Quinacrine greatly enhances plasma concentration and sojourn in the body. Doses are given daily for curative purposes.

**DRUG-RESISTANT STRAINS**

Resistance may be acquired, or a strain may be naturally insensitive, or relatively so, to a particular agent. Acquired resistance may be the result of ‘overgrowth’ of the naturally occurring resistant mutants, or the resistance can be induced by inadequate blood levels of the therapeutic agents.

A high degree of resistance can be induced against chloroquine and pyrimethamine, less easily so against the 4- and 8-aminoquinolines and acridine derivatives. Quinine is usually helpful against these multiresistant strains, but should resistance to this alkaloid develop, recourse is taken to the use of combinations, e.g. pyrimethamine with either a sulphonamide or dapsone, or trimethoprim with a sulphonamide.

**PREVENTING OR LIMITING RESISTANCE**

The use of a combination of drugs prevents or limits resistance. The combination must be chosen so that the half-lives of the components are similar (to ensure a continuous combined effect), e.g. chloroquine and pyrimethamine or the latter with either a long-acting sulphonamide or dapsone. One particular combination should be employed until proof of the emergence of a resistant strain is evident. Only then should the reserve combination be administered. Likewise, combination drugs should be held in reserve for treatment of the acute attack, until evidence exists that strains in that area are resistant to the conventional drugs (4-aminoquinolines).

Intermittent and inadequate chemosuppression of non-immune and partially immune populations, who are constantly being reinfected from indigenous reservoirs of parasites, greatly favours the emergence and spread of drug-resistant strains of malaria. Immune populations should not be given chemosuppressives unless dosage regimens are adequate and strictly adhered to.

In this context two factors must be stressed, i.e. the unreliability of patients in taking medication, and factors affecting bio-availability of the drug in question. The adequacy of the treatment regimen can in many cases be assessed by determination of plasma levels of the drug, and reliability of ingestion of the drug by a qualitative urine test.

Many so-called drug-resistance cases may be the result of inadequate drug levels at the site of action.

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**Malaria Control in the Northern Transvaal**

**C. F. HANSFORD**

**SUMMARY**

Malaria epidemiology relating to control operations is briefly reviewed. Control methods are discussed and reference made to the staging of control programmes. Details are given of current control operations in the northern Transvaal, with particular reference to aspects of importance to medical practitioners.


An attempt is made to give a brief background of malaria epidemiology as it affects control operations in the Transvaal followed by an outline of control operations and aspects which may affect medical practitioners and the public.

**State Health Department, Pietersburg, TVL**


Paper presented at the Malaria Symposium held at Nelspruit, Eastern Transvaal, on 27 January 1973 under the auspices of the Lowveld Division of the Northern Transvaal Branch of the Medical Association of South Africa.

**IMMUNE STATUS IN RELATION TO STABLE AND UNSTABLE MALARIA**

In this country *P. falciparum* is responsible for over 95% of malaria infections and remarks are confined principally to this type of malaria. Malaria may be classified as stable or unstable. Stable malaria is present where temperatures are high and vector mosquitoes are common and have a moderate to high longevity. Malaria transmission is regular and the vast majority of the population becomes infected and reinfected from an early age, thus developing a strong immunity. In these areas of high malaria transmission (holo-endemic) spleen rates are often over 75% in the 2-10-year age group, falling to lower levels in adults. Infant mortality is high, but adults are relatively free from clinical malaria in spite of a considerable proportion showing low parasitaemia on blood examination.

Malaria is unstable where either climatic conditions are subject to marked seasonal variations or the vector is short-lived and less efficient. There are marked seasonal and annual fluctuations in the incidence of malaria,
resulting in a variable but generally lower immune status of the population. This results in acute malaria infections developing in all age groups.

