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THE INCIDENCE, PREVENTION and TREATMENT OF MALARIA IN INDIA.

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I. Introduction

In India not less than one million deaths annually are due to Malaria, and cases of sickness from this cause alone amount to a hundred millions per annum. It has been estimated that such figures imply an annual unproductive expenditure of £17,000,000 to £20,000,000, by reason of loss of wages, expenditure during sickness, and concomitant circumstances.(i) The vitality of the nation is sapped by the scourge, and, though local antimalarial measures have reduced the incidence in certain districts and among selected communities, there are no signs of a general decrease of the numbers affected by the disease, and India still remains the most malarious country in the world.(2)

A sojourn in India of several years' duration, associated with medical duties in war and in peace, in cantonment and in jungle, in civil and in military employ, afforded opportunities of making special observations on the incidence of the disease in different localities and under varying conditions, and on the measures adopted for prophylaxis and treatment.

Firstly, a period was spent in cantonments in Peshawar, in the North West Frontier Province. Though comparatively free from malaria for nine

months of the year, in the late summer and autumn malignant tertian infections abound, and the lower temperatures recorded during the winter months tend to cause relapses of latent infections. Irrigation of a stiff, retentive soil, as was pointed out by Dempster as long ago as 1845,[3] is still the main cause of the high endemicity of the disease.

A punitive expedition against a refractory Frontier tribe, conducted in the height of the malaria season, and the high incidence of the more severe forms of the disease afforded an opportunity of studying the problems involved, and suggested measures which might be adopted to lessen the number of casualties from "fever" in similar circumstances. Among other points, the inadvisability of making long marches in the heat of a tropical day, and the dangers of camping in close proximity to infected native villages were two that were emphasized.

A further period of active service, this time in Palestine, afforded an interesting comparison of the antimalarial measures employed in the two countries under active service conditions. The absence of native population, the enthusiasm of the medical officers, many with Macedonian experience, and the ease with which large parties of men could be obtained for minor or major measures, rendered malaria prevention comparatively easy at the stage of the campaign

during which the writer was with the Egyptian Expeditionary Force.

After weathering the storm of aestivo-autumnal infection in Peshawar and the hardships of the hot weather Frontier campaign, the writer fell a victim to benign tertian infection, contracted on the banks of the watercourse known as the Wadi Ghuzzeh, in the brackish pools of which larvae of A. Turkhudi were found. In the absence of an infected native population it was considered that these anopheles became infected by the Eygptian ambulance drivers, or by troops transferred from Macedonia.

A return to India in a civil capacity with sanitary inspection and medical control of a large number of railway communities, scattered over a large area, embracing portions of Rajputana, the Punjab, the United Provinces, and Central India, gave further opportunities for observation and research. The incidence of malaria in these communities varied very much with the district in which they were situated. In Eastern Rajputana the endemicity was low, and the predominant type was benign tertian. The porous nature of the soil, the moderate rainfall, the absence of extensive irrigation, and the scattered population accounted for the low incidence. Eastern Punjab was also an area of low endemicity for the same reasons, though there were small foci of higher endemicity. A heavily populated wheat and

rice growing area, comprising the extreme East of Rajputana, the South of the Punjab, and the West of the United Provinces, had moderately severe endemic malaria, but was liable to fulminant epidemics. A factor in the spread of malaria in India which is not often mentioned is the number of the native population who travel by rail. It is estimated that the Indian railways carry the large number of 62 million passengers annually. Many of these are pilgrims and come from places where the endemicity of malaria is high, and it can easily be imagined how a new type of malaria can be introduced or a non-malarious locality become malarious by the halt of some hundreds of these travellers at a wayside station under conditions favourable for infection of the local anopheles.

Lastly, a return to military employment and the medical command of several stations in the area known as the Malakand, which lies to the North of Peshawar, enabled further points to be noted.

In one station the incidence of malaria closely resembled that of Peshawar, in another the altitude and the rocky nature of the soil rendered infection less common, in a third the situation on the banks of the Swat river, the proximity of flooded land under cultivation, and presence of suitable anopheles formed ideal conditions for the spread of the malarial

infection. The effect of moving a body of non-immune troops into the latter area was exemplified by the disease assuming epidemic proportions and an entire garrison being hors de combat, so far as strenuous fatigues or tactical exercises were concerned.

As a result of the experiences of the writer in these different parts of India, and under different conditions, some insight has been gained into the malarial problem of that country. It is intended in this thesis to discuss the incidence, prophylaxis and treatment of malaria in India, to record the observations made, and to suggest measures which might be helpful in combatting the disease.

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2. Historical Outline

Malaria has been in existence since the infancy of the human race. There is evidence that the ancient Egyptians had some knowledge of the disease, and in Greece and Italy it has been known to exist for more than 2000 years. Investigation of the disease, carried on through the centuries, culminated in the discovery by Laveran of the parasites in the blood. Rational treatment commenced with the introduction of Cinchona; and scientific prophylaxis dated from the immortal discovery of Ross that the mosquito was the vector of the disease.

Firstly, the disease was recognised and divided into its different forms, then the advent of the microscope and the institution of microscopic examination of the blood led to the discovery of its parasitic nature.

Hippocrates, among Greek writers, in the fifth century B.C. differentiated malaria from the continuous fevers and described quotidian, tertian and quartan varieties of the disease. Celsus, in the first century A.D., described practically all the forms of malaria fever recognised to-day, including two types of tertian fever; and many other Roman writers have mentioned the disease and associated it with marshy ground. Little was added to the knowledge of the disease until the introduction in 1640, of

Cinchona. Following this, Morton, in 1697, was able to separate those fevers which were cured by it from those which were not, and thus instituted a method of diagnosis of malaria which is still employed. Lancisi in 1717, described the eteological connection between marshy ground and malaria, and studied mosquitoes as a possible cause of the disease, but came to the conclusion that the drinking water was contaminated by their larvae. Sydenham, in 1723, accurately described malarial fevers, and ably defended cinchona, upon the use of which there was much controversy at this time. Torti, in 1753, wrote an exhaustive treatise on the various forms of malaria, and his description of the pernicious forms is often quoted at the present day.

The malaria parasites themselves were observed by several investigators, such as Virchow and Meckel, but none realised their significance, and their role in the etiology of the disease until Laveran, in 1880 discovered that he was dealing with a living parasite of the human red corpuscle. Using a 1/6 inch dry lens he observed the gametes in the blood; and, though he did not know the nature of the phenomenon at the time, he detected micro-gametes issuing from the male cell. It was not till 1898 that it was demonstrated by W. G. MacCallum that these microgametes or flagellae represented male sexual elements analogous to spermatozoa. Following the lead given by Laveran's discovery, numerous other investigations were made which

advanced our knowledge of the disease. In 1884, C. Gerhardt proved that healthy persons can be inoculated by injection of the blood of paludic patients. C. Golgi, of Pavia, in 1886 discovered that the parasites reproduce by spontaneous sporulation, that febrile paroxysms occur when the spores are liberated, and that a morphological difference existed between the parasites of mild tertian and quartan fever. A little later Marchiafava and Celli differentiated the subtertian parasite from the other two, and showed that in this form of the disease sporulation is seldom observed in the peripheral blood.

The theory that mosquitoes were agents in the spread of malaria was advanced by many, but notably by Koch and Laveran in 1884, by Manson in 1894 and by Bignami in 1896. To Manson belongs the credit of regarding the exflagellation of the parasite as a preparation for an extracorporeal existence. Inspired by his views Ross, in 1898, after more than two years of persistent searching, found pigmented bodies in the stomach wall of a dapple-winged mosquito which had been fed on a malaria patient. He confirmed his discovery by experiments with the proteosoma of birds, a parasite nearly allied to that of man, and traced all the stages of the sexual cycle. Others were not slow in following up this epoch-making discovery. In Italy, Grassi, Bignami and Celli traced the corresponding stages of development of the human parasite,

which circumstances alone had prevented Ross from doing. Additional observations in confirmation were made by Koch, Daniels, Stephens, Cristophers and others. Finally, Manson performed the classical experiment, in which his son, P. Thurburn Manson, was bitten by anopheline mosquitoes infected in Italy with benign tertian malaria, subsequently developed typical malaria, and placed the truth of the mosquito malaria theory beyond doubt.

Such is an outline of the series of observations and discoveries, the most outstanding of which are those of Laveran and Ross, leading to our present almost complete knowledge of the disease. Further details are added from time to time, and the treatment of cases of general paralysis by malaria has led to further facts being elucidated, and has opened a wide field for experimental research.

The introduction of Cinchona into Europe in the year 1640 is a great landmark in the history of Malaria. The efficacy of the bark of cinchona was first known to the Indians in the region of Loxa, Ecuador, and when the wife of the viceregent of Peru, Countess del Cinchon, fell ill with intermittent fever, this local remedy was tried with success by the court physician, Juan del Vego. As a result of this the bark was introduced into Spain on the return of the Viceroy from Peru in 1640. Here it was employed mainly by the Jesuits, hence the name "Jesuits Bark," and they took it to Rome in 1649. Introduced into

England in 1671 by Sir Robert Talbot, an eminent quack, who is reputed to have cured Louis XIV of France by the remedy, the drug met with a mixed reception. It was used by Morton in 1697, and Lancisi was a strong supporter of it. • In 1714 Ramazzini wrote that should a patient die of fever it was a crime not to have used Cinchona. Pelletier and Caventou isolated the alkaloid quinine from the bark in 1820, and since then a number of alkaloids have been isolated, the most important of which are, quinidine, cinchonine, and cinchonidine. The institution of quinine plantations in Java in 1854, in Ceylon in 1859, and in India a year or two later caused a drop in the price of quinine, which was formerly worth its weight in gold. Steps are now being taken to make India self-supporting in the supply of quinine by steadily increasing the areas under cultivation in that country.

In India, Malaria has been in existence in all probability, for as long as in other parts of the world. Ancient Hindoo writers describe the remittent and intermittent fevers, and the "fevers" mentioned in the Charaka Samhita are most probably malarial[4]. It is stated that Susruta, an ancient Sinhalese writer who lived more than 1400 years ago, connected fever with mosquitoes. Though he may have been referring to the irritation caused by their stings, rather than to a mosquito theory of

etiology, the fact remains that he was describing malarial fever.(5) With the exception of the appreciation of the necessity for drainage in malarious areas, little was known of the nature of the infection. As in Europe small headway was made until the introduction of Cinchona. It was first used by Dr. Bogue in Calcutta in the malaria epidemic of 1657. It appears to have met with a better reception there than in Europe at first, and about 1760 James Lind and John Clark established a treatment by Cinchona nearly as effective as that of to-day. There are records of 500 cases being treated by this means with only two deaths. However, in 1804 Dr. James Johnson went out to India for a few weeks, and on the basis of his experience wrote a treatise on tropical diseases which remained the standard text book for nearly forty years. He taught that it was dangerous to give Cinchona during fever and recommended large doses of calomel, pushed till salivation was produced. This treatment was universally and enthusiastically accepted, and in one hospital alone 13,300 grains of calomel were used in a month. The mortality was appalling; and in 1837 a doctor is reputed to have been turned out of Bombay for publishing the results of the mercurial treatment. In 1847, Dr. Hare found the writings of Lind and Clark and recommenced Cinchona treatment, with the result that the fever mortality

fell at once and the position of Cinchona has never since been assailed.(6)

The alkaloid quinine was introduced into Bombay in 1826. The determination of the amount of endemic malaria by estimation of the spleen rate, or splenic index, lies to the credit of Surgeon Major D.Dempster I.M.S., who studied the problem in the United Provinces about the year 1846. It was he also who pointed out that the chief cause of the malaria in India was the presence of countless numbers of infected indigenous children. It was Vandyke Carter in India who alone of British observers appreciated the importance of Laveran's discovery.(7) In the years that followed important antimalarial work, chiefly of the nature of drainage and sanitary measures generally, was carried out through the instigation of a succession of British medical officers, among whom may be mentioned Sir Joseph Fahrer, Sir Leonard Rogers, and Sir Patrick Hehir. It was in May 1895 that Ross commenced his efforts to solve the malaria carrier problem. Working at Bangalore he attempted to infect mosquitoes with the blood of malaria patients. Though exflagellation could be observed in the mosquito's stomach the cycle could not be followed further. The mosquitoes employed were all culicinae of the sub-orders culex and stegomyia, so the results were uniformly negative. However, at last, while in Secunderabad, after more

than two years continuous research, he observed the zygotes of the parasites of malaria in the mid-gut of two large dapple-winged mosquitoes, which had been bred from larvae, and fed on a malaria patient with crescents in his blood. Owing to circumstances he was obliged to follow out the life history of the parasite in culices infected from birds whose blood harboured the plasmodium danilevski, and his efforts were triumphant at last.(8) In 1901 J.W.W. Stephens and S.R. Cristophers went to India and made further investigations of the life history and habits of the anophelines, and of the endemicity of the disease. In 1902, an experimental antimalaria campaign was conducted at Mian Mir in the Punjab, on the lines suggested by Ross after his first visit to Sierra Leone. Though the results of this campaign were reported on unfavourably by S.P. James, in 1903 and S.R. Cristophers, in 1904, and the possibility of mosquito reduction in India ridiculed, Ross points out that the conditions in that cantonment were not suitable for such an experiment, and the manner in which the campaign was carried out was unsatisfactory. In 1910 C.A. Bentley published a report on Bombay, incriminating A. Stephensi as the local carrier of the disease, and suggesting a campaign by strict legislation against house holders and property owners in that city. Since that time Bentley has done important work in Bengal. A laboratory for malaria

research has been instituted at Kasauli and anti-malarial measures are now undertaken by the provincial governments. Prior to the great discovery of Ross various hypotheses of the etiology of malaria were advanced. In marshy districts Paludic miasmata, or infecting emanations from the marsh, were supposed to be the causal agent; in places where no marsh existed telluric miasmata, or the emanations from humid or newly disturbed soil were held responsible; and in one place, Hong Kong, the prevalence of malaria was supposed to be due to the emanations from decaying granite. The only known method of prophylaxis was by the limitation of irrigation and by drainage. Ross put malaria prophylaxis on a scientific basis, and soon after the publication of the results of his investigations and of the antimosquito measures he recommended, an immense amount of antimalarial work was performed in all the malarious parts of the world. In some quarters reliance was placed on quininisation, and antimosquito measures were given a secondary place; in others the principles of Ross were followed more closely.

The immense value of prophylaxis, and, particularly, of a steady and persistent anti-mosquito campaign was exemplified by the work of Col. Gorgas, in Panama. By his efforts an engineering feat, which had been considered impossible owing to the ravages of disease, was carried to a successful conclusion. The deaths

among employees in the Panama Canal zone fell from a maximum of 11·59 per 1000 in November 1906, to 1·23 per 1000 in December 1909, and what was considered a white man's grave became as healthy as New York.(9)

Ross's own campaign in Ismailiah, though small in comparison to the others, was an unqualified success. It is an example of what scientific prophylaxis and attention to detail can do. This township was comparatively healthy prior to being supplied with fresh water by a newly constructed canal from the Nile in the year 1877. In that same year 300 cases of malaria occurred, and the numbers rose steadily to a maximum of 2500 in 1891. In the latter end of 1902 antimalarial measures were commenced, and in 1903 the number of cases fell to 214, while from 1905 to 1908 there were no fresh cases.(10) This striking result was brought about by anti-mosquito measures alone. A visit to this town in 1918 satisfied the writer that so complete an eradication of the disease in so short a period must have entailed a high degree of efficiency both in the measures adopted, and in the manner in which they were carried out. In Port Said E.H. Ross conducted an anti-mosquito campaign, and in Cairo H.C. Ross did much to reduce the incidence of the disease.(11) In Havana the efforts of the American Army Medical Corps practically stamped out malaria.(12) The brothers Etienne and Edmond Sergent conducted a campaign on similar lines in Algeria.

