"MALARIA PREVENTION AND TREATMENT WITH SPECIAL REFERENCE TO CONDITIONS IN LAGOS".

by

Oyewole Lekunle
K. A. ABAYOMI,

M.B., Ch.B., D.T.M. AND H. (Edin.)

A THESIS PRESENTED TO THE FACULTY OF THE UNIVERSITY OF EDINBURGH FOR THE DEGREE OF DOCTOR OF MEDICINE.

A.D. 1936.

INDEX.

---*---

INTRODUCTION.

The prevention and treatment of Malaria in the Tropics has at all times presented to practising physicians a problem of great difficulty.

The widespread nature of the disease and the chronic invalidism of large sections of the population has created a problem not easy of solution.

Clinically the protean nature of the disease and the various syndromes under which it may manifest itself with resultant difficulties in diagnosis and delay in the commencement of treatment have complicated the task of those engaged in combating the disease.

Another matter of great importance is the economic problem due to the incapacity or invalidism of the large number of individuals that are affected. For this reason no apology is needed in recording in the present Thesis my observations on the conditions found in Lagos where I am in private practice. The present work is based on a survey of 200 cases of Malaria among Africans and 30 cases among Europeans, Syrians and Indians. The records of these cases extend over the period 1930-1935 and all were under my care whilst at Lagos.

TYPE OF DISEASE.

All the cases observed showed Subtertian Malaria, and although Ovale Tertian Malaria has recently been connected with West Africa yet none of the cases showed Ovale Tertian clinically and

microscopically. It may however be that owing to the mild infection of the Ovale Tertian, that the natives did not seek any medical aid until the symptoms of infection had passed off.

Vectors.

Anopheles Costalis was chiefly responsible for the infection but recently Anopheles gambiae has been identified [30].

Some native medicines tried with the specific drugs have been included in this material with a view to a study of the active ingredients.

Lastly the work and the observations have been undertaken with a hope that they would prove of some use in advancing the knowledge of the disease already gained, and the scope of the present Thesis is to describe the kind of cases met with and the prophylaxis and treatment used.

HISTORICAL OUTLINE.

(a) General.

Malaria indeed has a very striking historical significance as it was known even before the birth of Hippocrates in about B.C. 500 [17), 32)].

It was however then referred to as Paludism (Marsh Fever) holding rightly that the disease was definitely connected with marshes and that animacules were carried by inhaled gases which subsequently caused troublesome diseases [32)].

Even as far back as the first Century, Colunella [32)] in his enunciated theory stated "that bogs breed swimming and creeping insects which are armed with stings, and these insects cause obscure and pestilent disease". This indicates clearly that marshes have been incriminated with the disease - production for several years past.

In about the fifth Century B.C. Hippocrates [17)] recognised the periodic fevers and classified them according to their periodicity.

Again, among the ancient Greeks although the connection of the disease with marshes was held yet they also supposed the actual causation of it to be due to the action of demons or gods who if prevailed upon by prayers or offerings or coerced by those who knew the proper incantations, could after the usual ritual appease the wrath of the gods or demons in order to effect a cure; and towards this end sacrifices were made for propitiation [17)]. During

the Christian era and towards the 17th Century the cloud of superstitions around medicine was clearing gradually and the horizon of empiric methods was looming beneficially over the zealous clinicians whose methods were vigorously employed to classify the different fevers separately according to the symptoms and the re-actions to medication. This tense anxiety continued and the recovery of the Countess de Chinchon, the wife of the Spanish Viceroy of Peru from a severe fever in 1638 through the medication of the decoction of a special bark obtained locally, gave a strong fillip to further interest. This bark was sent to England for identification and was subsequently named Cinchona after the Countess[32].

In 1640 under the leadership of Martin, Tort and Syndeham, Malaria was treated with the preparations of Cinchona and later on several of its alkaloids were extracted - the chief one being quinine which could be made into different soluble or less soluble salts. Thus Cinchona and its derivatives have become the sheet-anchor in Malaria therapy.

The question of human infectivity was however still unsolved, and researches upon researches went on, until Meckel[32] discovered the characteristic malaria pigment of the viscera in 1847, this discovery was confirmed by Virchow and later by Planer. Laveran[32] in 1880 discovered malaria parasites and called attention to the crescents with the eruption of the long and motile flagella.

But there was still a gap in the mode of infection and the vectors must be known to complete the chain of infectivity, and thus Manson reasoned incessantly that the "flagellation" took place not in the circulating blood but after its withdrawal from the body and concluded that it represented the first stage in extra-corporeal life. Summing up these facts backed up by his ripe experience of the other blood parasites, e.g. Filaria Brucei, he strongly suggested that there must be a definite intermediate host and he suspected a species of mosquito. Working on this analogy Ross discovered in India in 1895 - 1897[32] a similar protozoan disease of bird-Plasmodium praecox, and later confirmed the mosquito theory as the chief intermediate host,[32] and subsequently Grassi and his collaborators extended this theory to human Malaria and showed the connection of the infection through anopheles mosquito.

The criterion of the theory was reached when Manson under the auspices of the Colonial Office and the London School of Tropical Medicine sent Doctors Sambon and Low with Mr. Tersi and their servants in 1900[41] to the most malarious districts of Romana Campagna - Ostia. These people mixed freely with the natives of the districts and did many things in common with them save that they retired at sunset to their hut which was excluded from the mosquitoes by a simple arrangement with a wire gauze on the doors and windows. After living for sometime there they returned to England un-infected. Again, this experiment was

confirmed by getting the mosquitoes fed on infected persons in Rome and taken to England to bite Dr. Thurnburn Manson and Mr. George Warren who developed typical symptoms of Malaria although they had never been abroad. So the mode of infection through mosquito Anopheles has now been proved beyond doubt.

LAGOS:

Here for many centuries before the discovery of West Africa by the Portuguese explorers in the 15th Century, the natives knew that those who stayed close and around the marshes developed more severe periodic fevers than those staying on the dry up-land partitioned by thick forest; and as the infection became very severe and mortality high, especially among the children, the infected families gradually moved to the interior dry-land for safety. They also noticed that several mosquito bites not only led to irritation of the skin but also to severe fever following a few days after, hence they used mosquito nets freely to protect the children especially. The nets used unfortunately were of very close mesh and stuffy during use. Again, they knew also that children who had been repeatedly bitten by mosquitoes and who developed fevers generally had large swellings on their left sides. Experience also taught them to appreciate the relief that followed the sweating stage of the fevers and they therefore invariably used diaphoretic decoctions or infusions to accelerate this stage in any seen patients. They also treated the left side enlargement by blood letting or scarification

over the swelling.

Should however an epidemic break out in spite of their different primitive treatments, the chiefs would consult together and like the ancient Greeks resolve to appease the wrath of the gods or demons through sacrifices. Later on as more Europeans settled down in the country the same old theory of vitiated marsh gases causing the disease made those who were staying close to the marsh to build their houses in such a way as to allow the minimal amount of obnoxious gas in; so that even today there are still houses at Lagos bearing the vestiges of this old 'hall-mark'.

However, after the cession of the island about seventy-five years ago by King Docemo to the British Government sanitation began to spread gradually although not without a resistance from the natives who were used to squalor, and to enforce the sanitation, laws were passed to the effect of making anything contrary to sanitary progress, an offence punishable by heavy fines or imprisonment. Governors after Governors pushed up the degrees of the sanitation, and in 1902, Sir William McGregor, M.D., the Governor of Lagos from 1899 - 1904, fired by the enthusiasm of the new discovery of the mode of Malaria transmission to human beings and strengthened by his medical back-ground invited Sir Ronald Ross[32] as an expert adviser to Lagos. On Sir Ronald's arrival he strongly advised a big campaign against Mosquitoes by filling up the marshes and rendering the mosquito breeding places impossible, and strongly emphasised human

protection by a careful use of good mosquito-nets and daily quinine taking. Thus sanitary laws and methods have been engrafted into the country but the complete extermination of the Anopheles is still a problem.

As a prophylatic measure also the mass education of the public has been adopted in order to obtain the useful public co-operation in the anti-Malaria campaign, and thanks to the Sanitary and Hygiene Societies in London, a Health Week Committee was formed in Lagos about 10 years ago. This Committee arranges a Health Week bi-ennially and the last one was in 1934; and during that week elaborate demonstrations were given showing the causation of different Tropical diseases and Malaria having the most prominent place. The demonstrations could well be imagined in that Lagos stood first and won the coveted shield offered by the Sanitary and Health Societies in London for the best practical hygiene-demonstrations among the Colonies and Dominions.

Undoubtedly this mass education has taken very well with the general public and Malaria incidence is on the decline.

MELANO-FLOCCULATION TEST.

J. Gordon Thomson [31] in 1919 suggested a complement-fixation test for Malaria and prepared his antigen from Malaria parasites. He carried out the technique on the same principles as those of Khan or Wasserman Reaction and found out that Malaria cases gave positive results. Even those cases which showed scanty or no parasites at the peripheral circulation

but which were diagnosed only on clinical history, viz. Splenic enlargement, definite rigors, irregular high temperatures and high percentages (15 or more) of large mononuclear leucocytes - were also positive. The high percentage of large mononuclears with other clinical symptoms is very suggestive of Malaria infection - Stephens and Christophers [36].

He also found that quinine administration whether orally or parenterally did not negative the test but other diseases as syphilis did, as the test was also positive for them.

In a report presented to the Association Francais l'Advancement des Sciences at Constantine, Henry (1928) describes certain serological tests for the diagnosis of Malaria. These have been based on the observations that the sera of Malaria patients were found to flocculate solutions of the Metharsenate of Iron and Melanin pigments. The former phenomenon is termed "ferro-flocculation" and the latter - more sensitive, the Melano-flocculation test [38], [39]. Henry regards it as an outcome between pigments and a corresponding anti-Melanin agglutinin developed in human sera after Malaria infection [9]. Other observers including (Chorine and Gilles, 1933) suggest that the phenomenon is due to an increase in the serum globulins accompanied by a disequilibrium in the other soluble constituents of serum. They state further that negative may be transformed into positive sera by the simple addition of four volumes of 1 : 2000 formalized distilled water; and that positive sera may be rendered

negative by heating at 55°C. for half an hour, and the Melanin pigment - used for the test proved to be non-antigenic by animal immunization. These controversies went on and as there have not been British or American records of the test, Greig and others[9] worked on the test for confirmation or otherwise. They used human hair as a source for the Melanin pigment-extraction instead of from the ox-choroid membrane used as Antigen by Henry and others. The reason for the substitution being that the aqueous solutions of the ox-choroid membrane are relatively unstable and that such solutions contain a too large proportion of protein tissue to make a delicate serological work accurate.

