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Contributors

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THE CAUSATION AND PREVENTION

OF

MALARIAL FEVERS;

A STATEMENT OF THE RESULTS OF RESEARCHES.

DRAWN UP FOR THE USE OF ASSISTANT SURGEONS, HOSPITAL ASSISTANTS, AND STUDENTS.

BY

CAPTAIN S. P. JAMES, M.B. (LOND.), I.M.S.

Issued under the authority of the Director-General, Indian Medical Service.

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PREFATORY NOTE.

THE first edition of 5,000 copies of this pamphlet was soon exhausted. In preparing a second edition Captain James has enlarged the scope of the work so as to make it an easy introduction to the study of malaria.

B. FRANKLIN, *Surgn.-Genl.*,
Director-General, Indian Medical Service.

SIMLA.
October 1903.

THE
CAUSATION AND PREVENTION
OF
MALARIAL FEVERS.

IN the following statement I shall endeavour to describe as clearly as possible the cause of malarial fevers, the method by which they are contracted, the main characteristics of the malarial fevers met with in India, their treatment, and the means by which they may be prevented.

The cause of Malarial Fevers.

In the year 1880, Laveran, a French army surgeon, discovered that malarial fevers are caused by the presence of a large number of micro-organisms in the blood of patients suffering from the disease. These micro-organisms, which live inside the red blood corpuscles, are not bacteria; they are small animals belonging to a grade of the animal kingdom called the *protozoa*. *Protozoa* is the name applied to the lowest grade of the animal kingdom. The animals in this grade are sharply distinguished from all the rest of the animal kingdom (known collectively under the name *metazoa*) by the fact that they are structurally single cells of protoplasm—they are essentially unicellular animals. A number of such cells may, as the result of the process of fission (cell-divison), be grouped together in contact with each other, but each cell thus formed is quite independent of every other cell and pursues its own life apart. In contrast to this even the simplest of all other animals consist in the first instance of two layers of cells (which are structurally and functionally distinct from each other) arranged around a central cavity, the common digestive cavity, which is in open communication with the exterior by a mouth.

All *protozoa* are provided with a nucleus, and the substance of which their bodies is composed has the same general properties as the protoplasm of the cells which build up the tissues of the higher animals; it is irritable, it moves, it assimilates food, it grows and divides, and it produces, by chemical processes which take place in its body, a variety of chemical compounds.

The malaria parasite,—for this is the name given to the particular *protozoon* which causes malarial fevers—is only one among a very large number of parasitic animals included among the *protozoa*. The animals in which a parasite passes its life and at whose expense it lives are called its hosts, and the hosts of the malaria parasite are man and mosquitoes. In man the organism is found in the red blood corpuscles, and in the mosquito in the tissues of the stomach wall and in the salivary glands.

The group of *protozoa* to which the malaria parasite belongs multiply themselves by two methods. Firstly by an asexual method, consisting of the simple division of a parasite after it has grown to a certain size, into a number of small parts, each of which can enter a new corpuscle and become a young parasite exactly similar to the original one; and secondly by a sexual method, consisting of the union of two cells which have acquired different properties (male and female), followed by the growth of the resulting fertilized cell and its division into a number of parts which are capable of becoming young parasites exactly similar to the original ones. It may be said that, as a general rule, all *protozoa*, at the commencement of their life, multiply themselves only by the asexual method, and that after a certain number of generations have been thus produced, sexual forms appear, which are capable, under suitable conditions, of carrying on multiplication by the sexual method. Without sexual reproduction the organism would, after a certain number of asexual generations, become worn out and die. It is impossible here to give the reasons why, when the energy with which a *protozoon* started life is almost all used up in multiplying itself by simple division, sexual forms appear. The answer to such a question would involve a consideration of the whole question of the origin of the sexes. It is sufficient with regard to the malaria parasite to say that after a certain number of asexual generations have been formed, sexual forms appear, which, *if transferred to the body of another host* *(the mosquito)*, can, by a process of fertilization and subsequent growth and division, produce forms which, when retransferred to the original host, develop into entirely rejuvenated young parasites with as much energy for asexual reproduction as had the original organism.

Man is only the intermediate host of the malaria parasite because in his blood only asexual multiplication by cell division of the parasite occurs, and if the organism had no other method of multiplying itself than this, it would die out with the death of the man.

The mosquito is the definitive host because in its body sexual multiplication, by which the parasite is rejuvenated and enabled to start its life afresh, whatever may afterwards happen to the mosquito, takes place.

With this preliminary explanation we are in a position to describe the complete life history of the malaria parasite.* For the sake of simplicity we may commence with the young form of the parasite [*schizont*]† as it is found inside one of the red corpuscles of a man's blood. It will be seen under the microscope as a small unicellular mass of protoplasm, undergoing amœboid movement and occupying but a small portion of the whole corpuscle (Pl. I, 2). It gradually grows larger, feeding upon the substance of the red blood corpuscle and converting the hœmoglobin into dark granules of pigment (melanin), which may be plainly seen in the parasite (Pl. I, 3). When it has grown to its full size, so that it nearly or quite fills the corpuscle, the grains of pigment collect together into a mass and the parasite begins to divide up into a number of small parts, (Pl. I, 4, 5), each of which is capable of becoming a new parasite identical in all respects with the original one. These parts or segments ("spores") [*merozoites*] remain in contact with each other for a short time, and then burst through the red blood corpuscle—which forms at this time little more than a thin shell round the parasite—and become free in the blood (Pl. I, 6.). Each of them now seeks out and enters a fresh red blood corpuscle, in which it begins to grow in the same way as the original one did, ultimately reaching its full size and dividing up into a fresh number of embryo parasites

* A careful study of Plate I will render the following description easily understood. The diagrammatic figures in this plate should also be carefully compared with the photographs of actual parasites in Plates VII and VIII.

† The correct names of the different stages of the parasite are inserted between square brackets. It is not necessary for the beginner to remember these names.

which again enter other corpuscles and go through the same cycle. This is the asexual method of multiplication [*schizogony*] by simple division of a full grown parasite into a number of small ones, and it is clear that even if originally only one corpuscle contained a parasite, a very large number of corpuscles will, by this method, soon become infected.

After this method of multiplication has gone on for a certain number of days, some of the parasites in the red blood cells instead of going on to their full size and dividing up into a number of segments, proceed to the formation of *sexual* forms [*gametes*]. These sexual forms are, as a rule, readily distinguished from the full grown asexual forms. Two kinds are present, *viz.*, male forms [*microgametocytes*] and female forms [*macrogametocytes*]. Having attained to their full size they appear as coarsely pigmented round or crescent shaped bodies enclosed within the thin shell or envelope of the red blood corpuscle (Pl. I, 8, 9). In the blood of man they undergo no further development. If, however, a mosquito bites a man with these sexual forms in his blood, some of them are carried into the mosquito's stomach with the blood which the insect extracts. If the mosquito is of a particular kind (*viz.*, one belonging to the *anopheles* genus), further development of the parasites in its stomach occurs. As a result of the mixture of the blood with the fluids in the mosquito's stomach, aided perhaps in part by the digestive action of the stomach juices, the thin envelope of red blood corpuscle which protected the parasite while it was in the blood of man, becomes disintegrated, and the parasite escapes and is free in the fluid of the mosquito's stomach.* Immediately following its escape from the corpuscle great changes are seen to take place in the character of the parasite. The female sexual form becomes a granular spherical body (Pl. I. 13). The pigment of the male sexual form is first seen to be violently agitated, and then, from the periphery

* It will be seen by those who have studied the subject that this description differs in detail from that usually given. It is usual to say that the gametocytes escape from the red blood corpuscles and become free in the blood plasma while they are actually in the blood of man, although it is said that, for some unknown reason, the male gamete does not flagellate while it is in the man's blood. That flagellation really does not take place in the blood of man is proved by the fact that flagellated bodies can never be found in freshly drawn blood. It appears to me probable that the reason of this is that the sexual parasite has not, *of itself*, the power of escaping from the corpuscle, but that some external influence such for example as the effect of osmosis in a moist-chamber, or in the mosquito's stomach, is necessary to break down the enclosing envelope of the red cell. As soon

of the parasite, three or four long filaments (flagella) [*microgametes*] are suddenly protruded (Pl. I, 12). After lashing about for a few moments the flagella break off from the main body of the parasite and swim about in the fluid in the mosquito's stomach. They are the true male element in the sexual process. When one of them meets a female sexual form it enters it and fertilizes the true female element [*macrogamete*] contained in it (Pl. I, 14). After this act of fertilization has occurred, the female parasite acquires new characters. Changing from the shape of a sphere to that of an ovoid with a pointed end [*ookinet*] (Pl. I, 15), it begins to move about, and making for the inner wall of the stomach of the mosquito it passes through the internal coats and comes to rest between the epithelial and muscular layers. Here it forms a capsule round itself and begins to grow, until in a few days it has attained a comparatively large size (Pl. I, 16). At this stage it is usually called a *zygote*, [*oocyst*]. By a process of division an enormous number of embryo parasites called *sporozoites*, elongated in shape and provided with a nucleus, are formed in the full grown zygote (Pl. I, 17, 18). After a time the capsule of the zygote bursts and the sporozoites are liberated into the lymph sinuses which surround the outer surface of the stomach. Thence they are conveyed by the circulation to the salivary glands, and penetrating the outer wall of the gland cells they come to rest in them and in the salivary duct, which has its external opening at the point of one of the piercing stylets of the proboscis which enter the skin in the act of biting. When the mosquito next bites a man it injects some of these sporozoites into his blood with the salivary or poison fluid.* Having got into the blood of man again the sporozoites after a certain time are found in the red blood corpuscles as young parasites identical in all respects with those from which the cycle was commenced.

These two cycles of the malaria parasite are represented

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as the male parasite has escaped from the red corpuscle it is able to throw out its flagella.

This explanation would also account for the fact that phagocytic leucocytes do not attack sexual forms while they are in the blood of man, although as soon as they have escaped from the protecting envelope of the red corpuscles and changed into flagellated bodies, they do so readily, in the same way as such leucocytes are able to attack the free spores of the asexual parasites as soon as they have escaped from the red cells.

* It should be particularly noted that the tube down which the salivary fluid and sporozoites pass when injected into man, is quite separate from that through which blood is sucked up by the mosquito.

diagramatically in Plate I, and photographs of the parasite in its more important stages in man and in the mosquito are shown in Plates VII and VIII.

The method by which malarial fevers are contracted.

From what has been said above it will readily be seen how malarial fevers are contracted. A mosquito of the *anopheles* genus bites a man who has been suffering for some days from malarial fever, and who has sexual forms of the parasite in his blood. These sexual forms are taken into the mosquito's stomach with the blood which it sucks in, and there they undergo the development that I have just described, resulting after some days in the formation of numerous sporozoites which lodge themselves in the salivary or poison gland of the mosquito. When this mosquito next bites a healthy man, it injects some of these sporozoites into his blood with the salivary fluid, and so produces a malarial infection in him similar to that of the man from whom it originally sucked blood.

Fortunately every kind of mosquito cannot act as a suitable host for the human malaria parasite, and in all probability only mosquitoes of one genus, *viz.*, the *anopheles* genus, can do so. Malarial fevers can therefore only be contracted by the bite of an *anopheles* mosquito. It must be remembered also that malarial fever cannot be contracted even by the bite of an *anopheles* mosquito, unless that mosquito has sporozoites in its salivary glands. This means that it must have bitten a man with malarial fever a week or more previously, and that the temperature and other factors necesssary for the development of the parasites in the mosquito's body, were favourable. Again it is not sufficient for an *anopheles* mosquito to have bitten a man with malarial fever unless sexual forms of the parasite (which alone can develop in the mosquito) were present in the man's blood at the time he was bitten, and in addition the sexual forms must have been fully developed, for as a general rule, sexual forms cannot proceed to further development even in an *anopheles* unless they have reached a certain stage of maturity. Thus in order that an *anopheles* mosquito may be able to carry infection it must have previously bitten a malarial fever patient *at a particular period of his case.*

In malarious places, however, cases of malarial fever are so frequent, and the number of *anopheles* mosquitoes is so great, that many opportunities occur for all the required conditions to be fulfilled, so that it is always possible in malarious places to find a number of *anopheles* mosquitoes with sporozoites in their salivary glands.

It has been proved almost beyond any possible doubt that there is no other method by which malarial fevers can be contracted than by the bite of a properly infected *anopheles* mosquito. We cannot contract malarial fevers from drinking impure water, or from the soil, or by breathing impure air, and water and air are only indirectly connected with malarial infection in the sense that they are the homes of the malaria-carrying mosquitoes.

What we have learnt so far may be summed up as follows :—
Malarial fevers are caused by the presence in the blood of the patients of a small parasitic animal belonging to the lowest grade of the animal kingdom, the *protozoa.* This parasite passes its life in two hosts, *viz.,* man and *anopheles* mosquitoes. In man it multiplies itself by a process of simple division for some days, and then produces sexual forms, which for their further development, require to be taken into the body of a mosquito of the *anopheles* genus. This is effected when such a mosquito bites a man with these forms in his blood. In the mosquito's body the female sexual form is fertilized by the male, the cell which results being called a *zygote.* By the growth and division of the zygote an enormous number of new forms of the parasite called *sporozoites* are produced, which lodge themselves in the salivary or poison gland and duct of the mosquito, so that when this mosquito next bites another man, some of the *sporozoites* are injected into him with the salivary fluid. In his body they develop into the young parasitic animals in the red blood cells exactly identical with the original ones.

As the malaria parasite does not, in all probability, pass any part of its life in any other environment than men and mosquitoes, it follows that men and mosquitoes are the only sources of infection of malarial fevers. The life history of the parasite which has been described fulfils every requirement for its nourishment and continued life, and it is therefore extremely improbable that it has yet another phase existing perhaps in water, or in the air, or in some other medium, because such an additional phase is unnecessary for the continued existence of the parasite. For this reason, as well as on account of many experiments that have been made in this connection, we may say with some certainty that the only way by which malarial fevers can be contracted is by the bite of a properly infected mosquito of the *anopheles* genus.

The conditions on which the prevalence of malarial fevers in different places depends.

It has always been recognised that some districts are more malarious than others, and it is necessary to refer briefly to some of the conditions which determine a greater or less prevalence of malarial fevers in one place than in another.

From what has been already said it is evident that the prevalence of malarial fevers in any place will depend on the following factors :—

(1) The prevalence of the carrier of infection, that is the prevalence of the particular kind of mosquito in which the parasites can develop.

(2) The prevalence of the source of infection, that is the prevalence of suitable cases of malarial fever from which the mosquitoes can become infected.

(3) The presence or absence of favourable conditions for the passage of the parasite from man to the mosquito and for its growth in the mosquito.

(4) The presence or absence of favourable conditions for the communication of the parasite from the mosquito to man and for its growth in man.

We will consider these factors in order.

(1) *The prevalence of the carrier of infection.*—The prevalence of adult *anopheles* mosquitoes in any village or town will depend on the number of suitable breeding places, the distance of these breeding places from the village, and the presence of favourable climatic conditions for the life of the mosquitoes. If there are many suitable breeding places near, and if the weather is hot and the air moist, numerous *anopheles* mosquitoes will usually be found in the houses of a village, and, as a general rule, it may be said that a direct relation exists between the extent and nearness of breeding grounds, the abundance of adult *anopheletes* * and the prevalence of malarial fevers.

* The plural form of the word *anopheles* is *anopheletes*; that of the word *culex* is *culices*.

It must not be thought, however, that there are no exceptions to this rule. Although no place has yet been found where malarial fevers exist in the absence of *anopheletes*, it is possible to find many places in India where they are abundant and yet where malarial fevers are almost unknown, although every condition, including all the other factors enumerated above, appear favourable for the development of the disease. How can we explain this condition of things? Recent observations have shown that the explanation for some places of this nature lies in the fact that *all* anopheles *mosquitoes are not equally good carriers of malaria in nature.* It is therefore possible to have in one place numerous *anopheletes* of a species which is a bad carrier accompanied by little or no prevalence of malarial fevers, and in another place comparatively few *anopheletes* of a species which is a good carrier accompanied by great prevalence of the disease.

This fact is a very important one in connection with the conditions which determine the prevalence of malaria, and very important in connection with efforts at destruction of mosquitoes.

(2) *The prevalenee of the source of infection.*—We have already seen that the source from which the mosquito derives the malaria parasite is man. It has recently been shown that in malarious parts of India a large proportion of the young native children have malaria parasites in their blood and suffer from malarial fever, although, in spite of this, they are often able to run and play about without showing the marked symptoms which are usually at once brought to our notice in an adult. In certain parts of India as many as 70 to 80 per cent. of the native children under ten years of age harbour the malaria parasite, which runs its course in their blood unchecked, because the parents of the children (though they often recognise that the children have "fever") do not, as a rule, think it worth while to bring them for treatment. Many of the children have enlarged spleens reaching as low as the level of the umbilicus or more.

It will be easily understood that, as these children are untreated, the parasites are able to develop in great numbers in their blood, and that sexual forms of the parasites are very commonly met with. *These native children form in fact the chief source from which* anopheles *mosquitoes become infected.*

(3) Conditions favourable for the passage of the parasite from man to the mosquito are the presence of abundant sexual forms of the

parasite in a large number of individuals, the presence of a large number of suitable mosquitoes, and many opportunities for the mosquitoes to bite the infected persons. These conditions are met with in every malarious town or village in India. The chief condition necessary for the growth of the parasite in the mosquito is a suitable temperature; this condition is also necessary for the continued life and activity of the mosquito.