Among other measures they instituted the measure of conducting water by two channels, each being used for a week only, and the other being allowed to dry up, thus ensuring that any larvae present in the water were killed by dessication. They also advised curative quinine for chronic cases, and considered that the soundest method of making a region healthy.(13)

In Italy, Professor Angelo Celli conducted an antimalarial crusade. After an attempt at the Herculean task of the extermination of mosquitoes in country districts, he fell back on quinine. "He who takes quinine every day and therefore has a supply of quinine in his blood stream can undergo with impunity inoculation of blood full of malarial parasites, and can expose himself with little or no danger to the bites of infected mosquitoes." Such was the opinion held at that time, but the fallacy of this doctrine has now been proved. Celli drafted laws on state quinine to facilitate quininisation of the exposed population.(14) Constantine Savas, discussing antimalarial measures in Greece, showed that much antimosquito work was done, but the success of the Italian campaign led that country to follow the example set by Celli and to pass State laws facilitating the distribution of prophylactic and curative quinine. Cardamatis, by antimosquito measures alone, reduced the incidence of malaria in

Athens.[15] As a result of antimalarial measures undertaken in the German Colonies malaria was reduced. V. Schilling[16] came to the conclusion that the simplest and cheapest method was quininisation, but the relative importance of quininisation, screening, and anti-mosquito measures could only be decided upon according to the local conditions.

In the Federated Malay States Malcolm Watson[17] in 1901 commenced his great fight against the disease, and he has conducted an incessant warfare against the mosquito for over a quarter of a century. At one time it appeared as if many towns and rubber plantations would have to be abandoned on account of what he describes as the "Silent War", but now the commercial prosperity of the country is assured. During the great War the work of Major E.E. Austin[18] and of Manson-Bahr[19] in Palestine showed what could be done to prevent malaria under active service conditions; and the investigations of the Malaria Enquiry Laboratory, which included Wenyon[20] added to our knowledge of the measures to be adopted when conducting military operations on a large scale in a hyperendemic area, such as Macedonia.

Since the War, important work has been done by the International Health Board under the auspices of the Rockefeller Foundation. The areas investigated so far have been Brazil, where good results have been obtained without quininisation of the

of the people, Palestine in 1924, and Italy. In the latter country a general survey of the malaria was made at the invitation of the Government, as a result of which screened houses are now supplied to Government employees, and a premium is offered to private individuals who screen their houses in malarious districts.(21)

Such is an outline of the history of malaria and prophylaxis. It appears as if the progress in India has not been so rapid as in smaller and more happily situated countries, but the immense size of that country, extending over an area of 1,870,000 square miles, and the population of over 320,000,000 must be remembered before a comparison is made. The problem of malarial prophylaxis in that country is a great one, but is not incapable of solution in the course of time provided that progress, however slow it may seem, is made, and an unremitting warfare waged against the mosquito.

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3. Etiological Consideration

India lies wholly within the zone where Malaria may be met with; that is, between the latitudes of 60° N. and 40° S.[22] The presence of endemic malaria in a district depends on four main factors, and in the absence of one of these factors such malaria will be absent. The factors are, firstly, the presence of anopheles capable of carrying the protozoon; secondly, meteorological conditions favourable for the development of the oocysts in the body of the mosquito, thirdly, the presence of persons with gametocytes in their blood; and, fourthly, the presence of persons to whom the anophelines may convey the infection. Many instances can be given where three of the factors were present, but the absence of a fourth has accounted for the absence of malaria. In India there are many small localities where the absence of the first factor, malaria carrying anopheles, has rendered the area non-malarious, but as notable instances of this the cases of the islands of Mauritius and Barbados may be mentioned. Mauritius had been quite free from malaria in spite of a suitable climate, the presence of Indian coolies and African negroes with parasites in their blood, and a large non-immune population. However, in 1861, the disease became epidemic, and it has been endemic in the island ever since. This was proved to be due

to the introduction of an anopheles capable of carrying the protozoon, namely P. Costalis, an African species, most probably introduced from that country. Barbados had been free from endemic malaria until quite recently, The climate favoured it, infected persons from the other West Indian Islands were present, and there was a large non-infected population. In October last 300 cases of a fever, which proved to be malignant tertian malaria, occurred, and, on investigation, it was found that the island, hitherto free from anopheles, now harboured A. Albimanus in considerable numbers. It is thought that the mosquitoes may have travelled in the holds of small ships from the neighbouring Antilles.(23)

Instances of the absence of the second factor, that is meteorological conditions favourable for the development of the sexual stage of the parasite in the body of the mosquito, causing the disappearance or preventing the prevalence of malaria, are equally numerous. The nonprevalence of malaria in this country is, in part, due to the absence of this factor. It has been found that a sustained mean temperature of 58° to 60° Fahrenheit is necessary for the development of benign oocysts in anopheles. The last unusual prevalence of malaria in this country coincided with the hot summers of 1857 and 1859, and the cold summer of 1860 caused a marked deline in the incidence of

the disease.[24] In this part of East Sussex anopheles (A.Maculipennis) are numerous, breeding places abound, and cases of malarial relapse frequently occur among those residents who have returned from malarious countries, yet fresh infections are extremely rare. In India the instances of this are usually found in the hills. C. A. Gill[25] found no lack of malaria carrying mosquitoes, such as A.Maculipennis, A.Fuliginosus and A.Willmori, at 6000 to 8900 feet in the Himalayas and in Kashmir, but absence of malaria owing to the low temperatures.

The third factor, presence of persons with gametes in their blood, is seldom, if ever, absent in India. It is the most potent cause of malaria in that country. Most probably the main cause of the non-prevalence of malaria in this country even in hot summers, is the comparatively small number of carriers of the disease. The elimination of this factor is brought about by the screening of the sick, and by their treatment to a final cure.

The fourth factor, presence of persons to whom the anophelines may convey the infection, is rarely absent. Even in so-called immune communities there is a constant supply of non-immunes, in the shape of new-born babies. The potential absence of this factor can be secured by screening and by like measures or, as recommenced by Stephens and Cristophers in 1902, by the segregation of Europeans in hyperen-

demic areas.

It is proposed to deal with the predisposing and exciting causes of malaria as they act directly or indirectly through these four main factors.

PREDISPOSING CAUSES

Climate and meteorological conditions

Climate has an indirect and a direct influence on the incidence of malaria. Indirectly, high temperatures and work in the sun favour relapses and increase the number of infective persons; low temperatures, especially the low evening and night temperatures following a hot day, which occur towards the latter end of the Autumn in Northern India, cause the resistance of the body to be lowered and also favour relapses. Rainfall has the same effect by the chill and wetting often experienced. A warm climate and the consequent lack of clothing favours infection and spread of the disease.

The direct influences of climate are the more important and act in two ways, firstly, by effecting the breeding of anopheles, and, secondly, by effecting the maturing of the oocysts in their bodies.

Temperature

In India this affects the breeding of the anopheles, the development of the malaria parasite on the anopheles, and the multiplication of the parasites

in the blood of man. Firstly, the effect of temperature on the mosquito will be considered. Long before the role of the mosquito was discovered Hirsch[26] maintained that the isobar of 59° to 60° Fahrenheit of mean summer temperature indicated the malaria limit. Macdonald[24] corroborated this with regard to England. Col. S.P. James[27] investigated the length of life of mosquitoes kept under artificial tropical conditions. He found that the mortality of A.Maculipennis was high at 24° Centigrade, about 50% dying during each of seven to ten days of life, at 22°C. it was less, but the time taken to become infected was longer, fresh feeds of blood being required daily, at 26°c. nearly all the mosquitoes died before the sporozoites reached the salivary glands. Possibly the Indian species are more resistant to heat for Hehir[28] states that at 40°C. A.Stephensi, A.Culicifacies, and A. Pulcherrimus are full of life. James[27] found also that at low temperatures, such as 4° to 6° C. infected mosquitoes lived for 2½ months, and retained their infectivity. Exposure to the direct rays of a tropical sun kills mosquitoes in a few minutes. Another effect of the temperature is to cause breeding places to dry up and to kill larvae and ova by dessication. In Northern India the anopheles hibernate during the winter months. In the spring when the days become warmer, they emerge from their

resting places, and lay their eggs and give rise to fresh broods of mosquitoes. With the advent of the hot weather, in April and May, the temperature becomes too high for the mosquito, and, most probably, numbers die. The continuity of the species is secured by the survivors aestivating, as observed by Stevens and Cristophers,[29] in cool and dark places. In the late summer, when the days become cooler, and anopheles again come forth and breed freely until the cold weather drives them into shelter once more. This may be taken as the typical cycle of events, though the habits of the individual mosquito varies with the species. Thus, A. Culicifacies hibernates in the larval stage, and others hibernate in the egg stage. The effects of the temperature on the habits of the anopheles accounts for the seasonal influence of malaria, and this is most pronounced in Northern India where the variations in temperature are greatest.

The second influence of temperature is the effect on the development of the sexual stage of the malaria parasite in the mosquito. It has been found that a mean temperature of 60°F. is necessary for the development of benign tertian oocysts and this must be maintained for 16 days, a higher temperature being needed in the case of subtertion infection. C.A.Gill[30] in India found that there was no transmission of malaria when the mean temperature was below 60°F. Jancso[31] has shown that the zygote ceases to develop in the

mosquito at 60°F. (15.6°C), and that above this limit development goes on more rapidly, so that it may be completed and sporozoites formed in as short a period as six or seven days. Intermittent low temperatures were found to delay, not prevent development; but a prolonged low temperature causes degeneration of the sporozoites, in the salivary glands. Wenyon[32] in the Balkans found normal oocysts in A.Superpictus when hibernating in barns and cowsheds below human habitations during the winter months. When the development of the oocysts is retarded by cold it is continued when the weather becomes warmer. Temperature may have an influence on the prevailing type of infection. A.Pagnier and P.Schrumpf-pierron[33] studied this question in the Near East and found benign tertian malaria prevalent during the spring months, when the temperature rose from 0°C. to 30°C. and subtertian only in September to November, when the temperature was from 25°C to 30°C., but dropping when it fell to 5°C.

Humidity

Moisture is essential for the development of the eggs and larvae of the mosquito, and a certain degree of humidity is essential for the existence of the mosquito itself. Laboratory experiments show that mosquitoes live for much longer in humid than in dry air. Lt. Col. Hodgson, I.M.S.,[34] has shown as a result of experiments that in dry air the temperature

of the body of the mosquito approximates to the wet bulb temperature; in a nearly saturated air it approximates to that of the atmosphere. He has shown that exflagellation and fertilization of the malaria parasite in the stomach of the mosquito occurs only when the wet bulb is between 18° and 22° Centigrade, and holds that malaria prophylaxis is necessary only when this condition is fulfilled. C.A.Bentley(35) found, when determining the sporozoite rate of A. Stephensi in Bombay, that it varied directly with the humidity. High atmospheric humidity favours the infection of mosquitoes, and the development of the parasites in their bodies. C.A.Gill(30) found that transmission of malaria did not take place when the humidity was below 63% at 8 a.m. The same observer(36) carried out extensive experiments with culex fatigans and proteosoma grassi as the parasite. He found that at 27°C. the culex could not survive more than five days, if the humidity were less than 48%; if the humidity was over, 48%, growth proceeded normally and oocysts developed in the stomach wall; if the humidity was over 50% successful feeding was assured. There is evidence that anopheles are more resistant to high temperatures. In the high temperatures of the Punjab, successful feeding does not take place unless the humidity is above 40%. It is highly probable that the humidity factor in the spread of malaria in India is more important than the tempera-

ture factor. High atmospheric humidity such as occurs after rainfall increases the activity of anopheles and their thirst for human blood, as all who have lived in the tropics well know.

Rainfall

Rainfall has in India an important influence on the prevalence of malaria. It lowers the temperature and increases the humidity of the air, and provides breeding places for the anopheles, and so increases the incidence of the disease. On the other hand excessive rainfall, by washing away the larvae, has the opposite effect, and in swampy districts rainfall usually results in a diminution of malaria owing to the flooding of the breeding grounds. In some parts of India the influence is more remote. For instance in the irrigated areas of the Punjab and North West Frontier Province, where the rainfall is scanty, the incidence of malaria depends on the rainfall in the Himalayas and the resultant swollen rivers and canals. The association of rainfall and malaria is more or less constant. C.A.Gill (37) has shown this association to be so regular in the Punjab, that from the precipitation in July and August the Autumn incidence of malaria can be forecasted with a certain degree of accuracy. Years with heavy monsoon rains predispose to epidemics. Leonard Rogers demonstrated that high annual rainfall meant an increase of malaria

with reference to Chota Nagpur and Assam, in 1895 though the reason was not known then. In Eastern Bengal decreased rainfall means increased malaria, for, owing to the earlier subsidence of the floods, a longer time is allowed for the mosquitoes to breed under favourable conditions of temperature. In Darjeeling, C.Strickland[38] found the malaria season to be the dry warm one from April to July, later the heavy rains washing away the stream breeding. In Shillong, the same observer[39] found that the incidence of malaria bore an inverse relationship to the rainfall of the previous year. In the districts investigated by the writer the rainfall had a more or less direct influence. In Eastern Rajputana and Western Punjab the malaria incidence varied directly with the rainfall. Scanty rainfall in July meant that the two succeeding months were extremely hot, and the breeding places of the anopheles dried up. In the Western United Provinces and in the south of the Punjab malaria was always moderately endemic owing to the number of irrigation canals and rivers, but heavy rains meant hyperendemicity.

In the North West Frontier Province the scanty rainfall, often less than 20 inches per annum, had little influence. Irrigation was the most direct cause of hyperendemicity. Heavy rains in the hills caused the rivers and canals to overflow their banks and also led to hyperendemicity. Thus it can be seen that the influence of rainfall varies with the

district and the local conditions.

Irrigation

In India the average amount of land irrigated annually by constructed irrigation canals varies from 26 to 28 million acres.(40) With the opening and completion of the Sukkur Barrage in Sind a further six million acres will be under irrigation. The main cause of the high incidence of malaria in the North West Frontier Province and in the Punjab is the canal irrigation of a naturally dry country and in the United Provinces the substitution of canal for well irrigation. Robertson(41) found that the canal irrigation was the main cause of the high incidence of malaria in Saharanpur, and the curtailment of such irrigation for a distance of ¼ of a mile from the boundaries of the city resulted in a lowering of the malaria incidence for many years. The same officer pointed out that well irrigation has a tendency to lower the level of the subsoil water, while with canal irrigation the level may be only from three to five feet from the surface of the ground after the rains. Dempster(42) pointed out in 1845 the dangers of irrigation of a stiff, retentive soil, and advocated, with reference to Peshawar, the prohibition of canal irrigation within a mile of the Cantonment Pillars. Irrigation alone is responsible for the high incidence of malaria in the Peshawar valley, and in most parts of the North

West Frontier Province. The extremely low endemicity of Rajputana where well irrigation only is employed contrasts with the higher endemicity of the neighbouring canal irrigated United Provinces. In most parts of India the incidence of malaria varies directly with the level of the subsoil water. Hehir[43] noted this phenomenon in 1880 in Chudderghaut, and Leonard Rogers[44] noted the same relationship in the Dinajpur district. The danger of canal irrigation is the raising of this level to above 10 feet from the surface of the ground. In well irrigation a proportion of the water drawn up evaporates and the subsoil level is found to fall. In Bengal, where the ground is flat and swampty, C.A.Bentley[45] found that raising the level of the subsoil water reduced the incidence of malaria and more extensive irrigation was advocated; but conditions in Central and Northern India render the control and local curtailment of irrigation essential.