Greig and his co-workers[9] suggested, the term Melano-precipitation reaction instead of the Melano-flocculation test because they find that the phenomenon is no true flocculation following inter-action between antigen and antibody. They recommend the test for Malaria and throw in suggestions for further observations as to its confirmation from other workers.

However, after several other experiments carried out on the test, Greig and others[10] found out that the reaction is not specific for Malaria as it has been found to be positive also in Kala-azar and therefore conclude that:-

(1) Reaction has no obvious relationship to the concentrations of albumin, total globulin, cholesterol or chlorideion in the serum.

(2) One of the globulin fractions, i.e.

Euglobulin is responsible for the precipitate and that this increase of Euglobulin is present both in Malaria and Kala-azar in which the test is positive. This view is also held by Lloyd and Paul.

(3) That Melanin acts only as an indicator and the active principles in the so-called antigen are the concentration of sodium chloride and pH. of about 9 - 12.

(4) Since the reaction is also negative in Syphilis, a condition with high Euglobulin index, the phenomenon cannot be explained on the grounds of an increase in euglobulin alone and they suggest that protein-lipoid complexes enter into the question.

PLASMOCHIN.

The first synthetic drug to compete with quinine for about 300 years in Malaria treatment [24], is a compound produced by Schulemann, Schonhofer and Wingler (1924) and is a derivative of quinoline.

The experimental work and the therapeutic dosage was carried out by Roehlin on canaries infected with Preteosoma (Plasmodium relictum) and it was found that small quantities of the drug when injected into the alimentary canal of the birds would banish the parasites from the circulation [13), 19), 24)].

Given to man in a dosage of 0.06 grm. daily for five consecutive days it has a specific action on the gametocytes and the crescents of the Subtertian parasites (which persist for weeks in the circulation in quinine therapy) disappear after four days with plasmochin therapy. Plasmochin also reduces splenic

enlargement. Unfortunately in heavy subtertian infections especially with large doses it produces cyanosis, probably due to the conversion of haemoglobin into methaemoglobin. It also produces acute spasms of abdominal pain especially on the left hypochondrium and this is supposed to be due to the violent contraction of the spleen from the effect of the drug. Plasmochin is 60 times as strong as quinine in action.

PLASMOQUINE-COMPOUND.

Made in tablet form, is a combination of quinine 0.125 grm. and plasmochin 0.01 grm. to each tablet. It is found that quinine combination counteracts the action of plasmochin and lessens its toxic effect. Gametocytes and crescents of the subtertian Malaria are acted upon by the plasmochin in this compound but the quinine is rather too small to produce a quick and effective destruction of the Schizonts. Children tolerate the compound fairly well 1), 7), 8), 20), 25), 26), 38), 39), 40)

ATEBRIN.

It is a compound containing acridine and exists in a yellow powder which dissolves in water at 40°C. in 7% solution. It was first synthesized by Mietsch and Mauss in 1930. The first experiment was in avian parasites. Kikuth has shown that Atebrin has a specific action on the Schizonts of all Malaria parasites but no direct action upon the gametocytes especially of the subtertian parasites. First it attacks the rings, then the developmental forms and

finally if the Atebrin is continued long enough the gametocytes disappear. Manson-Bahr and Walters[26] have shown that it does not affect the exflagellation in the least as the minute dose of plasmochin does. It has a most striking effect in heavy infections of subtertian Malaria. It is the safest drug to administer when Blackwater fever is threatening as it has been shown that it has no haemolytic action as with quinine. It is practically toxin free and large doses have been taken with impunity. It gives a yellow discoloration of the skin due to the Acridine dye and not to jaundice. This yellow pigmentation generally disappears after atebrin has been fully excreted from the system, which may be as long as thirty days after stopping Atebrin treatment. It is fairly slow to be excreted and this fact of continuous saturation of the blood reveals its more advantageous secret in preventing Malaria relapses than quinine. Hoops[15] and others have shown that it acts as a cerebral excitant and may show symptoms not unlike alcoholic intoxication. It has also been reported to produce mild or transient psychosis and this has been explained to be due to the intense liberation of the Malaria toxin from the effect of the drug - the toxin affecting the cortical centres. Some suthorities suggest the combination of Atebrin and quinine treatment in severe cases of Malaria, especially subtertian; this view however, is not supported by the Third General Report of the Malaria Commission of the League of Nations, which emphasizes

that Atebrin or quinine must be used seperately [38]. Atebrin is in tablets containing 0.1 grm. each and is given three times a day on a full stomach. It reduces splenic enlargement more rapidly than quinine. It has been proved that it is well borne by children and is safer for pregnant women than quinine which sometimes leads to abortion.

It has also been prepared in the form of soluble Atebrin-Musonate for intravenous injections and the strength of the solution is 0.125 grm, equal to 0.1 grm. of Atebrin. This proves very satisfactory when parenteral administration is indicated as seen in the recent case of Malaria in Ceylon. Injection equal to 0.2 grm. of Atebrin has been given in cerebral Malaria without any toxic effect [3), 14), 23), 26), 27), 38), 39)].

Row and others [34)] have proved the same effect of Atebrin on monkeys.

ETIOLOGICAL CONSIDERATIONS.

All the features discussed under this heading refer in particular to the conditions at Lagos.

Predisposing Causes.

(1) Absence of good food.

(2) Debilitated conditions. e.g. Anaemia of any form or wasting diseases.

(3) Gastro-intestinal troubles - Diarrhoeas, dysentric conditions or helminthic intestinal infections.

(4) Fatigue - following a strenuous exercise or overwork.

(5) Traumatism - after severe injuries.

(6) Sudden chills, damp or wetting. Common in people who have been heavily soaked by the rains.

(7) Intercurrent diseases: pneumonia, etc.

(8) Anxiety, sorrow, shock or fright - conditions lowering the action of the sympathetic nervous system.

(9) Alcohol, especially in excess.

(10) Paturition especially with previous Anaemia.

(11) Neglect of regular quinine taking, especially among the Europeans, Syrians and Indians.

Climate and Hygienic Conditions.

The climate is fairly warm and damp. The heavy rains begin about the middle of April and last until the latter part of September. The rainfall for the

period of five years when the observations for this Thesis were made, i.e. 1930-1935, was equal to an average of 71.36 inches yearly [30]. After the rains, the climate is very hot up to the end of March. The temperature - average for each year of the five, was equal to:-

Absolute shade maximum 92°.

Absolute shade minimum 67°.

Major hygenic measures are under the full and judicious control of the health authorities who work strenuously to make the place ideal but who several times are hampered by the actions of the majority of the population whose sanitary habits are far below the ordinary. For it is not uncommon to find empty bottles, empty tins, etc. in dwelling places which, are usually filled with rain water and invariably neglected thereby facilitating breeding places for mosquitoes.

Under the hygenic measures it is interesting to quote from the Nigerian Report on the Medical and Health Services 1934 [30].

"Malaria - Although no major drainage or other works have been possible, general anti-malaria measures have been carried out as in previous years. These consist chiefly of the use of Paris Green and larvicidal oils, canalisation of streams, extension and maintenance of ditching and drainage or reclamation of borrow-pits".

"In the vicinity of Lagos extensive areas of the township have in recent years become more favourable

to mosquito-breeding owing to the indiscriminate felling of trees for firewood or charcoal burning or as a preliminary for farming. In this way much thick comparatively dry bush has been converted into open flat stretches which are often flooded and which are covered with a coarse grass (Paspalum vaginatum). Such areas speedily become extensive breeding places for Anopheles gambiae. Action has been taken to put a stop to this dangerous form of clearing and measures of re-afforestation are being undertaken".

"The Medical Officer of Health, Lagos, records a striking example of the production of swamp conditions resulting from tree felling and bush clearing at Apapa. Here a long narrow swamp was effectively drained by means of a central ditch cut a few years ago leaving thick bush on either side. The ground along the south side of the ditch has since been cleared for farming with the result that it is now a collection of numerous water-holding depressions, whereas the north bank which is still thickly covered with bush, remains quite dry".

Geographical and Geological Formation.

Lagos is the principal port and the capital of the British Colony and Protectorate of Nigeria, West Africa. It is situated 6° 26' North, and 3° 23' East, (see map attached) and has a population of 160,000 - (Nigeria has a population of about 20 millions - Census of 1931) [30]. It has a birth rate of 27.89 per 1,000 and the death rate is 13.05 per 1,000 [30]. It is a low land,

lying just a few feet above the sea-level and is surrounded by marshy areas.

It attracts many immigrants both for trade and education and the influx is from overseas as well as from the hinterlands. It is an island and is linked to Iddo Island by the Carter Bridge - 2,600 feet long.

Exciting Causes.

(1) Humidity: Relative humidity for the five years of observation - average 84.5.

(2) Type of mosquito - Anopheles Costalis and Anopheles gambiae.

(3) Time and place of breeding.

The vectors breed chiefly and more abundantly after the rainy season, but commonly at any season except if the rains are very heavy and incessant. Common places are around the dwelling places and in the marshy areas. In the dwelling places any recepticle holding water affords a good breeding place, e.g. flower vases, broken bottles in the yards, etc.

Water Supply.

Lagos is supplied with pipe-borne water from a fountain at Iju, about 20 miles from Lagos. The storage, filtration, etc., are all done at Iju and the water comes down to Lagos through thick and large metallic pipes. The water is tested every time especially at Iju and all precautions are taken to prevent contamination. There is an analyst who publishes a monthly report of the state of the water as to the purification, lime content, etc.

TREATMENT.

PROPHYLACTIC.

(A) Major Anti-Malaria Measures.

These are under the full control of the local Health Authorities with an efficient staff of Europeans and Africans, and the measures adopted vary and are wide in order to cope with the local species of Anopheles Costalis and Anopheles gambiae which are ubiquitous and adaptive in their bionomics. However, a few of these measures might be mentioned, viz.:- The care of drainage, the reclamation of swampy areas, trimming up hedges around streams, weekly house to house inspection, house to house distribution of imported larvicidal fish (minnows) for unused wells with wire gauze covers, oiling stagnant pools, Paris Green to large marshes - all these methods "inter alia" are judicially undertaken to foster a high hygienic standard.

