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PRACTICAL MALARIA CONTROL

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A Handbook for Field Workers

BY

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Foreword by

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FOREWORD

THE problem of Malaria, its prevention and its treatment, is the outstanding problem of tropical life. It is estimated that at least five million human beings die from this disease every year. The loss of time in invalidity must be enormous. To the newcomer from areas free from the disease it may be a life or death struggle. Economic disaster awaits neglect of preventive measures in large undertakings.

Dr. Carl Gunther has spent many years as Medical Officer of a large industry in the Mandated Territory of New Guinea. Here at Bulolo is the centre of the gold dredging, right in the midst of the tropical jungle, and in a highly endemic area of malignant tertian malaria. In 1934, on his annual leave, he obtained the Diploma in Tropical Medicine in Sydney.

Gunther is an entomologist of repute as well as a student of clinical and preventive work and fully acquainted with its literature. He gives in this book the results of his many years' experience in the control of malaria and nothing is recommended that has not been tested out to the full.

Admitted that many of the questions that arise are controversial, Gunther's first hand experience must be listened to with appreciation. For the practitioner who meets Malaria for the first time it is invaluable. For the practitioner with more or less acquaintance with the disease it is of the greatest interest.

In the Military definite lines of action are drafted both for the prevention and treatment of the disease. Gunther's monograph supplies an excellent background by which to understand and use even more effectively the methods officially laid down.

—HARVEY SUTTON

FOREWORD OF THE AUTHOR

THIS little handbook is offered in the hope that it may help those who are meeting malaria in the field with only an academic knowledge of that complex and fascinating disease. It does not pretend to be a treatise on malaria, but is merely an outline of the practical problems involved. The opinions expressed are my own. I offer no apology for them, even though I am aware that some are radical, and some are unscientific, and that most are expressed dogmatically. This could hardly be otherwise in a condensed review of this nature.

As my only experience has been gained during ten years in New Guinea, my methods have naturally developed along lines suited to local conditions, and I have tried not to go beyond the limits of my own experience. Nevertheless I believe that most of what is presented here can be applied elsewhere, and I present it to all those whose work on malaria lies in undeveloped districts with widely-scattered populations, where time and expense are big factors, and where many questions arise which can only be answered out of hard-bought experience.

Bulolo, T.N.G.

C.E.M.G.

PART I

ANTIMALARIAL MEASURES

1. ELIMINATION *versus* CONTROL

GENERAL

In any district where malaria is endemic, there may be two general lines of attack. The disease can either be eliminated entirely, or by supervision and control it can be reduced to minor proportions.

ELIMINATION involves the eradication of all *Anopheles* breeding places within and around the district, and the treatment of all inhabitants so as to render them non-infectious to mosquitoes. The former requires permanent works, usually of considerable magnitude and expense; it is practicable in towns and certain types of developed country. In undeveloped country the benefits would only justify the expense in rare instances. The latter requires not only a sure means of destroying gametocytes in the blood stream; it requires also the wholehearted co-operation of every inhabitant, or else the means and authority to enforce treatment and to establish an effective quarantine. It would possibly work quite well in a gaol.

Elimination must be complete and permanent. If it be incomplete, much money and effort will have been wasted; if permanence cannot be guaranteed, the effect of a breakdown after a few malaria-free years would be disastrous, since the population would have lost its tolerance and partial immunity. It also requires a large, well-trained staff and a long purse. It should be obvious therefore that

unless conditions are truly favourable for successful elimination, and unless facilities and finances are adequate, it is useless to attempt it; and the problem then resolves itself into achieving the most effective reduction of malaria possible, for a reasonable cost.

MALARIA CONTROL aims at reducing the important breeding grounds, protecting the majority of inhabitants from mosquitoes, and reducing the number and severity of attacks of malarial fever per inhabitant. By comparison with elimination its cost is negligible; it does not interfere with tolerance or relative immunity; and it achieves results which are satisfactory for all working purposes. The point of greatest importance is to assess the probable effect in relation to the cost of the measures to be applied. Local conditions will influence all of these, but there are certain basic principles which have a universal application, and these will be discussed in their place.

PERSONAL

In treating patients, the same choice between elimination and control is offered. It is usually possible, in most cases, to eliminate malaria from the system by an intensive course of treatment. Where a general policy of malaria elimination is followed, every effort must be made to eliminate infection in every patient; but where the general policy is one of control only, the personal policy should conform, except in young children, where elimination should always be aimed at. Under control conditions there is always a good chance that many individuals may become infected, and it would be economically unsound then to try to eliminate all infection in the individual, since this involves an intensive course of treatment, often more unpleasant than the disease itself, with at least two weeks spent in hospital, or at any rate in bed under constant medical supervision. The heavy expense and loss of working time would not be justified when the patient runs much risk of being re-infected within a short time. In addition,

he would suffer more severely from any subsequent re-infection because of the absence of any degree of relative immunity.

PERSONAL MALARIA CONTROL aims at treating all attacks of malarial fever thoroughly, not with the object of eliminating the infection entirely, but rather of reducing its intensity to a negligible degree and maintaining it at a level low enough to prevent recurrent attacks.

A person otherwise in good health may for years carry a properly-controlled malarial infection, yet never have an attack of fever, or suffer any apparent impairment of his general health. He may take a regular dose of five grains of quinine daily without suffering any ill effects. Even should he develop occasional attacks of fever, under proper control conditions they will be infrequent, mild, and easily subdued.

2. THE RESERVOIR OF INFECTION

The indigenous inhabitants of a malarious district, while themselves possessing a high tolerance for the disease, provide a reservoir from which any introduced inhabitants can easily be infected. On the other hand, the introduction of any considerable number of non-immunes will stimulate a local increase in the virulence of the disease, to a point where the tolerance of the indigenous immunes is insufficient to cope with it. So a vicious circle operates for a time, until equilibrium is regained. Consideration of the reservoir of infection in relation to malaria control therefore provides the first practical problem.

The fact that a relatively primitive indigenous population owes a large part of its primitiveness to the braking action of centuries of malaria is no immediate concern of the medical officer. Recovery from this state of affairs is a matter, not of a few years, but of many generations, and will automatically take place provided the indigenous population survive the many disadvantages of contact with civilisation long enough to enjoy some of its advantages.

The facts concerning the indigenous inhabitants that really matter are these:

1. Having survived repeated malarial infections since infancy, they have a very high degree of tolerance or relative immunity, which must not be interfered with.

2. Massive infection, local increase in virulence following the introduction of non-immunes, and diseases causing a temporary lowering of general resistance, are the chief factors which will produce attacks of fever in them.

3. They constitute a reservoir of infection for the introduced non-immunes, to their own ultimate disadvantage, because of the increased virulence factor.

4. They will not carry out personal measures of control, or measures requiring personal co-operation, with any useful degree of efficiency. The more severely they suffer from malaria, the less are they likely to help themselves.

The measures to be taken to control their malaria are these:

1. Prevent chances of massive infection by mosquito control.

2. Give quinine as a routine measure to patients in hospital, as a substitute for their loss of general resistance due to disease.

3. Do not give any prophylactic treatment while they are in good health, for fear of interfering with their tolerance.

4. Separate the living quarters of immunes and non-immunes. Local conditions will influence the details, but useful general rules can be laid down. The ideal, usually an easy one to achieve, is to keep the two groups well apart, each in its own quarter. Unless the customs of the country absolutely prohibit this, the following is the best procedure in laying out, say, a small station with a compound for native servants and labourers:

i. The breeding habits of the local species of *Anopheles* having been ascertained, the chief breeding places around the proposed sites are mapped out.

ii. The direction of the prevailing evening breeze is ascertained.

iii. Working upwind from the worst breeding place, or from the one which promises the hardest and longest task in clearing it, put first the stables and byres, then the native quarter (immunes), and last the white quarter (non-immunes).

The evening breeze is selected as the deciding factor because it is in the evening that the *Anopheles* sallies forth to seek her prey, and although she might like to travel upwind towards any victims she may scent, a brisk breeze will carry her downwind in the greatest numbers. Towards dawn she is again active, but most of her prospective victims will then be safely asleep under nets or in screened houses; and unless she is already on the spot, or is helped by the dawn wind, she will not travel far before daylight drives her to shelter. On the sea coast, however, because the dawn wind is usually as strong as, and in the opposite direction to the evening breeze, a different arrangement must be adopted. The breeding places having been located, the direction of any offshore current must be ascertained. Then, working away from the breeding place in the opposite direction to the flow of the current, put first the stables, then the native quarter, and last the white quarter, in line along the coast (this, not because of malaria, but because of possible fouling of beaches; for similar reasons, where it is necessary to locate both quarters on a river bank, the white quarter should be upstream).

It is not unfair to the natives thus to place them in the forefront of the battle. In the first place, the presence of any stock will usually divert most of the mosquitoes. In the second, while protecting the non-immunes from infection is very much to their advantage; it is of advantage to the immunes also, because of the virulence factor. With the immunes placed between the main breeding places and the non-immunes, fewer mosquitoes will reach the non-immunes; if the breeding ground is reasonably well controlled, there is no likelihood of massive infection of the

immunes, and all will be well. If, instead, the two groups are placed side by side across the line of the prevailing wind, mosquitoes will reach each group in equal numbers and there will be considerable lateral traffic between them, to the disadvantage of both. Finally, it may be objected that mosquitoes which do reach the non-immune quarter, and become infected with malaria of increased virulence, can travel down wind again to the immune quarter. However, once fully fed with blood, they will obey the urge to lay their eggs, and only after that will they again seek food. In any case, under proper control conditions only a small proportion of the non-immunes will be infected; still less will become infective to mosquitoes; and only a very few of the infected mosquitoes will escape from the houses. So much cannot be said of the immunes.

This ideal arrangement has as its main advantage the fact that only general control measures are necessary among the indigenous inhabitants; no enforcement of personal measures is necessary. But under certain circumstances it may be impossible to separate the two groups, either because the custom of the country is for native servants to occupy quarters attached to or adjacent to the European households, or because lack of foresight has allowed the dwellings of immunes and non-immunes to be mixed up. If this arrangement cannot be overcome, it will be necessary to enforce personal control measures among the immunes, who will not carry them out at all unless forced, nor properly unless constantly supervised.

When dealing with native populations, it must be emphasised that under no circumstances should labourers from non-malarious districts be brought to work in malarious districts. The adults within malarious districts only survive because of their tolerance to the disease, acquired steadily since birth. The effect of sudden exposure to infection on natives who do not possess this tolerance is disastrous.

3. MOSQUITO CONTROL

ANTI-LARVAL MEASURES.

Control of mosquito larvæ and their breeding places depends wholly on knowing which of the local species of *Anopheles* are vectors, and what their breeding habits are. There are experts who can, and will, supply all essential information by return post—and there are many traps for young players. Consider the medical officer who found swarms of anopheline larvæ in certain large swamps, and therefore sited his township well away, on a hillside near some clear springs and streams. In spite of this, malaria was rampant, and expert advice was sought. It was found that the swamp-breeding species was not a vector in that district, and that the vector was a species which bred in the clear sunlit running streams. But the solution of the problem was not to move the township away from the hillside breeding places; it was to grow shade trees and shrubs overhanging the streams, since exclusion of direct sunlight made them unsuitable as breeding places for that particular species. This is an actual example of the type of problem which may be met with. In other circumstances, clearing and draining of swamps might drive away certain shade-loving species, but encourage the breeding of even more dangerous sunlight-loving species. It is only necessary to attack the larvæ of such species as are actual vectors. Therefore, the numbers of undifferentiated adults about do not constitute any measure of the effectiveness of anti-larval measures.

If the district is part of a region which has had a mosquito survey made, the local Public Health Department should have full information about vectors and their breeding habits. Failing that, the nearest school of tropical medicine, or national museum, or the British Museum, might be able to oblige. If no survey has been made, the best thing to do is to collect adult *Anopheles* and post them to one of the above authorities with a request for information. All available specimens must be sent, and

nothing may be taken for granted; in New Guinea, for instance, the common species on the coast has entirely different habits from the allied, almost identical variety found only a few miles inland.

Collecting adults is easy. They may be caught fully developed, or bred out from larvæ. For the first method, only a cyanide tube is needed. It is made by putting about one-quarter of an inch of chipped sodium or potassium cyanide into a strong test tube; this is covered with one-quarter of an inch of plaster of paris, and well rammed down; then another quarter of an inch of plaster, mixed to a thin cream with water, is poured in. When it has set and dried out, a thin layer of cotton wool is pressed over it, and a suitable cork is inserted. By searching with a flashlight in the darker corners of native dwellings, many adults can be found resting on walls and clothing, and may be caught by deftly capping them with the open tube and holding it until they collapse. Both day and night collections must be made. For practical purposes it is sufficient to know that the *Anopheles* rests with its body, head, and proboscis in a straight line, at about 40 degrees from the perpendicular, as distinct from other genera, whose bodies rest parallel to the surface with head and proboscis bent down at an angle. When sorting dead specimens the straight tapering shape and the row of dark spots on the anterior margin of the wing are a sufficient guide to the genus.

To breed out adults from larvæ, slightly more elaborate equipment is needed. For catching the larvæ, a small aluminium or white enamel ladle to scoop them from the water; a six-inch length of one-quarter inch glass tubing with a rubber teat on one end, to pick them out of the ladle without getting too much water with them; and a bottle with a moderately wide neck, in which to carry them home. Anopheline larvae lie with their bodies along the surface of the water, while those of other genera hang by their tails from the surface film. It is not easy to distinguish between pupæ, but the adults can be sorted out when they hatch. A breeding cage is necessary; a simple

one can be made by cutting the ends out of a tin (a petrol tin would be unnecessarily large, but quite suitable). Over one end is tied a plain piece of mosquito netting; for the other end a long cone of netting like a butterfly net is made. The wide opening is tied over the tin, and the tip of the cone is cut off to make an inlet for the hand about three inches across. By tying a loose knot in the cone the cage can be effectively closed. More elaborate cages with a wooden base bearing a wire frame over which is stretched a shaped net with a sleeve let into one end, can easily be devised. The larvæ and pupæ are put into small dishes in the cage, with enough water to prevent total loss by evaporation, and when they emerge the adults can be caught with the cyanide tube.

For packing specimens chip pill-boxes are the best containers. A drop of beechwood creosote on the floor of the box, with a few crumbs of camphor dropped in, will serve to preserve them. Cover the floor of the box with a wisp of cotton wool, put in a layer of mosquitoes, then more wool, and so on until the box is full. Then some more camphor and a drop of creosote inside the lid. Make a note on the lid of the number of layers enclosed. Packed in a strong outer box and endorsed "Entomological specimens, dead and preserved," they will travel safely through the post and should satisfy any Customs regulations. Information as to location, altitude, type of breeding water, and season when collected, should be sent. It would be well to ask for identification, capacity for transmitting malaria, breeding habits, and the best means of combating breeding.

To make an original investigation covering these points requires more time and knowledge than is possessed by the average medical officer.

No useful purpose can be served by detailing here the special methods of control applicable to individual species; they will be given by the expert when he reports on the specimens. But there are certain general methods which are always useful:

GENERAL METHODS OF TREATING BREEDING PLACES

Water can be classified as:

Permanent: rivers, lakes, streams, and swamps.

Semi-permanent: collections of moderate size which are likely to persist throughout the wet season, either being maintained by soakage, or requiring to be replenished occasionally by rain.

Temporary: small shallow accumulations which disappear by evaporation unless replenished by rain every few days.

These three classes require different methods of treatment.

PERMANENT WATER: Surface-feeding mosquito-eating fish offer the simplest single measure for permanent water, if they can be acclimatised. *Gambusia affinis* adapts itself to a very wide range of conditions; it is viviparous and multiplies rapidly, and a few liberated in a swamp will, after a few months, be found to have populated every stream and pool connected with the swamp. There are a few useful points concerning these fish: being surface-feeders, they are easily caught with a ladle or small net by a quick flick of the wrist. To transport them, a wide-mouthed jar is best, so that ample air can reach the water; they must not be crowded, and if they are kept in the jar for any length of time the water must be aerated by dipping it out and pouring it back repeatedly. They must be kept in water from a pool rather than in clean rain-water. They will live in such water for several days without artificial feeding (they are cannibals, and will look after themselves), but are likely to die if given bread or biscuit crumbs.