(4) Conditions favourable for the communication of the parasite from the mosquito to man are the presence of a large number of infected *anopheletes* in a thickly populated district. The indifference of the native (especially native children) to mosquito bites, and the fact that they usually sleep with the greater part of their bodies uncovered, gives them a special liability to infection.

An individual may be bitten by a properly infected mosquito and yet not develop an attack of malarial fever, that is he may, for some reason or other, be immune against the infection. Very few individuals are absolutely immune from malaria, but a relative immunity may be acquired by repeated infections and reinfections. Thus in very malarious places, although almost all the young children may have malaria parasites in their blood and be suffering from malarial fever, few or none of the adults may be found infected. The only possible explanation of this fact is that the adults have, by repeated infections during childhood, become relatively immune. This immunity of adult natives in India applies only to those whose lives have been spent in certain very malarious districts, and the majority of adult natives enjoy little or no immunity.

To any one who has followed the preceding remarks carefully it will be apparent that a fairly complete knowledge regarding mosquitoes, and especially regarding mosquitoes of the *anopheles* genus, is necessary not only to explain the facts regarding the endemiology and epidemiology * of malaria, but also because

* Endemiology means the knowledge resulting from the scientific study and investigation of endemic disease.

An endemic disease is one to which the inhabitants of a particular country are peculiarly subject and which for that reason may be supposed to proceed from local causes.

Epidemic means generally diffused and prevalent. A disease is said to be epidemic in a place when it appears in a great number of cases at the same time in that locality, but is not permanently prevalent there. If it is permanently prevalent it is said to be endemic.

it is essential to be able to recognise the malaria carrying species of mosquitoes before any measures against them can be undertaken.

A short account of mosquitoes will therefore be given here.

The general characters of mosquitoes.*

The general appearance of a mosquito is probably well known to all, but it may be necessary to mention that mosquitoes may be distinguished from other flies (such as "sand-flies," etc.) which seem to resemble them, by the following characters :—

(1) They have a long sucking proboscis.

(2) The veins of the wings are covered with scales (which can be plainly seen with a small magnifying glass). The veins of the wings of other flies have no scales.

The following are the stages through which mosquitoes—like all other insects—pass before they reach the adult state. An adult female mosquito lays its eggs on a pool or other collection of water. In a few hours these eggs hatch into small animals called *larvæ*, whose life is spent entirely in water. The larvæ of mosquitoes can be seen in almost any old tin or tub that has been left full of water in a garden for some days. After a variable time, depending chiefly on the temperature, the larvæ change their shape and character, and become small comma-shaped creatures called *pupæ* which spend their time struggling to the bottom of the water and floating up to the surface again to breathe. After one or two days the pupæ are transformed into the adult insect or *imago*, which emerges at the surface of the water from the skin or pupa-case enclosing it, and which it leaves behind in the water. After resting for a while on the surface of the water, the adult mosquito flies away to seek its food from the blood of some animal or man.

The appearances of the various kinds of mosquitoes differ in all these stages of the insect's existence, and it is important to know these differences in order that we may be able to distinguish the malaria-bearing from the harmless mosquitoes.

For purposes of classification, mosquitoes are divided into a number of *genera* or families, each of which contains many *species* or varieties, but for our present purpose it is only necessary to have

* For the different parts of the mosquito, which are referred to in this description, see Plates II—IV.

a knowledge of two genera, *viz.*, the *culex* genus and the *anopheles* genus.*

The differential diagnosis between these two genera is very important, because, as we have already learnt, only mosquitoes of the *anopheles* genus are capable of carrying malarial fevers.

The distinctions between CULEX and ANOPHELES mosquitoes.

The differences between the eggs, larvæ, pupæ, and adult insects or *imagines*, may be taken in order.

(1) *The eggs of* culex *and* anopheles.—The eggs of the *culex* genus of mosquitoes are laid on the water in small black masses consisting of several hundred eggs joined together. These "egg-rafts" or "egg-boats" as they are called, look like small lumps of soot floating on the surface. They can be seen on almost any tin or tub of stagnant water that has been left lying about out of doors.

The eggs of the *anopheles* genus of mosquitoes are tiny rod-shaped bodies which, as each egg is laid separately, can only be seen plainly with the aid of a lens. Each egg is provided with a delicate rim or float so that they can be easily distinguished from the individual eggs of *culex* mosquitoes which have no float (Plate IV).

(2) *The larvæ of* culex *and* anopheles.—If any one who has not seen a mosquito larva, will look in almost any tin or tub of water that has remained unemptied in his garden for some days, he will find there a number of small, very active creatures about $\frac{1}{16}$th to $\frac{1}{4}$th of an inch long, which wriggle about in the water, now diving to the bottom and then coming up to the surface to breathe, which they do by means of an air-tube attached near the tail. If some of these little animals are put into a glass bottle and watched from the side, it will be seen that, when they come to the surface to breathe, they hang obliquely with their heads downwards and with only the tips of their air-tubes at the surface of the water.

These are the larvæ of the *culex* genus of mosquitoes. The

* The words *culex* and *anopheles* are here used in their original sense and must be understood to include the new genera separated by entomologists on account of differences in scale structure. Thus the word *culex* as here used includes the genera *Culex*, *Stegomyia*, *Panoplites*, etc., and the word *anopheles* includes the genera *Myzomyia*, *Pyretophorus*, *Myzorhynchus*, *Nyssorhynchus*, etc., of the new nomenclature. In spite of their new names the species comprised in these so-called new genera (which formerly all came under the term *anopheles*) still remain prominent malaria carriers, and from this point of view it is unfortunate that they should be separated into different genera.

larvæ of *anopheletes*, on the other hand, have no external air-tube and the result of this is that they lie *flat* at the surface of the water. They move along at the surface, when disturbed, in a backward direction, by a series of darting, jerky movements. They are thus easily distinguished from *culex* larvæ ; an *anopheles* larva lies flat at the surface, and a *culex* larva lies with its head and body sloping downwards beneath the surface in an oblique direction.

(3) *The pupæ of* culex *and* anopheles.—The pupæ are small comma-shaped creatures bearing no resemblance to the larvæ, and they breathe by means of two trumpet-shaped projections attached to the head, so that they lie with their heads at the surface and their tails downwards.

The trumpet-shaped breathing tubes of the pupæ of *culex* mosquitoes are longer and more slender than those of the *anopheles* genus.

(4) *The adult insects.*—Before we can distinguish between the adult insects of these two genera, it is necessary to know the differences between a male and female adult mosquito. The chief difference is that in male mosquitoes the antennæ or feelers are covered with long hairs, so that each antenna forms a feather-like tuft in front of the head. In female mosquitoes the antennæ have no long hairs and are nearly bare. (See Plate III, Figs. II, III, IV.) In females too it may often be seen that the abdomen is distended with eggs, or the stomach may be full of blood, and as only female mosquitoes suck blood, we know at once that mosquitoes containing blood must be females.

The following are the ways by which adult *culex* and *anopheles* mosquitoes may be distinguished from each other :—

(1) The correct way is to make a careful examination of the palpi and proboscis of the mosquito with a lens. In *anopheles* mosquitoes the palpi are the same length as the proboscis in both sexes, so that *female* anopheletes *have long palpi.* In *culex* mosquitoes the palpi of the male are long but those of the female are very short; *female* culices *have short palpi.* (See Plate III, Figs. III, IV.)

(2) The attitude of the majority of *anopheletes* when resting on a wall or roof is very characteristic and quite different from the attitude of *culex* mosquitoes. When an *anopheles* is resting on a wall it keeps its proboscis, head, thorax and abdomen in one line, and the hinder part of its body projects outwards from the wall so that the insect frequently appears to be standing on the tip of its

proboscis. With *culex* mosquitoes the body is either kept parallel to the wall, or the tail end is even nearer to the wall than the front part of the body, so that a *culex* appears "hunch-backed." We must remember, however, that this attitude of *anopheletes* does not apply to the whole genus. There is one very important *anopheles* (*A. culicifacies*) which when sitting on a wall looks exactly like a small brown *culex* and keeps its body parallel to the wall as a *culex* does.*

(3) As a general rule it may be said that most *anopheletes* have spotted wings while in most *culices* the wings are quite plain and uniformly coloured. We must be careful, however, to avoid using this character as a test without subsequent careful examination of the palpi, for in India there is at least one species of *culex* (*C. mimeticus*) with well marked spots on the wings, and at least two species of *anopheletes* (*A. immaculatus* and *A. Aitkeni*) with quite unspotted wings.

We should, however, aim at something more than a knowledge of the distinctions between the two genera *culex* and *anopheles*: we should try, if possible, to ascertain what species of *anopheles* we are dealing with. The importance of this has already been indicated in the remarks on the conditions which determine differences in the prevalence of malaria at different places. It was noted in those remarks that some species of *anopheletes* are better malaria carriers in nature than others, and it is especially important therefore to be able to recognise the species which have been proved to have most influence on the spread of malaria in India. Owing, however, to the comparatively large number of species of *anopheletes* that exist in India, and to the fact that many of these species resemble one another very closely, it is a matter of some difficulty to correctly identify any particular specimen of *anopheles*. The subject is however a very important one, which will well repay the expenditure of much time and trouble. One of the most important things in a study of malaria in any place is to collect and identify the various species of *anopheletes* prevalent in the district, and to find out as far as possible by a study of the habits, relative abundance, seasonal prevalence, and other particulars of the life history of each species, what connection it has with the prevalence of malaria. To do this it is necessary to know how to collect *anopheletes*, how to mount and preserve them, and how to examine and identify them.

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* At least one of the unspotted winged species of *anopheles* referred to later also adopts the attitude of *culex* mosquitoes when resting on a wall.

How to collect adult anopheletes.

One of the habits of *anopheles* mosquitoes is that they only fly about after dusk and during the night; in the daytime they seek some dark shed, outhouse, or stable, where they rest on the walls and roof, until evening. In these places they can be easily caught, the necessary implements being a few dry test tubes and a large dry bottle. When a mosquito is seen sitting on the wall or roof, the mouth of a test tube is placed very gently over it. It will fly into the tube, the mouth of which can then be closed with a plug of cotton wool. As each mosquito is caught it may be transferred to the large glass bottle by placing the mouth of the tube over that of the bottle and removing the cotton wool plug. The mosquito will fly into the large bottle and the tube can be used again. If *anopheletes* are at all abundant twenty or thirty can be caught in this way in a very short time. The best places in which to search for them are outhouses, cowsheds, woodsheds, and thatched unoccupied rooms with dirty smoke-blackened walls and many cobwebs. It is almost useless to search in a new whitewashed house. Even in places which appear favourable, mosquitoes are often difficult to detect, and some species hide among the straw of a thatched roof or in holes and corners of the wall with great success. For searching the roof a ladder should be used, so that the eye is not more than a foot or so off the roof, and every part of the thatch should be carefully examined. The commoner *anopheletes* are light coloured and stand out against the black background of dirt and soot like little white thorns hanging from the roof, but even an experienced observer may sometimes miss the small brown species which, as we shall see, are so important from the point of view of malaria.

How to mount and examine anopheletes.

The mosquitoes that have been caught should be killed by placing a drop or two of chloroform on the muslin cover of the bottle. The dead mosquitoes are then turned out on to a clean white sheet of paper and mounted as quickly as possible.

The following articles are necessary for mounting a mosquito :—

(1) A supply of fine silver pins, No. 20 size.
(2) A pair of forceps for holding the pins.
(3) Small discs of thin cardboard.

(4) Ordinary pins.
(5) A box in the bottom of which a layer of cork or pith is fixed.

Mosquitoes which are required for identification should never be touched with the fingers. A pin or needle should be used for moving them when this is necessary. A card-disc should be taken and one of the No. 20 silver pins thrust through its centre, so that about half the pin projects each side. The mosquito to be mounted is turned over on to its back, and the point of the pin carrying the disc is entered into its thorax at the point of origin of the legs, and made to emerge through the dorsum of the thorax. On turning the disc over, the mosquito will be found to be mounted in its natural position, right side uppermost, and its legs and wings can be gently arranged on the card-disc with the aid of a pin. An ordinary pin is now thrust through the edge of the card disc to attach it to the cork in the bottom of the box. (See figure 1.)

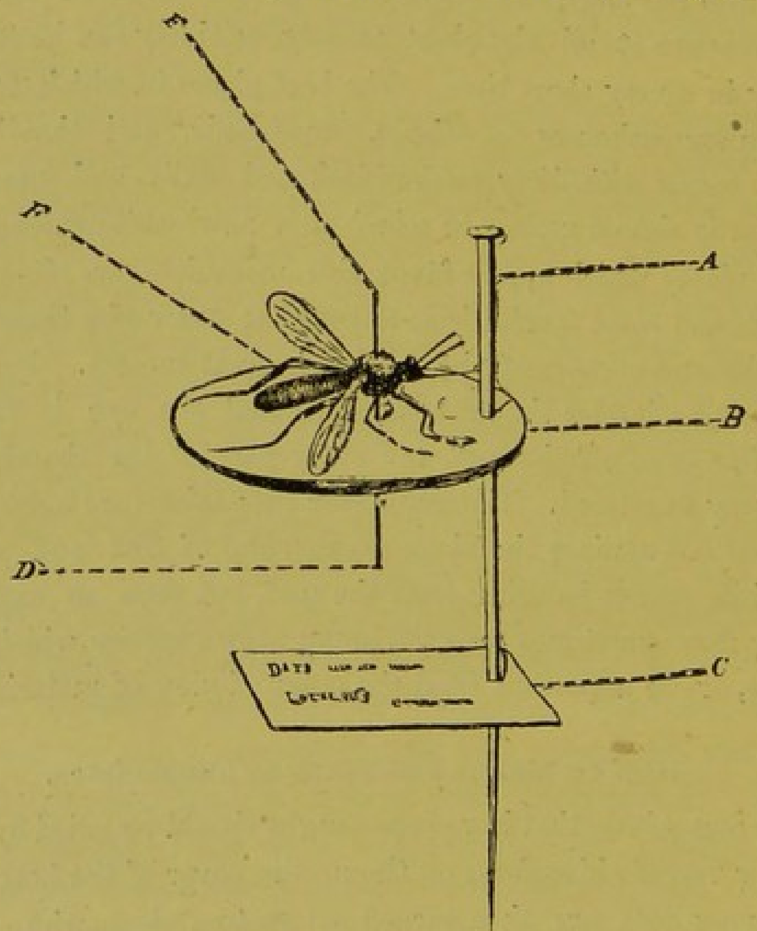

FIGURE 1.
(*After Theobald.*)
METHOD OF MOUNTING A MOSQUITO.

a. pin through card disc, (*b*); *c.* label for date, locality, etc.; *d.* No. 20 pin through card disc (*b*) and mosquito (*f*); *e.* point of *d* through thorax of mosquito.

For the proper examination and identification of adult mosquitoes a low power microscope is almost a necessity, but in the absence of this it will be found that most of the markings and characters, except those relating to the shape of the scales, can be made out, though less easily, with a hand-lens.

For the examination under a microscope, the mosquito, which has already been mounted on a card-disc in the manner above described, is fixed by a pin thrust through the edge of the disc to a flat piece of cork about an inch square. This cork carrying the mosquito is placed on the microscope stage and can be moved about at will, so as to bring all parts of the mosquito under the lens.

It is best to begin with an examination of the palpi and to work backwards, noting every marking and character that presents itself. The palpi, proboscis, and antennæ will be first examined, and from the length of the palpi we shall be able to see whether the mosquito belongs to the *culex* or *anopheles* genus, and from the character of the antennæ whether it is a male or female. At the same time we shall note whether the palpi have any white bands, and if so their number and relative width, and also whether the tips of the palpi are white or black. On the head we shall note the upright forked scales which are so characteristic of the *anopheles* genus, and on the dorsum of the thorax there will probably be a number of small white spindle-shaped scales, and some white or brown hairs. Passing on to the abdomen we shall find that in most species it is thickly covered with long brownish hairs, but that very few if any scales are present. In one or two species however we shall find that the abdomen is very thickly covered with broad silvery scales, and we shall recognise that this is a very important aid in the identification of these species. In the examination of the legs we shall note that each consists of a femur, tibia, and five tarsal segments, the terminal of which is very short and carries the *ungues*,—very sharp-pointed horny structures which enable the mosquito to rest in any position on a wall or roof without falling. In some species we shall see that the legs are of a uniform brown or black colour without any white bands at the joints, in others there will be a more or less broad white band at each joint, and in some the whole of the last one, two, or three, tarsal segments of the hind legs will be pure white. In addition to the bands at the joints, the femora and tibiæ may in some species, be brilliantly speckled with white scales. In the examination of the wings we shall note that some of the scales are white and others dark coloured, forming alternate black and white scaled areas ("spots"), and taking each vein separately the number of dark and light scaled areas will be noted.

Having in this way noted the markings and characters of each structure, we shall, in the majority of instances, be able to correctly identify the species by means of the following table.

TABLE OF THE INDIAN SPECIES OF ANOPHELETES.

I.—WINGS UNSPOTTED.

A.—PALPI UNBANDED.

A. Aitkeni (James).

B.—PALPI WITH WHITE BANDS.

A. immaculatus (Theobald).

II.—WINGS SPOTTED.

A.—PALPI UNBANDED.

A. Lindesayi (Giles)	The wing has one large white spot near the apex. Femora of hind legs with a broad white band.
A. barbirostris (Van der wulp).	A very large species with black densely scaled palpi.
A. gigas (Giles)	A very large hill species.

B.—PALPI WITH FOUR WHITE BANDS.