(B) Minor Measures.

It was found that 85% of the Africans treated did not keep to a high standard of sanitary habits. 35% were new arrivals at Lagos from places where sanitation was at its lowest ebb, and the remaining 50% who are town-dwellers were very neglectful in sanitary habits also in spite of the drastic measures in the Anti-Malaria campaign undertaken by the local Government, hence the following measures were adopted by me:-

(1) Demonstrations:

Before discharging any patients either in my

Nursing Home or in their own homes, I made it a rule to demonstrate different stages of the life of mosquitoes from egg to imago, to them. These specimens were kept in weak formalin solution in my laboratory. The importance of mosquitoes in causing Malaria fever was usually stressed, and that in order to minimise the incidence of Malaria fever it was the duty of every one of them to see that any of the stages demonstrated should not be allowed to develop. This would mean not to allow broken bottles, empty tins, etc., to lie carelessly in the yards which would ultimately be filled with rain water. It was also pointed out that it should be a habit amongst those who kept flower vases to empty them daily. It was also impressed on all patients that a constant over-hauling of their dwelling places should always be undertaken, because by so doing the mosquitoes lurking under beds, in unlit corners and behind cup-boards, etc., could be easily got at and killed.

The importance of opening the windows day and night was also stressed as the current of air would not only benefit the house occupants but it is also disadvantageous to the mosquito-flight.

That it was the duty of every good citizen to co-operate with the Health Authorities to break down the chain of infection, and if they followed these detailed methods they would be contributing their own share to the reduction of Malaria fever.

(2) Bonification:-

This aims at raising the general standard of the

mode of living among the patients and thereby creating a sense of well-being which is one of the most important forces of natural defence and as several of the patients were under-nourished and lacked the usual compensatory factors of good health they were told:-

(a) To eat good and mixed foods with plenty of vegetables.

(b) To avoid excesses especially in alcohol.

(c) To take regular exercise of some kind to reinforce the heart-activity and all summed up in short, that they should try to live well.

(3) Mosquito-netting:

The free use of netting had been adopted for several years, and 45% of the cases treated were using nets which invariably were of a very close mesh, and several of them did not know how to use the nets properly. I recommended the standard net of 26 holes to a square inch sold locally and usually I demonstrated its proper use, i.e., a net should be hung inside between bed-poles and not outside them, and that it should be made ready at about 5 p.m. before sunset; also that it should always be tucked with its calico edge right under the mattress, and that great care should always be exercised to see that the already made net had not a mosquito inside. The natives adopted this measure of prophylaxis very quickly. Among the Europeans, Syrians, and Indians treated, the use of nets was carefully adopted.

(4) Drugs:

The natives as a rule could hardly be convinced of the importance of taking any drug regularly as a prophylaxis after they had been pronounced cured; and out of the discharged patients interviewed six months later not one kept up the regular drug-taking ordered them for even a period of three months. However, the Europeans, Syrians, and Indians always took quinine daily and after their discharge I recommended Atebrin 0.1 grm. daily as most of the quinine tablets sold locally had been proved to be insoluble even in dilute acids, e.g., hydrochloric or sulphuric.

(5) Importance of early treatment:

This was repeatedly stressed to the patients especially the natives, to seek medical aid and not to indulge ignorantly in self-treatment with nostrums, and that only through the propper medical treatment could sterilization of the system be expected and that the more sterilized persons would mean fewer channels for mosquitoes to carry infection from.

(6) Mass Education:

As a member of the Lagos Health Week, I urged on all my discharged patients to attend the Health Week demonstrations which took place twice during these observations. On each occasion during the whole week elaborate Cinema demonstrations and lectures were given, and the individual responsibility of killing mosquitoes was emphasised.

(B) Curative.

General treatment:-

Rest in bed - every patient was kept in bed until

the temperature was normal for four days in succession. Much fluid - this consisted of Soda Water, lemon juice and oranges. Milk - 2½ pints daily given in acute stage and plenty fruits - bananas, pine-apples, etc., and when the temperature became normal for a few days they were allowed light solid diet.

Cold stage - Hot blankets and hot water bottles.

Sweating stage - Sponging with warm water and some vinegar in it to avoid chills.

Great restlessness - Pulv. Ipecac. Co. grs. X at once, and repeated if necessary.

Ordinary forms of Malaria.

Regular intermittent and irregular remittent forms:- Oral medication of quinine, plasmoquine compound, Atebrin, decoction of Cassia Occidentalis cum Rauwolfia (18) and decoction of Emilia Sagitata (18).

Comatose Form.

(1) Unconscious type:-

Intramuscular injection of either Quinine Bihydrochlor or Atebrin-Musonate. Quinine Bihydrochlor grs. X dissolved in 20 mins. of sterilized normal saline. The skin around the gluteal region properly sterilized with weak Iodine tincture and the syringe and needle properly boiled before use. Atebrin-Musonate in solution already in prepared ampoule - a dose equivalent to 0.1 grm.

Point of injection:

The intersecting point of the two lines drawn from:-

(a) Anterior Superior spine to the top of inter-gluteal furrow.

(b) Posterior Superior spine to Ischial tuberosity.

This point avoids the sciatic nerve. The injected part was always thoroughly rubbed down and in no case was there any abscess formation from any of the forty cases injected.

Five per cent warm glucose saline 3 pints daily was given per rectum after washing the rectum with Sodium Bicarb. grs. XXX to half a pint of warm water.

When the patients recovered from unconsciousness they were put on oral medication as indicated for ordinary types with the usual procedure of light diet.

(2) Hyperpyrexial type:

Temperature 103°F. and above - intramuscular injection as in the unconscious type. Cold baths and one pint ice-cold 5% glucose saline per rectum every four hours after the rectum had been washed with Sodium Bicarb. as in unconscious type. Temperature and pulse of the patient were carefully watched and immediately the temperature fell two degrees below the the hyperpyrexial height and pulse was about 100, the hydrotherapy was stopped. When the patient's temperature came down as stated then the oral medication was started as forementioned with light diet.

Algid Form - Adynamic:

Type with extreme prostration and weakness:- Warmth around skin - hot water bottles, blankets, etc. Stimulants, Brandy alone or with hot milk and sugar. Camphor grs. III in Olive oil 2 c.c.

intramuscularly.

The intractable vomiting:-

Tr. Iod. Mit. m3 in half a pint of hot water and if still persistant:-

℞

Glucose	5	5
Sodium Chloride	1	
Hot Aq. Destil.	100	

Half a pint every two hours and if still intractable - Tr. Opii m X would be added to the hot glucose saline.

Intramuscular injection of Quinine Bihydrochlor or Atebrin-Musonate to be followed by oral medication after getting rid of the shock-stage.

Choleraic Type:

Treated exactly like adynamic type.

Bilious remittent form:

Treated like the Algid form but with the following additionals:- Epigastric pain - hot fomentation or hot bottle on the region.

Hiccup:

℞

Pot Brom.	āā	grs. X
Chloral Hydras		
Aq. ad.	℥i	

To be taken in a wineglassful of hot water thrice daily untill the hiccup stops.

During Pregnancy:

0.1 grm. Atebrin, as the native women are highly susceptible to quinine.

During Convalescence:-

℞

Syr. Eastoni	ʒ ss
Aq. ad.	℥i

To be taken thrice daily after food and continued after recovery for two months.

Methods of oral administration of the various drugs used.

(1) Quinine

Always given preceded by Alkaline mixture, viz:-

(A) Alkaline Mixture.

R

Sodium Bicarb.	3ī
Sodium Cit.	grs. XL
Aq. ad.	3i

(B) Quinine Mixture.

R

Quin. Sulph.	grs. X
Acid Citric.	grs. XXX
Mag. Sulph.	3 p
Aq. ad.	3i

Dose. (a) Adult - "A" mixture to be started first and given thrice daily alternating with "B" at half hour intervals between.

(b) Infants 0-6 months - 3 p of each twice daily.

(c) Infants 6 months - 2 years. 3ī of each thrice daily.

(d) 2 years - 12 years. - 3ii of each thrice daily.

(e) 12 years - 16 years. - 3 p of each thrice daily.

(f) 16 years and above - adult dose.

In case of severe vomiting per se or following the administration of quinine mixture, Tr. Opii m X - 3ī would be added to the Alkaline mixture and given thrice daily until the vomiting ceased, but should it still continue intramuscular injection would be

given and hypertonic glucose saline given by the mouth as in the adynamic type. Once the vomiting stopped opium was omitted in the Alkaline mixture and continued thrice daily but should it still continue, intramuscular injection of quinine would be given to save time.

The two mixtures were generally given for seven days, then an interval of five days allowed and they were repeated for another seven days, and then 3 t daily for three months and if no relapses, the patients would be told of all the prophylactic measures to be taken. If there were relapses the same treatment followed.

(2) Plasmoquine Co.

In tablets containing plasmochin 0.01 grm. and quinine 0.125 grm.

For an Adult.

7 days 2 tablets twice daily
4 days interval
7 days 2 tablets twice daily
4 days interval
7 days 2 tablets twice daily
4 days interval
7 days 2 tablets twice daily
4 days interval
7 days 1 tablet twice daily.

For infants.

0 - 1 year ½ tablet daily
1 - 3 years 1 tablet daily.

Children. 4 - 5 years 1 tablet twice daily
6 - 10 years 1 tablet thrice daily

Above 10 years adult dose.

(3) Atebrin:

In tablet containing o.1 grm.

Adult. One tablet thrice daily for seven days, then

an interval of five days was allowed, and the treatment repeated for another seven days.

For infants.

	0 - 1 year	½ tablet daily
	1 - 3 years	1 tablet daily
Children	4 - 5 years	1 tablet twice daily
	6 - 10 years	1 tablet thrice daily

Above 10 years - adult dose.

(4) Decoction of Cassia Occidentalis (Native name Réré) with Rauwolfia Vomitoria (native name - Asofeyeje).

The dried leaves of each were mixed together and made into a decoction - 20% in strength.

Adult Dose:

A wineglassful thrice daily for two weeks; an interval of a week was allowed and then another two-weeks treatment was given.

