm was reported by Kries. Sull observed 17 cases of similar haemorrhages, the majority unilateral. Almost all the patients were over 40 years of age (Mannaberg).

Chiarini also notes the occurrence of albuminuric retinitis in association with malarial nephritis and accompanied by oedema and albuminuria, where amblyopia and amaurosis have been complained of. These have usually occurred in cases of malarial cachexia, and the retinal trouble has been secondary to the renal lesion rather than due to the direct action on the retina.

W. H. Manson, who gives a resumé of the ocular sequelae in 12,000 malarial cases, points out that it was exceedingly common to find a slight icteric tint of the conjunctiva after each attack. The yellow colouring, sometimes considerable, involved the retro-tarsal fold, extended forward onto the bulbar conjunctiva and disappeared as the patient recovered. He suggests that this may be a valuable suggestive symptom in the diagnosis of pyrexial conditions of uncertain origin.

Ulceration of the cornea was the most frequent sequel and was not very common. It was never seen accompanying the primary infection and the parasite was benign tertian, though some of the cases had M. T. superadded. The condition began with hyperaemia, and watering of the eyeball, followed by the formation of a small bleb pushing up the corneal epithelium. The condition when first seen had generally a small streak of ulceration on the cornea, but in the most pronounced cases there was a definite dendritic ulcer, when the deeper corneal layers may be involved. It was often central and therefore interfered with vision. They were very painful, healed slowly, and recurred with each malarial attack. Iritis was a frequent accompaniment, though it did not occur as an isolated lesion in this series. Local treatment was normal saline and atropine. Absolute alcohol was discarded on account of pain. In one case Herpes Zoster Opthalmicos accompanied the ulceration.

Wauban during malarial epidemic in Macedonia in 1916 was struck with the frequency of ocular pains and conjunctival injection. Patients arrived pretty constantly with eyes red and lacrimosed. In 72 malarial cases, mostly acute, he found ocular disturbance 55 times. In these 55, 20 times there was no ocular pain, and 22 times there was no conjunctival injection.

Werner describes three cases of retinal haemorrhage of malarial origin. Good plates accompany the original article. He summarised

the literature on the subject, and distinguished between small peripheral retinal haemorrhages and large peripapillary and macular haemorrhages. He considered that these haemorrhages depended less upon the kind of parasite, and more upon the degree of anaemia present. According to him, the macula lutea is the sight of election for these haemorrhages, and in two out of three of Ziemann's cases of malarial retinal haemorrhage, the macular was alone involved. Prognosis was generally good, and recovery with resorption is largely parallel to recovery from the accompanying anaemia.

One of Werner's cases is given as an example.

CASE I. Retinal haemorrhage in Malaria (Werner).

Salesman, aged 28. Ill with malaria in 1903, in the Cameroons, and recurrent attacks since.

23:1:10. Blackwater fever, attacks severe and lasting several days. Since then has complained of defective vision—defective definition.

16:2:10. In hospital—pale and slightly icteric. Spleen enlarged down to umbilicus. Numerous M. T. parasites in blood. Basophilia, polychromatophilia.

Eye Examination: Both eyes show visual defects. R $\frac{1}{6}$, L $\frac{5}{6}$. Double central scotoma. Ophthalmoscopic exam. of right eye shows large haemorrhage in the macula, and three smaller haemorrhages in the course of the larger veins. Left eye also shows macular haemorrhage, though less than in right eye.

Gradually increasing doses of quinine given until after 8 days gram doses are taken. Parasites and temperature diminish rapidly to normal in a few days. Vision steadily improved and haemorrhages diminish rapidly so that patient left hospital on 10:3:10 before absorption was complete, feeling well, wearing dark glasses, and proceeding with quinine.

Wood noted marked failure of accomodation in a malarial subject in East Africa. Headache was complained of, together with inability to stand sunlight and inability to read. After a severe malarial attack, tenderness to light lasted about a week, but difficulty in reading lasted longer—a month or so, if no further attack

occurred to keep it going. Neutral tint glasses and an allowance for reading of a dioptre or more were required. Similar cases are noted by Bull, Stellwag, and Stilling (Mannaberg).

Optic neuritis has been observed with moderate frequency both in acute and chronic form. Ribon, writing on different forms of meningitis, says that optic neuritis is more common with malarial meningitis than with tubercular meningitis, that there is thrombosis of central vein of retina, retinal haemorrhages, and irido-choroiditis. He also notes that malaria often gives rise to eye troubles (Columbia), such as asblyopia and amaurosis, often transient; conjunctivitis, keratitis, corneal herpes; and retinal haemorrhages with or without neuro-retinitis. Cases have been recorded by MacNamara, Jacobi, Sulzer, Poncet, Guarnieri, Chiarini, Duigeon and others.

Signorelli describes a case of optic neuritis in a girl of 16. She had had malaria for 10 days, which disappeared under quinine but she remained weak. After two months apyrexia, she suffered from headache and vomiting for about a week. Then suddenly she lost the sight of the left eye, and the following day, of the right eye. There was no fever, but liver and spleen were swollen. Malignant tertian parasites were found in the blood. The fundi showed double neuritis and papillary stasis. Malarial optic neuritis was diagnosed and large doses of quinine were given with complete recovery.

Leonard Duigeon describes a case of malignant malaria in a soldier who died comatose in the Balkan Area during the War. The vessels of the retina, iris, and optic nerve, as well as the vessels of the white matter of the brain, were packed with parasite-laden red cells, with thrombosis and punctate haemorrhages (see Figs. 1 and 2)

Henry Smith records six cases of night blindness in natives of the Punjab, where night-blindness is very common. They were of both sexes, and their ages ranged from 9 to 25 years, and all showed progressive retinal degeneration at various stages. All had a malarial history. He also records three other cases of malarial retinitis, one that of a male native who lost his sight suddenly four years before during severe malarial fever with vomiting, which lasted for one and a half years. Ophthalmoscope showed atrophy of both retinae.

Hemianopsia may be unilateral or bilateral. Pennoff observed

lateral hemianopsia preceding the paroxysms. De Schweinitz reported a case of temporal hemianopsia with malarial parasites in the blood which was cured by quinine.

CASE II. Homonymous hemianopsia in Malaria. (A. L. Weakley).

Patient was lieutenant, aged 28. Admitted to hospital with malignant malaria and examined by the author on account of bad sight. The pupils were slightly larger than normal and reacted sluggishly to light. The vision of the right eye was 6/24ths., and left, 6/36ths. The fundi were healthy, and the discs of good colour. The fields showed right homonymous hemianopsia, absolute and complete, for colours and white.

The condition began suddenly three weeks previously with severe head pain followed by a period of unconsciousness. He now has loss of memory, and confusion of thought.

There is probably a lesion near the angular and supramarginal gyri, and the posterior part of the internal capsule on the left side; possibly a blockage of a vessel or vessels by malarial parasites.

Dyschromatoxia has been less frequently observed (Pennoff, De Schweinitz, U. Raynaud).

According to Mannaberg, hemeralopia, amblyopia, and amaurosis are the most common functional visual derangements. Séqari met them frequently in Madagascar; Sulzer and Poncet mention them, and U. Raynaud gives several examples.

Ischaemia of the fundus, associated with amblyopia, was observed by M. Raynaud, and Moursou—both times in association with local asphyxia of the extremities. Ramorino and Decrem observed cases of ischaemic intermittent amaurosis which were cured by quinine. The ischaemia is characterised ophthalmoscopically by contraction of the vessels and pallor of the disc.

Paralysis of extra-orbital muscles have been observed and then not uncommonly with other nervous symptoms. A case of this kind is recorded by Britto.

CASE III. Extra-orbital muscle paresis. (Britto).

Man aged 27 at Bahia, Brazil, with ocular palsy affecting the right eye. There was paralysis of all the muscles except the external rectus, with marked dilatation of the pupil and ptosis of the right eyelid. Tumour and gumma were considered and excluded. There was a marked large mononuclear increase, and malarial parasites and pigmented leucocytes were found in the blood.

Malarial neuritis of the right third and fourth cranial nerves was diagnosed, and energetic quinine treatment resulted in complete recovery.

CASE IV. Left hemiplegia, with left 5th and right 6th nerve paresis (Descomps and Quercy).

Left hemiplegia, with paralysis of the right sixth nerve, and paresis of left 5th nerve came on suddenly in course of benign tertian attack in a man of 24 who had contracted ague in Macedonia 10 months previously. Otherwise quite healthy. After 8 months, power had been regained almost completely in the limbs, but the condition of the cranial nerves remained unchanged. Examination of the C-S. F. at this time -ve.

W. H. Manson records three cases (Wassermann -ve) in otherwise healthy men, shortly after malarial attacks; one of external rectus paresis with recovery; one of paresis of accommodation with recovery; and the third a total ophthalmoplegia of the left eye occurring 10 days after an attack of malaria. The paralysis did not recover.

Hypersecretion of tears has been frequently observed in latent supraorbital neuralgia, and cases have been noted apart from neuralgia, both during and before paroxysms. Moursou saw a marine with paroxysms consisting of fever, vaso-motor disturbances on the right half of the face, transient amblyopia, and hypersecretion of tears. Later this last symptom occurred alone without fever until cured by quinine (Mannaberg).

MALARIAL and QUININE AMBLYOPIAS.

It is well known that quinine produces in some people mild or severe toxic effects (See Section on Quinine Poisoning in Chapter 30.)

All sorts of complaints, indicating varying degrees of hypersensitiveness to the drug have been recorded, sometimes with quite small doses, at other times with large or massive doses. Symptoms noted as associated with quinine poisoning include pressure on the stomach region, vomiting, ringing in the ears, vertigo, deafness, erythema, urticaria, purpura haemorrhagica, neuralgia of the fifth nerve, (Schulz) diuresis, polyuria, pain in the ears, stupor, confusion, delirium, dyspnoea, with or without great anxiety and sense of impending death. Amblyopia has been recorded in varying degrees by various authors, in some cases going on to complete blindness, transitory, partial or permanent. Geschwind found in a case of amblyopia following continuous administration of quinine, a filaceous clouding of the vitreous humour, which might explain the persistence of the derangement of vision (Mannaberg). Fatal cases have been recorded as a result of quinine anaphylaxis.

Roberts observed the following symptoms in a woman after 8,0 quinine sulphate; unconsciousness, fall of temperature, general lividity, slowed superficial respiration, small thready pulse, (45 to the minute), pupils widely dilated, staring, abolishment of tendon and skin reflexes, coffee-ground vomit, in addition to deafness that lasted a week and blindness that continued 5 months. (Mannaberg).

Conti (Sardinia) considers that quinine amblyopia is distinguished by

1. Quinine in large doses.
2. Sub-cutaneous quinine followed by deafness.
3. Pupils dilated and not reacting to light.
4. Vision quite lost for some time.
5. By ophthalmoscopic examination: ischaemia of retina and optic nerve.
6. Thinned fundal vessels, and yellow spot changing colour.
7. Condition lasts a long time.
8. Defect of vision, especially with regard to colour.
9. Benign prognosis—even after amaurosis of months.
10. Cure by suspension of quinine.

Dosage need not be large, however, to produce ocular

phenomenon—hypersusceptability with a small dose may produce the same result. Seeligsohn (quoted by Ziemann) describes in a case of quinine amaurosis—narrowing of the vessels, slightly swollen papilla, diffuse whitish clouding of the retina, and a cherry-red spot in the macula lutea.

These features are largely borne out by Traquair, who has written so comprehensively and concisely on this subject that his article with three examples is largely embodied here. He says that considering the amount of quinine consumed every year for various conditions, permanent visual damage is rare in this country. The following three cases recorded by him are worthy of note.

CASE V. Quinine Amblyopia. (Traquair).

Miss M.M., aged 23, seen in July, 1916, had been feeling "run-down" and had been taking quinine as a tonic. About as much as would go on a threepennybit was taken two or three times a day for three weeks. Then on one occasion, rather more than a teaspoonful was taken in one dose (these amounts correspond to about 1 gr., and about 20 grs. respectively of ordinary crystalline sulphate of quinine). Stupefaction, tinnitus aurium, and loss of sight ensue. 30 hours later, the stupefaction and tinnitus were better, but vision remained "quite gone" for a week. An ophthalmic examination two days after the quinine had been taken showed absence of perception of light in each eye; pupils dilated and inactive to light. The fundi were found normal. Vision gradually returned, and four months later was 6/24ths in each eye, fields of vision much contracted, pupils unequal but reacting to light. In July, 1918, after nearly 8 months, I examined her eyes. Vision was now 6/9ths partly with the right, and 6/9ths with the left eye after correction for astigmatism. The pupils were of normal size in ordinary daylight, but tended to dilate slightly after primary contraction to light. The fields of vision were greatly contracted even for comparatively large objects. Central colour vision was good. The fundi showed optic atrophy, with much contracted retinal vessels. She complained of bad vision in the dusk, and of inability to "see if things fall".

CASE VI. Quinine Amblyopia (Traquair).

E.P., aged 28, female. In May 1918, her doctor informed me she had " a bad, almost hopeless pneumonia". Hypodermic injections (she was not able to swallow) containing 15 grs. quinine-urea hydrochloride were given every four hours, commencing late on the first day, and ceasing early on the third day. In all, 8 injections were given, equal to 120 grs. of the combined salt. Tinnitus began after the third injection, and the next day, she was very deaf. Early the following morning, after the last injection, vision became very dim, and a few hours later total blindness supervened. The quinine was stopped and hydrobromic acid given. 8 days later perception of light began to return, and a week afterwards colour could be detected. Improvement continued for the next three weeks, but was not noticeable after that time. When seen by me three months later, the vision of the right eye was 6/6ths partly, and of the left eye 6/36ths. The fields of vision, especially for colour, were much contracted. The optic discs were pale and the retinal vessels constricted. She complained of "dimness" over the eyes, and when last heard of described her vision as "very unsatisfactory" and not improving.

CASE VII. Quinine Amblyopia. (Traquair).

J.R., male, aged 53. In July, 1918 had influenza. Quinine was taken for one night only, every four hours in cachets, containing 3-5 grs. each Tinnitus soon came on, and when he got up after two or three days, he found he had to be led about as he was unable to see. As far as I have been able to ascertain, the total amount of quinine consumed in about 12 hours was under 30 grains. The memory of the circumstances is very hazy; evidently a certain amount of intoxication was soon produced. Two months later he was seen at the Royal Infirmary by Dr. Sym, who kindly allowed me to use his notes. His vision was 6/9ths in the right eye, and 6/18ths in the left. The fields were contracted. A trace of pallor was noted in the optic discs, especially the left one. No reduction in size of the retinal vessels was seen. A month afterwards, he came under my observation. Vision was now 5/12ths in each eye. In

bright light, the pupils were equal and normal in size, in subdued light, the right pupil was rather larger than the left. Both pupils contracted well to light, but the right dilated slightly after primary contraction. The fields of vision were greatly contracted, especially the right field. The fundi showed pallor of the optic discs and constriction of the retinal vessels, both changes being more marked on the left side. His chief complaint was difficulty in reading.

Author's Comments: It will be noted that two of the cases were associated with the recent epidemic of influenza and pneumonia. In one case, the amblyopia was caused by a relatively small dose, in the other two, comparatively large, but by no means massive doses had been received.

The first symptom was tinnitus. Blindness was quickly reached and slowly recovered from. The patients were left with good central vision but restricted fields, partial optic atrophy, and contracted retinal vessels. It is noteworthy that in spite of the good central vision, all the patients complained of inability to see satisfactorily, showing the importance of para-central and intermediate zone vision. An interesting point, bearing on the pathology of the condition, is exemplified by cases V and VII, which had already been examined before they were seen by me. In these cases, the fundus changes had evidently developed after the blindness, and had continued to develop while vision was improving. In case VII also, the fundus changes did not correspond to the visual symptoms in the two eyes.

Two views have been advanced as to the mode of production of quinine amblyopia—one that their action is primarily vaso-motor on the retinal vessels, the retinal cells and nerve fibres suffering secondarily, and the other that the toxic action is primarily on the retinal cells, the visible fundus changes being secondary. The late development of the optic pallor and vascular constriction has been noted by several observers, and is in favour of the second view, which is also supported by the authority of de Schweinitz.

Several points of practical importance deserve consideration. We have seen that the dose need not be excessive or even large. Big

doses are naturally more likely to cause ill-effects, but cases are on record in which amblyopia followed doses as small as 22 grs in 3 days; 15 grs. in 24 hrs., 12 grs. in one dose, and so on. It is hardly necessary to mention that enormously larger doses are quite commonly taken without harm. Idiosyncrasy evidently plays an important role, and it is not possible to state definitely what constitutes a dangerous dose of quinine. There is good evidence that an absolute or relative overdose may produce a state of increased susceptibility, and that persons who have once suffered from quinine poisoning should use only minimal doses or avoid the drug altogether.

The diagnosis of quinine poisoning should not be difficult. Vision is lost, the pupils are dilated and inactive, hearing is affected, headache, drowsiness and even stupor may be present. Such symptoms may be confounded with the result of the disease under treatment, and it is necessary to avoid any such mistake. The opthalmoscopic signs are pallor of the optic discs and constriction of the retinal vessels—features which, as already stated, may not appear for a little time. Later, when some vision has returned, the contraction of the visual fields can be made out. The prognosis is usually good, as regards central vision, but bad as regards peripheral vision. Only in mild cases is completely satisfactory vision recovered, while permanent blindness is the result of only the most severe cases. Improvement is fairly rapid at first, and then goes on more slowly for some months, or possibly even longer.

Treatment, apart from stopping the quinine, is of little avail. A number of drugs have been advocated from time to time, and as is often the case, their diversity indicates their inefficiency. Strychnine, caffeine, hydrobromic acid, digitalis, iodides, and other drugs have all been recommended. Measures directed towards increasing the retinal blood supply, such as the recumbent position, or the exhibition of nitrites, appear somewhat more rational, but their value is doubtful. Obviously, to be of use, treatment must be adopted early.

The main point which should be born in mind is that quinine amblyopia is a condition which can be recognized and checked in its [illegible] by the general practitioner, who is on the spot.

spot

Specialists practically always see the cases too late to be of any service.

In 12,000 malaria cases, W.H. Manson saw no instances of quinine amblyopia or optic atrophy, although it was customary to give up to 60 grs. of quinine by mouth daily, in 30 grs doses. He records two cases of quinine amaurosis, one of whom recovered completely while the other became totally blind. In each case, at least 80 grs. of quinine had been taken at one dose.

While quinine amblyopia may follow large dosage with quinine, the following case by R. H. Elliott exhibits this effect from a very small dose of the drug.

CASE VIII. Quinine Amblyopia, following very small dosage of quinine. (Elliott).

A dispensing chemist stated that within a quarter of an hour of taking a low dosage of ammoniated tincture of quinine for colds, he had headache, deafness, difficulty in seeing clearly, and contraction of the field of vision. The author experimented with him, and gave him 2 grs. of powdered sulphate of quinine in cachet. Before the experiment, the fundi were examined, and found slightly blurred, and surrounded by faint halves, suggesting previous mild optic neuritis. Colour normal. He stated that some years before, he had had influenza, and that his sight had not been the same since.

30 minutes after the 2-grain dose of quinine, he had headache, deafness, and was slow in manner. The optic discs were paler than before, and the arteries slightly but definitely less in colour. Increased difficulty in reading, marked restriction of the fields of vision in both eyes occurred. Three-quarters of an hour after the quinine was given these signs and symptoms were more marked. A control case was unaltered in these respects. A cup of coffee relieved his symptoms. The author considers that the interest in this case lies in the fact that this is the lowest dose of quinine recorded as causing amblyopia.

The differential diagnosis, then would rest with the evidences for malaria on the one hand—parasites in the blood obtained readily, or by the methods adopted in the chapter on latent malaria, etc.

and the features detailed above on the other.

II. THE EARS.

Mannaberg quotes several writers--Weber-Liel, Voltolini, who record ear affections the result of malaria. Weber-Liel mentions intermittent otitis with sharp pain in the ear coming on with chill, sensations of fulness, and ringing in the ears, and vertigo. These symptoms are followed by sweating, pass and recur again, with tertian or quotidian periodicity. Sometimes an exudation is found in the tympanic cavity. The tragus is insensitive to pressure. Puncture of the tympanum or spontaneous rupture does not relieve, but quinine cures. Voltolini has reported cases of intermittent otalgia of malarial origin, cured by quinine.