A. sinensis (Wiedmann) and its allied species *A. nigerrimus* (Giles).	Tarsal joints banded but none of the hind tarsal segments pure white.
A. pulcherrimus (Theobald).	Abdomen covered with broad white scales. Legs speckled. The 3rd, 4th and 5th hind tarsal segments pure white.
A. leucosphyrus (Dönitz)	Legs banded and speckled, but none of the hind tarsal segments pure white.
A. karwari (James)	Legs not speckled, but with bands at the joints. The 5th tarsal segment of hind legs pure white.

C.—PALPI WITH THREE WHITE BANDS.

I.—Tips of palpi black.

A. Turkhudi (Liston)	None of the hind tarsal segments white.
A. nagpori (James)	The 4th and 5th hind tarsal segments pure white.

II.—Tips of palpi white.

One or more of the hind tarsal segments are pure white.	*A. fuliginosus* (Giles)	Tarsal joints banded but legs not speckled. The 3rd, 4th and 5th hind tarsal segments pure white.
	A. Jamesi (Theobald)	As above, but with speckled legs.
	A. maculipalpis (Giles)	As above, but with legs and palpi speckled.
	A. Theobaldi (Giles)	Only the 4th and 5th hind tarsal segments are pure white.
	A. maculatus (Theobald)	Only the 5th hind tarsal segment is pure white.
	A. Willmori (James)	Differs from *A. maculatus* in having many scales on the abdomen.
Tarsal joints banded but none of the hind tarsal segments pure white.	*A. Rossi* (Giles)*	The legs are not speckled.
	A. Stephensi (Liston and James).	The legs are speckled. Abdomen covered with scales.
Legs uniformly coloured without bands or white segments.	*A. fluviatilis* (Liston and James).	Third longitudinal vein of wing white scaled. Six white patches on wing fringe.
	A. jeyporiensis (James)	Seven white patches on wing fringe. Faint white spots at some of the joints of the legs.
	A. culicifacies (Giles)	Third longitudinal vein of wing black scaled. Faint white spots at some of the joints of the legs.

A few examples will serve to illustrate the method of using this table.

Example 1.—A female mosquito with palpi as long as the proboscis, *i.e.*, it belongs to the *anopheles* genus.

* When a mosquito is named after any person the accepted rule for forming its specific name is to add one *i* to the person's name. This well known mosquito for example is named after Major Ross, I.M.S., and not after an Italian named Rossi. Its specific name should therefore be *Rossi* and not *Rossii* as usually written. (Dönitz. Zeitschrift für Hygiene, XLIII, 1, page 238.)

Wings.—Spotted.

Palpi.—With three white bands or rings, one broad ring including the tips (which are therefore white), and two narrower ones.

It therefore comes under the group C, sub-group II.

Legs.—There are white bands at the tarsal joints but none of the hind tarsal segments are pure white, and there is no speckling of the legs in addition to the bands.

Diagnosis.—*A. Rossi.*

Confirm by careful examination of the wing markings.

Example 2.—A female *anopheles.*

Wings.—Spotted.

Palpi.—With three white rings, the outermost of which includes the tips. In addition to the three complete rings there are one or two small patches of white scales, which do not amount to a complete ring or band, on the upper surface of each palp; *i.e.*, the palpi are marked with three bands and are speckled in addition.

Legs.—The 3rd, 4th, 5th, and the apex of the 2nd tarsal segments of the hind legs are pure white. There are white bands at the other tarsal joints and the femora and tibiæ are brilliantly speckled with white scales.

Diagnosis.—*A. maculipalpis.*

Example 3.—A female *anopheles.*

Wings.—Spotted.

Palpi.—With three white rings and the tips white.

Legs.—Uniformly coloured without bands at the tarsal joints.

Diagnosis—*A. fluviatilis.*
A. jeyporiensis or
A. culicifacies.

Separate by careful examination of the wing markings.

The breeding places of CULEX and ANOPHELES mosquitoes.

Having learnt how to find and distinguish the different kinds of adult mosquitoes, we shall next desire to know something of the places where they breed. This is very important because in the first place it is much easier to kill mosquitoes in their larval condition in water than it is to kill the adults, and in the second if we can do away with all breeding places, it is evident that no adult insects can be produced.

We have seen that *culex* mosquitoes have no connection with the transmission of human malaria, but as it has been proved that they are the agents by which another very important disease of India, *viz.*, elephantiasis, is transmitted, it is well to destroy their breeding places wherever we can do so. Our great object should be, however, to find and destroy the breeding places of *anopheletes.*

If we can find mosquito larvæ in any collection of water we know that such a collection is a breeding place of the particular kind of mosquito whose larvæ we have found, and it is therefore necessary to know how to collect larvæ and how to breed them out into adult mosquitoes, before we can tell what are the breeding places of any particular kind of mosquito.

How to collect larvæ and breed them out.—When going out to collect larvæ it is best to take a large tin mug with a handle and some wide-mouthed bottles. As *anopheles* larvæ are often difficult to see, we should not leave any pool or stream because we cannot *see* larvæ in it, but should stoop down at the edge of the water and scoop the tin quickly through it under the grass at the edge, bringing it out full of water. Then, if the tin is allowed to stand on the ground for a few moments, any larvæ that have been dipped up in it will rise to the surface and be easily recognised. By fishing in this way at the edges of several parts of a pool or stream we shall either catch a good many larvæ, or make certain that the pool or stream is free from them.

If any are caught they should be transferred with some of the water into one of the wide-mouthed bottles, keeping the larvæ from different pools in different bottles. The mouths of the bottles should afterwards be covered with a piece of coarse muslin, and after a few days the larvæ will develop into pupæ and then into adult mosquitoes, which can be transferred to another bottle, killed, and mounted for examination. In this way we shall learn after a time exactly what species of *anopheletes* are found in the different breeding places.

Culex larvæ may be found in abundance in almost any collection of water that has remained on the ground, or in a tin, tub, *gumlah,* or tank for some days. From the few drops of water which collect at the base of the leaves of trees in a wood to the largest tank or irrigated rice field ; in the smallest and dirtiest puddles by the road side, or in the eddies and back-waters of a mountain stream ; in the foul water of a cesspool or in the clear rain or well water kept in an iron tank or fire bucket ; in broken *chatties*, old bottles, in any thing in fact where a few ounces of water can lodge, *culex* larvæ may be found.

Anopheles larvæ may also be found in any or all of the above situations. This is a very important fact because it shows that when searching for *anopheles* larvæ we must not neglect to examine every collection of water of whatever kind it may be.

Although in referring to the whole genus *anopheles* we may say that their larvæ are found in any collection of water, still when we come to examine the subject more closely we shall note that all the different species of the genus are not equally common in all breeding places. A breeding place which is suitable for one species is not so for another, so that while we find one species always breeding in shallow muddy pools near houses, the larvæ of another species are always found in more or less swiftly running streams, and of another in the clean stagnant water of wells, *gumlahs*, etc.

We have already seen that the prevalence of *anopheletes* in a village depends on the number of breeding places near, and we may now add that the prevalence of any particular species will depend on the number of suitable breeding places for that species. Thus in a place surrounded only by shallow muddy pools we shall find only that species to be prevalent which breeds successfully in such collections of water ; in a place near which there are many small streams we shall find a stream-breeding species, and so on.

It is important therefore to know the favourite breeding places of the more important species of Indian *anopheletes*, and this subject has been rendered easier by the fact that, as regards habits and breeding places, the different species may be divided into certain natural groups, the members of which are alike in these respects.

The chief and most distinct of these groups are as follow :—

Group I.—Species breeding in open water with much aquatic vegetation, at some distance from houses, such as deep ponds, swamps, marshes and deep pools under trees or in a wood.

A. barbirostris.

A. sinensis.

A. nigerrimus.

The adult insects of this group are very rarely found in houses; they are essentially "wild" mosquitoes.

Their relation to the prevalence of malaria.—Although the species in this group feed on the blood of man and are capable of transmitting malarial fevers, yet from the fact that they are rarely met with in houses it is probable that they exert very little, if any, influence on the prevalence of malaria.

Group II.—Stream breeding species. The larvæ of these species are almost always found in more or less swiftly running streams. Irrigation watercourses form the chief breeding places in the Punjab for one of the members of this group (*A. culicifacies*).

A. fluviatilis.

A. jeyporiensis.

A. culicifacies.

In places where such breeding places are common the adult insects of this group are abundant in the houses.

Their relation to the prevalence of malaria.—The members of this group form the chief malaria-carrying species in India and Africa. Wherever malarial fevers are very prevalent one or other of these species will be found, and although other species may be present as well, observations have shown that the prevalence of malaria is to be ascribed chiefly, if not entirely, to the presence of a member of this group.

Group III.—Pool breeding species. The most important of these species is *A. Rossi*, which is almost always found breeding in shallow muddy pools in the vicinity of houses. As would be expected from the nature of its breeding grounds, this species is the most widely distributed in India, and may be found in enormous numbers in the houses after the rains. It is essentially a "domestic" species.

Its relation to the prevalence of malaria.—Although this species is so abundant and so widely distributed, it appears to have little if any influence on the prevalence of malaria in nature. Like all other *anopheletes* with which experiments have been made, it has been proved to be capable of transmitting malarial fevers under experimental conditions, and the reason why it does not usually do so in nature is unknown. It is possible, however, that this species feeds for preference on the blood of domestic animals such as cows, goats and horses, rather than on that of man.

With the above remarks as a guide it should not be difficult for anyone to find the favourite breeding places of the different species of *anopheletes* prevalent in his district.

The habits of anopheletes.

The fact that some species of *anopheletes* are always found near human habitations ("domestic" species), while others are rarely found in houses ("wild" species), has already been mentioned, as have also the important facts regarding the selection of different breeding places by different species. Another important characteristic of *anopheles* mosquitoes is that they bite almost exclusively at night, *i.e.*, between sunset and sunrise. During the day time they hide away in some dark corner of the room or in the outhouses, coming out again as soon as twilight begins. For this reason there is more danger of catching malarial fever at night than in the day time.

Anopheletes do not habitually fly very far, and for this reason they are seldom found in places which have no suitable breeding places near at hand. If the nearest breeding place to a village is over half a mile away the village will be practically free from *anopheletes* and even if the nearest breeding place is only a quarter of a mile away comparatively few may be found. It is possible, however, that under certain conditions *anopheletes* can fly a long distance. If for example all the breeding places round a village were suddenly done away with, it is probable that the majority of *anopheletes* would desert the village for a more favourable one, and again at the onset of the severe cold in the north of India a possible explanation for the sudden and complete disappearance of adult *anopheletes* is that they have migrated to more favourable conditions further south.

Regarding the length of life of *anopheles* mosquitoes, their seasonal prevalence, and the means by which they tide over the severe cold of winter, very little is in fact known, and extended observations on these important points require to be made. The generally accepted idea that adult *anopheletes* are able to remain in a hybernating condition in houses without feeding or laying eggs for many months is very improbable. Recent work has shown that all species do not tide over the winter by the same method, and some species are undoubtedly able to resist cold better than others. *A. fuliginosus* for example is able to live, feed and lay eggs throughout the winter in the Punjab just as it does in the autumn. *A. culicifacies* on the other hand tides over the Punjab winter solely by means of hybernating larvæ. Although all adults of this species die off or disappear during the winter, some of its larvæ remain in permanent pools, in a more or less resting condition, without developing into pupæ and adults until the spring. Both adults and larvæ of other species, *e.g.*, *A. Rossi*, disappear entirely from the Punjab during the winter, and do not return again until the following July, some time after *A. culicifacies* has become fairly prevalent.*

The characteristics of the malarial fevers and parasites of India.

We must now briefly consider the results of the presence of malaria parasites in the blood.

It is well known that the most prominent symptom caused by an infection with malaria parasites is *fever* of a very definite and peculiar character. This character may be summed up in the words *Intermittency* and *Periodicity*. By intermittency is meant the fact that the fever ceases at intervals; the temperature alternately falls to normal or below, and rises again. On this account the name "Intermittent fevers" is well applied to malarial fevers. By periodicity is meant the habitual tendency of the fever to recur at stated intervals of time. Thus the fever may recur at intervals of 24 hours (Quotidian periodicity) or at intervals of 48 hours (Tertian periodicity) or at intervals of 72 hours (Quartan periodicity). It may be said that, almost without exception, all cases of fever due to the presence of malaria parasites in the blood will *if left untreated*, sooner or later exhibit these two characteristics of intermittency and periodicity. Unfortunately the terms "malaria" and "ague" are often applied in a loose manner to many continued and irregular fevers, the nature of which is not wholly clear, and at the outset I would strongly urge you to guard against making a hasty diagnosis in any continued or irregular fever; and would advise you to err on the side of those who do not consider any case of fever

* For further information on these points see Scientific Memoirs by officers of the Sanitary and Medical Departments of the Government of India, New Series, No. 6. "First report of the anti-malarial operations at Mian-Mir, 1901—1903" by Captain S. P. James I.M.S.

as malarial, until the character of the temperature chart, or an examination of the blood, plainly proves it to be so, rather than on the side of those who regard every case of fever as "malaria," until, after several weeks of ineffectual treatment, this diagnosis is proved to be wrong.

Before describing the clinical types of malarial fevers we must say a few words regarding the process by which the malaria parasite produces fever.

I have already described how the parasites in the red blood corpuscles gradually grow larger and larger until they attain their full size and divide up into a number of segments or spores, which burst through the thin remnant of the corpuscle and become free in the blood plasma, ready to enter fresh corpuscles. It has been found,—and the observation may be verified by any one who examines the blood of a typical case of malarial fever,—that the onset of the attacks of fever from which the patient suffers, always corresponds in point of time with the stage of sporulation or segmentation of the parasites. During the interval of apyrexia only young and medium-sized parasites, enclosed within the red blood corpuscles, can be found, and it is only when the parasites are in the segmenting stage and escaping from the corpuscles that the attack of fever begins. There is thus a very intimate connection between the sporulation of the parasite and the attack of fever, and it is probable that during the growth of the parasite in the red blood cell it produces a pyrogenetic or fever-producing chemical substance, which, when the parasite bursts from the red cell in the act of sporulation, is liberated into the plasma and so becomes able to exert its influence and cause fever. As long as the parasite remains inside the envelope of the corpuscle the pyrogenetic substance cannot escape, so that during the time the parasite takes to grow to its full size the patient does not suffer from fever. As soon as the parasite divides and bursts from the corpuscle the pyrogenetic substance escapes and causes fever.

From this you will readily understand that a parasite which sporulates every 24 hours will produce Quotidian fever, one which sporulates every 48 hours will produce Tertian fever, and one which sporulates every 72 hours will produce Quartan fever.

In India there are three species or varieties of the malaria parasite which sporulate at the above intervals respectively, and which cause the three clinical types of malarial fevers, Quotidian, Tertian and Quartan, which are so commonly met with. It will be apparent that if a parasite should, for some reason or other, complete its asexual cycle in a less period than 24, 48, or 72 hours, a different clinical type of fever will result, and also that a different clinical type may be produced by the presence in the blood of two or more groups of parasites which sporulate at different times.

The three species of malaria parasites referred to above are called respectively :—

(1) The Malignant Tertian parasite.

(2) The Benign Tertian parasite.

(3) The Quartan parasite.

The general description of the life cycle of the malaria parasite in man and in the mosquito which I have already given, applies equally to all these species, but they differ from each other not only in the time which they take to complete their asexual cycles respectively, but also in other particulars, such as their size and appearance, their amœboid movements, the character of the pigment they produce, the number of segments into which they divide up, and the characters of the sexual forms. These differences are considered sufficient for them to be regarded as distinct species.

I shall describe first the results of an infection with Benign Tertian parasites, because this is the species most commonly met with in India, and afterwards note the differences which result from infections with the other two forms.

1. *Benign Tertian infection.*—Supposing a man to have been bitten by a mosquito infected with the sporozoites of the Benign Tertian parasite, he will probably not feel any ill effects until about twelve or fourteen days afterwards. This is the incubation period during which the parasites have been gradually multiplying in his blood, but have not been present in sufficient numbers to cause any symptoms. Towards the end of the period he may feel some aching of the bones, headache, or other premonitory symptoms, and his temperature may be somewhat raised. After these indefinite symptoms have gone on for a day or two the regular attacks of "ague" begin. These consist of a series of attacks of fever which recur, in infections with the Simple or Benign Tertian parasite, at definite intervals of 48 hours. Each attack is represented clinically by a "cold" stage, a "hot" stage, and a "sweating" stage. At the

beginning of the cold stage the patient feels chilly ; after a short time the feeling of cold spreads all over his body and becomes so intense that his teeth chatter and he shakes from head to foot. His temperature however, in spite of the feeling of cold, begins to rise. After a time the shivering stops and the patient begins to feel hot, the skin becomes dry and burning, and the temperature rapidly rises to 103°F. or 104°F. or more. After an hour or so the hot stage passes off, the patient begins to perspire profusely, the fever quickly declines, and in a short time all the acute symptoms have disappeared and the patient feels almost well. As a rule he is able to get up and go about his occupation until the next day but one, when he will again have another attack of fever similar to the first one. If untreated these attacks may recur every other day for many weeks, gradually declining in severity as time goes on. In the meantime the patient's spleen has become enlarged and he has become pale and anæmic. After the fever has apparently left him for good it may return at irregular intervals for many months (Relapses). These relapses of fever may be brought on by almost any exciting cause such as chill, over fatigue, over-anxiety, exposure to the sun, etc., *and have no connection whatever with mosquitoes.* They are simply due to the fact that all the parasites of the first infection have not died out, and when the patient's resisting power is lessened by any of the exciting causes just mentioned, the parasites are able to develop rapidly again and produce their ill effects.