(5) Decoction of Emilia Sagitata (Native name - odúndún Odo).

The dried leaves were made into 20% decoction and given to adults at the dose of a wineglassful thrice daily for two weeks; an interval of a week allowed and another two weeks treatment given.

RESULTS.

Quinine Medication.

Immediately the treatment was started the temperature fell within ten hours even in the cases which had shown continued pyrexia and if it did rise again the peak would not be the same height as before the treatment. The drug increased the sweating very much and among the natives - tinnitus - transient

deafness and in some cases a generalised rash has been observed. Some patients were extremely intolerant to the drug and the intolerance was sometimes manifested by intractable vomiting. Again, there were some who developed extreme palpitation after only two doses of the quinine mixture. Native women aborted quite easily with the smallest dose of the drug; e.g. 2 grs. thrice daily.

The Europeans, Indians and Syrians too suffered from tinnitus and transient deafness when they were saturated with the prescribed dose but these toxic effects were not so marked in them.

There was a European case that developed a severe diarrhoea after the curative oral dose which had to be stopped and Atebrin substituted. During the treatment, crescents were seen right to the 14th day in some cases and were not affected by the drug as their number did not diminish from day to day. The other stages of the parasites from the trophozoits to the Schizonts were noticed to diminish from the 2nd day and were not seen after the 6th day in most cases. Ten per cent of the cases treated showed recurrence after nine months to one year but they never reported ill with Malaria fever after the second treatment was given. The intramuscular injection had a very sharp effect on the disease in bringing the temperature down rapidly in the hyperpyrexial type, and controlling the shock in the adynamic type. In the choleraic and the bilious remittent types it also had a very marked action and within six hours of the injection

improvement generally set in.

The combination of the intramuscular treatment with the oral medication when necessary, did not diminish the parasites in the peripheral blood earlier than with the oral therapy alone.

Plasmoquine Co.

It was used only in ten cases and the toxic effects in five were so severe that its use was stopped.

With the Natives:

There was always a deep cyanosis of the lips, especially the lower one, and around the gums. The gastric symptoms were also very severe and in one case the treatment simulated "Acute Abdomen" with general 'boarding' of the whole abdominal muscles with severe vomiting, and the treatment had to be stopped and three pints 5% glucose saline, was given daily for three days before the severe symptoms abated, and the patient was switched on to quinine alone.

With Europeans:

The only two cases treated had the same toxic effects as mentioned above but in a milder degree. The asexual stages of the parasites persisted for 14 days in most cases although no crescents were found from the third day.

Atebrin. Orally:

The natives preferred it to quinine as it never gave tinnitus or transient deafness. It was used for 20 pregnant cases without any signs of abortion. It has a very weak toxicity on the whole as two patients who were treated in their homes and who were

anxious to get better very quickly took three tablets thrice daily and finished the bottle of 15 tablets in less than two days. In each case when the patients were seen the following day, there was no marked serious effect in either of them except that they were somewhat excited, and talked as if they had had some alcohol.

The intramuscular route had a quicker effect than that of quinine. Whether intramuscularly or orally the parasites were reduced from the second day and all asexual stages disappeared by the fourth day in most cases. The crescents however could still be found till about the fourteenth day. The natives on the whole tolerated the drug quite well and did not show any discoloration or severe intoxication of violent vomiting, severe headache and any excessive cerebral excitement - mania , and fits as reported by Hoops [15].

The Europeans:

Four were treated and each tolerated the drug quite well also. There was a slight discoloration in two cases which persisted for six weeks after the curative treatment was stopped. None of them showed any cerebral symptoms.

There were no relapses or recurrences either among the Africans or Europeans who were treated.

The chief factor against the drug however is the expense, as it is very dear at Lagos - a bottle of 15 tablets costing 3/6.

Decoction Cassia Occidentalis with Rauwolfia Vomitoria:

This decoction is used frequently among the natives for the treatment of fevers and it was used as an experiment during these observations to find out its effect. It was used in ordinary forms of Malaria where only oral medication was indicated and on adults only. It had a very sharp diaphoretic effect and when administered it resulted in a profuse perspiration greater than that produced by quinine medication in less than three hours; moreover it controlled the vomiting which was present in all the cases. It also had a mild laxative effect. It has no toxic effect whatsoever as the natives in their own ways of treatment as a rule took about 2 - 3 pints of a stronger decoction daily. It had a weak effect on the parasites and after ten days the asexual and sexual forms were still present but after the 14th day, only the crescents were still present in small numbers in the peripheral blood.

Decoction Emilia Sagitata:

Its action is similar in all respects to that of Cassia Occidentalis cum Rauwolfia Vomitoria.

Neither of the two native preparations was used for the treatment of infants or children during the observations owing to its uncertain action.

Description of Modified Melano - precipation test (9) - a newer method of diagnosis.

25 grams of human hair are refluxed with 100 c.c. of 50% hydrochloric acid (by volume) for five to six hours. The dark brown hydrolysate is filtered through paper and the black insoluble residue

discarded. Darker hair yields a greater insoluble pigment than brown or less dark hair which is preferable for the experiment.

The hydrolysate is then distilled in vacuo to remove the bulk of the volatile acid, at least three distillations should be made, water being added each time as soon as the residue becomes pasty. The residue is completely soluble in distilled water, giving a very dark brown solution.

The remainder of the hydrochlor acid and a considerable portion of the Amino-acids present are removed by dialysing the mixture in a collodion sack against running tap-water. After six to ten hours, depending on the completeness of the vacuum distillations the solution is only slightly acid to litmus paper and dialysis is then stopped. The mixture inside the sack is transferred to a 4 inch porcelain basin and 10 percent Sodium hydroxide solution is added until the reaction is slightly alkaline to litmus. The bulk of the precipitate should dissolve on this treatment, but warming on the steam bath may be necessary. Any remaining precipitate is removed by filtration. In all case a dark brown water clear solution should be obtained. It may be sterilized by transferring into test-tubes which are heated in a boiling water bath for twenty or thirty minutes and sealed off as soon as they are removed. The colloidal solution of Melanin so prepared appears to keep indefinitely. It does not give a positive ninhydrin reaction, is completely free

from iron but contains some compound of sulphur which gives a positive nitro-prusside reaction after fusion with sodium.

The solution may be compared calorimetrically against a solution containing 10 grms. of ferri alum per 100 c.c. of distilled water. Assuming that a standard represents 1 unit of Melanin per 100 c.c. then a stronger solution representing about 4.8 to 5.0 units per cent appears to be most satisfactory. The colorimetric comparison is not accurate, for the shade of colour depends upon the type of hair used.

TECHNIQUE.

A row of ten Wassermann tubes are laid out on a rack with a corresponding row of narrow agglutination tubes opposite them.

To each of the Wassermann tubes (1) to (10) inclusive, 0.4 c.c. of distilled water is added and in (1) 0.4 c.c. of 1:2 dilution of serum present there and add it to (2) from which in turn is withdrawn the same amount and the process repeated until tube (9) is reached from which 0.4 c.c. is removed and discarded. With a clean pipette sterilized by boiling next add 0.4 c.c. of Melanin to all ten tubes (1) to (10) inclusive. The 1 c.c. measuring pipette is now discarded and a Pasteur quill tube substituted with which mixtures are transferred from the Wassermann tubes to the narrow agglutination tubes commencing with (10) and working backwards. The ultimate dilutions of patient's serum are thus: 1/4, 1/8, 1/16, 1/32, 1/64, 1/128, 1/256, 1/512, 1/1024 respectively,

the control tube (10) containing Melanin solution plus distilled water. The entire series should on examination be clear and transparent in appearance with no trace of particles in suspension; it is now incubated at 37°C. for five hours and the results read at the end of that time.

INTERPRETATION OF RESULTS.

Positive readings are easily observed on naked-eye examination and may be detected by the presence of a fine grannular white precipitate at the foot of the tube with slight cloudiness of the upper column. The usual reacting titre of patient's serum during the course of a benign tertian infection is generally from 1/32 to 1/128 which yields adequate information.

At Lagos.

The test carried out by Dr. Smith, the Senior Pathologist, on several occasions gave varying results so that he considered it fallacious in diagnosis.

However, Colonel Greig, one of the experts of the modified Test informed me that the several errors detected there might be due to the incorrect pH.; the pH (9 - 12) concentration is very essential in carrying out the test properly. Moreover, as it has been stated, the test even when properly carried out is also positive for Kala-azar and other infections where the euglobulin fraction is raised, and is therefore not specific for Malaria.

CLINICAL NOTES - CASES.

Diagnosis:

Clinically - the history of irregular fevers with high temperatures, rigors and occasional splenic enlargement was always suggestive.

Histologically:

Blood films - thin and thick.

Method:- Blood taken from the pulp of a finger after cleansing with alcohol and the needle sterilized in a spirit-lamp flame. No pressure applied to the finger before taking the blood.

Thin Film;

Two clean slides were used. On one end of a clean slide, half inch from the edge, a drop of blood was placed, and the edge of the other slide dipped into part of the blood and spread on until it tapered.

Thick Film:

On the same slide as the thin one, it was gently spread with a pipette.

Staining:

Leishman's stain was used. The two films were partitioned by grease pencil marks; distilled water was poured on the thick one and stain on the thin one and left for one minute. Then the stain was diluted with four parts of water and flooded over to the thick film as well and left for five minutes after which the slide was washed off in distilled water, dried and examined.

Confirmatory Test:

Usually the thick film showed parasites and crescents more, and in absence of parasites, differential counts of white cells were made and the presence of large mononuclears of 14 percent and above was taken as highly indicative of Malaria, taking the other clinical signs into consideration (normally, large mononuclears, hyalines, monocytes, 4 - 8 percent - average 5%).

Table showing the number of cases with the percentage of parasites and crescents found.

AGE	No. of CASES	PARASITES IN DIFFERENT STAGES PRESENT IN	CRESCENTS FOUND IN
0-4 Mths.	20	75%	5%
4Mths-3Yrs.	70	98%	25%
4 - 10 Yrs.	60	65%	13%
11-16 Yrs.	35	48%	10%
17-35 Yrs.	25	25%	8%
35 Yrs. & over	20	20%	4%

The table shows low parasites and crescents in infants up to 4 months after which it rose to the highest percentage between four months and three years and subsequently fell slowly until the age of 16 years. After 16 years there is a steady decline in direct ratio to the advancing age.