Failing fish, more or less permanent works involving sometimes considerable expense may have to be undertaken. Because of the expense, careful attention to breeding habits and capacity as vectors must be given before undertaking them, to ensure that the correct larvæ are

attacked. Some of the following methods are fairly extensive, and may almost be regarded as more applicable to expensive elimination projects than as simple control measures. Yet, with cheap native labour they may be made quite efficient for a reasonable cost.

Slow rivers with breeding places in the pools and backwaters along the banks are best treated by channel control. During a dry spell the main channel is outlined with closely-set bamboo stakes; rows of stages are set transversely between the edges of the channel and the banks; in the swifter parts, stake-and-stone weirs in the shallows control the current. The whole effect is to aid the river to cut out its main channel more deeply, while silting up the more sluggish shallows.

Smaller streams may need to be cleared of rock and log barriers; and lakes, pools, and creeks may have their banks treated for shade—according as the local vector likes or dislikes sunlight, so the banks may be planted with suitable shade bushes, or sloped back and denuded of overhanging vegetation. Another method of treating small streams possessing many pools and backwaters has recently been suggested: dams with sluice gates are constructed at intervals; by closing the gates periodically the breeding places are drained or isolated. Then the gates are opened, and the ensuing flood scours out these spots, carrying the larvæ down the main stream.

Low-lying swamps near the sea can be treated by the low tide-level system of De Verteuil and Spence. Culverts are built at low water level, running into the swamps, and fitted with gates which are opened at high tide, then closed when it has ebbed. Not only is sand gradually carried in to fill the swamp, but the raised salinity of the swamp water may prove distasteful to the larvæ. However, some species of *Anopheles* thrive in brackish water, and certain others may become accustomed to quite high degrees of salinity.

Swamps can sometimes be drained effectively by a single channel with a few lateral branches. It must be emphasised

however that the construction of drainage channels of any length is a trap for inexperienced workers; it is wise to get a surveyor to run levels and lay out all drains—without some such expert aid it is easy to spend much time and money merely proving that water will not run uphill. Often a convenient lower level to which water from a swamp could run cannot be found. Such a swamp should be silted up; any relatively high ground nearby is cleared, and steep stormwater channels are cut in it, leading directly into the swamp. Erosion may be aided by judicious undercutting of the channel banks. If the larvæ are shade-loving species, the vegetation can be felled and left lying to act as a silt-trap. Quite large swamps can be silted up in a single wet season by this method. Once the low level of the floor of a swamp has been raised by silting, a channel can be cut to carry away surface water.

SEMI-PERMANENT WATER: If semi-permanent water cannot be drained, filled, or silted up, it may be periodically stocked with fish. If these are not available it must be oiled. Oiling is best done with knapsack sprayers. The Vermorel "Eclair" knapsack sprayer Model No. 1, fitted with oil-proof valves, is my preference. It would be well to order three extra Air Chamber Covers (spare part No. 17) and six extra Lid-bands (spare part No. 41) with each original sprayer. This model is mechanically simple and capable of being satisfactorily operated by natives. It is a French product, but for the Orient it is easiest to obtain it from the Britannia Engineering Company, of Calcutta.

The cheapest oil is waste oil from engine sumps, thinned with kerosene. All sump oil from garages and machine shops should be run into drums; a cock can be screwed into a drum and the requisite proportions of kerosene and oil can be mixed in the sprayer itself. Undiluted oil clogs the jet, and does not spread well. Kerosene alone evaporates too rapidly in the heat of the sun. A mixture of from one to four parts of sump oil to one of kerosene, according to climate, should be satisfactory; a little experimenting will determine the proportions most suitable

for local conditions. Oiling must be done once a week, regularly. The usual hatching time is about ten days, so that spraying every seven days is necessary to catch all forms. It has been shown that more expensive oils, specially developed with respect to their spreading power, film persistence, and toxicity to larvæ, are more economical than cruder oils because they go further with less labour; but in places remote from the source of supply, where there is cheap native labour, they cannot compete with the mixture recommended above.

TEMPORARY WATER lies in small holes, road ruts, pockets in gutters, hoof marks, post holes, borrow pits, and the like; such breeding spots should be classified as preventable. If roads, gutters, and drains are kept in good repair; if post holes and stump holes are always filled in; if road-repair gangs, builders, and gardeners are prohibited from making casual borrow pits; if soft ground is thickly grassed with couch or some similar grass to bind the surface and prevent deep footmarks being made; then there will be little casual water about.

The difficulty about such breeding places is that not only are they often hard to locate, but being small, they overflow every time it rains, and oil is floated off. They must, of course, be eliminated by filling—a long and tedious job; meanwhile paris green should be dusted on them. Paris green floats on the surface for half-an-hour or so, and the surface-feeding anopheline larvæ are poisoned. It is very cheap, and easy to use, but unlike oil, its effect does not last, and it does not kill eggs or pupæ. It has the advantage that it does not need to be sprayed on to each individual small pool as oil does—a light cloud blown out to windward will reach all the pools over a moderate area, and will not hurt the vegetation in between. It is applied as a mixture of one part of paris green powder (200 mesh, American) to one hundred parts of sifted wood ash.

The Hudson No. 604 Dust Gun, supplied by the Dunham, Carrigan, and Hayden Company, of San Francisco, is most satisfactory; it is slung in front of the operator

and driven by a rotary handle. The Blue Bird Dust Gun, manufactured by the Peerless Dust Gun Company, of Cleveland, is of the same type, and has a good reputation. A knapsack type of sprayer can be obtained from the Central Industrial Workshop, Bangalore. It would be well to specify "For use with paris green" when ordering. Prices (sterling in 1939) at the factory were approximately as follows:

Hudson 604	£3 0 0
"Blue Bird"	4 10 0
Knapsack (India)	2 0 0
"Eclair" (oil)	2 10 0

Difficulties of exchange, freight charges, etc., can most easily be overcome by ordering through a bank, "Cash against documents."

It is a good plan to make periodical surveys of semi-permanent water and temporary water after rain, and flag them with different colours for oil and paris green. Then nothing can be missed on the weekly spraying days, and the flags will also serve as guides for the gangs employed in filling and draining.

ANTI-ADULT MEASURES

The most important single measure against malaria, under control conditions, is complete screening of houses. There will always be some mosquitoes about, and to be bitten by only one infectious mosquito is to contract the disease; and it is not possible for anyone in the open to maintain a constant guard against an almost invisible foe, evening after evening, with any reasonable hope of success.

The *Anopheles* flies and feeds in the half lights—around dusk and dawn; all day in dense jungle; all the evening, under chairs and tables, while the lights are lit; and all night when the moon is clear and bright. The usual routine of dwellers in the tropics is: drinks at sundown, a late dinner, a book or a game of bridge, and so to bed. By the time a man is safely asleep under his net, provided

the moon or any other outside light does not shine directly into his room, the *Anopheles* will have retired too, only to emerge again with the light that precedes the sunrise. Hence a net affords protection only through moonlit nights and at dawn. A screened bedroom has the extra advantage of permitting undressing at leisure, and of offering a sanctuary for reading or writing.

There remains the period from sundown to bedtime. Certainly if mosquito-proof clothing be worn there will be little risk of being infected; but it is not likely that many men would adhere to such a costume, while no woman could be comfortable, or happy, wearing it, especially in the evenings. Mosquito-proof clothing is hot and uncomfortable, and is worn usually as a protection against the annoyance of swarms of mosquitoes in the open air. When working out of doors at night, it might offer the only possible means of protection against malaria. It consists of a veil hung from the hat brim and tucked into the neck of the shirt or tied around the chest; a high-necked shirt with long sleeves without plackets, buttoning at the wrists; high boots and breeches; and light gauntlets. The shirt and breeches must be made of closely woven material. Instead of high boots, very thick socks may be worn under ordinary slacks, or two pairs of long stockings under a long skirt, since mosquitoes cannot penetrate two layers of any but the sheerest openwork silk.

Screening the dining-room will not entirely solve the problem; the kitchen and connecting passage must be included, or the constant opening of the door by the table boys will admit mosquitoes; also the noise of the door is a source of irritation not to be underestimated, provided the boys do not prop it open most of the time.

The real difficulty is in the style of building. Tropical houses are usually designed primarily for coolness and shade, on a plan which does not lend itself to the economical use of screens; nearly always there is a group of tiny rooms surrounded on all sides by wide verandahs, with the kitchen and bathroom tacked onto the back corners,

The verandahs make for coolness, but the rooms are always dark and usually stuffy. They offer excellent shelter for mosquitoes during the day, and but little inducement to human occupation during the evenings—the cool airy verandahs are much more enticing. But the cost of putting screens all around a house of this type is high, particularly if rust-resistant gauze has to be used because of the proximity of the sea. If only a part of the verandah be screened, the rest becomes just so much waste space where lumber accumulates.

It is possible, however, to plan a house which is more compact; to make the rooms larger at the expense of verandah space; to keep it almost as cool by employing good methods of ventilation, and building extra-wide eaves; and to have the rooms lighter while eliminating glare by building on deep window awnings. Because of its compactness, such a house will show a saving in roofing material which will about balance the extra timber required, while the screening will amount to less than five per cent. of the total cost of the building.

An important point is that the possible entries for mosquitoes must be reduced to two outside doors; they must be fitted with spring hinges or automatic closers, and with rubber stops to prevent noise and jarring. The toilet should be included within the screening. If water can be spared and a satisfactory sewage outlet can be found, a water closet should be installed. The initial cost of a septic tank is surprisingly low; it will be partially repaid by the saving in sanitary charges where a pan system would otherwise be used, and more than repaid by its many advantages and conveniences. A pan can be maintained inside without unpleasantness if its box is fitted with a good lid and an outside ventilator. Pans must be emptied, washed, and tarred daily (thus necessitating two pans, to be used alternately), and a deodorant must be used freely—the correct method is to put four inches of water and a tablespoon of disinfectant into the fresh pan. When an outside pan hatchway is installed, care must be taken to see that it is mosquito-proof.

Children and servants must be taught not to hold or prop the door open, and to reduce running in and out after sundown to a minimum. Adults should not stand with the door held open while speeding the parting guest with prolonged last-minute conversation.

Every night, when the servants have cleared away and are ready to leave, their last duty should be to spray the house out with a pyrethrum preparation. This is the best time for two reasons: there will be no more coming and going through the back door with consequent introduction of mosquitoes, and the occupants of the house are most likely to be settled on the verandah at that time, and will not be inconvenienced by the spraying. A couple of puffs under beds and tables and behind other pieces of furniture should never be omitted. It is usually necessary to prove by demonstration to the staff that one small whiff of the insecticide is sufficient to kill an insect within a short time, otherwise natives are prone to keep squirting until they drown it; which method is expensive. A cheap pyrethrum spraying solution can be made by macerating one pound of *Pulv. pyrethri flor.* (powdered dried immature chrysanthemum buds) with one gallon of kerosene for a week, and straining. The addition of four ounces of methyl salicylate or saffrol improves the effect slightly.

Where these points are well observed, there will be no need for mosquito nets, except for young children, who must be given this extra protection just in case of accidents.

When it is necessary to go outside after sundown, all movements must be brisk, so as to offer no opportunity for mosquitoes to alight and feed. Club houses, picture theatres, and any other buildings used at night should be screened, and sprayed out just before the usual evening influx of patrons. In the case of workshops, power houses, and similar buildings which cannot be screened, much can be done to protect night workers if electric light is available. Naked bulbs arranged under desks and benches, above the rafters, and in dark corners behind machinery, prevent mosquitoes from lurking in these spots. The

modern safety measure of painting machinery some light colour aids this by increasing light reflection. Where men have to work out of doors at night, they can be provided with a portable lighting outfit consisting of a string of sockets on heavy flex, fitted with 100-watt globes and white enamel reflectors, and provided with a fuse box and switch which can be plugged in on any available power supply; these lights can be hung in a circle, pointing inwards, to eliminate shadows.

When screened sleeping quarters are out of the question, a mosquito net (mesh 24-26, cotton 40/60) must be used. Where sandflies are prevalent cheesecloth nets are necessary, but they are close and depressing, and should be dispensed with as soon as the sandfly season is over. The net should be as wide and as long as the bed, with a high top made of calico; it should have a calico band around the bottom for tucking under the mattress. It is a good plan to fasten the corner tapes to strong indiarubber rings (thin strips cut from an old inner tube are excellent) which stretch if the net is pulled on, saving it from being torn. Restless sleepers who are prone to lie with arms and legs against the net may have extra calico bands put on the sides, coming up to about eight inches above the level of the mattress. Such bands must not be carried across the head or foot as well, as they would then interfere too much with air circulation. The net is let down and tucked in before sundown, care being taken to kill any mosquitoes which may be found inside. A flashlight should be taken to bed, and after crawling in through the smallest possible opening and tucking the net in again, an inspection must be made to see that no mosquitoes came in too.

A spare net of this type can be made into a mosquito-proof "room" by hanging it with its edges lying on the floor. There is space within for an easy chair and a small table, or even for two small chairs and a tiny table. If the floor has cracks in it, a mat or blanket should be laid down. More elaborate netting rooms can be made, with overlapping flaps to serve as an entrance. They are useful

for camping, or where wire gauze is temporarily unobtainable, but because of their size they are very liable to become torn, and they are unmanageable in even a moderate breeze.

Mosquito repellents for application to the skin depend on their odour; either they are distasteful to the mosquito, or they so disguise the skin odour that the mosquito fails to recognise a possible source of food. While not unpleasant, they are somewhat overpowering on the hands and face. Few have a lasting effect. They have the serious defect that when they are used repeatedly on the skin they are liable to set up a dermatitis, more especially in the tropics where the mouths of the pores are pouted and sodden from continued sweating.

Anti-adult measures, it has been shown, require intelligent co-operation. Unless this can be obtained from the indigenous native population they had better not be attempted, as not only will much money be wasted, but a false feeling of security will be engendered. Anti-larval measures will protect the natives from massive infection, and anti-adult measures among the non-immunes will help them indirectly. However, in places where the indigenous immunes have their quarters close to the houses of the non-immunes, it is absolutely necessary to employ some anti-adult measures. These should be limited to screening their houses and seeing that they do not prop their doors open, and teaching them to use a pyrethrum spray properly.

4. PERSONAL MEASURES

Certain antimalarial measures depend entirely on the individual, who must be educated to understand them and the need for carrying them out in their entirety. Malaria is a disease of countries where doctors are usually few and far between. That the general run of patients like to treat their own malaria, and will treat it, at least until it gets out of hand, is an established fact, and must be accepted. Only when a heavy attack of fever supervenes on a suc-

cession of imperfectly-treated ones, and fails to respond to the usual haphazard home treatment, is a doctor consulted. Education should take the form of teaching the population a few simple essentials about prophylaxis, diagnosis, and treatment. Patients could be given a brief talk on the habits of the *Anopheles*, how to avoid infection, the usual early symptoms of an attack of fever, and the need for early vigorous treatment. They should be warned not to fly to quinine for every fancied illness, but to report any suspicious symptoms at once so that the diagnosis of malaria can be properly established. They must also be convinced of the very real necessity for carrying on with the full course of treatment once it is commenced, and that a "mild" attack of fever cannot be properly treated with a correspondingly reduced course of quinine, no matter how quickly it responds. Especially must they be taught that if an attack of fever is treated correctly at its onset it can never reach serious proportions, whereas a delay of a few days permits what should have been a minor ailment to develop into a serious illness; that this can happen so often in a disease whose onset is normally so clearly defined and so easily capable of being accurately diagnosed, and which responds so well to early treatment, is largely due to failure of patients to co-operate owing to their lack of even elementary knowledge.