Water Supply

Wells are the chief source of the water supply of India. In towns they are a source of malaria, and collections of water in the vicinity of public wells are responsible for much local infection. In the country the wells are usually situated at some distance from the houses, and their etiological importance is less. In the larger Railway Communities there are large storage tanks of water to supply the

locomotives, and these are raised a considerable distance above the ground, so as to obtain a sufficient head or pressure of water to allow the boilers of the engines to be filled rapidly. A pipe line from these tanks supplies the station buildings and the larger bungalows. It is a common sight to see Indians drinking and bathing under the taps on the platforms of the stations. As a source of anopheles these tanks are not of much importance. Their depth, their steep sides, and the lack of vegetation render the breeding of malaria carrying anopheles in them unlikely, though Culex and a few A.Subpictus larvae have been found.

The tanks themselves are supplied with water pumped from a neighbouring river bed, for instance those in Kotah are supplied from the River Chambal. Drawn from a stream on the banks of which numbers of Natives perform their morning evacuatory rite, and fouled with the excreta of crows and kites, the water from this source, unless boiled, is highly dangerous for drinking purposes.

Domicile

The fact that malaria is a household disease has been brought into prominence recently.(27) It is thought that mosquitoes feed and become infected in one particular house or quarter, and even return to it after ovipositing. Such being the case the condition of the houses in India calls for comment.

It is a well known fact that mud forts, such as those at Peshawar, Shabkadr, Jamrud and other places on the frontier are highly malarious. Their proximity to native villages and towns has been the cause usually assigned to this. It seems as if it were the condition of the forts themselves that is responsible for their unhealthiness. Their walls are intersected with cracks and crevices where anopheles may hibernate and aestivate, and no measures short of reconstruction can ever clear them of mosquitoes. The sundried clay or mud and straw bungalows found in so many of the military stations are little better, The construction of the ceilings alone, where matting is affixed to the beams and the whole covered with a more or less dilapidated sheet, affords an ideal roosting place for myriads of mosquitoes. As a contrast the stone built bungalows and quarters of the Railway Communities, though hotter in summer and colder in winter were comparatively easy to keep free from mosquitoes, and their lime-washed interiors provided few hidingplaces for lurking anipheles. The type of bungalow which is most pernicious is the thatched one. Many dak bungalows or rest-houses are of this nature. It is impossible to keep such a bungalow free of mosquitoes. That mosquitoes hibernate in the thatch has been observed, and as many as sixteen anopheles have been found in a single straw.(46) The housing of the Indian population is

worse. It is highly probable that the condition of the houses is no mean factor in the etiology of malaria in India.

Personal Predisposing Causes

Hygienic Conditions. Malaria is much more prevalent among the ill-fed, the ill nourished, and the poorly housed. The agriculturists suffer most. Living in wretched shacks of bamboo or in huts of sunbaked mud, scantily clad, exposed to the extremes of temperature, and often on a deficiency diet they stand little chance of resisting the disease. In the Railway communities the population could be divided into four categories or grades. Grade I. consisted of European and senior Eurasian officials, grade II consisted of European and Eurasian sobordinates, grade III of Indian subordinates, and grade IV consisted of coolies, gangmen, gate keepers and the conservancy personnel of the station. It was in the fourth grade that the incidence of malaria was greatest, and the incidence decreased proportionally up to grade I, but even in the lowest grade the incidence was less than among the agricultural population. Regular pay, good stone-built quarters and sanitary supervision accounted for the difference. This comparison was made in an area of low endemicity, so the immunity of the inhabitants was negligible. Anything

lowering the resistance of the body tends to make attacks of malaria more common and more severe. Hence infections and relapses are more frequent in the army during the stress and strain of active service than under peace conditions.

Age: Children under ten years of age are the most often attacked. From the custom of allowing Indian children to run naked for the first six or seven years of life they are more exposed than the adult, in addition they have more sensitive skins and, sleeping sounder, are more prone to be bitten during the night. The infected native children are the main source of malaria in India, as was pointed out by Dempster in 1846, but was lost sight of for many years.

Sex: is only influential in so far as the individual by occupation or by dress is more or less exposed to the bites of mosquitoes. Women are prone to relapses during the menses and the puerperium. The writer saw a fatal case of cerebral malaria in a Eurasian originally suffering from a miscarriage.

Race: Europeans and particularly new-comers are more prone to attacks than the Indians, Eurasians are reputed to share the susceptibility of their European progenitors, but the writer considers them rather less susceptible than the pure European, but more neglectful of protective measures. Indians are less susceptible, and acquire a condition of so-called immunity in endemic areas.

Previous attacks predispose to relapses, but not necessarily to fresh infections. Numerous previous attacks, especially when dating from infancy and untreated by quinine often cause immunity in the Natives.

Immunity. It has long been known that the adult Indians living in hyperendemic areas remain free from attacks and that parasites are not found in their blood. Investigation has shown that in such highly malarious areas the children up to two years of age live in a condition of almost continuous acute infection of malaria. The mortality is very high, but the survivors commence to acquire immunity after the age of four. The attacks or rather the latent immune infestations become less frequent, and after the tenth or twelfth year parasites disappear from the blood, the spleen becomes reduced in size and immunity is more or less complete. In a moderately infected place the rise of parasitic and spleen rate is not so high, but the fall is more gradual and only slowly is immunity acquired.(47) Anything lowering the vitality causes a loss of this immunity. Loss of immunity occurs also when moving to a new locality,(48) and there are instances of immunity to one species of parasites not protecting against the others.(49) The high incidence of malaria among the Indian troops in the North West Frontier was

due in part to their non-immunity to the type of local malaria, but, mainly, from their having come from districts of low endemicity in the South of India.

Exciting Causes

It has been seen that when three of the factors of etiology are present the addition of a fourth results in the occurrence of malaria. So any one of the four factors may be the exciting cause. In India the third and fourth factors, the presence of persons with gametocytes in their blood, and the presence of persons to whom the anopheles may convey the infection, are more or less constant, so the exciting cause will either be the presence of anopheles, or meteorological conditions favourable for the development of the parasites. Now, there are few areas without one or more of the ten proved malaria carriers present, so the exciting causes can be narrowed down to meteorological conditions being favourable for the breeding of the mosquitoes and for the maturing of the occysts. It is usually to the meteorological conditions that one must look for the exciting cause, and for the cause of seasonal variation in the incidence of malaria in any district in India.

Description of the Districts

For purposes of description the districts may be divided into four areas. Firstly, Eastern Rajputana;

secondly, the south west of the Punjab; thirdly, West of the United Provinces and South Punjab; and fourthly, the North West Frontier Province and the trans-frontier terrain.

Firstly, the portion of Eastern Rajputana, including the towns of Bharatpur, Alwar, Jaipur, Ajmere and Kotah, was an area of mild malaria. This area forms part of the Central Indian Plateau, is for the most part over 1000 feet in height, and is composed geologically of Basalt, and chiefly granitoid gneisses. It is by no means a table land, as might be assumed from the name, but is a picturesque region with hills and valleys, for the most part open jungle, but with scattered townships and villages, and adjacent areas of cultivation. The surface of the land is intersected with ravines, representing the dried channels by which the land is drained in the rainy season. There are comparatively few permanent collections of water, and these are mostly in the neighbourhood of the rivers Irrigation is carried out by the husbandman drawing water from the wells by a bullock drawn leather bucket, or by the primitive water wheel. The rainfall is small. There are a few showers in December and January, and mosquito breeding commences in the middle of February; a few cases of malaria occur in the two succeeding months. From the beginning of April the temperature rises steadily and the humidity

falls, till at the end of that month no mosquitoes are to be seen, and so great is the dryness of the air that life is only tolerable if grass screens, kept moist by some automatic device or by the attentions of a coolie, are placed in front of the windows and doors that face the scorching wind. At the end of June or beginning of July the rains break and the temperature falls a little. In August and September the temperature rises again and, unless the rains have been heavy, the pools soon dry up. Towards the end of September mosquito breeding commences and continues until November. So, malaria may prevail to a slight extent in the Spring, and again in October and November, the prevalence being dependent on the rainfall.

The second area is situated in the South West of the Punjab, and includes the towns of Sirsa, Rewari and Hissar. The soil is sandy and the rainfall small in amount. The arid nature of the district and the scattered and small population render the endemic malaria moderate in amount. The meteorological conditions much resemble the first district, though the humidity is less. When the wind blows from the West from the direction of the Indian Desert the hot weather temperatures become excessive. In small areas only, where local conditions provided breeding grounds for anopheles, was malaria prevalent to any extent.

The third area comprised a portion of the South of the Punjab, and of the West of the United provinces, and included the towns of Delhi, Agra, Muttra, Farukhabad and Cawnpore. A densely populated alluvial tract, under 1000 feet above the sea level and lying for the most part in the gangetic plain, this area had moderately severe endemic malaria, but was liable to fulminant epidemics, extending most likely from the Punjab. This large wheat and rice growing district was irrigated by numerous constructed canals and rivers, and to a less extent by wells. The incidence of malaria depended on the amount of the rainfall, and in many districts the peak of the malaria curve followed the melting of the snows in the hills and the consequent flooding of the rivers and canals.

The fourth area consisted of a portion of the North West Frontier Province and included the towns or military stations of Peshawar, Nowshera, Mardan, Dargai, Malakand and Chakdara. In this area extremes of temperature are met with and the rainfall is scanty, often less than 20 inches per annum. The incidence of malaria is almost independent of the amount of rainfall, and is mainly due to the irrigation of a naturally dry soil. However, in the valleyes of the rivers the malarial incidence is dependant in part on the rainfall in the hills

among which the rivers take their origin. Heavy rainfall in the hills means swollen and flooded rivers, and the inundation of large areas of land which provide countless breeding grounds for anopheles when the waters are subsiding. Most of the district is over 1000 feet in height, Peshawar being 1179 feet and Malakand 2375 feet above the sea level. It is a region of barren hills and plains, but with fertile areas where irrigation and cultivation had been carried out. The soil of the hills is rocky, the foot-hills are stony, and the valleys have outcrops of clay. The soil is impermeable and pools of water are soon formed when the land is irrigated. The malaria is characterised by a spring rise of short duration and mostly of the benign tertian type, and a large and more protracted rise of aestivo-autumnal infection towards the latter end of the year. The most malarious place in which the writer resided was in the Fort of Chakdara. It is situated 10 miles beyond Malakand on the banks of the Swat river, and in close proximity to flooded paddy fields. After the monsoon rains had fallen in the hills, this river became swollen, and overflowing its banks, flooded the surrounding country even up to the walls of the Fort. As the waters subsided numerous pools were left and mosquito breeding began apace. The quarters and barracks soon swarmed with anopheles, A.Listonii, A.Fuliginosus and A.Culicifacies being

identified, all dangerous malaria carriers. Though the Indian troops themselves had come from a healthy district in the South, permanent residents in the Fort, such as gai-wallahs or milkmen, and small shop-keepers and their wives and families, provided an ample supply of malignant gametocytes. Epidemic malaria prevailed among the troops, and few escaped heavy subtertian infection. The civil hospital, within a stone's throw of the Fort was thronged with fever-stricken villagers attending as out-patients for their dose of quinine. It is interesting to note that the old civil hospital and dispensary situated on dry and stony ground at about half a mile from the river and Fort was comparatively free from malaria. The occupant, the Indian Political Agent, congratulated himself that the authorities had thought fit to move the hospital and had provided him with such a healthy residence. Had the troops been moved to this site, or even further from the river the epidemic might have been avoided. The temperature is falling during the malaria months of September, October and November, and the whole garrison, with the exception of a picket to man the Fort, could have gone under canvas during that time.

Such is a sketch of some of the more important etiological factors of malaria in India. Although wholesale eradication of the disease is not a feasable proposition at present, it is thought that much could

be done to lessen the incidence of malaria in all these localities.

... ...

4. TREATMENT. (a. Prophylactic (b. Curative

a. Prophylactic

Referring again to the four main factors of etiology, it has been found that the elimination of one of these factors is all that is necessary to break the vicious circle and bring the incidence of malaria to zero in an endemic locality. The second factor, favourable meteorological conditions for the development of the sexual stage of the parasite, cannot be influenced as a rule, but even if elimination of one of the three remaining factors is impracticable, a diminutive of one or more of them will result usually in a diminition in the incidence of malaria. It is only in very fortunate circumstances that a factor can be eliminated entirely. Ross's (50) campaign in Ismailiah so reduced the number of anopheles that the malaria incidence fell to zero. In Havana (51) the same result was brought about by the efforts of the American Army Medical Corps more than a quarter of a century ago, Koch (52) and Celli (53) recommended wholesale quininisation of infected populations with a view to killing the parasite in the human host, and so reducing or eliminating the third factor. The fourth factor is reduced by segregation of the healthy, or by

protecting them from the bites of infected mosquitoes.

In conducting an antimalaric campaign it is usually best to concentrate every available effort on one carefully selected method, which can be bought to a high degree of perfection(54). The success of Malcolm Watson in the Federated Malay States was due mainly to his choice of method, namely an anti-mosquito campaign and to his consistency in adhering to his choice throughout.

Firstly, the measures employed with a view to elimination or diminution of the first factor, namely, the presence of malaria-carrying anopheles, will be considered. These measures aim at the primary destruction of the mosquito throughout all stages of its development, as advocated originally by Ross. In the early days of antimosquito measures a campaign against all mosquitoes was recommended, but experience has shown that this is unnecessary, is costly, and is even harmful, for destruction of the breeding grounds of a comparatively harmless species may provide ideal conditions for the multiplication of a potent carrier of the disease. It is essential that the local malaria carrying anopheles be identified, and their habits carefully studied before antimosquito measures are commenced.

Antimosquito measures aim at the destruction of the mosquito in the Larval and egg stage, and in the adult stage. The methods employed to prevent the

breeding of mosquitoes or to destroy them in the larval and egg stage are, firstly, drainage, filling operations, the regulation and control of irrigation and wet cultivation, and the submersion of marshy districts: secondly, petrolege, the use of larvicides, and the introduction into breeding grounds of larvivorous fish.

Drainage is the oldest method of malaria prevention. It was employed by the ancients, and it was recommended and carried out in certain districts in India long before the rationale of the method was understood. As Ross was the originator of scientific prophylaris, so was Malcolm Watson the pioneer of scientifically applied anti-malarial drainage. The problem of drainage depends on local conditions and these must be carefully studied before any drainage scheme is formulated. In marshy districts the aim is to lower the level of the subsoil water, and the most important means of bringing this about are by the laying of land drains or subsoil pipes, or by the construction of open ditches. The latter method is the one usually employed in India. It has been found that the construction of properly graded surface drains to a suitable outflow is initially the most comprehensive and econimical means of reducing the incidence of malaria. Where a

collection of water is separated from its natural outflow by an impervious stratum vertical drainage may be employed. A shaft of considerable diameter is bored through this stratum and the pond or marsh allowed to drain away. Much of the malaria in the districts investigated could be prevented by measures of a minor nature, such as the drainage of local collections of water, the regular supervision of all open drains, and the clearing and, if necessary, rough canalisation, of the beds of small rivers and streams.

Filling operations are quite satisfactory on a small scale, but expensive and laborious as a major work. Filling is the most satisfactory method of dealing with small collections of surface water and is the method most used by mosquito brigades and the conservancy personnel of the Railway ~~Committees~~ Communities. Freshly made borrow-pits in the vicinity of human habitation may be disposed of by this means. Malcolm Watson(55) emphasises the inadvisibility of dealing with a swamp or large collection of water by filling operations unless drainage is an absolute impossibility.

It has been seen that the main cause of the malaria in Northern India is the canal irrigation. Unless carefully supervised and controlled such irrigation is a danger to the health of the inhabitants of the irrigated areas. There may be leakage

or seepage from the canals themselves, which are often above the level of the land through which they flow, and consequent formation of pools and marshes; there may be overflooding of the fields irrigated, with the result that they become waterlogged, and, instead of drying up in the periods between irrigations, form breeding grounds for anopheles; the cutting off of the supply of water during the months following the rains, namely in August, September and October, allows the formation of pools of stagnant water in the canal beds at a time when the malaria season is at its height. The remedies recommended are construction of the canals so that leakage is prevented, regulation of the supply so that waterlogging of the land is avoided, and, throughout the year, a weekly flush of from six to twelve hours duration of all canals to prevent mosquito breeding in their channels. The canals themselves should have sufficient flow to prevent breeding and their banks should be kept clear of vegetation. Should these measures be unsuccessful, canal irrigation should be prohibited within a radius of from $\frac{3}{4}$ to one mile from the boundaries of a town.