Table showing total number of cases treated at different ages with the drugs used.

AGE	No of CASES	DRUGS				
		QUININE.	PLASMOQUINE. Co.	ATEBRIN.	CASSIA Co	EMILIA SAG.
0-4 Months	21	10	1	10	-	-
4Mths-3Yrs.	42	20	2	20	-	-
4 - 10 Yrs.	51	25	1	25	-	-
11-16 Yrs.	38	10	2	10	8	8
17-35 Yrs	44	10	4	10	10	10
35 Yrs. & over	34	-	-	-	17	17
Total	230	75	10	75	35	35

Special Cases with reference to the treatment.

A. QUININE

Cases showing comatose forms.

(1) Date 15 : XI : 30. F. O. Male African, aged 15 years.

Suffered from what the parents called "Influenza" six months before and was confined indoors for about two weeks. No qualified doctor attended him during the so-called Influenza and the treatment was purely native, consisting of some decoctions etc. He recovered and went back to school. He joined in a football match and had a very strenuous time during the match, and returned home quite wet with perspiration. He went to bed and next morning developed a very high temperature - he was unconscious and muttered a lot of meaningless sounds.

Examination:-

Patient was very hot with a sharp acrid odour. Temperature per rectum - 102°F. Urine taken with catheter examined and found to contain no sugar, acetone or albumen.

Blood:-

Histologically - parasites of different stages numerous, on several fields were found. Crescents were also found but in the proportion of one crescent to eight of the other parasites.

Treatment:-

Absolute rest in bed. Intramuscular injection of Quinine Bi-Hydrochlor grs. X dissolved in 20 mins. of normal warm saline. Within ten hours patient recovered consciousness and was put on oral treatment of the "A" Alkaline mixture alternating with the "B" Quinine mixture thrice daily as already described.

General:

Light diet of milk, soda water, oranges and fruits. When temperature became normal for four days he was put on light solid diet.

After a week of Quinine treatment he was allowed up and to move about, he had five days interval from treatment, which was repeated for another seven days.

The recovery was uneventful and he was sent back to school after a month's treatment. He was told to continue quinine, 5 grs. in liquid daily for three months. He also had Easton's Syrup in 3 p doses during convalescence.

(2) Date 4 : IV : 31. A. M., European, aged 25 years.

A merchant who arrived in Lagos about seven months ago. Went to work and complained that he was not feeling too well. Returned home in the evening and took some whisky for the cold. Next morning his boy-servant went to the room as usual and found that he was talking "something funny" to himself. The servant at once summoned medical assistance.

Examination:

Patient was very restless and soaked with perspiration. He had a small icteric tinge on the conjunctival and on the mucous membrames of the lips. His temperature was 101° F. per rectum. His lower limbs were very tremulous. Urine by catheter - nothing abnormal. Blood - different stages of parasites with crescents.

Treatment:

Quinine Bi-Hydrochlor intramuscularly as in the first case. One pint 5% warm glucose saline per rectum. Patient recovered consciousness in about eight hours and was put on oral quinine treatment. Light diet was prescribed with plenty of fluids, soda water, orange juice, etc. Patient recovered quite well and resumed duty in two weeks but was strongly told to continue quinine grs. X in solution daily for three months. After the third month he was advised to take Atebrin 0.1 grm. daily as prophylaxis.

(3) Date 5 : III : 33. A Syrian trader, aged 28 years.

He had toured the suburbs and had been caught in a very severe rain, he returned to Lagos at about 9

p.m. quite wet, had a cup of coffee and retired to bed. Next morning he felt little cold and remained in bed, and about 9 p.m. next day he was found to be unconscious. Temperature per rectum 103° F.

Examination:

Patient was extremely hot and dry. Very restless and occasionally sank into deep quick breaths. Urine taken with catheter showed nothing abnormal. Blood - histologically - numerous parasites and crescents found. Marked increase of large mononuclears - 15%.

Treatment:

Quinine intramuscularly as in case 2. Patient recovered consciousness in fifteen hours. Oral quinine medication started with light diet. Quinine continued for three months and he was advised to take Atebrin 0.1 grm. daily as prophylaxis.

Several other cases gave similar pictures and were treated accordingly.

Cases of hyperpyrexial types.

(1) Date 3 : III : 31. A Syrian Merchant, aged 35 years.

This patient gave a history of previous mild attacks of malaria and he had been taking 3 grs. of quinine daily but when he went to the Northern Province he did not take any quinine until he returned to Lagos about nine months ago and had since been taking 3 grs. daily. Patient was quite well until two days ago when he attended a dinner party. On his return home he felt extra warm and took a cold bath before going to bed. Next morning he had several

attacks of shivering and he remained in bed. At 12 p.m. he took his temperature and found it to be 103°F. He was very alarmed and sent for a doctor.

Examination:

His temperature when taken was 104.8° F. He was very much agitated and was weeping bitterly. His face was flushed and his tongue was very dry. He had a very angry look and was desperate. Blood - examination showed numerous parasites and crescents.

Treatment:

Quinine Bi-Hydrochlor intramuscularly. Hydro-therapy: rectal ice-water 2 pints. Cold sponging of the body. Temperature dropped to 102° F. and he was put on oral quinine medication with light diet, etc., as in previous cases. He was told to take liquid quinine, grs. X daily after discharge for three months and then Atebrin 0.1 grm. daily. He was cured within seventeen days and resumed his work.

(2) Date 10 : II : 32. An Indian shop assistant, aged 23 years.

Had Black-water fever at Bombay two years ago. Had been at Lagos for over fifteen months. Took quinine irregularly and only when he felt chilly. Took ill at the shop and was asked to go home. He went to bed immediately he arrived home and started shivering. His looks were dull and although he was conscious his speech was incoherent. He showed disorientation for time and place within ten hours of the fever.

Examination:

Patient was talking about some bazaar in Bombay and that several people bought goods from him there and ran away without paying. When asked about the time or the place where he was, he was utterly confused and gave wrong answers. A thorough systematic examination was made and nothing found except the blood which showed numerous malaria parasites (sub-tertian) in different stages with crescents. His temperatures at the axilla was 104°F. and per rectum 105° F.

Treatment:

Quinine intramuscularly and Hydro-therapy of cold sponging; rectal ice-water till temperature dropped to 102° F. Then patient was put on oral medication with the same routine as already stated. He recovered within five weeks and was advised to go home on leave but to keep on with Atebrin 0.1 grm. daily.

Algid Cases - adynamic.

(1) Date 10 : XII : 33. An African woman, aged 27 Years.

She was confined three weeks ago. During the gestation she was very weak and had swollen legs from the fifth month - had full time labour unaided, and was looked after during puerperium by some relatives. Had no appetite.

Examination:

Patient was very weak and her skin was very cold and the temperatures, at axilla 97° F. and per rectum 100° F. respectively. Extreme pallor of the mucous

membranes of the conjunctive and lips. Abdomen showed a scaphoid appearance. Blood - few parasites and crescents.

Treatment:

Warmth - blankets and hot-water bottles around the patient. Stimulants - brandy 3ii , Ideal milk 3iv, glucose 3i , hot water 3ii every four hours.

Intramuscular injections of quinine bihydrochlor - grs. X in 20 min. of warm sterilized saline. Patient was then put on the "A" Alkaline and "B" Quinine mixtures orally but showed intractable vomiting after taking quinine and was given

R

Glucose	5	5
Sodm. Chloride	1	
Aq. Dest.	ad 100	

with equal quantity of hot water, and given a half pint to be sipped every two hours. The vomiting stopped after the hypertonic glucose saline had been given for six hours. She then started her quinine mixture comfortably.

As she was so weak Camphor grs. iii in 2 c.c. olive oil was also given intramuscularly to reinforce the action of the heart. Her recovery was protracted and took over two months to build her up properly with Easton's Syrup as well in 3 p. thrice daily doses with judicious dieting.

(2) Date 14 : X : 34. A male African, aged 2 years.

Had severe diarrhoea for three weeks previously which was cured by native treatment. Patient also suffered from mild cough six months ago. He became listless and subsequently took to bed and refused

meals.

Examination:

Stools - not pathological. Chest, nothing abnormal found. Heart sounds were weak but pure and close. Blood - numerous parasites in all stages with heavy infection of crescents. Temperature 97.8° F.

Treatment:

Warmth - blankets - hot lemon drinks with sugar frequently; hot coffee - freely. Intramuscular quinine bihydrochlor grs. iiii in 20 mins. warm sterilized saline. He was then put on "A" Alkaline and "B" quinine mixtures thrice daily alternately - dose 3 iii of each. The mixtures were continued for a week, five days interval allowed, and repeated. He made an uneventful recovery in 16 days but the parents were told to continue liquid quinine for three months - 3 iii daily.

Three other Algid cases had similar treatment.

Choleraic Cases.

(1) Date 18 : IV : 31. A male African, aged 10 years.

Had very severe vomiting with frequent motions - stools were watery and colourless and not unlike the so-called rice-water stools of cholera (with white flakes of rice-like deposits). Severe cramp all over the muscles, especially those of the lower extremities.

Examination:

Patient was very cold. Temperature per rectum 100° F. Stools - no pathological organisms, blood - parasites and few crescents.

Treatment:

Exactly as in the adynamic type. Intramuscular quinine injection - grs. V in 20 mins. of warm saline. Fluids and milk allowed freely. He was put on "A" Alkaline mixture with Tr. Opii m $\overline{iii}$ - 3 $\overline{ii}$ doses thrice daily and given quinine mixture of the same dose alternately. Hot fomentations and massage for cramp. Patient recovered very slowly and took about two and a half months to convalesce. He was strictly warned to take liquid quinine daily for three months.

Four other Choleraic cases were treated on the same lines.

Bilious remittent Cases.

Date 18 : IX : 34. An Indian Trader, aged 23 years.

Started vomiting severely from about 8 a.m. and was unable to retain anything. He even vomited soda water when it was sipped. He became very weak and sent for medical aid at 12.30 p.m. Patient admitted that he took no quinine as prophylaxis and that he had had several mild attacks of malaria in India.