Before considering personal measures in detail it must be pointed out that persons who suffer from certain conditions should not attempt to live in malarious districts because of the bad effects which either malaria or its treatment might have. The more important of these are: arteriosclerosis; corneal ulcer, past or present; cholecystitis; diabetes mellitus; gastric or duodenal ulcer, past or present; and syphilis. Most of these are discussed later.

A good standard of living and of general health must be maintained if frequent attacks of fever are to be avoided. There must be prompt attention to small sicknesses which might lower the general resistance and encourage a latent infection to develop; the periodical medical overhaul

should not be omitted; and rational exercise must be obtained—it is difficult for anyone to keep in good training in the tropics, but daily exercise entirely dissociated from that obtained in the regular routine of work should be encouraged. As for alcohol, in moderation it does no harm, but excesses favour the development of attacks of fever in those carrying a latent infection, while habitual over-indulgence engenders carelessness about taking the necessary precautions against contracting an infection.

These, however, are all minor matters alongside the daily taking of so-called “prophylactic” quinine* by the introduced, non-immune population. Under control conditions the reduction of breeding grounds, the screening of houses and the taking of prophylactic quinine are complementary; together they produce excellent results, but the slackening of any one causes trouble. The term “prophylactic quinine” has been out of favour since it has been proved that there is no known drug which by its presence in the body in safe amounts can kill sporozoites or prevent their development when injected by a mosquito. The term need not be abandoned, however, if it is accepted as implying prophylaxis against attacks of malarial fever rather than against acquiring a malarial infection.

It is important that there be no exaggerated claims made on behalf of prophylactic quinine. It has its limitations, and these must be recognised and allowed for. The most that can truthfully be said is that a person enjoying normally good health can take a dose of five grains of quinine daily for many years without suffering any ill-effects whatever, and that the benefits he will receive are that he will suffer fewer attacks of fever, and these attacks will be less severe and more easily and rapidly controlled.

Of plasmoquine and atebirin for prophylaxis I have had little experience. I have found quinine so effective and so safe for general use in the field that I have not thought it necessary to look further. In any case, in view of the greater toxicity of the synthetic drugs and their

* Usually now termed the “suppressive” dose.

much higher rate of idiosyncrasy, I would hesitate to issue them in large quantities to the general population for unsupervised use. Apart from this, the taking of a tablet of quinoplasmoquine daily has no advantage over the taking of quinine, since the patient is getting $4\frac{1}{2}$ grains of quinine anyhow, together with $\frac{1}{6}$ th grain of plasmoquine which is reputedly only really effective in killing gametocytes, from which no fever can arise. For this he is paying two and one-half times as much for plain quinine. Atebrin, which is recommended to be taken at the rate of two tablets (each of $1\frac{1}{2}$ grain) on each of two days in each week, may be of value for prophylaxis, but the intermittent dose is of less value than a continuous series, and the drug is capricious in its effects. The recommended dosage costs two and one-half times as much as does the regular daily programme of quinine. There cannot possibly be a difference in the action of the three drugs as great as the difference in prices, and so quinine offers much better value for the money.

Because I have obtained such excellent results, within the limits of the local conditions, by using quinine for prophylaxis, I insist on its use by every member of the non-immune population over the age of ten years. Young children, although they tolerate relatively large doses over a short period very well, do not react satisfactorily to a suitably small continued dosage; after a few months their appetite decreases, they become pale, and they do not put on weight fast enough. For this reason it is better for them to take no prophylactic quinine, but to sleep under a net even in a screened house, as an additional precaution in case of accidents; and should they develop an attack of fever, it must be treated drastically in an endeavour to eliminate the infection.

From ten to sixteen years the daily prophylactic dose is $2\frac{1}{2}$ grains; over sixteen, 5 grains. The classical time to take it is at dinner, after the soup (since soup stimulates the secretion of acid, making this time the one best suited for rapid absorption of the quinine); but as this time was

originally laid down when it was believed that the presence of the quinine in the circulation would destroy any sporozoites which were injected during the evening feeding hours of the *Anopheles*, and we now know that this is not the actual action of the drug, the time at which it is taken is really of no importance.

Quinine sulphate is satisfactory for prophylaxis. It has been stated that its slower rate of absorption, due to its low solubility, gives protection over a longer period, and that this is an advantage which it possesses over the more soluble salts. Be that as it may, I found no appreciable difference in malaria statistics when I changed over a population of 300 from the bihydrochloride to the sulphate for prophylaxis. There are, however, two practical advantages: the sulphate is a very stable salt, and large stocks can be held without risk of their deteriorating; the same cannot be said of the bihydrochloride, which breaks down if exposed to damp air. Also, sulphate capsules cost about one shilling per hundred less than the bihydrochloride. Where the two salts are stocked, they must be put up in differently coloured capsules to avoid risk of confusion; the addition of a little cochineal to one set of capsules during manufacture can easily be arranged for at no increase in cost.

There are certain points of importance concerning the taking of prophylactic quinine: the daily dose of 5 grains must not be exceeded—this amount is not harmful, but I have seen several cases of mild quinine intoxication after taking 10 grains daily for upwards of six weeks. In any case, if 5 grains is not sufficient to give satisfactory protection, 10 grains is hardly likely to be much better. The form in which the quinine is dispensed is very important. Liquid quinine is a barbarous preparation, and besides its impossible taste, its high content of acid makes short work of amalgam fillings. The substitution of citric acid for the usual sulphuric acid will avoid this latter trouble. The traditional powder rolled in a cigarette paper or stirred into a generous spot of whisky is haphazard and

wasteful, and unpleasant to take. Compressed tablets are very unreliable in their rate of disintegration in the stomach; many may pass through the bowel unabsorbed. Sugar-coated tablets are useless, since they are completely insoluble. Gelatin capsules offer the only satisfactory way of dispensing quinine; they are tasteless, accurate, and economical, although they are costly.

Many patients find that for several days after they first commence to take quinine they are troubled by tinnitus and perhaps indigestion. It is often necessary to encourage them to persist for a week or so until they become accustomed to the drug and cease to feel these effects. Many women are forced to discontinue it either shortly before or during the menstrual period, because it causes menorrhagia. Most of these find that after a few months they are able to carry on with it without distress, as they gradually become accustomed to it. Pregnancy does not constitute a contra-indication to quinine—on the contrary it is of the utmost importance that it be taken throughout; the daily dose of 5 grains has not the slightest tendency to interfere with the pregnancy, but offers protection against attacks of fever which would do so. An added advantage is that a pregnant woman who does develop an attack of fever in spite of daily prophylactic quinine can be put immediately on a dosage of 30 grains daily without any risk, whereas if she were not accustomed to the drug she would need to be started more cautiously on it, with subsequent loss of time and risk of miscarrying. But during lactation it may be advisable to discontinue it if the infant cannot be accustomed to the taste of it in the mother's milk. Every effort should be made to carry it on, for if the infant should develop an attack of fever it is best treated by giving the mother full doses of quinine; the mother needs its protection, for if she should develop an attack her milk supply may be so seriously interfered with as to necessitate weaning the child—even if this does not happen, she will have to be treated by full doses, and the infant may the more willingly accept the presence of large amounts in the milk if he is accustomed to the smaller daily dose.

When quinine is used regularly as a contraceptive (this is emphatically not to be recommended) the problematical amount absorbed from the vagina may need to be considered in relation to the daily prophylactic dose. The usual dose of quinine contained in "tonics" is about $1\frac{1}{2}$ grains; this amounts to taking $4\frac{1}{2}$ grains per day, which is near enough to a sufficient prophylactic quantity; hence these tonics should not be prescribed, or else the patient should be warned not to take prophylactic quinine at the same time.

Patients with a history of previous gastric or duodenal ulceration should be very cautiously introduced to prophylactic quinine, as it often causes sufficient irritation to light up the original condition. It is usually best for them not to take it, trusting to general measures for protection. Patients with hypochlorhydria will probably not absorb enough quinine sulphate to do them any good. They may benefit from the bihydrochloride. Where prophylactic quinine is found to afford no protection, this condition should always be suspected and tested for. If liquid quinine is the only alternative, it may perhaps be given in capsules, but the patient should rather trust to general measures. Latent pyelitis may be lit up by the irritation caused by the presence of excreted quinine in the urine; if the pyelitis cannot be cleared up with sulphanilamide, prophylactic quinine may have to be abandoned. Other factors such as chronic tonsillitis, chronic constipation, and conditions similarly producing lowering of the general body tone, may intervene to neutralise the protective effect of prophylactic quinine, and must be searched out and eliminated.

Some patients may suffer from severe indigestion when taking the sulphate, but may tolerate the bihydrochloride; the reverse sometimes happens. I know of no explanation of this, but a check should always be made to ensure that some concurrent gastric upset is not responsible.

There is another system for taking prophylactic quinine, wherein the whole week's supply is consumed in one day.

It is not a good system, since it lacks the continuity of effect of the regular daily dose, which is to kill any parasites which may emerge from the protection of the red blood cells during the time when the quinine is circulating. By reducing this time to one day per week instead of seven half days, many chances are lost. Also, after the first few days the unpleasant effects of quinine are lost under the daily system, whereas they are reproduced in a more intense form each week under the intermittent system.

The use of prophylactic quinine among the indigenous immune population is wrong. Apart from the fact that it would interfere with their tolerance, there is the fact that they will not take it regularly or for any length of time. But it is a good plan to give all natives in hospital who are running a high temperature, 30 grains daily for three days, in order to eliminate any possible attack of fever coincident with the main illness, but masked by it.

Temporary visitors to malarious districts are in a separate category. They will shortly be returning to a non-malarious country where they will not be able to acquire a re-infection. They do not need to keep a latent infection under control for long periods, as do the permanent dwellers; their interests will be best served if, having acquired an infection, they discover it as soon as possible and start treatment at the earliest possible moment. Therefore, while taking as much advantage of general protective measures as possible, they should not take prophylactic quinine, and should seek drastic eliminative treatment if they develop an attack of fever.

5. CONTROL UNDER TEMPORARY LIVING CONDITIONS

So far, consideration has been given only to control measures which can be adopted where permanent settlement of malarious districts is in progress. But preceding such settlement there will be, possibly, two phases where numbers of non-immunes are living in endemic areas for comparatively long periods under camp conditions: there

must be prospecting and surveying, and before these there might be military operations. Anti-malarial measures have been divided into three main groups: measures against larvæ, measures against adult mosquitoes, and personal measures; and these groups have each been considered in relation to the introduced non-immunes and the relatively immune indigenous population. But it must be obvious that so complete and orderly an arrangement cannot be applied even to peaceful penetration of new country, while the problems presented by a military campaign are still more formidable. In each case new factors are present, and the principles involved must be modified.

PEACEFUL PATROLS AND SURVEY PARTIES

Peace-time activities may be divided, roughly, into two types: official patrols exploring, making contact with isolated natives, or conducting administrative tours and health surveys; and private enterprise prospecting, surveying, or carrying out preliminary work for development. Official patrols have the advantage that they can command, and obtain, whatever co-operation they wish from the indigenous population, and they usually cover the same routes periodically and so are able to develop certain improved conditions at their regular resting places. Private parties have not these advantages. One of the main points about this difference is that official parties usually spend the night in association with native villages, where the mosquitoes must be assumed to be heavily infected; but private parties can more easily and profitably remain out in the bush where the wild mosquitoes are not infectious. This is very important, since it determines the degree of thoroughness to be employed in applying anti-adult measures. Near a village precautions must be taken with extreme care. The white men may have a mosquito-proof tent and pyrethrum spray, or they may have camp cots and full-sized nets. Often, however, they will sleep on the ground. A good net for ground sleeping has its base 7 feet long by 2 feet 6 inches wide, with extra-wide calico bands to tuck in

between the blanket and the groundsheet; the ends and sides are triangular, the whole forming an oblique four-sided pyramid with its apex about 3 feet above the sleeper's head, thus providing a single point of suspension, from which a light cord can be attached to the branch of a tree, or the ridge pole of a tent or shelter. A rubber ring must be used as a shock absorber to prevent tearing.

If the blankets are sewn up to form a sleeping bag, a head net may be used. It is a smaller pyramid, cube, or hemisphere, pegged to the ground around the head, with a slack front which lies across the chest and is tucked under the blanket, or preferably tied with tapes to loops on the sleeping bag. The pyramid shape is best, since it requires only a single cord suspension, while the others must be stretched over wire or cane frames. These bivouac nets are not very secure, and easily become torn.

Natives use smudge fires to keep mosquitoes away. Inside a tent or hut they are effective provided they are kept going all night. They are useless for white men, since the concentration of smoke must be almost suffocating to be effective; natives tuck their blankets over their heads and seem to be little inconvenienced.

Out in areas which are definitely uninhabited and unfrequented by natives, there will be plenty of mosquitoes, whose attentions may necessitate carrying out anti-adult measures; but wild mosquitoes are never infected with malaria. The natives with the party will act as a reservoir of infection for wild mosquitoes, of course; but as it takes at least ten days under favourable conditions for an infected mosquito to become infectious, if camp is moved a few miles every fortnight there will be little danger of the white men becoming infected from wild mosquitoes. The *Anopheles* will not follow for any distance except in the thickest dark jungle. It must be remembered that a return to a previous camping locality within three months may mean encountering mosquitoes which were infected on the last visit. Because of the latent period before the wild mosquitoes which are infected from the natives can become

infectious, it is obvious that it does not matter how close together white and native quarters are placed in temporary camps.

Anti-larval measures in the bush are manifestly impossible. But the taking of daily prophylactic quinine is essential, both for whites and natives. It may just succeed in keeping the almost certain infections of camp life under control for long enough to let the job be finished; as for the natives, it can be regarded as the only certain insurance against attacks of fever. As it will only be needed for a few months, it can be given to them without serious risk of interfering too much with their tolerance. They will need careful supervision to ensure that they take it.

MILITARY CAMPAIGNS

The problems of malaria control presented by a prolonged campaign in an endemic country differ peculiarly from those of peacetime activities. The success of a whole operation can be jeopardised by malaria. History is full of instances, many of them quite recent, where thousands of casualties from this disease could have been avoided if a few careful plans had been made in advance. The danger is in the first few weeks, when there are seldom any serious cases, but when failure to protect the troops from infection may be laying up a store of future trouble.

In the establishment of a Base, it must be remembered that the best of civilian public health services will inevitably break down under the strain imposed by the influx of an army; among the first troops landed should be hygiene units capable of carrying out extensive anti-larval measures in a very short time. These should also be available in numbers sufficient to clear the Line of Communication as it is extended. In addition, anti-adult measures could often be carried out from the beginning; fully-screened accommodation for all permanent troops at the Base and on the L. of C. should not present much difficulty if a simple type of screened hut is planned, and a supply of suitable mater-

ials arranged for. Extra gauze for screening existing buildings could be allowed when these are likely to be occupied. The vigorous application of anti-larval and anti-adult measures from the very beginning would ensure freedom from serious hindering of administration, communications, or supplies, and the enforcement of personal measures would add to the security thus obtained. The construction of screened sleeping quarters for troops passing through to the Front would be of the greatest additional value.

Once the troops reach the Front, however, and go into action, they cannot be so well protected. Field Hygiene Sections may be able to follow them around and carry out some anti-larval measures, but they will not be able to control sufficient country for efficient prevention. Nor may the areas in which the army is to operate be chosen for anything but their tactical advantages. When a position is occupied for any length of time the country behind our own lines can be reasonably well cleared of breeding places; the enemy may perhaps be relied on to do the same; but the intervening zone will be a rich source of mosquitoes. Dusting large areas with paris green sprayed from low-flying aeroplanes might be helpful, if practicable.

Whether the war be one of movement or of position, the most valuable of the anti-adult measures, the screening of buildings, will not be available. The fighting troops will hardly be able to avoid the vicinity of native villages, and must expect to encounter large numbers of heavily infected mosquitoes. It will be necessary therefore to rely on individual anti-adult measures; nets, mosquito-proof clothing, and repellants. As regards nets, the difficulties are those of transportation; full-length nets cannot possibly be carried on the man, and even bivouac nets would make an awkward addition to marching order, and would be almost impossible for battle order. The only type to be considered would be the small pyramidal net with single point suspension, since the others need cane or wire frames as well.