The relation of the parasites to the different clinical stages.—If the patient's blood be examined at the onset of fever, that is, during the cold or rigor stage, it will always be found that (as we have already noted), the majority of the parasites are in the stage of division or sporulation. The onset of fever and the rigor correspond in point of time to the sporulation of the asexual forms of the parasite. From the point of view of treatment this is an important point to remember. By the time the hot stage approaches all the parasites have divided up and are entering, or have already entered, fresh corpuscles. During the last part of the hot stage, during the sweating stage, and during the interval of apyrexia, the parasities are enclosed in the red blood corpuscles, growing and developing pigment. Between any two similar stages of the parasite an interval of 48 hours elapses, *i.e.*, the Benign Tertian parasite takes 48 hours to complete its asexual cycle.

These points and the clinical characters of Benign Tertian malarial fever are illustrated in Chart. I.

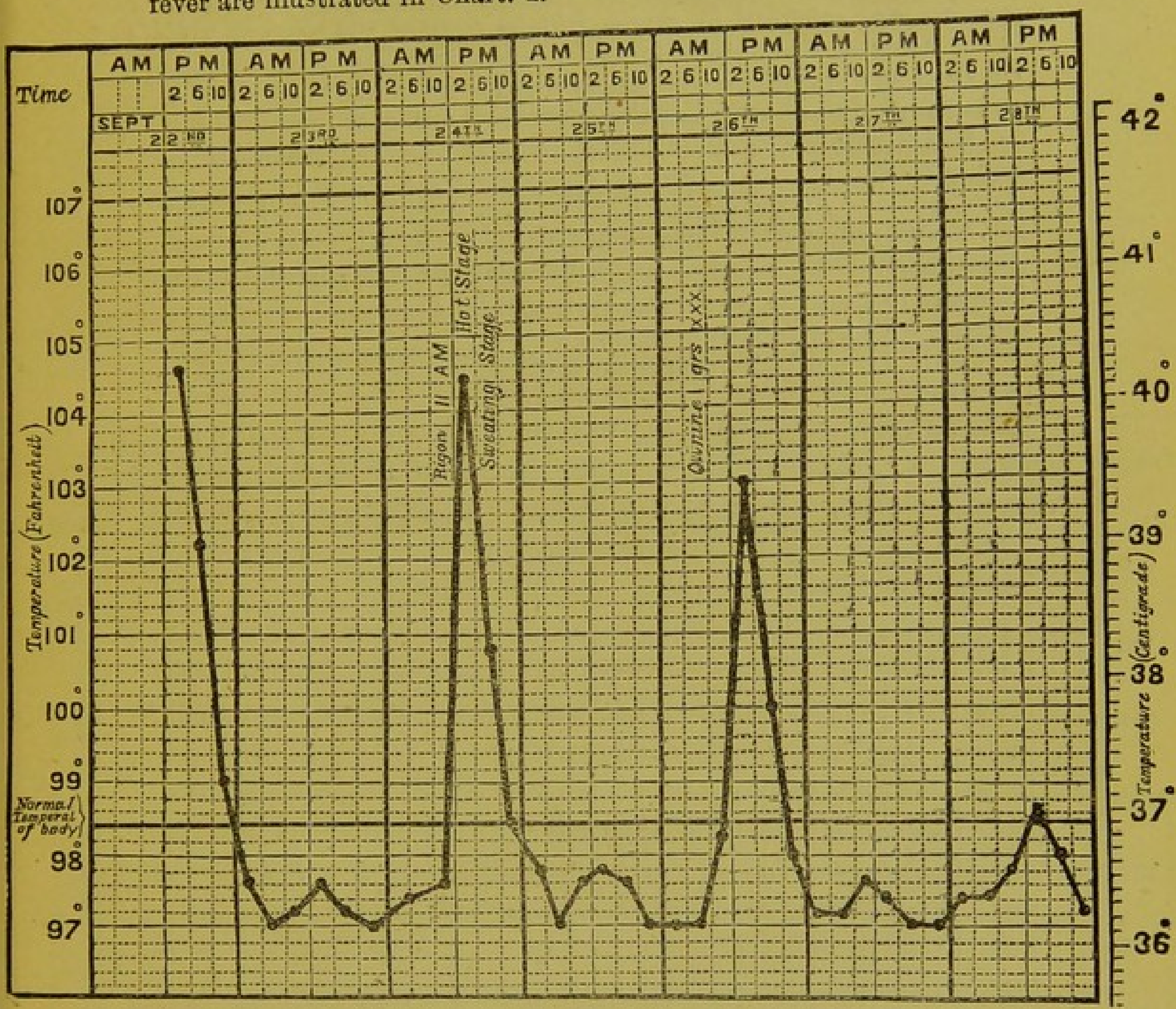

Chart No. I.

Malarial fever. Benign Tertian infection.
Name.—Gunner T—. *Age*—25.

This chart. shows three typical paroxysms of ague occurring at the same time on alternate days. Each attack lasted from about 11 A.M. until about 8 P.M. At 12 noon, during the shivering stage, sporulating forms (from which the photographs in Plate VII, Figs. 3, 4, were taken) were found in the blood, and at 7 P.M. very young forms, which had lately entered the corpuscles, were present. The sudden rise of the fever and its quick fall are characteristic of Benign Tertian infections. The administration of thirty grains of quinine at 7 A.M. on the 26th, though it did not prevent the onset of the attack on that day, stopped all future paroxysms and practically cured the case. (See page 36.)

After the attacks of fever have gone on for a few days, sexual forms of the parasite which, in the case of the simple Tertian parasite, are spherical in shape, will be seen in the blood as well as the asexual sporulating forms. These sexual forms, however, do not cause any symptoms, and unless they are taken into the body of a suitable mosquito they gradually degenerate and die.

2. *Quartan infection.*—The symptoms produced by an infection with the Quartan form of the malaria parasite are similar to those produced by the simple Tertian form, except that the interval between the onset of the attacks of fever is one of 72 hours instead of 48 hours. The reason of this is that the Quartan parasite takes 72 hours to complete its asexual cycle instead of only 48 hours as is the case with the Tertian parasite.

Chart II illustrates the results of an infection with Quartan parasites.

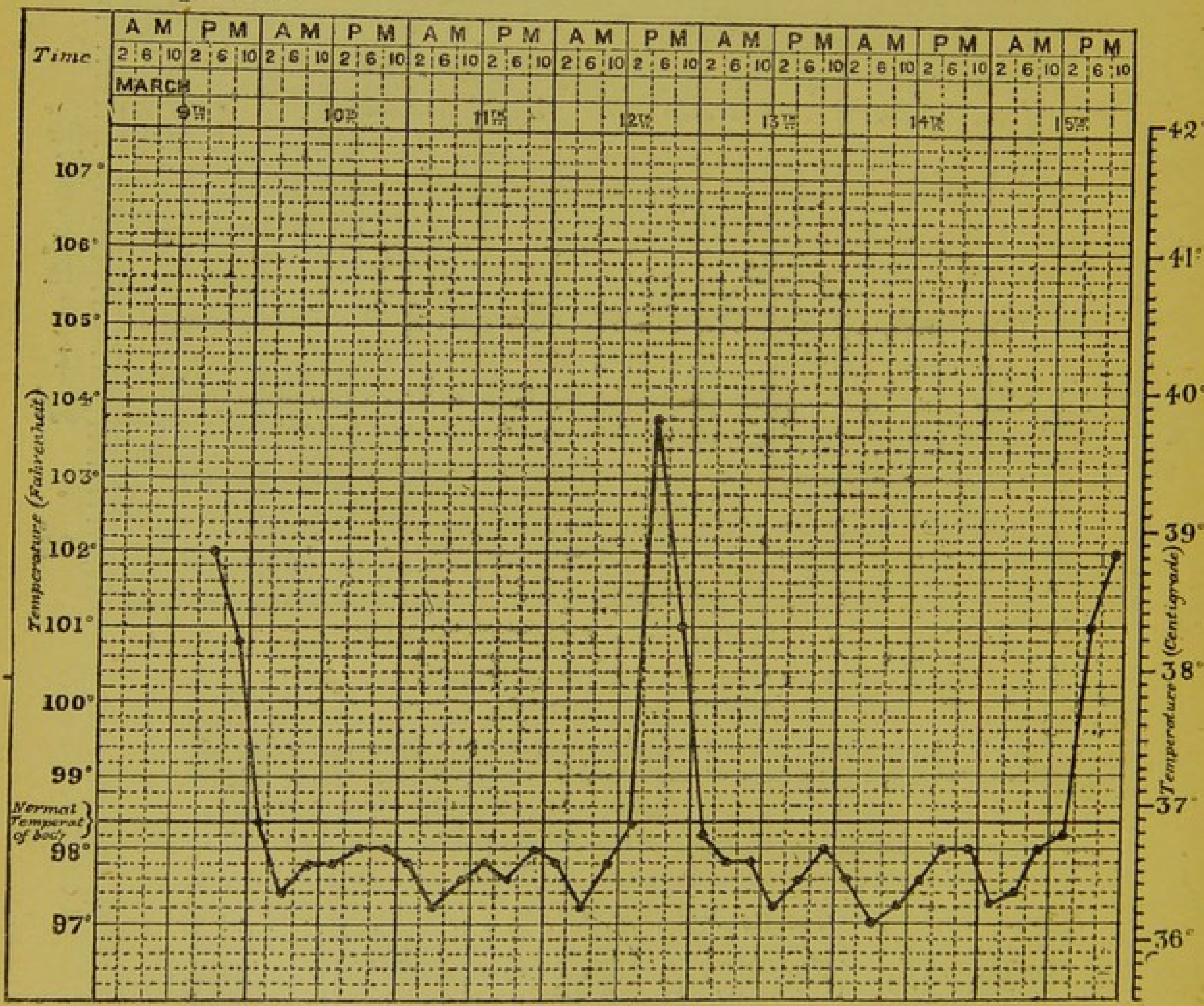

CHART No. II.

Malarial fever. Quartan infection.

Name.—Chetty. *Age.*—10 years.

On the 10th young Quartan parasites were found in the blood of this case; on the 11th medium sized forms (Plate VII, Fig. 6) and on the 12th at 5 P.M. pre-segmenting and segmenting forms (Plate VII, Fig. 7).

3. *Malignant Tertian infection.*—There are marked differences between infections with the malignant Tertian form of the malaria parasite and those with simple Tertian or Quartan parasites, and the term "malignant" has been applied to this species of parasite in opposition to the term "benign," which is applied to the parasites of simple Tertian and Quartan fevers, because dangerous symptoms, such as hyperpyrexia, coma, delirium, etc., are much more liable to arise in the course of an infection with this form of parasite than with the others. The malignant Tertian parasite, like the simple or benign Tertian, takes 48 hours to complete its asexual cycle, and for the first few days of a case this fact is often apparent from the temperature chart (see Chart III). With this form of parasite, however, there is a great tendency for the parasites to complete their cycle in a shorter time than 48 hours, often indeed in as short a time as 24 hours, so that after a day or two the patient usually has an attack of fever every day. Again there is a tendency for the parasites to complete their cycles in different periods of time instead of their all doing so at the same time as in the case of simple Tertian and Quartan infections. As a result of this it not infrequently happens that the temperature does not fall quite to normal for several days together, and the chart may be remittent in character.

In untreated cases the fever continues in this way for about a week or ten days and then ceases, leaving the patient very weak and anæmic but otherwise apparently well. After an interval of apyrexia varying from six days to a week or more, a second series of attacks of fever, exhibiting a Tertian or Quotidian periodicity exactly similar to the first attacks, occurs. These relapses may be repeated at more or less constant intervals of a week or more for two or three months, gradually getting shorter and less severe until they die out altogether, leaving the patient with an enlarged spleen and extremely weak, anæmic and emaciated.

These points are well illustrated in Chart III, which is from a case of malignant Tertian fever in a child.

For the first four days this chart shows a definite Tertian periodicity. Then follow daily paroxysms until the 9th, after which an interval of six days' apyrexia occurs. This is followed by a series of relapses occurring at varying intervals, and in this case the relapses were still occurring at fairly definite intervals four months after the primary attack. The temperature is intermittent throughout the case. It should be noted that as the temperatures in this case were only taken twice daily, they are not by any means a record of the highest temperature reached on any particular day. In order to obtain a correct temperature chart it is necessary for the temperature to be recorded at least every four hours.

The malignant Tertian parasites are much smaller than those of the benign group of fevers. Their amœboid movements are very active, and it is very common to see several parasites in one corpuscle. Only the young forms of the parasite are seen in the peripheral blood, segmentation occurring for the most part in the deeper viscera, such as the spleen and bonemarrow. Towards the end of the first series of attacks of fever, that is, about a week after the commencement of the disease, sexual forms appear in the blood. Their number gradually increases, and they are very abundant after the fever has quite left the patient. It is certain therefore, that these sexual forms have no connection with the production of fever. They may still remain in large numbers when the patient has apparently quite recovered and gone about his occupation. In malignant Tertian infections the sexual forms are very easily recognised because they are crescent-shaped (Pl. VII, Fig. 10), the sexual forms of the simple Tertian and Quartan parasites are round and more difficult to recognise, because they look something like the full grown asexual forms (Pl. VII, Fig. 5).

4. *Mixed infections.*—Combined infections, with different species of the malaria parasite, occur not infrequently in India, and may produce irregular charts. A combined infection of simple and malignant Tertian parasites is perhaps most commonly met with, but combinations of simple Tertian and Quartan parasites are

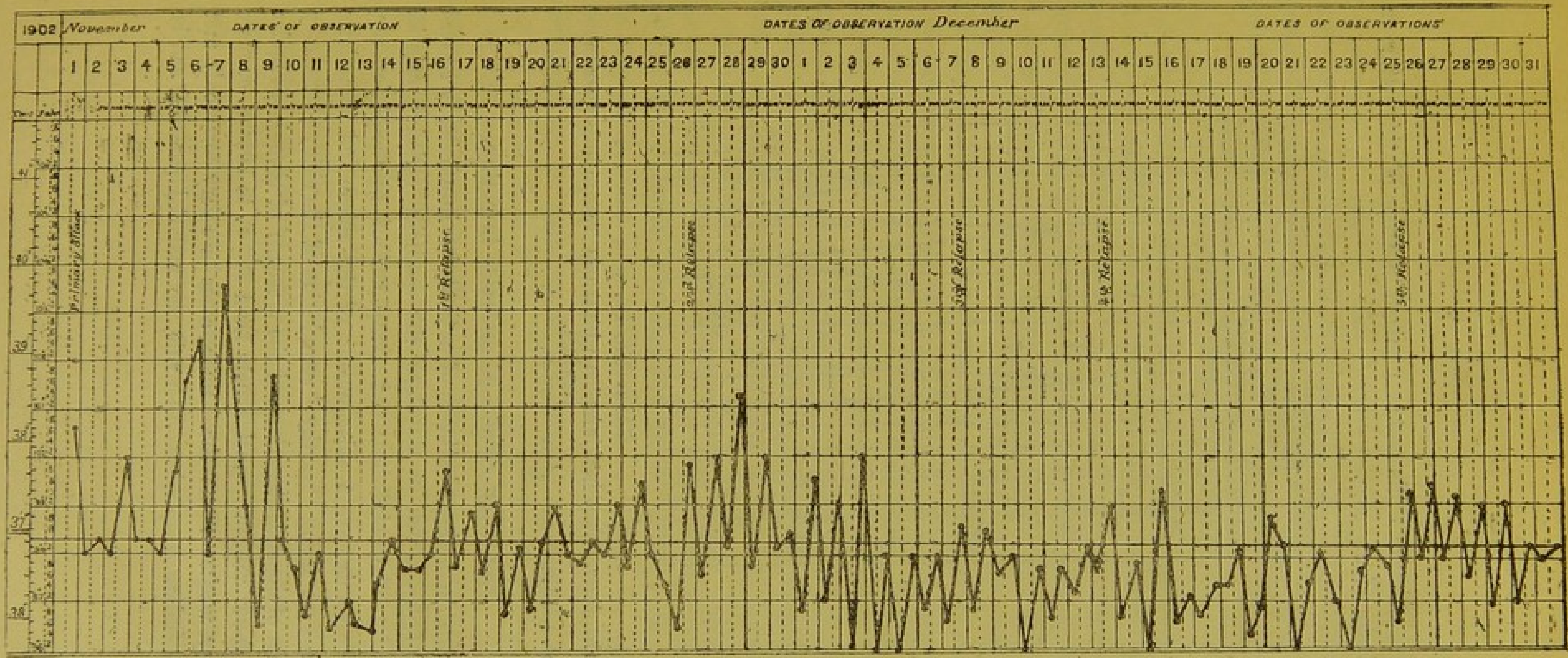

Chart No. III.

Malarial fever. Malignant Tertian infection.

Name.—Rangu. *Age.*—$1\frac{1}{2}$ years.

also seen. Chart IV illustrates a mixed infection of this nature in a child aged four years.