Examination:

He was very weak when seen and said he had vomited much fluid. The colour of the vomit was greenish and watery. Thorough examination revealed nothing abnormal in the alimentary tract. Blood - showed parasites and a few crescents.

Treatment:

Alkaline mixture "A" with Tr. Opii m V - 3$\dot{i}$ thrice daily until vomiting stopped. Intramuscular quinine injection. He was put on liquid quinine treatment alternating with the Alkaline mixture without opium

later. Fluids and light diet. He recovered in nine days time but was rather weak. He had Easton's Syrup treatment for this weakness, and was told to continue liquid quinine daily for three months and then to start Atebrin 0.1 gr. daily.

Four other similar cases were treated as above.

Ordinary irregular remittent forms.

Date 25 : XI : 33. A male African, aged, 30 years.

He went to the office in the morning and felt severe cold while in the office. He was given permission to go home and he went straight to bed.

Examination:

He was seen at 9 p.m. Temperature in the mouth 101° F. He admitted having had a rigor. Blood - few parasites and crescents.

Treatment:

Patient was put on Alkaline and Quinine mixtures but developed a generalised rash all over the whole body the third day of the treatment. The rash was intensely itchy. Apart from the rash which subsided four days after the quinine treatment was stopped the recovery was uninterrupted.

Four other cases showed generalised rash similarly.

Ordinary regular intermittent forms with pregnancy.

Date 10 : X : 32. An African woman, aged 23 primipara.

Period of gestation - 6½ months. Had a severe fever for three days. Slight vomiting - loss of appetite.

Examination:

Blood - showed numerous parasites and crescents.

Treatment:

Patient put on Alkaline and Quinine mixtures, but 2 grs. quinine used instead of the usual 10 grs. On the sixth day of the treatment she started to show signs of abortion which became complete on the eigth day in spite of all sedative measures taken to arrest it. During the threatening abortion she was given liquor Sedans 3ṯ in water thrice daily and kept quietly in bed.

Four other pregnant cases with the same small doses of quinine aborted likewise.

Total cases treated with quinine 75.

Total cases treated with intramuscular quinine and oral administration 30, viz:

(a)	Comatose	10
(b)	Hyperpyrexial	5
(c)	Algid - Adynamic	5
(d)	Choleraic	5
(e)	Bilious remittent	5
		30

B. PLASMOQUINE Co.

Ten cases were treated with plasmoquine Co, - six Africans, two Europeans, one Indian, and one Syrian.

Date 11 : XI : 32. A male African, aged 2 years.

Had a very severe fever of four days duration. Slight vomiting and mild diarrhoea.

Examination:

Patient was weak, with temperature at 101° F. Spleen enlarged and tender. Blood - numerous parasites and crescents.

Treatment:

Rest in bed, light diet - plenty fluids etc. Plasmoquine Co. - One tablet daily divided into three doses and powdered before taking. He developed left epigastric pain on the sixth day of treatment and the gums and lips were cyanosed. The drug was stopped for five days, and the pain lessened but the cyanosis faded only slightly. On resuming treatment with the drug again the patient developed the same pain on the third day of the second course of treatment and the drug had to be stopped and he was put on "A" Alkaline and "B" Quinine mixtures, 3 ii t. d. s. alternately for one week. He had no return of pain with 'quininisation' and recovered in fifteen days time. During convalescence he had Easton's Syrup Min. XX in water thrice daily after food.

Date 12 : XII : 32 A female African, aged 22 years.

Had fever for three days, became unconscious and her relatives were forced to send for a doctor after their native treatment had failed.

Examination:

When seen, she was partially unconscious. She muttered meaningless words for sometime and then said something sensible. Catherterised urine - normal; Blood - numerous parasites and crescents; Spleen - not enlarged; Temperature 100° F.

Treatment:

Plasmoquine Co. - Adult dose of two tablets twice daily with four days interval - a full course was given. (See page 27).

Patient had cyanosis of the gums and lips but no marked epigastric pain.

Patient recovered quite well after the full course.

Date 13 : IV : 33. A male African, aged 16 years.

Had fever for about two weeks and admitted having had many rigors.

Examination:

Enlarged spleen. Temperature 101.6° F.
Blood - numerous parasites and crescents.

Treatment:

Plasmoquine Co. Adult dose - two tablets twice daily according to the course (see page 27). He developed very marked cyanosis of the gums and lips, severe abdominal pain with extreme "boarding" and severe vomiting resembling "acute abdomen".

The drug was stopped and the patient put on three pints 5% warm glucose saline per rectum daily for three days after which the grave signs subsided and the patient was then put on Alkaline and Quinine mixtures for a week.

Two Europeans also treated with plasmoquine Co. had mild cyanosis of the gums, lips and face but no marked epigastric pain. Neither had an enlarged spleen.

C. Atebrin.

Total cases treated with this drug, 75, out of

which there were ten intramuscular injections of Atebrin-Musonate (one ampoule Atebrin solution is equivalent to 0.1 grm. Atebrin) in combination with oral administration.

Cases treated with Atebrin-Musonate with subsequent oral Atebrin.

COMATOSE	HYPERPYREXIAL	ALGID-ADYNAMIC	CHOLERAIC	BILIOUS REMITTENT
2	2	2	2	2

COMATOSE FORM.

Date 7 : XI : 32. An African male clerk, aged 24 years.

Had several attacks of fever during the past seven months. His health had been very poor and he was becoming very thin. Felt very weak for some time past. Developed very severe fever about 7 p.m. and by twelve o'clock midnight he was unconscious and restless.

Examination:

Patient unconscious, temperature 102° F. Catheterised urine - normal. Blood - different stages of parasites with crescents, numerous.

Treatment:

One ampoule Atebrin-Musonate intramuscularly. One pint 5% warm glucose saline per rectum. Patient became conscious in about five hours and was put on Atebrin 0.1 grm. thrice daily for seven days. Five days interval was allowed and Atebrin given in the same doses for another seven days. Patient recovered

within seventeen days and put on weight.

Another similar case was treated likewise.

HYPERPYREXIAL FORM.

Date 4 : V : 33. A female Syrian trader, aged 32 years.

Had not been feeling too well and had been taking two grs. quinine irregularly whenever she felt 'out of sorts'. She thought she had contracted cold and went to bed, started shivering and developed high fever.

Examination:

Temperature 104° F. All the systems were gone through carefully but nothing abnormal was found except the blood which showed parasites and crescents.

Treatment:

Atebrin-Musonate, one ampoule intramuscularly. No hydro-therapy given and the temperature dropped to 101° F. in three hours time. She was then put on the adult two courses of oral Atebrin of seven days each, with five days interval. She recovered about the tenth day. She showed slight yellowness of the skin which persisted for about six weeks after the drug was stopped.

Another similar case had the same treatment.

ALGID FORM.

Date 10 : X :34. An African male, aged 16 years.

He was brought from one of the suburbs to Lagos for treatment. His relatives said he had not been well for about two months and could not move about owing to weakness.

Examination:

Patient was extremely cold, weak and prostrated. His pulse was 40 per minute and the heart sounds, very weak. Blood - parasites and crescents numerous.

Treatment:

Atebrin-Musonate, one ampoule intramuscularly; warmth produced by blankets, hot water bottles. Stimulants - Brandy 3ii , Ideal milk 3ii , glucose 3i and hot water every four hours. Camphor grs. iip in 2 c.c. of olive oil intramuscularly as well. He was also put on oral Atebrin adult dose - courses. He recovered very quickly and regained his strength in about ten days time. He was kept in my Nursing Home for a month and discharged after he had been properly toned up with Easton's Syrup, 3 p. doses.

Another similar case receiver the same treatment.

CHOLERAIC TYPE.

Date 15 : XII : 34. A male African, aged 27 years.

Complained of several motions a day which had continued for ten days. He used chlorodyne and different native medicines to stop the motions but failed and as he was becoming weaker he sought medical aid.

Examination:

Specimen of stools was found to be watery and showed white rice-like deposits. Stools showed no pathogenic organisms. Blood - parasites and crescents. High percentage of large mononuclears 15%.

Treatment:

Fluids - oranges, milk and soda water.

Atebrin-Musonate intramuscularly with oral Atebrin in the usual courses. The stools stopped the third day and patient had to be given liquid paraffin ℥ i the fifth day as he was constipated. He had Easton's Syrup 3 p doses during convalesence and was discharged cured in a month.

Another Choleraic type had the same treatment and behaved exactly as the case detailed.

BILIOUS REMITTENT.

Date. 17 : III :35. An African female, aged 30 years.

Had slight fever for three days previously and woke up with severe head-ache and repeated vomiting which was intractable. Her condition was grave when seen. She was extremely costive.

Examination:

The specimens of vomit were watery, copious, mucous and bilious. No food particles were seen. Patient looked very toxic and pale. Pulse fast - 100 per minute. Other systems - nothing very special to note except the blood which contained parasites and crescents.

Treatment:

Atebrin-Musonate - one ampoule intramuscularly. Soda water and oranges only. Patient reacted very well within four hours after the injection as the vomiting stopped and she was then put on the oral Atebrin, the usual adult dose - the same courses as already detailed. She recovered in eighteen days time.

Another bilious remittent type had the same treatment and reacted well.

Twenty pregnant cases of different periods of gestation from four months to nine months were treated with oral Atebrin without a single case of abortion. The dose given in each case was the full adult dose and the same two courses of treatment.

D Decoction Cassia Occidentalis with Rauwolfia Vormtoria. (Native herbs).

Total cases treated were 35.

Two typical cases showing the action:

Date 13 : II : 33. A male African, aged 34 years.

Had repeated attacks of fever and was slightly weak. He had no appetite. He was very constipated.

Examination:

Tongue heavily furred and dry. Temperature 101° F. Blood - parasites and crescents. Total count, red cells 3,500,000. No megalocytes - large mononuclears. - 13%. Red cells rather small.

Treatment:

Liquid diet of milk, soda water and oranges. Decoct. Cassia Co. A wine glass full thrice daily for two weeks, an interval of a week allowed and repeated for another two weeks.

Patient started to perspire profusely in less than three hours after treatment and had to be dried often. After the third dose of the Decoct. he had a motion and kept on having three motions daily during the treatment in spite of the fact that he was habitually constipated for several days.

Patient recovered very slowly and was discharged after 1½ months.

Date. 14 : I : 34. An African Female, aged 35 years.