No really successful pattern of "two-in-one" shorts, with a cuff worn turned up during the day and buttoned down over the knees at night, has yet been designed. Therefore, if shorts are chosen for daytime wear slacks must be carried, and time and opportunity found every afternoon for changing into them. Obviously slacks over thick stockings or tucked into short leggings would be the better wear. Dark green or brown veils (white interferes with vision, especially at night) and light canvas gauntlets complete the items required; with the net, a supply of quinine, and a tin of repellent cream, they could be carried in a small special haversack. There is then only one further difficulty: sentries, pickets, outposts, and the like would be hampered too seriously by wearing veils and gauntlets; each unit in turn supplies details for these duties; and therefore every man must sooner or later run the risk of being infected, under the doubtful protection of a mosquito repellent alone. But even if an infection is acquired it can be controlled, often for long periods, by taking prophylactic quinine, and this measure should be insisted on. A check can be kept by periodically collecting random samples of urine and testing them for the presence of the drug.

Neither bivouac nets, mosquito-proof clothing, mosquito repellents, nor prophylactic quinine is very efficient if used alone, especially under war conditions; but quite good control can be effected by securing the full co-operation of the troops (education to this end is just as necessary for the soldier as for the civilian) in making the greatest possible use of a combination of all four.

PART II

DIAGNOSIS

6. CLINICAL FORMS OF MALARIAL FEVER

Malaria is a protean disease, and often its diagnosis presents a nice problem. For practical purposes there is little to be gained by sorting out each attack of fever into its bacteriological type, except in a few rare cases whose severity of resistance to treatment needs special attention. It is wise to make a survey to determine the local types of infection, but this is best done by examining films from a large series of the indigenous inhabitants, after provocative doses of atabrin if necessary. The various types of malaria will respond equally well to vigorous treatment if it is commenced early; quartan offers the most stubborn resistance. In any case, under the system of prophylaxis and treatment outlined here it is usually difficult to find parasites in the peripheral blood. Valuable time will be lost by waiting until parasites are identified before commencing treatment; under control conditions it is of the highest importance to be able to recognise the disease in its various clinical forms in the earliest stages. These forms are: the classical, gastric, muscular, and algid forms, the subacute and the fulminating cerebral forms, chronic malaria, and "low fever." The question of whether the attack is primary, secondary, or concurrent with some other disease, has a considerable bearing on the diagnosis also.

PRIMARY ATTACKS are usually heralded by up to three weeks of vague symptoms. Patients complain of lassitude, easily-developed fatigue, headaches, loss of appetite, and even slight nausea.

SECONDARY ATTACKS, provided the previous attacks have been even moderately well treated, strike out of a clear sky. It is common to hear that on the morning of an attack the patient felt more than usually well.

The progress of these groups differs also. It takes a little longer to bring primary attacks under control than it does secondary attacks. The reason for these differences is that although no absolute immunity to malaria can be developed, there can be a high degree of tolerance or relative immunity, and there appears to be a certain threshold intensity of infection beyond which an individual will suffer from an acute attack of fever. While the number of parasites per cubic millimetre of blood is increasing, the non-tolerant individual suffers to some extent from the smaller total amounts of toxin they produce, whereas the tolerant patient suffers no inconvenience until the threshold is passed. The presence of such tolerance also determines that the patient can usually throw off an attack more rapidly and with less actual sickness than the non-tolerant patient, given the same treatment.

ATTACKS COMPLICATING OTHER DISEASES are generally due to flaring up of a latent infection when the concurrent disease has sufficiently lowered the general resistance. In such instances there is sure to be a fair amount of relative immunity, and the response to treatment is rapid; the only real difficulties arise when the concurrent disease interferes with treatment—gastric ulcer, dysentery, and cholecystitis are examples. These difficulties can always be overcome with a little ingenuity and patience. The important point is to decide whether malaria is present or not; the rule which demands that a double diagnosis may never be made, but all signs and symptoms present must be fitted to the one condition, does not apply in malarious countries. The number of occasions when malaria complicates another disease, and either masks it, or is masked by it, is astonishing.

The **CLASSICAL FORM** is introduced by a rigor (in children there may be convulsions). The intense cold felt

by the patient is due to peripheral vaso-constriction and cannot be relieved by heat or by taking alcohol. From the onset there is a low-sited backache and a typical trembly, weak feeling down the backs of the thighs. The spleen is more or less enlarged and tender and there is tenderness over the gall bladder. After the cold stage, which may last from a few minutes to two hours, there is a hot stage, accompanied by severe headache, hot dry skin, and slight flushing of the face. During both of these stages bilious vomiting is usual. Delirium during the hot stage is not uncommon, even at comparatively low temperatures. The hot stage lasts from one-half to four hours. The stage of sweating supervenes suddenly; the hot dry skin becomes moist and greasy, then a profuse sweat breaks out, delirium ceases, and headache disappears or at any rate becomes much less, and vomiting stops. There is an intense desire to sleep; many patients are ravenously hungry and can eat a heavy meal with enjoyment, but anorexia is the usual feature. It is important to note that many women, and some children, do not sweat heavily; their skin becomes moist, and their temperature falls by slow crisis over several hours. By the next morning the patient usually feels well, except for the backache, which persists. In primary attacks the symptoms are not so clear-cut and do not pass off so completely; a certain amount of nausea remains, and the temperature does not fall quite to normal. Without treatment the cycle repeats itself in approximately 48 hours, or in 72 hours in the quartan type, or in 24 hours when there are two swarms of parasites maturing alternately. Subsequent cycles become successively more severe. A light jaundice develops, the temperature does not fall so low in the remissions, nor does the patient feel so well. The bilious vomiting increases and possibly diarrhœa develops. After five days or more the condition merges into the subacute cerebral form.

The GASTRIC FORM is distinguished by the fact that the vomiting, which is very severe during the cold and hot stages, does not disappear after the sweating stage, but

persists at frequent intervals through the remissions. There is intense thirst, but even sips of water cause racking vomiting. There are attacks of dry retching, and periodically bile is present in the vomitus. Hæmatemesis due to rupture of small gastric vessels often occurs. Diarrhœa is present early. The patient may become partially dehydrated and exhausted. Without adequate treatment the subacute cerebral form supervenes after some days.

The **MUSCULAR FORM** is a modification of the classical attack in which severe aching, tenderness, and stiffness of various groups of muscles predominate. The neck and shoulders, the back, and the calves are most often affected, sometimes for a few days before the onset of the fever. It is convenient to include under this name even those attacks in which the calf muscles are affected to the extent of a peripheral neuritis—a rare form, in which there is weakness, flabbiness, and tenderness of the muscles for as long as six weeks after.

In the **ALGID FORM** there is no definite onset and the symptoms include nothing prominent or clear-cut enough to help in making a diagnosis of malaria. There is no defined rise of temperature at regular periods, but rather a confused succession of small rises to perhaps 100° Fah. This form is probably due to many small swarms of parasites maturing at irregular intervals, and it is almost invariably of the nature of a primary attack. The onset is gradual, with headache, perhaps slight backache, and usually nausea. Vomiting, and sometimes diarrhœa, are present, though neither is very severe. The spleen may be enlarged but does not become particularly tender until later. Progressive weakness is an alarming feature. This is the form in which examination of the blood for parasites is the chief aid to diagnosis. If untreated the vomiting and diarrhœa become extreme and the temperature falls to below normal. It finally merges into the subacute cerebral form.

The **SUBACUTE CEREBRAL FORM** is really the end-result of untreated attacks. There is an irregular high

temperature with a relatively high pulse rate. The pulse is fluttering, the tongue is coated and dry, sordes appear on the lips and teeth, and the patient remains sunk in a semi-coma. The urine is dark and scanty, diarrhoea is usually present, and urine and fæces may be passed into the bed. The blood contains enormous numbers of parasites (over 20,000 per cubic millimetre is not uncommon). The spleen is enlarged and very tender. This form is often seen in infants, where it supervenes rapidly on other forms if there is any delay in starting treatment; convulsions frequently occur in such cases.

The **FULMINATING CEREBRAL FORM** is of a different nature. At its worst, the onset is sudden, resembling a "stroke"; the victim collapses and passes rapidly into a fully comatose state. In children there are repeated severe convulsions, often Jacksonian in type. More commonly the first indication is a series of unbearable headaches, which may be spasmodic or continuous. The theory of the causation of this form is that a group of enlarged parasitised red cells or a clump of parasites forms a cerebral embolus. If untreated, cerebral irritation and death may rapidly supervene. The spleen is often moderately tender. Absence of parasites from the peripheral blood in the early phase may make diagnosis difficult, but unless an early diagnosis is made the patient may die before treatment can be given. An intramuscular injection of atabrin musonate may act provocatively and bring out enough parasites to help, but it is safer to assume that any sudden loss of consciousness, unless obviously due to alcohol or trauma, is due to malaria, and to proceed accordingly, waiting until later to sort out the other possible causes.

CHRONIC MALARIA is due to insufficient treatment. When an attack of fever is treated with too little quinine, and no follow-up course is given, a recurrence can be expected within a few weeks. Under the same conditions of treatment subsequent recurrences appear more and more frequently, although they do not become much more severe

since a certain amount of tolerance is developed. Nevertheless the effect on the patient is severe; he becomes anaemic and lightly jaundiced, his sleep and appetite are interfered with, he loses weight and becomes "nervy." The spleen reaches record sizes and is so tender as to produce a feeling of fullness and discomfort under the left costal margin, and even sharp pain with deep inspiration. This state of malarial cachexia, if associated with a sub-tertian infection, is one of the antecedents of blackwater fever; it has been described as the "pre-blackwater state." Parasites are often scanty in this form.

"LOW FEVER" might be described as an indefinite, prolonged, very mild attack. It occurs usually in those who are taking prophylactic quinine, either when there is some slight concurrent cause of lowered general resistance, or when there is some irregularity in taking the quinine. It does not progress beyond the stage of malaise and loss of appetite and energy. There are no severe symptoms as in chronic malaria, and the temperature chart shows no rises, while the spleen is not tender, although it may be just enlarged enough to be palpable. This form often clears up spontaneously, or may culminate in a classical attack after some weeks. It gives the impression that there is an infection of subliminal intensity which is just being held under control by the prophylactic quinine. The delayed period of onset described above as accompanying primary attacks is more or less of this nature. An interesting point is that if quinine is discontinued there immediately results a feeling of well-being for some days, followed by an attack of fever.

Naturally clear-cut examples of these various clinical forms do not always occur; there is shading and overlapping as a rule, but most attacks of fever conform more or less to one of them. It cannot be too strongly emphasised that recognition of the main features of the different clinical forms, regardless of the type of parasite involved, is the key to early diagnosis.

7. CLINICAL SIGNS

The constant clinical signs of malaria are well worth separate discussion:

ENLARGEMENT OF THE SPLEEN: This sign is usually of value only in non-immunes; the indigenous immunes always have a grossly enlarged spleen which gives no help in determining whether they have at the moment an attack of fever or not. Among the non-immunes the spleen becomes enlarged with each attack of fever, but shrinks almost to normal size with prompt efficient treatment. It remains enlarged, and increases in size, if treatment is inadequate and a state of chronic malaria is allowed to develop. It is tested for by pressing the fingers below the left costal margin just lateral to the nipple line and telling the patient to draw in a deep breath. If the spleen is grossly enlarged it will be felt as the fingers are applied, and the anterior margin with its notch can easily be traced out. In less severe cases the edge will be forced down during inspiration and can be felt to touch the fingers. Lesser degrees of enlargement can only be felt with the patient sitting or standing, with the body inclined slightly forward and the abdominal muscles slack. Dullness on percussing laterally along the perpendicular bisector of the line joining the left nipple to the umbilicus is indicative of enlargement of the spleen.

TENDERNESS OF THE SPLEEN: This varies; with gross enlargement there is a feeling of fullness and discomfort in the left hypochondrium, and pain on coughing. With this, and even lesser degrees of enlargement, there may be referred pain over the lower ribs about the anterior axillary line. In these cases even slight pressure on the abdominal wall below the costal margin causes sharp pain. In cases where the spleen can only be felt on inspiration, the patient will wince just as the fingers feel the pressure of the edge as it descends. Immunes rarely develop tenderness of the spleen, since its chronic fibrous thickening prevents rapid engorgement at the onset of an attack of fever.

TENDERNESS OVER THE GALLBLADDER: If the fingers are placed just below the tip of the ninth right costal cartilage and the patient instructed to breathe in, he will wince and complain of pain. No mass can be felt, nor is the patient ordinarily conscious of discomfort, but tenderness elicited in this way is a constant sign, present from the onset of an attack of fever. It is not affected by the patient's having previously been in the habit of taking prophylactic quinine, whereas tenderness of the spleen is. When no prophylactic quinine has been taken the spleen is always more tender than the gallbladder; if the spleen is less tender than the gallbladder, it can be assumed with certainty that prophylactic quinine has been taken regularly.

LOW-STITCHED BACKACHE often precedes the actual attack of fever by some hours and persists, in spite of rest or exercise, heat, aspirin, and even morphia, until quinine at the rate of 30 grains daily for two days has been taken. It disappears on the fourth day of a standard course of atebirin.

MUSCULAR ACHES are present inconstantly in most forms of fever, although most marked in the muscular form. An invariable accompaniment to all forms is a weak, trembly feeling, not quite an ache, down the backs of the thighs.

HEADACHE, frontal or bitemporal, more marked on bending down or turning or shaking the head, appears while the temperature is raised, but usually disappears after the sweating stage is well established. In primary attacks and when prophylactic quinine has not been taken, it persists until the temperature has been brought under control with adequate treatment. It responds readily to aspirin, but recurs when the effect of that drug has worn off.

BILIOUS VOMITING is a regular feature while the temperature is high, but normally ceases during the remissions.

The **MASSIVE SWEATING** of the third stage is characteristic. It is almost unbelievably profuse, soaking

through sheets and blankets, and well into pillow and mattress. The moisture can literally be wrung out of the bedclothes. It can be stimulated by a sweat caused by taking aspirin in other conditions where the temperature is raised, and a massive sweat which is not spontaneous is not necessarily diagnostic of malaria. Women and young children often fail to exhibit it in such a marked form. It may be only slight in gastric attacks because the body has already been deprived of all surplus fluid by the vomiting and diarrhœa.

The TEMPERATURE presents certain characteristic features. Although there is no fixed hour of the twenty-four at which an attack of fever must arise, malaria is the only disease which can produce a rise of temperature followed by a fall before the afternoon, hence such a phenomenon is diagnostic of malaria. As well, a rise and fall occurring regularly every second or third day at about the same time, with complete remissions on the intervening days, is diagnostic. Sometimes it is even possible to trace such rises in a chart which shows a steady, moderately raised temperature from some other conditions, such as XK typhus. On the other hand, when there are two swarms of parasites maturing on alternate evenings, a malaria chart may exactly simulate the hectic appearance of a septic condition.

The PULSE RATE in malaria rises in conformity with the temperature, at the rate of ten beats per minute for every degree Fahrenheit.

The TONGUE is ordinarily clean during an attack of malarial fever. This is a very useful feature, especially in children. But constipation is a common precipitating cause of an attack of fever in children and in natives, in which case the tongue may be white and thickly coated from the onset. Also, heavy sweating combined with the constipating effect which large doses of quinine have on many patients may cause the tongue to become coated in the later stages of an attack of fever which has not received prompt treatment.

The TOTAL LEUCOCYTE COUNT is normal in malaria. This is of the greatest importance, because a count can be carried out much more quickly and simply than a search for parasites, and gives enough information to narrow the diagnosis down to a very few conditions which can usually be sorted out with ease. Besides being quicker and easier, a leucocyte count gives definite information at all times, and is therefore often of much greater value than a parasite search—admittedly the finding of parasites is definite enough, but there are so many intervening factors that a negative result is indefinite and quite valueless.

