

Malaria Symposium — Opening Address

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In contrast with our present tragically drought-stricken state, we all longingly recall the previous season when nature gave her abundance with that memorably high rainfall. We also, however, recall the very real scare of malaria which then arose, particularly in this area; a scare which had medical and political repercussions throughout the country, right down to an important building at the opposite tip of the Republic of South Africa. Dr Hein Pretorius and the local branch of the Medical Association are therefore to be congratulated on their initiative in taking a closer look at this thorny theme, one of the endemic problems in this beautiful and bountiful region of our country. Very wisely, they have also invited colleagues from neighbouring countries such as Rhodesia and Mozambique to pool their knowledge and experience of a problem common to all.

LIFE-CYCLES

As a first point of perspective allow me to reformulate a truth which might appear self-evident but still needs to be stated in order to see our position quite clearly. It is the basic fact that man, despite his eminence in nature, is still to be seen as an incidental, physically available, biological reservoir and thus a participant in the life-cycles of the teeming organic life obtaining in his habitat. He ever remains part of the broad biological system, desired as a most suitable host by other organisms which use him in their particular biological life-cycles to ensure their own existence.

Man can exist without the other two participants (parasite and mosquito) in our three-linked problem, but he does, by way of his mobility and way of life, become involved in the natural setting or life-cycle of those two participants. His mobility, both as regards occupation and recreation when he roams far afield as a tourist, brings him from otherwise safe areas into endemic malarious regions. Within the endemic area his way of life is in addition a very real factor in maintaining malaria as an endemic infection. In this regard our Black population, by virtue of their way of life, their habitation and habits, very easily become earth-mates to the two other actors in our drama. For the one, our most important mosquito, *Anopheles gambiae*, man is a very welcome source of food and is, in the range of available food sources, surely to be classed as a delicacy on the menu of this feeder. That statement I found on the fact that man's exposed, thin and practically

hairless skin, which provoked the epithet 'the naked ape', offers the best opportunity for the mosquito to penetrate through this covering and obtain its meal of blood. Were we to protect our skin by going cloaked from head to foot, we could literally shrug off the problem of malaria. Man's skin is thus an invitation to the vector. For the other actor, man is a most suitable host in the developmental cycle of the parasite from its basic form into the schizonts, as well as in producing the gametocytes essential for its further existence outside man.

In its own life-cycle the mosquito can do without man and also does not need the parasite, but, fortunately for us, is very dependent on ecological conditions such as water, an optimal temperature range and height above sea level. As mentioned, man is for *A. gambiae* the most suitable and easily available feeding ground. The mosquito is, of course, essential for the sexual life-cycle of the parasite, thus firmly linking up with the third actor in our drama.

Of our three actors in 'Drama Malariae' the parasite is the most dependent on the other two members of the trio, certainly as regards the two most important forms in our setting, namely *Plasmodium falciparum* and *P. vivax*. It is fortunate for man that of the many types of *Plasmodia* existing in nature, only a restricted number are established human pathogens, and that of these we have a single predominant to deal with. In this regard it is well to remember that these parasites are subject to different natural lifespans: our major one, *P. falciparum*, she with the sickling sex, has a very restricted lifespan, usually only 3-4 years, compared with the second most important, *P. vivax*, whose very name reminds us that it has a long lifespan, at times extending even up to 30 years.

With the broad biological system which has pertained over centuries, the *Plasmodium* has thus firmly established itself within the two other life-cycles: of mosquito, in which it completes its sexual cycle for its own further existence; and of man as a very fitting host for its primary development in the liver and the disease-flaring schizonts in the erythrocytes. Here is the differentiating point where *P. vivax* has revealed itself to be the tougher, although less malignant, of the two, by maintaining itself in the basic form in tissues outside the red blood cells. From this maintained existence, which need not necessarily affect the host, further periodic developmental cycles in the erythrocytes can repeatedly flare up as clinically evident disease in the host. Safely ensconced in the depths of the tissues, it is this form of the long-life parasite, *P. vivax*, which makes it so difficult to eradicate.

The particular suitability of man as a host in this developmental cycle is emphasised by the fact that the healthiest specimens of man, particularly with abundant haemoglobin, are indeed the most desirable hosts from the point of view of the parasite.

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We still need more precise knowledge of the metabolism both of the malaria parasite and of the host during infection. The tissue damage, more specifically cerebral damage, appears to be based on anoxia due to a combination of local and general circulatory disturbances coupled to histotoxic effects of metabolites.

The physiological and pathophysiological responses by the host to the infection are largely non-specific, and in some respects applicable to other acute medical conditions. This, in large measure, accounts for the wide range of differential diagnoses always to be considered. The circulatory disturbance appears fundamental in the pathogenesis: a hyperstimulated autonomic nervous system coupled with a disturbed endocrine balance and the pharmacological effects of circulating kinins and kininogenases, creating a chain effect with the brunt on blood vessels and membranes.