Had not been feeling too well since the birth of her last child six months ago. She was a multiparous and had five children. This morning she woke up with slight fever and started to vomit repeatedly. All her friends efforts to stop the vomiting failed.

Examination:

Patient emaciated and anaemic - mucous membranes of conjunctival and lips were pale. The copious vomit collected showed different colours.

Temperature per os 100.8° F. Blood - parasites and crescents.

Treatment:

Decoct. Cassia Co. in the same doses and courses as fore-mentioned. Vomiting stopped after the first dose. Patient put on liquid diet of milk and oranges for seven days until the temperature became normal and she was switched on to light solid diet. She recovered very slowly and took 2½ months. She was given Easton's Syrup during convalescence.

The thirty five cases treated with Decoct. Emilia Sagitata showed similar reactions as those treated with Decoct. Cassia Co.

Supplementary pharmacologic details of the drugs used.

QUININE.

Found in the bark of various species of Cinchona which are natives of South America but are now cultivated also in the East. Cinchona bark was

introduced into European Medicine in 1640 and was named by Linnaeus after the Countess of Chinchon who was successfully treated by it. Quinine was isolated from the bark in 1820 by Pelletier and Caventon[24] and since the use of the Alkaloid has replaced the crude bark. Cinchona bark contains a large number of Alkaloids (quinine, quinidine, cinchonine and cinchonidine), and about one half of the total being quinine. Generally the other Alkaloids resemble quinine in constitution and action but none of them equals it in importance. Quinine has a complicated structural formula which is believed to include a quinoline

and a piperidine group. Quinine differs from most Alkaloids in having no high degree of selective action. It kills all living cells in sufficient concentration, hence it is sometimes called a general protoplasmic poison. It is also an antiseptic but relatively less efficacious against bacteria than against protozoa like the Malaria parasite. Its chief features of action are that in a relatively low concentration it diminishes the activity and vitality of protozoal organisma; hence its action in Malaria. It acts only on different stages of asexual forms. It acts as an antipyretic by diminishing heat formation.

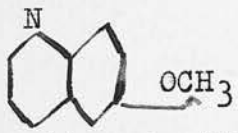
Low concentrations such as occur in the blood after medicinal doses may cause increased contraction

of involuntary muscles especially that of the uterus, hence its use in labour though not comparable in power to pituitary or ergot. Large doses or continued maximal therapeutic doses produce disturbances of the senses of hearing and sight - ringing in the ears, deafness, vertigo and contraction of the field of vision (cinchonism). Usually these effects are transient and disappear when the quinine is stopped. Marked idiosyncrasy to quinine affects some people who suffer from disorders of hearing and sight even from much smaller doses; others again suffer from skin rashes.

The salts of the Alkaloid used during the observations were quinine sulphate and quinine bihydrochlor. Quinine sulphate occurs in feathery crystals which are intensely bitter and soluble 1 in 800 in water. Quinine bihydrochlor has a solubility of 1 in 1 in water.

PLASMOCHIN.

It is a compound derived from quinoline and has a structural formula

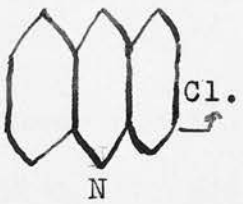


It has a specfic action on the sexual stages of Malaria parasites especially the cresecnts. The therapeutic dose is estimated as 1 mg. for each kg. of body weight. It is intensely toxic leading to cyanosis and severe epigastric pain - (See also page 11).

Its compound with quinine - plasmoquine Co. - containe plasmochin ~~0.01~~ 0.01 grm. and quinine 0.125 grm. in each tablet. It is supposed that the action of quinine in combination counteracts the toxic effects of plasmochin but this is not absolutely true. It is comparatively tasteless and it is also believed to be more efficacious than quinine in preventing relapses. (See also page 11 for the historical data and page 27 for doses and the usual courses of treatment).

ATEBRIN.

It is an acridine compound with a structural formula



And its chief pharmacologic actions with doses have been described on pages 12, 13, 27 and 28.

Atebrin-Musonate of which 0.125 grm. corresponds to 0.1 grm. of Atebrin-dihydrochlor was used intramuscularly during the observations and not intravenously.

CASSIA OCCIDENTALIS.

It is a very common plant in Nigeria and grows wildly in different places. The natives use nearly all the parts of the plant - bark, roots etc. - for medicinal purposes. The decoction of the dried leaves is believed by the natives to have a distinctive effect on infantile convulsion and to control adult fevers. As a rule the leaves are generally combined with the dried leaves of Rauwolfia Vormitoria in equal

quantity made up into a decoction in order to produce a synergetic effect. The dosage allowed by the natives is large and may range from a tumblerfull (10 ozs.) or more thrice daily.

During the observations the combinations of the two kinds of leaves was used in decoction of 20% which was allowed to boil for one hour and the dosage given was a wineglassful thrice daily.

The effects noticed were :

(1) It controlled the excessive vomiting;

(2) It has a strong diaphoretic action and is mildly laxative;

(3) It has a weak toxic effect on the asexual parasites but none on the sexual forms.

EMILIA SAGITATA.

This is also a common plant in Nigeria. The dried leaves in decoction are used by the natives for fevers - infantile and adult. They also give large doses of the decoction. During the observation the dried leaves were made into a decoction of 20% and allowed to boil for one hour. Dose - a wineglassful thrice daily. Effects - similar in all respects to those of the leaves of Cassia Occidentalis with Rauwolfia Vomitoria.

SUMMARY.

Two hundred and thirty cases of uncomplicated Malaria Fever had been studied at Lagos with a special regard to prevention and treatment.

As far back as thousands of years the ancient Greeks connected Malaria Fever with marshes and called it, Paludism. The specific drug - cinchona and its chief alkaloid, quinine has been long known. The authentic knowledge of the mode of infection through an intermediate host, - anopheles, was indirectly initiated by Sir Ronald Ross and confirmed later by other research workers.

The ancient inhabitants of Lagos also connected fevers with marshes and mosquitoes long before the scientific proof. They therefore took various precautions against infections. Sir Ronald Ross visited Lagos through the invitation of Sir William McGregor, M.D., and the former suggested definite anti-malaria measures which ~~have~~ have been magnified through time.

J. Gordon Thomson suggested complement fixation test for Malaria on the basis of Khan or Wassermann Reaction. Later on Henry developed the Melano-Flocculation test which was subsequently modified by Col. Greig and others and re-named Melano-precipitation Reaction.

Plasmochin introduced for Malaria therapy and was later combined with quinine - Plasmoquine Co.

Atebrin followed Plasmoquine Co. after some years.

Malarial patients at Lagos had definite

predisposing causes.

The climate and constantly interrupted chain of hygienic measures offer a suitable prospect to the highly adaptive local species of Anopheles costalis and Anopheles gambiae, the intermediate hosts.

The Major Anti-Malaria measures are efficiently controlled by the local Government.

Minor preventive measures stressed by me consisted of: (1) Demonstrations, (2) Bonification, (3) Mosquito-netting, (4) Drug-taking, (5) Importance of early treatment and (6) Mass education. Curative treatment was:-

(a) General.

(b) Drugs - Quinine, Plasmoquine Co., Atebrin, Decoct. Cassia Co., and Decoct. Emilia Sagitata.

Cases treated were:-

75	with quinine.
10	with Plasmoquine Co.
75	with Atebrin.
35	with Decoct. Cassia Co.
35	with Decoct. Sagitata.
230	

CONCLUSIONS.

Since Malaria has long been known for centuries past as a severe endemic disease in the tropics and the sub-tropics and judging from the comparatively low mortality of the disease from numerous infected cases, there must be some relative immunity developed among the people in the highly malarious countries. During the observations spreading over five years it was found that the parasites were low in infants up to four months and then rose rapidly and reached a

maximum of 98% at the age of three years, subsequently it fell slowly until the age of 16 years and then fell steadily again in direct proportion to the advancing age. This infection rate seems to be constant at Lagos as the record is practically in accord with that of another independent observer - W. Fletcher[37]. Again, Christophers[37] during his observations in India in 1924 gave statistics coinciding with those obtained at Lagos as regards to periods of heavy and light infections.

During the observations at Lagos it was found that the index of splenic enlargement was highest at the period coinciding with the highest infection, that is from four months to three years. These views seemingly point to two facts, (1) that there must be some relative immunity in early infant life before four months which subsequently got attenuated. (2) That owing to the immunity there was a check on the parasites which reaction caused the enlarged spleen.

However the immunity must be taken as a low one and cannot be called a sterilizing one but an infection immunity resulting from a latent infection; such an ~~infection~~ immunity has been called "premunition" by Sergeant, Parrot, and Donatien in 1925[37].

Christophers[37] holds that the length of time taken to attain this kind of immunity might be due to the existance of many different strains of parasites in the locality with each of which the individual must be'salted'. This view is equally applicable to the

people at Lagos who have been passing through different strains of parasites for several years.

Melano-precipitation Reaction.

As already stated this test is not specific for Malaria and all the observations made at Lagos in different cases of Malaria varied. Like all laboratory tests, however, it has to be interpreted in terms of clinical signs and although the main factor determining a positive reaction depends on the blood serum with high euglobulin fraction and the successful method of carrying out the test with the required pH. yet the test should still hold a serological value. Even we know that the reputed Wassermann or Khan's test is sometimes negative when clinical signs are positive, hence in obscure cases of Cachexia when other diseases with high euglobulin fractions in the blood, e.g. Kala-azar Trypanosomiasis - have been excluded the test in conjunction with other clinical signs should be very helpful to clinch the diagnosis of Malaria.

At Lagos the predisposing causes (page 15) to Malaria were many and all put together could be said that anything that lowers the tone of the body predisposed to the disease, and apart from the climate that is extremely hot and distressing sometimes, the local species of Anopheles costalis and Anopheles gambiae are highly adaptive in their methods of breeding and they develop very rapidly thus enabling them to take advantage of any temporary water. This view is also held by W. Fletcher [37].

Prophylaxis.

The major anti-malarial measures though useful cannot alone efficiently cope with the conditions at Lagos[37]. To any observer, mass education with major anti-malaria measures is the most important factor. Unless the natives understand the methods of infectivity and willingly co-operate with the Sanitary Authorities, the constant breach in the chain of infection since the visit of Sir Ronald Ross about thirty five years ago, will still be maintained; and in full agreement with Manson Bahr sanitary measures can rarely be carried out effectively without the co-operation of those whom they are intended to benefit and this cannot be secured unless the rationale of their co-operation is understood.