8. DIFFERENTIAL DIAGNOSIS

Because of its many forms, malaria is often missed for some days, and conversely, many other diseases are first diagnosed as malaria. Those diseases which enter most frequently into the differential diagnosis of malaria are: dengue fever, influenza, the XK type of typhus, amoebic abscess of the liver, dysentery, typhoid fever, food poisoning, cerebral hæmorrhage, cerebral embolus, meningitis, epilepsy, and cholecystitis. Each clinical form of malaria is associated with some of these more than with others. Even the classical form may be involved—it is almost invariably diagnosed instead of XK typhus, which has a sudden onset with a rigor, rapid rise of temperature, headache, and enlarged (though not particularly tender) spleen. Unless a primary eschar is found, or particular notice taken of the low pulse-temperature ratio, the diagnosis of malaria may stand until it is realised that there has been no response by the temperature to quinine treatment after 48 hours or so. When the typhus patient is seen first in a later stage, a diagnosis of subacute cerebral malaria is often made; the low pulse-temperature ratio, the eschar, and the very low leucocyte count of XK typhus are the distinguishing points.

Gastric malaria may be confused with food-poisoning, but in the latter the temperature is not raised, and the

spleen is neither enlarged nor tender. Dengue fever and influenza must be distinguished from the muscular form. In dengue fever the peculiar nature of the pains, the extremely flushed face, injected conjunctivæ, and painful eyeballs, should be sufficiently distinctive. Sore throat and extreme weakness, and the absence of a rigor, may distinguish influenza. But these two conditions more than any other are liable to be complicated early by malaria, and a careful watch must be kept on spleen and gall-bladder to guard against missing the double condition.

The algid form may resemble dystentery, especially the Shiga type. Much diarrhœa in the gastric and algid forms of malaria may lead to the presence of blood and mucus in the stools in the later stages, and this confuses the diagnosis, while parasites may be few and hard to find. The normal leucocyte count of malaria is helpful here, as is the bilious vomiting, which is more marked in those forms most likely to be confused with dysentery. The response to quinine is rapid in those forms too, and often provides the final proof.

Amoebic abscess of the liver is almost always diagnosed at first as chronic malaria, or as a mild attack of the classical form. The recent history of much loss of weight should raise suspicion, and the low pulse-temperature ratio ought not to be missed, but too often the diagnosis is only changed when there is no response to quinine treatment after two or three days.

The fulminating cerebral form has to be distinguished from the various other causes of unconsciousness. Rapid diagnosis is here vital, since only early injections of quinine can be of any value. The rule to follow is that in a malarious country unconsciousness not obviously due to alcohol or injury must be regarded as of malarial origin until proved otherwise, and quinine injections must be given immediately. No harm will be done by following this rule, and lives may be saved. Once sufficient injections have been given, further sorting out of possible

causes of the unconsciousness may be attempted. Parasites may be few, and missed, until treatment drives them out into the peripheral blood—an intra-muscular injection of atabrin musonate will do this most effectively. The finding of parasites may be the only possible way of deciding between this form of malaria and apoplexy.

Meningitis, especially in children, can easily be confused with the subacute cerebral form. A total leucocyte count will show the way. Where there are convulsions epilepsy may be suspected, but there is little similarity between the spasms. Apart from all these, malaria is only too often diagnosed as septicæmia, pneumonia, appendicitis, cholecystitis, and gastric ulcer. The leucocyte count alone is sufficient to weed out most of these. Actually, the ability to perform a reliable leucocyte count is of much more practical value than to be able to stain and find parasites (a much more difficult operation), provided the various clinical forms of malarial fever can be recognised, and the diseases with which they are more likely to be confused are remembered. The following table shows these in a convenient form :

<i>Clinical forms of malaria—</i>	<i>Conditions most closely related—</i>
Classical	XK typhus (early stages)
Gastric	Foodpoisoning, cholecystitis
Muscular	Dengue fever, influenza
Algid	Dysentery
Subacute cerebral	XK typhus (later stages), meningitis
Fulminating cerebral	Heatstroke, apoplexy
Chronic	Amœbic liver abscess

9. LABORATORY AIDS TO DIAGNOSIS

There are only two laboratory investigations of real practical value for the diagnosis of malaria in the field: total leucocyte counts and examinations of blood films for parasites. However, it is convenient to include here erythrocyte counts and hæmoglobin estimations for determining the progress of chronic malaria or blackwater fever, an approximate total parasite count which is of value in estimating the prognosis of very severe neglected attacks of fever, and urine tests to check whether treatment is being followed correctly. All of these are easy to carry out and require no elaborate equipment. Every medical officer is familiar with the ordinary use of the microscope, hæmacytometer, and hæmoglobinometer. In this chapter will be discussed special points of technique applicable to malaria.

EQUIPMENT

BEDSIDE TRAY: It is very convenient to assemble all the small items needed to collect material for these tests as a self-contained unit which can be taken to the bedside. With a few wide-mouthed half-ounce bottles and a shallow cigar box a handy tray can be made in half an hour. The lid of the box is removed and cut with a fretsaw into strips to make the partitions. Ordinary pins are quite satisfactory to nail the strips in place. A row of six bottle compartments is made along the back of the tray. About two inches at one end of the remaining space is separated off. On the floor of the large space which is left, a one-quarter inch strip is fastened at a convenient distance to prevent slides resting with one end on the front edge of the tray from slipping down and becoming scratched. The first four bottles contain respectively Toison blood fluid, 5 per cent. acetic acid, distilled water, and alcohol. The next is packed with half-inch cotton-wool swabs. In the last is lysol, and a straight triangular-pointed needle is set in its cork. The end compartment holds two Wright's capsules, an ampoule

cutter, two wire paper-clips, and a lamp of plasticine stuck in the corner. Four inches of soft narrow rubber tubing for a finger tourniquet, and a spreader (which is an ordinary slide with its corners nipped off with a pair of pliers) lie in the larger compartment. A linen cover keeps dust out.

The hæmacytometer pipettes would normally be kept in their case and only put on the tray when required. Slides are stored in alcohol and taken out as needed. When these have been added, with the Tallqvist book laid on top of the cover to prevent its blowing away, everything is ready for all the above tests. The paper clips are to be sprung on the tubes of the pipettes to prevent leakage; the ampoule cutter is for opening the Wright's capsules, and the plasticine to seal them. Such a tray will ride safely on a car seat; for more awkward trips, a few selected items can be packed in a small box and carried in the pocket. With a little ingenuity a compact travelling case could be designed.

SLIDES should be cleaned with "Bon Ami" or "Old Dutch Cleanser," rinsed in clean water, and stored in alcohol. When needed they are rinsed in water and dried and polished with a soft well-washed linen cloth; they must be handled by their edges. The thicker slides, with a light greenish tint, are the best. A glance along one edge will show that they are very slightly curved from end to end; if the film is spread on the convex side the slide will not rock on the stage. They should always be rested against a ledge, with the film underneath, to protect it from dust and scratching. When quite dry they may be rolled in clean writing paper without causing any damage to the film.

The NEEDLE, if set in the cork of a bottle containing lysol so that its point is immersed, will not rust, is always sterile and ready for use (after wiping with alcohol), and is easy to handle.

SOLUTIONS: Toison blood fluid for erythrocyte counts is very convenient, since it can be made up from Burroughs

Wellcome "Soloids." One tube of six will last a long time. This solution must be watched for moulds. For leucocyte counts 5 per cent. acetic acid is used. Methylated spirit is satisfactory for cleaning the needle and the finger.

The hæmacytometer pipettes must be washed and dried with distilled water, absolute alcohol, and æther.

The distilled water for diluting stains must be freshly neutralised; to do this, traces of 1 per cent. lithium carbonate in distilled water are added in a small beaker with a glass rod. A drop or two of saturated brom-thymol-blue in distilled water is used as an indicator; it is yellow with an acid reaction, blue with an alkaline; the neutral point is a yellowish green.

STAIN: Leishman's method for thin films is probably the simplest, and gives excellent results within limits. Thick films require great skill, and the solutions must have a very accurately adjusted P.H. They are not here included among practical field methods. Burroughs Wellcome "Soloid" Romanowsky stain is very convenient; the same firm put up methyl alcohol in 15 c.c. ampoules. One tablet is ground in small glass mortar and scraped into the drop-bottle, and 15 c.c. methyl alcohol added (the instructions issued with the stain recommend 10 c.c., but the larger amount is preferable in warm climates). The stain should be shaken occasionally for two days, by which time it will be ready to use. When more than three weeks old it may deteriorate in hot weather. It is hygroscopic, and if exposed to moist air it will precipitate on films. A petri dish to cover the slide during staining and a small pipette with indiarubber teat for diluting and mixing the stain are needed.

URINE-TESTING REAGENTS: Mayer's reagent for quinine consists of 10 per cent. mercuric potassium iodide in 5 per cent. acetic acid; it is stable. For atebirin are needed amyl alcohol and 5 per cent. sodium hydroxide. The chloranil reaction for plasmoquine is too complicated for field conditions.

A DARK-ROOM TIMBER is a most useful accessory.

MAKING A BLOOD FILM

It is important to make films at the stages in the developmental cycle of the parasites when they are likely to be visible. A rigor marks the release of merozoites from the erythrocytes. For a time they are free in the serum; then they are to be found as applique forms, which do not, alone, afford a good basis for diagnosis. Only when they have grown into young ring forms are they easily to be found and identified by simple methods of examination; this does not occur until some twelve hours after the rigor, by which time the diagnosis should have been established by clinical means, and treatment should be well in progress.

A drop of blood is expressed from a finger near the base of the nail, or from the lobe of the ear, and is lightly touched with a slide about an inch from one end in the midline; too much blood must not be picked up. The spreader held at about 45° to the slide is brought up to the drop; two or three short lateral movements will distribute the blood across it, and the spreader is then pushed briskly along the slide, drawing the blood after it. The film is rapidly dried by blowing on it or waving it in the air; slow drying encourages distorting of the cells. The patient's name can be scratched in the thick end of the film with the corner of the spreader. Two films should always be made so as to have one in reserve in case anything goes wrong with the staining; this takes little extra time, but on occasion may save hours.

STAINING THE FILM

The film must be quite dry; twenty minutes in an incubator, or ten minutes in direct sunlight or within a few inches of an electric light bulb, usually suffices; the slide must then be allowed to cool to room temperature. If this preliminary drying and cooling is not done properly, stain will precipitate in granules on the cells. Then place the

slide on two pieces of glass rod or match sticks on a level surface, film upwards. drop on enough stain to flood the film area and immediately cover with half a petri dish. Leave it for one minute to allow the methyl alcohol to fix the film; during this time neutralise an ounce or two of distilled water. Then with a small pipette run onto the slide four or five times as much water as there is stain, mixing thoroughly; re-cover the slide and allow it to stain for four minutes. Rapidly rinse it with the rest of the neutralised water and gently blot it with clean blotting paper; it must then be carefully dried out again for at least ten minutes, because immersion oil will not "take" on the damp cells. Before applying the oil dust the film gently with a camel hair brush. The staining must be checked by examining first a few leucocytes—their pinks and blues must both be of good value.

Faulty staining may be due to the stain's being too old or too new, to failure to neutralise correctly the diluting and washing water, to the presence of strong acid or alkaline ions contaminating the distilled water (as, for instance, when the water has been run into a container which previously held acid, and which had not been neutralised), or to failure to dry or cool the film properly. If the staining is faulty check all solutions and technique, and then prepare and stain a film made from your own finger; if this behaves properly then stain the reserve film taken from the patient. It may not be convenient or politic to go back for more if the reserve film is experimented on and also fails.

EXAMINING THE FILM

The top end of the film will usually be too thick; an area must be found towards the lower end where the erythrocytes are evenly spread and not distorted. A rapid search is made using the x5 eyepiece and concentrating only on the centre of the field; this search will discover all the clear, obvious parasites, and the x8 eyepiece is kept handy

to check doubtful structures. Enlarged parasitised cells such as occur most often in benign tertian malaria will tend to congregate along the edges of the film and towards the lower end. If no parasites are seen after ten minutes' search the result may be recorded as negative, but it must be remembered that a single negative result is absolutely meaningless, not only because the film may have been made at the wrong stage of the parasite cycle, but also because about fifty parasites per cubic millimetre may give rise to an attack of fever, and to find even one of these in a thin film is largely a matter of luck. If three successive films taken at twelve-hour intervals show no parasites (the patient receiving no anti-malarial treatment meanwhile) then the absence of an active infection can be assumed. But the influence of even small doses of quinine must be reckoned with—if five grains has been taken within the twenty-four hours preceding the search for parasites, there is every chance that the number in any film will be so small that they will easily be missed.

It does not fall within the scope of this discussion to give descriptions and illustrations of malaria parasites. These can be found in appropriate reference books.

OTHER TESTS

There should be no need to go into detail about the everyday tests. The total leucocyte count can give valuable negative information about malaria—a count below 5000 per cubic millimetre would be against malarial fever and in favour of XK typhus; a rise beyond 10,000 could not be due to malaria, but would indicate some other process (which of course might yet be occurring concurrently with malaria).

Hæmoglobin estimations by the Tallqvist scale are accurate enough for all ordinary malaria work. Together with erythrocyte counts they are useful in determining the degree of anæmia present in chronic malaria and in black-water fever, and will be discussed in their place.

TOTAL PARASITE COUNTS

Total parasite counts are of some prognostic value in very severe cases. A simple method of obtaining an approximate count is as follows:

A total leucocyte count is made. Then a stained film is examined, leucocytes (undifferentiated) and parasites are counted, and the ratio between them is worked out. Thence a simple calculation will give the number of parasites per cubic millimetre. For example, if the total leucocyte count is 7000, and there are 80 parasites for every 100 leucocytes, then there must be 5600 parasites per cubic millimetre. At least 200 leucocytes must be counted.

It must be emphasised that this test gives only an approximation, and in practice it is of no value unless there are very large numbers of parasites; but in a non-tolerant patient, if there are more than 50,000 parasites per cubic millimetre, the prognosis is extremely serious, and a count near that figure would indicate the urgent need for rapid, drastic measures. Among highly tolerant Asiatics counts of over half a million have been frequently made in patients who subsequently recovered, but the mortality rate is very high over 100,000.

QUININE IN URINE

Boil the urine, acidifying if necessary. If albumen is present filter it off. Cool, and add Mayer's reagent drop by drop. Turbidity indicates the presence of quinine. Other alkaloids are never taken in amounts sufficiently large to give a positive reaction. It is stated that plasmoquine gives this reaction, but the point is immaterial, since it is rarely given without quinine.

ATEBRIN IN URINE.

Make the urine definitely alkaline with sodium hydroxide. To 10 ccm. add 0.25 ccm. amyl alcohol, shake well, and allow to separate. Set up a duplicate test with normal

urine. Atebrin produces a typical yellow colour, much more distinct than that given by urinary pigments, in the layer of amyl alcohol.

THE PLACE OF LABORATORY DIAGNOSIS IN FIELD WORK

One reads so often that the diagnosis of malaria must be based on finding parasites in the blood—that quinine injections should never be given until parasites have been demonstrated—that it is important to determine the species of parasite involved—but in the field these things and many like them are purely of academic interest. I have a first-class laboratory, and I use it all the time; but, off-hand, I can remember five patients with cerebral malaria during the last ten years who owed their lives to injections of quinine given promptly on clinical evidence alone—four of them at least would almost certainly have died by the time the diagnosis was confirmed by laboratory methods. For several years it was a commonplace for me to travel twenty miles by aeroplane, four by car, and then two on foot, or to walk ten or twelve miles by bush tracks, fording a breast-high river three times *en route*, to reach numbers of my patients. They could not afford the expense, nor I the time, for many such trips. How would they have fared if I had been dependent on my laboratory for help in diagnosis? Or consider the plight of a Regimental Medical Officer in a tropical campaign if he is not thoroughly grounded in the clinical manifestations of malaria, which will be responsible for at least 60 per cent. of his casualties—he has no microscope, nor would he have any chance to use one.