In South Africa, before control operations, malaria was stable in northern Natal and over large parts of the Transvaal lowveld. Swellengrebel in 1931 reported that in parts of the eastern Transvaal up to 88% of White children had enlarged spleens on account of malaria. Unstable malaria existed over most parts of the central and western Transvaal from the Zeerust district northwards. As a result of control operations previous unstable malaria areas have become malaria-free and the stable areas converted into unstable areas with resulting decline in the immune status of the population. During recent malaria outbreaks it was noted that over 95% of patients attending clinics and hospitals for treatment did so within 2-3 days of the onset of symptoms on account of feeling severely ill. Relatively few symptomless carriers were found, except in areas adjoining the lower Crocodile, Komati, Letaba and Mutale rivers. These findings suggest that the immune status has fallen to very low levels except in these low-lying river areas where low-level transmission has persisted.

MALARIA MOSQUITO VECTORS

*A. funestus* and *A. gambiae* are the principal malaria vectors in central and southern Africa. *A. funestus* prefers breeding in permanently shaded water; in the Transvaal such conditions are generally limited to the escarpment foothills. This vector is very susceptible to residual insecticide hut-spraying and nowadays is rarely found biting man.

*A. gambiae*, on the other hand, prefers shallow open pools such as those formed by receding waters, seepage and animal hoofprints after heavy rains. These breeding sites often become very extensive during February and March after prolonged rains and a tremendous increase in the numbers of *A. gambiae* frequently follows. It is these conditions, combined with the presence of a few malaria gametocyte carriers, that cause our malaria outbreaks.

In addition to the actual number of mosquitoes present, the longevity of mosquitoes is an important factor in determining the extent of malaria transmission. Under warm conditions the *P. falciparum* parasite takes approximately 12 days to complete its cycle in the mosquito, and if the average mosquito longevity is prolonged beyond this period, malaria transmission will be increased proportionally. MacDonald has made a mathematical study of the factors influencing malaria transmission and has evolved the concept of a critical reproduction level below which transmission will diminish and finally cease. The major factors affecting the level of transmission were shown to be the biting frequency, proportion of infected mosquitoes, mosquito longevity and duration of the extrinsic cycle. The extent to which the transmission rate is influenced by a change in any of these factors may be calculated, and this has in practice been used to predict the effects of different control measures.

INTERUPTION OF TRANSMISSION

Vector

Interruption of transmission has been successfully achieved by a reduction of mosquito numbers, combined with a shortened longevity as predicted by MacDonald. Total eradication of the vector is seldom practical or necessary. The vector mosquito may be controlled at the larval and adult stages. Larval control includes the elimination of suitable breeding sites by draining and filling in the propagation areas of predators such as gambusia fish, and the use of oils and insecticides. In practice the latter have resulted in the most dramatic control, but must be applied at frequent (usually weekly) intervals, restricting their economic use to the more densely populated areas. Difficulties may be experienced in controlling inaccessible marshy areas and with pools of water after heavy rains.

Adult mosquito control has been revolutionised by the introduction of the newer insecticides. When DDT or BHC is applied to protected surfaces such as the interior walls of dwellings, it has a prolonged insecticidal action of 3-6 months. Adult mosquitoes frequently rest on these surfaces before or after feeding on man, and a high proportion pick up a lethal dose of insecticide. Female mosquitoes take a blood feed, rest for a day or two while digesting the blood and, developing a batch of eggs, seek suitable water for depositing the eggs and then return for another blood feed. This gonadotrophic cycle takes 2-4 days, necessitating at least 4 blood feeds during the period of 12 days that it takes the malaria parasite to multiply and mature in the mosquito. Thus if only 50% of vector mosquitoes are killed each time they enter a dwelling, malaria transmission will be greatly reduced.

Where vector mosquitoes feed only on man and only inside dwellings, this type of residual insecticide control is extremely effective. Originally *A. gambiae*, our principal vector, was thought to conform strictly to these habits and its numbers were dramatically reduced as a result of this type of control. Later it was found that many of the surviving *A. gambiae* were feeding on animals as well as man, and also feeding on man outdoors. Further investigations showed that what was previously considered to be a single species of *A. gambiae* was actually a morphologically identical group of at least 3 species with differing habits. Species A is an indoor man-biting mosquito probably responsible for transmitting the majority of malaria before control measures were applied. It is now only present in limited numbers and it is presumed that species B, which feeds on man and animals both indoors and outdoors, is responsible for a large part of the remaining malaria transmission. On account of its habits species B is not as susceptible to residual insecticide control. Further investigations are required to confirm the relative importance of these 2 species in different districts and to devise improvements to present control measures.