De Rossi claims to have encountered intermittent otalgia in malarial subjects, the curative action of quinine being very evident. Politzer also asserts the existence of malarial intermittent otalgia. S. L. Frank of Baltimore reported a case of intermittent tinnitus of malarial origin, which was cured by arsenate of quinine. Sugiyama records two cases of malarial otalgia, before and during attacks.

Richardson records several cases of otitis associated with malaria. Porot records a case with painful buzzing in the left ear recurring with each malarial attack, in a man of 39, with quiescent otitis dating from infancy.

Ferreri reports two cases of labyrinthine vertigo. The first was a patient who had suffered from malaria for two years, then recovered, and was again attacked with fever lasting four months. During this latter period, every febrile paroxysm was preceded by deafness and tinnitus and then followed by extreme vertigo and retching. The vertigo was so marked that the patient felt as if he were falling down, and he would actually fall unless he sat down at once. With the appearance of the chill and fever, the vertigo ceased, leaving the patient deaf and bewildered. Recovery took place at about the end of a month under treatment with quinine.

The second case was that of a hunter who had acquired malaria

~~malaria~~ at Sersoneta, a very malarious region, and had had two severe attacks. After many slight aural symptoms in Oct. 1889, he was seized after a febrile paroxysm with deafness and ringing in the ears, and with such severe vertigo that he fell to the earth, the face being drawn at the same time over to the right shoulder. This attack was repeated three times in the course of 10 days, and the patient then consulted a physician, who found an enlarged spleen and aestivo-autumnal parasites in the blood; there was deafness, especially on the right side, together with bilateral tinnitus. He was cured by quinine in two months. The Menière syndrome therefore, though not common, does occur as the result of malaria.

Wolff and Gellé record cases of deafness as the only manifestation of malaria, periodic, and generally with fever, and curable only by quinine. It may occur without fever, replacing the paroxysm.

T. Barr says that malarial fevers may often be associated with labyrinthine deafness, and adds that quinine may contribute to this condition.

Ferreri records a case in which, after two weeks of malarial fever without the use of quinine, the patient lost his hearing in the right ear, and had marked tinnitus; otoscopic examination showed an apparently normal organ. In another case, Ferreri observed a loss of hearing on the right side, following an attack of delirious pernicious fever in a lad of 16 years; objective examination revealed no middle ear disease. Ferreri also records two cases who during the course of malignant tertian infection developed deafness, tinnitus, and vertigo, which he considered, after careful examination, were due to to labyrinthine haemorrhage of malarial origin, (Marchiafava and Bignami).

Alexander records a case of VII and VIII cranial nerve neuritis due to malaria.

CASE IX. Malarial cutaneo-facialis neuritis (G. Alexander).

Man aged 29. Healthy till 22nd March, 1918, when he had a malarial attack with fever, headache, vomiting, difficult hearing in both ears, ear noises affecting both ears, attacks of giddiness with swaying to left and right, and generally associated with nausea and vomiting. He was admitted to hospital and treated for the

malarial attacks which ceased after a few weeks, but deafness and ear noises continued. After three weeks, the vertigo had ceased, except with light exercise, as standing up quickly, rising from bed, etc. There was also tiredness of the legs. At the end of Aug., 1916, another malarial attack, with marked ear noises, nausea, attacks of vertigo and vomiting. Weekly attacks occurred and patient continued in hospital with short intervals till March, 1917.

On March 10th, 1917, a complete left-sided facial paralysis occurred, and at that time, the patient noticed an increase of the deafness and ear noises of the left ear, together with vertigo attacks, nausea, swaying to the right, and vomiting. Alcoholism and syphilis were denied.

Otological examination: 23:3:17. Showed otoscopic findings negative. Loud whisper was heard by right ear at 8 metres, left ear 1 metre. Tuning fork test indicated involvement of both internal ears. Labyrinth: spontaneous nystagmus of small amplitude, and moderate frequency, and rotatory with horizontal component towards the left looking towards the left. Labyrinthine reflex excitability on both sides normal. No attacks of giddiness, but slight feeling of giddiness; moderate swaying to side and marked swaying forwards in the Romberg position; can stand on one leg with swaying; walks backwards with closed eyes on broad track.

The right facial nerve was normal, the left showed complete peripheral paralysis with reaction of degeneration and absence of faradic excitability. Tear secretion increased, soft palate intact. General nervous system normal. Blood and C-S. F. Wassermann tests -ve.

Diagnosis: Slight right-sided and marked left-sided cochlearis affection; left-sided labyrinth involvement, and left-sided peripheral facial paralysis, due to malaria.

The bilateral neuritis began after the first malarial attacks, improved with quinine treatment, and recurred with the malarial attacks 7 months later. The patient was six weeks in the ear department, and had energetic malaria treatment. Galvanism was applied to both auditory nerves (electrodes in both tragi), and left facial daily, later thrice weekly (four milliampères for 5 minutes). After 6 weeks of this treatment, the facial paralysis was almost normal,

and later completely recovered. No recurrence of vertigo attacks while in ear department. The spontaneous nystagmus completely disappeared after three weeks treatment. Hearing of left ear improved to 6 metres whispered voice. Hearing of right ear unchanged. No giddiness on rising; a trace of lateral and forward swaying in Romberg attitude.

Otitis Media:- Acute malarial middle ear disease is described in two forms. In one there is simple hyperaemia of the tympanum with a serous or muco-serous exudation; the other is a true purulent otitis media. The first of these is probably that mentioned by Weber-Liel and Hotz, where there is intermittent otalgia, often violent, and cephalgia presenting all the symptoms of the most grave suppuration of the drum, while otoscopic examination shows nothing but a slight tympanic hyperaemia. De Rossi (Rome) and others claim to have observed suppurative middle ear disease of malarial origin. It may be that some at least of these cases are mixed infections, where the malarial parasite has lowered the resistance of the host to other organisms in the ear, throat, and nose. A case of this class is recorded by Ruttin.

CASE X. Acute otitis and malaria. (Ruttin).

A. P., aged 24, came to Russian Front, 20:10:15, and was sent back through general weakness. 25:8:16, Italian Front. 30:3:17, fell from a rock and was about 2 hours unconscious—had fractured right arm.

8:4:17. In Reserve Hospital, with arm in Plaster of Paris. Had headache, giddiness, ear pain, no ear discharge, and no ear noises.

11:4:17. Discharge right ear: formerly ears quite sound.

15:4:17. Purulent discharge right ear. Meatus red at inner end. Drum red and anterior lower quadrant perforated. Pain in mastoid, especially at point. Left ear meatus dry; in anterior lower quadrant of drum a thin scar.

Diagnosis: Purulent otitis media. Strabismus divergent of right eye. Intracranial complications. Transferred to Vienna.

Ear Clinic, Vienna, 15:4:17, reports: Left ear—drum and

function normal. Right ear—irum red, swollen and bulged. Perforation, anterior lower quadrant. Tenderness of mastoid. Hearing for conversational voice, 1 metre; whispered speech, at the concha. Weber—to right. Rinne, -ve. Schwabach, normal. C_1 and C^4 positive; no spontaneous nystagmus; no fistula, calori c reaction typical.

Blood, 19:4:17. Leucocytosis. No malarial parasites.

Operation, 21:4:17. (Ruttin). Usual incision, mastoid sclerotic. Attic filled with pus. Sinus bared 2½ cms. Seems normal. Dressed. Temperature normal. Bacteriological examination of pus shows streptococcus pyogenes. Rise of temperature to 40°C from day after operation, with tertian periodicity. Tertian periodicity of temperature also existed for three days before operation, though no parasites were got in the blood. Maybe due to sepsis or malaria.

26:4:17. Tertian parasites found in the blood—recovery.

Conti records that the Roman school holds that the nuclei of the acoustic nerve may be involved by hyperaemia, haemorrhages, and embolism (Ferreri). He considers that hyperaemia, and thrombosis of the middle ear, and thrombosis of the inner ear and the labyrinth explains how malaria produces auditory disturbances. The changes most noted have been:

1. Intermittent otalgia.
2. Labyrinthine giddiness—curable by quinine.
3. Deafness labyrinthine, and labyrinthine haemorrhage.

This deafness treated by quinine usually disappears rapidly.

It would appear then, that the ear comes in for a share of disturbance by this blood-borne parasite, though ear disturbances do not often bulk large in the symptomatology.

III. THE THROAT AND NOSE.

Disturbances of taste and smell have been occasionally recorded as consequent on malarial infection. It is probable that they are

more frequent than the literature would suggest, as they are probably associated with more imposing cranial lesions in diffuse forms of encephalitis, meningitis, bulbar paresis, etc, and less frequently occur as isolated disturbances.

Da Matta (quoted by Ziemann) observed a woman near Manaos who, in association with a malaria attack, had a severe headache spreading to eyes and nose. It lasted for a few hours in the forenoon and then suddenly subsided. No fever, but exhaustion. Loss of sense of smell was noted. No parasites were got in the blood, but the author considered the condition as due to malaria and recovery from the neuralgia and loss of smell followed treatment by 30 cgms. of quinine daily, within four days.

The following case recorded by Richarison, simulating frontal sinusitis, is of additional interest as showing some disturbance of taste.

CASE XI. Frontal sinusitis. (C. W. Richardson).

J. W. S., fireman, aged 24, came complaining of intense frontal head pain. Marked tenderness over left frontal region, especially marked at floor of sinus. Nasal and post-nasal regions normal.

Admission to Hospital, 28:12:15. History: Lives in Maryland. Mother, 47, alive and well. Father 51, alive and well. Both grandmothers alive and well, and aged 74 and 75 respectively. Had measles at 2 years; chicken pox at 4: whooping cough at 10; malaria at 8 years.

Physical Examination: Weight, 180 lbs; 5ft.10½ ins. Chest, 38/40ins. Waste, 33 ins. Robust, well-formed. Heart, lungs, liver, joints, etc., normal. Tenderness and pain over left eye, increased on pressure. He lives in a swampy poorly-drained district. Uses tobacco moderately. Uses alcohol moderately, a glass of beer or whisky each day, sometimes two; more if on party. Rises at 5 a.m., retires at 10 p.m. Sleeps well, but takes no precautions against mosquitoes which are plentiful in his district.

Present illness: 5 weeks ago he had a cold on the chest, later extending to naso-pharynx. This illness began by severe rigor, accompanied by pains in the head, particularly at the frontal pains in

region. Bitter taste in the mouth. Fevered the first week, pains in backs and legs, malaise, no appetite, bowels regular, frequent micturition. The pains in the head increased, so that he was sent to Ear and Throat Hospital. On admission, pain and tenderness over left frontal region of forehead. No abnormal nasal discharge. Pain was not increased by the reclining posture.

Clinical Examination: Urine normal. Many tertian malarial parasites in the blood. Leucocytes, 5000 per c.mm., later 12,000 per c.mm. No evidence of any septic focus.

Treatment: Quin. Sulph., grs v. three-hourly for four days. Parasites decreased markedly. 5th day, increase of parasites. Quinine, grs v., two-hourly. Parasites almost disappeared. Pain over left eye cleared up, and the patient was discharged. Considered as malaria involving frontal sinus.

It is interesting to note that this patient never had a chill or fever, during the fortnight he was under treatment for frontal headache. The temperature was normal throughout. The blood was teeming with parasites—hardly an erythrocyte free of a parasite.

De la Mothe, who studied the laryngeal complications of malaria in Macedonia during the War, records that they were almost exclusively of a motor character. He found that aphonia might develop suddenly, generally after severe attacks, and associated with asthenia. It may be due to two causes—more or less paresis of the constrictor of the glottis, and tensors of the vocal cords; and a true recurrent paralysis of one vocal cord, which was less frequently met with and might or might not end in recovery. Prognosis is generally favourable, improvement occurring parallel to recovery from the asthenia, and assisted by faradisation and re-education.

Two exceptional conditions were observed by him.

1. A case of paralysis of the dilators of the larynx, the right vocal cord being immobilized in the median position. Being unilateral, this phenomenon was not accompanied by any disturbance of function. This paralysis, if double, would lead to closure of the glottis, respiratory distress, and necessitate tracheotomy.

2. Several cases of motor inco-ordination, difficult to interpret, in which the laryngeal disorders are associated with

speech disturbance, resulting from the affection of other centres.

Any group of muscles may come in for special attention so that spasm, atrophy, inco-ordination of musculature may be exhibited at times.

Pansini records a case of laryngeal atony, with attacks of suffocation in a man of 30, a malarial subject.

CASE XII. Malarial laryngeal atony. (Pansini).

A man of 30, was admitted to hospital for attacks of suffocation which had followed a typical paroxysm of tertian malaria. Laryngeal examination showed no throat inflammation. Injections of strychnine, atropine, local iodine, guaiacol, massage and faradism, were all ineffectual, but the condition subsided after quinine, given hypodermically.

Ziemann records a case of intermittent spasm of the larynx due to chronic malaria. This case is detailed in the chapter on periodicity.

Monier-Vinari, who studied the neurological affections in 64 malarious soldiers, found 9 with laryngeal troubles associated with those of extremities, such as paresis or spasm, single or bilateral of constrictor muscles or dilators of the glottis.

A case of laryngeal paralysis due to malaria is recorded by Cold. (quoted by Cariamatis). After febrile attack, the patient, a clergyman, complained of hoarseness, and laryngeal examination showed the left vocal cord quite immobile,—paralysed. In speaking, the right cord passed over the middle line and touched the left one, which was quite toneless.

Deutsmann records a case of hypoglossal paralysis, with dysarthria, and ataxia of the left arm.

Vernueil records two cases of toothache in healthy teeth consequent on malaria.

The naso-pharynx then appears to bear its share, if on the whole a comparatively small one, of the incursions of this versatile parasite.

CHAPTER XXVII.

LATENT MALARIA—FORMS AND DIAGNOSIS.

All who have handled large numbers of malarial subjects are quite familiar with a class of case with a very wide range of symptomatology, where no parasites can be found in the blood upon repeated examination, and yet subsequent evidence has come forward, as by post-mortem examination or by ultimately getting the parasite in the peripheral blood, or by spleen puncture, that malaria has been the cause of the trouble. Many cases of this kind are attending malarial and other clinics, and hospitals, throughout the world—repatriated soldiers with all sorts of complaints, often of a neurological nature, who became infected with malaria in the malarious war zones of Macedonia, Palestine, East Africa, Italy, India, etc. There are also many instances in civil practice of old malarial subjects with obscure complaints, where the malarial infection of many years back, if not forgotten altogether, has apparently but not really severed its connection with the present state of the patient, through difficulty in establishing the continued existence of the parasite in a subdued form within the host.

Many of these cases of repatriated malarious soldiers attended neurological clinics under the Ministry of Pensions and it was the duty of the Medical Officers, of whom the writer was one, to determine how much the particular complaint of the applicant was due to Service conditions in general, and malaria in particular, in order to assess or discontinue his pension, and to administer appropriate treatment.

In the case of those with a history of malaria infection, there was often a great difficulty of diagnosis—a difficulty of deciding whether the parasite still lived in the host in a subdued form, with occasional exacerbations of sporulation, maybe at long intervals, and sometimes enough to make a frank malarial paroxysm, but often too slight to do that, though not too little to produce a state of fluctuating ill-health which was apt to increase when the patient subjected himself to any strain such as an attempt to work, or

exposure to rough climatic conditions or extremes of temperature. This state of affairs consitutes what is known as latent malaria, where the parasite lives on in the depots especially spleen, bone-marrow, and liver for periods of varying duration—sometimes only for a few months after the patient has left the malarious district, sometimes for longer periods—up to 20 years or more. The mimicry for which the masquerading parasite is famous is exhibited in its lesser degrees of activity, as in its greater. This being so as wide variation of disturbances and complaints may emerge from a relatively subdued survival of growth of the parasite in the internal organs of the host, where it carries on guerilla warfare with exacerbations of growth from time to time. These exacerbations of growth may be excited by anything that puts a strain upon the patient, such as insolation, fatigue from any cause, traumatism including surgical operation, anaesthetics notably chloroform, alcoholism, change of climate or temperature, intercurrent disease and so on. It will thus be seen, that unless malaria is thought of and looked for, it will often escape notice under cover of the agency that excites renewed growth of the parasite. Even if looked for, it may easily escape notice for long periods—unless artificial means for demonstrating the parasite are adopted.

It has been found as we have seen from the medico-legal chapter, that a small proportion of these latent malaria cases exhibit abnormal conduct of an anti-social nature, that brings them into contact with the law, and with these especially is it important to be able to demonstrate the parasite, since it may be a matter of capital punishment, and judge and jury are not apt to be impressed with any evidence for malaria short of finding the parasite.

How malarial infections may escape notice with serious consequences, even with the most capable observers, is exhibited in this record by Osler. This is not exactly a case of latent malaria (which presumably would have been still more difficult to diagnose) as the parasite was evidently not looked for until too late, but it shows how apparently insolation, or indeed any other irritant, may mask the malarial factor in, or cause of, the condition, all the more readily if the parasite is looked for and not found, though present.

Case I.

Masked malaria. Diagnosed post-mortem. (Osler).

L.K., admitted July 18, 1889, complaining of pains in the head and of coldness and numbness of the feet and hands. He has enjoyed fairly good health and for his age is a vigorous, healthy looking man. On the 9th, while picking berries in a field in Anne Arundel Co., he had a heat stroke; was unconscious for two hours and had to be carried home. He was up the next day, and was able to work; has not felt well since, and has had headache, and occasional feelings of sensation of cold.

On the 18th, the following note was made: Healthy looking, much sunburnt, pulse full, vessel walls soft, no oedema of feet. Lungs are clear in front and behind. Respiration prolonged. Apex beat of heart is neither visible nor palpable; the sounds are weak, the second is scarcely audible at the base. Area of liver dulness reduced. Spleen not enlarged; urine bright yellow in colour, sp. gr., 1,010; no albumen or casts.

I saw the patient only during the first four days of his stay at hospital, and thought that he was suffering from the effects of a sunstroke. He was given a tonic mixture. The patients temperature was normal, but on the 20th and 21st the morning record was 97·6°F and 97·8°F.

On the 25th at 11.30, he had a chill and temperature rose to 105°F, and remained high all afternoon. At 7.30 p.m., it was again 105°F, and he had a greadusted bath. Throughout the 26th, temperature fell, but did not get below 101°F. Pulse rapid and feeble.

On the 27th, temperature, 8 a.m., 100·6°F; rose in afternoon to 103°F, and in evening was 100·3°F; pulse 104, extremely irregular and intermittent. There were feeble rales, with high pitched percussion note in right infrascapular region. Towards evening, the patient sweated profusely, and the breathing was of the Cheyne-Stokes' type.

On the 28th, temperature fell rapidly, sinking from 103°F at 4 p.m. of 27th to 97·3°F at 8 a.m. of 28th, and to 95·5°F at 10 a.m. Pulse very feeble and irregular. Vomited twice: no expectoration. There was marked feebleness of breathing at right base. Throughout

afternoon of 28th, temperature rose and at 8 p.m. was 100°F.

29th. Cheyne-Stokes' respiration persists—has had slight diarrhoea. He speaks with difficulty, but appears to be conscious.

Throughout 30th, and Aug. 1st, he gradually sank and died on the morning of the 2nd.

I did not see this patient from the date of his chill until the morning of the 2nd just before his death. The case was regarded as one of low anomalous pneumonia. The day after the chill it is stated in the note that the blood was examined with negative results, but there is no initial to indicate by whom the examination was made.

AUTOPSY: (by Prof. Welch)

Anatomical diagnosis, malarial fever with malarial parasites in blood and spleen.

Pigmented spleen, soft, swollen, length 13 cm., width 8 cm.

Pigmented and myristicated liver.

Pulmonary emphysema.

General muco-purulent bronchitis and pulmonary oedema.

Catarrhal colitis.

Heart small, of deep brown colour; slight thickening of aortic and mitral valves.

Lungs markedly emphysematous and much carbonized. Dependent parts congested, and there is moderate general oedema. No pneumonia.

Kidneys—no special changes.

Blood Examination by Dr. Welch: Blood from finger shows small number of malarial organisms namely, spots of shape and size of red corpuscles with pigmented plasmodia, free round pigmented corpuscles, varying in size from blood plates to twice that size, and pigmented crescents, the pigment in a ring in the middle.