In suitable circumstances the greatest assistance can be obtained from the laboratory in malaria work, but in the field proper malaria control depends on early diagnosis, which in turn depends on a thorough understanding of the clinical signs of the disease and of the various clinical forms which it assumes rather than on laboratory aids to diagnosis, which are really of little use or help in the early stages.

PART III

TREATMENT

10. GENERAL PRINCIPLES

Treatment of malaria must have two aims: first, to cut short any attack of fever as soon as possible, and, secondly, to reduce the frequency and severity of recurrences. To achieve the best results treatment must interlock with the principles of control already laid down; these, if correctly applied, will ensure that the majority of cases will present early, will be mild, and will respond readily to treatment.

It is surprising how little quinine or atabrin is needed to clear up an attack of fever—but even a mild attack, if insufficiently treated, will develop into a severe one; or if treated only with a view to clearing up the immediate symptoms, will lay the foundations for an early, severe recurrence.

Under control conditions the chances of becoming re-infected are far from remote, and there can be no sense in giving long heavy courses of treatment aimed at eliminating all infection from the individual. Instead, it is better to give a short intensive course to clear up the symptoms rapidly and enable the patient to return to work at once, and then a follow-up course, heavy enough to kill off lingering parasites and thus reduce recurrences, yet light enough to permit working in comfort. Prompt, vigorous treatment has the extra advantage of preventing patients from becoming infectious to mosquitoes, by forestalling gametocyte production.

There is little to support the theory that the patient's tolerance may be increased if one or two rigors are allowed to pass before treatment is commenced. Tolerance is much more likely to be developed during a relatively long struggle to maintain control over a chronic infection, in the course of which the tissues become accustomed to the continual discharge of small amounts of toxins. Delayed treatment merely permits the patient to become weaker and increases the loss of working time. If treatment is started immediately after the first rigor the patient may be fit to commence work on the third day, but if it is delayed until after the second rigor five days will almost certainly be lost.

THE ACTION OF THE VARIOUS ANTI-MALARIAL DRUGS

It is not convenient to go any further until we have formulated a working hypothesis as to the mode of action of the anti-malarial drugs. What follows here may not be quite accurate technically, but it matches the facts well enough and its application produces satisfactory results.

Quinine is directly toxic to all types of malaria parasites at all stages. Its efficacy is directly proportional to its concentration in the blood, and depends on the salt used, the method of its administration, and the accessibility of the parasites at the time it is circulating. The sulphate is the cheapest and the most stable, but it has a very low solubility; in the stomach it is so slowly dissolved that absorption is but little faster than excretion, and it probably never reaches high serum-concentrations. The bihydrochloride has a very high solubility but is unstable and slightly more expensive; it is absorbed much more rapidly than it is excreted and can reach relatively high serum-concentrations. Absorption once the drug has left the stomach practically ceases, due to the alteration of the reaction of the bowel contents from acid to alkaline.

Injections give the highest concentrations; the intramuscular route is preferable, since subcutaneously there

are intense pain and abscess formation, and intravenously even very dilute solutions given very slowly may cause clotting with fatal embolism. For intramuscular injection the bihydrochloride in 30 per cent. solution is used, and the site is the gluteus muscles. The injection is rather painful and the muscle remains stiff and sore for several days. The injected area degenerates and later becomes infiltrated with scar tissue. Abscesses of the buttock following injections of quinine are not uncommon, but can usually be traced to faulty asepsis or technique, and particularly to giving a second injection into the same area before it has had time to heal. Later injections into healed scarred muscle are much less rapidly absorbed.

In very low serum-concentrations quinine can kill any merozoites which are released while it is circulating, but it probably reaches only a few of the trophozoites contained within the erythrocytes; in higher concentrations more trophozoites will be destroyed; while six hours after an intramuscular injection about 60 per cent. of the intracellular parasites can be seen to be disintegrating.

In a chronic malarial infection large numbers of parasites may live and multiply in the swamps of the reticulo-endothelial system, only a few escaping from time to time into the general circulation. Even abnormally high serum-concentrations of quinine fail to reach these; they remain to all intents completely inaccessible until flushed out into the main stream by the engorgement accompanying an attack of fever. A single dose of 30 grains of quinine bihydrochloride, for instance, will immediately clear up an attack of fever (while, of course, making the patient very sick, and preventing the administration of any follow-up course), but within a fortnight there will be a recurrence of considerable severity.

A dose of 5 grains by mouth causes tinnitus, but after a few days on regular prophylactic dosage this effect is lost. Patients who are used to the drug usually develop some tinnitus again if they are put on 30 grains daily dur-

ing an attack of fever, but they rapidly become accustomed to the larger amounts. Where prophylactic quinine has not been taken the effects of large dosages can be very distressing, while patients who have had any serious middle-ear disease may suffer acute pain. Quinine in therapeutic doses does not of itself cause vomiting, although patients not accustomed to it sometimes complain that it causes indigestion and even nausea. In gastric fever, and particularly during the period of morning sickness in pregnant women, it is often impossible for patients to retain quinine—this is more marked if it is taken with food, and sometimes there will be no vomiting if it is taken between meals.

True *idiosyncrasy* to quinine is rare. Among over one thousand white persons selected indiscriminately I found the following: one woman who commenced to menstruate, without regard to her regular cycle, after three daily doses of 5 grains; two men who complained of peripheral fogging of vision after two days on 30 grains daily, although neither suffered any ill-effects on 15 grains daily for seven days and one man who developed hæmaturia on 30 grains daily, but who suffered no ill-effects from 5 grains daily.

Quinine poisoning may be chronic or acute. The chronic form occurs chiefly in children, who do not tolerate well even small daily doses over long periods. Prophylactic quinine is usually responsible for the typically thin, pale, languid "tropical" child. Adults who exceed the daily prophylactic dose of 5 grains may develop chronic poisoning after some weeks; the symptoms are loss of appetite, indigestion, loss of weight, moderate anæmia, and nervous irritability; the condition may easily be confused with "low fever"; it clears up rapidly when the drug is discontinued.

Acute quinine poisoning is due to taking massive doses. Amounts of the order of 30 to 40 grains do no permanent damage; there are severe tinnitus, giddiness, and deafness, persisting for from twelve to twenty-four hours; there may be considerable fogging of vision, worst at the periphery

but present over the whole field; there is usually intractable vomiting for several hours; and there may be pain and tenderness in the renal regions. After two or three days nothing is left but some visual fatigue and gastric irritability, which may take two or three weeks to settle down. Doses of from 50 to 90 grains cause greater damage; the tinnitus and deafness do not last for much longer than twenty-four hours, but the giddiness may endure for a week. There will be very severe fogging of vision, usually amounting to total blindness lasting from a few hours to many days or even weeks. Peripheral fogging and nyctalopia may persist for weeks after the vision returns, and visual strain and fatigue much longer. Of larger doses I have had no experience, but permanent blindness, coma, cerebral irritation, and Jacksonian convulsions have been reported. In patients with myocardial disease even therapeutic doses may cause serious upsets, heart block being the commonest phenomenon. In children coma and a Jacksonian type of convulsions certainly occur, and it may be impossible to distinguish clinically between fulminating cerebral malaria and acute quinine poisoning; when there is any doubt atebirin should be used until the diagnosis is settled.

Atebrin is not directly toxic to malaria parasites except in relatively high concentrations. It is given by mouth as tablets of $1\frac{1}{2}$ grain, varnished to cover its bitter taste and to prevent its corrosive action on the tongue. It is apparently absorbed from the stomach and upper portions of the small intestine and excreted largely in the bile. A cumulative cycle is thus set up, upon which its successful action depends, because although large doses quickly cause atebirin poisoning, most patients can be habituated to the drug by repeated small doses and can tolerate high concentrations if they are built up gradually. It takes usually four days on three tablets per day to reach an effective concentration, which is indicated by yellow staining of all tissues. Once full concentration is attained, but not before, all symptoms subside rapidly. Higher concentrations with safe doses can be obtained more quickly by intramuscular

injections of atebtrin musonate ($5\frac{1}{2}$ grains is the normal adult dose), and the effect of such injections is more prolonged, since the drug can be found in the urine for as long as eight days afterwards. Atebrin musonate is not so painful as quinine, and in the usual strength is no more likely to cause abscesses. Two, or at the most three, injections is the limit of safety; more may cause atebtrin poisoning.

Part of the action of atebtrin is possibly a direct stimulation of the reticulo-endothelial system to resist or destroy parasites. At any rate, once full saturation is reached the spleen decreases very rapidly in size—much greater reduction of chronically-enlarged spleens is produced by atebtrin than by quinine. It is probable that the low relapse-rate claimed in selected cases for atebtrin is due to this action, full saturation being responsible for destroying many more of the parasites in the reticulo-endothelial system than can be reached by quinine.

Atebrin given by mouth is erratic in its action. In my experience about 10 per cent. of patients are highly sensitive to it and suffer from symptoms of poisoning on the normal dosage, while on another 10 per cent. it has no effect whatever. Those patients who do tolerate it suffer no unpleasant effects beyond the staining, which may be so intense as to cause yellow vision; many complain of epigastric pain, but this is usually due to taking it on an empty stomach—it is essential that it be taken after meals. A breakdown in the cumulative cycle is presumably responsible for its failure in certain instances; these patients do not stain yellow, and their malaria is not cured.

Atebrin poisoning is marked by racking, intractable bilious vomiting lasting from 12 to 24 hours. It is apparently due to toxic effects on the liver; pre-medication with glucose has been recommended, but is not always successful. It may occur with full force after only one tablet has been taken.

Plasmoquine has practically no effect on the vegetative stages of malaria parasites. If given for treatment of an

attack of fever it is always reinforced with quinine, as "plasmoquine compound" (insufficient quinine) or "quino-plasmoquine" (1/6th grain plasmoquine and 4½ grains of quinine sulphate per dose). It is reputed to be of much greater value in destroying gametocytes than either of the others, and its only real value is to render non-infectious to mosquitoes those patients in whom gametocyte production has not been forestalled by early, vigorous treatment. In therapeutic doses it may cause acute epigastric pain, hæmoglobinuria, or multiple joint pains; about 10 per cent. of patients may suffer from one or other of these effects.

Atebrin with plasmoquine has entirely gone out of use. The combination is intensely poisonous: cyanosis, severe intractable epigastric pains, and extreme mental depression are the chief effects, and are suffered by at least 60 per cent. of patients.

THE RELATIVE MERITS OF THE VARIOUS ANTI-MALARIAL DRUGS

Considering the first aim of treatment—to cut short an attack of fever as rapidly as possible—obviously intravenous injections will have the quickest effect. There is little to choose between quinine and atebtrin for effectiveness, and there are neither failures nor poisonous results with the latter in normal doses. But injections are painful; they require quite a lot of preparation, especially when patients are not in hospital; and abscesses are not unlikely. They should not be used for ordinary straight-ahead cases, but should be reserved for emergencies or for attacks where oral administration is difficult or impossible.

For oral administration quinine is unquestionably far superior. Prompt treatment will always prevent a second rigor, and the patient may be back at work on the third day; whereas it takes four days to reach saturation with atebtrin and terminate an attack, and the patient will in the meantime have become so much more weakened that he will rarely be fit for work before the sixth day. Moreover,

except for the occasional patient with achlorhydria, quinine can always be relied on, while atebtrin will be responsible for further delay not only in those patients who suffer from poisoning for the first twenty-four hours, but also in those who fail to show successful results by the fourth day, due to absence of the cumulative effect.

The reduction of the number and severity of recurrences is the second aim of treatment. It is never sufficient to cease treatment as soon as symptoms subside—a follow-up course is always necessary. With quinine the follow-up course can run straight on; but since the normal therapeutic course of atebtrin is also the normal maximum safe dose, an interval of at least a week must elapse before giving any more. (In spite of the claims made for it, the relapse rate for atebtrin is not nearly so low that a routine follow-up course can be neglected.) The question of cost enters here: at wholesale rates a single course of atebtrin costs slightly more than a full course of quinine bihydrochloride in capsules; at retail prices the difference is much greater.

Nevertheless, in severe attacks of neglected fever, especially when the spleen is much enlarged, quinine alone is not nearly so effective in reducing relapses as it is when diagnosis is early and treatment prompt. Here is the real value of atebtrin—it is still not so effective as quinine in checking the fever rapidly, but if added to the quinine follow-up course it produces first-class results. The combination is much more than twice as effective as either of the drugs alone. This combination may also be applied to patients who cannot tolerate full doses of quinine, such as those who have had bad middle-ear trouble; a full course of atebtrin combined with a smaller dosage of quinine will clear up an attack much sooner than will atebtrin alone. It must be emphasised, however, that the combination is not necessary if the conditions laid down for good malaria control have been carried out; nor is the extra expense involved by using atebtrin justifiable if satisfactory results can be obtained by using quinine alone. Ate-

brin only comes into the picture when difficulties are met with.

To sum up: The oral administration of quinine bihydrochloride, in powder form, in gelatine capsules, is the treatment of choice. When oral administration is not possible either quinine or atabrin musonate can be given intramuscularly until oral administration becomes possible. When full doses of quinine cannot be tolerated modified doses reinforced by atabrin should be given. Neglected malaria and gross enlargement of the spleen respond best to an initial course of quinine with a combined follow-up course of the two drugs.

11. ROUTINE TREATMENT

In malaria, even more than in many other diseases, treatment is dependent on the individual peculiarities of each patient, so that no hard and fast rules for routine treatment can be laid down. In the previous chapter four main variations were discussed. It is proposed now to outline the details of standard courses of treatment, for normal adults, on those lines; these should meet average requirements; later, special points about treating children and pregnant women, and the various clinical forms of fever, will be dealt with.

A.—SPECIAL TREATMENT

STANDARD ORAL COURSE OF QUININE

To secure the best results by oral treatment it is necessary to give a total of about 200 grains daily of quinine bihydrochloride over a period of seven to ten days. Either 30 grains daily for seven days, or twenty grains daily for ten days, would achieve this, but neither of these courses is quite satisfactory. To secure the most rapid termination of an attack 30 grains must be given on each of the first three days—but by then the patient is fit to resume work, and he cannot work comfortably on this amount of quinine; so the follow-up course must be lightened. An easily-

remembered formula is: 30 grains daily for three days, 20 for three days, and 15 for three days. This totals 195 grains in nine days, and gives excellent results.

Five grains of quinine bihydrochloride in a single dose is big enough. Ten grains produces much more tinnitus, is just as soon excreted, and probably kills no more parasites. In practice, better results are obtained by taking six doses of 5 grains each than three doses of 10 grains. The doses can be conveniently spaced at breakfast, morning-tea, lunch, afternoon-tea, dinner, and bedtime. At the twenty-grain stage the morning and afternoon doses are dropped; the bedtime dose is omitted at the last stage. If it is found that for any reason this course is too light, it can easily be extended by increasing each stage by one or two days. This should rarely be done, however, if atabrin is available and can be tolerated.

During the rapid rise of temperature which initiates an attack of fever, vomiting almost always occurs. To take quinine at this stage is therefore wrong—it will be lost, and the patient, tasting it on its return, will be firmly convinced that it was responsible for the vomiting, and will not take any more even after the tendency to vomiting has passed. Accordingly no quinine should be given until the sweating stage is well established; then 5 grains is taken, and after that the routine programme is picked up and carried out for the rest of that day. The full standard course starts the following morning.

It must be admitted that this routine will often not prevent recurrences, but it will terminate any ordinary attack of fever with dramatic suddenness and enable the patient to return to work. And if all recurrences, however slight, are treated with the same course, there will be only two or three of them, each less severe and spaced at longer intervals. Moreover, such a course represents about the maximum which the average patient will bother to take—once free of direct medical supervision there is a tendency to backsliding, and the follow-up course must be short and light if it is not to be neglected.