Other factors which assist in the reduction of transmission are the siting of dwellings away from mosquito breeding sites, the gauging of dwellings and the habit of remaining indoors at night. Malaria case investigations
have shown that a high proportion of Whites contract their malaria during an evening *braai* held outdoors.

**Parasite**

Antimalarial drugs now available are extremely effective and single-dose treatment given to semi-immune patients will cure over 90% of *P. falciparum* infections. However, many control schemes based on chemotherapy alone have failed on account of difficulties in reaching the whole population. Where vector control programmes are undertaken, large-scale chemotherapy is a valuable help in reducing the time required to lower the parasite rate, and it is essential in eliminating residual foci remaining in the later stages of control programmes. It is also the best method of combating a sudden outbreak.

In the Transvaal we have reached the stage where every case of malaria is a danger and must be detected, given adequate treatment to cure the patient and to sterilise gametocytes which may remain infective and continue circulating in the blood for a further month after clinical cure. It is essential that all proved malaria infections are promptly reported to the health authorities for investigation.

**STAGES OF MALARIA CONTROL PROGRAMMES**

The World Health Organisation has standardised malaria control and eradication programmes into the following 4 stages:

**Preparatory Survey**

The preparatory survey investigates the presence, incidence and factors influencing malaria transmission, existing health services, and administration, following which a decision is made as to whether control is feasible and, if so, how it should be carried out.

**Attack Phase**

The second stage is the attack phase, where insecticides are applied to control the vector. After 3-4 years the incidence of malaria should have dropped to low levels enabling a surveillance system to be built up to trace and treat remaining malaria infections.

**Consolidation Phase**

When transmission has virtually ceased, the programme progresses to the consolidation phase, where insecticidal control ceases but surveillance measures are continued.

**Maintenance Phase**

A few years later, when it has been shown that transmission has not recurred after the withdrawal of insecticidal control, surveillance measures are discontinued and the maintenance phase commences. This involves the detecting and reporting of malaria infections only by the curative services, all other measures having been discontinued.

**THE PRESENT MALARIA SITUATION**

In the Transvaal malaria control has advanced in a similar manner. The attack phase was introduced from the late 1940s, progressing from districts in the central and western Transvaal to the lowveld. A considerable amount of larval control was done in the early stages, but as the advantages of adult residual insecticidal control became apparent, this method gradually superseded larval control. In the western Transvaal attack phase (insecticidal) measures are still being continued over a 0-kilometre-wide strip adjacent to the Limpopo and other large rivers northwards from the Ellisras district. This year, owing to malaria transmission near Alldays, this area and most of the country north of the Zoutpansberg have been returned from the maintenance to the attack phase. In the eastern Transvaal most of the country below the escarpment has remained in the attack phase. Owing to the increased incidence of malaria during the past 2 years, the Sigasi district of White River and the Crocodile River valley up to Nelspruit have returned to the attack phase.

Attack phase measures include the spraying of all interior wall surfaces of dwellings as well as the undersurfaces of roofs both inside and outside. DDT wettable powder is used on porous wall surfaces, giving an effective life of 4-6 months. It is unsuitable for better-class wall surfaces with painted finishes. Fenitrothion is used at present for this purpose giving protection for 3 months, but trials are in progress with other DDT and Lindane preparations to find a suitable longer-acting insecticide. House-spraying operations commence annually from September to October, the first round being completed from December to January. From January onwards dwellings in the higher-risk areas are given a second spray. Surveillance operations, incorporating house-to-house visits for the detection of malaria infections, are also carried out in Komatipoort and in part of the Sibasa district.

At present 25 teams are employed on control operations, each team controlled by a team leader with vehicle. A total of 382 Black supervisors and spray labourers are employed in these teams which in turn are under the control of health inspectors employed by the State Health Department. In recent years an annual total of 250 000 to 300 000 huts have been sprayed.