Rice and other crops growing in flooded fields are a frequent source of malaria. There are several solutions suggested for this problem, one is that the fields should be flooded completely and not allowed

dry up during the malaria season. Others recommend that the water in the flooded rice fields should be kept constantly moving at the rate of 10 to 12 yards a minute, and so prevent breeding of anopheles[56]. The prohibition of rice growing in hyperendernic areas is suggested, and the Provincial governments advocate the prohibition of rice growing near certain towns[57]. The affluent and effluent should be kept clear from vegetation, and the use of a double channel as employed by the Sergents[58] in Algeria has much to recommend it. The flooding of paddy fields by rivers overflowing their banks, as met with in the North West Frontier Province is a source of malaria difficult to avoid. The land will be inundated whether cultivated or not, and it is questionable whether mosquito breeding was more prevalent in the paddy fields than in the uncultivated areas that had been submerged.

Submersion or flooding of marshy or swampy ground washes away the larvae of anopheles, and renders the area submerged unsuitable for breeding. This method has been employed since the time of the ancient Greeks. C.A. Bentley[59] strongly advocates this measure for Bengal, the aim being to raise the subsoil water level by flush irrigation, and to keep it as high as possible during the wet season to

benefit the crops and reduce the malaria. This measure of malaria prophylaxis is inapplicable to Central and Northern India.

The more direct and the less satisfactory methods of dealing with the breeding grounds of anopheles are petrolege, spreading a film of oil such as kerosine over the surface of the water, the use of chemical larvicides, and the instillation into suitable collection of water of larvivorous fish.

Petrolege. The process of petrolege of stagnant water was first employed in the United States of America by O. Howard[60] in the year 1892. It consists of spreading a film of oil over the surface of the water to destroy the larvae and ova of mosquitoes, together with those adult mosquitoes that come to oviposit. It was thought formerly that the larvicidal action of the oil was purely a mechanical one, a surface film being found on the water, the breathing tubes of the larvae being clogged, and death occurring from suffocation. By colouring the oil with a mineral dye it has been observed that the oil enters the siphons by capillary attraction and causes death by suffocation and toxaemia in from 30 to 60 minutes. The oil has a possible further effect of altering the chemical composition and surface tension of the water, and rendering it unsuitable for the breeding of mosquitoes. Petrolege is a method largely used in India, rather

too frequently used in the opinion of the writer. It is a method that appeals to the native mind, for pouring a little oil over the surface of the water is a much less laborious undertaking than drainage or filling operations, and the film of oil on the water is a visible proof that something has been done whether it has been successful in preventing mosquito breeding or not. The use of petrolege should be strictly confined to small and temporary collections of water, or where the use of any other method of mosquito prevention is impractible. The more efficient the anti-mosquito measures the less need there is for kerosine. The solution recommended and most commonly used in India is a mixture of kerosine 66 parts, heavy oil 33·5 parts and crude castor oil 0·5 parts per cent. The approved methods of applying the oil are by mechanical sprayers, by drip cans in the case of running water, and by oily rags or waste thrown into the water where the collection of water is very small. Sprayers are rarely seen in India, and the methods of applying the oil to the surface of the water are more or less crude and involve much waste of oil.

On damp and sodden ground where a surface film cannot be produced by petrolege sawdust soaked in a mixture of kerosine and crude oil in the proportion of 1 to 3 can be sprinkled.

Larvicides have a more limited application owing to their poisonous nature. They are specially useful for the edges of large collections of water and for stagnant pools in uneven drains. The Panama Canal larvicide consisted of a mixture of resin, caustic soda and crude carbolic acid, but its use has been discontinued in that region. Soap and water are nocuous to larvae, hence the absence of mosquito breeding in the vicinity of a dhobie ghat or native laundry. In America[61] Paris green mixed with 100 parts of road dust or fine sand and sprinkled widely has been used as a larvicide with success. It is stated to do no harm to plants or cattle, but it was not employed in India. Cresol is an effective larvicide. It has been found that a mixture of 1 in 10 million kills larvae in 12 hours, and 1 part of cresol in 1 million parts of water kills larvae in four hours. Its poisonous nature renders its use dangerous in India unless under supervision. It was much used by the conservancy staff in the Railway Communities, and was most efficacious in dealing with collections of water in the larger drains.

The use of larvicides in India is very restricted. The presence of an uncivilised or semi-civilised indigenous population, who use any collection of

water for drinking, bathing, rinsing their mouths, watering their cattle and irrigating their crops, renders the use of a poisonous chemical larvicide impracticable. Could a larvicide be found innocuous to any other kind of animal or vegetable life it would be advantageous to use it, but even then it is doubtful whether the religious principles of the people would allow its general use.

Several investigators have made a careful research into the composition of the water in which anopheles breed. R. Senior-White[62] has examined the mosquito breeding waters of Ceylon, has determined the limits of hydrogen ion concentration of the water within which anopheles are able to breed, and has studied the algae growing in the observed waters. The influence of the hydrogen ion concentration and chemical composition of the water is supposed to be an indirect one, acting on the pabulum on which the larvae feed, rather than on the larvae themselves.

Various aquatic plants reported to be injurious to the breeding of anopheles have been investigated, but the use of these on a large scale is not considered a practical solution of the problem. Malcolm Watson observed the growth of felted algae in pools which had been oiled previously, and noted that these pools were not selected by A.Maculatus for oviposition. Further research may reveal a simple

biological method of preventing the breeding of anopheles, but in the present state of our knowledge clearing away vegetation of any kind from the breeding grounds of anopheles is the wisest course to adopt. Few anopheles will breed in water without visible vegetation.

The introduction of larvivorous fish. In other countries the introduction of larvivorous fish has been a pronounced success. In the United States[63] it is found in some parts a cheaper method than oiling or ditching. In Spain[64] the introduction of Gambusia from the United States in 1921 has given good results. Unfortunately, the fish most used for this purpose, known as "millions" or Girardinus Poeciloides, though introduced into India some twenty years ago by the government of the United Pronvinces did not thrive and multiply. There are numbers of indigenous fish which might be used, but the subject requires local investigation and experiment. At present this method of larval destruction is not used to any extent in India. Destruction of the adult mosquito has formed a part of almost every antimalarial campaign, but more importance is now attached to this method of prophylaxis by the finding that malaria is largely a household disease, and by recent discoveries pointing to the possibility of infection being retained by hibernating mosquitoes. It has been estimated[65]

that each adult female mosquito surviving the winter is a potential producer of 7½ million descendants, so that the destruction of hibernating female mosquitoes is of considerable importance. The condition of the majority of the houses in India renders this method of attacking the disease particularly difficult. Much can be done by the recognised methods of mosquito destruction; but there are few houses which can be cleared completely of mosquitoes by this means. The methods usually employed for destruction of adult mosquitoes are fumigation, spraying with insecticide solution, and the destruction of mosquitoes by traps or by hand.

Fumigation is usually carried out by closing all the windows and doors, if necessary, covering over the chimney, and by exposing the mosquitoes so trapped to the effects of a poisonous gas. The gas most commonly used is sulphur dioxide, and this is generated by burning crude sulphur in an iron vessel standing in water. It is estimated that 2 lbs of sulphur per 1000 cubic feet of air space are required. Where procurable, cylinders of compressed sulphur dioxide may be used, or the gas may be generated by a Clayton apparatus, but this is seldom done in India. In the United States a mixture of camphor and carbolic acid is often used, especially to destroy the stegomyia callopus, or

vector of yellow fever. Equal parts of crystallised carbolic acid and camphor are dissolved by gentle heat and put in a small pan and suspended over a spirit stove for two hours. It is estimated that 4 ounces of each ingredient per 1000 cubic feet of air space are required. This method has the advantage that the room may be used immediately after the fumigation. Cresol may be substituted for the carbolic acid.

Formaldehyde gas may be used, generated from paraform tablets, but several hours exposure is necessary and the rooms must be thoroughly ventilated afterwards. Of other methods the two most applicable for use in India are the burning of "country" or native Indian tobacco and by the use of smoke from a wood fire. In the former method a quantity of country tobacco, one pound per 3000 cubic feet of air space, is saturated with kerosine oil and set on fire in the closed room; in the latter a wood fire is lit in the room, the chimney closed, and all the windows and doors opened, so that the mosquitoes are driven out; or all the windows and doors are covered with dark cloths, except one window, which is covered with a white sheet, from which the mosquitoes may be collected and killed. Fumigation should be used preferably at the end of the breeding season in the Autumn, in the early spring, and again just before the rains set in; but the times selected will depend

on the habits of the local anopheles. The destruction of hibernating and aestivating mosquitoes is aimed at.

Spraying with insecticide solutions may be employed to destroy anopheles in places where fumigation cannot be carried out satisfactorily. Formalin in a one per cent solution may be used, or creosote. The latter substance has been found to have a repellent influence on the anopheline mosquitoes and has been used for this purpose in the houses of the negroes in the Southern States of America.(61)

The mosquitoes themselves may be caught in traps such as T. Bainbridge Fletcher's box trap, or by the large garden trap devised by S.P. James in 1913. The box mosquito trap is commonly used in all parts of India. Simpler measures are the use of some adhesive substance spread on strips of paper, such as tanglefoot, which is a mixture of resin and country castor oil; the killing of mosquitoes by fly swats; or by catching them in test tubes and subsequently killing them by tobacco smoke or chloroform. If the occupant of every house or quarter were to make a point of daily searching out and killing every mosquito he could find in the house, the effect upon the number of infected mosquitoes would be appreciable. The practice of clearing

the bungalows for the hot weather, which consists of taking down all curtains and hangings and making the rooms as bare as possible has much to recommend it, and the curtains should not be replaced till the end of the malaria season. In the absence of curtains bamboo screens can be used to keep out the heat and glare of the day. Animal screens to divert mosquitoes from attacking human beings have been recommended by some. Roubaud[66] advised the building of cowsheds near human habitations with the idea that the mosquitoes will be attracted by the cattle and leave the houses alone. However, in this case A.Maculipennis was the vector, and the method was a failure in the Dutch East Indies, where A.Listonii, the local carrier, was not attracted by the cattle. In India cattle are usually tethered in close proximity to the houses of the Indians, and there is no diminution of malaria on this account. Much can be done to lessen the numbers of mosquitoes in a district by clearing the ground. Gorgas in Panama recommended clearing the bush for a distance of 200 yards from human habitations; but the distance usually advocated is half a mile, and Wenyon in the Balkans[67] found even that distance insufficient and suggested a mile limit. However, much can be done by clearing ground round dwellings, cutting down a percentage of trees, and by reducing the irrigation of gardens

and lawns to a minimum during the breeding seasons of anopheles. In areas of virgin jungle extensive clearing operations must not be undertaken lightly. The experiences of Malcolm Watson[68] in the Federated Malay States show that such districts may become intensely malarious as a result of clearance and drainage. A preliminary study of the habits and distribution of the local malaria-carrying anopheles is all important in such cases.

Such is a description of the measures most commonly employed with a view to the extermination of the anopheles in all stages of its development. The Second Factor, namely favourable meteorological conditions for the development of the oocysts in the bodies of the infected mosquitoes, cannot be influenced as a rule, unless the effect of drainage on a large scale or extensive irrigation is to alter the humidity and temperature of the air. Investigation carried out under natural conditions and in the laboratory show how the development of the sexual stage of the parasite is affected by alterations in meteorological conditions.

The Third Factor, namely, the presence of persons with gametes in their blood, can be influenced in several ways. It can be eliminated by the screening of infected persons, by efficient quinine treatment, or by the removal of infected cases to a place where there are no mosquitoes. Isolation or screening of

the infected can be carried out only in hospital and under favourable conditions. The efficient treatment by quinine of all acute and chronic cases of malaria is all important. Malaria prophylaxis by this means is known as the method of Koch, and it has many advocates. W. B. Orme[69] came to the conclusion that unless the campaign against malaria is strengthened by an attempt to reduce and, if possible, to destroy its incidence by dealing with the human carriers of the disease the efforts at present exercised are doomed to failure. The malaria commission in Spain[70] gave the place of honour to treatment of the sick to a final cure. The Sergent brothers in Algeria considered the cure of chronic cases the soundest method of making a malarious region healthy. The cure by quinine of the highly infected native children would do much to lessen the incidence of malaria in India; but, unfortunately, that measure is at present impracticable. The presence of millions of uncivilised or semi-civilised people renders such a means of reducing the disease much more difficult than in civilised countries. It has been suggested that infected Europeans should be removed to hill stations, where the possibility of re-infection and spread of the disease is nil, until completely cured. This has not been carried out to any extent and is not of practical importance. In Macedonia during the great War[71] there was initiated

in 1918 a wholesale removal of chronic and relapsing cases to the United Kingdom and other non-malarious places under the famous "Y" scheme, and this resulted in a considerable reduction in the incidence of malaria.

Early and efficient quinine treatment raises the question of prophylactic quinine, which is in practise the earliest form of treatment. It was thought originally that the administration of varying doses of quinine was true prophylaxis, and that the presence of a certain concentration of quinine in the blood destroyed the sporozoites introduced by infected mosquitoes. Now there is ample evidence that so-called prophylactic quinine is really curative. Yorke and Macfie[72] have investigated this subject, dealing with patients suffering from general paralysis, and experimentally infected with malaria. They found that sporozoites injected by an infected mosquito are not destroyed or even harmed when the patient is taking as much as 30 grains of quinine daily. Also, the same observers found that 18 grains of quinine taken daily for five days before and seven days after being bitten by an infected mosquito failed to avert an attack of malaria, but if the quinine were continued for ten days after infection the attack was prevented. They found also that infection produced by the inoculation of malarial blood was cured by

from 3 to 10 grams of quinine without relapse, but in cases infected by mosquitoes 57% relapsed with this dosage.(73) So it is now almost an established fact that the sporozoites are unaffected by quinine, but it is the earlier stages of the schizogenic cycle that are attacked. The failure of quinine taken prophylactically to prevent attacks of malaria among persons living in hyperendemic areas has caused it to be condemned by many authorities. A.Macdonald(74) concludes that quinine has no position in sanitary administration, and that the facile relief from malarial attacks by the taking of quinine has disastrously postponed sanitary administration in the tropics. Col. Rawnsley and others(75) came to the conclusion that prophylactic quinine in small doses is useless if not dangerous, and recommended 30 grains daily for not longer than four weeks; and the same writer concludes later(76) that prophylactic quinine is a waste of time and money. C.M.Wenyon(77) from an extended trial of quinine administered prophylactically in doses varying from 5 to 30 grains daily, came to the conclusion that the prophylactic use of quinine on so vast a scale as employed in Macedonia was not worth the labour and expense involved. He found that the regular administration of quinine daily prevented a certain proportion of relapses in already infected men, but sooner or later

attacks of malaria developed more difficult to cure on account of the previous continual dosing with quinine. Many others, such as Anderson[78] and Waugh Scott[79] condemned the use of prophylactic quinine, and in a leading article of the Lancet[80] it was stated that 5 or even 10 grains of quinine daily was useless as a prophylactic. Leonard Rogers[81] advanced the view that the reported failures of quinine prophylaxis were due to the inadequacy of the measures used in the particular cases. Harford[82] thoroughly approved of a daily 5 grain dose for Europeans in Tropical Africa, and it is interesting to note that a similar dose of the bi-hydrochloride of quinine is employed daily in West Africa by Europeans of the Colonial Service. Pringle[83] found that regular takers of a 5 grain dose of quinine were free or nearly free from attacks and when attacks occurred they were mild in character. It was stated in a leading article in the Lancet[84] that one of the reasons for the failure of prophylaxis was the fact that no quinine was taken during the night. Aldo Castellani gave his opinion in favour of quinine prophylaxis combined with anti-mosquito measures in combatting malaria as a result of his experiences in the Balkans and in the Piave Valley in Italy.[85]