COMBINED INTRAMUSCULAR AND ORAL COURSE

Under certain circumstances it is necessary to commence with one, two, or even three injections before going on to oral treatment. Each injection should consist of 9 grains of quinine bihydrochloride in 2 ccm., or $4\frac{1}{2}$ grains of atebtrin musonate in 5 ccm., given into the buttock. No matter how dramatic the effect of the injections, they must not be regarded as more than a preliminary—oral treatment must be substituted as soon as possible, and properly followed up. As a rough guide to the total dosage when injections are given, let each day on which one or more injections are given be regarded as replacing one of the thirty-grain days in the standard course outlined above. For example, for a true gastric attack one might give an injection on each of the first two days, and then, by mouth, 30 grains for one day, 20 grains for three, and 15 for three; or for a fulminating cerebral attack three injections at intervals of six hours on the first day, then two days on 30 grains, three on 20, and three on 15.

ORAL QUININE REINFORCED BY ATEBRIN

A course of this type is used for neglected and unduly severe attacks of fever in the hope of keeping down recurrences. The usual quinine, 30 grains for three days and 20 for three days, is given; but then for the next five days 5 grains of quinine with $1\frac{1}{2}$ grain of atebtrin are given three times a day. There is a little more quinine in this than in the standard course, but this is all to the good.

REDUCED QUININE COURSE, WITH ATEBRIN

This course is for those who cannot tolerate full doses of quinine. It is rarely necessary. The quinine is cut down to $2\frac{1}{2}$ grains three times a day, 5 grains twice a day, or 5 grains three times a day, depending on how much the patient can take. This dosage is continued for from seven to ten days, and on the first five days $1\frac{1}{2}$ grain of atebtrin is given three times a day as well.

ATEBRIN ALONE

In selected cases a standard five-day course of atebtrin (1½ grain three times a day, after meals) may be given alone. If this is not fully effective in checking the fever it can be extended for one day more. If it does not prevent recurrences the course should be repeated after an interval of ten to fourteen days. Such a repetition is preferable to increasing the amount or duration of a course.

STANDARD COURSE FOR INDIGENOUS IMMUNES

With the immune indigenous population the position is very simple. It has already been pointed out that because of their vast tolerance they suffer attacks of fever as a rule only when some other condition lowers their resistance, and that the giving of 30 grains of quinine daily for three days to all hospital patients whose temperature is raised will almost entirely eliminate the problem of their malaria. As a routine course for all attacks of fever they should be given one tablespoonful of a 4 per cent. solution of quinine sulphate (with 10 minims of dilute sulphuric acid to the ounce to aid solution) three times a day for three days. Natives have no amalgam fillings in their teeth to be harmed by the acid. Quartan malaria will be found to be far too stubborn to respond to such a course, and a longer course combined with atebtrin will be necessary.

Native children and adolescents whose spleens, although perhaps grossly enlarged, have not yet become sclerosed and friable, should be given two standard courses of atebtrin with a month between; their tolerance will not be seriously interfered with, but the great reduction in the size of the spleen will undoubtedly be beneficial. Atebrin has no useful effect on the "ague-cake" spleen of adult natives.

(It might with advantage be mentioned in passing that when employing natives for work in malarious districts those with no palpable enlargement of the spleen should be rejected since they are likely to have no tolerance, while those adults with greater than "plus three" spleens should

be rejected not only because their efficiency is likely to be low, but also because they will be dangerously liable to suffer rupture of the spleen from even a slight accident.)

B.—GENERAL TREATMENT

The strain imposed on the system by an attack of malarial fever is severe, and rest in bed as soon as the rigor starts is essential. Very little can be done to relieve the intense cold of the first stage—three blankets and a hot-water bottle give the most help. As the temperature rises there will be some vomiting, but frequent small drinks of water, lemon squash, soda water, and similar drinks should be given in spite of this, and should be continued through the hot stage. Once the shivering has stopped, only a light cover need be kept on, sufficient to ward off draughts and prevent a chill. Delirium is common during the hot stage, and when it is present a constant watch should be kept to see that the patient does not harm himself in any way.

The onset of the sweating stage is presaged by the hot dry skin becoming moist and greasy. When this occurs the patient should be wrapped in a blanket. Heavy sweating is likely to go on for an hour or more, and there is no sense in changing the bedclothes until it is finished; there will not be too much discomfort if the blanket is kept well wrapped around and the face is wiped frequently. Once the sweating is well established the headache and delirium clear up and the vomiting ceases (except in true gastric attacks). Quinine may be given then; and many authors recommend 1 grain of calomel (to be followed by a dose of epsom salts next morning). I consider that at such an early stage the calomel is unnecessary, but is only indicated when treatment is delayed and the tongue has become dirty.

When the sweating has ceased the patient should be given a warm bath—many are quite well enough to get up and have a shower. He should remain in bed for at least

twenty-four hours more; he may then get up and sit around for the rest of that day, and in most cases will be ready for work the next morning.

During the hot stage the headache may be unbearable, or the delirium may be alarming. In such cases it may be necessary to give 10 grains of aspirin, but this drug should be avoided if possible. It produces a massive sweat and gives great relief, but as soon as its effect wears off the temperature rises again. The normal sweat of malaria, which only comes on when all the toxins have been eliminated, is delayed, and the premature sweating due to the aspirin exhausts the body fluids. As a consequence the normal sweat is then not so profuse, the temperature falls more slowly, and the general relief is not so great. At the onset of the sweating stage, however, aspirin can be given with benefit, especially to women, who do not usually sweat so profusely as men.

There are no diet rules—the patient may eat what he likes. In the more severe forms no harm is done by restricting the diet to bland fluids for several days.

12. SPECIAL TREATMENT

CLINICAL FORMS OF MALARIAL FEVER

For completeness and ease of reference the modifications of treatment usually necessary for all the various clinical forms of malarial fever are listed here. This outline should only be regarded as a guide, and the personal peculiarities of each patient must be given full consideration.

Classical form: Give the standard oral course of quinine, increasing it by one or two days if treatment has not been commenced until after the second rigor.

Gastric form: Give one injection daily, up to three injections, until the vomiting ceases and oral quinine can be substituted. A mixture containing sodium bicarbonate and

either bismuth carbonate or *Pulv. rhei co.* often helps to control the vomiting, but must not be taken at the same time as the quinine, since the alkali will interfere with absorption.

Muscular form: Give the standard course of quinine. For subsequent neuralgia or muscular weakness give sodium salicylate or strychnine, and massage.

Algid form: If diagnosed before the vomiting and diarrhœa commence, give the standard oral course of quinine; if they have started, give the combined intramuscular and oral course. Follow up with a gentian and strychnine tonic.

Subacute cerebral form: Give up to three injections at intervals of 12 hours, then oral quinine.

Fulminating cerebral form: Give three injections at intervals of 6 hours, then oral quinine, followed up with combined atebirin and quinine. Rest in bed for at least a week.

Chronic malaria: If the patient's general condition is poor, one injection may give a better start off. Usually oral quinine reinforced by atebirin is enough. Give full doses of dessicated liver and a good tonic such as "Metatone."

"*Low fever*": Discontinue all quinine and wait until a definite attack of fever develops, then treat according to form. Attempts to treat "low fever" with quinine or atebirin will not clear it up; they will either only postpone it for a few days, or develop a quinine-resistant strain of parasites, or precipitate an attack of blackwater fever.

COMPLICATING CONDITIONS

Certain conditions interfere with the effect of quinine, and need special consideration:

Achlorhydria: Often a course of atebirin will succeed, where quinine has failed because of lack of acid to aid its absorption. If atebirin is not tolerated, or fails, an acid sodium phosphate mixture may be taken with each dose of quinine. One or two injections might be necessary.

Dysentery: In this, and allied conditions, the rapid passage of the stomach contents prevents quinine or atebtrin remaining for long enough to be absorbed, and a concurrent attack of malaria would need to be aborted with an injection on each of three successive days, oral treatment being postponed until the main disease subsides.

Gastric and Duodenal ulceration: The taking of oral quinine or atebtrin may seriously irritate an ulcer. Injections should be given; three on successive days will at least abort an attack of fever, and repetitions for subsequent recurrences would be justified.

Alcoholic gastritis: Oral quinine or atebtrin may cause severe vomiting in this condition, and a considerable hæmatæmesis may result. It may be necessary to give injections alone.

Indigestion: Not this condition itself, but the large doses of alkaline powders which many patients take for it, may interfere with the absorption of quinine. At the same time, the indigestion may be aggravated by the irritant effect of quinine or atebtrin. Judicious spacing of alkali and drug will overcome this trouble.

Menstruation: Full doses of quinine may cause dysmenorrhœa and menorrhagia, although often the quinine is blamed when the malaria is really at fault. It may be necessary to interrupt a course of quinine for two or three days at the beginning of a period, or to switch to atebtrin.

PREGNANCY

An attack of malarial fever may terminate a pregnancy if left untreated for even three days—if left any longer there will be no doubt about it. There are two ways by which abortion may be produced: either the malarial toxins set up uterine contractions and cause the contents to be expelled (compare malarial menorrhagia), or else the pyrexia, or the malarial toxins, or perhaps even a trans-

mitted malaria infection, kills the foetus. In the latter case the uterine contents are usually not expelled at once, but are retained for a month, or until the next due menstrual date, when a macerated foetus is delivered. A malarial abortion of this type is always complete, clean, and uncomplicated.

When a pregnant woman is harbouring a latent malarial infection she may of course suffer an attack of fever at any time, but the commonest times are around the eighth week and the eighth month. During the period of morning sickness there is a lowering of resistance, prophylaxis is often interrupted because of the gastric upset, and the onset of the fever is masked by the vomiting and malaise. There is thus every chance that diagnosis will be delayed and treatment interfered with, and consequently most malarial abortions occur at this time. Any sudden increase in the vomiting, especially if much bile is present, should be regarded with suspicion. Early confirmation of the diagnosis may be available if the spleen is enlarged or tender, but often it is necessary to record the temperature four-hourly for forty-eight hours to make certain.

Attacks of fever occurring after the third month are quite easily recognised, and early treatment prevents any damage being done to the child. The majority of these attacks occur during the eighth month. When there is an attack of fever at this late stage it can be anticipated that labour will probably come on up to three weeks ahead of the due date. If this happens the labour is usually precipitate; in most cases the membranes rupture without warning, and the child is born within three or four hours. Occasionally a very serious complication occurs: sometimes when labour is premature, often when it goes on to term, and nearly always when it is delayed, primary uterine inertia develops within a few hours. The uterine contractions become very weak and the head ceases to advance, usually at a point too high for forceps. It is necessary, as soon as the head stops advancing, to give a few hours rest with morphia; then, with the aid of a dose of castor oil, labour will recommence

with sufficient vigour to bring the head within reach of low forceps.

QUININE AND ATEBRIN DURING PREGNANCY

Normally, quinine has very little effect on the pregnant uterus until after the seventh month, when a dose of 10 grains will usually induce premature labour (provided the patient is not used to the drug through daily prophylaxis).

Prophylactic quinine should be taken from the onset of pregnancy. It may ward off attacks of fever altogether; or if it fails to do this it will at least ensure that any attack will be of moderate severity and will respond readily to treatment. In addition, since the patient is accustomed to quinine, a full therapeutic course may be given without fear of untoward effects. A serious difficulty is that if morning sickness is excessive it will interfere with the taking of prophylactic quinine at the very time it is most needed.

To prevent an abortion prompt treatment with full doses of quinine on the lines previously laid down is essential. Because of the vomiting, it will be necessary during the period of morning sickness to start with one or two injections; there is little chance that oral treatment can be instituted in time to save the child, and time should not be wasted in attempting it.

During the later months preliminary injections should not be necessary except when complications are present.

Atebrin has no effect whatever on the pregnant uterus, but is so slow in its action that death of the foetus will usually occur before the fever is controlled. It should therefore not be used except by injection when prophylactic quinine has not been taken, and when there is therefore some risk that the uterus may be upset by suddenly starting full doses of quinine. Even in such a case, when an injection of atebrin musonate on each of the first two days will rapidly control the fever, quinine should be given concurrently. Five grains twice on the first day, and four

times on the second, will be sufficient to lead up to the full dosage of 30 grains on the third day. If there is any doubt about this course, 10 to 15 grains of potassium bromide three times a day may be given—this will certainly neutralise any bad effects of the quinine on the uterus.

THE PUERPERIUM

An attack of fever can be anticipated during the puerperium if prophylactic quinine is not started early. Treatment should be on standard lines. Full therapeutic doses of quinine have no effect on involution, either to stimulate it or delay it. In women who have had much malaria involution is often slow. It must be remembered that in a patient accustomed to quinine there is not likely to be any response to the quinine in "Mist.Q.E.S." should such a mixture be needed; common humanity therefore demands that the "Q" be omitted from this vile concoction in such cases.

LACTATION

The taking of prophylactic quinine does not interfere with lactation, but enough may be excreted in the milk to make it taste. The infant will know no better if he is accustomed to it from the start, but if he is suddenly introduced to it after some weeks he may object. Still worse will it be if, because of the lack of prophylaxis, the mother develops an attack of fever. Interference with the milk supply may be so great as to necessitate weaning the child. In any case, on the days when there are pyrexia and sweating all milk should be expressed and discarded, and the child given substitute feeding.

CHILDREN

There are two chief factors affecting the treatment of malarial fever in children: first, since they do not tolerate prophylactic quinine over any length of time very well, and therefore do not normally take it, an attack of fever

occurs reasonably soon after the infection has been acquired, and is usually a sudden, well-defined (though not always easily recognised) entity; secondly, they tolerate relatively greater doses of quinine over a short period than do adults, and respond very quickly to its action. Hence any delay in establishing a diagnosis is compensated for by rapid response to treatment. In the absence of prophylaxis, children must have nets even in screened houses, and must be strictly trained not to run about out of doors after sunset.

The difficulties met with in making an early diagnosis are due to the fact that the three classical stages may be poorly defined. A rigor occurs only with a very heavy infection, and many children do not sweat heavily. Also, splenic enlargement and tenderness are often absent, since the infection has been of very short duration. The most useful signs are the sudden onset and rapid rise of temperature accompanied by bilious vomiting, marked facial pallor, and a heavy stupid look about the eyes. The remarkable recovery which takes place once the temperature has fallen is typical; a child who has suddenly become alarmingly ill, and has been delirious for two hours, may in another hour be running around apparently none the worse. Nevertheless, the chief diagnostic aid is the temperature: a rise in the morning, with a fall and a great improvement in general appearance by the afternoon, is a certain sign; rises at intervals of forty-eight hours leave no doubt; a double infection, with alternate swarms of parasites maturing on alternate evenings, may simulate any condition, and blood films may have to be taken before a decision can be made; the result of a leucocyte count may eliminate septic infections of various kinds.

NURSELINGS

In the case of breast-fed infants the administration of quinine is very easy. It is done by giving the mother a standard oral course—the proportion of quinine excreted in the milk will be enough for the baby.

OLDER CHILDREN

Since children tolerate large doses of quinine, the usual calculation of the fraction of the adult dose of any drug

$\frac{\text{age}}{\text{age} + 12}$ can be modified with advantage. My practice

is to calculate the age to the nearest quarter of a year, and to give daily for seven days the following fraction

of the normal adult dose: $\frac{\text{age}}{\text{age} + 9}$. This can be divided

into two, three, or four suitable doses. For example: for a child aged 18 months the daily amount needed will be

$30 \times \frac{1\frac{1}{2}}{1\frac{1}{2} + 9} = \frac{45}{10\frac{1}{2}} = 4\frac{1}{2}$ grains approximately. This

is best given as $1\frac{1}{2}$ grains three times daily, for seven days.

Fractions may be omitted over the age of three years. For a child of six the calculation will be:

$$30 \times \frac{6}{6 + 9} = 12 \text{ grains daily.}$$

Between the ages of 10 and 16 a daily prophylactic dose of $2\frac{1}{2}$ grains can be given without bad effects. The above formula can be used to calculate the therapeutic dosage. After sixteen the prophylactic dose is 5 grains daily, and a standard therapeutic course of 20 grains daily for seven to ten days can be given.