I found in one specimen of splenic pulp two actively free flagella.—In the capillaries of the brain are a few pigmented corpuscles.

Osler says: "In this case, the history of a sunstroke and the occurrence of pulmonary symptoms threw us off our guard, and the case was regarded as one of low pneumonia. A more careful and systematic examination of the blood, would, no doubt, have led us to a correct diagnosis".

This difficulty of finding the stranger within the gates, often even when thought of, let alone when not thought of, has given rise to a mass of literature which deals with the features by which the surreptitious parasite betrays its presence to the close observer, and it also deals with methods for inducing him to leave his lens, and emerge into the peripheral blood, where he may be recognised in the usual way. A goodly list of clinical features characteristic of latent malaria has been tabulated by Gordon Ward, and the writer proposes to use that list as a basis for dealing with the subject, modified and extended somewhat by the work of other observers, including himself. Ward's observations were based upon a study of 1000 cases of soldiers under treatment for malaria in England and France, and are largely confirmed by the experience of most of those dealing with large numbers of malarial subjects. The following features, do not, of course, appear all in one case, but are more or less marked characteristic of latent malarials as a whole. They often occur, that is, in varying groups in individual cases.

Common characteristics of latent malaria.

1. *Any abortive attack:* shaking, hot and sweating stages without rise of temperature. Dutmann and Porak, who have examined many hundreds of malarial charts from Macedonia, Greece, Italy, North Africa, have noticed several types of periodicity in the apyrexial periods of malarials. The types noted have been, tertian periodicity, subnormal to normal, 95°F to 98·6°F or so, maybe; or tertian periodicity in drop of temperature. Septan periodicity has also been noticed similarly both ways in different cases, and is very common. Decan, and quartan rhythms have likewise been noted, but are less common than the other two, tertian and septan. These variations have no doubt to do with sporulation of parasites in varying degrees, in their depots.

2. *Headache:* generally frontal or parietal, most often supraorbital, in any case over the trigeminal distribution area. Sometimes occipital, but not vertical. Hyperalgesia at margins of areas where pain felt, or from lower lids to vertex.

3. *Pains in legs or back, or both:* Leg pain generally

down front and sides of thighs, or above and below knees in front. It may be more general, affecting whole limb, bones, muscles, which may be tender to touch, and resembling "rheumatism". It is often fleeting, but recurrent. The pains in the back are most often in the lumbo-sacral region (1st Lumbar to 3rd Sacral segments).

4. *Eyes:* Pain behind eyes. Supraorbital tenderness. Conjunctivitis, photophobia, amaurosis, slight nystagmus. Rarely strabismus.

5. *Pain in left side*, worse on standing long or walking. Often dispelled by deep breathing. Splenic adhesions? Sometimes only a feeling of heaviness in splenic region.

6. *Perisplenitis:* slight friction rub in 7th or 8th left intercostal spaces. This is intermittent, but useful when present—pleurisy excluied.

7. *Splenomegaly:* uncertain, but useful when present. More often with severe attacks and with jaundice.

8. *Pharyngitis, and laryngitis to bronchitis:* generally about time of attack, and usually not long after.

9. *Jaundice:* some patients seem specially liable to jaundice after malarial attack. A slight yellow colour is suggestive in chronic cases.

10. *Fraud:* generally fine—of tongue and hands, rarely of lips, and only for a few days after attack.

11. *Pigmentation:* At times seems to increase with attacks and diminish between them. (Sympathetic fluctuation of irritation phenomena).

12. *Tachycardia:* Common—continuous, or on exertion. Perhaps related to thyroid and sympathetic irritation.

13. *Hyperidrosis:* Not infrequent, though not often complained of. Chronic tendency apart from acute attacks. Affects chest, hands, axillae, without any apparent provocation; at other times on mild excitement or exertion.

14. *Transient urticaria or oedema:* anywhere, but mostly fingers, hands, or legs. Passes off in a half to a few days.

15. *Raynaud's Syndrome:* "Dead" fingers; cold feet—up to complete syndrome.

16. *Weakness:* unaccountable feeling of weakness, either without

exertion or out of proportion to given exertion. May be associated with anaemia or wasting, or not.

17. Hyperaesthesia of skin: in 8th cervical, 1st Dorsal, 7th Dorsal, 1st to 5th Lumbar distributions. Frequent for few days after attack at least, maybe longer and most constant in 7th Dorsal distribution. (Carmalt Jones).

18. Periodicity: tertian, quartan, of any symptom or sign whatever, from hiccough to mental confusion, or from herpes or urticaria to neuralgia. Anything that recurs at the same hour every day, or every second or third day should be considered in this connection.

19. Blood films:

(1). Parasites.

(2). Pigmented whites—leucocytosis without parasites in apyrexial phase is probably not malaria.

(3). Leucopenia. (2,000 to 3,000 per cu. mm.) with relative mononucleosis (about 15%); not quite constant, but nearly so.

(4). Eosinophils increased—5-10% in chronic phase.

(5). Endothelial cells with frayed protoplasm—sometimes two together.

(6). Large (new) reds, and maybe nucleated reds (young forms).

20. Urinary Pigment: centrifuge urine. There may be found pigment in

(a). Very fine granules massed together.

(b). Large granules arranged in groups.

(c). Large masses varying in form.

(d). Granules within leucocytes, and hyaline casts. (Urriola)

21. Urobilin: in Urine and Stool: is often found in malarial subjects, and in urine can be readily detected by Schlesinger's test, viz:

1 Schlesinger's solution { Zinc acetate. 1 part. / Alcohol. 10 parts.

2 Tincture of Iodine.

3. Sample of urine.

Take test-tube third full of unfiltered urine, and add equal quantity of well shaken Schlesinger's solution. Add a few drops of

tincture of iodine, as this hastens the reaction. Filter mixture, and if urobilin is present, the filtered mixture shows a more or less distinct fluorescence. The test is very delicate, and can be got after diluting the urine with 200 parts of water. Quite healthy urine does not give the reaction, as it contains only at most, the slightest amount of urobilin.

Many other diseases have it, of course, such as cirrhosis of the liver, liver abscess, and many infective diseases, but notably malaria (after Atkinson).

A few cases by Ward exhibit some of these features: Cases with symptoms lasting 5-10 years after return to malaria free climate are not infrequent, and in one case, plasmodium vivax was found 15 years after the patient's return from India.

CASE II.

Example of apyrexial rigor. (Ward).

Pte. T., aged 28, had two typical rigors during which plasmodium vivax was found and he was then put on quinine and came under my care. 16 days later, his morning temperature was 97·4°F, pulse 72. At 10.30 a.m., he was seen by me and was then sweating profusely, and showed marked rigor which he attempted to control in vain. His eyes were suffused but he had no pain or headache. His temperature was 98·6°F, and his pulse 114, regular and full. He appeared very flushed and was hot to the touch. At 11 a.m., he was still sweating, but the rigor had almost ceased. His temperature was 98·2°F, pulse 96, and respirations 40. At 11.10 a.m., he was no longer shaking, but complained of nausea.

Blood was negative for parasites.

At 12.45 p.m., temperature 98·6°F, pulse 88, respirations 30.

At 2.10 p.m., he had headache, which had come on about an hour previously. He had no longer any sweating. Two days later he had a similar but less severe attack, characterised by feeling cold, then hot, and sweating, and finally by headache. On other occasions, he had similar attacks, but his temperature never rose above 99·4°F, while he was taking quinine.

In this case the rigor happened to be very marked, and the patient looked and no doubt felt as ill as a man with a temperature

of 104°F. He lay curled up in bed, covered with blankets and evidently very unhappy. He had already been promised evacuation to England and had nothing to gain by simulating attacks. Nor would it be possible to simulate such an attack as he had. His temperature was taken with three different thermometers, and I counted his pulse and respirations myself. It may be noted that his haemoglobin two days before the attack was 76%. During the attack, it was 82%, the sweating producing concentration of the blood. Two days later it had fallen to 50%, and not till four days later was it above 80% again.

Minor lapses are not usually so flamboyant as this.

CASES III, and IV.

Latent malaria—minor type. (Ward).

Patient had two rigors of usual type before he came under my care, and plasmodium vivax was demonstrated in his blood. He was then put on quinine. As soon as he was allowed up, he began to have an evening pyrexia between 99° and 100°F. Each evening, also, he had symptoms which he himself recognised as malaria—e.g. feeling of cold, followed by flushing, sweating and headache. His blood, taken on one such occasion showed no parasites, but the leucocytes were increased, and the polymorphs 80%—just as is commonly the case at the onset of an ordinary malarial relapse.

Ward notes a similar case in which blood was examined three or four times and a few parasites were found on one occasion only. (Plasmodium vivax). This man had not been exposed to reinfection for 15 years.

But while these features tend to occur and are suggestive of chronic malaria, there are a few of them which tend to be more constant and rather more reliable.

The writer had found spleen friction, heard best with the patient lying on his back, in the 7th or 8th left intercostal spaces, indicating chronic perisplenitis, a very useful sign in the absence of pleurisy. It is not always present in patients where it does occur, but recurrent examinations at a few hours or days interval

often elicits it. It is often very fine in quality, requiring close attention.

The next most useful sign, in the experience of the writer, is leucopenia (2,000-6,000) with mononucleosis; or alternatively, a leucocytosis of 16,000 or more in absence of other causes (Acton and Knowles, David Thomson). Large numbers of malarial parasites on sporulating cause a leucopenia, while a very small number on sporulating produce a leucocytosis. During the rigor and temperature in malaria, the mononuclear leucocyte percentage (more especially that of the large mononuclear variety) is low. With the fall of temperature, however, the mononuclear percentage rises very high, sometimes even to 90% of the total leucocytes. This fluctuation in the percentage of total mononuclears occurs also long after continuous quinine treatment, and is observed for months and even years after the last attack of fever. (David Thomson).

15% or over of large mononuclears is highly compatible with chronic malarial infection, with a leucopenia where 500 or more white cells have been counted (Stevens and Christophers).

A fluctuating leucocyte count with a high mononuclear percentage at the leucopenic stage is very suggestive that malarial parasites are still present somewhere in the body (Acton and Knowles). There are, however, exceptions to this rule, especially in patients repatriated for a year or over (Rieux, Alcock and O. Löwy).

Finally there are the steps taken to find the parasite. If repeated examinations of the blood, especially by the thick film method, have failed, then artificial means may be adopted to induce the parasite to appear in the peripheral blood. These means have been very various, and a host of different methods have been recommended by Continental and other workers—such as adrenalin injections, application to the splenic area of heat, or cold, or sunlight, quartz lamp, ultra-violet rays, X-rays; subcutaneous injections of horse serum, strychnine, lactic acid, anti-typhoid vaccine; intramuscularvinjections of 10-20 ccs. sterile (boiled) milk, neosalvarsan etc., and induction of fatigue.

Sassen, who surveys all the methods used, considers adrenalin

and ultra-violet rays the best. Horse serum injections is well spoken of by Biedl and Brauer. Dorendorf prefers the serum and milk methods. Thaller prefers milk—5 ccs. heated to 100°C for 10 mins. on water bath, and injected intragluteally. It failed in 5 cases out of 30 to induce a malarial attack in from 1 to 14 days. Löwy used milk injections + small doses of quinine (Copi).

Adrenalin has many favourites—Shittenhelm and Schlecht, Dazzi and others. It is the only method of which the writer has any experience, and it has been found very useful on the whole. The method used has been to inject 10-20 minims of 1 in 1000 fresh adrenalin solution, i.e. 1 agm, (Parke, Davis and Co) and examine thick blood films of blood taken an hour after, two hours after, the same night, next morning, and so on at increasing intervals for two days or so. If the result is negative, repeat the process in a few days. The patient should be lying down. He often becomes pale, may feel faint, and may have rapid pulse, or not. The writer has seen no serious accident from its use. It is important to see that fresh material is used, otherwise its results may be disappointing. Two cases dealt with in this way by Schaefer are recorded; also two cases by Sachs, using spleen hot douching and serum and anti-typhoid vaccine as provocative agents, are given.

CASE V. *(Shaefer).*

Prisoner, Russian front, got malaria in 1914. Healthy previous to this. Typhus, 1916. 1917, recurrent malaria. A few quinine tablets taken. Since then no complaints till May, 1919. Then out of sorts—general malaise.

Examination: pale, indisposed. Spleen enlarged to percussion; liver enlarged. Secondary anaemia. Mononuclears, 12%.

16:5:19. Adrenalin, 1 agm., intramuscularly, without reaction.

24:5:19. Adrenalin, 2 agms., intramuscularly, without reaction. Wassermann reaction negative.

26:5:19. Sun exposure over spleen, for 15 minutes, without reaction.

2:6:19. Sun exposure over spleen for 30 minutes, after which shivering, and temperature 37·6°, with feeling of lassitude. Tertian parasites found in the blood. Quinine given.

19:7:19. Feeling well—clinically cured.

CASE VI. (Shaefer).

Soldier who had served in the East, not Macedonia. Healthy pre-War. No malaria, therefore no quinine given. For several weeks he had some periostitis of the left forearm and tibia, for which he was being treated. Six days before, he had profuse diarrhoea—sudden onset. Then sudden rise of temperature which was diagnosed as typhoid, 26:6:19.

Examination: Moderately well nourished. Some bony thickening and tenderness of left lower arm. Spleen enlarged. Leucocytes, 5,200. Mononuclears, 4%. Temperature normal. Gruber-Widal -ve. Diarrhoea.

31:6:19. Adrenalin, 1 mgm., without reaction. Spleen normal.

6:7:19. Sun exposure over spleen for 15 mins. without reaction.

10:7:19. Sun exposure over spleen for 30 mins., followed by shivers, and temperature 39°. Spleen enlarged. Many tertian parasites found in the blood.

CASE VII. (Sachs).

Man complained of headache, pains in the chest for 14 days, cough. General condition good, well-nourished, strong looking. Lungs—moist râles. Liver and spleen normal in size. Otherwise findings negative. No anaemia.

After 12 days treatment, no improvement. Blood negative for parasites.

17th. Spleen hot touch.

18th. Blood negative for parasites.

19th. Crescents found. Quinine + Salvarsan.

CASE VIII. (Sachs).

Man, 21:11:17. No history of malaria. For some days noticed yellow tint of skin. Otherwise no complaint.

Examination: strong, well-nourished. Icterus. Heart and lungs negative. Liver enlarged and tender. Spleen enlarged. Blood -ve for parasites. Urine—bile, urobilin +ve. Stool light brown;

urobilin +ve. Dieted, carlsbad salts.

24:11:17. Horse serum, 15 ccs.

25:11:17. Blood negative for parasites.

27:11:17. " "

28:11:17. Feels well. Jaundice less. Blood negative for parasites. Discharged.

30:11:17. Returned.

1:12:17. Sines day before, fevered, headache, pains in the neck. Temperature up, but no other change. 2nd, 5th, and 8th Dec., blood negative for parasites.

10:12:17. 2 ccs. of antityphoid vaccine subcutaneously.

11:12:17. Crescents found in the blood, followed by quinine treatment.

17:12:17. Jaundice better.

While cases of latent malaria may exhibit almost any degree or kind of incapacity or complaint, we are concerned for the present mainly with the neurological aspects that may occur. The cases with which the writer had to deal complained of such things as incapacity for sustained effort through weakness for which they could often not account, headaches, depression, lack of interest in life in general, "rheumatic" pains, often in the legs, weakness of the legs, excitability, sleeplessness, palpitation, occasionally diarrhoea, loss of appetite, restlessness, feelings of suffocation, giddiness, loss of memory—generally in the form of difficulty in remembering things. A few, however, had lacunar amnesia, when there were total blanks in their memory for hours, so that they wandered away, or stopped what they were doing at the time and had no recollection of what was happening for a given period. Feelings of unaccountable anxiety affected some, and friends or wives reported such things as irritability of temper, unreasonableness, impulsiveness, cruelty, a few were even threatening in their attitude at times, and that to those who knew and liked them best. Wives and intimate friends have reported changes of character so that a man who was formerly "one of the best" had become altered and "impossible to live with" through ill-temper or impulsiveness or some form of unreasonableness. Most were depressed at times, many had lost heart and interest in their work, while some had become epileptic and thereby unable to keep their

jobs.

A few of the author's cases are appended, and a few more are included in the medico-legal chapter, especially the first four, in one of which (case III) adrenalin had to be used in order to demonstrate the presence of parasites.

CASE IX.

J. McC., aged 26, sergeant R.A.M.C., married, 3 children ploughman pre-War.

History: Joined the army in Jan., 1915. France, Sept., 1915. Macedonia, Oct., 1915. Took malaria during 1917. He was severely ill with it, and has been out and in the hospitals ever since. Was discharged from the army in Feb., 1919.

Attacks are now less frequent—about 1 month since the last. He now suffers from very severe headaches every other day, and pains in the left side (splenic region). He feels very weak, and tremulous when he tries to do anything. Not a heavy smoker or drinker. At present he is able to spend some time on his father-in-law's farm, but is not fit for such. At first he had attacks about every 10 days, and had a very serious attack in Sept., 1917—was told he was delirious.

29:11:20. General condition poor. He is thin, pale, emaciated and apathetic looking. Tongue clean and moist. Teeth satisfactory. Pulse 120. Heart's action weak and rapid. No enlargement. Lungs negative. Deep reflexes brisk.

He complains of pain and tenderness over the splenic region. Spleen is not palpable, but area of dullness increased. Mentally he is dull, lethargic and depressed, and lacks self-confidence. Put on iron, arsenic, quinine and nux vomica.

13:12:20. Improving. Pulse 108. Still pale and short of breath.

13:1:21. Malignant tertian parasites found in the blood two hours after 1 cc. of 1 in 1000 adrenalin solution given subcutaneously. Quinine given.

18:1:21. Feeling of depression, apathy, lack of interest, alternating with periods of betterment. Spleen tender, but not palpable. Area of dullness enlarged. Liver not enlarged, nor

tender.

25:1:21. Markedly better. No further attack.

3:3:21. Improvement being maintained—putting on weight.

12:5:21. Progress satisfactory. This man continued his treatment with iron, arsenic, quinine and adrenalin, and his general health slowly improved so that he was able to resume full-time work on the farm by Autumn, 1921.

CASE I.

W.T., aged 39, rough rider, married, three children. Coachman pre-War.

History: Health good pre-War: never had a day's illness. Enlisted Jan., 1916. Lemnos, Mar., 1915. Egypt, April, 1915. Salonica, Dec., 1916. Under air raid fire, not wounded. Septic sores, both hands; about middle of 1916. Malaria about Aug., 1916, and in hospital with it 3-4 weeks. Invalided England, Nov., 1916, with neurasthenia. Frequent attacks thereafter during 1917. Discharged July, 1917. Has done 9 months work since then—light work. Has complained of weakness, occasional giddiness, pains in back of head.

Wife states that he is very irritable, easily worried, impulsive, depressed at times, easily tired and lacks former interest in things. Starts up in his sleep. He is unlike his former self, for he was a "good husband". General condition fairly good. No anaemia.

Physical signs: Heart and lungs negative. Spleen palpable. Liver not enlarged. Knee-jerks brisk. Pupils normal.

Mentally: looks apathetic, dull, and shows slight mental retardation.

Sleep indifferent. Shivering attacks about once a fortnight. Sweats thereafter—clamminess rather.

Splenic friction heard over 7th interspace. Blood Pressure: Systolic, 122 mm., Diastolic, 85 mm. Hg.

25:7:21. Spleen friction well marked. 20 minims 1 in 1000 adrenalin—shivering turn with pain in back, headache. Pallor of hands and face. Malignant tertian parasites found in the blood.

9:8:21. Quin. Sulph., grs. X., t.i.d., week about with

Ferroarsine (colloid), drs i., t.i.d., p.c.

23:8:21. Worrying about loss of sleep, and emotionally unstable.

6:9:21. Improving steadily and looking for work.

1:11:21. Improving on the whole, but during interview to-day had one of his "turns". He came in deadly pale, and looked as if he were going to faint. Pulse small, easily compressible and a little rapid (95 per min); but revived after rest and a drink of water.

This case attended the Army Pension Clinic where he was under treatment for about a year with quinine, iron, and arsenic, adjusted from time to time to suit his requirements. He steadily improved regaining much of his old self-confidence, and settled down to work as a market-gardener.