P. Bassett Smith recorded the undoubted value of prophylactic quinine in the Royal Navy during the late War, in reducing the number of infections and preventing loss of man power. Thus it can be seen that as a result of the use of quinine prophylactically on a large scale during the period of the Great War opinions as to its efficacy were very much divided, and, on the whole the balance of opinion went against quinine. It has been advanced by W.Yorke and Macfie[86] as a theory of the action of quinine, that a certain number of malarial parasites are destroyed by the drug and a large amount of soluble antigen is set free. This antigen, by stimulation of the hosts tissue, provokes the formation of immune body, and the remainder of the parasites are destroyed. For a cure to occur, firstly a sufficient quantity of antigen must be set free, and secondly, there must be a capacity on the part of the host fo react to the antigen and produce a sufficient quantity of immune body. It may have been the failure of the tissues of the troops, subject to the strain of active service conditions, to respond by formation of thes immune body that caused the lack of success of quinine, used both prophylactically and curatively, during this period. In Palestine in 1917, prior to the great advance, it was found impossible to treat cases of malaria in the Field, and all such cases were sent to the comparative

comfort of the Base for a two months course of treatment. That the resistance of all concerned in the World War was lowered is an established fact, and the high mortality of the influenza epidemic of 1918 was mainly due to this cause. Recent reports are more in favour of prophylaxis. In Italy, B.Grassi has recorded good results from prophylactic quinine in the marshy parts of Tuscany. In Palestine I.J. Kligler[87] reports that the use of the drug prophylactically has reduced the loss of working days to less than one sixth of those not taking the drug; however 25% showed parasites in their blood four days after ceasing quinine, the infection being masked while they were taking the drug, and work being possible. In the extremely malarious part of New Guinea prophylactic quinine failed to avert infection during an epidemic, but the generally mild nature of the attacks enabled work to be completed. In Tropical Africa reports from the Belgian Congo show that 15 grains of quinine twice a week in the hands of H. Seidelin[88] rendered malarial infections few and mild. The Sergent brothers[89] and others in Algeria found that the prophylactic use of quinine was no absolute protection against attacks, but if taken daily rendered them less dangerous. The experience of the writer with reference to the epidemic encountered on the

Indian fronteir agrees with this latter view. At first the failure of a daily prophylactic dose of 10 grains of quinine bi-sulphate in solution to prevent infection gave the impression that the views held of the futility of prophylactic quinine were correct; but an analysis of the records of infection, which showed that nearly 100% were infected chiefly with subtertian malaria, revealed the fact that the mortality and permanent invaliding figures were both nil, and that the nature of the attacks were on the whole less severe than what one would expect from heavy infection with the malignant parasite. J. Thomson(90) found that the prophylactic use of quinine in hyper-endemic areas, even when it does not prevent infection, yet prevents them from becoming severe and pernicious, and maintains the general health; the experiences of the writer agree with this conclusion entirely.

The Fourth Factor is the presence of persons to whom the anopheles may convey the infection. This factor may be eliminated or reduced by segregation of all uninfected or non-immune persons, by screening them from the bites of mosquitoes, and to a certain extent by the use of repellents.

Segregation, first recommended by Stephens and Christophers in 1902, is practised to a varying extent in India. The military cantonments in India, planned and built long before the role of

the mosquito in the etiology of malaria was thought of, are situated usually at some distance from the native city. This must have a beneficial effect on the health of the European population. However, with the increase in the number of Indian shops in the cantonments a new native population has sprung up, and the original segregation of European is threatened.

The purely Railway Communities have a more or less constant population, are well laid out, and have no native quarter comparable to the Sadar Bazaar or Indian shopkeepers' quarters of the military cantonments, so the effect of segregation on the European population is more marked. ~~a potential source of malaria.~~ Segregation cannot be regarded as a practical means of reducing the incidence of malaria in India.

Protection from the bites of infected mosquitoes can be secured by screening, by the use of mosquito nets, and by the use of veils, gloves and mosquito boots. Screening is most useful in endemic localities, where more active antimalarial measures are impossible or are in the process of being carried out. The screening of houses, hospitals and barracks must be complete, and every possible means of entrance of anopheles must be considered. Most of the bungalows and hospitals examined by the writer and supposed to be efficiently screened were ineffective, and in many

cases, the building were acting as large mosquito traps. Hehir puts the number of well screened buildings observed in India as 40 per cent, but in the opinion of the writer even this figure is too high. The chief causes of the lack of success of screening were in order of frequency :- uncovered openings, such as bath-room drainage holes, loop-holes and ventilators, warped and ill-fitting doors, broken and damaged screenes, partial screening, which is worse than useless, and the employment of gauze of too large a mesh. Screening must be complete to be effective, and constant supervision is necessary to have any damaged screens repaired, to see that the swing doors are fitting efficiently and that they are not propped open by careless servants and others. One hospital under the care of the writer was well screened, but a row of loopholes overlooking an evil smelling ditch had to be dealt with before anopheles could be excluded. A bungalow occupied by the writer was perfectly screened, but the mesh of the gauze was less than 12 to the inch, and, though a protection against flies and flying ants and such larger insects, was no bar to mosquitoes, A mesh of at least 16 to 20 to the inch is necessary.

Mosquito nets are efficient when carefully used and when kept in perfect repair. They were issued to the Indian troops in the fort of Chakdara but it

was most difficult to ensure their correct use. The use of mosquito nets does not account for the period from sundown, till the time for retiring. This is a period of great activity of mosquitoes, and, even though a person is awake and often moving, he is sure to be bitten many times, when mosquitoes are numerous, before gaining the shelter of the net. For troops, screened barrack rooms, or even light mosquito-proof huts, as described by Wenyon,(91) would solve this problem.

Veils and gloves were never seen in use in India, but mosquito boots, in the form of ordinary mess boots or Wellingtons, were invaluable. Mosquitoes have a habit of resting under tables and chairs, and in the evenings they often fly close to the ground to avoid the wind from the punkah and the glare of the lights, hence the ankles are a vulnerable part. The punkah or the electric fan is a great protection against mosquitoes, and with the electric fan playing on one's person few mosquitoes will approach.

Various repellents are used smeared on the face and hands or on any exposed part of the body. The commonest in use in India are the oil of citronella, and the common Army modification Bamber oil. The latter consists of citronella 1½ parts, kerosine 1 part, cocoanut oil 2 parts and carbolic acid 1 part. It is supposed to retain its activity for

two or three hours, but mosquitoes have been observed to bite within half an hour of its application. Possibly the duration of protection depends on the voraciousness of the local mosquitoes.

The question arises as to which of these methods of malaria prophylaxis is most suitable for use in India. Each has its place in the prevention of malaria, but the method adopted depends on the local conditions. Generally speaking the only possible way of reducing the incidence of malaria is by anti-mosquito measures. Quininisation is impossible for, apart from the question of cost and the difficulty of administration of the drug, the world's annual output of quinine is insufficient to treat the actual cases of malaria occurring among the civil population in India, without providing for its prophylactic use. Screening is impracticable, except for the European population and for the better class houses Indians, and it is a costly and uncertain method of prophylaxis. Of the Anti-mosquito measures drainage and the supervision and control of canal irrigation are of paramount importance. In many small cantonments and railway townships minor anti-mosquito measures systematically and thoroughly carried out will suffice to reduce the incidence of the disease. In several of the stations visited by the writer antimosquito measures were

in abeyance, or were but superficially carried out. The campaign against the mosquito must be continuous, and any lack of continuity of effort due to the frequent changes of staff which are incidental to life in India must be guarded against. Screening has its place in the protection of Europeans and others in malarious localities. In military service there is the great advantage of discipline and control, and the incidence of the disease in the Army in India might be reduced still further. The rates of admission into hospital of the Indian troops do not give a true estimate of the incidence of malaria. Only the more serious cases are admitted into hospital, and the maximum will be the number of beds the hospital contains; the remainder are classed as "detained" or "excused duty" and treated in their quarters. When the site of a fort or barracks accounts for the high incidence of malaria among the troops, and anti-mosquito measures are not successful in reducing the incidence of the disease, a new site should be selected without delay. The occupation of the same malarious site for year after year, and decade after decade must account for a considerable amount of sickness and a considerable number of deaths.

On active service on the Frontier few anti-malarial measures were carried out, and troops were often quartered in close priximity to highly infected native villages; the fort and village of Shabkadr is a case in point, no quinine was issued and no nets were supplied. It appeared to the writer that the small bivouac nets, such as were used in the Balkans during the War, could be used with advantage on these occasions. They are light and portable and the conditions of frontier warfare, with the absence of shell-fire and the formation of perimeter or walled camps, were most suitable for their employment.

In one camp, near Subhan Khwar, the Mohmand fighting ground, there were swarms of anopheles, one could not move a blanket in ones tent without disturbing numbers of them, and at dawn they could be observed entering the tents in myriads. Much of the malaria could have been prevented by the use of bivouac or other mosquito nets, and by the employment of portable mosquito-proof huts in which the men could sit during the evening hours. Failing these measures, or in addition to them, a prophylactic daily dose of from 5 to 15 grains of quinine, according to the severity of the malaria, was indicated. If the military situation permits, marches should be as short as possible, at the commencement of the campaign,

and should be conducted during the cooler hours of the day, or even during the night in the hot weather. The initial march of this campaign from Peshawar to Shabkadr, a distance of 20 miles, conducted in the heat of a September day, accounted for numbers of casualties from malaria, many being fatal comatose cases.

The omnipresence of malaria in India has often led to its acceptance as a matter of course. The anti malarial measures found most suitable for any district or condition of life must never be relaxed, for it is only by a persistent struggle that the incidence of the disease can be lowered and malaria eventually eradicated.

.. ..

Treatment (b) curative

Early and efficient treatment of all cases of malaria is true prophylaxis, for by such treatment attacks are cut short, the output of gametocytes is diminished and finally arrested, and the cycle of etiology is broken. Quinine is the universally accepted drug in the treatment of malaria, and including the other crystallisable alkaloids of cinchona, is the nearest approach to a specific which we possess.

After a brief reference to its mode of action on the plasmodia, it is proposed to consider the time of administration of quinine, the dosage, and the manner and form in which it should be given. In addition, a few other remedies that have been tried and their limitations will be mentioned.

The mode of action of quinine on the plasmodia:

Originally, it was thought that the manner in which quinine acted on the plasmodia of malaria was a simple one, and that all that was necessary to ensure disinfestation of a malaria patient was to administer sufficient quinine to secure a concentration in the blood inimical to the parasites. Laveran[92] in 1881 found that the addition of a solution of quinine of a strength of 1 in 10,000

caused the death of the malaria parasites, and Binz[93] stated that to destroy the protozoa a concentration of quinine in the blood of 1 in 5000 was essential. Recent experiments have contradicted these assumptions. P.Muhlens and W.Kirschbaum[94] found that defibrinated tertian blood mixed in vitro with a 1 in 5000 solution of quinine hydrochloridge still produced infection when injected into healthy persons after 12 hours incubation at 37°centigrade, and with double that strength of quinine, after 5 hours incubation. Ramsden,[95] in 1918, found it extremely difficult to get a higher concentration in the blood than 1 in 500,000 without severe toxic symptoms. However, Acton[96] found that after a single dose of 20 grains of quinine sulphate the maximal concentration of quinine in the blood was 1 in 150,000, and after a single dose of 10 grains 1 in 250,000, and that for treatment to be efficacious the concentration of quinine in the blood must be maintained between these limits continuously for a period of at least three to four weeks. The action of quinine is not a direct one, and, though numerous hypotheses have been advanced to explain its action, none are conclusive, and the question is still unanswered. J.Morgenroth,[97] from a series of experiments, concludes that quinine is stored or held in the red cells, and that the curative or

prophylactic effects of the drug are due to the negative chemotaxy or repulsion exercised by the cinchonised red cells on the attacking parasites. The theory of Warrington Yorke and J.W.S. Macfie[86] has already been mentioned, and their views explain the occurrence of relapses and the importance of the individuality of the patient in resistance to the disease. It is stated by Acton and Knowles[96] that quinine circulates in the blood as a quinine base, in whatever form it may be administered, and is present in the plasma and on the surface of the erythrocytes, but not within them. Hence such parasites as have become intracellular escape its action. This view does not account for the resistance of the sporozoites injected by the mosquito. It is possible that it is not quinine itself that acts on the parasites, but some metabolite[98] of the drug and that further research will modify our views with regard to the mode of action of the drug. However the plasmodicidal effect of the drug be produced, the following facts are fairly well established. Quinine is most lethal to the amoebulae or spores thrown into the circulation by the process of schizogeny or sporulation. It has less effect during the intracorpuscular stage, but has a more lethal effect on the younger forms of the parasite before pigmentation commences in the red cell. It has little or no

effect on the fully developed schizont and does not prevent it from sporulating. It causes all parasites except the subtertian gametes to disappear from the peripheral circulation in a few days in cases of simple infection. Its action on the gametes is less clear. It is thought that quinine has no direct action on the crescents or subtertian gametocytes, but reduces their number by destroying the asexual forms of the parasite and so cutting off the source of supply. W.M. James[99] agrees with this view, and adds that those gametes that have begun to develop from asexual forms will continue their growth, irrespective of treatment, and will persist for the duration of life of the red cell, which is about 30 days. Bruce Mayne suggests that emasculation of the gametes of plasmodium vivax by quininisation accounts for the persistence of subtertian, but not of benign tertian infections after the administration of the drug. Thus it can be seen that the mode of action of quinine on the plasmodia is still unknown. The effect of the administration of quinine and other alkaloids of cinchona has been closely observed and various theories have been advanced to account for the effects produced, but none are conclusive.

The time of administration of quinine

The ideal time for administration of quinine is a definite period before the next attack of malaria is due to occur, so that the maximum quantity of the drug is present in the circulation when sporulation of the parasite takes place. Cardamatis[100] attaches supreme importance to the time of giving quinine, namely from seven to eight hours before a paroxysm is due, so that the act of schizogeny and the moment of maximum absorption of quinine synchronise. Ross[101] recommends a single dose of quinine daily, four hours before the anticipated rigor. J.D. Thomson[102] concludes that the first essential in the administration of quinine is accurate timing, bearing in mind that it is in the act of schizogeny that the merozoites, being free in the plasma, or merely attached to the red corpuscles, are most vulnerable. Acton and Knowles[103] come to the conclusion that the administration of quinine should be so timed that it reaches the blood stream at the moment when the latter is at its most alkaline tide, and this has been found to be 2½ hours after a meal. Ochsner has advised that 2 grain doses of quinine should be given two hourly day and night for 48 hours, the doses during the night being ensured by the use of an alarum clock; but the results of such treatment have

been unsatisfactory and the method tedious in the extreme. W. S. Dawson[104] however, has found that repeated small doses given throughout the night as well as the day were indicated in the subtertian type of infection with continued fever, met with in East Africa during the war. When a patient is first seen at the commencement of a paroxysm, on the supposition that the younger the form of parasite the more vulnerable it is, quinine should, strictly speaking, be given at once, and there are many who advocate immediate administration of the drug. By what has long been known as the "English method" a diaphoretic, such as aspirin, is given during the hot stage and quinine is withheld until the temperature is falling and the sweating stage has begun. According to Hehir[105] quinine given during the acme of the fever would set up nausea and, perhaps, vomiting. Gordon Ward[106] considers that the oral administration of quinine should be delayed until the temperature has begun to fall. Aldo Castellani[107] holds that the time for giving quinine in malaria in the tropics and malarial countries is "at once." In India the so-called English method is the one in general use, unless there are signs of severe and intense infection, when there must be no delay.