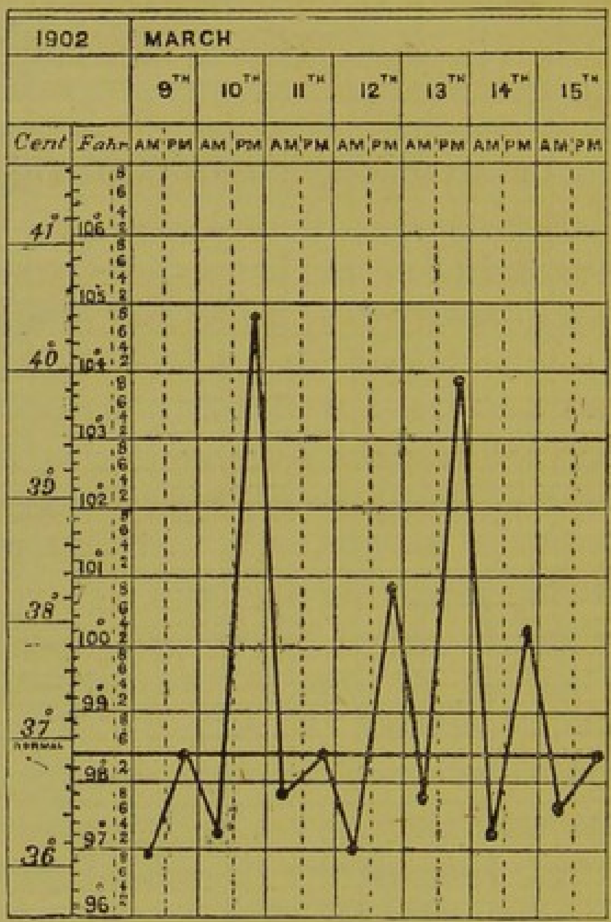

CHART No. IV.

Malarial fever. Combined infection with simple Tertian and Quarian parasites.

Name.—Uligammah. *Age.*—4 years.

The after effects of malarial infection.

After a succession of attacks of untreated or insufficiently treated malarial fever, a patient develops the condition called " malarial cachexia." The chief signs and symptoms of this condition are, marked anæmia, great enlargement of the spleen and sometimes of the liver, a sallow "earthy" complexion of the skin, a tendency to œdema of dependent parts, and the presence of chronic irregular "low" fever ranging continuously from 99° F. to 101° F. or more for many weeks or months. Such cases are very commonly met with in Indian hospitals. As a rule, no malarial parasites can be found in the blood of these patients, and for this reason they are not amenable to quinine. The chronic low fever from which they suffer in all probability is not connected in any way with the presence of malaria parasites, but is a secondary result of their general condition.

The treatment of malarial fevers.

Quinine is the only reliable drug in malarial fevers, and if given in a proper manner and in sufficient doses it seldom fails to effect a cure. It is a mistake, however, to commence the treatment of a case of fever with quinine until the diagnosis is absolutely assured. If we get into the habit, as many of us are apt to do, of treating all cases of fever indiscriminately with quinine, on the supposition that they are possibly malarial, our faith in the efficacy of the drug will soon diminish, because we shall find that it does not by any means cure all the cases of fever with which we have to deal. An accurate diagnosis is essential for successful treatment. In the absence of a microscopic examination of the blood the diagnosis of malaria rests chiefly on the character of the temperature chart. Tertian and Quartan periodicity only occur in malarial fevers, and if the chart exhibits either of these characters a diagnosis of malaria is almost certain. In the great majority of cases of malarial fever occurring in India, *which are not treated with quinine*, the temperature chart does exhibit either a Tertian or Quartan periodicity, and even in malignant Tertian infections a Tertian periodicity can be made out in the majority of cases. If quinine is given in small doses at the beginning of an attack of malarial fever, the temperature chart becomes irregular, and an accurate diagnosis is rendered very difficult. The fever may continue in an irregular or continuous manner in spite of the usual doses of quinine, until after a week or so we become hopelessly confused as to the real nature of the case, and begin to suspect that the case may not after all be one of malarial fever. But if from the commencement we had abstained from giving quinine, until our diagnosis could be made with certainty, we should have been saved the anxiety caused by a possible error in diagnosis, and if the case turned out to be really one of malarial fever, we should be able, with one or two adequate doses of quinine given at the proper time, to cut short the attack almost at once. We should also be in a position to tell our patient exactly what type of malarial fever he was suffering from, how long he would have to continue treatment in order to completely eradicate the parasites, and how to protect himself from future relapses. All these points are very important, because it must be remembered that malaria, like syphilis, requires many months of continuous treatment for its eradication, and for this reason requires the same care and accuracy in diagnosis.

As soon as the diagnosis of malarial fever is assured, it is best to begin treatment with quinine at once, irrespective of the stage of the fever, and to keep the patient slightly cinchonised * by repeated doses of the drug until he is cured.

We should note, however, that quinine acts most effectively on the parasite when it has escaped from the red blood corpuscles in the act of sporulation. As we have already learnt, this corresponds in point of time with the onset of the paroxysm (the cold stage), and whatever other doses of quinine we give the patient during the day we should always make sure that he receives one large dose (say of 20 grains) shortly before his paroxysm is expected. One dose given at this time will, in the ordinary regular Tertian and Quartan fevers, probably stop all future paroxysms, though it will not of course prevent the one which is actually impending (see Chart I).

Euchinin which is tasteless, is quite as effective as ordinary quinine and can be easily given to children. *It must be given in the form of the powder, as, if dissolved with the aid of acids, its bitter taste returns.*

Quinine is much more effective if given hypodermically than in any other way. Tabloids of the bi-hydrochlorate or some other soluble salt should be used, dissolved in distilled water. A new syringe, kept solely for the purpose, should be employed, and great care taken to thoroughly boil the needle, syringe, and solution and to render the skin thoroughly aseptic before carrying out the operation.†

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* The first symptoms of cinchonism are buzzing noises in the ears and deafness.

† A convenient case containing all necessaries for the hypodermic administration of Quinine can be obtained from Messrs. Burroughs, Wellcome & Co., London.

From two to five grains is usually a sufficient dose hypodermically, given, if possible, just before the onset of the paroxysm, but as much as ten or fifteen grains may be given and repeated on the same or subsequent days as may be necessary. It is easier and better to give the quinine hypodermically than intramuscularly, but care must be taken to get the point of the needle actually under the skin and not between its layers, or a painful lump will result. Arsenic has no action on the malaria parasite and is only of use as a tonic after the attack is over.

As in syphilis, continuous treatment is necessary for some months after all symptoms have passed off to ensure freedom from relapses. It is probable that a very large number of the cases of malarial fever admitted into our hospitals are relapses, the result of insufficient treatment during and after a first attack, and the practice which pertains in our hospitals of sending a patient out as "cured" almost as soon as the fever has left him, is no doubt responsible for the large number of cases of chronic malarial cachexia that occur in India.

Prophylaxis.

Under this heading two closely allied, yet quite distinct, subjects must be considered, *viz.* :—

(1) The prevention of malarial fevers.

(2) The extirpation of malarial fevers.

In considering first the prevention of malarial fevers we may recall these facts :—

(1) *Anopheles* mosquitoes are the carriers of the disease.

(2) People with malaria parasites in their blood are the source from which *anopheles* mosquitoes become infected and able to carry the disease.

Attempts at prevention may, therefore, be directed either against the carrier, (*anopheles* mosquitoes) or against the source, (infected people) or against both.

The chief methods of prevention that have been recommended are as follow :—

(1) The extermination of *anopheles* mosquitoes.

(2) The protection of everyone from the bites of *anopheles* mosquitoes.

(3) Segregation.

(4) The use of prophylactic drugs.

Methods (1) and (2) are directed against the carrier of the disease and method (3) against the source. Method (4) is an empirical one and disregards both the carrier and the source.

The plan of attempting to exterminate or to reduce the number of *anopheles* mosquitoes in malarious districts, was initiated by Major Ronald Ross, I. M. S., the discoverer of the facts upon which all modern systems of prophylaxis are based. This method may, therefore, be called the method of Ross.

The plan of attempting to protect everyone from the bites of infected *anopheles* mosquitoes, by covering in the doors and windows of houses with mosquito-proof netting has been chiefly advocated by Professor Celli in Italy, and it may, therefore, be appropriately called the method of Celli.

The third plan, that of segregation, differs from segregation measures usually carried out in the case of other contagious diseases, in that it has for its object not the segregation of the sick but that of the healthy. It has been chiefly advocated for the protection of *Europeans* who are obliged to live in malarious districts, and it has its foundation in the fact that natives, and especially native children, in malarious countries form the chief source of infection of *anopheles* mosquitoes. It assumes also that such mosquitoes do not habitually fly more than half a mile, and that they bite only at night-time. On these grounds it is advocated that no European house should be built within half a mile of a malarious town or village, and that no native servants or their children should be allowed to sleep at night in the compounds of European bungalows, but that their quarters should be placed as far as possible from the bungalow.

This method of prophylaxis goes by the name of "The segregation of Europeans", and was initiated by Drs. Stephens and Christophers, who consider it to be the most efficient way of protecting Europeans from malaria in certain parts of Africa.

As regards the fourth method it may be said at once that the only drug which is of any service as a prophylactic against malarial fevers is quinine, and that the correct way to employ it for this purpose is to administer a dose of 15 grains on two successive days every 9th and 10th days throughout the time the individual remains in a malarious place.* Small doses of 3—5 grains taken every day, as recommended by some authors, are of little or no use in preventing new infections, though perhaps such doses, if taken continuously, would serve to ward off relapses of old attacks.

Having thus briefly summarised the different methods of prophylaxis recommended, we may now apply our knowledge to the following particular cases: —

(1) Prophylaxis as applied to the individual.

(2) Prophylaxis as applied to any particular body of individuals such as a regiment of soldiers.

(3) Prophylaxis as applied to communities.

1. *Prophylaxis for the individual.*—In considering the prevention of malarial fevers from the point of view of the individual it is necessary to distinguish carefully between two points which are frequently confused, *viz.*:— (1) the prevention of *first* or new infections; and (2) the prevention of relapses of former attacks.

There is no doubt that any individual who wishes to do so, may effectually protect himself from a first or a new infection, wherever he may be living, by taking measures to prevent himself from being bitten by mosquitoes. This fact has been thoroughly proved, and at the present time is not doubted by anyone who is capable of forming an impartial opinion on the matter.

The chief precautions to be taken are:—

(1) Never go to sleep except under a good mosquito curtain.

(2) Never go out in the evening or sit in the house or verandah without wearing sufficient clothes to protect the whole body from mosquito bites.

Especial care should be taken to protect the feet and ankles by wearing high boots or putties. The reason for this precaution will be obvious to anyone who has lived any time in the tropics. Theoretically it would also be necessary to protect the hands by

* The method of Dr. Robert Koch.

wearing gloves and the face and head by wearing a gauze net covering; but in actual practice it is unnecessary to take these extreme precautions, because most people, except during sleep, take care to prevent mosquitoes from biting their face or hands.

Anyone who carries out the principle of always protecting himself from mosquito bites by the simple method outlined above, can live in the most malarious country with impunity. There are, however, certain additional safeguards for the individual which no wise man would neglect.

The chief of these is an application of the prophylactic method known as the "segregation of the European" which has already been referred to, and which of course is equally applicable to any individual native who chooses to make use of it. Remembering that this method arises out of the fact that natives in malarious districts are the chief source of danger, and that *anopheles* mosquitoes seldom fly more than half a mile, care should be taken when camping out never to pitch one's tent within half a mile of a native village. Travellers in Africa, as a rule, disregard this precaution entirely, with the result that they suffer a great deal from malaria. In India also a night spent in the *dâk* bungalow of most villages very frequently results in a bad attack of malaria, unless the strictest precautions have been taken to guard against mosquito bites.

If, for some reason or other, an individual is not able to carry out the directions given above, he must fall back upon the plan of attempting to ward off malarial fevers by taking prophylactic doses of quinine, according to the method already described. The uncomfortable effects produced by the large, but necessary, dose of quinine twice every 9 or 10 days renders this method a very trying one, which no one would resort to unless it were quite impossible for him to employ the simpler and more effective method of protecting himself from being bitten by mosquitoes.

The prevention of relapses of former attacks.—Relapses only occur in cases in which a former infection with malaria parasites has not been completely cured.

They have no connection whatever with mosquitoes and may be brought on by almost any exciting cause such as a chill, overfatigue, exposure to the sun, etc. The best way to avoid these relapses is to go through a thorough course of quinine treatment similar to that which will be described later under the heading of the "disinfection of infected individuals." It is almost useless to take a dose or two of quinine occasionally, in an irregular manner.

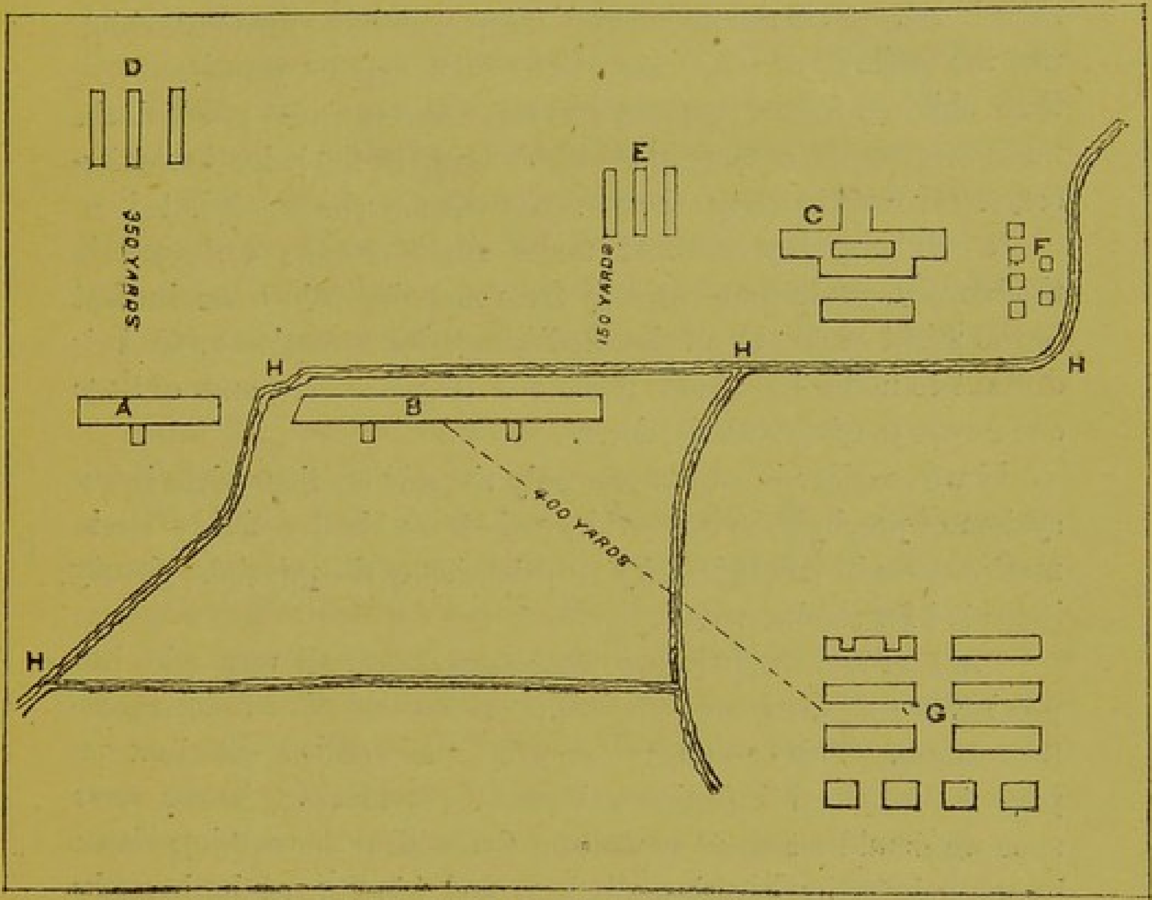

Figure 2.

A. B. Barracks of the men. C. Hospital and Prison. D. Syce lines. Infection of children 35 per cent. E. Syce lines. Infection of children 56 per cent. F. Hospital Followers. Infection of children 60 per cent. G. Regimental bazaar. Infection of children 40 per cent. H. H. H. Irrigation watercourse. Breeding place of *anopheles* mosquitoes.

2. *Prophylaxis for a particular body of individuals.*—We may next consider the case of a number of individuals, such as a regiment or company of soldiers living together in one or more barracks, surrounded on all sides by native bazaars and by breeding places of *anopheles* mosquitoes. I refer, for example, to such a condition as is illustrated above (Figure 2), a condition which is commonly met with in Indian cantonments.

A. and B. are the barracks of the men. C. is the hospital and military prison. D. and E. are syce lines containing perhaps 200 children, from 40 to 60 per cent. of whom have malaria parasites in their blood. F. is the hospital followers' quarters, containing perhaps 40 or 50 children, 60 per cent. of whom have malaria parasites in their blood. G. is the regimental bazaar containing numerous children, the majority of whom are infected with malaria parasites. All these children form a constant and abundant source from which the numerous *anopheles* mosquitoes which breed in the irrigation water-course (H.) and in many other watercourses near, become infected.

It will be readily seen that under these conditions the men in the barracks must suffer severely from malaria. They are in fact in the midst of an area of infected *anopheles* mosquitoes and it is difficult to understand how, under the circumstances, any of them can escape getting malarial fever.

If we consider in such a case only the soldiers themselves in our system of prophylaxis, it is evident that we shall probably attain most success in prophylaxis by an extension of the principles already indicated for the individual.