The following case is included to illustrate the versatility of the parasite in varying symptomatology. It will be easy for the reader to realise, that a lesser degree of sporulation and therefore infection than presumably exhibited in this case, with a corresponding lesser degree, though no change in kind, or maybe varying the picture still further, could make a very baffling problem for the medical attendant to explain, and consequently deal with adequately. It will be easily seen, therefore, how readily the epithet "malingering" can be quietly or openly attached to these patients to explain a picture which inadequate acquaintance with its nature has failed to do.

CASE XI.

4 malarial attacks, with different nerve symptoms each time, under inadequate treatment. (Busquet).

Busquet reports a case of a patient who had four distinct attacks of malaria fever in three months, each of which was associated with interesting nervous phenomena. In Nov., 1897, the patient while in Madagascar had a pernicious comatose paroxysm. After his recovery he began to suffer from girdle pains, which, however, yielded to treatment to-gether with quinine. January, 1898, he began again to have attacks of intermittent fever with a rapidly developing anaemia, as a result of which he was sent to Marseilles.

On May 16th., patient had a chill. There was marked paresis

of the right arm and leg, the right arm showing a rhythmical tremor which persisted during effort, and as a result of which he found it difficult to feed himself. The right leg during fever showed spontaneous epileptoid tremor, with oscillations of great amplitude; general sensation good. The right patellar reflex was greatly exaggerated, and accompanied by clonus. Left was exaggerated; there was ankle clonus on right side; plantar reflex absent on the right, increased on the left. There was incontinence of urine. Blood showed malarial parasites—of acute cycle and crescentic.

Under quinine, fever and all nerve symptoms entirely disappeared. In four days most of the symptoms had yielded. In two weeks, treatment was stopped. In five days nerve symptoms reappeared, and three days later incontinence of urine. On June 10th, there was a febrile paroxysm, and on the following day, incontinence of faeces. Under treatment by quinine, symptoms again cleared up in a few days, though the incontinence of urine lasted eight days.

Treatment by quinine was stopped after 10 days. Four days later, incontinence of urine reappeared, and on following day was another febrile attack. He was then given two grams of hydrochloride of quinine hypodermically, and afterwards, one gram a day for eight days, then 0·6 G. up till July twelfth. Three days later, fever and incontinence of urine again developed, which yielded once more in a few days to quinine. On July 26th, patient left hospital feeling well.

The author believes that the nervous phenomena were probably due to the indirect* irritation of the central nervous system by the parasites in the circulation.

The failure to find parasites either through not having adopted other than the simplest means to do so, or through having tried and failed, may easily lead to an awkward situation, or even to the adoption of a line of treatment wich may have disastrous consequences for the patient—either in the sense of being operated on unnecessarily or in the medico-legal sense of not attaching abnormal and illegal conduct to malarial infection where it exists.

*Why indirect?—W.K.A.

A difficulty of this kind is illustrated by Goodall's case which might have unmistakably revealed its secret if one of the provocative methods of enticing parasites into the peripheral circulation had been adopted.

CASE XII.

Case of clinical cerebral malaria, reacting to quinine, without parasites being found in the peripheral blood. (Goodall).

Pte. L., aged 32, admitted to hospital on 10th Oct., He had reported sick on 3rd Oct., with headache, vomiting, and pains in the legs. He had no previous malaria. On admission temperature was 101·5°F. Pulse 100. The tongue was furred; there was slight icterus and some sickness. The spleen was enlarged, but not palpable. Parasites were not found. He was ordered quinine, 40 grs. daily by the mouth, but as he became dull and drowsy later in the day, he received 18 grs. by intramuscular injection. Next day he was better, but as he had occasional vomiting, the intramuscular injection was repeated.

On the 12th, the temperature was 103°F, and patient became delirious. He received an intravenous injection of 24 grs. of quinine, at 2 p.m., and an intramuscular injection of 18 grs. at 9 p.m. On the 13th, he seemed better, and the temperature was normal. He received 40 grs. of quinine by the mouth. At 9 p.m., he became restless and delirious—said there were people below his bed. On the 14th, he was quieter, and seemed better, but had delusions of suspicion. On the 15th, he became maniacal, and argued fiercely that he should not be shot without a court-martial. He had hallucinations of sight and hearing. The tongue was furred, the knee-jerks were sluggish, the speech was thick and slurring. A consultation of experts was now held. An asylum superintendent thought the patient had general paralysis of the insane; a gynaecologist thought he suffered from quinine poisoning; while our eye specialist maintained that the true diagnosis of delirium tremens. Fortunately for the patient, my surgical colleague strongly supported my view that the case was one of persistent cerebral malaria. Acting on this opinion, we administered 18 grs. of quinine intravenously at 11 a.m., and again at 6 p.m. On the 16th, patient was drowsy and heavy, but quite

rational. Quinine was continued by the mouth. He steadily improved, and was practically well by the 29th. By this time the spleen had become palpable, but parasites, inspite of the repeated search, were never found.

How easily the correct diagnosis can be missed in a case of malarial infection in a child is illustrated by the following:

CASE XIII.

Latent malaria in a child. (David).

7:3:19. A child of 8 years of age had for some time slowly increasing lassitude, no desire to play, and increasing drowsiness. There was some cough, fever, with a feeling of heat, but no digestive disturbance. Pale, non-muscular, rachitic skull, and enlarged lymphoid glands. Spleen enlarged. Reds, 2,600,000. Whites, 22,400.

18:3:19. Seen again—shivering fits in interval since last visit. Very sleepy. No fever. Spleen bigger. No albumen, or sugar, or diazo reaction in the urine. X-Ray of chest -ve.

24:3:19. Seen again, temp. 38°. Blood exam. again, large mononuclears, 12%, polymorphs, 50% lymphocytes, 34%, eosinophils, 4%. Ring form of tertian parasite found this time. It turned out, that the child had been in a malarious area the preceding summer. It is to be noted that until then no apparent attacks had occurred—the child had been below par, or had "failed a bit", but there was no marked complaint, and no history of febrile attacks until this appeared.

While the omission to realise and remember the subtlety of the debilitating effects of the parasite in the individual patient under consideration may be embarrassing, or disappointing enough in the end, it seems to be serious on a larger scale when applied to armies on the field or large bodies of men at work in malarious districts, as in the case of the construction of the Panama Canal. This "concealed inefficiency" is dilated on by Capt. Smallman, R.A.M.C., thus:

"Let us consider for a moment the nature and the amount of the inefficiency caused by malaria and compare it with that caused by enteric fever. Its chief characteristic is that the inefficiency due to it is what may well be called a concealed inefficiency. The man who contracts enteric fever goes to hospital and may be looked upon as a non-effective for the next six months or so. He thereby drops out of the reckoning for that length of time.

"A man suffering from malaria is often comparatively fit, and is usually able to carry out his ordinary duties without trouble, and his inefficiency is not revealed until the time comes when a little extra strain, privation, cold or fatigue brings on another attack of fever and renders his useless for the duties of a soldier for the next few days. He is in fact, exactly the type of man who is useless or worse for the purpose of field service.

"In amount the ineffiency is often great and occasionally massive. It has happened before now that a regiment in apparently good physical condition has been marched off to the frontier only to find that with the access of the usual aided strain of campaigning, its numbers have been so reduced as to render it unfit for service, and it has been sent back again.

"It sometimes happens in a malarious station in India that a so-called "strong as possible" parade is a sight little short of melancholy. The small number of those able to parade owing to the presence of many in hospital, the cachectic and debilitated appearance of those on parade, and the fact of a certain number of those on parade being obliged to fall out, all combine to produce a sad impression".

The distribution of parasites throughout the circulation has a bearing on latency and has been specially studied by Bastianelli and Bignami. They distinguish the following varieties of distribution

(1) Cases in which parasites (M.T.) are abundant in the vessels of all the organs and which often end in coma. Symptoms may be referable to any or all organs. Or parasites may be abundant in the spleen, bone-marrow, and peripheral blood, but scarce in the brain, in which case there is a lack of cerebral phenomenon.

(2) Cases in which the parasites are absolutely and relatively

scarce in bone-marrow, spleen, liver and peripheral blood, while they are concentrated in other organs, e.g. (a) brain and meninges, either in sporulation stage, or in all stages, with clinical cerebral phenomena. (b) Stomach and intestines, generally with the more mature forms of parasite, and with gastro-intestinal phenomena clinically.

There is often discrepancy between the findings in the peripheral blood, and those in the internal organs. Generally speaking, the finding of the more adult forms in the peripheral blood favours prognosis, while abundance of pigment in peripheral parasites suggests accumulation of parasites in internal organs with correspondingly graver symptomatology.

Often enough the disproportion between peripheral and central blood findings is considerable and surprising, and may be exhibited by a protracted and obstinate course of the infection, or by a grave sequel, or both.

Marchiafava records a case where localisation was almost exclusively in the brain. Bastianelli and Bignami record a case which died at the beginning of the fourth attack of malarial quotidian fever, after two days in hospital on quinine treatment. There is no record of state of blood as regards parasites before treatment was begun, but at the autopsy two parasites in three preparations were found in the blood from a vein in the arm. In the spleen pigment was so scarce that malaria could not have been diagnosed by the naked eye, and by microscope very few pigmented leucocytes were seen. After a long search, a sporulation form or two were found. The liver and bone-marrow were in the same condition, but in the brain pigmentation was visible to the naked eye, and in the vessels of brain and meninges numerous sporulation forms were found. In this case, these authors maintain, it would have been impossible to foretell so grave a prognosis, which occurred suddenly with cardiac weakness and pulmonary oedema, nor would there have been any help from splenic puncture since the spleen was so poor in parasites.

This type of case, however, is more the exception than the rule, and so far in their experience the cases in which the disproportion between the parasitic contents in the peripheral

blood and internal organs was so considerable, were only those in which there was cerebral localisation.

Usually in malarial blood there is a leucopenia with mononucleosis; but sometimes there is a polymorphonuclear leucocytosis apart from any inflammatory accompaniment, such as pneumonia or erysipelas, which is of great import. This may occur in cases with severe diarrhoea, with severe anaemia, and cases with haemoglobinuria.

In some fatal cases, under active treatment with quinine, few or no parasites may be found in the internal organs or peripheral circulation, but severe tissue damage may be found in brain or other vital organ,—the parasites being killed off in process of treatment, but not before serious damage incompatible with life has been done.

These observers record a case illustrating the disproportion between the gravity of the patient's condition, and the number of parasites found in the circulation post-mortem.

CASE XIV.

Latent malaria, with disproportion between gravity of condition and parasitic content of blood. (Bastianelli and Bignami).

A robust youth of 17 was brought to hospital at 2 p.m. on 17th July with a history of only two or three days' illness. He is stuporous, cannot tell his name, and there is slight fever. At 3 p.m., fever rises, and he has convulsions. At 4 p.m., temp. is 40·6°C, and he is comatose and does not react to stimuli. Pupillary reactions present. Eyes turned upwards, arms and legs rigid and extended. Abdominal muscles rigid. Patient turns to right and left and occasionally arches his body. Contortions increase so that he is put in a straight jacket. Spleen enlarged. Blood shows a few plasmodia (M.T.) without pigment. 2 gms. quinine injected. He gets worse and dies comatose at midnight of day of admission.

Autopsy: Outside appearance of body normal.

Cranium: Dura mater distended: cerebral hyperaemia, no melanosis.

Thorax: Both lungs show in lower lobes numerous patches of broncho-pneumonia: peribronchial glands calcified. Heart normal.

Abiosem: Organs in normal position. Spleen slightly enlarged, length 15 cm. Follicles very visible, and pulp brown in colour. Liver looks normal. Stomach normal in size, with numerous recent haemorrhagic erosions. Gastric contents like coffee-grounds. Kidneys normal in size and capsules easily stripped. Relations of cortex and medulla normal. Bladder full. Intestines healthy, apart from a slight hyperplasia of the follicles. Peyer's patches normal.

Microscopically:

Brain: Intense hyperaemia of most vessels. In a few capillaries are odd pigmented parasites seen.

Spleen: pigment scarce. A few leucocytes pigmented and very few parasites seen. No semi-lunar forms.

Bone marrow: No parasites found—only some leucocytes with a little pigment.

All the organs were the same as regards scarcity of parasites. No micro-organisms were found in broncho-pneumonic patches in the lungs, though there was alveolar haemorrhagic exudate.

Here then is a robust youth with grave cerebral symptoms who dies after a very short illness, living only 12 hours after the injection of quinine. The malarial parasites in the patient's blood during life are very scarce, as also post-mortem, and the scarcity of pigmentation seems to make it clear that the last illness could not have been preceded by grave malarial attacks.

The authors consider a picture of this kind exceptional and inexplicable. They suggest two possibilities—one, another agent of disease with the malaria; the other that the virulence of malarial ~~was enough to determine~~ toxin was enough to determine the fatal result.

They consider as possible that sunstroke not uncommon in Southern Italy may have contributed to the fatal result in this case, in the absence of the evidences of tissue damage which are likely to have been wholly of malarial origin.

A type somewhat similar to this—called toxic—is considered in the chapter on coma.

It will be seen then, that with parasites hibernating in the vessels of the internal organs, going through a life cycle there,

probably often in numbers too small to produce symptoms, and only occasionally taking on spurts of overgrowth when the vitality of the host is temporarily lowered for any reason, that not only has the host a treacherous enemy within the gates, but for long periods he may be unaware of it, until such overgrowth occurs. For long periods also, no parasites may be detectable in the peripheral blood, and other phenomena suggest that they are there and may encourage their pursuit both etiologically and therapeutically.

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CHAPTER XXVIII.

PERIODICITY.

A Chapter on periodicity has been included for several reasons. In the first place, it was by this curious habit of tertian or quartan sporulation of parasites with febrile accompaniment that the disease was recognizable in the writings of the ancients. In the second place it is a highly characteristic feature of the disease in its fully developed and untreated form. Thirdly, it is found in clinical experience that almost any conceivable symptom or sign may recur with quotidian, tertian, or quartan periodicity with, or more remarkably without, the usual febrile accompaniments.

Lastly, and by no means least, for medico-legal reasons, when that symptom which is periodic in its recurrence happens to be an abnormal mental state in which the unfortunate patient has committed homicide, or some lesser offence—and in the eyes of the law is now a culprit until proved to be an invalid—or should a short period of loss of memory be associated with it, the judge and jury are apt to remain unconvinced, unless the fitful habits and defects of this will-o'-the-wispish parasite are convincingly brought home to them.

It is well known to all handling malarial patients that although periodicity of symptomatology in general and periodicity of febrile attacks are highly characteristic of the disease, this periodicity does not always occur at all stages, and in all forms of the infection. During the primary stage, for instance, especially if there is a mixed infection, the temperature, though often high and remittent, has not the tertian or quartan periodicity that it develops later on. Then again, after the periodicity phase, which may last for days or weeks, even if untreated, the temperature tends to abate and immunity asserts itself, leaving the patient with a normal or sub-normal temperature, likely with occasional febrile exacerbations, out of the former rhythm. This, furthermore, will

be more liable to happen sooner in treated cases, where application of quinine usually interrupts the periodicity and leaves the patient with a temperature normal, sub-normal, or at any rate with broken rhythm. But where periodicity of symptomatology does occur, it is often useful in diagnosis, and a survey of its range prepares the observer for unusual and rarer forms of it, especially in the mental field, which may lead to the correct diagnosis and this particularly in cases having a legal bearing.

Periodicity of temperature change and symptomatology generally in malarial infections is more subtle than at first appears. Gutmann and Porak found some interesting phenomena on examining great numbers of temperature charts of malarial subjects from Macedonia, Greece, Italy, and North Africa. They point out that we are so accustomed to see and note the classical rises of temperature, that we have omitted to observe temperature changes in the apyrexial periods of the infection. They have found the basal temperature sub-normal, coming up to normal or a little above it, with periodicity. The periodicities noted were largely tertian and septan—more rarely lecan and quartan. The rhythms tertian and quartan are known from antiquity, as we have seen. The rhythm septan is very frequent, and Grall puts a value on it.

Periodicity in drop in temperature was also noted—to 35°, or towards 35°. The types of drop most seen by these authors were septan and quartan.

It is often with these periodic fluctuations of slight rise and slight drop in temperature that subtle symptoms and signs in wide variety arise—often unrecognized until the parasite is thought of and looked for. And many of these cases form a large proportion of the instances of latent malaria, where endless trouble may have to be taken before the parasite is finally found.

From the literature, some representative examples of tertian and quartan periodicity of symptoms and signs have been gathered together, where in some instances at least, the periodicity was the feature which gave the clue to the true nature of the case. In tropical malarious countries, the medical practitioner is perhaps more likely to be on the outlook for the malarial parasite, to explain his cases usual or unusual, but in less malarious

countries like Britain, where most of the cases are infected repatriated Colonials or soldiers, the parasite, especially in its less typical symptomatological dress is liable to be readily forgotten and overlooked. Almost any and every variety of symptom or sign has been observed as replacing or accompanying the temperature with tertian or quartan periodicity. Prominent among these have been neuralgias, often trigeminal or sciatic, headaches, splanchnic neuralgia with digestive disturbances, skin eruptions such as urticaria, different varieties of erythema, hiccough, angiospasm, aphasia, hemiplegia, ~~amnesia~~, peripheral neuritis, and even mental confusion and amnesia. Da Matta describes a case of intermittent hiccough and plantar hyperaesthesia in masked paludism. F. Schweitzer describes intermittent neuralgias of the cervical and accessorius region, tonic contractions of the sterno-mastoid extending to the neck muscles; also intermittent myospasm affecting lumbar muscles, adductors, quadriceps femoris etc. He found the "rheumatic" syndrome common. Also he found intermittent sweating, paraesthesia, formication, joint pains and swelling in hands, feet, tongue etc., and notes that angiospastic phenomena were commoner than vaso-dilator phenomena. In some patients, extreme vaso-dilation intermits with vaso-constriction. In peripheral paraesthesias, the radial artery was found contracted on the affected side on which the pulse was smaller and the blood pressure higher, and pulse tracing showed the pulse smaller than normal, and also smaller than in the free interval. He indicates that spasm may affect the coronary arteries, producing false angina, and asthma of both cardiac and pulmonary origin.

A case of tetany with tertian periodicity is recorded in Chapter XXIII (Hebert and Bloch).

The following examples will illustrate the range of this fitful symptomatology.

CASE I. Rubella-like rash, with quotidian periodicity. (Billet).

F.R., soldier, embarked at Marseilles, 3:1:05, to return to his regiment in Oran. He took a violent attack of intermittent fever, a recurrence of fever got at Oran in Sept., 1904. There was

severe lassitude, headache, giddiness, and nausea. Too fatigued to continue, he was conducted to hospital, where it was noted that temperature at 2 p.m. was 39°-5, and attention immediately arrested by a rash-like German measles on abdomen, and front of forearms. They were easily effaced by digital pressure, and did not itch. He was therefore isolated.

Temperature at 6 p.m., 40°-6, which subsided after that with sweating.

4th January, 5 a.m. Temperature normal. At 8 a.m., the erythema had completely disappeared. 9 a.m., temperature, 37°-6 with renewed attack of sweating. 12 noon, tempt., 40°-3, erythema reappeared with same localisation as before. 2 p.m., sweating, with commencing disappearance of rash. 6 p.m., temperature normal, rash disappeared.

The author thought it rubeola, but intermittency suggested malaria. Blood showed abundant M.T. parasites.

5th January. Symptoms repeated as above. No evidence of syphilis, and patient had not taken quinine for a long time. 1 gm. of hyirochloride of quinine given at 12 noon—thereafter no recurrence, and parasites disappeared from the general circulation.

CASE II. Scarlatiniform rash, with quotidian periodicity. (Billet).

K.F., a Zouave soldier, aged 21, was admitted to hospital at Constantine, 29:8:01, for scarlatina. He presented over different parts of the body large red plaques on the anterior aspect of forearms, thorax, back, front of thighs, all with the appearances of scarlatina symmetrically distributed. Tonsils and soft palate a little red, with slight dysphagia, but without marked swelling or membrane. —

29:8:01. Temperature, 39°-6 at 10 a.m. Said he had fever on the 25th, but no eruption until the 28th. Fever not continuous, occurs in the morning, and normal in the evening with sweating abundant. Put on observation, with milk diet, nasal and mouth washes. No medicines since the 25th, except purgative on the 27th.