In ordinary cases the delay of a few hours before the temperature begins to fall is not of sufficient consequence to warrant immediate quininisation. The rule adopted by the writer was to commence quinine treatment, provided that no contra-indication was present, whenever the diagnosis of malaria was established by microscopical examination. Timing of the doses in relation to the paroxysms of malaria was possible only in private practice and when the cases of malaria were few. During the malaria season when the hospitals were crowded and the hospital staffs were working at high pressure such a method of treatment was impracticable.

The dosage of quinine

The dose of quinine given is of the greatest practical importance. The "tonic" doses given in the early days of the Great War by medical officers inexperienced in the treatment of tropical disease are well remembered, and at the present day in this country prescriptions of moderate doses of quinine are often returned by the dispensers. Towards the end of the War the pendulum swung to the other extreme and massive doses, such as 90 or even 120 grains daily, were given in an endeavour to prevent relapses. (108) With reference to these large doses Ross points out that the organism subjected to them seems to sense, so to speak, the risk of poisoning, and

throws them out with increased rapidity, so the amount of quinine circulating is lessened not increased by toxic doses. There are numerous standard treatments recommended by different authorities. They usually commence with a dose of 30 grains a day, and decrease in amount until at the end of three or four months 5 grains a day is reached and the course is completed. The maximum efficacious dose may be taken as 45 grains a day, and this is what is recommended at the commencement of the Panama Canal Zone Standard Course for 1925.(109) A series of benign tertian relapse cases were treated by short courses of quinine in doses of from 5 to 120 grains a day by J.W. Stephens(110) and others during the War, and it was found that 10 grains or more on each of two consecutive days caused a cessation of febrile paroxysms and the disappearance of parasites from the cutaneous blood; over 30 grains on each of the two days were necessary for cure, and this curative effect was more marked as the dose was increased from 45 to 90 grains on each of the two consecutive days; by that maximum dose 62% of cases were prevented from relapsing. Experience has shown that, though possible in the United Kingdom, the administration of such large doses is not without danger in a

tropical country, and that 30 grains a day is the maximum safe dose in India. Hehir recommends for use in India a standard course of quinine lasting for twelve weeks. During the first week 30 grains a day are given for three or four days alternating with 20 grains a day according to the type of infection, then 15 grains, 10 grains, and lastly 5 grains a day are given for the remainder of the period. The United States' Standard Course[111] consists of 30 grains of quinine sulphate daily for three or four days or for as long as the fever persists, and then 10 grains nightly for eight weeks. It is claimed that 90% of cases are cured by this course, but it is not sufficient for Tropical countries such as India. In South Africa J. Pratt-Johnson and K. Gillchrist[112] recommend 10 grains of quinine three times a day for three weeks, twice a day for one month, and once a day for two months. In the military hospitals in Northern India during the War a course of 30 grains of quinine daily for three weeks reduced the number of relapses to the low figure of 6·5%. The writer has personally experienced two quinine courses. One consisted of 30 grains of quinine sulphate in solution daily for one week, 20 grains for two weeks and ten grains daily for two months, and was undertaken while doing full duty in the desert of Palestine. No relapse occurred but it was considered that the debilitating effect of

the course under active service conditions was more severe than the occasional attack of benign tertian malaria had been.

The second course, this time for a fresh infection of malignant tertian malaria, was of approximately the same dosage, and duration, but it was commenced in hospital, continued in convalescent camp and while doing light duty so that ill effects of the treatment were not appreciable. Different courses have been tried in India, and there was no pronounced difference in the results obtained. Usually, 30 grains a day was given for the first week and the patient was kept in bed for this period, then 20 grains a day was given for six days a week for two or three weeks according to the severity of the infection, and then from 7½ to 10 grains a day often combined with iron and arsenic, for six days a week for two months. It is considered that it is the patient who must be treated rather than the disease. The adoption of hard and fast rules for quinine administration and standard quinine courses for each type of infection rather overlooks the personal factor of the natural resistance to the disease. The question of the dosage of quinine according to the age and sex of the individual is usually considered, but not so often the question of dose in proportion to weight. The dose of quinine should be less for debilitated

patients who are below the average weight for their age and height. In convalescent and ambulatory cases the ill effects of quinine must be watched for, not necessarily the classical signs of cinchonism, but gastric and intestinal catarrh, loss of weight, and a lowering of the vitality, and the dose of quinine reduced accordingly. Care must be taken to distinguish cases in which the symptoms are not due to the effect of quinine, but to latent malaria, in which an increase of the dose of quinine will cause a disappearance of the symptoms.

The manner of administration of quinine

Quinine may be administered by the oral, intra muscular, intravenous, rectal and subcutaneous routes. The advantages of taking quinine by the mouth are sufficiently obvious; it can be taken and given by anyone, no skilled medical attendance is required, and the dangers are infinitesimal. The disadvantages are the unpleasant taste of quinine, the occasional inducement of nausea and vomiting, and the diminished amount absorbed when gastric and intestinal catarrh is present. Quinine idiosyncracy is so rare that it need not be considered. For unconscious and comatose patients, where nausea and vomiting is pronounced, and where a rapid effect is essential, the oral route is contraindicated. The disagreeable taste of quinine

can be overcome by the use of powders taken in moistened rice wafers, by the use of tabloids, tablets, capsules or pills, or by the use of a tasteless preparation of quinine. Some of the more insoluble salts of quinine are practically tasteless, such as quinine ethyl carbonate or euquinine, and the tannate of quinine. The former drug is very expensive and has to be given in large doses to be effective; the latter was much used, often in combination with chocolate, in Italy and also in Greece in the early days of anti-malaria measures, but the results were not satisfactory and the drug is little used now. During the period the writer was in India quinine sulphate in solution was used almost exclusively, but it is said that nowadays tabloids of the sulphate or bi-sulphate of quinine are used in the army in India. It has been shown (113) that quinine appears in the urine from 2 to 2½ hours after the oral administration of tabloids of quinine, that it reaches its maximum concentration between 5 to 10 hours, and disappears 27 hours after administration. The oral route is the channel of administration par excellence. It is the route employed universally in India, unless the indications for another mode of administration are imperative.

Intramuscular injection

There are many schools of thought with reference to intramuscular injections. There are some who recommend the treatment of acute cases by intramuscular injections alone; others commence treatment with a series of intramuscular injections and continue with oral quinine; others who reserve this treatment for grave cases and for cases which cannot absorb or take quinine by the oral route ; others again consider that this route should never be employed. During the War period, the apparent failure of oral quinine to cure cases of malaria and to prevent relapses, and the number of severe types of the disease encountered led to the extensive use of this method of treatment, and the results obtained were not always satisfactory, Possibly the same factor that rendered oral quinine inefficacious, namely the lowered resistance of the individual, led to the frequent ill effects of intramusuclar injections; The dangers of this form of treatment are, the production of local necrosis of tissue, the paralysis of nerves adjacent to the site of injection and more rarely tetanus.(114) The necrotic effects upon the tissues of intramuscular injections of quinine has been studied by Manson-Bahr,(115) who examined at autopsy the sites of

infection in fatal cases, and from his experiences came to the conclusion that quinine so injected has its distinct beneficial usage, but is liable to abuse, and that injections in debilitated, anaemic and emaciated subjects are to be avoided. H.W. Acton[116] ascribes this local necrosis to the effect of the strong acid solutions injected and not to the quinine itself. The strength of the solution has been attacked and dilute solutions are recommended by the brothers Sergent[117] who state that the strength should not exceed 3%. The three cardinal rules of[118] 20 years ago, namely strict asepsis, deep injections and dilute solutions, hold good to-day. There is considerable difference of opinion with reference to the harmful and beneficial effects of intramuscular quinine. Acton and Knowles[119] condemn the practice and consider that it should be given up. Fletcher[120] came to the conclusion that after intramuscular injection, quinine is absorbed less rapidly than after oval administration, and that the method does not maintain an effective concentration of quinine in the body for a longer period than does quinine orally. On the other hand, in the severe subtertian malaria of Tropical America Mac Phail[121] uses intramuscular injections in all grave cases and has given 15,000 injections without mishap. Roche[122] obtained rapid and complete sterilisation of malignant malarial cases in Africa by eight intra-

muscular injections of 7½ grains of bi-hydrochloride of quinine. C.G. Stephen[123] looks upon intramusuular injection of quinine as a sheet-anchor in all obstinate and chronic forms of the disease. Leonard Rogers[124] recommends the use of intramuscular cinchonine hydrochloride, and in severe cases of malaria, during prevalence of pernicious forms, and for patients who vomit orally administered quinine, he advised intramuscular injections of cinchonine acid hydrobromide. From experiments on rabbits he found that the latter drug causes no local necrosis of tissue and is more completely absorbed than quinine. The same authority found intramuscular injections most useful in chronic and relapsing cases chiefly of benign tertian type. Intramuscular quinine has a definite place in the treatment of malaria. In obstinate cases and in those which have gastric symptoms one or two injections will cause complete cessation of the paroxysms and complete disappearance of the asexual forms of the parasites from the peripheral circulation, and in most cases oral treatment can then be commenced. Severe cases of subtertian malaria and those with an exceptionally large proportion of parasites in the cutaneous blood call for intravenous rather than intramuscular quinine. Strict asepsis and attention to detail is essential in intramuscular injection. The solution should be

boiled or carefully sterilised in an autoclave. The dose usually administered was from 10 to 15 grains of the bi-hydrochloride in from 2 to 5 c.c.m. of normal saline. From a number of intramuscular injections given by the writer no bad results can be recorded.

Intravenous Administration of Quinine

It is stated that this mode of administration of quinine was introduced by Bacelli in 1890(125). This method was used extensively during the War, and there was much conflict of opinion with regard to its application in the treatment of the disease. Some held that such treatment should be reserved for pernicious cases: others that resistant and chronic cases should be given an intravenous course of quinine; others again that it should form part of the routine treatment of the disease. The chief superiority of this form of administration is the certainty and rapidity of absorption of the drug, but the action is a transient one, and Ramsden and Lipkin(126) state that 90% of the quinine given in this way disappears from the blood stream within one minute. There are definite dangers associated with intravenous quinine. There is the risk of sepsis; there is a fall of blood pressure which may be accompanied by heart failure; the rapid destruction of parasites may flood the body with liberated malaria toxins and paralyse the cardiac mechanism. Some

observers have given a large number of injections without untoward symptoms, for instance Cantlie and Moubarek[127] in a Soudan epidemic gave 2,484 intravenous injections with fainting on two occasions only, but the general concensus of opinion is that such treatment should be confined to grave cases and that it should not be undertaken lightly. The unfortunate results of intramuscular injections and the failure of oral quinine to prevent relapses led many to turn to intravenous methods of quinine administration during the war period. Leonard Rogers [128] recommended vigorous treatment of primary attacks by intravenous injections followed by prolonged oral administration of quinine. J.D. Thomson[129] concluded that the intravenous route has special advantages during the active periods of the disease, for by this route the full quantity of quinine can be concentrated against the parasite when it is most vulnerable to the action of the drug. Henri Soulie[130] considered the intravenous and intromuscular the best methods of administering quinine in all cases. R. Knowles[131] concluded that the intravenous administration of quinine was the quickest and surest method of cutting short a febrile attack of malaria, that it was a perfectly safe method and was infinitely preferable to intra-

muscular injections from every point of view, but that it could not be relied on to exterminate the parasite from the patient's system amd should be supplemented by an oral course of quinine. However, Leonard Rogers[132] now states that the method is no more efficacious than the oral route and should be confined to grave cases, to cases of cerebral malaria, and to cases where 12 or more parasites are observed in one miscroscopic field. In Macedonia A.G. Phear[133] noted many cases of cerebral malaria saved by intravenous quinine. As in intramuscular injections attention to detail is all important. Strict asepsis must be observed. From 7½ to 15 grains of the acid hydrochloride in from 10 to 20 c.c. of sterile saline should be used. Rogers[134] found the acid hydrobromide of quinine les toxic and just as efficacious and that salt is recommended by Acton and Knowles[135]. Should the blood pressure be low and circulatory failure possible, 5 minims of a 1 cm. 1000 solution of adrenalin may be added. The injection must be made very slowly and with the patient in the recumbent posture. The intravenous route is used much less in India than the intramuscular. It must be remembered that fully qualified medical men are relatively few in that country, and that the method involves a degree of skill and precision which all who are called upon to treat cases of

malaria do not possess. In skilled hands this mode of administration of quinine is invaluable, and by the timely injection of intravenous quinine many lives have been saved.

Rectal Administration

This method of administration of quinine has fallen into disfavour of recent years. It has certain advantages. It is easily and safely administered by subordinate medical officers, and it is comparatively painless. In an epidemic and in districts where more skilled medical attendance cannot be obtained these points are of the greatest importance. On the other hand, many have found that the absorption of quinine is irregular and small when this method is used, and that pain, tenesmus and even dysenteric symptoms may be produced. Fletcher(136) found that quinine was not well absorbed after rectal injection, and by testing the urine found that little was excreted, and that the method was liable to cause pain, irritation, and severe dysenteric symptons. On the other hand H.B. Newham(137) states that the method is safe and effective. Henri Soulie(138) concluded that the rectal method gave no results and was badly borne. It is an uncertain method, but of value when the drug is not retained by the mouth, and in the treatment of children. Twice or thrice

the oral dose must be given and, if rectal irritation be feared, 10 to 15 minims of the tincture of opium may be added to each dose. The injection should be made slowly through a rubber tube or catheter and should be given as high up as possible. The acid hydrochloride of quinine should be used dissolved in saline with the addition of the minimum quantity of hydrochloric acid, or better still, tartaric acid, necessary for complete solution. The strength of 1 grain of quinine to 1 dram of saline is recommended. In one hospital taken over by the writer, this method was used extensively by the assistant surgeon in cases where oral quinine could not be given or failed to reduce the temperature. There were no ill effects from the treatment and the results were quite satisfactory, though the numbers so treated was not sufficient to be conclusive. In severe cases the use of the method was not attempted, but recourse was had to intramuscular or intravenous administration. The method is of considerable value in the treatment of children, and hourly rectal injections of from 2 to 5 grains of quinine in half an ounce of normal saline are well borne in cases of malarial convulsions.

Subcutaneous administration

This method was first employed by Bourdon[139] in 1863. The writer has never used this method, nor

seen it used in India. Hehir[140] mentiones this mode of administration only to condemn it. It has some supporters. N. Pende[141] of the Italian army recommends the use of quinine subcutaneously in physiological salt solution and with ½ c.cm. of a commercial solution of adrenalin added to each dose, and advises that the treatment be kept up for two months. C.A. Johnston[142] alone of writers in India recommends the use of subcutaneous injections. He uses a dilute solution of 4 grains of quinine bi-sulphate in 20 c.cm. of sterile saline solution. This method is seldom if ever used in India.

Though many other remedies have been tried in the treatment of malaria, at present quinine has no serious rival in the field. There are signs that cinchona febrifuge, which contains a percentage of quinine and which was used originally in the treatment of malaria in India, may again replace the use of the single alkaloid in the future, but the position of quinine still remains unassailed. Among other drugs that are used in the treatment of malaria salvarsan, plasmochin, arsenic and iron will be considered.