Our first aim would be to thoroughly cure all men who had previously suffered from malaria and who would therefore be liable to relapses. This would be done by the method described on page 45 for the disinfection of infected individuals. At the same time we should set about protecting the soldiers from being bitten by mosquitoes, by covering all doors and windows of the barracks with mosquito-proof netting, and as a further safeguard by giving each man a mosquito curtain. In most Indian stations this plan of protecting the men against mosquito bites would be impracticable, owing to the fact that the intense heat during the summer nights would render it quite impossible for men to sleep under mosquito curtains in mosquito-proof barrack rooms. In such stations therefore the best plan would be to adopt, in a modified form, the method of segregation already described; that is *to remove the native lines and the bazaar to a greater distance from the barracks, so that the men may be if possible half a mile from any source of infection.*

If neither of these methods could be carried out we should have to fall back upon prophylactic doses of quinine.

3. *Prophylaxis for communities.*—Either the method of protecting all the men from mosquito bites, or that of segregation, would doubtless protect the particular body of individuals referred to from getting malarial fevers. No system of prophylaxis however, can be considered satisfactory which aims only at the protection of a few, however important these few may be, while it leaves the great mass of the inhabitants of a place in the same condition. The object of a good malarial prophylaxis should be to render *everyone* less liable to contract malaria, to transform, in fact, a malarious place into a healthy one. Measures which aim at anything short of this are of more scientific interest as proving that protection from the bite of infected mosquitoes ensures protection from malaria, than of real practical value.

How then can we set about turning a malarious place into a healthy one?

We know that if we can exterminate all malaria-carrying mosquitoes from the place we shall entirely get rid of malaria there, and this is therefore the method which must be attempted.

The suppression of anopheles *mosquitoes.—Anopheles* and other kinds of mosquitoes are, as we have already seen, much more easily dealt with in their larval condition in water than in their adult state. The main object of all efforts directed to the suppression of mosquitoes is therefore to get rid of all places where they can breed. This is comprised in the words "effective drainage." From the earliest times it has been recognised that malaria may be diminished and in some places banished altogether by drainage and drying of the soil. It is almost certainly by these means that large tracts of country in England, Holland, France and many other places which formerly were very malarious have been rendered healthy and productive. It is also for this reason that large towns such as Rome in Italy, Calcutta, Bombay and Madras in India, are far less malarious than the outlying villages which surround them, though in the latter cities a great deal in the way of effective drainage still remains to be done. In our large towns in India, in proportion as we effectively prevent the formation of stagnant pools of water, and in proportion as we carry out measures for drying the soil and lowering the level of the subsoil water, so will the number of malaria-bearing mosquitoes and in consequence the prevalence of malarial fevers, diminish.

In isolated villages we should aim at carrying out the same principles—the draining away of large areas of water, the filling in of all small tanks and pools, and the removal of stagnant water wherever it may be.

In many parts of India irrigation by means of canals is the chief cause of the prevalence of malaria. We have already seen that the chief malaria carrying species of *anopheles* mosquitoes breed almost entirely in the running water of irrigation water-courses, and apart from this the effect of bringing in large supplies of water to a district which already is improperly drained, is to further increase the water-logging of the soil and the formation of numerous pools where mosquitoes can breed.

The same result is produced by bringing in a drinking water supply to a town from outside without first providing for the efficient drainage of all superfluous water.

There is little doubt that, at any rate in cantonments, where the chief need for irrigation is in the making of flower gardens, irrigation by means of wells should be substituted for the present method by canals. For these purposes well-irrigation is quite effective, and has the great advantage of lowering the level of the subsoil water and drying the soil.

Any superfluous water which cannot be drained away, may be made an impossible breeding place for *anopheles* mosquitoes by covering it with a layer of kerosene oil, which not only kills all larvæ, but also any adult mosquitoes that may come to lay their eggs on the water.

If irrigation canals, streams, etc., cannot be done away with in any place, they may, to a certain extent, be rendered inhospitable breeding places by keeping their edges very smooth and clean and free from weed and grass.

The extirpation of malarial fevers.

Quite distinct from the foregoing measures for the *prevention* of malarial fevers,—though the ultimate aim of both is the same,—is the proposal of Dr. Robert Koch to exterminate all malaria parasites, by the systematic treatment of all infected individuals with quinine. Dr. Koch compares the campaign against malaria to that which is carried out against cholera. Just as in cholera it is necessary to search out all the sick, the convalescent, and the healthy who harbour the cholera vibrio and to isolate and disinfect them, so in a campaign against malaria it is necessary to search out and disinfect all people who harbour the malaria parasite. The method is carried out in the following way. The blood of all the inhabitants of the district which it is desired to free from malaria, is systematically examined, and all those in whom infection with malaria is found are treated by the following plan for "the disinfection of the infected." A dose of 15 grains of quinine is administered on each of two or three successive days and repeated at intervals of eight days throughout a period of three months. If during the course of the treatment the individual gets a relapse of fever, or if, even without a relapse, malaria parasites are found in his blood, he receives five consecutive days' treatment with quinine given in the following doses :—On each of the first and second days 30 grains of quinine (15 grains in the morning and 15 grains in the evening) and on each of the third, fourth and fifth days 15 grains. The after treatment is then continued in the same way as before, *viz.*, 15 grains on two or three successive days every eight days for three months.

By this method Dr. Koch and his assistants have obtained successful results in a number of malarious districts under different conditions.

In carefully selected malarious places in India, and especially in cantonments, where all the inhabitants are under supervision, it is a measure which is likely to prove of the greatest service in spite of its apparent impracticability. Looking back at the illustration on page 41 (Fig. 2), the syce lines, the hospital followers' quarters, and the bazaar are practically the only centres of malaria from which all the *anopheles* mosquitoes in the lines become infected. If we were to treat all the infected natives in these groups of huts with quinine, we should not only greatly benefit the people themselves but we should also do away with the main sources of infection of *anopheles* mosquitoes. This would not be by any means an impossible task, and as a matter of fact the experiment has already been tried in a modified form in the cantonment from which our illustration is taken.

All the children living in one of the syce lines (over 100 in number) and all the children in the hospital followers' lines (35 in number) were treated systematically with quinine from August to November 1902. Each child received from five to ten grains of quinine according to age daily for the first ten days and afterwards ten grains twice a week on consecutive days.

As a result of this treatment no parasites were found in any of the children of the syce lines, and in only 16 per cent. of the hospital followers' children, during the fever season of 1902, although during the previous year a very large number were infected. The spleen rate of the children was also markedly reduced, and the best result of all was found in the fact that scarcely a single case of fever occurred throughout the year among the *adults* (the syces and hospital followers) although they themselves received no quinine. During the year 1901, although the adult syces and hospital followers received a prophylactic dose of quinine, they suffered so severely from malarial fever that more than half their number were frequently incapacitated from work.

This is a very good proof that the children are really the chief source from which *anopheles* mosquitoes become infected, and that if we can get rid of the parasites in them we shall do much towards reducing the prevalence of malaria and the liability to infection in any place.

We have now briefly considered the different measures which have been recommended for the prevention of malarial fevers as well as Dr. Koch's plan of attempting to eradicate all malaria parasites, and it only remains to say that it is impossible to lay down hard and fast rules for a campaign against malaria that will be applicable to every place. Before measures in a district are undertaken, it is essential that the conditions under which malaria prevails there should be thoroughly known, *and the practicability of each measure thoroughly weighed before the campaign is begun.* If this were always done, much money would be saved and much disappointment prevented.

APPENDIX.

Methods of examination of the blood.

Any one who wishes to fully understand the life history of the malaria parasite or who desires to be able to diagnose and treat cases of malarial fever successfully, must be thoroughly familiar with the appearances assumed by the parasite in human blood. In order to acquire this knowledge it is absolutely necessary to be able to make preparations of blood for examination, and to be able to recognise the parasite in such preparations. For the sake of any student who wishes to take up the study of malaria seriously a few remarks on the methods of examining blood for malarial parasites may therefore be added. It should be noted however that no directions given in a book are of any value compared to the actual demonstration of real parasites by one who is familiar with the subject, and no student should leave college without having made it his duty to obtain such a demonstration from one of his professors.

"*It is impossible to make reliable examinations of the blood for malarial parasites without first being familiar with the ordinary appearances of normal blood and the more common pathological changes.**"

This axiom cannot be too strongly impressed upon all who enter upon the microscopic study of malaria parasites, and many pages might be filled with the errors that have been made by observers who have confused normal constituents of the blood, such as blood platelets and even leucocytes, to say nothing of such common pathological changes in the red corpuscles as vacuoles, crenations, fissures, etc., with malaria parasites.

Before commencing to study the appearances of malarial blood it is essential, therefore, for every one to make themselves familiar with the appearances of normal blood, and to be able to distinguish differences in the colour, size, and shape of the red corpuscles, and to recognise such changes in them as crenations, vacuoles, and fissures, and also to be thoroughly familiar with the different varieties of leucocytes and with the blood platelets.

For the examination of malaria parasites a good microscope with a one-twelfth inch oil-immersion objective is necessary. The blood may be examined either in the fluid state or in dried and stained preparations. The advantage of examining fluid specimens is that the living movements of the parasite and the changes that take place in it can be watched, but in stained preparations the detailed structure is more readily seen. Whenever possible both methods should be employed simultaneously and results compared. The articles required for preparing fluid specimens of blood are :—(1) Thin cover glasses, (2) glass slides, (3) a pair of forceps for holding the cover glasses, (4) alcohol, (5) a surgical needle.

The thinnest and best cover glasses and slides only should be used and they should be absolutely clean and well polished. Immediately before being used the slides and cover glasses should be rewashed in alcohol, thoroughly dried and polished with a silk cloth, and placed on a sheet of white paper under a glass

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* Lectures on the Malarial Fevers by W. S. Thayer, M.D., Professor of Medicine in the Johns Hopkins University.

tumbler in order to keep them free from dust. The palmar surface of the patient's finger tip where the prick is to be made is then thoroughly cleaned with alcohol. The prick is best made with an ordinary surgical needle. If it is made without hesitation, sharply and not too deeply, no pain will be felt by the patient; but even this simple operation requires some practice. The first drop of blood which appears should be wiped off, and before the second drop is squeezed out a cover glass should be taken up in the forceps and held ready over the finger. As soon as the second drop of blood—which should not be larger than a pin's head—appears, the centre of the cover glass is made to touch it. The drop of blood comes away on the cover glass which is then quickly laid on to one of the glass slides. If the operation has been done successfully the blood immediately spreads out in a thin film between the cover glass and the slide. A slight tap with the end of the forceps on the upper surface of the cover glass sometimes assists the blood to spread out more easily, but if the slides and cover glasses are perfectly clean this should not be necessary. After waiting a minute or two, the edge of the cover glass may be ringed with vaseline in order to prevent evaporation. The specimen will then keep good for several hours.

The preparation should first be examined with a one-sixth inch objective, and if it is a sucessful one, the red blood corpuscles in many parts of the specimen will be found to be lying flat in a single layer with their edges nearly touching each other but not overlapping, and these are the parts of the specimen to be specially examined for parasites. Nearer the edge of the cover glass the corpuscles will be found heaped up and overlapping each other. Having found a suitable field, a small drop of cedar-wood oil is placed on the cover glass and the oil-immersion lens turned on. A substage condenser and a low eyepiece must be used, and the iris diaphragm should be nearly closed so that only a moderate amount of light passes through the specimen. If the illumination is too brilliant the parasites may be easily missed.

A beginner should not at first attempt to find small unpigmented parasites; he should search for large pigmented forms, and above all he should remember (1) that the parasite must be looked for inside a red blood corpuscle, and (2) that it is a very definite organism which, if once seen, cannot well be mistaken for anything else.

On searching each corpuscle carefully the observer will presently come across one in which fine black dots of pigment are seen. On focussing carefully he will find that these dots are contained in a transparent mass of pale protoplasm which is undergoing amœboid movement inside the corpuscle. After a short time the movements will become less marked and the outline of the body will become more distinct. Careful watching will convince the observer that he is looking at a living parasite. Once having found a parasite, the beginner will know what sort of body to look for, and will easily be able to educate himself to pick out the smaller forms.

The reason why beginners make so many mistakes over malaria parasites is partly because they are not thoroughly familiar with the appearance of normal blood, and partly because they do not search in suitable cases at the commencement of their study. The majority of men who are commencing the subject expect to find parasites in the most unlikely cases,—cases with charts showing no sign of periodicity, or cases of chronic cachexia which have been drenched with quinine. Even an experienced observer would probably be unable to find parasites in such cases, and to any one who has had little or no practice in the examination of blood I would say, (1) Do not commence to search for parasites until you have found a typical case like that of chart I or chart II (page 29); and (2) Do not search in any case that has been given quinine even in small doses as this drug quickly causes the majority of the parasites to disappear from the blood.

If typical cases like those of charts I and II are not available, the following plan may be recommended. Go to a native village in the evening and take the temperatures of half a dozen children with enlarged spleens. It will almost certainly be found that at least one or two of the children have a rise of temperature, though they may be playing about apparently quite well. In return for a small present these children will allow their blood to be examined as frequently as may be desired, and the finding of parasites in their blood is generally an easy matter. Among the children of most Indian villages a greater variety of cases of pure malarial fever will in fact be encountered than are likely to be met with during many months' examination of hospital cases.

For making stained preparations dried blood films must be used. A straight surgical needle, the eye of which has been removed with a pair of forceps, and glass slides are all that are necessary for taking these films. Cover glasses are not required.

The finger is pricked and a clean glass slide is lowered on to the drop of blood that exudes so that it touches the drop about half-an-inch from one end of the slide. The slide is then held between the finger and thumb of the left hand and the shaft of the needle (which is held by the point) is placed crosswise on the slide over the drop of blood. (Fig. 3).

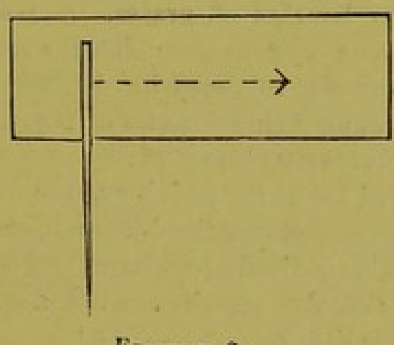

FIGURE 3.

The blood will run along the under surface of the needle which is then drawn evenly along the slide to the end, thus making a broad thin film of blood.

Films prepared in this way should be allowed to dry in the air and then fixed by immersion in absolute alcohol for half-an-hour.

It is better for the beginner to get accustomed to one stain than to attempt many different methods, and the best stain for malaria parasites is undoubtedly that recommended by Romanowsky. This is a triple stain consisting of a combination of a particular kind of Eosin and medicinal methylene blue. It can now be obtained in the form of compressed tabloids * and is therefore very convenient to use. Each tabloid should be dissolved in 10 cubic centimetres of

* From Messrs. Burroughs, Wellcome & Co., London.

pure methyl alcohol, and the stain is then ready. *If this stain is used, previous fixation of the blood films is unnecessary.* After the film has dried in the air it is covered with a few drops of the stain. Half a minute afterwards an equal quantity of *distilled* water is added to the stain, and the slide is moved about so as to thoroughly mix the water with the stain. This mixture is allowed to remain on the film for from ten to twenty minutes, and is then washed off with a gentle stream of distilled water. The slide is then allowed to dry in the air and examined. It is not necessary to cover the film with a cover-glass; the oil for the oil-immersion lens may be placed directly on the film of blood.

By this method the red blood corpuscles are stained pink and the blood platelets and the nuclei of the leucocytes a deep ruby-red.

Polynuclear leucocytes will be recognised by their large irregular nucleus. Their body protoplasm is unstained and contains fine red granules (Plate VII, Fig. 11).

Large mononuclear leucocytes have generally a large oval or horse-shoe shaped nucleus and faintly blue stained body protoplasm which is free from granules. *They may contain grains of intensely black malarial pigment (melanin) which should be carefully looked for as they are a sign of recent infection* (Plate VII, Fig. 12).

Lymphocytes have a round, ruby-red nucleus surrounded by a thin rim of blue stained protoplasm.

Eosinophile leucocytes have generally two pear-shaped nuclei joined together at the top, and numerous large, round, red granules scattered through the cell, which make them very easily recognisable.

The blood platelets are deep ruby-red, and will generally be found in groups looking something like bunches of grapes. A few are seen in Plate VII, Fig. 11. Many beginners mistake them for the spores of malaria parasites. Malaria parasites are very easy to detect in the red blood corpuscles by this method of staining. Young "ring" forms of the parasite in the red blood corpuscles present the following characters :—

(1) A brilliant red dot at the periphery, (the nucleolus of the parasite) ;
(2) A clear space almost unstained (the nucleus of the parasite) ;
(3) A circle of blue stained protoplasm surrounding the clear nucleus (the body of the parasite). Such a parasite is represented in Plate VII, Fig. 8.

Larger forms of the parasite present the same characters, *viz.*:—

(1) One or more red patches of chromatin ;
(2) A clear space ;
(3) A large blue stained body, in which grains of black pigment can be plainly seen (Plate VII, Fig. 1).

The red corpuscles containing parasites may be variously altered. In simple Tertian infections, for example, the corpuscles containing parasites may be swollen to more than double their original size, and with this stain they may be infiltrated with red stained dots to such an extent that the parasite itself is almost hidden (Plate VII, Fig. 2). When corpuscles studded with these red dots are seen, we may be sure that the case is one of an infection with simple Tertian parasites. When the parasites have arrived at the segmenting stage it will be seen that the patches of chromatin have divided up into a number of parts, each of which represents a "spore." A thin rim of corpuscle may still be seen round the group of red stained spores, and near the centre of the group a mass of black pigment will be collected. (Plate VII, Figs. 3, 4, and 7.)