30:8:01. Calm night, apyrexia. 6 a.m., temperature rises slowly to 39°-8 at 10 a.m. Eruption, which had almost disappeared

during the night, reappeared with its former intensity, and was highest between 9 and 12 a.m., and parallel with the temperature. By 4 p.m., it had almost disappeared again. Intermittency suggested malaria. Blood literally swarmed with parasites—10-12 in a field. Leucocytes, 25,000 per c.mm. Of mononuclears, 70% were large ones, i.e. mononucleosis. At 4 p.m., 1,50 quinine given.

31:8:01. Temperature normal all day. No erythema and no parasites found in the blood. Apyrexia 1, 2, 3, 4, and 5 and 6th Sept. Slight desquamation of skin seen.

8:9:01. Apyrexia—no erythema.

9:9:01. Fresh attack: temperature, 40°-5 at 9 a.m., and reappearance of erythema on thorax only. Some parasites seen in blood again. 2 gms. quinine sulph.

10:9:01. Apyrexia, daily quinine.

11:9:01. No further erythema.

18:10:01. Patient left the hospital in a cachectic condition.

It is of interest to note that this case was mistaken at the beginning for scarlet fever.

Billet also records a case of cardiac dyspnoea, with the symptoms of angina pectoris, which recurred with malarial febrile attacks with tertian periodicity. This case is detailed in Chapter VI.

CASE III. Urticaria, with quartan periodicity. (A. C. Pross, Brazil).

The patient was a coloured woman, a cook, aged 25, who suffered from urticarial manifestations every four days at 11 o' clock, without any other symptoms. No fever, no chill, no perspiration. When first seen by the author, she said she had had the condition for two months, and that she had never had malaria, notwithstanding that she had lived in a malarious district in Bahia.

Physical examination showed only some pain on pressure in the epigastric region at left lobe of liver. Spleen not palpable or painful, but slightly increased in size by percussion and phonometry.

Malaria suspected because of periodicity—blood immediately examined, and found many parasites of p. malariae.

The patient was observed for a fortnight, and urticaria never

failed to appear every four days during that time. After quinine, the sickness diminished gradually and disappeared, notwithstanding the fact that some quartan parasites remained in the blood. Quartan fever is not common in Bahia.

Masked paludism in Bahia more often shows as neuralgias, hepatic colic, headaches, lethargy, coma, convulsions, etc.

CASE IV. Urticaria, with other anaphylactic phenomena in tertian periodicity. (Ettinger).

Man took ill, 18:8:02, with severe indigestion.

20:8:02. Developed a typical measles rash, with suffusion of the eyes, nasal mucous membrane, and larynx. Spleen not palpable. No parasites found in the blood, either during or after this attack.

21:8:02. Temperature normal—total absence of rash.

22:8:02. Temperature, 40°. Whole body showed urticarial rash. With each attack, there were general symptoms of collapse, urticaria, abd gastro-intestinal disturbance, and suffusion of throat, nose, and eyes. Spleen not palpable, at this time. Many parasites found during this attack.

26:8:02. Spleen palpable for 6 days after this date. No recurrence of symptoms after quinine treatment. 0.6 gm. twice daily begun, and no desquamation of skin visible.

CASE V. Angio-spasm, with tertian periodicity (F. Schaudinn).

A. R., brought up in Jersey City, aged 28 years, was robust until three years ago, when he began to be ailing. He had frequent chills, general pains, and was usually very tired and depressed. In May, 1904, he complained to me of paraesthesia in his limbs. Four months before, he had first noticed them in his feet, then in his arms often, and now often in his head and tongue. He had good and bad days alternately, and always slight fever, ranging from 99°F to 101°F.

Examination revealed a hard and very large spleen, large liver, slightly melanotic skin, and very anaemic blood with plasmodia of the tertian type and one semi-lunar body; the urine and blood vessels were normal.

Four weeks of anti-malarial treatment brought some relief, but he is not yet entirely free from attacks of numbness. It seems as if he had been injured permanently, as if he would have great difficulty of getting out of his anæmic condition. Author considers it probable that angio-spasms represent the chill.

CASE VI. Tongue swelling with tertian periodicity. (Schweizer)

Woman, a hospital case, complained of intermittent swelling of the tongue. Every second day at 6 p.m. her tongue swelled up to such a size that she had to keep her mouth open to allow it to protrude to keep from suffocating. Quinine given after the third attack brought prompt relief. The spleen was very large, and although blood slides were not taken, the author considers the condition due to malaria.

Moscato describes a case of angio-neurotic oedema affecting the left half of the upper lip in a boy of 12, and recurring with quotidian periodicity, which is recorded in Chapter VI, under the section on Oedema.

CASE VII. Intermittent swelling of thyroid gland. (Kaufman, quoted by Schweizer).

This case, seen by Dr. Kaufman, showed intermittent swelling of the thyreoid gland. The swelling was so great, and the ~~extent~~ tension of the gland at times so painful, that a surgeon suspected an abscess or tumour. Several probatory punctures proved negative. As the patient's spleen was very large, quinine was prescribed with success; the gland resumed its normal size and consistence, and for six years has shown no signs of disturbance.

CASE VIII. Fever and diarrhoea, with tertian periodicity. (Gloëner).

Frau S., 27th June, complained of shivers between 9 a.m. and the afternoon. Temperature at its highest was 39°·8. During the fever period, there were ten movements of the bowels—thin, yellow, without blood, mucus, or pain. For the next 24 hours,

there was no movement at all. Third day, another shivering with profuse diarrhoea. Spleen slightly enlarged. Malarial parasites in the blood. Fever and diarrhoea disappeared after two doses of quinine—1 gm. quinine chloride.

Glogner has seen many cases of this kind with intermittent symptomatology. The following is a severer case of this class:

CASE IX. Fever, abdominal pain, and diarrhoea with tertian periodicity. (Glogner).

Male patient, admitted to hospital, 28th May, with fever, abdominal pain and diarrhoea. Fever occurred each morning at 7 a.m., and lasted till 12 noon. At 2 a.m., at this time he felt warm for a short time. Complained of loss of appetite, epigastric pain, tenesmus, during bowel movement, pain on pressure over ascending colon, especially in ileo-caecal region. Spleen and liver enlarged. Malarial parasites in the blood. Stools thin with mucus and blood.

28th May. Fever early, highest temperature, 38·6°C. Afternoon temperature normal. At 4 p.m., 36·3°C. 1,2 quinine given in apyrexial period.

29th, 30th May, 1st and 2nd June, in early morning hours, slight fever. Absent till 8th June, when another attack same as before. Thereafter normal.

30th May, at noon, temperature was 37·8°C, breathing short, pulse 96, respiration 36; this was repeated on third of June.

31st May—less blood and mucus in stool, and pain is less.

2nd June. No blood in stool.

9th June. Stool formed—no mucus or blood; three times in 24 hours. Soon after this, patient is normal. Parasites slowly diminished and disappeared with pain and diarrhoea on quinine treatment.

CASE X. Clonic contractions of sterno-mastoid muscles in malaria. (Gaz. degli Osped., 7th January, 1906).

Woman, aged 30, showed synchronous clonic contractions of both sterno-mastoid muscles. Every movement caused her head to bend

The spleen was large and soft. There was intermittent fever and numerous semilunar parasites in the blood.

Every attack while in hospital was accompanied by clonic contractions of the head, the maximum intensity of which coincided with the height of the fever, and the contractions disappearing with the pyrexia. Under quinine injections, fever and contractions disappeared. After two weeks pyrexia, patient was discharged. The writer contributes contractions to tonic action on central nervous system.

CASE XI. Laryngeal spasm with quotidian periodicity.
(Ziemann).

A young salesman, previously quite healthy and with good personal and family history, had been two years in the Cameroons. He took no quinine prophylactically. He had occasional slight attacks of fever after being six months in the country, during which he took a little quinine.

He came complaining that, beginning four days before, about four in the afternoon daily, he had a feeling of cramp in the muscles of his throat associated with difficulty in breathing; unaware of fever at these times.

Examination, 11 a.m. Well-built man; temperature and pulse normal. Internal organs negative. Larynx looks normal. Voice on breathing free. After long hunt, found two M.T. gametes. Hb, 78%. Sent to Hospital.

4 p.m. Cramped feeling in throat. Temperature, 37·4°C. Dyspnœa during inspiration. Voice soft—anxious. Crico-thyreoid muscles stretched and hard. Examination with laryngeal mirror impossible; after cocaine, just possible. Epiglottis in normal position. True vocal cords stretched, and show only a small space of about 2·5 mm. during energetic phonation. In blood, no gametocytes but after long hunt, some pernicious schizonts. Attack over in about hours.

The following day, 1·5 gm. quinine bihydrochloride intramuscularly; at 1 p.m. with Quinke's hot air-bath. At 4 p.m.—same phenomenon, spasm, temperature, 37·3°C. Up to the third day, the same, though on the third rather less than formerly, both temperature

and spasm. Fourthday, still less. Fifth day, 1 p.m., 1,0 quinine and hot air-bath. No spasm. From that date parasites disappeared, as also the spasm.

The patient was put on strict quinine treatment, 1,0 quinine daily for three days, then every second day for 14 days, then every fourth day, 1 gm. He remained free from spasm, which the author considered as having been wholly due to malaria.

CASE XII. Neck-swelling, with quotidian periodicity. (Schwyzer).

A woman came complaining of recurrent swelling of the neck. At the first interview nothing was to be seen. She came back at 8 o'clock one night, with a red oedematous neck, and said the swelling always occurred at this hour. Malarial parasites were found in the blood. Quinine removed the swelling at the time, but she came back twice within a year with the same complaint.

CASE XIII. Aphasia, with tertian periodicity. (Schwyzer).

Man aged 40 who had had malaria for a long time complained of " a sleeping" feeling of the right hand, and after a few minutes of the right leg also. This was followed by giddiness, and aphasia which lasted a few hours. The patient could move the limbs quite well. The writer considered it at first a small cerebral haemorrhage. This combination of symptoms, however, recurred every second day at the same hour, when malaria was suspected, and examination showed parasites in the blood. The spleen was enlarged, and temperature rose during attacks, with apyrexia between.

Quinine in large doses stopped the temperature and sweating, but aphasia and angio-spasm affecting the arm and leg continued for a time.

CASE XIV. Meningeal symptoms, with tertian periodicity. (Poro

A. M., aged 17, had had malaria a year before, when he had repeated severe attacks during 8 days. On 1st May, 1909, he was taken suddenly during the night with violent shivers, headache, and vomiting. Temperature rose rapidly, and remained up all day but towards evening it fell, headache disappeared, and next day patient

felt well. Then followed four fresh tertian attacks, but the doctor, struck by the slow pulse (60 per min) and high temperature (40°C), by the stiff neck, retraction of abdomen, sent the patient to hospital with the diagnosis of cerebro-spinal meningitis.

8th May. Temperature normal (37°). No headache, but neck still stiff and abdomen retracted, reflexes a little brisk, pulse 50.

9th May. Febrile attack, temperature, 39°C, pulse 60. Headache, stiff neck, Kernig. While temperature fell next day, headache and Kernig disappeared. Cerebro-spinal fluid shows marked hypertension. Visible deposit, which gives 50% polynuclear cells. No parasites found, but quinine given. Slight pupillary inequality.

28th May. The patient left hospital feeling well, though the pupils were still a little unequal, and the reflexes a little brisk.

CASE XV. Mental confusion, with tertian periodicity (Pepper).

E. C., female, aged 69, was admitted to the hospital in a state of semi-unconsciousness, having been taken suddenly ill on a train. On admission she was mentally confused and her circulation was in a very alarming state of weakness, pulse very rapid and thready, and myocardial tone very poor. Temperature, 99·6°F. Urine contained a faint trace of albumen and many casts. Blood count: Hb, 80%. Reds, 4,890,000: Whites, 11,800: polymorphs, 82%: lymphocytes, 8%: large mononuclears, 8%: transitionals, 2%.

A diagnosis of myocardial weakness and cerebral anaemia was made, and cardiac stimulants were given. Within two hours, her condition improved materially, and the next day, she had recovered sufficiently to desire to continue her journey. She then gave a history of having been in Brooklyn on a visit in apparent good health until the 21st of the month, when she was taken with a chill and felt drowsy. A physician was called and diagnosed fever trouble. She continued drowsy, and on the 23rd became worse, vomited, and had some epigastric pain. On the 24th, she felt well, but on the 25th had a second chill, but felt well enough to start for her home in Delaware. On the trip, she became partially unconscious, and was sent to the hospital.

She states that she had three or four attacks during the past year somewhat similar to the present one, but these former attacks were always associated with slight outbreaks of erysipelas on her ankles, to which she attributed the chills and malaise. This history was obtained on the 26th and at this time the patient seemed in excellent condition.

On the morning of the 27th, the patient was found to be irrational, and at times stuporous. Her temperature abruptly rose to over 103°F, and she showed signs of circulatory collapse. The blood pressure fell, and did not respond to any stimulant until after the temperature fell. There was no chill, and the spleen was not palpable. The patient became clear mentally, but could not remember what had happened. The following day she appeared entirely recovered. On the 29th, the chill was repeated, and for the first time, a few tertian parasites were found in the blood. No further attacks developed after treatment with quinine was instituted.

Within but a few hours this patient would change from a condition of satisfactory circulation and blood pressure into what appeared to be an alarming circulatory collapse, only to recover almost as rapidly.

An interesting observation was made on the urea content of the blood. It has been shown in the past, that there occurs an increased urinary output of urea during a paroxysm, and that this increase begins several hours before the attack attains its maximum during the cold stage, and declines to normal at the end of the paroxysm. Our case was being investigated from a renal standpoint, and blood was taken for the determination of the blood urea nitrogen at a time when the temperature was normal. An hour later, the patient had a chill, and the high reading of 42 mgms. per 100 cc. of blood is probably to be correlated with the increased output of urea which is known to occur at this time. A later estimation after all chills had been stopped by quinine showed that the reading had fallen to 25 mgms. This second reading is still far above normal.

CASE XVI. Delirium with quotidian periodicity. (Blocca).

A man who was delirious for a few hours at the same time on three successive days during malarial rigors. Temperature moderate (37.8°C) first two days, while on the third day, the delirium occurred without any rise of temperature. The delirium subsided with the sweating stage of the rigor and between times, the man was mentally quite clear. Malarial parasites were found in the blood, and the condition cleared up with quinine. The patient was a chronic alcoholic which the author considered had a morbid influence, the malaria doing the rest.

CASE XVII. Tertian periodicity of symptoms in a diabetic. (C. S. Crispin).

M. was seen on February 5th, 1918, suffering from fever (temperature, 101°F), headache, vomiting, constipation, cold extremities, and cardiac distress. Spleen and heart normal, but pulse weak. He was a known diabetic, and had 4·76% sugar in the urine a month previously. He was passing extremely little urine of high colour. It contained acetone, diacetic acid, & β-oxybutyric acid. Blood films negative for malarial parasites; no mononuclear increase; distinct polymorphonuclear increase.

Patient was immediately put on a fluid diet, and given 30 grs. bicarbonate of soda every two hours, and the same evening was better, the cardiac distress and vomiting having ceased. Bowels moved by enema.

Feb. 6th, 1918. Much better, no fever, headache, vomiting. Urine scanty, contained sugar, no casts, no diacetic acid, and was alkaline; slight albuminuria and phosphates. Sodium bicarbonate continued.

Feb. 7th. Condition same as on the 5th. Bad night. Blood films negative for parasites. 24 hrs. urine specimen contained 3% glucose, slight albumen, no casts and was alkaline. Bowels relieved by enema.

Feb. 8th. Much better. Urine alkaline, trace albumen. Sod. bicarb. stopped.

Feb. 9th. Return of all the symptoms, and his condition caused some anxiety. 3·7% glucose in the urine. Pulse very weak. Spleen

not enlarged. After consultation, diuretics, and cardiac stimulants were given—digitalis and nux vomica.

Feb. 10th. Better in the morning but recurrence of the ~~sympto~~ symptoms in the evening.

Feb. 11th. Symptoms persisted—condition unsatisfactory. Urine amphoteric, with trace albumen, and no diacetic acid. Blood films negative for malarial parasites, and there was no mononuclear increase.

Struck by the periodicity of the symptoms, I decided to try quinine, as several cases of malaria had occurred in the neighbourhood where he lived. A 10 gr. dose was ordered, but only 5 grs. were taken in the morning, and in the evening he got 10 grs. by injection.

Feb. 12th. Very much better. All medicines stopped, except 10 grs. quinine injections, which were repeated daily for a week, during which progress was uninterrupted.

Feb. 14th. For the first time, blood films showed sub-tertian rings and gametocytes.

Feb. 17th. 24 hrs. specimen urine showed 2·37% sugar, slightly acid, trace albumen, no diacetic acid.

Feb. 18th. Quinine, 10 grs. daily, by mouth instead of by injection.

Feb. 23rd. Malarial crescents in blood. Urine, 3·6% sugar.

March 5th. Patient perfectly well—no fever. Urine acid, 2·52% sugar.

April 13th. Has kept well. Urine acid, no acetone, and contains 2·48% sugar.

The absence of the malarial parasites in the blood, with no mononuclear increase, and no enlargement of the spleen, with presence of acidosis, were the causes that gave rise to error in diagnosis. The blood films were all carefully examined by the same man, and whereas a most thorough search on the 5th, 7th, and 11th showed no parasites or mononuclear increase, parasites were present in abundance on the 14th. The only indication of malaria, therefore, until then, was the periodicity of the symptoms.

CASE XVIII. Malarial colic, colitis, dysenteric diarrhœa with tertain periodicity (Billet).

F, soldier, Algeria, evacuated 13th October for dysenteriform diarrhoea.

13th Oct., 11 p.m. Admitted to hospital very weak, and with severe colic, and bloody stools. Temperature, 37·8°C.

14th Oct. Some improvement. Complains of slight tenesmus and weakness. Temperature, 36·4°C, morning: 36·2°C evening. Caffeine, milk diet, alcohol, (warm), 25 gms. Mag Sulph.

15th Oct., 1 p.m. Violent colic recurs, with meteorism, and great tenderness of abdomen to pressure. Tongue furred, dry. Face pinched; body covered with cold, viscid sweat, but no shivering. Temperature rises rapidly to 39·6°C at 4 p.m., and remains so till 6 p.m., by which time there is diarrhoea, with mucus and blood in stools, and continues during all the time the temperature is above normal. Some relief of pain follows each evacuation. During the evening, symptoms gradually abate.

16th Oct. Temperature, 36·6°C at 6 a.m. Bismuth and opium, milk, alcohol. A quiet day. No diarrhoea. Apyrexia restful.

17th Oct. Again a dysenteric attack same as above, at same hour in the evening. 4 p.m., temperature, 39·6°C. Ring forms of M.T. parasites, 6-10 per field, found in the blood. Mononucleosis. 1 gm. quinine given hypodermically on 18th, 19th, and 20 th Oct.

18th Oct. Apyrexia.

19th Oct. Very slight evening diarrhoea. Temperature, 37·8°C at 4 p.m.

20th and 21st. Apyrexia. Malaise only. Able to sleep. Very weak—cachectic.

22nd Oct. Crescents. Mononucleosis. Recurrence of dysentery attack in the evening. Temperature, 38·8°C at 4 p.m., but not so violent as formerly. Parasites recur.

23rd, 24th, 25th Oct. Quinine injection daily. Apyrexia since the 24th, and thereafter rapidly improved, cachexia disappeared and by 28th Oct., patient was able to get up.

12th Nov. No recurrence of dysenteriform attack since last note—continues quinine daily.

Another case, one of cardiac dyspnoea, with tertian periodicity of symptoms, is also recorded by Billet (Cf. Chapter 6).

A case of recurrent colic by Job and Birtzmann is also recorded in Chapter 8.

PERIODICITY OF SYMPTOMS NOT OF MALARIAL ORIGIN.