CEREBRAL MALARIA IN CHILDREN

This is the most serious form of malarial fever; it is difficult to diagnose and difficult to treat. Breast-fed infants whose mothers take prophylactic quinine may escape it, but among young children who have not this protection cerebral malaria is tragically common. Prophylactic quinine is undesirable, and general anti-mosquito measures often break down; in the absence of a rigor the first and even the second rise of temperature may be missed or attri-

buted to teething or something similar. Before anything has been done there comes a prolonged convulsion followed rapidly by coma. In a malarious district convulsions followed by coma in a child must always be regarded as due to malaria, with one proviso: acute quinine poisoning may cause the same signs, and a rapid check must be made to ensure that the child has not swallowed any quinine capsules, which are commonly quite accessible in all tropical households. If there is any doubt of this, atebryn must be used. Without waiting to go into a long differential diagnosis, immediate injections must be given. Either atebryn musonate or quinine bihydrochloride may be used; the dose of the latter must be very carefully estimated, since its rapid action when injected may lead to poisoning. The usual formula is applied to the normal adult doses (9 grains of quinine in 2 ccm., and $5\frac{3}{4}$ grains of atebryn musonate in 5 ccm.), but it is easier to work on the volumes of the solutions than on the actual doses of the drugs. Thus for a child aged 16 months the calculation for quinine

$1\frac{1}{4}$

would be: 2 ccm. x $\frac{1\frac{1}{4}}{1\frac{1}{4} + 9} = 0.25$ ccm. This is given intramuscularly.

Following this injection warm soap and water enemata are given until the bowel is completely clear. Tepid sponging must be used to reduce the temperature to 102° F., and maintain it there. Other possibilities suggested by the symptoms may then be investigated.

If the child is not fully conscious after four hours another injection must be given. There will have been time to prepare for this, and half a grain of quinine bihydrochloride in 10 ccm. of normal saline may be given intravenously, very slowly. This is rather a forlorn hope, because if the first injection does not produce very definite improvement within two hours the prognosis is practically hopeless.

Once the child is conscious oral quinine can be given on standard lines. A continuous watch must be kept for

twitchings, stiffenings, or rolling up of the eyes, which might threaten a return of the convulsions. A further injection will be necessary if they occur. Oral quinine should be continued for a clear week after the symptoms have subsided, and it can be reinforced with half a tablet of atebirin once or twice a day for five days.

Children who are too young to swallow capsules may have the powder rubbed in butter; a little warm milk is best to wash it down. If this is not satisfactory they can be given either quinine or atebirin in solution; the requisite amount with a trace of acid can be put up as a teaspoon dose three times a day. There is a so-called tasteless quinine salt, "Euquinine," but it is far from tasteless and has a very low solubility; there is no advantage in using it.

PART IV

COMPLICATIONS OF MALARIA

13. BLACKWATER FEVER

ETIOLOGY

Except that it is a complication of malignant subtertian malaria, and that its occurrence is associated in some way with the taking of anti-malarial drugs, nothing is known about the etiology of blackwater fever. Clinically, it appears as if something which is liberated when a swarm of merozoites emerges acts on many other unparasitised erythrocytes and hæmolyses them; methæmaglobin is formed, and the breakdown products are removed by the liver and kidneys; this causes excessive bile production and the passage of typical smoky-black urine. Usually, but not invariably, there is a history of many attacks of fever, insufficiently and irregularly treated; physical strain, low general health, and exposure to cold often appear to be predisposing factors. The mortality is 25 per cent.

ONSET

Occasionally it strikes out of a clear sky, but the usual history is that what appears to be an ordinary attack of malarial fever is placed under ordinary treatment; the second rigor, however, is not aborted, but is prolonged, and the patient becomes very weak and perhaps a little breathless. The backache early becomes severe. The liver and spleen are enlarged and tender. The first sample of urine passed after this rigor is an intense smoky black. Jaundice develops after a few hours. Thirst is intense, and there are pitiless bilious vomiting and diarrhœa. It is the

exception to find parasites in the blood after the onset. Either quinine, plasmoquine, or atebirin may act as the precipitating agent.

PROGRESS

Further progress depends on the type of attack. The urine may continue black for from one to four days, paling through red and pink to normal, or it may clear slightly and become black again with successive rigors. It is useful to keep serial samples of urine for comparison, and to estimate the hæmoglobin percentage daily, in order to follow the progress of the hæmolysis.

CLASSIFICATION

Attacks may be classified as follows:

FULMINATING TYPE: Here the initial breakdown of red cells is tremendous—up to 40 per cent. may be lost in half an hour, and more with successive rigors at short intervals. There may be a total drop to 30 per cent. in thirty-six hours. There is serious collapse. This type is accompanied by intense toxæmia, and the patient becomes comatose within a few hours. Death from respiratory and circulatory failure occurs on the second to fourth day.

SUBACUTE TYPE: Here the initial breakdown is not so great—often only 15 or 20 per cent.—and the toxæmia is less. Coma does not occur. The urine remains dark for two or three days, fluctuating a little, and the hæmoglobin value falls to perhaps 45 per cent. Then the urine gradually clears and the patient goes on to a slow recovery.

INTERMITTENT TYPE: This is a chronic type, marked by repeated small breakdowns occurring perhaps daily or on alternate days for ten days or more. The hæmoglobin may fall to 30 per cent., but there is no serious collapse because the loss is gradual. Spontaneous cessation of the process is not uncommon, but treatment is usually needed to bring it to an early stop. Death is rare in this type.

ANURIC TYPE: In this type it has been stated that the kidney tubules are blocked by the debris of broken-down erythrocytes, but this is not the whole story, because the van den Bergh reaction differs from that in each of the other types. In the present state of our knowledge, however, the distinction does not matter. What happens is that two or three days after the onset of what appears to be a subacute attack, production of urine suddenly ceases. In spite of all efforts the anuria persists for ten days, and massive œdema develops. Mentally the patient remains quite bright. Usually the hæmolysis ceases after some days, and by the tenth day of anuria the breakdown products have been eliminated as bile and the jaundice has faded; the excess fluid may have been all eliminated by sweating, vomiting, and diarrhœa and the œdema has subsided. A little straw-coloured urine may even be passed at the later stages; but invariably after ten days the patient becomes comatose and dies within a few hours. The coma is uræmic in type.

PSEUDOANURIC TYPE: A somewhat fine distinction must be drawn between this type and the previous one. In the true anuric type the kidneys are somehow intrinsically involved, but the pseudoanuric type occurs in patients whose kidneys were previously damaged; they cannot stand the strain imposed by the excessive elimination demanded of them. In such a case a subacute or intermittent attack of blackwater fever may respond very well to treatment, and the anuria may not come on until after the urine has cleared. The anuria may be only relative. The patient dies in uræmic coma after ten days.

SEQUELAE

It is obvious that with the profound anæmia developed in this disease any strain on the circulation will seriously affect the heart muscle. Blackwater fever patients have been known to sit up in bed suddenly, and drop back dead from myocardial failure. The cerebral anæmia makes patients cross, irrational, and resistive.

Except in elderly people the anæmia responds rapidly to treatment, and patients may be got out of bed three weeks after the urine has cleared. Another month should see them fit for work.

Apparently those parasites whose emergence sets up the hæmolysis are involved in the process and destroyed for the most part; in the intermittent type some go on invading new erythrocytes and following out their cycle for two or three weeks. But the usual statement that an attack of blackwater fever eliminates all malaria parasites is definitely incorrect. In almost every case some remain unharmed in the reticulo-endothelial system, and once the urine has cleared they take advantage of the patient's lowered resistance to multiply. Unless steps are taken to prevent it, an attack of malarial fever will always develop on the tenth to the twelfth day after the urine has cleared, and quite often this precipitates a recurrence of the blackwater fever.

Acute cholecystitis is a not uncommon sequel to blackwater fever, presumably initiated by the severe strain imposed on the bile-eliminating mechanism. In one instance I was compelled to drain the gall bladder on the tenth day after a subacute attack.

Some permanent damage to the heart and kidneys is inevitable, but is rarely gross enough to be disabling.

It is probable that one attack predisposes to others.

DIAGNOSIS

The smoky black colour of the urine in blackwater fever may be simulated by poisoning with phenol, resorcin, or sulphonel, but the history and other symptoms should prevent error. Sometimes quinine, and often plasmoquine, cause hæmoglobinuria, and as these are likely to produce this effect in conjunction with an attack of malarial fever, blackwater fever may be simulated very closely. The urine

is more red than black, and exacerbation of the hæmoglobinuria is associated with taking one of these drugs in an apyrexial interval rather than with the occurrence of a rigor.

TREATMENT

There is no specific treatment. The fulminating and anuric types are always fatal—in the former, blood transfusions are useless because of the rapidity with which the brain and heart are starved and poisoned simultaneously; in the latter, elimination of toxins by collateral routes cannot compensate for the retention due to complete failure of the kidneys, and there is no known method of stimulating the kidneys to resume their function.

The three great points in treating blackwater fever are to conserve the heart by absolute rest and careful nursing, to give copious fluids so as to flush the kidneys, and to keep the patient “on the alkaline side.”

The extreme sudden anæmia makes absolute rest imperative, but the resistant attitude of the patient in this disease makes nursing an arduous and exhausting task. An attendant must be at the bedside all the time—bilious vomiting; frequent bowel and bladder actions, often uncontrolled; small drinks every ten or fifteen minutes; frequent small feeds; kidney packs if the urine is scanty; measuring and recording every sample of urine; and controlling the constant restlessness, make a programme full and overflowing when the wellbeing of the patient requires that he be assisted in everything and not be allowed to do anything for himself. On the nursing alone depends the successful outcome.

A curious point is that after the first twelve hours transporting the patient for any distance usually ends in disaster. Apparently muscular movements in response to the jolting, exhaust the patient and favour further hæmolysis. Hence there is extreme urgency, once the diagnosis is confirmed, in getting the patient into hospital. Hand carrying on a

good stretcher with relays of bearers is necessary. The bushman's rule—"Build a hut around them where they lie"—is the fruit of many bitter experiences.

A high fluid intake is vital. There is a colossal fluid loss from vomiting, diarrhœa, and sweating, and the kidneys are embarrassed by the toxins and the debris of broken-down erythrocytes. A minimum excretion of 20 fluid ounces of urine in the twenty-four hours must be maintained, but the optimum is about 45 ounces. To achieve this at least two gallons must be taken every 24 hours. Half of this can be made up of a variety: plain water, soda water, barley water, aerated drinks, tea, and coffee. This variety is important, because the other gallon must be water with one teaspoonful of bicarbonate of soda to the pint; this is hard to take, and dries the tongue and lips, but it is apparently useful in limiting hæmolysis. The patient will rebel against it early, and must be persuaded and bullied, and bribed with alternate drinks from the list above. If the vomiting interferes, small warm saline enemata of 4 or 6 ounces may be given, but they will seldom be retained. Subcutaneous saline or intravenous glucose-saline, one pint every eight hours, will be more successful, but any œdema at all constitutes an absolute contra-indication.

If the urine is scanty, or if there is any œdema, cloths wrung out in hot water should be applied continuously over the loins; this is ineffective in the anuric types.

Food is important but difficult. Milk increases the bilious vomiting. Jelly, light gelatine puddings, clear broths, sweetened tea and coffee, and effervescing glucose drinks such as "Dexsal" will be the mainstay until the bilious phase has passed and a bland diet can be introduced. Habitual drinkers should be given judicious amounts of brandy.

In the unlikely event of constipation, small enemata may be given, but care must be taken lest racking diarrhœa be initiated.

BLOOD TRANSFUSION

Blood transfusion may do much harm while hæmolysis is actively going on, although many authors advise it as soon as hæmolysis commences; but once the urine has cleared it may help in relieving the heart of strain and shortening convalescence. It is hardly worth while transfusing a patient whose hæmoglobin value is over 70 per cent, and it is not essential unless the value is under 45 per cent. Sometimes in the intermittent type it is necessary to give a transfusion in the interval between two breakdowns so as to tide the patient over until hæmolysis ceases.

In selecting a donor special care must be exercised. There must be direct two-way typing, because although in ordinary transfusions only the action of the donor's serum on the patient's corpuscles is of real importance, in black-water fever and breaking down of the injected corpuscles by the patient's serum is a serious matter. To find a suitable donor under these circumstances may be a long job, and so a fairly large sample of the patient's blood, say 5 ccm., should be taken. Half is citrated; the rest is allowed to clot and the serum is drawn off. One ccm. of the prospective donor's blood is similarly treated. It is convenient to have slides with three hard paraffin rings; in the centre ring is a drop of citrated blood with a drop of normal saline, for reference; the two direct tests are set up in the end rings. A damp chamber may be made by cementing a piece of soft blotting paper inside the cover of a petri dish and moistening it; this cover must be kept over the slide while awaiting the completion of the test. Clumping in either end ring indicates incompatibility.

Should a second transfusion be necessary the same donor may not be used without testing again. The first reaction was as *a* against *b*, whereas the second will be as α against $b + a$, and this is not necessarily a compatibility.

Any œdema at all, and the presence of any active breaking down of the patient's blood, as indicated by dark urine, constitute absolute contra-indications to transfusion.

It is quite likely, however, that injections of plasma given before the urine has cleared, so long as they do not coincide with a rigor or the period shortly following it, would be harmless and beneficial. I have had no opportunity of trying this, but I feel that it should be investigated.

ANTI-MALARIAL TREATMENT

It has already been pointed out that quinine, plasmoguinine, and atebtrin are all apparently capable of acting as precipitating agents in the causation of blackwater fever. It is likely that once sensitisation has been accomplished the taking of further doses of the precipitating agent cannot make matters much worse, but the risk is great. Yet it is often necessary rapidly to reduce the number of circulating parasites in order to lessen the possibility of a series of rigors, each accompanied by further hæmolytic. It is a good rule to give, in the intermittent type, atebtrin if quinine was associated with the onset, or quinine if either atebtrin or plasmoguinine was to blame. One-sixth of a grain of atebtrin or 5 grains of quinine bihydrochloride three times a day for five days should be enough. If vomiting interferes, 3 grains of quinine or $1\frac{1}{2}$ grains of atebtrin musonate intramuscularly on each of the first three days should suffice.

It has also been mentioned that numbers of parasites survive the acute phase of the disease, apparently sheltering in the reticulo-endothelial system. In every case an attack of malarial fever arises ten or twelve days after the urine has cleared, unless something is done to forestall it; such an attack often precipitates a recurrence of the blackwater fever. If quinine has already been given as outlined in the previous paragraph, normal prophylaxis can be started on the fourth or fifth day after the urine has cleared. But if no quinine has so far been given during the course of the disease, and especially if quinine was the apparent precipitating agent, greater caution must be exercised. On successive days, starting on the fourth day after the urine clears, give: $\frac{1}{2}$ grain; two doses of $\frac{1}{2}$ grain; two doses of 1 grain; two doses of $2\frac{1}{2}$ grains; and then one dose of 5

grains daily. The few early fractional doses may more conveniently be given in solution. Once this "desensitisation" has been carried out full therapeutic doses may be given should the need arise later.

LIVER THERAPY

Intramuscular injections of "Campolon" have been recommended, but it does not seem to have any active therapeutic value. Possibly it gives greater impetus to the regenerative mechanism. Dessicated liver can be given once the bilious phase is over. The peculiar flavour is very well covered by soup, "Bovril," or warm milk. It appears to be of real value in aiding blood regeneration.

14. HERPES

Herpetic sores on and around the lips and nostrils, the so-called "fever sores," are a very common feature. Less common sites are the forehead and external genitals. Their appearance usually marks the end of the active phase of an attack of fever. Zinc cream containing $\frac{1}{4}$ per cent. of methol is a useful application.

The cornea is involved under ordinary circumstances very rarely, but in patients who have previously suffered from corneal ulceration from any cause, a recurrence after an attack of fever is not unlikely. Concurrently with the appearance of herpes labialis or frontalis, the eye becomes painful, red, and watery; staining with fluorescein reveals an ulcer. Usually there is an accompanying iritis. Standard treatment with a sodium salicylate mixture, atropine, and acriflavine, will clear it up.

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