Cinchona febrifuge consisted originally of the mixed alkaloids extracted from the bark of cinchona succirubra. With the increased demand for the alkaloid

quinine, a policy began to be adopted of replacing C. Succirubra on the plantations by species yielding larger quantities of quinine, and the constitution of cinchona febrifuge became altered, so that after 1903 it came to represent a mixture of the residual alkaloids remaining after extraction of quinine from the barks of C. Ledgeriana and its hybrid with C. Succirubra, a certain amount of quinine being added to make it approximately similar to the original cinchona febrifuge. The treatment of malaria by cinchona febrifuge has been successful in many hands. Acton and Knowles(143) record good results, and have adopted the use of cinchona febrifuge as a standard treatment of malaria. W. Fletcher(144) found it as efficacious as quinine, and investigations are still in progress comparing the efficacy of the two drugs. The chief disadvantages in the use of cinchona febrifuge are the inconstant composition and the difficulty of standardisation of the drug. Could the febrifuge be standardised, and should it be proved as effective as quinine, its use would mean a great economy, for its price is only Rs. 9 per lb. as compared with Rs. 29 per lb for the sulphate of quinine. Moreover, the cultivation of C. Succirubra could again be taken up, and, that species being hardier and yielding more bark than the others, a

further economy would be made. The writer seldom used this drug in the treatment of malaria, supplies of the dependable quinine always being available.

Salvarsan was much used during the war, and immediately after, in the treatment of malaria. It was chiefly used for chronic and relapsing cases, more particularly those of benign tertian type. Investigating the effects of a single intravenous injection of this drug in acute cases of malaria, J.W.W. Stephens[145] and others came to the conclusion that the fever was controlled and parasites disappeared from the cutaneous blood in one day in simple benign tertian cases, but that the curative effect was nil. J. Norcott d'Esterre[146] reported that 20 cases of malaria, 12 benign tertian, and 8 subtertian, were treated with a series of intramuscular injections of novarsenobenzol without a single relapse. The experiences of many observers have led to the following conclusions:- Salvarsan and its congeners are contra-indicated in subtertian malaria, for occasionally, disastrous effects are produced; in chronic cases of benign tertian malaria the drug is fairly successful, but rather on account of its general tonic action, than a specific action on the parasites; in acute cases of benign tertian malaria it causes the parasites to disappear from the peripheral circulation more quickly than when quinine is

used.

Plasmochin is a synthetic "Bayer" drug recently introduced. It is fairly successful in the treatment of benign tertian malaria, but in the treatment of cases of subtertian infection must be combined with minute doses of quinine to be effective. It differs from all other known drugs in that it causes the rapid disappearance of crescents, the gametocytes of malignant malaria, from the peripheral circulation. It has a low margin of safety and overdose causes cyanosis, methaemoglobinaemia, and, in severe cases of overdosage, methaemoglobinuria and death. This is the first synthetic drug which has been prepared with a specific action on the malaria parasites, and it may be regarded as the beginning of a new series of antimalarial drugs. Tartar emetic has been given intravenously by Rogers[147] in the hopes of killing the crescents of malignant tertian malaria, but the results were not conclusive. It has no effect on the asexual forms of the parasite, and Hughes[148] considers that it is rather a general protoplasmic poison, than a specific poison for the malaria parasite.

Arsenic has been reputed to cure malaria, but experience has shown that it has no direct effect on the parasites. It is merely a haematinic, and its tonic properties render it of great use in the treatment of chronic and relapsing malaria. It is often

combined with the quinine in the latter months of a quinine course, and is invaluable in malarial cachexia. Iron is largely used in chronic malaria to combat the anemia. In the military standard quinine course recommended by Ross[149] during the War, iron strychnine and arsenic are combined with the quinine throughout the course. According to Gordon Ward[150] the administration of iron for the anaemia of malaria is unnecessary, is often not well borne, and so is actually undesirable. This observer holds that numbers of red cells are destroyed by the parasites and by toxic haemolysis, and that a large proportion of the iron is retained in the internal organs, so that further administration of iron is not required. The writer considers that arsenic is more efficacious than iron in the treatment of post-malarial anaemia.

The majority of the above methods of treatment by quinine aim at the destruction of the malarial parasite. Referring again to the hypothesis of Yorke and Macfie[86], the destruction of the parasites by the action of quinine is only part of the treatment. The resistance of the individual must be maintained or increased, so as to ensure a sufficient output of immune body and so eradicate the parasites from the system. Rest in bed is essential during the first week of treatment and while large doses of quinine are being taken. The bowels must be kept

open, and a preliminary dose of calomel is usually indicated. For the same reason a saline aperient such as the sulphate of magnesia is often prescribed with the quinine throughout the course of treatment. Nourishing food and complete rest of mind and body are essential for a cure. The principle of evacuating all cases of malaria for a two months course of treatment at the Base, which was initiated in the latter years of the War, was a sound one, Though a man may appear fit to carry on, after an attack or two his vitality is lowered, he is prone to fall a victim to other diseases, and he is a source of danger to his comrades. The mental effect of repeated attacks of malaria and of large doses of quinine accounted for many cases of so-called acute mania which occurred among troops in the front line. Hospital treatment, and preferably base hospital treatment, is essential in time of War. In India under peace conditions the problem is a different one. After a period in hospital cases occurring among Europeans during the hot season should be sent to a hill station for the remainder of the treatment. For Indian troops a long period of light duty is recommended, for leave to return to their homes would most likely mean a discontinuance of quinine.

On one occasion, the blood of all Indian soldiers

returning from home leave was examined for malarial parasites, and no less than 75% of the films examined were positive.

The oral course administered consisted of ten grains of quinine sulphate in solution three times a day for seven days, then 20 grains a day in three doses for six days a week for three weeks, then 10 grains a day in two or three doses for two months. Europeans were often given quinine bi-hydrochloride in powder form in gelatine capsules for the first three or four weeks of the course, and the same drug in tabloid form for the remainder of the course.

Intramuscular injections were reserved for cases with gastric symptoms and for cases where oral quinine failed to reduce the temperature or arrest the paroxysms. One or two such injections of 10 grains of the bi-hydrochloride of quinine usually sufficed and then the oral course was commenced.

Intravenous injections were given to grave cases only, namely those with severe cerebral, abdominal and pulmonary symptoms. In comatose cases with signs of cardiac embarrassment, a preliminary injection of one or two pints of normal saline intravenously was given, after abstraction of venous blood, when the blood pressure was high. The usual dose of quinine in the intravenous injection was 10 grains of the bi-hydrochloride in 10 C.CM. of normal saline.

Rectal injections were given with success for the same indications as the intramuscular injections. A few cases, however, did not respond to this treatment, and required an intramuscular injection of quinine before the temperature fell or the paroxysms ceased.

Subcutaneous injections were never given.

Cinchona Febrifuge was seldom used owing to the difficulty of standardisation, and the adequate supply of quinine available. Salvarsan was tried in several cases of chronic benign tertian malaria. One or two injections were given of 0.3 grains of Novarsenobillon, but the results were in no way superior to those obtained after a complete oral course of quinine. Plasmochin had not been introduced when the writer was in India, Iron and arsenic were found to be of definite value in cases of malarial cachexia, and were often combined with the quinine in the oral course. Rest and general tonic treatment was found to be of an importance little inferior to the use of quinine in the treatment of malaria.

... ...

5. CLINICAL CASES

In this section it is proposed to record a few notable cases, to give the results of treatment, both prophylactic and curative, and to mention the diagnostic methods employed and other noteworthy points.

The most resistant cases of malaria encountered were due to the benign tertian parasite. These cases resembled the chronic and relapsing cases of the War period, and the only satisfactory treatment was their transference to a hill station, or better still, to the United Kingdom. In the opinion of the writer these resistant forms of malaria were less common among the Indian troops than among the Europeans. The following two cases are illustrative of this form of the disease.

Case I. European, Lieutenant Mahrattas, aged 22 years. The patient was infected with benign tertian malaria in Muscat in Persia, 12 months previously. He had been treated by oral courses of quinine, by intramuscular injections, and by intravenous injections of salvarsan, but was still subject to severe attacks of malaria. He was anaemic and his spleen extended a hand's breadth below the left costal margin. He was put on a course of quinine, iron, and arsenic, and sent before a

medical board for invaliding to the United Kingdom. Though discharged from the Army on medical grounds, the result of treatment in this country was so satisfactory that he was enabled, subsequently, to take up a permanent appointment in the East.

Case II. European Captain Mahrattas, aged 28 years. The patient was infected with benign tertian malaria in India six months previously. There were frequent relapses of malaria, the spleen was palpable and enlarged, and the patient was very anaemic. Any extra exertion or chill brought on an attack, though the attacks were not so severe as in the case above. He had been treated by oral quinine courses, and by intramuscular injections. He, also, was put on a course of quinine, iron and arsenic and sent before a medical board. Sick leave to the hills was granted, but the result was not satisfactory, so the patient was invalided to the United Kingdom, where he was cured.

The severe or pernicious forms of the disease were due, usually, to infection with the subtertian parasite, though one case, at least, was due to benign tertian malaria. These pernicious forms of malaria may be classified into cerebral, abdominal and pulmonary types. Early diagnosis and early treatment is essential. Of the cerebral types of

malaria the commonest variety encountered was the comatose. These comatose cases occurred, almost without exception, among subjects of latent, untreated or insufficiently treated malaria. The usual history was that the patient had been feeling out of sorts for a day or two, and then, suddenly, often while on parade or engaged in physical exercise in the heat of the day, collapsed from what was supposed to be sun-stroke. On admission to hospital the patient was unconscious and hyperpyrexial and active treatment was essential to save his life. Patients admitted into hospital suffering from malaria of ordinary severity rarely, if ever, pass into coma.

The first cases of this nature occurred during the initial stages of the Indian Frontier Campaign. The column set out from Peshawar and marched the 20 odd miles to Shabkadr in the heat of a September day. So many men fell out from malaria and heat-stroke that the following ambulances were soon filled, and civilian tongas had to be requisitioned to convey the serious cases back to Peshawar hospitals. Many of the cases diagnosed as suffering from heat-stroke were found to be due to malignant malaria, and there were many deaths. Being on the march, with only such medical equipment as could be carried by pack mules, all that could be done for these cases

of severe and comatose malaria was to evacuate them to hospital as quickly as possible. That such cases stand rapid evacuation badly was the experience of Manson-Bahr[151] during the Palestine campaign, but there was no alternative under the conditions of frontier warfare.

The following cases are typical of those met with under peace conditions.

Case III. Punjabi Mussulman Transport driver, aged 28 years. The man was present on the sick parade in the morning and complained of headache and lassitude. His temperature was normal, and on examination, no abnormal physical signs were detected. He gave no history of recent illness or fever, but appeared to be dejected and fatigued. A tonic was prescribed and he was excused duty for the day and ordered to report for further examination on the following morning. At 3 p.m. word was brought that the man had collapsed while crossing the parade ground, and had been brought into hospital in an unconscious condition. On admission to hospital his temperature was 105°F. and he was comatose. Ice packs were applied, and, after venesection, an intravenous saline injection was administered, but the patient died one hour after admission. The temperature rose to 108.2°F. and

remained high for some time after death. This was the highest temperature ever recorded by the writer. A blood film taken from this case revealed a heavy malignant tertian infection. The severity of the infection, and the condition of the patient contra-indicated quinine.

Case IV. Churka Rifleman, aged 25 years. The man was taken ill while on parade and was admitted to hospital in a semi-conscious condition with a temperature of 103.8°F. A blood film was taken and revealed the heaviest infection of benign tertian malaria ever seen, many forms of the parasite being present, including mature schizonts. The patient became comatose soon after admission. An intravenous injection of 10 grains of quinine bi-hydrochloride was given, and later, intravenous saline, but the patient died four hours after admission to hospital.

Case V. Eurasian woman, aged 30 years. She had been treated for a miscarriage two days before admission to hospital by the Indian assistant surgeon. He stated that her temperature, which had previously been normal, suddenly went up to 104°F. and that she became unconscious; so he sent her into hospital. On admission she was moribund, and she died soon after. A blood film showed malignant tertian parasites.

Numerous other cases could be given, but these three fatal cases are mentioned to show the sudden onset of this type of malaria and its liability to occur in latent cases untreated by quinine.

Severe abdominal types of malaria were not so common under peace conditions as they were on active service on the Frontier.

The abdominal cases encountered could be divided into three varieties: firstly, those with dysenteric symptoms; secondly, those with symptoms of an acute abdominal condition; and thirdly, those with symptoms of cholera, the so-called choleraic form of malaria. Those of the first variety were the most common. The symptoms were usually of anorexia, sometimes nausea and vomiting, and pain, tenesmus, and frequent evacuations of blood and mucus. A temperature chart, and microscopic examination of the blood and faeces, alone can distinguish these dysenteric forms of malaria from cases of true dysentery, though an enlarged and tender spleen suggests malaria. The possibility of the co-existence of malaria and dysentery must be borne in mind. Practically all the deaths which occur in the Indian villages from this form of malaria, are returned officially as being due to dysentery, for it is seldom possible for the layman or unqualified

practitioner to distinguish between the two conditions.

Case VI. Jat cavalryman, aged 22 years. The patient was admitted to hospital as a case of dysentery. He had a coated tongue, his temperature was elevated, and he had an enlarged and tender spleen. He was passing frequent stools containing blood and mucus. A blood film revealed malignant tertian parasites, and the administration of oral quinine resulted in a cessation of the dysenteric symptoms and eventual restoration to health.

Case VII. Captain, Indian Army, European, aged 24 years. The patient had a history of mild attacks of fever, of diarrhoea of moderate severity, chiefly after meals, and of having on two occasions passed blood with the stools. On admission to hospital the patient was apyrexial, the spleen was not palpable, but the tongue was coated, and the patient appeared to be anaemic and ill. The stools were formed, but contained mucus. On microscopic examination of the faeces, neither amoebae not cysts were found, but a blood film revealed benign tertian parasites. The diagnosis of malarial enteritis was made and an oral course of quinine was commenced and resulted in a complete cure.

The second variety of abdominal malaria was not so common. One typical case will show the difficulty of diagnosis from an acute abdominal condition.

Case VIII, Lieutenant, British Army, aged 21 years. The patient, while supervising the construction of wire entanglements on the Frontier, was seized with acute abdominal pain. The pain was situated in the right hypochondrium and was agonising in character. Nausea was felt, and retching was caused, but only a little mucus was vomited. The passage of a copious semi-solid green coloured stool gave a little relief, but the pain was still intense. An ambulance was sent for and the patient was brought into the Field Hospital in a collapsed condition. On admission the patient looked pinched and anxious, his pulse was 126, his extremities were cold, yet the temperature was 102·4°F. On abdominal examination, rigidity of the right rectus was noticed, and there was tenderness on pressure over the right hypochondrium. A blood film showed malignant tertian malarial infection. Ignoring the blood film, the condition suggested acute cholecystitis or other acute abdominal condition. An intramuscular injection of 10 grains of quinine bi-hydrochloride was given, and the pain went away as suddenly as it had come on. On the following day tenderness could not be elicited, and there were no abdominal symptoms. The patient made an uninterrupted recovery and was put on a course of oral quinine.

The third variety of abdominal malaria is the choleraic. The following case occurred at Chakdara during the malaria season, and the fact that the patient was a follower and not a soldier, suggested that the issue of prophylactic quinine had not been taken.

Case IX. Hindu Follower, aged 20 years. The patient was admitted to hospital as a case of cholera. His temperature was subnormal, his pulse was rapid and barely perceptible, and he was vomiting, retching, and passing copious water evacuations. The watery stools were almost colourless and the difference from a typical cholera stool must have been very slight. A blood film was taken, and an intravenous saline was given at once. The film showed malignant tertian parasites, so 10 grains of quinine bi-hydrochloride were given intravenously, and as soon as the gastric symptoms had abated, an oral course of quinine was commenced. The recovery was uneventful.

The pulmonary type of malaria was fairly common under active service conditions, but not so common in time of peace. The following case, the first of this type of malaria met with, suggested to the writer before the diagnosis was established that pneumonia in India must be quite different from the same disease in Europe; that the resistance of the Indian to that disease must be very small; or

that there must have been an error in diagnosis.