While tertian or quartan periodicity of symptoms may be the only clue to malarial infection, the need for substantiating the diagnosis by other means, preferably by finding the parasites is important. For other conditions than malaria sometimes give rise to symptomatology of tertian or quartan rhythm. Several cases of gastric carcinoma simulating malaria because of rhythm of symptoms have been recorded by Rovsing. One, a man of 49, began to have chills, followed by fever rising to 104°F, with occasional vomiting. These febrile attacks returned every third or fourth day, but sometimes the fever kept up for four of five days at a time. He was treated with quinine and arsenic for malaria without results, and no parasites were found in the blood. By the fourth month, he began to have a sensation of oppression in the epigastrium with nausea and vomiting after meals, and occult blood was found in the stools. The man was restored to clinical health by resection + gastro-enterostomy, and he survived for over three years before death from recurrence of adeno-carcinoma. At the first operation, it was found to have involved both stomach and duodenum, and some lymph-glands, and it pressed against the pancreas.

Rovsing has found 5 similar malaria-like cases of gastric cancer on record. One (Halla) was a necropsy surprise after ineffectual quinine treatment of "four day fever". In one of Wanpeln's three cases, the patient was dismissed from the hospital as the "malaria" had proved refractory to a course of quinine treatment, but the man returned three months later with a large tumour in the epigastrium. Necropsy confirmed the cancer.

Periodicity, then, is a feature in symptomatology, which, when present, is useful in putting the observer on the right track, though of course it exists in affections other than malaria, and careful discrimination has to be made. At any rate, timely suggestion of malaria as an explanation of an obscure case, or one

that has resisted previous treatment, may lead to the finding of the parasite or even to cure by empirical use of quinine. Furthermore, observation of a well constructed chart may reveal the fact, by reason of periodicity of temperature, either hyper- or hypo-thermic, that parasites in subdued form or numbers, still exist in the host.

It is of special interest for medico-legal purposes to note that where the periodicity of symptomatology is mental, that coincident abnormality of conduct, homicidal or otherwise, is quite consistent with mental clarity on alternate days, and ultimate irresponsibility. (Cf. Chapter XXI).

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CHAPTER XXIX.

SURGERY AND MALARIA.

Malaria has been found to complicate surgical conditions in several ways, the best known of which are as follows:

1. Simulation of "acute" abdomen.
2. Chloroform anaesthesia in malarial sunjects is apt to produce pernicious symptoms.
3. Operation may induce an attack of malaria.
4. Trauma, especially of long bones, ribs or spleen may induce an attack of malaria.
5. Surgical spleen.
6. Malarial gangrene of extremities.
7. Tendency to haemorrhage in malarial subjects.
8. Tendency to delay, or failure in healing of fractures, or wounds, in malarial subjects.
9. Increased susceptability to other infections in malarial subjects.
10. Wounds of the head may closely simulate cerebral abscess in malarial subjects. (W. White).
11. Drainage of the abdomen in malarial cirrhosis of the liver.
12. Quinine abscess.

Malaria therefore again simulates syphilis in its modifying detrimentally the course of surgical as well as medical conditions; especially is this referable to the delayed healing of wounds. In malaria, however, the effects are apt to be more dramatic, with sudden and considerable rises of temperature, onset of coma, etc.

1. Simulation of acute abdomen.

This has been noted by many observers—Alamartine and Vandenbosche, Parsons, Jackson and Capps, White, Falconer and

Anderson, Craig, Gallot, Soulié, Rosenburg, Dudgeon and Clarke, Castellani, Ross and Daniels, etc. The commonest form appears to be the simulation of appendicitis, and instances of this are already recorded in Chapter VI.

Abelario records a case of operation for apparent appendicitis in a malarial subject, in whom, while under chloroform anaesthesia, alarming symptoms occurred. The patient's temperature rose markedly and he showed cerebral symptoms. Malaria was suspected, but in spite of 1 gm. of quinine and restoratives, the patient died. Malarial crescents were found in the blood after death. Death was considered due to malarial cerebral congestion, and the author thinks that a pernicious attack was induced by the combined effect of operation, and chloroform anaesthesia inducing coma in one with latent malaria.

Craig reports a case of malarial appendicitis with recovery.

CASE. Malarial Appendicitis. (Craig).

The patient was an officer of the U. S. Army, who was transferred to the Army General Hospital at San Francisco with a diagnosis of suspected appendicitis, transfer being made with a view to operation if the diagnosis was verified. He gave a history of having had intermittent malarial attacks in the Phillipines, which did not necessitate admission to Sick Report. He had not been feeling well for some time, and on the day before admission to the hospital he had an attack of pain in the region of the ascending colon. Upon admission, he complained of pain in this region, at times very severe; his tongue was coated; bowels regular; and his pulse and temperature about normal. A blood count was made and a slight leucocytosis was found.

Physical examination showed no rigidity of the muscular wall, but he complained of pain in the right iliac region on pressure, and after careful examination, operation the next morning was determined on.

That evening he had a slight chill, and his temperature rose to 104°F. A blood examination showed tertian aestivo-autumnal parasites. Quinine was promptly administered, resulting in an immediate fall

of temperature, and complete recovery.

In this case an operation would undoubtedly have been performed in the morning for a condition essentially malarial in character.

Castellani saw several cases of this kind in the Balkans, and two in Ceylon. In one, the surgeon operated and found the appendix macroscopically normal. On the third day after the operation, the patient had a very severe rigor, and complained again of pain in the "caelo-colon" region, though more diffuse; his temperature jumped to 105°F, the spleen became palpable, and sub-tertian rings were found in the blood. After intramuscular quinine, the temperature became normal within 36 hours. Castellani says that in these cases the polymorphonuclearleucocytosis of true appendicitis is often absent, while he points out that there are exceptions to this rule.

Goodall found malarial appendicitis common in Macedonia, and difficult to deal with. The questions that arose in these cases were whether they were pure malarial, or septic only, or sepsis in a malarial subject. Blood examinations were generally relied on for a decision. Presence of parasites was helpful, but insufficient. Generally speaking, a polymorphleucocytosis decided for surgical treatment. Only once did the leucocyte count lead astray. The patient appeared to have a definite appendicitis, with a high leucocyte count, and a high percentage of polymorphs. On the strength of this the appendix was removed, and found to be only slightly congested. Cure was completed by quinine. He says that the more serious error is less likely to occur as an appendicitis demanding operation does not occur without disturbance of the leucocyte count.

Falconer and Anderson saw 12 cases of appendicular type of malarial origin, and found the chief features vomiting, pain in the right iliac fossa, associated with moderate pyrexia and marked tenderness and rigidity in the right fossa. In most cases, it was possible to show that the rigidity was not constant. In some of the cases the tenderness was most marked above McBurney's point; in others it corresponded exactly with this point. In all cases, there were either parasites in the blood, or definite enlargement of the spleen. None showed a leucocytosis, and all had the typical relative lymphocytosis of malaria. All rapidly cleared up with quinine.

A few of them showed so severe pains and rigidity as to suggest acute abdomen, but these also cleared up rapidly with quinine.

Gillot records several cases of interest in this connection. One is that of a woman of 21 years in the 5th month of pregnancy who developed signs of peritonitis, but who had malarial parasites in the blood, and was cured by subcutaneous quinine, and left hospital without mishap to the pregnancy. A case simulating extra-uterine pregnancy, and sent to hospital for operation, is detailed in Chapter VI. (Capps). Gillot indicates that many of these cases simulate generalised peritonitis with generalised pain and tenderness, meteorism, incessant vomiting, small pulse, pinched face, and loss of voice. He records the case of a woman who was brought to Hospital in Algiers, and was for several days in a typhoid state, and rapidly developed signs of peritonitis. It was thought she had a typhoid perforation of the intestine, although the serum test was negative. The surgeon did a laparotomy, and found—no typhoid lesions, no perforation—nothing. The patient died next day. Malarial parasites were found in the blood post-mortem.

Another similar case of Soulié's, quoted by Gillot, recovered on quinine treatment.

CASE. Malarial peritonitis. (Soulié).

Woman of 41, admitted to Hospital at Algiers, 26:8:90. Fevered for 5 days, and complaining of headache and general lassitude. Never had malaria till then. Temperature, 40°C, pulse 120. Next day abdomen painful, meteorism, vomiting. Ice to abdomen and opium prescribed; next day worse—can keep nothing—vomits constantly. Face pinched, abdomen very painful and ballooned up. Pulse 130. Temperature, 41°C.

Peritonitis diagnosed. Malarial parasites, and pigmented leucocytes, found in the blood. 1,50 quinine bichloride given hypodermically. From next day temperature 38·4°C: abdomen less painful, but meteorism, vomiting less. Another injection of 1,50 quinine in the evening lowers temperature to 37·4°C. Next day vomiting ceased: meteorism much diminished.

31:8:90. Temperature rises to 39°C. Vomiting, meteorism,

and abdominal pain reappear. Ice-bag applied with quinine. 1,50 quinine bihydrochloride. From the next day fever normal, and vomiting and pain disappear. Quinine continued for two days. The patient leaves cured on 30th Sept. The author considers this a rare example of malarial infection.

Rosenburg records a case diagnosed as peritonitis in which operation showed no such thing. Capillaries were stuffed with parasites and pigments, found after death on the third day. A second similar case with parasites in the blood was cured on quinine treatment.

Jackson reports two cases—one diagnosed as pelvic peritonitis with pain, tenderness, and resistance in the right iliac fossa. Spleen enlarged. Malarial parasites in the blood: leucocytes, 5,100 per c.mm. Another case with repeated malarial attacks and acute epigastric pain with each recurrence. After subsidence of the fever, marked epigastric tenderness persisted for some days.

Castellani reports a similar case of pseudo-peritonitis in a lady in Skopolje. She had low feber, pinched face, vomiting, severe pain and tenderness, all over the abdomen, and was supposed to be suffering from petitonitis from some old uterine disorder. Spleen impalpable, but palpation was difficult owing to muscle rigidity. The blood was found teeming with malarial parasites, and quinine cured the condition in a few days.

Capps reports a case diagnosed as acute salpingitis. There were chills and fever to 103°F daily. Spleen enlarged. There was acute abdominal pain, mostly in the lower zone. Leucocytes, 5,800. Also another case diagnosed as gall-stones. For six days, the patient had fever, headache, vomiting, and pains in the epigastrium so acute as to require morphia; he was then admitted to hospital for operation for gallstones, or perforating gastric ulcer. Spleen enlarged. Leucocytes, 8,900—which was considered against peritonitis. Malarial parasites were found in the blood.

Castellani saw three cases suggesting acute cholecystitis all cured by quinine.

Alamartine and Vandenbosche record two cases of violent

abdominal pain, incessant vomiting and rigidity, which suggested perforation of stomach or duodenum and were nearly operated on.

While the majority of the cases recorded with abdominal symptoms appear to be malignant tertian infections, benign tertian infections with acute abdominal disturbances are recorded by Parsons, Jackson, Capps, etc.

Parsons records a case of a private soldier, aged 47 years, who had malaria with benign tertian parasites in the blood. He had been on the Struma Front for six months and had taken quinine regularly. This was his first attack of malaria, when he reported sick 14:12:16, with pain in the left side, headache, shivers, fever, vomiting and shortness of breath. On Sept. 17th, admitted to hospital. General condition fair, temperature 98°F. Tongue clean; heart and lungs clear. Complains of acute pain in the lower left axilla. Great tenderness over left side of the abdomen and splenic area, and rigidity of the left rectus muscle. Spleen enlarged, and palpably tender. B. T. parasites in the blood. Dec. 18th.: Marked rigidity of left side of abdomen, more so in upper part, and extending across epigastrium to middle line. Left rectus much firmer than right. On deep inspiration, spleen palpable and very tender. No cough. Left side of chest clear—no signs of pleurisy. On Dec. 22nd, there was still a little rigidity of upper quadrant of left abdomen. Spleen palpable. Left side of chest clear. Gradual cure by quinine.

Acute haemorrhagic pancreatitis (already referred to in Chap. VI) has been recorded by many observers, viz. White (2 Cases, one of which is recorded in Chap. VI), Castellani, Ross and Daniels, Flu, Duigeon and Clarke, etc. Generally no sugar in the urine, and only traces have been observed in these cases.

Castellani's case was that of a man of 42 who appeared to be in excellent health until he took ill suddenly with violent pain in the epigastrium without any apparent reason; this was quickly followed by very severe vomiting and complete collapse. There was a certain circumscribed area of very severe tenderness over the upper portion of the epigastric region, which was tympanitic, and somewhat swollen. The case was diagnosed as probably acute haemorrhagic pancreatitis, and an operation suggested, but the blood

was found to be swarming with malarial parasites.

For the diagnosis of malarial "acute" abdomen, these observers have relied on finding parasites in the blood (mostly sub-tertian, but sometimes benign tertian), enlargement of the spleen, the absence of a leucocytosis with relative mononucleosis—i.e. a malarial blood picture. Parsons is the only observer quoted who found a leucocytosis in all his cases of "acute" abdomen of malarial origin not including one case where a count was not made).

The reason for this varied "acute" abdomen picture, with its localisation of pain in different organs, rests largely in the pathology of the solar plexus. We have seen that a large part of the initial malarial paroxysm (Cold Stage) has the features of sympathetic stimulation. There is much collected evidence to suggest that pain referred to appendix, gall-bladder, stomach, or other abdominal organ, is not so often due to inflammatory changes in these organs, as to a neuritis of the solar plexus or its ramifications supplying these organs. Laignel-Lavastine has shown that the solar syndrome is determined, not so much by inflammation of the peritoneum itself, as by inflammatory changes in the cells and filaments of the plexus itself—swelling, leucocyte invasion, sclerosis, pigmentation of the nerve cells of the solar ganglia, and even ultimate disappearance of these cells. This agrees with the clinical pathology of malarial "appendicitis" and allied conditions, where often enough no naked eye appearances of inflammation are present and generally also no polymorphonuclear-leucocytosis; and while some of these cases may be explained by an endarteritis of the appendix from localisation of parasites there, it is highly probable that malarial neuritis of the solar ganglia and its branches explains others, and allied conditions.

2. *Chloroform anaesthesia* in malarial subjects, has been found to induce pernicious symptoms, and in not a few recorded instances has led to fatalities. A case of this class recorded by Abelardo is detailed above. White and Fuller both testify to the risks with chloroform anaesthesia in malarial subjects, and advise the use of ether. Alamartine and Vandenbosche emphasise the danger of collapse with chloroform in malarials, and say they have

noticed that attacks have been more frequent and severe after it than after ether. They had three cases who died with icterus and pernicious malaria after administration of chloroform, and several times had instances of haemoglobinuria. In more than a thousand anaesthesias in patients, 80% of whom were malarial subjects, they lost three cases due to chloroform anaesthesia, but had no liver accident with ether or ethyl chloride, which they recommend as less likely to produce hepatic insufficiency.

Cioffi considered this subject from the medico-legal standpoint —that is, in how far traumatism on the one hand, and chloroform anaesthesia on the other, gave rise to the occurrence of malaria, which went to complicate the original injury. He made inquiries at a large number of Italian Hospitals, where numerous malarial subjects are admitted, and found that in those clinics where chloroform is used, it is extremely common for simple operative procedures to be followed in a day or so by malarial attacks, but in those where chloroform has been abandoned, nothing of this kind has been observed. He also made observations on 80 railway employees, who were known to have suffered from malaria, who were injured, and in whom there was at a later period evidence of persistence of malarial parasites in the blood, and in none of them was an attack determined by the trauma, even when it concerned the bone. Cioffi investigations seem to show conclusively that chloroform as an anaesthetic should be abandoned. Ether and ethyl chloride appear to be the safer anaesthetics.

8. *Operation* may induce an attack of malaria especially if it concerns the long bones, ribs, joints, or spleen. While this is maintained by many observers, there is much to suggest that many recurrences at or after operation are due to the anaesthetic chloroform, rather than to the operation (see Cioffi's investigations referred to in last section). Alamartine and Vandenbosche, who have used chloroform, ether, and ethyl chloride as anaesthetics in malarial subjects, and are alive to the dangers in the using the first, indicate the frequent recrudescence of malaria—sometimes violent after operation, and maintain that it sometimes reveals latent malaria in subjects where its presence was not suspected.

They induced malarial attack generally occurs during, or from 24 to 48 hours after, operation, and especially, according to White, is this so in bone and joint cases. The patient complains of severe pain in the wound, which looks unhealthy, and joints become swollen and exquisitely painful. Temperature, if sub-normal, goes up in a few hours to 105°F or 106°F. Quinine is indicated intravenously or intramuscularly. According to Cioffi, observations of discretion (such as hernia) can be undertaken with security, so long as chloroform is not the anaesthetic.

Moore records two cases who had had malaria for two or three months, one of whom had the uterus curetted, and the other, who had pyosalpinx and one ovary removed with post-operative febrile attack, associated with malarial parasites in the blood, controlled by quinine. Billet, Bell, and Steward record similar cases (Ziemann). Ziemann had a case of an African Negro who, 20 hours after removal of his right leg (thigh), developed fever with malarial parasites in the blood, which subsided after a few days under quinine.

Prampolini had 9 surgical cases who, though they had had no evidences of malaria for a long time, and some of them not at all, developed post-operative febrile malarial attacks.

There are numerous instances of puerperal fever of malarial origin, complicating the puerperium, and suggesting sepsis, until the true nature of the condition has been recognised and dealt with by quinine.

Marchiafava and Bignami indicate the occurrence of post-operative "surgical" fever of malarial origin, and indicate the tendency of the puerperium to excite malarial attacks in latent or more acute infections. They quote Thayer, who recorded a case of malarial fever occurring after operation for cancer of the tongue, and clearing up on giving quinine intravenously.

Moreau reports 14 cases of wounded soldiers who had recurrence of malaria after injury, including operation, but does not distinguish between the effects of operation and the effects of chloroform. He found that recurrence may occur during any time from 24 hours to a month—not infrequently, 2-4 weeks after. It may occur in a recent case or in those who did not know they had malaria.

The majority were M. T. infections, the others S. T. Wounds and fractures healed slowly in infected cases, until quinine was given. Abscess incision often gave violent reaction, and were occasionally fatal.

Bertrand emphasises the importance of keeping post-operative temperature records in malarial countries, as in this way much assistance is afforded in the differential diagnosis between malarial recrudescence and sepsis.

4. Trauma, especially of the long bones, joints and spleen, may induce an attack of malaria, just as insolation or exposure to cold may do. According to Alamartine and Vandenbosche malarial attack occurs as a rule from two to three days after injury, the degree of which does not appear to matter in many instances. A fracture or seton may induce a very violent attack, just as operation may do. They indicate that malarial recrudescence is more constant and more marked if an anaesthetic (espec. chloroform) is required, and in some cases only occurred when it was used. The temperature in different cases was remittent, continued, or intermittent. With quinine, the wounded and those operated on became rapidly apyretic.

Moreau indicates that recurrence of attack, or appearance for the first time, is usually just after a wound, but is very variable, and may be any time up to a month afterwards.

Vieusse records 5 cases of trauma with recurrence of malaria long after last attack.

Nicoll relates of a boy of 5 who, after a visit to Cuba, was not well for six weeks with indefinite trouble, but which was thought to be malarial. In July 1905, he got a wound of his foot, and two days after was somnolent, and complained of pain in his neck. Temperature, 38·9°C. After a few hours, the neck became very painful, and convulsions appeared imminent. Malarial parasites were found in the blood. 1,20 of quinine was given in 24 hours, and improvement was rapid.

5. *Surgical Spleen.* The malarious spleen, being apt to be

very fragile, it has not infrequently to be removed after rupture by accident or spontaneously. Palpation or direct injury of the same organ has been noticed to induce a malarial attack sometimes. This part of the subject is dealt with further in the medico-legal chapter. Torsion, suppuration, and bullet-wounds of the malarious spleen require splenectomy. A spleen unusually large, and having resisted medical treatment, especially in cachectics, may be removed advantageously. According to Alamartine and Vanlenbosche, surgeons in malarious countries have had good results by splenectomy, in malarial cachectics, and quote in this connection Tricomy (Italy), Jonnesco (Buscharest), and Michailowsky. Vanverts collected 29 cases, 21 of which were cured, 7 continued to have malarial attacks, and one died shortly after operation. Jonnesco considers all spleens should be removed in chronic malarias that have resisted prolonged medical treatment. Sabadini also reports favourable end-results from this operation.

Degorce, on the other hand, has found that splenectomy does not disinfect and may induce immediate and fatal relapse.