In rural areas considerable grouping of the population into villages has recently occurred, making larval control a more practicable proposition. This additional control measure is being practised where feasible in, and adjacent to, the larger villages where dangerous breeding sites exist.

Local authorities at Nelspruit and at Phalaborwa are responsible for mosquito control within their areas, including non-malarial mosquitoes. On account of the high density of houses, residual spraying is not economic, and
intensive larval control is practised over these limited areas.

What has happened to the vector mosquito as a result of these control measures? We now find that instead of the 30 or more *A. gambiae* per hut in some areas before control, there are now less than one per 100 huts. *A. gambiae* larvae are still found in variable numbers depending on climatic conditions, and entomological observations suggest that these remaining vectors bite man outdoors, especially in warm areas where many Blacks sleep outdoors. *A. funestus* is now rarely associated with man but is still found feeding on cattle. As stated earlier further investigations are required to determine the extent of outdoor transmission, and it is hoped that these will be intensified now that facilities at Tzaneen have been expanded. Investigations are continuing to assess the sensitivity of vector mosquitoes to insecticides. Resistance to DDT and BHC has not so far been a problem, but must be detected at an early stage if effective countermeasures are to be taken.

Extensive mass blood-smear examinations have been undertaken to determine the incidence of malaria and to detect asymptomatic malaria carriers. Apart from the recent outbreaks a steady decline in incidence has been noted and fewer carriers found. For example in the Bushbuckridge district, during the second half of 1970, only 6 out of 25 000 blood smears showed parasites, and yet the following years after good rains over 200 infections were detected. It is difficult to determine the origin of these infections—local carriers or infected visitors from elsewhere. It is known that malaria parasites may be scanty or only circulate intermittently in the blood of semi-immune people and thus be missed on examination. For these reasons the principal method of carrier detection has recently been changed from mass blood smears to the examination of blood smears obtained during house-to-house surveillance and from patients with pyrexia and other illnesses, attending clinics and hospitals. This change has proved to be justified and has enabled more carriers to be detected and a wider area covered without increasing the number of blood smears examined. At present 8 members of the Tzaneen staff are employed to examine blood smears and up to 100 000 smears are examined annually. The use of malaria antibody testing to detect carriers with intermittent parasitaemia will be investigated shortly.

Close contact is kept with all laboratories and hospitals in the region and arrangements made with them for the immediate notification of all infections detected. All malaria patients are investigated as soon as possible, preferably before discharge from hospital. Details of recent movements, previous illnesses, the presence of other individuals ill with possible malaria, are obtained from the patient and confirmed if possible by relatives and neighbours. A search is made in the patient’s dwelling and adjacent area for vector mosquitoes and further malaria infections. Insecticidal spraying is undertaken if indicated, blood smears are taken and single-dose chemotherapy given to people living in close proximity to the presumed site of the original infection. These measures are aimed at the detection and treatment of carriers, and to eliminate the malaria focus. They are considered extremely important at our present state of malaria control, and for this reason medical practitioners are requested to make an accurate diagnosis of malaria with the use of blood-smear examinations and to report infections promptly. Where practitioners examine smears themselves it would be appreciated if they could notify infections to the local State Health Office or local authority immediately by telephone, and also forward the smear to a recognised laboratory for confirmation.

This year some practitioners have reported patients with malaria-like illnesses apparently responding to anti-malarial therapy, but with negative blood smears. In retrospect these illnesses were probably due to one of the mosquito-borne viruses, possibly *Chikungunya* virus. The Arbor virus unit of the SAIMR is interested in the incidence of these infections and practitioners may forward blood samples for examination. Two samples should be forwarded, one taken in the early stages of the illness and one after recovery to detect a rise in antibody titre.

In known high-risk malaria areas such as the Komati-poor and lower Letaba areas, the State Health Department has also undertaken mass blood surveys combined with single-dose chemotherapy during January and February, in an attempt to reduce the number of carriers immediately prior to anticipated outbreaks.