Case X. Sikh artilleryman, aged 30 years. The patient was admitted into the Field Ambulance as a case of pneumonia. His temperature was high and there were signs of slight congestion of both lungs. A blood film was examined but the result was reported to be negative. He was evacuated to hospital forthwith as an early pneumonia. It was reported later that the patient had died in hospital a few hours after admission and that by a further examination of the blood a diagnosis of fulminant pneumonic malignant malaria had been made. As mentioned above, the severe types of malaria were more prevalent during the Frontier campaign than under peace conditions. It was noticed that there was a seasonal maximum incidence of the three types.

During the height of the hot weather cerebral cases were more frequently met with; as the temperature, especially the night temperature, fell and autumn approached, dysenteric cases were more numerous; and, as the day and night temperatures fell still lower and the cold weather set in, the pulmonary type prevailed. The occurrence of cases of heat-stroke, true dysentery, and pneumonia during these same periods rendered the diagnosis more difficult. Fatal and pernicious cases were more prevalent when the troops were on the march or engaged in active operations against the enemy, than

when they were stationary. Maniacal types of cerebral malaria were occasionally seen. The following case, though not proved to be malarial, might well have been a suicidal type of the disease, occurring as it did during the height of the malaria season on the Frontier campaign, when pernicious forms were prevalent.

Case XI. Jat Pioneer, aged 24 years. The patient had been on the morning sick parade complaining of debility. The regimental medical officer gave him a tonic and marked him for duty. That night at about 2 a.m. a shot was heard and the sentries, on entering the tent in which he was quartered, found that he had shot himself through the head, with his service rifle. The other nine occupants of the tent knew nothing of the occurrence till awakened by the report of the rifle.

Under peace conditions the diagnosis and treatment of all forms of the disease was less difficult. Early microscopic diagnosis is all important. The following case illustrates the difficulty of diagnosis of cases of continued fever in the tropics, and the fallacy of assuming that, because malarial parasites are found in the blood, the condition is wholly malarial.

Case XII. Mahratta Sepoy, aged 32 years. The patient was admitted to hospital as a case of

"clinical" malaria. A blood film showed the parasites of benign tertian malaria, though the temperature chart was not typical and resembled at first that of subtertian malaria. There were physical signs of chronic bronchitis. The spleen was palpable, but neither tender nor much enlarged. Quinine was administered orally, rectally, and intramuscularly, yet the temperature remained elevated and after a period of irregularity began to swing regularly betwee 100°F. in the morning and 102°F. and 103°F. at night. The sputum was examined, but no tubercle bacilli were found. A specimen of blood was sent to the laboratory for a Widal test, but the result was negative. The pyrexia continued with little variation and the physical signs in the chest became very suggestive, but it was not until the third week that, after repeated examinations, tubercle bacilli were found in the sputum and the diagnosis of pulmonary tuberculosis was established.

The small epidemic of malignant malaria at Chakdara is typical of what occurs in military posts on the Indian Frontier, where the endemicity of malaria is high. The situation of the Fort has been described above, and the possibility of preventing the incidence of malaria by anti-mosquito measures alone was remote, for nothing short of removal of the garrison would have been efficacious. The garrison consisted of the headquarters and two

companies of an Indian infantry battalion recently transferred from Belgaum, an area of low endemicity in the south of India, a detachment of artillery, an Indian Station hospital staff, telegraphists, servants and followers, in all approximately 600 men. In addition there was a permanent civilian population of approximately 100 persons, consisting of the Indian post office staff, shopkeepers, dairymen and their wives and families. When the writer assumed medical command of the station he was instructed to use his own discretion with regard to the administration of prophylactic quinine, and to employ whatever form of treatment was considered necessary. The malaria season had commenced and major antimosquito measures being impracticable, it was decided to rely on minor measures, the use of mosquito nets and repellents, and on prophylactic quinine. In August a prophylactic issue of quinine was commenced. This consisted of 10 grains of the sulphate of quinine in solution, administered under personal supervision between 5 and 6 p.m. daily, this time being most convenient for the troops. The civilian population did not attend the quinine parades and did not come to the military hospital, for treatment, so that an important source of infection of the anopheles could not be controlled.

Towards the end of August cases of malaria began to occur, and these increased in number throughout

September, until in the middle of October, the cases of malaria on the morning sick parades averaged between 80 and 90. The hospital was soon filled and extra accommodation had to be found for the malaria cases in empty quarters in the Fort, and, when these were filled, cases had to be treated in their barrack rooms. The Indian troops were supplied with mosquito nets, but the writer was not satisfied that these were used correctly, and in any case, the men were exposed to infection during the evening hours. Bamber oil was issued to men on guard duty at night, and a supply was sent to each barrack room for use during the evening. The prophylactic dose of quinine was well borne, but apparently, had small effect in reducing the incidence of malaria. So great was the number of cases that occurred after any military operations or exercises, that these had to be suspended and the minimum amount of work carried out. By the end of October a large proportion of the garrison was on a course of quinine, and the number of cases of malaria commenced to fall.

The following cases are typical of those met with during the epidemic.

Case XIII. Havildar, 117th Mahrattas. Admitted to hospital with a temperature of over 103°F. A blood film showed benign tertian rings. He had

three days quotidian fever in spite of 30 grains of quinine sulphate orally per diem, and then the fever became tertian. Two intramuscular injections of 10 grains of quinine bi-hydroch-loride on two successive days in addition to the oral quinine caused a cessation of the parozysms, and the oral course was then continued.

Case XIV. Sepoy, 117th Mahrattas, admitted to hospital as a "clinical" case of malaria with a temperature of 102°F. A blood film showed malignant rings. An oral course of quinine was commenced and resulted in a fall of temperature on the third day and no relapse.

Case XV. Sepoy, 117th Mahrattas. Admitted to hospital with a temperature of 103. A blood film revealed a heavy malignant infection. The temperature remained elevated for three days in spite of oral quinine, so three rectal injections of 20 grains of quinine hydrochloride in 2 ounces of normal saline were given at intervals of two hours. The temperature fell to normal on the fourth day and the oral course of quinine was continued.

Case XVI. Lieutenant, British Army. Admitted with typical attack of malaria. A blood film revealed malignant tertian rings. An oral course of quinine was commenced and the temperature fell on

the fourth.day. The spleen was slightly enlarged and there was tenderness on pressure over the liver. Slight icterus developed and persisted for several days. An examination of the blood during the second week after the initial attack showed malignant crescents. Convalescence was accompanied by great depression of spirits, and the patient was transferred to the United Kingdom.

Case XVII Sepoy, 117th Mahrattas. Admitted with a typical malaria attack, but suffered from nausea and vomiting. A blood film showed malignant tertian rings.. Oral quinine being contra-indicated three doses of 20 grains of quinine hydrochloride in 2 ounces of saline were given rectally every two hours. On the second day oral quinine was commenced and the patient made an uninterrupted recovery.

Case XVIII Sepoy, 117th Mahrattas. Admitted with attack of malaria. Spleen enlarged and tender. A blood film showed benign tertian parasites. Oral quinine was given and caused a cessation of the paroxysms, but a relapse occurred on the eighth day. Two successive daily intramuscular injections of 10 grains of quinine hydrochloride were given and the oral course of quinine was continued. The patient had no further relapse while under observation.

Case XIX Sikh artilleryman. Admitted to

hospital with severe malaria and congestion of the lungs, a blood film revealed malignant rings. Oral quinine was given and in addition 10 grains of quinine hydrochloride intravenously. The patient made a slow recovery and was granted sick leave before returning to duty.

Case XX. European male child, aged two years. The child had a severe convulsion after complaining of feeling tired and of his legs aching. A blood film was taken and showed malignant rings. The temperature was over 104°F. Three hourly injections of 2½ grains of quinine bi-hydrochloride dissolved in half an ounce of mucilage were given per rectum, and when the convulsion had passed off 5 grains of euquinine was given orally, and the same dose was continued three times a day for seven days, and once a day for one month, when the child left for the United Kingdom.

It was reported later that the child had been given quinine continuously during the voyage, but that the drug had been discontinued when England was reached, and that there had been two relapses, one nine months and one eleven months after the attack in Chakdara. Had the quinine been continued for a longer period, the relapses might have been avoided. The primary attack, which occurred before arrival in Chakdara, had been treated by quinine for a few days only.

When cases were admitted to hospital no quinine was administered until blood films had been taken and examined microscopically. When time permitted blood examinations of all cases by both the thick and the thin film method were made, but when the pressure of work became great thick films alone were examined. The number of positive films was large in spite of the issue of prophylactic quinine, but a certain number of cases with negative blood films were diagnosed clinically as suffering from malaria and treated accordingly. The withholding of quinine and daily examination of the blood of all such cases as recommended by Hehir(152) is an ideal to be aimed at under normal conditions, but is impracticable in time of epidemic. Of 1272 positive thick films examined 72% showed subtertian parasites, 24% benign tertian parasites, less than 4% mixed infection, and less than 1% quartan parasites. The proportion of serious cases and severe types of the disease was very small. The one choleraic case occurred in a Follower who may not have been taking prophylactic quinine. The most resistant type of case appeared to be the quotidian benign tertian, and it was in these cases that rectal or intramuscular quinine had to be given most often to control the paroxysms. Simple benign tertian came next in order of resistance to treatment and lastly the subtertian type. According to the findings of James and Shute from their

observations of artificially inoculated malaria (27) simple tertian infection commences with two or three days of gradually increasing fever, and then succeeds a period of ten days quotidian fever, and, finally, the fever becomes tertian in type. It may have been that these so-called double tertians were primary simple benign tertians at an early stage.

Usually, both thick and thin blood films of every case were examined. In the case of the thick film a drop of blood is spread over an area of about half the size of a threepenny piece on a slide, the resultant film is allowed to dry thoroughly, half an hour being necessary for this, and then stained for one hour with a 1 in 20 solution of Leishman's stain in distilled water. So successful were the thick films that when the number of cases of malaria became great, thick films alone were employed until the number fell to reasonable proportions. It is more difficult to distinguish one type of parasite from another in thick films, but the great saving of time and the increased number of positive results fully compensated for this disadvantage. The thick film method has many advocates. J. Pratt-Johnson (153) after an experience of 250,000 thick film examinations recommends the staining of the unfixed films in a solution of 2c.cm of 1% eosin diluted with 220 c.cm. distilled water and 4c. cm. of 1% azur II or methylene

blue added for 20 minutes. G.Bini (154) advised staining the thick films for two or three minutes in a solution of one drop of Giemsa to 1c.cm. of distilled water, draining off, and covering with Leishman's stain in the same proportion of distilled water for eight minutes. H. Seidelin[155] found the thick film the only satisfactory method. J. A. Sinton and A.C. Bannerjee[156] have given up their films in favour of thick ones, and find that there is a saving of time and that there are better results. All cases diagnosed as suffering from malaria were put on a full quinine course, and further blood examinations were made to control the treatment. Crescents were common in the sub-tertian cases in spite of the regular quinine treatment. Relapses, unfortunately, were also fairly common, though many of the so-called relapses must have been fresh infections. The inability of quinine to prevent malaria where fresh infection cannot be excluded was thus exemplified. There were no deaths, and all cases of uncomplicated malaria were able to return to duty in due course of time. The inadvisability of sending the Indian troops on home leave until their course of treatment was completed was shown by the fact that when an order was issued that the blood of all men returning from such leave was to be examined for malaria

parasites, no less than 2/3 of the films taken were positive.

As a result of the observations made during this epidemic the following points were emphasised.

1) The inability of prophylactic quinine to prevent infection in an area of hyperendemicity.

2) The absence of pernicious and severe forms of the disease, even when subtertian malaria predominates, when quinine is administered prophylactically.

3) The inability of a course of quinine to prevent so-called relapses when fresh infections are numerous and cannot be excluded.

4) The apparent resistance of quotidian or double benign tertian malaria to orally administered quinine.

5) The regular appearance of crescents in cases of subtertian malaria in spite of treatment by quinine.

6) The success of the thick film method of examination of the blood, when cases of malaria are numerous, and the time for examination is limited.

... ...

6. SUMMARY AND CONCLUSIONS

The observations of the writer in the different districts led to the following conclusions with reference to the etiology, prophylaxis and treatment of malaria.

The most important factors in the etiology of the disease were the canal irrigation, and the condition of the houses and forts. No material progress can be made in lowering the incidence of malaria in Central and Northern India until canal irrigation is controlled, and, if necessary, prohibited in the neighbourhood of towns. The condition of the habitations of all classes of people calls for great improvement. Old forts and barracks situated in malarious places should be pulled down and rebuilt on healthy sites.

As regards the prophylaxis of malaria in India the only measures which have a general application are those which aim at the destruction of the mosquito. General quininisation of the infected population is impracticable, and screening has only a limited application. In areas of low endemicity minor measures will suffice, if efficiently and thoroughly carried out. The small incidence of malaria should be no excuse for the relaxation of antimosquito measures. In regions of moderate and high endemicity major measures are usually

necessary in addition; and of these drainage and the control of canal irrigation are the most important. Until these measures have been carried out screening has an important place in the prevention of malaria among Europeans and better class Indians. The screening of houses, barracks and forts is of small use unless the buildings themselves are in a sufficiently good state of repair to render such screening effective in excluding mosquitoes. On Frontier campaigns the use of bivouac nets and mosquito-proof huts would do much to lessen the incidence of the disease. Prophylactic quinine has a definite place in the prevention of malaria in India. It is indicated particularly for administration to troops and Europeamson Frontier campaigns and in hyperendermic areas; and, though attacks of malaria may not be prevented by the use of prophylactic quinine under such circumstances, they are rendered less severe and are less liable to become pernicious.

The treatment of malaria is true prophylaxis and can be summarised in one word - quinine. The drug should be given by the mouth in ordinary cases. The maximum safe dose of quinine for India is 30 grains a day and rest is essential while large doses are being taken. Quinine orally administered in

the form of a Standard course does not prevent re-infection in hyperendermic areas. Intramuscular injections of quinine are of use in the treatment of severe cases, and of those unable to take quinine orally; and in selected cases give good results. Intravenous injections are safe and effective in skilled hands and are indicated in pernicious cases and where a speedy effect is desired, but the method is unsuitable for general use in India. The transient effect of intravenous injections necessitates a supplementary course of oral quinine. Rectal injections of quinine are uncertain in their action, but have given good results under the supervision of the writer. Subcutaneous injections cannot be recommended. No drug treatment of malaria is successful unless the resistance of the patient is maintained or increased by rest, nourishing food, and general tonic treatment.

The pernicious forms of the disease are most common in times of hardship and strain, as on active service. Cerebral cases are most likely to occur during the hot weather, and in subjects of latent malaria who are not taking quinine and are performing strenuous exertion in the heat of the day.

Abdominal and pulmonary types of malaria are more prevalent during the autumn months. Benign

tertian malaria is more resistant to quinine treatment than malignant tertian, and early diagnosis and early treatment of all cases is essential.

The eradication of malaria in India can only be attained by constant and scientifically applied warfare against the mosquito. The malaria carrying anopheles of every district must be identified, their breeding places mapped out, and measures taken to destroy them. By general improvement of the housing conditions the possibility of the hibernation of adult mosquitoes will be lessened. As in other countries, education should hold a prominent place in the prevention of the disease. Coincident with general education a practical knowledge of malaria should be imparted to every scholar. The progress of education among the indigenous masses of India is necessarily slow, but it is proceeding gradually. The prophylactic measures adopted by the Europeans and educated Indians should form an object lesson to the uneducated classes. Agriculture should be encouraged and the conditions of the peasant improved; for agriculture scientifically carried out prevents malaria and the consequent prosperity of the agriculturalist renders him less liable to fall a victim to the disease. It is true that the wholesale eradication of malaria will take many years, but the time can be shortened and the incidence

lessened by whole-hearted efforts to prevent the disease. Antimalarial measures may seem costly, but the disease is still more costly, and anti-malarial measures alone will render India, with its unlimited wealth and resources, a healthy and prosperous country.

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