Contra-indications are:

1. Cirrhosis of the liver.
2. Peritoneal adhesions which are troublesome.
3. Marked ascites.
4. Pleurisy.
5. Bad general condition, especially with visceral, hepatic or renal complications.

It is of interest to note that this procedure with the malarious spleen is similar to what Mayo has said (Surgical Congress, London, 1923) with regard to the spleen in syphilis. He maintains that in some cases of syphilis the spirochaete lodges in the spleen and resists all forms of medical treatment, and the blood Wassermann reaction does not remain negative. In a number of these cases, he has performed splenectomy with satisfactory results clinically and biologically, the Wassermann reaction becoming, and remaining, negative. Here again there is a parallelism between malaria and syphilis.

6. *Malarial gangrene*, oftenest of the extremities, but also

of ears and skin of body. Many instances of this are recorded throughout the malarial literature, and several cases are detailed in Chapter VI. Paisseau and Lemaire and others have shown that the ganagrene is associated with endarteritis.

Alamartine and Vanlenbosche record cases, one a man of 35 with malarial gangrene of the left leg from endarteritis and thrombosis of the femoral artery. Asputation at site of election resulted in cure. Syphilis and alcohol were excluded, and P. falciparum were found in the blood. Microscopically there was found to be an endarteritis of the posterior tibial artery.

A second case, a Serb aged 22, had gangrene of the left leg which was amputated at the thigh and showed endarteritis of all the arteries of the leg.

A third (fatal) case showed gangrene of the right arm and leg. The liver and spleen were packed with parasites. There was arteritis of the popliteal, tibial, and peroneal vessels.

These authors quote le Dantec as recording a case of a Doctor of Medicine, who after malaria had gangrene of the feet which were amputated, then the legs, and finally the thigh.

7., *Tendency to haemorrhage*, in malarial subjects, has been noticed by many observers. Variations in blood coagulability has been studied by many authors. At a part of the prodromal stage of a malarial attack, Abrami and Senewet record an increased coagulability, but the bulk of observations go to show that the blood of those infected with malaria is for the most part deficient in coagulation power, though it varies considerably from time to time. (Cf. Chapter VI).

Monier-Vinard found the blood coagulation time often very slow (20 minutes to two hours) and indicated that it is apt to show marked variations from day to day. In one patient, for instance, blood coagulation time was 1hr 20mins, and next day 50mins. He records 8 haemorrhagic cases—generally epistaxis, recurrent, and retinal haemorrhage. Paisseau and Lemaire have dwelt on the haemorrhagic syndromes of malaria.

Malcolm Watson (Selangor) notes a case with a scalp wound where after the injury there was haematuria, and although the

temperature was normal, there were many quartan parasites in the blood.

Ziemann saw a case of violent epistaxis in a sailor in the Navy, who bled to death. Nasal and peripheral blood showed enormous numbers of parasites. Billet saw epistaxis 14 times in 40 Algerian malarious cases of typhoid type.

Alamartine and Vandenbosche indicate that in their experience malarials bleed easily—epistaxis, haematuria, petechiae, ecchimosis Caillé, (quoted by them), noted delayed coagulation and observed that clot showed only a slight degree of contractility, and led to secondary haemorrhage.

White indicates that, in her experience, cases with malarial purpura haemorrhagica should not be operated on unless absolutely necessary, and that then every precaution should be taken to prevent haemorrhage. Even the extraction of a tooth has had a fatal result in cases of this kind. In her experience, quinine has very little if anything to do with the tendency to haemorrhage in malarial patients. In cases pre- or post-operative, she gave quinine hydrochloride in small doses with large doses of calcium lactate and if necessary horse serum.

Castellani records an outbreak of so-called scurvy with which he had to deal in Serbia in 1915. It affected a Serbian regiment, and the men had haemorrhages in and under the skin, petechiae affecting the whole body, and some with tense indurated subcutaneous extravasations of blood. In many there was bleeding from the gums and nose; in two from stomach and intestine; in one from lungs and bronchi; in another from kidneys and bladder. They were all very anaemic. The condition proved to be of malarial origin, and recovery took place when the men were treated with quinine without any change in diet.

Tendency to haemorrhages has also been recorded by Marchiafava and Bignami, who indicate that epistaxis is the most frequent form, but that skin, bowel, mucous membrane haemorrhages are not uncommon, and even haemorrhages from the ear. Retinal haemorrhages have been frequently noted as indicated in the Chapter on Special Senses.

8. *Tendency to delay in the healing of wounds and fractures*

has been noted by White, who says that wounds look unhealthy, granulate over, only to break down in a few days. She says that "some of them resemble syphilitic sores, and often it is only with a negative Wassermann, and response to quinine therapy, one becomes convinced that malaria is the aetiological factor".

Schwyzer noted that wounds and fractures in malarial subjects often healed badly.

Moreau records the retardation in the healing of wounds and fractures in malarials and advises quinine treatment as hastening the process of repair.

Marchiafava and Bignami also record the tendency of malaria to delay the healing of wounds.

Verneuil (1881-82) was probably the first to emphasise the importance of dealing with the malaria in the surgical conditions of malaria subjects. He quotes Morsly, who records a case of simple fracture of the leg in a robust man of 30 after having had several attacks of malaria. The leg was splinted, and two days after the accident he had a malarial attack which was stopped by quinine sulphate. On removal of splints 35 days later, the fracture was found to be un-united. Two days thereafter, another febrile attack, treated by quinine. The fracture healed 7 months only after the accident.

In another case of Verneuil and Petit—a robust young man who had had malaria for a long time and who sustained a compound fracture of the leg. Twenty months after the accident, the limb was still not quite healed.

9. *Increased susceptibility to other infections.* Marchiafava and Bignami emphasise this tendency in malarial subjects. While they (and Ascoli) have found it eminently so in regard to pneumonia in the Roman clinics, it occurs in more surgical conditions also. According to Alasartine and Vandenbosche, infections play the same role as trauma in awakening latent malaria. Very often an abscess, cold or otherwise, sinusitis, appendix abscess, etc. may precipitate an attack. Intercurrent infection may often affect the course of chronic malaria. Likewise temperature may be normal, with

abscess, between attacks. These authors were struck with the frequency of ischio-rectal abscess or pelvi-rectal fossa abscess, and abscess of liver, in Macedonia. They record a case of deep ischio-rectal abscess, masked by sub-tertian malaria with parasites in the blood, who was gravely ill, but recovered after operation, and quinine. Another case with dysenteric abscess of liver, and lumbar abscess masked by sub-tertian malaria, made a good recovery after operation, emetin, and quinine. They had many such cases and as a result of their experiences, consider that malaria prepares the patient for intercurrent infection.

Sepsis anywhere may light up a malarial attack, producing cerebral symptoms such as coma, which may simulate cerebral abscess (see next section).

Malcolm Watson has recorded the readiness with which other infections take place among the quartan malaria patients in Selangor. He says that among new infections, diarrhoea and dysentery are by far the most important, and that they accounted for 5 of 8 fatal cases. In 5 cases, the patients had abscesses, in 3 single, in 2 multiple. They are frequently large and comparatively painless, and they are frequently the complaint which brings the patient to the doctor.

He records the case of a Chinaman, aged 30, admitted to hospital, 26th March, 1903, with multiple abscess, complaining of pain and swelling of left arm and leg. Patient was anaemic, and gave no history of dysentery, diarrhoea, or fever. On 28th, abscess in arm was opened. On 31st, one in the thigh was opened. By the 2nd April, temperature chart suggested quartan malaria, but a careful examination on the 5th discovered no parasites. On the 8th, however, an unpigmented and a pigmented quartan parasite were found. On the 11th April, a large gluteal abscess was opened. On the 13th another in the thigh, and on the 20th yet a third on the same thigh. Patient then appeared to make satisfactory progress, until onset of diarrhoea on 26th April. This continued till death on the 29th May. The urine contained a trace of albumen but no casts, and was passed in quantities ranging from 25-50 ounces in the 24 hours. A pure culture of staphylococcus pyogenes aureus was grown from the abscess in the buttock.

Watson records another case of multiple abscess in a Tamil woman of 22, with quartan malaria—and recovery.

Castellani saw a case of malaria simulating abscess of the liver in Ceylon. The patient had developed his disease up-country where malaria is almost unknown. There was a history of dysentery 10 years before. When seen by Castellani, he had been suffering for two months from intermittent fever which had not yielded to quinine by mouth in 30 grs. doses daily. There were profuse sweatings, loss of flesh, impalpable spleen, liver enlarged and very painful but not very hard. The blood was reported negative for malaria, on each of four examinations. Castellani, however, found a few malarial crescents. After intramuscular quinine, supplementing that given by mouth, all the symptoms disappeared within three weeks. Castellani points out "that mistaking abscess of the liver for malaria is a far more common error than mistaking malaria for abscess of the liver; while I have come across only one case of malaria diagnosed as abscess of the liver, I have seen a great many cases of abscess of the liver diagnosed as malaria and drenched with quinine for months and even years".

10. Wounds of the head may bloody simulate cerebral abscess in malarial subjects. In these cases, cerebral malaria may be exhibited with signs of meningitis, or coma, or both. White emphasises this type of case, and records a case of cerebral malaria secondary to sepsis, simulating brain abscess.

CASE: Malaria simulating brain abscess. (F. White).

Patient aged 31. Service, three and a half years. Had been in Salonica, one year. Admitted to St. Elsa Hospital on diagnosis of gunshot wound of right elbow joint. No history of malaria, or dysentery; had been well up to time he was wounded. On admission, temperature 102°F, pulse 118. Patient very weak and anaemic; great pain in arm; headache, dizziness, and ringing in ears. Examination revealed very little apart from the wounded arm, which was swollen, cyanotic, and tender from shoulder to finger-tips. Elbow especially swollen; pus streaming out of a pin-point opening on anterior side, just over brachial artery. Glands in the axilla

were enlarged and tender. Day after admission, severe headache; face very flushed. He had several fainting attacks; proposed operation for drainage of elbow joint postponed. Temperature, 102°F; pulse 130, very weak and intermittent. Strychnine and digitalis were given during the day.

Next day his general condition had improved somewhat, and under ether anaesthesia, the elbow joint was drained. No attempt at resection on account of serious condition. During the next two days he improved greatly. Temperature not above 99°F, and pulse 100; ate well and slept well; complained of nothing but a feeling giddiness, which he said he had for some weeks before he was wounded.

On the evening of the second day following his operation, without any warning and while talking, he had three severe epileptiform convulsions, became very violent, and relapsed into unconsciousness. Next morning, as he was still unconscious, a lumbar puncture was done: spinal fluid under greatly increased pressure, but clear. A white blood count was made, and film taken for malaria. Catheterised specimen of urine showed a faint trace of albumen, but no casts. The bacteriological report of spinal fluid negative; sugar reaction present. Films negative to malaria. White blood count was 8,600: polymorphs, 60%; lymphocytes, 38%; large mononuclears, 6%. Patellar reflexes were absent; Babinski and Kernig's sign absent; some slight retraction of head. Eye report negative.

During the next 24 hours, patient still remained unconscious; temperature 102°F; pulse, 130; involuntary urination and defaecation. Lumbar puncture; fluid still under greatly increased pressure, but clear. Bacteriological report as before; films again negative to malaria. The arm looked unhealthy, and the edges of the wound gangrenous, with a very offensive odour; amputation was discussed, but decided to try intravenous quinine first. Quinine hydrochlor. grs. xv, in 10 ozs. normal saline given; another lumbar puncture at same time. Two hours after the injection, he commenced to perspire profusely; 16 hours later, perfectly conscious; temperature 98°F, pulse, 90; patient very weak.

From this time recovery was uninterrupted, quinine hydrochlor.

grs xv, was given daily, intramuscularly, for a week; then twice a week for four weeks. The arm cleared up rapidly. During the next 10 weeks in hospital, he had no further rise of temperature and was sent to England as a walking case. Malarial parasites were never found in the blood, and the spleen was only just palpable.

Author's Comments: This was a case of camouflaged malaria, where all symptoms indicated some other illness. The septic condition of the arm, followed by the sudden coma pointed to an extension of the infected foci to the brain, with a resulting cerebral abscess, especially with the negative history of malaria and the absence of parasites in the blood. The white cell count, and the absence of any localisation of symptoms, were the only two factors in the probable diagnosis of a cerebral malaria. Later, the prompt response to quinine therapy, and the rapid recovery, left no doubt as to the diagnosis.

11. *Drainage of abdomen in malarial cirrhosis of the liver.* White indicates this operation, but gives no results.

Malcolm Watson records a case of a Tamil, aged 35, admitted to Hospital, 8th Dec, 1902. He complained of swelling of the abdomen of three months duration; history of malarial attacks for two years, but said he had had no fever for a month. He also admitted taking alcohol to excess. There was slight oedema of legs. Ascites marked. Heart normal. Dulness and weakness of respiratory murmur over lower two-thirds of right lung. Pulse, 84: respiration 20: no cough. Urine contained a trace of albumen, and casts hyaline and granular. Quartan parasites in all stages were found in the blood from the 11th to the 18th. On the 17th, the temperature rose to 102·4°F, but patient was absolutely unconscious of it. He felt neither hot nor cold, and had no sweating after it. This was the only day fever was present. Quinine was given on 20th Dec.

The record in this case thereafter was mainly a series of tappings, which failed to do any permanent good. Oedema increased in the legs, and began to spread up to the thighs. The urine became very scanty. Albumen, which had disappeared from the urine, returned, and the prognosis was very gloomy.

On the 14th February, I incised the abdomen and stitched the omentum to the parietes. The operation occuped 30 minutes. The patient seemed to do well for a couple of days, but then diarrhoea started, the urine beame very scanty, and death occurred on the 20th.

Castellani indicates that, in his experience, malarial cirrhosis of the liver is not very common. He treated a typical case in Serbia in 1915. A soldier, aged 23, had ascites, and typical hepatic facies. After tapping, liver and spleen were felt to be enlarged and hard. Ascites recurred, and feet and legs became oedematous. After a second tapping, the liver was found to be much smaller. After repeated examination of the blood, malarial parasites were found, and patient very slowly recovered on quinine.

12. *Quinine abscess.* According to Alexandrine and Vandenbossche (and others), this is very rare apart from sepsis. These authors had only four cases in a thousand injections.

Prat-Plottes and Violle indicate that it usually occurs after 10 injections on the average, of chlorhydrate of quinine. After a forthight, it usually showed as a small focus, indolent and hard. Left to itself, it sloughed and spread. Treatment consisted in free and deep incision, and 46 cases were so treated, with excellent results.

Duigeon produced experimentally necrosis of muscle, nerve, and artery, with quinine injections.

White mentions another surgical procedure in malarial subjects, tried in Malta—namely decapsulation of the kidney for suppression of the urine in cases of blackwater fever, but no results are given.

So it would appear that the surgeon dealing with possible malarial subjects would do well to study the habits of this subtle parasite.

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CHAPTER XXX.

TREATMENT.

Treatment of mental and nervous conditions of malarial origin falls naturally into four sections.

(1). Treatment of mental conditions.

(2). Treatment of nervous conditions.

(3). Treatment of the malaria.

(4). Treatment of the general physical deterioration that often accompanies these conditions, of which they form a part, and which react upon them.

(1). The care of those mentally deranged as a result of malarial infection is that common to the insane in general, which usually means institutional treatment with trained attendants. The melancholic must be prevented from harming himself, the maniac from harming others. Isolation in some form or another with trained attendants and control are fundamental.

Where the case has a medico-legal bearing, it is important to see that by correct diagnosis in the first place and adequate presentation of the facts in the second, that justice is done. This aspect of the subject is developed in the medico-legal chapter.

The mental patient once installed in a suitable environment, treatment appropriate to his physical and mental state can be proceeded with as indicated subsequently.

Where excitement, restlessness, or sleeplessness forms part of the nervous instability, the usual sedatives with necessary precautions may be advantageously employed—paraldehyde, trional, sulphonal, hyoscine hydrobromide, bromides, luminal, medinal, dial, chloral. Hyoscine is best avoided where there are pulmonary or renal complications, as it is apt to lock up secretions. Chloral is best avoided in the aged. Tepid baths are a useful sedative in some cases. Nourishing and easily digestible food, and attention to bowels are all important.

Simple occupations, in accordance with the taste of the patient, and with strict avoidance of fatigue, is a useful adjunct to treatment in the convalescent stages, always with the surveillance necessary to ensure that no undue risk is incurred in the use of cutting instruments, and that the ingenuity of the melancholic will not outwit the vigilance of the attendants in attempts at suicide.

Careful and well-adjusted policing then is the first requisite for the mental patient, malarious or otherwise.

(2). Treatment of nervous conditions. This is comprised largely by the treatment of the condition of the patient as a whole, as outlined in the next two sections, combined with the treatment of nervous conditions in general. In the earlier stages, timely treatment for the malaria may be all that is required, as it may be all that is required for menacing cerebral conditions; but in the more chronic forms where more permanent nerve damage had been done, the usual procedure of massage, electricity, and passive movements are useful, together with more general neurological treatment, such as high-frequency current, tepid baths, hot-air baths, etc., where these things are specially indicated.

(3). Treatment directed against the parasite in mental and nervous conditions is largely the treatment of malarial infections in general, namely quinine.

That spontaneous recovery does take place has been known, of course, for a very long time, and no doubt this has accounted for many recoveries before quinine came to be used, as it has done since. Metchnikoff showed that the macrophages of the spleen and bone-marrow are actively phagocytic, and Bignami who had paid special attention to this in relation to malaria found that the macrophages of the spleen and bone-marrow took up large numbers of parasites in every stage of development, and that in a lesser degree the endothelium of the spleen, hepatic and cerebral vessels were phagocytic for parasites. Vascular endothelium, Kupffer cells, and leucocytes all play a role in phagocytosis, so that the mechanism of spontaneous cure has been traced to this extent. It was therefore found sufficient in some instances of malarial mental and nerve disturbance, to remove the patient from the area of

infection, and to conserve the body economy by mental and physical rest, good food, etc. Repatriation with the congenial society of friends, also conduce to recovery.

But as a rule, quinine bulked largely in the treatment of these cases, whether of the acute or the chronic form.

It is not intended here to give an account of the devious paths of treatment adopted by innumerable writers for malaria in general, which, so far as quinine administration is concerned, is largely that of malarial nervous conditions in particular, but simply to give a brief summary of up-to-date methods that have been found most useful. For more extensive details, the reader is referred to standard works on tropical diseases.

It is important, of course, in mental and nervous conditions, which have been found most commonly associated with malignant tertian infection, but not uncommonly with benign tertian, while more rarely with quartan infection, to get rid of the parasite. For this, three main methods of administrating quinine are in favour.

(1). The Standard Treatment of the United States National Malaria Commission specially advocated by Bass (1921). 30 grs. (2 gm) daily of quinine sulphate so long as clinical symptoms continue, or for three or four days in three doses of 10 grs. each, and thereafter 10grs. daily for 8weeks, this course being held to disinfect 90% of cases.

Proportionate doses for children are: Under 1 year, 1·5 grs; 1 year, 3 grs; 2 years, 6 grs; 3 and 4 years, 9 grs; 5, 6, 7 years, 12 grs; similarly 8, 9, 10 years, 18 grs; 11, 12, 13, 14 years, 24 grs; 15 years and older, 30 grs, in three equal parts daily, and one part continued for 8 weeks after the temperature is normal.

(2). Nocht's Treatment. 1 gm. daily of the bisulphate of quinine in powder in fractional doses of 0·2 gm. two-hourly (or four doses of 0·25 gm) from 6 a.m. to 2 p.m. for 10 days continuously. Then 2 days interval. Then
3 days of 5 doses, 0.2 gm., with 3 days interval. Then
2-3 " " 4 "
2-3 " " 5 "
2 " " and so on with 5 day intervals for at least 6 weeks. After a week's interval, begin again.

(3). Ross's Treatment. 15 grs. of sulphate or hydrochloride of quinine in solution daily for two weeks, and thereafter 10 grs. daily on 6 days a week for about 10 weeks, and finally 5 grs. daily for another month, to be raised to 10 grs. daily in the event of relapse.

For the great majority of cases, the oral route in above doses generally suffices. But others have found larger doses, e.g. 45-60 grs. daily more serviceable in severe cases met with in large numbers in Macedonia and the Balkans during the War. (Castellani, Goodall, Abrami, etc).