**RECENT MALARIA OUTBREAKS**

Until recently many people were under the false impression that malaria had been eradicated in South Africa. Malaria eradication was a widely-used term 10-15 years ago when dramatic improvements followed the use of insecticides, but it soon became apparent that eradication was rarely feasible except in temperate climates or in isolated communities where reintroduction of the parasite or vector could be prevented. In Southern Africa malaria control rather than eradication must be the objective for the foreseeable future. It has already achieved remarkable results in reducing former high malarial incidences to the 0.5% experienced during this epidemic year when 5 000 estimated malaria infections developed among a population of 100 000 at risk. It has also enabled the lowveld to be intensively developed, this in itself being a factor which has considerably increased the malaria risk.

The principal reason for the increase of malaria during the past 2 years has been the high rainfall experienced. During the past season rainfall was double the average each month from October to April in all the potentially malarious districts, causing ideal conditions for mosquito breeding and increased longevity. During 1971 high rainfall was experienced in the lowveld south of Acornhoek, resulting in a malaria outbreak in this area, while to the north, where dry conditions prevailed, the incidence of malaria was low. In 1967 the malaria outbreak followed a cyclone. Macdonald has shown that extremely small numbers of malaria carriers are sufficient to initiate an outbreak if conditions are favourable. In some districts these persisted from previous low-level transmission, and
in other districts outbreaks were noticed to follow population movements both inside and across the country's borders.

This year the distribution of malaria infection followed previous patterns, the majority of infections being contracted adjacent to the major rivers. The following number of local infections were detected during the period July 1971 to June 1972:

- Eastern Barberton district: 1300
- White River: 120
- Bushbuckridge: 600
- Klaserie: 100
- Letaba: 300
- Sibasa: 600
- Messina: 250
- Zoutpansberg: 80

A total of 132 Whites and 3556 Blacks, who contracted infections locally, were detected, i.e. confirmed by blood smears, and an additional 154 were imported from outside the country.

During the period July to December 1971 only 83 local infections were detected, 43 of these being carriers. The peak of the 1972 outbreak lasted from mid-March to mid-April, approximately 3000 infections (85%) being detected during this period. Similar findings were recorded during the 1971 and 1967 outbreaks.

THE MEDICAL PRACTITIONER AND MALARIA CONTROL

Advice on chemoprophylaxis is a common request which is not easy to provide. The following are factors which increase the risk of contracting malaria and should be considered in formulating this advice:

1. Residence in a high-risk area, especially if occupation involves outdoor night activity;
2. The February-April period associated with good rainfall;
3. The presence of malaria transmission in the vicinity;
4. Travel to areas of adjacent countries where malaria incidence is known to be high;
5. Individuals in poor health, after splenectomy, on steroid treatment in infancy and old age, are more likely to contract malaria and to become severely ill.

Unless the danger of malaria is very real, the enthusiasm for taking prophylaxis rapidly wanes and after a few months one finds that dosage often becomes irregular. It is probably best to advise prophylaxis only to those groups at higher risk and for limited periods only. It is much more important to warn persons that if they develop a pyrexial illness not due to an obvious cause such as coryza, they should obtain medical advice without delay, advising the practitioner that they had been in a malarious area. The gauzing of houses, the use of a pyrethrum knock-down spray and the wearing of protective clothing in the evenings are also important aspects of personal prophylaxis.

Fortunately the majority of practitioners in the eastern Transvaal are malaria-conscious, and it is rare that a malaria infection is not promptly detected. Practitioners in other districts are rarely confronted with malaria and consequently frequently omit it from the differential diagnosis of a pyrexial illness. If patients are questioned on recent movements, malaria and other illnesses acquired by the travelling public will automatically be considered. Experience during the recent outbreaks has confirmed that malaria is not such a dangerous illness when diagnosed and treated in the early stages. It is among those patients who have delayed seeking advice or where the diagnosis has been missed, that the mortality is high.

During outbreaks of malaria busy practitioners holding clinics find it difficult to spare the time to take blood smears from suspected infections, and the Health Department may as a result have incomplete information on the extent of the outbreak. If practitioners feel that they are unable to manage they should contact the local State Health Department office and assistance will be provided.

Finally, one must repeat the importance of accurate diagnosis, adequate treatment and prompt reporting of malaria infections.