In minor measures of Malaria - control the hygiene of individuals stands paramount and thanks to the School Authorities who enforce the study of hygiene in most schools; and assuming that such a knowledge is put into practice by different pupils in their surroundings yet it still remains the great mass of illiterates. It is in this respect that the Health Week with its attractive demonstrations bi-ennially is very useful.

The proper use of mosquito-nets plays a strong role also, and judging that the natives prefer the use of nets to any drug taking, its importance cannot be over-rated in reducing Malaria incidence. The fact that there is no known drug that will prevent the sporozoites developing into trophozoites after the

former have been injected into human beings, is again in strong favour of the proper use of nets to prevent mosquito bites, and the lesson gained from the experience of Dr. Sambo and Dr. Low and others who stayed in Roman Campagna in 1900 without being infected with Malaria [41] must always be encouraged, and according to Wenyon [42] mosquito nets prevent infection more than all other methods of prevention taken together. The drug recommended as prophylaxis is Atebrin owing to its delayed secretion from the body. The Europeans, Indians and Syrians took it regularly and among them Malaria relapses or recurrences were never known. The yellow discoloration was the objection in many cases but with one tablet 0.1 grm. daily the discoloration was not very much noticeable. The natives as a rule never took drugs regularly in spite of all emphasis as already stated.

Curative Treatment.

Plasmoquine Co. gave degrees of cyanosis in every case which was very severe in debilitated cases with heavy infection of parasites. Again, the severe epigastric pain was very marked in cases with enlarged spleen; this might be due to the strong action of plasmochin on the spleen with subsequent violent contraction which led to the severe pain [24]. Although Muhlens [24] regarded the colicy pains as the effect of vasomotor disturbance.

The action of quinine was held by several authorities [24] to neutralize the toxic effect of

plasmochin but even in small doses (0.01 grm. in a tablet) in plasmoquine co. in the ten cases in which this compound was used, this neutralising effect was not seen to any advantage especially among the cases with enlarged spleen. Moreover, the severe epigastric pain in cases with enlarged spleen could not be attributed to idiosyncrasy alone as other cases without enlarged spleen also showed a lesser degree of epigastric pain. This view negatives the observations in Liberia[37] where it is stated that pure plasmochin up to the dose of 0.03 grm. was used freely among the natives without any untoward symptoms. As splenic enlargement is invariably a concomitant of Malaria, the observations lead one to conclude that plasmochin or its compound is not a safe remedy to use owing to its severe toxic action. Again, plasmochin or its compound - plasmoquine co. - in every case observed gave a cyanosis believed to be due to a compound analogous to Methhaemoglobinaemia similar to Pot. chlorate poisoning[24], and if such blood poisoning was exhibited even with so small a dose of plasmochin in plasmoquine co. could the drug be held in any way to be safe either for prophylactic or curative measure? The result of the observations gives a negative answer.

Atebrin versus Quinine.

As it will be seen the same number of cases (75) were treated with Atebrin and Quinine respectively. The observations put Atebrin a stronger and safer rival to Quinine. The slow excretion of Atebrin from

the system makes the blood more saturated than with Quinine administration which is very quickly excreted, hence the distinctive advantage of Atebrin over Quinine both for curative and prophylactic measures. In favour of Atebrin it has been shown that it actually penetrates the red blood corpuscles and has a specific action on Schizents [15), 16), 33), 37)] ; this claim has not been made in favour of Quinine and although it has a specific action in Malaria its real chemical action in vivo has not been proved. Atebrin from the observations made, is less toxic judging from the two cases that took over 15 tablets of 0.1 grm. in in less than 48 hours without any serious effect except a slight excitement. This however contradicts the views of Hoops in Singapore where toxic effects - mania, etc., were noticed but agrees with the author's view that Atebrin gives a sense of well-being in contradistinction to Quinine. Quinine even in small doses produced abortions in all cases in which it was used contrary to Atebrin that produced no abortions.

The intramuscular injection of Atebrin-Musonate acted much more quickly than Quinine and this is a distinct advantage in cerebral malaria forms where quick therapy is very much indicated. Against Atebrin is the yellow discoloration which persists for a few weeks after stopping the treatment and in the matter of expense Quinine is cheaper. The cases which reacted very quickly to quinine treatment developed tinnitus and partial deafness after a few days treatment which show a relatively cumulative

effect of the drug - these symptoms were never observed in any cases treated with Atebrin.

In Atebrin treatment there was no rash as seen in some cases treated with Quinine. The intractable vomiting following the administration of Quinine especially among children was not noticed with Atebrin treatment.

All the cases treated with atebrin showed no relapses or recurrences against Quinine which showed 10% of recurrences.

Decoct. Cassia Occidentalis Co. and Decoct. Amilia Sagitata.

Each decoction had a very strong diaphoretic effect and from the histological examination of the blood, the parasites receded slowly. Whether the recession of the parasites was due to the action of the drug or to the natural immunity leading to a cure is very difficult to say until the active principles of the herbs are known. Again, the cases treated showed 20% of relapses and this shows that the patients were either not properly sterilized during treatment by the action of the herbs or they got new infections. Whichever it is, the herbs were used with a view to open the way to further investigation which could only be completed when the active principles of the herbs are known.

Summary of Conclusions in order of importance.

THERAPY.

Prophylactic:

(1) Efficient major anti-Malaria measures with mass education.

(2) Mosquito-netting.

(3) Drug-taking - Atebrin.

Curative:

(1) Atebrin.

(2) Quinine.

BIBLIOGRAPHY.

1. British Medical Journal Vol 1. 1927 page 466

2. Chopra and Gupta. Indian Med. Gazette - 1933 - pp. 425, 493 and 558.

3. Chopra and Gupta. Indian Med. Gazette - 1934 - page 195.

4. Dawson, W. S., Malaria in the East African Campaign - Lancet 1921. 1. 248.

5. Deaderick. Practical study of Malaria 1909.

6. Delmege, J A., Malaria Prevention - Journal of Royal Sanitary Inst. Lond. 1920. 1. XLI. pp. 98 -102.

7. Fletcher and Kanagaraya - Plasmochin in treatment of Malaria. Ind. Med. Gaz. 1927. Sept. Vol. 52 No. 9. pp (499-506) (Experience with 97 patients).

8. Grieg, E.D.W. (Col.), - Lancet 30 - 6 - 34. p. 1393.

9. Greig, E.D.W. (Col.) and Others, Trans. Trop. Med. and Hygiene, 2 - 7 - 34.

10. Greig, E.D.W. (Col.) and Others, Trans. Trop. Med.and Hygiene, p. 175, 4 - 8 - 34.

11. Greig, E.D.W. (Col.) and Others, Trans. Trop. Med. and Hygiene, 1 - 10 - 34.

12. Hamilton - Malaria - Two years in Salonika. Journ. R.A.M.C. Lond. 1921. XXXVI pp. 361 - 369.

13. Hegner, Robert and Manwell - Effects of Plasmochin in bird Malaria - American Journ. of Trop. Med. 1927, Sept. Vol. 7. No. 5. pp. 279 -285.

14. Henderson - Trans. Roy. Soc. Trop. Med. and Hyg. 1933. Vol. 27. Nov. 30, p. 285.

15. Hoops, A.L., Trans. Roy. Soc. Trop. Med. and Hyg. No. 3. Vol. XXIX. Nov. 1935.

16. Hoskin, - 500 Cases of Malaria in Pensioners - B. M. J. 1921. p. 493.

17. Jones - History of Greek Therapeutics and Malaria Theory.

18. Kew - Bulletin Additional Series IX.

19. Lancet - 1926. Vol. II, p. 765. Brief Report of Dusseldorf Conference. also p. 1279.

20. Lancet - 1928. Vol. I. pp. 160 and 259.

21. Lotka, A.S. - Malaria Epidermiology - American Journ. of Hygiene. 1923. III (Supplement).

22. Macdonald, A.G. - Malaria Problems. Proc. Roy. Soc. Med. 1920. 1. XIV.

23. Macmahon - B. M. J. 1934. March 17. p. 477.

24. Manson-Bahr and Others - Proc. Roy. Soc. Med. (Trop. Dis. Sect.) Feb. and March 1927.

25. Manson - Bahr - Lancet 1928. Vol. 1. pp 25-26.

26. Manson - Bahr and Walters - Lancet 1934. Jan. 6. p. 15.

27. Manson- Bahr and Maybury - Trop. Dis. Buletin 1928. pp. 132-257.

28. McWalter, J.C. - Malaria as a present day problem. Med. Press. 1920. CX. p.348.

29. Meersemann and Lancour - Presse Medical 1934. June 20. p. 995.

30. Nigerian Report of Med. and Health Services 1934.

31. Ross, Ronald (Sir) with other Authors. Observations on Malaria 1919.

32. Ross, Ronald (Sir) - The Prevention of Malaria, 1911.

33. Ross, G. A. P. - Control of Malaria - Med Journ. South Africa, 1922-3 XVIII. pp. 134 - 146.

34. Row and Others - Journ. Ind. Med. Research. 1933. Oct. p. 295.

35. Smith Bassett - Malaria - Middlesex Hosp. Gaz. 1921. XXII. pp 54 - 62.

36. Stephens and Christophers - Practical Study of Malaria. 1908.

37. Tropical Diseases Bulletin. 1932 - pp. 331 - 362.

38. Tropical Diseases Bulletin. 1933. pp. 61-96. (Critical Review, pp. 193-202); pp. 458-502; pp. 819-871.

39. Tropical Diseases Bulletin, 1934. pp. 153-190; pp. 409-436; pp. 455-475. (Critical Review pp. 521-537). pp. 677-727.

40. Vad and Mobile - Place of Plasmochin in treatment of Malaria. Ind. Med. Gaz. 1927. Aug. Vol. 62. No. 8. pp. 430-434.

41 Walker, W. Observations on Malaria Prophylaxis - Dublin Med. Journ. 1920. 45. pp. 476-482.

42. Wenyon and Anderson - Malaria in Macedonia. 1915 - 1919. Journ. R.A.M.A. 1921. XXXVIII. 81.

--*--