Where for any reason the administration of plain quinine has to be modified, it is sometimes useful to give Warburg's tincture in 3ss doses once or twice a day; or Bacchelli's mixture modified (Quin. Bisulph, grs. viii; Ferri Perchlor. Ital. Pharm, grs. iii; Liq. Fowleri, mx; Aq. ad 3i) or Quin. Hydrochlor., grs. x; Tartar Emetic, gr. ½; Liq. Fowleri, mi; Syr., 3ii; Aq. Chlor. ad 3i —Two tablespoonfuls well diluted four hourly (Castellani). One or other of these mixtures sometimes acts well in cases of relapse. Similarly, Cinchona Febrifuge containing all the alkaloids extracted from Cinchona Bark (Quinine, 7-4, Quinidine, 22-83, Cinchonine, 18-58, Cinchonidine, 5-64, Ash, etc., 45-35) being cheap, is specially useful in benign tertian infections. Of the quinine alkaloids, Acton (1920) holds that the laevo-rotatory quinine and hydroquinine are specific for P. falciparum, while the dextro-rotatory quinidine acts more powerfully on P. vivax. He estimates the cure rates of the Cinchona alkaloids for P. vivax as—Quinine, 20%, Cinchonine, 40%, Cinchona Febrifuge, 50%, Cinchonidine and Quinidine, 60%, and Quinoidine, 0.

Euquinine or Euchinine, the ethyl carbonate of quinine, being almost tasteless, is useful for children or others.

With all these quinine preparations, experience shows it wise to see that if in tabloid form or sugar-coated they readily break down to ensure solution in the intestine; and that the bowels and liver are kept in good order with occasional doses of calomel and salts. Rest in bed with nourishing and easily-assimilated food and hot drinks are essential during attacks and for a few days

afterwards. Neosalvarsan (0·3-0·9 gm), Novarsenobillon (0·3-0·9 gm) and Galyl (0·3 gm) have been found useful, either alone, or with quinine in suppressing benign tertian infections, but are not so clearly useful against malignant tertian infections. Some cases are on record where latent M.T. infections have been lit up by these injections with fatal result (see Chapter 8).

All methods of administrating quinine have their respective advantages and disadvantages. By the oral route it is unpleasant, may cause indigestion, vomiting, and is more slowly absorbed than by the other routes. But intramuscular, subcutaneous, intravenous, and rectal routes are severally useful under special circumstances. These circumstances may comprise all acute abdominal forms, simulating dysentery, cholera, intestinal obstruction, appendicitis, cholecystitis; cerebral forms—coma, acute mental derangement as delirium, stupor, epilepsy, cerebro-spinal meningitis, and forms simulating sunstroke, etc.

Intramuscular injection. This may be resorted to where vomiting, indigestion, inability of the patient to swallow, or coma, or refractoriness prevents the patient receiving quinine by the mouth, or where more rapid action is required. The bihydrochloride in 5, 10, or 15 grs. doses in sterile water is usually given into the gluteus maximus muscle, or deltoid muscle, once or twice a day avoiding the sciatic and musculo-spiral nerves, under strict aseptic precautions. The disadvantages are pain, and a risk of thrombosis, abscess, and necrosis of muscle, nerve, or artery. The pain may be partly controlled by urethane, antipyrin, or opium, and the necrosis by avoiding the same site of infection on successive occasions. Films become negative sooner than by the oral method, but relapse is not necessarily controlled more readily by it.

Subcutaneous injection. This method is not so commonly used as the intramuscular method, but it is often not so painful. The bihydrochloride is again used (5 grs. in 1 cc. sterile water or saline) into skin of flank or upper arm, seeing that the needle point moves freely under the skin and solution spread about. Local massage is helpful after injection in preventing necrosis. Abram

recommends this method especially for acute (3 gms) and chronic (2 gms) cases in isotonic solution at 8 a.m. and 6 p.m. daily. Solution used is chlorhydrate of quinine, 10 grs: urethane, 3 grs: Aqua dest. 200 grs. 1,50 of quinine is given each dose, with 1 mgm. adrenalin added. Iron and arsenic and oral quinine given between pyrexial periods when injections are resumed.

Intravenous Injection: Where rapid access of quinine to the blood stream is imperative, as in hyperparasitism, mania, coma, or extreme forms of excitement, or acute symptoms during the febrile paroxysm, and in neuropsychiatry generally, this is the method of election. 10, 15, 20 grs. of the bihydrochloride may be diluted with 100-200 ccs. of normal saline. The dilution is important as W.M. James saw two deaths from a dilution of 1 in 10. Abrami advises for coma 1 gm. bihydrochloride or bihydrobromide at once; 1 gm. a quarter of an hour later, followed by subcutaneous injection of 1 gm. again in a quarter of an hour. These may be repeated until coma disappears. Then give two doses of 1 gm. each daily, until patient is apparently safe. In 21 cases of coma treated thus, there were 5 deaths in 4 hours, 3 deaths in 48 hours, and 13 recovered.

(anaphylaxis)

For algid, dysenteric, and haemorrhagic forms, Abrami commends intravenous injection of 2 mgms. adrenalin in 500-1000 gms Horse serum. He maintains that this intravenous route alone suffices in collapsed patients, and that quinine is secondary at this stage and in these cases.

The dangers of ~~this method~~ the intravenous method are the risks of quinine poisoning in one specially susceptible to it, but of course this will not weigh against the risk of extinction by pernicious malaria. Manson-Bahr warns against the risk by this method in those with weak hearts, where in hyperparasitism there is much malarial toxin suddenly set free in the circulation with consequent syncope. He also advocates the practice of spinal puncture, where cerebral oedema (as in coma) is expected.

Per rectum. This may be used in gastro-intolerance or in children. 20 grs. of the bihydrochloride or bihydrobromide in a few ounces of water with an ounce of mucilage of starch and perhaps a few drops of laudanum are used.

Pedro has used suppositories of 20 cgms. formate of quinine

(quinoform), 1 cgm., methylene blue, 2 gms. cocoa-butter, successfully in children of 20 months to 3 years, 1 suppository night and morning.

Quinine per rectum may sometimes produce necrosis of mucous membrane.

In refractory quartan infections, methylene blue, 1 gm., daily in five 0·2 gm. doses in addition to Nocht's quinine cure has been found useful by M. Mayer, Ruge, and others, but generally speaking, methylene blue is much less of a parasiticide than quinine. (Nocht and Werner), though it appears to have proved useful in individual cases where quinine results have not been clear cut, especially in association with quinine, when the dosage of that drug can be reduced.

Pregnancy. Pregnant women with malaria are liable to abortion or premature labour, to precipitate labour, or the birth of a dead child, or to have severe puerperal haemorrhage, puerperal septicaemia, pernicious anaemia, pernicious vomiting, or pernicious malarial attacks, with coma and death. Quinine may be given by any of the above methods according to the severity of the symptoms. Fowler's solution slowly increased to mv t.i.d. has been found useful in combating anaemia. Intravenous injections of the arsenical preparations are also useful, with the reservations defined elsewhere.

Children stand quinine well, and larger doses are with advantage employed in their treatment than are proportionately to body weight given to adults. 5 grs. of sulphate or hydrochloride may be given to a child of 10 with cinchonism, and even up to 10 grs. in case of need, with proportionate doses for younger children. It may be made up with olive oil, and given in milk, or it may be administered per rectum. Usually however euquinine is employed on account of its tastelessness. For a baby of 1 yr., 1½ grs. euquinine may be given 6-hourly; children, 3-5 years old, 5 grs. 6-hourly; children, 5-10 years, 7 grs (S. P. James).

Nagger found that new-born children could be satisfactorily treated by receiving quinine via the mother's milk.

Quinine Poisoning. In some people, as is well-known, quinine acts as a poison, and may give rise to a multiplicity of symptoms such as various degrees of ear noises, diminished hearing, specks before the eyes, lacrymation, malaise, nausea, anorexia, vomiting, dysphasia, headache, giddiness, pallor, urticaria, pruritus, fever, scarletiniform rash, skin haemorrhages, petechial or otherwise, mucous bleeding from nose, stomach bowel, or bladder, haemoglobinuria oedematous swellings of face, ears, eyelids, hands, feet, cyanosis of hands or feet, anxiety, confusion, excitement, tachycardia, dyspnoea, orthopnoea, amblyopia, amaurosis, optic neuritis and atrophy, blindness (see Chapter on Special Senses), apathy, depression, metrorrhagia, abortion, and collapse.

Any combination of these features may occur in individual cases, and give rise to difficulties of treatment in malarial subjects.

Haemoglobinuric fever, due to quinine, varies in frequency in different areas. In 16 cases if haemoglobinuric fever in Hospital in Daressalem, Koch found malaria only in 2: and the other 14 were considered as due to quinine. In 43 cases of haemoglobinuric fever, observed by F. Plehn, 24 followed the taking of quinine, and degree corresponded to period of greatest activity of the remedy. In 53 cases seen by A. Plehn, 48 were the result of quinine intoxication. The dosage necessary to produce this condition may be low—as small a dose as ½ gr. has been observed (Marchiafava and Bignami).

Roberts observed in a woman after 8,10 quin. sulph.—unconsciousness, fall of temperature, general lividity, slowed superficial respiration, small thready pulse (45 to the minute), pupils widely dilated and staring, abolishment of skin and tendon reflexes, coffee-ground vomit, with deafness that lasted a week, and blindness that continued 5 months.

Sailla records two cases of soldiers who took by mistake 12,0 quin. sulph. in solution. This was soon followed by intense ringing in the ears, total deafness, and cramps in the stomach. The skin became extremely pale, the pupils dilated, respiration became superficial, the skin cool, the pulse slow, small, irregular, and at times impalpable. The heart was scarcely audible by auscul-

tation, the sounds jerky and frequently running together. One died four hours later in syncope: the other recovered. The autopsy was negative. Cardiac poisoning appeared to be the cause of death in in this case.

Baermann (1909) records death after two doses of 0,5 quin. hydrochlor., with blood in the excretions, extravasation in the ~~organs~~ organs, and collapse.

Brugnatelli records a death after 15 gms. quin. sulph. A case is recorded in the R. A. M. C. Journal of a man who took by mistake 12-14 gms. of quinine. A hour and a half later, he was unconscious with stertorous breathing, imperceptible pulse, dilated and equal pupils, corneal reflex absent, and quite cold. Ether and strychnine, with hot bottles, and three quarters of an hour artificial respiration, but death followed two and a half hours after taking the drug.

In some, however, quite small doses have disturbing effects. Allwig observed shivering and urticaria after 3 grs. of quinine. 5 grs. produces sickness, giddiness, urticaria, semi-consciousness and collapse in a medical friend of the writer.

Van Poole observed a soldier who became comatose after 10 grs. of quinine taken prophylactically. The radial pulse became very slow, and hardly countable, pupils widely dilated and barely reacting to light, breathing stertorous. The patient recovered after washing out the stomach and applying stimulants.

Harrison records quinine idiosyncrasy in his own family traced through three generations, so that it always produced urticaria—in himself, even after 1 gr.

Many cases of haemorrhage are recorded. Baermann had a Chinese patient whom he was treating for Tertian Malaria. After ½ gm. quinine, temperature became normal, and no parasites could be found in the peripheral blood. After ½ gm. another day, vomiting. After ½ gm. that afternoon, smart bleeding from nose, and some hours later from bowel, with haematemesis, and bleeding into the skin and death. Post-mortem, all the organs showed extensive haemorrhages, as also in serous and mucous membranes, and muscle.

In many women, quinine produces menorrhagia, and even produces irregular bleeding between the periods. It may even cause abortion,

and should be given in small graduated doses in the early months of pregnancy. It is well borne in the 8th month of pregnancy, and it has been found that there is less disturbance of pregnancy taking careful administration of quinine than with malaria untreated (Ziemann).

A. Plehn has noticed in some people who have been taking quinine a long time, signs of cardiac neurosis similar to what occurs in nicotine poisoning—rapidity, irregularities, palpitation unduly easily produced or spontaneously. Ziemann has observed patients taking quinine twice a day prophylactically who have become nervous, with palpitation, who have become alcoholic in consequence and warns against this risk.

The following case is an example of anaphylaxis to small doses of quinine.

CASE: Quinine Anaphylaxis (Montel).

A European long resident in the East who had fever warned the author that any dose of quinine would occasion him erythema and dyspnoea. The author, sceptical, gave a cachet containing 0·25 gm. A few minutes later, he had a scarlatiniform eruption over the whole muco-cutaneous surface, swollen face, watering of the eyes, dysphagia, dyspnoea, tachycardia, anxiety, intense pruritus, especially in the soles and the palms, pains in the limbs, feeling of fatigue, etc.

These symptoms persisted for three hours and did not wholly disappear for 4 to 5 hours. The malarial state of the patient becoming worse and arrhenal failing to relieve him, it was decided to give him an intramuscular injection of 0·5 gm. quinine. It was well-borne, and was followed the next day by one of 1·0 gm., repeated for 5 successive days, without the slightest symptoms. The author discusses the case, comparing it with another, in which similar symptoms followed the injection as well as the ingestion of quinine, but is unable to explain it.

In some mild cases the difficulty is overcome by giving ~~recent~~ small repeated doses of quinine, maybe with alkali such as bicarbonate of soda.

Szent-Gyorgyi, starting from the observation that after

intravenous injection of a quinine salt, a strong local vaso-constriction is seen in the ear of a rabbit, sought to overcome this and the cinchonism of which it was the sign by the use of vaso-dilators of the nerv central nervous system. Of these, caffeine and aspirin proved effective, removing the symptoms of quinine intoxication; 0·2 gm. of caffeine and 1·0 gm. of aspirin were used to 1 gm. of hydrochloride of quinine. For use in man, caffeine is recommended for intravenous injection, either with or just before the quinine, and a combination of quinine with caffeine for oral administration.

For severe symptoms, tea, coffee, atropine, caffeine, aspirin, calcium chloride, adrenalin have been used beneficially.

Binz (quoted by Mannaberg) recommends the following in case of quinine poisoning, "Artificial respiration by rhythmic pressure over the region of the heart, in order to irritate this organ at the same time; hot baths (39°C) with cold douches; internally, hot strong coffee or tea, and probably atropine. In cases calling for large doses of quinine, the physician should ask himself whether any contra-indication exists in the shape of pulmonary or cardiac weakness".

Or the difficulty may be got over by using some other of the Cinchona alkaloids.

Sodium bromide and urethane have been useful for ear noises (Ziemann).

MacGilchrist and Duigeon have separately studied and experimented upon the ill effects of quinine upon the tissues. Duigeons observations which largely cover those of MacGilchrist are epitomised thus:

(1). Concentrated preparations of quinine produce more intense necrosis than dilute, but dilute preparations such as are of practical utility excite oedema and necrosis at the seat of inoculation. The difference between these two methods of quinine inoculation is not of sufficient value to justify active opposition to the method commonly employed. Inoculation of quinine in solutions so dilute as to avoid oedema and tissue necrosis is not of practical utility in the human subject.

(2). A concentrated solution of quinine is absorbed rapidly from the tissues as shown by chemical analysis eben in patients who are *in extremis*. It is not apparently stored as such in the liver, kidneys, or heart muscle.

(3). It is essential to realise that tissue necroses—spreading oedema and local blood destruction—are produced by the solvents employed for quinine aisinistration, and the effects are only slightly inferior to those excited by quinine salts and the alkaloids.

(4). No advantage was obtained by the addition of olive oil or fat, or by injecting the alkaloid dissolved in alcohol or ether, whether in a concentrated or a dilute solution.

(5). Tissue necrosis occurs immediately and persists for a considerable period. In some instances the fibro-myositis which results is associated with a fibro-neuritis, which causes various symptoms definitely related to the pathological processes.

(6). Necrosis of blood vessels in the area of inoculation is a common result. This leads to small haemorrhages into the tissues, and has caused severe haemorrhages in the human subject, and experimentally, from rupture of a large vessel. The destruction of the vessel wall is associated with an accompanying thrombosis.

(7). An extensive necrosis produced by an intramuscular injection of quinine, in the neighbourhood of an important nerve trunk, may result in nerve palsy. Experimentally, complete degeneration of the great sciatic and other nerves has been produced apart from any direct injury to the nerve at the time of the inoculation. In the Human Subject, this disastrous result may be due to spreading oedema and extensive tissue necrosis.

(8). Experimentally, no leucocytosis has ever occurred from quinine injections. On the other hand, a leucopenia may develop while an increase of large hyaline cells has been recorded on several occasions.

(9). No essential differences in the degree of tissue necrosis from intramuscular injections of quinine in malarial fever and or malarial fever associated with blackwater fever were observed.

(10). Repeated intramuscular injections of quinine should not

be given into the same area of muscle, or tissue directly adjacent, as otherwise permanent injury of muscle or nerves may occur.

(The gluteal regions, obtained from a man who had daily intramuscular injections of quinine, 9 in all, were shown at the R. M. A. Meeting in London, 1919. As a result of the injections wide tracts of muscle were necrosed, and only fragments of healthy tissue remained).

(4). The treatment of the general condition of the patient varies considerably according to the stage of the illness and degree and nature of the damage done. During the paroxysm, the patient should, of course, be in bed between blankets, and hot bottles and any other measures indicated to promote sweating—such as hot drinks, or even a hot bath, or hot air bath given in bed, as is used in nephritis. Attention to the bowels is important—preferably by calomel and salts. Ziemann commends warm, normal saline per rectum, twice or oftener daily, or cooled if given during the hot stage when it reduces the subjective feeling of heat. This procedure lessens the risk of vomiting during the paroxysm, but if this occur, intravenous quinine, ice to suck, hot foments over the stomach, or morphia may help. For the persistent vomiting during malarial attacks, Ziemann recommends a mixture of chloroform, 10 parts, gum arabic, 10 parts, powdered sugar, 20 parts, water, 200 parts, of which a tablespoonful or more should be given at intervals of one hour. Gastric lavage may be adopted in specially troublesome cases. Persistent hiccough, or cough, may be treated similarly.

Careful observation of the effects of disease and treatment on the vital organs—heart, brain, lungs and kidneys—should be carried out, and symptomatic features should be dealt with as they arise.

In convalescing stages, and in cachectics, it is important to have the patient removed from the area of infection and all measures adopted to conserve the body economy. For cachectics especially, a dry, warm, and sunny climate is indicated.

Where there has been loss of blood from haemorrhages, or severe anaemia, blood transfusion has been practised with success. Otherwise, iron and arsenic in most assimilable forms are indicated.

Fowler's solution in graduated doses is commonly used. The arsenical preparations intravenously, such as neosalvarsan, novarsenobillon, and galyl have often come in useful in restoring the activity of the blood-forming organs in anaemic conditions, but the risk in old cases of inducing a hyperparasitisation as has occurred even fatally in a few instances, has to be borne in mind.

In cases where low blood pressure with asthenia is a prominent feature, adrenalin (along with iron and arsenic) in 10-30m of 1 in 1000 freshly prepared solution by mouth, or 1 mgm. of the extract is advocated, especially by French observers, e.g. Paisseau and Lemaire. Abrami commends the use of adrenalin in algid cases, given with horse serum intravenously, as indicated above. Or in cases with hyperparasitism and great prostration, it may be combined with quinine in saline given intravenously.

In cases with achylia gastrica, or gastric sub-acidity—not uncommon in chronic malarial subjects, it is advantageous to supply 10-30m dilute HCl, with ℥iv-xx of water before each meal. In more sthenic types of chronic malarial subjects with irritable vagus, there may be a gastric hyperacidity, with indigestion as an element in the complaint, in which case measures to suppress the hyperacidity—atropine, belladonna, bismuth, alkalies such as heavy carbonate of magnesia, or other magnesium salts,—may be usefully employed.

A prescription frequently used by the writer is

℞

Liq. Atropinae. mxii.
Mag. Carb. Pond. ℥ii.
Liq. Bismuth. Hydratis. (Parke, Davis and Co) ℥iss
Aq. Chloroformi. ad ℥vi.
m. et s.

Sig/
℥ss in water t.i.d. between meals.

These broad principles may have to be varied according to the special requirements of the case—as where there is cardiac weakness, digitalis, strophanthus, caffeine, may be usefully combined with the other medicaments. In chronic cases, especially in women past the menopause, small doses of thyroid, ¼ - ½ gr. daily may greatly

assist the iron and arsenic given for anaemia.

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