The sexual forms of simple Tertian and Quartan fevers are difficult to distinguish in stained specimens from the full grown asexual forms, but the sexual forms of malignant Tertian fever, *viz.*—"Crescents," will be very easily recognised from their characteristic shape and from the grains of pigment collected at their centre. They are stained light blue with Romanowsky's stain, and near their centre, partly hidden by the pigment, a mass of red stained chromatin will be seen. (Plate VII, Figs. 10 and 11.)

Having learnt to find and recognise parasites the student will next desire to know how to distinguish the three forms, simple Tertian, Quartan, and malignant Tertian from each other. In the very young stage before the parasites have acquired pigment, this is a difficult matter, but in later stages it is comparatively easy. At a microscopical examination the points of distinction depend on the following observations :—(1) The stages of the parasite which are found in the peripheral (finger) blood ; (2) The effect of the parasites on the red blood corpuscles containing them ; (3) The character of the amœboid movements of the parasite ; (4) The number of spores into which the parasite divides up ; (5) The character of the sexual forms. (6) The character of the pigment seen in the parasite.

The differences in the three species of parasite in the above respects may be tabulated as follow : —

Species of parasite.	Stages found in the peripheral (finger) blood.	Effect of the parasites on the red blood corpuscles containing them.	Character of the amœboid movements of the parasite.	Number and arrangement of spores.	Character of the sexual forms.	Character of the pigment.
Quartan .	All stages .	The corpuscle is practically unaltered.	Very sluggish so that the parasite is generally oval or more or less rectangular.	8-10. Arranged with great regularity "like a daisy."	Round. Rarely seen.	Coarse black grains.
Benign Tertian.	All stages .	The corpuscle is very much swollen and decolourised.	Very active so that the parasite is irregular in shape.	20-23. Not so regularly arranged.	Round .	Fine brown granules or rods.
Malignant Tertian.	Only young "ring" forms and crescents. Very rarely an occasional segmenting form.	The corpuscle is generally shrunken and decolourised. Never swollen.	Very active and with a great tendency to assume the ring form.	9-10. The segmenting form only occupies about ⅓—½ of the red corpuscle.	Crescent shaped.	Fine brown granules or rods.

From the point of view of diagnosis by a microscopical examination the following hints may be useful.

If in a film we find a "crescent" (Pl. VII, Figs. 10 and 11), we know at once that we are dealing with a case of malignant Tertian fever.

If, at different examinations of the same case, we find nothing but small ring forms (Pl. VII, Fig. 8), no large forms being present, the case is also probably one of malignant Tertian. Small rings and crescents are characteristic of malignant Tertian infections.

If we find a large irregularly shaped parasite in a corpuscle which is distinctly larger than the surrounding ones (Pl. VII, Figs. 1 and 2), we may be sure that this is a simple Tertian parasite.

If we find regularly oval or rectangular parasites in corpuscles which are practically unaltered in size and colour (Pl. VII, Fig. 6), these are probably Quartan parasites.

If in a film stained by Romanowsky's method we find red corpuscles swollen and studded with red dots (Plate VII, Fig. 2), we may be sure that the case is one of simple Tertian infection. This stippling of swollen cells does not occur in Quartan or malignant Tertian infection.

The differences in the segmenting forms are well shown in Plate VII.*

Figure 7 is a pre-segmenting Quartan parasite. The different spores have not quite separated from each other, but it is seen that they are eight in number and that they completely fill the corpuscle which, however, is practically unaltered in shape and size.

Figure 3 is a segmenting benign Tertian parasite. The cell containing the parasite is much swollen and decolourised.

Figure 4 is a completely segmented benign Tertian parasite which has escaped from the red cell. About twenty-one spores can be counted and the round block of black pigment is plainly seen.

Figure 9 is a segmenting malignant Tertian parasite. These are very rarely seen in finger blood. It only occupies about one-half of the red corpuscle which, if anything, is smaller than the surrounding ones.

In examining blood films, two other blood parasites which have no connection with malaria but which sometimes occur in man, should be looked for, as, in the absence of malaria parasites, their presence may afford a clue as to the nature of the case. These parasites are, "Filariæ" and "Trypanosomatta," and in order to give an idea of their appearance in blood films I have added photographs of these important parasites (Plate VIII, Figs. 5 and 6). As is no doubt well known, the presence of filarial embryos in the blood is associated with such diseases as elephantiasis, chyluria, lymph scrotum, etc., and the presence of one species of trypanosome in animals is the cause of "Surra." A species of trypanosome has lately been found in the blood of man in Africa, though it has not yet been discovered in human blood in India.

Any student who desires to study practically the stages of the malaria parasite in mosquitoes will find the methods for doing so described by the present writer in the Scientific Memoirs of officers of the Medical and Sanitary Departments of the Government of India, new series No. 2. "Malaria in India," which may be obtained from the Superintendent of Government Printing, 8, Hastings Street, Calcutta, or from Messrs. Thacker, Spink & Co., Calcutta. (Price Rs. 1-8.)

* The photographs have lost much of their distinctness in the process of reproduction.

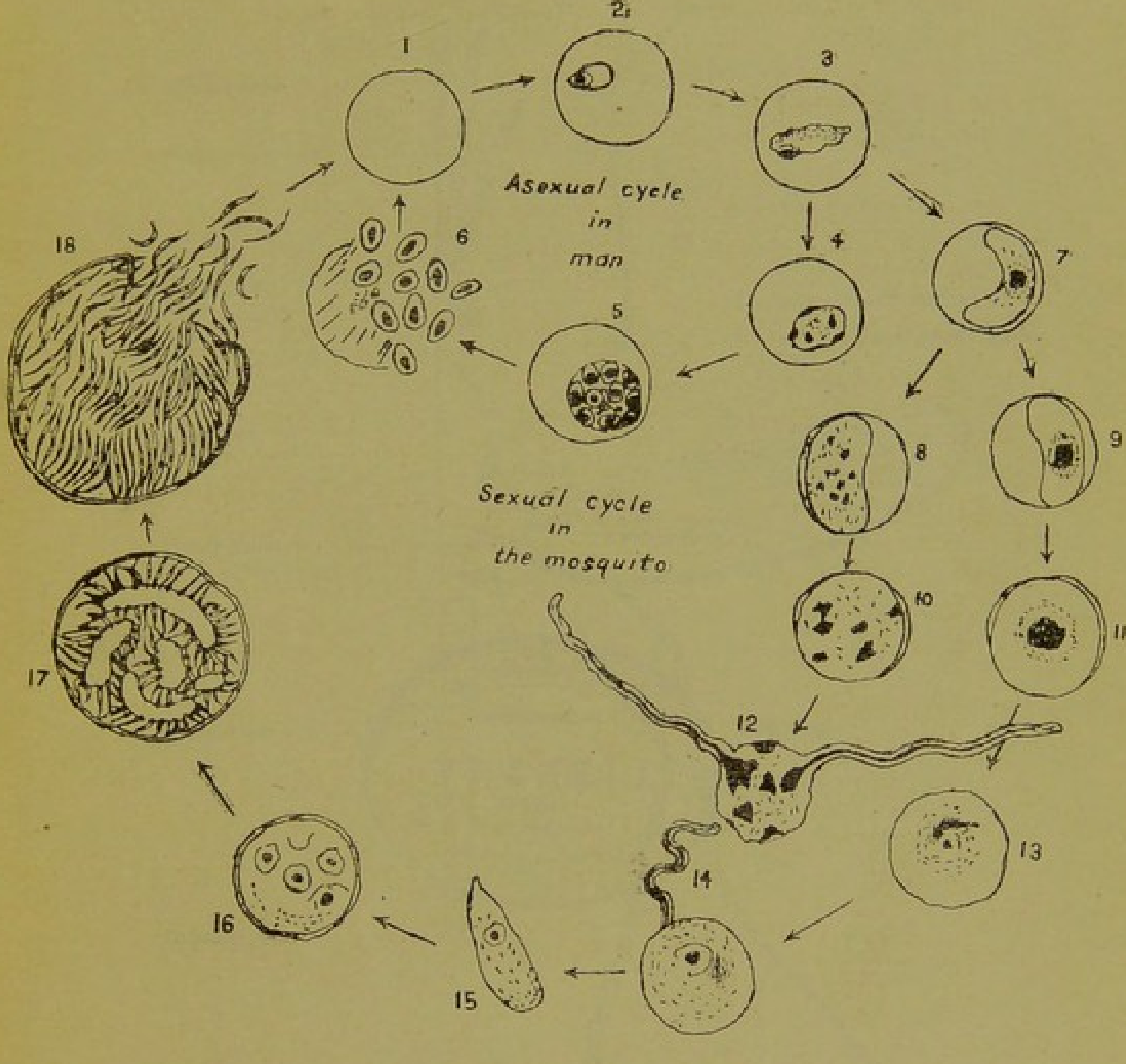

PLATE I.

1. Normal red blood corpuscle. 2. Red corpuscle containing malignant Tertian parasite. 3. Larger form of the same parasite containing pigment in short rods. 4. 5. Segmentation of the parasite. 6. The spores have escaped from the red cell and are free in the plasma. 7. A young sexual form (crescent) developed from a similar parasite to 3. 8. Male sexual form. 9. Female sexual form. 10. 11. Further development of these forms. The remains of the red blood corpuscle still surround them. 12. Free male form which has developed "flagella". 13. Free female form. 14. Fertilization of the female by a flagellum. 15. Travelling vermicule. 16. 17. Zygotes in the stomach wall of the mosquito. 18. The sporozoites fully developed have burst from the zygote.

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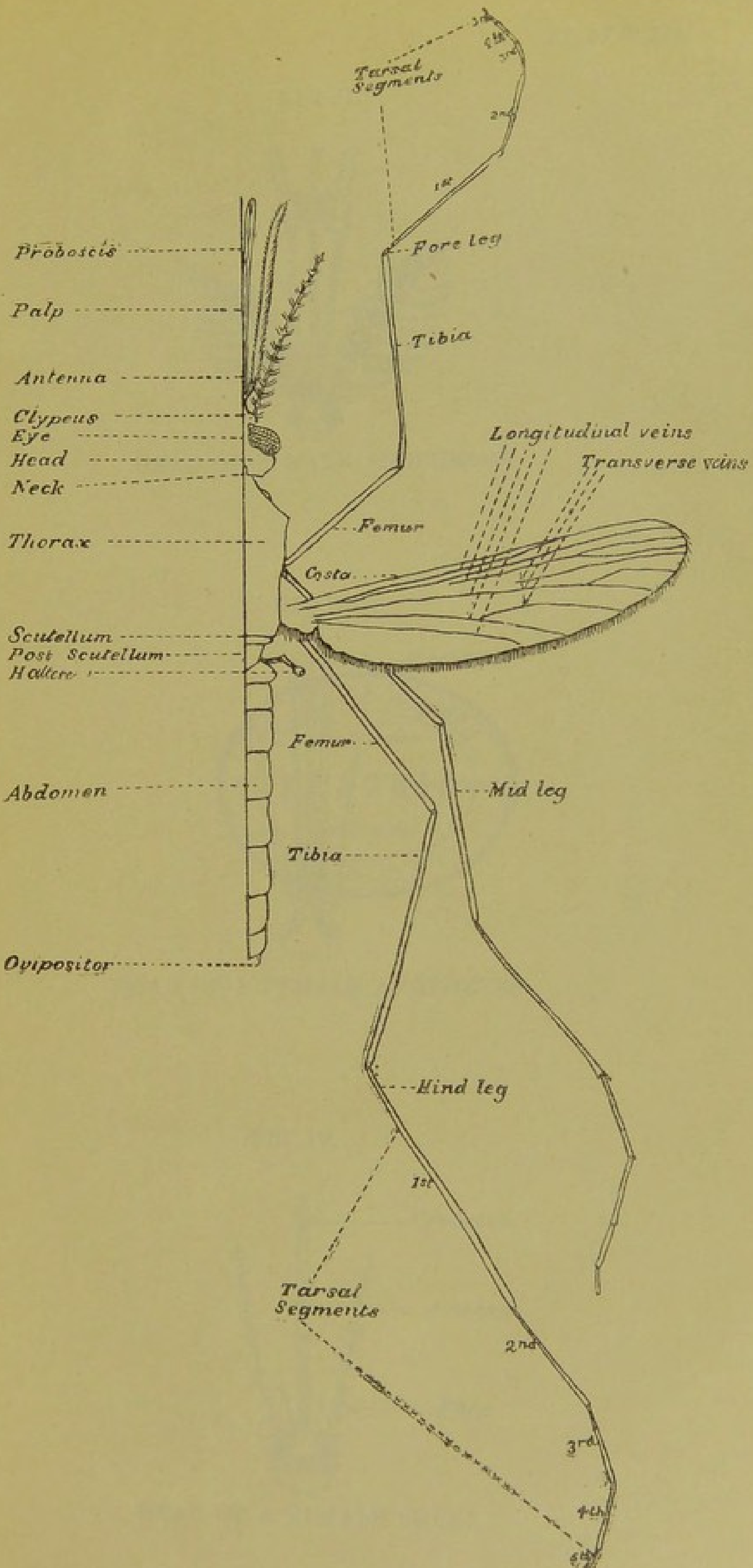

DIAGRAM OF A FEMALE ANOPHELES.

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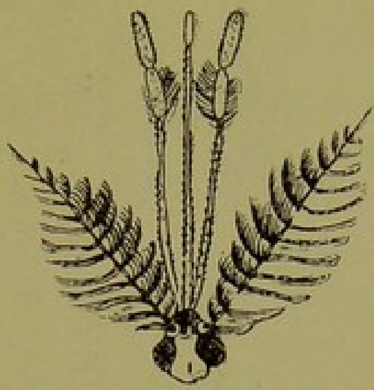
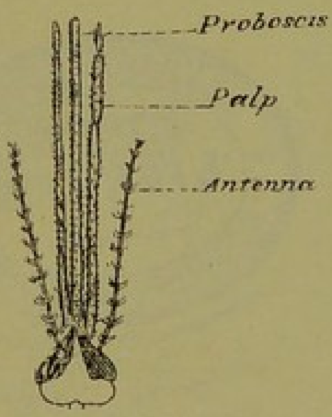
FIG II.



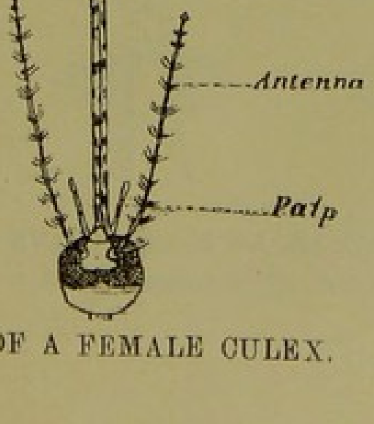
HEAD OF A MALE ANOPHELES.

FIG III



HEAD OF A FEMALE ANOPHELES.

FIG IV.



HEAD OF A FEMALE CULEX.

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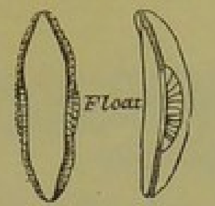
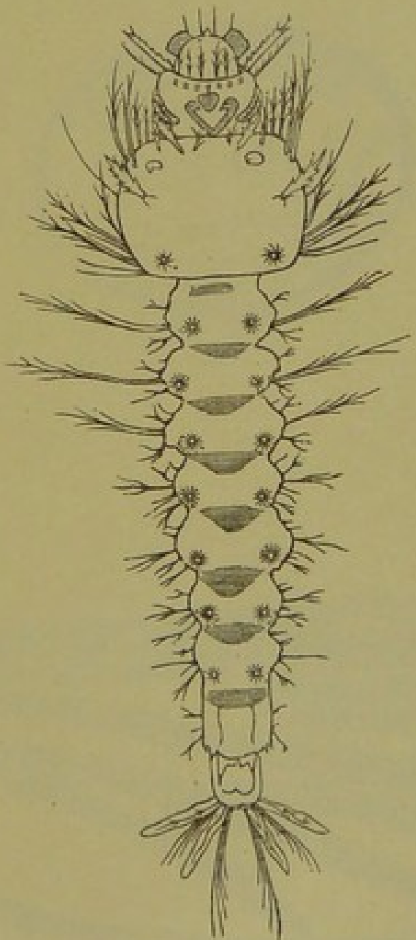
EGG OF ANOPHELES



a Front view b Side view



A FULL GROWN LARVA OF ANOPHELES CULICIFACIES

[*Drawn by S. R. Christophers M. B.* (*Vict.*)]

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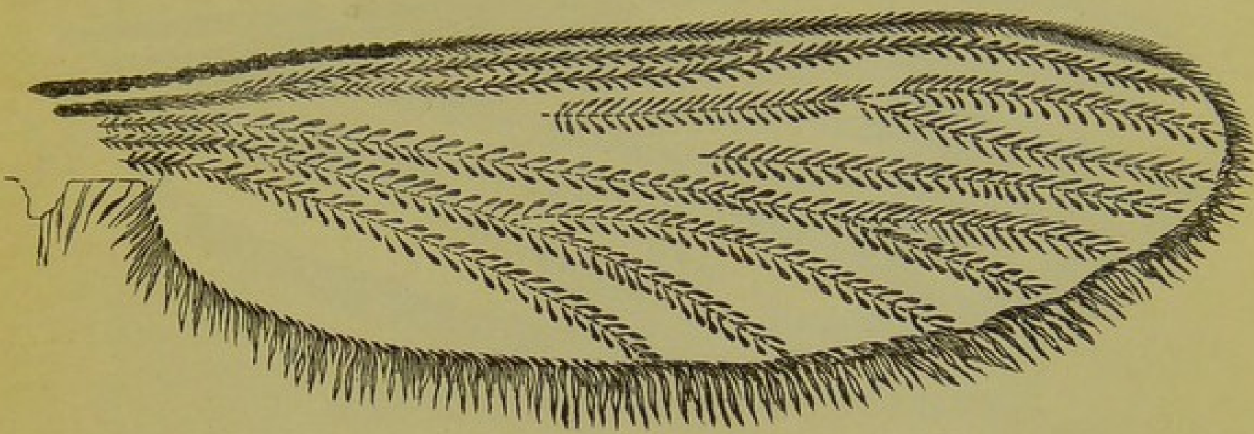
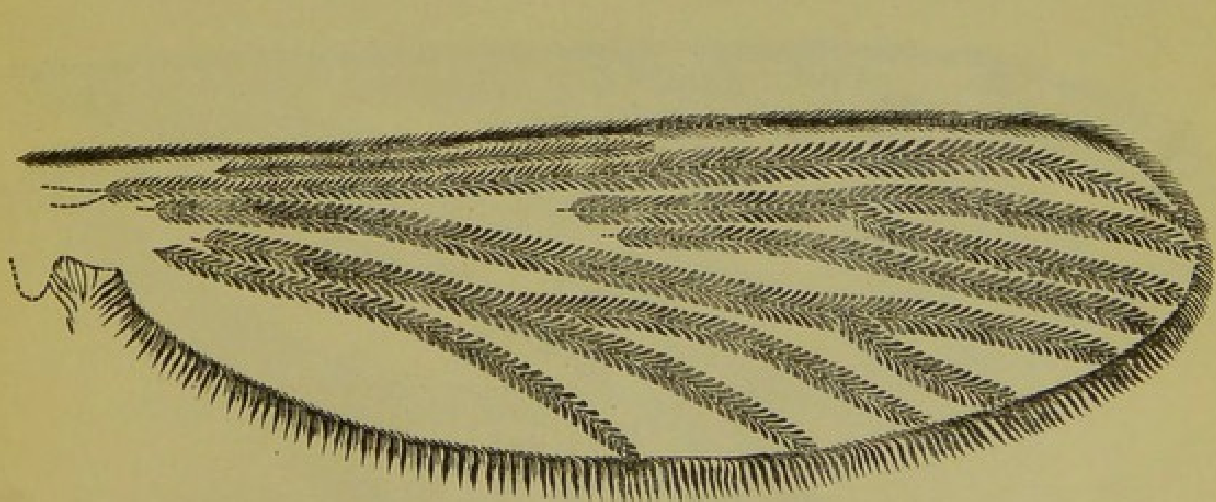


WING OF ANOPHELES CULICIFACIES (GILES)



WING OF ANOPHELES ROSSI

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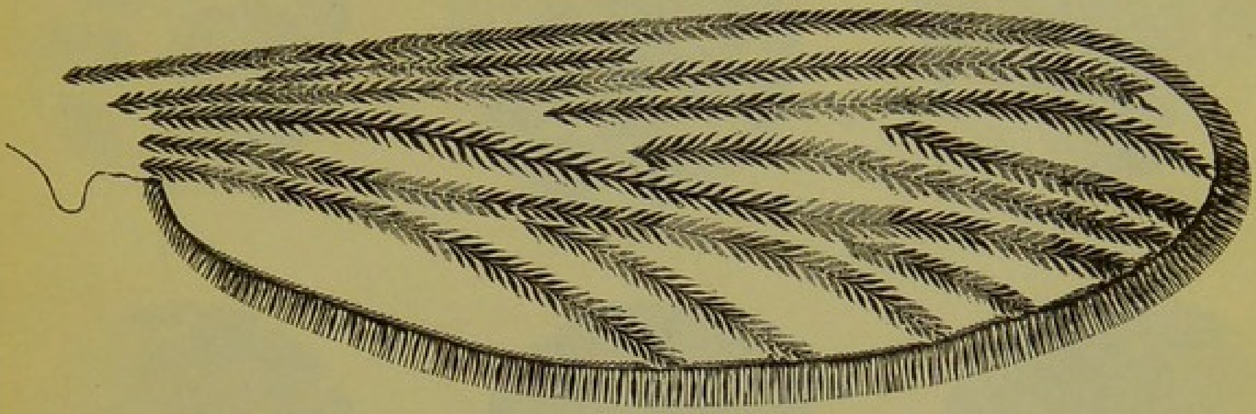
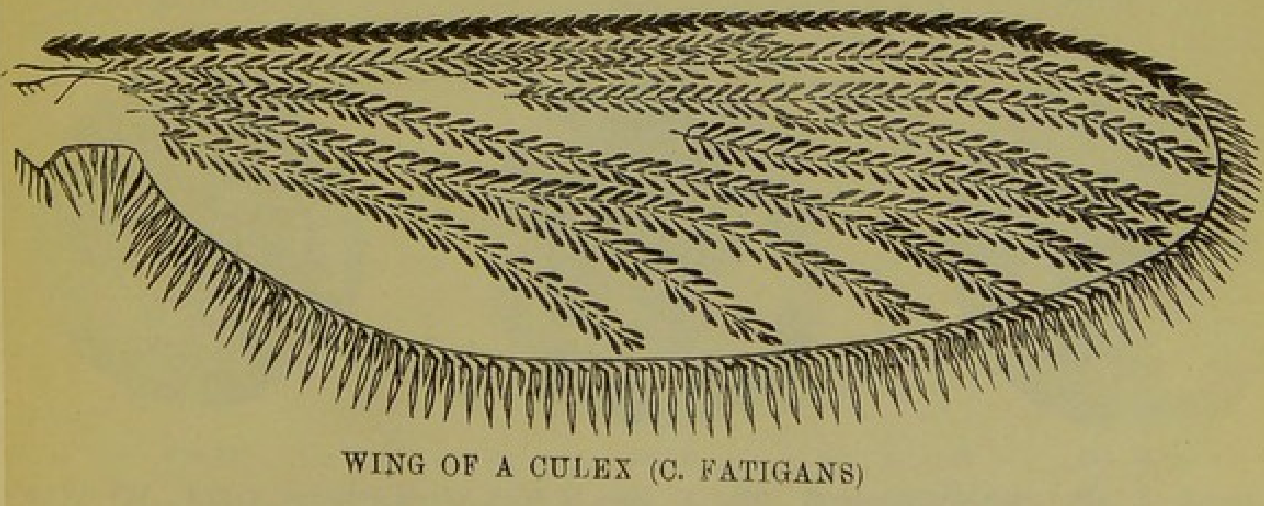


WING OF ANOPHELES JAMESI (THEOBALD)



WING OF A CULEX (C. FATIGANS)

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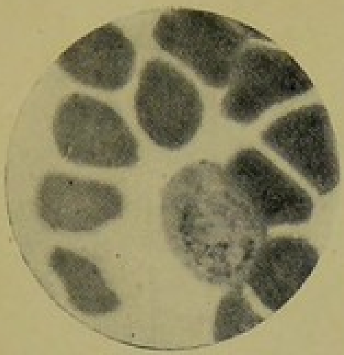

FIG. 1.

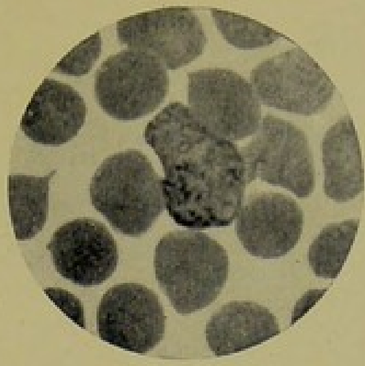

FIG. 2.

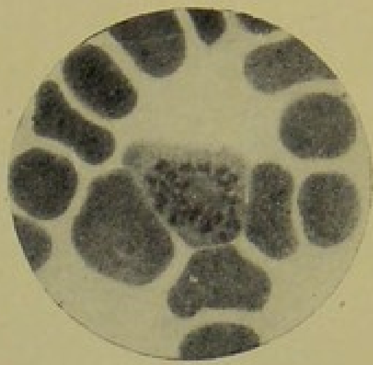

FIG. 3.

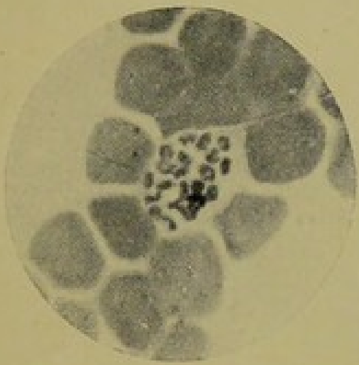

FIG. 4.

FIG. 5.

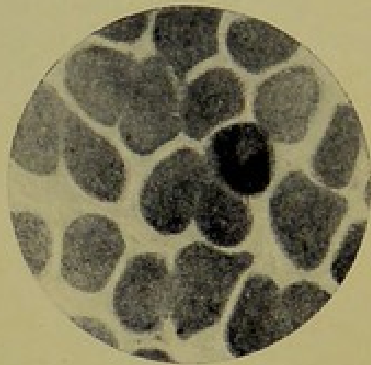

FIG. 6.

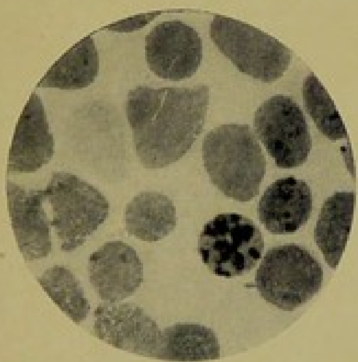

FIG. 7.

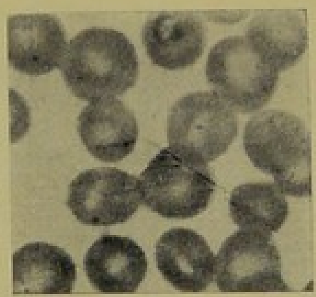

FIG. 8.

FIG. 9.

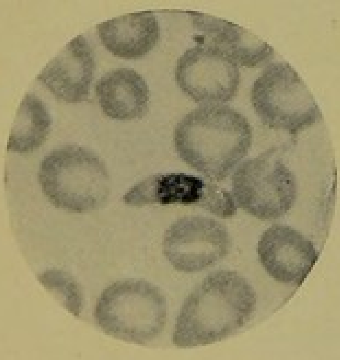

FIG. 10.

FIG 11

FIG. 12.

PLATE VII. Malaria parasites in the blood of man. X 1,000. Romanowsky's stain. *Fig. 1.*—Nearly full grown *Benign Tertian* parasite. The red corpuscle containing it is swollen and decolourised ; *Fig. 2.*—A similar parasite almost hidden by the stippling of the cell ; *Figs. 3 & 4.*—Segmenting stages of *Benign Tertian* parasite ; *Fig. 5.*—Sexual form of *Benign Tertian* parasite ; *Fig. 6.*—Nearly full grown *Quartan* parasite ; *Fig. 7.*—Segmenting stage of *Quartan* parasite ; *Fig. 8.*—Ring form of *Malignant Tertian* parasite ; *Fig. 9.*—Pre-segmenting stage of *Malignant Tertian* parasite ; *Figs. 10 & 11.*—Crescents (sexual forms of *Malignant Tertian* parasite). In Fig. 11, a polynuclear leucocyte and a few blood-platelets are also seen ; *Fig. 12.*—A "large mononuclear" leucocyte containing blocks of malarial pigment (melanin).

Microphotographs by Dr. C. Caleb, from the Author's preparations.

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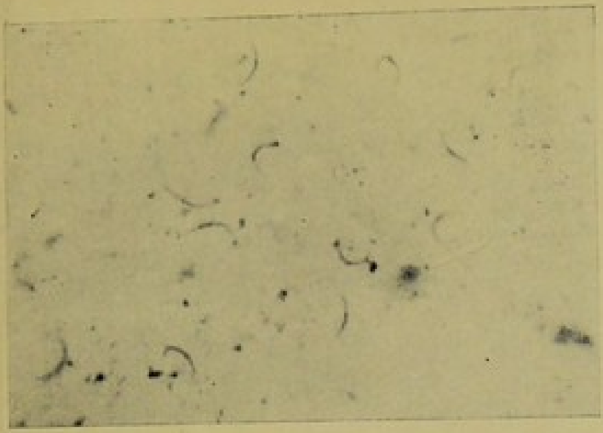

FIG. 4.

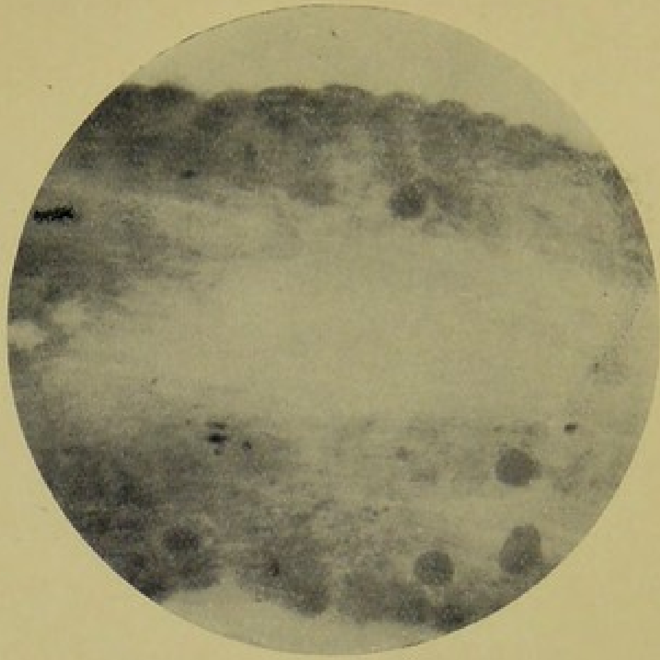

FIG. 2.

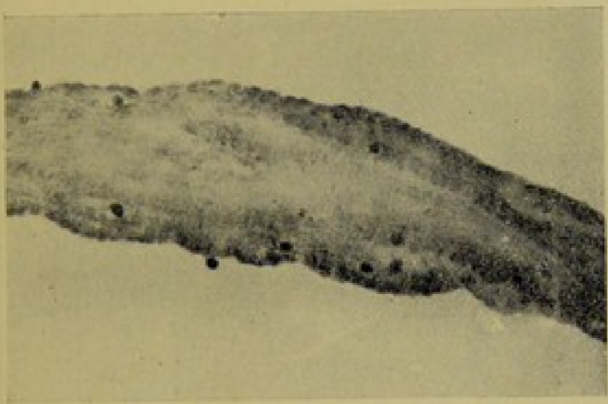

FIG. 1.

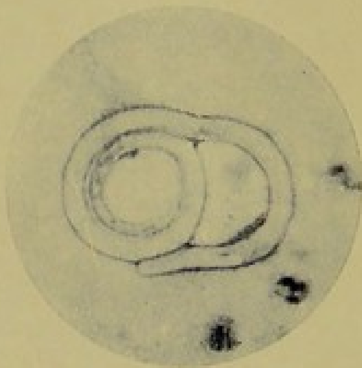

FIG. 5.

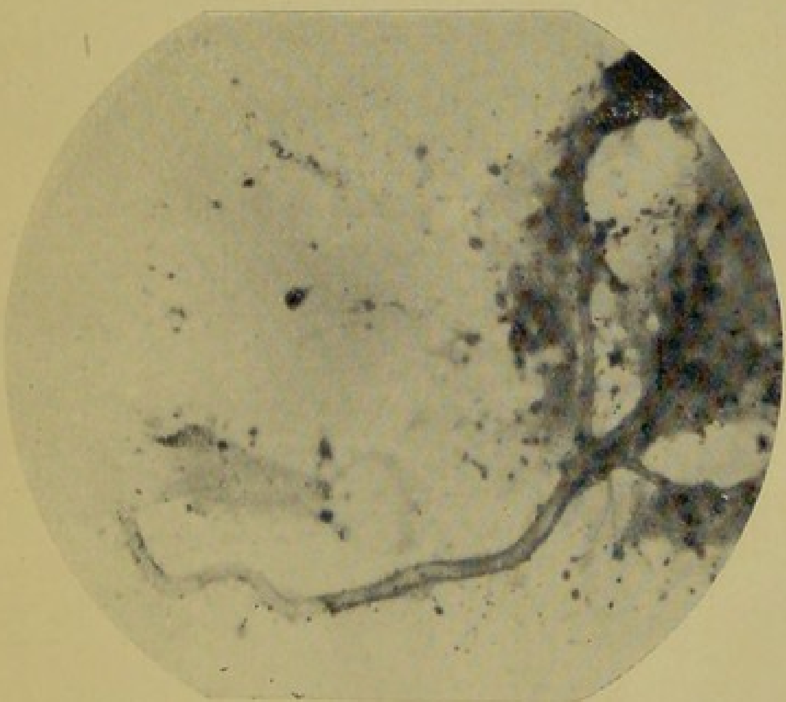

FIG 3.

FIG. 6.

PLATE VIII. *Fig. 1.*—Stomach of a mosquito showing "zygotes" × 60; *Fig. 2.*—The same × 300 showing five zygotes; *Fig. 3.*—The salivary gland and duct of an *Anopheles* as it appears when dried and stained. The sporozoites which were present in this preparation are not apparent in the reproduction; *Fig. 4.*—Sporozoites from the salivary gland of an *Anopheles*, dried and stained × about 700; *Figs. 5 & 6.*—Other parasites sometimes present in the blood of man; *Fig. 5.*—An embryo of "Filaria Sanguinis Hominis Nocturna"; *Fig. 6.*—The parasite of "Surra."

Microphotographs by Dr. C. Caleb, from the Author's preparations.

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