Man, thus involved and fighting for his own existence, must do one or more of three things: eradicate or control the particular mosquito as vector; eradicate or control the specific parasite; and protect himself as far as possible from becoming involved in their life-cycles.

LESSONS FROM THE PAST

I still recall clearly how in the middle 1930s, when I was still a medical student at the University of the Witwatersrand, epidemics of malaria occurred virtually annually. In one particular year, the notified cases in the Transvaal alone exceeded 10 000. This prevailed some 40 years ago with a considerably smaller population and far less tourist traffic. We have certainly advanced far from that phase to our present state. Let us then recall with due appreciation the active steps taken at the time by the Department of Health and, in particular, the very positive and vigorous contribution of the Transvaal Provincial Administration to combat the problem.

These efforts found their culmination in, and were most fruitfully exploited by, that great personality, our colleague Dr Siegfried Annecke. He and his team at that time, with patient and penetrating study, really delved into the habits of our vectors. They established their distribution as well as the ecological circumstances determining their breeding habits. They defined the various animals, particularly cattle, on which these mosquitoes also fed. Then came that wonderfully interesting and revealing study on the huts of our Black populations in the endemic areas. By spraying the huts with the insecticide Flit, and catching the dying mosquitos on white linen sheets spread on the floor of the huts, they could study a large population of mosquitoes intensively. Gradually the fact emerged that the female mosquito, the *femme fatale*, tended to settle in the peak of the hut after feeding. A point of attack was immediately suggested. Here she was captive to her own habits, weighted as she was with her meal of blood. This afforded a sure basis for the huge campaign which evolved from these studies with regular spraying of the huts during the important parts of the season, with the chlorinated hydrocarbons as residual insecticides. It is still the most profitable method of control, and even eradication, by breaking the mosquito's life-cycle and thereby

the transmission of the short-life parasite *P. falciparum* for periods long enough to end its allotted lifespan. It was here that Dr Annecke's enormous driving force, together with his team of trained and convinced partners, made a major breakthrough from which we today still pick the wonderful fruits.

Unfortunately ignorance, and thus resistance, were rife, so that health education had to go hand in hand with the control programme. But how, for example, could one obtain the essential co-operation of an elderly widow on a big farm with numerous huts of the Blacks and innumerable breeding sites, when she responded to Dr Annecke's advice on combating malaria: 'What do you want to tell *me* about malaria. I know everything there is to know. Haven't I already seen a husband and four children to the grave with malaria?'

This complex biological problem, the lack of interest and even irresponsibility on the part of many people and the restricted facilities, were all brilliantly overcome by a dedication ever to be revered. And annually one could follow the graphs indicating how the Lowveld was growing in population and in revenue as it became unfettered from the malarial yoke, developing into the beautiful and bountiful region as we know it now.

It has been a great source of gratification to me that I had the privilege of submitting the memorandum motivating the conferment of the honorary degree of Doctor of Medicine of the University of Pretoria on Dr Annecke, the first of the small series of highly selected honorary M.D.s in which I could participate. This reflection of deserved esteem was highly appreciated by Dr Annecke when he received the degree on 10 April 1954. His great contributions still serve as a basis and incentive for malaria control in South Africa.

CONTROL PROGRAMMES

Despite all our knowledge and advances it can still be said that, taken globally, malaria is still the most important of the indirectly transmitted diseases. Despite globally supported eradication campaigns directed at breaking the three linked cycles at vector point, breeding site, or human host, some 480 million of the world's population, outside China, live in ecological systems where they are still liable to contract the disease. According to the WHO most of these are in countries south of the Sahara where eradication programmes are not yet practicable. This biological guerilla war involves huge sums of money, for instance the R30 million supplied by international agencies over the 21 years from 1950 to 1971. It furthermore involves a large body of skilled manpower and it entails continuous study, education and over-all development of the populations concerned. On the latter score the WHO alone, over the 20 years from 1950 to 1970, has published some 22 technical reports drawn up by committees of experts on malaria. In Africa some 15 countries today receive WHO support, both financially in eradication programmes or control programmes, and in educational projects.

On the global map the dark malaria cloud over Africa still shows a threatening though lighter-shaded 'sickle' extending downward along our north-eastern frontier. This

contains the ever-present threat of darkening into endemic proportions or of flaring into epidemics if we relax our vigilance. Even the clear areas of our country are constantly exposed to the potential threat of infected vectors transported inland, or of 'imported malaria' through people already infected returning home. This has been a recurring experience of the big hospital centres in Pretoria and Johannesburg over the past 25 years. We know, furthermore, of the established pockets of malaria along the lower reaches of the Orange River, and even the extreme south-western part of the country, the Cape Peninsula, has experienced the heavy toll malaria can take. The inadequate medicinal protection by the individuals concerned, when visiting endemic malarious areas, emerges as a constant theme from these experiences. Why, in this modern era, should intelligent and informed people, even doctors, thus lose their lives to a parasite which already long ago, and deservedly, had been awarded the epithet 'malignant'?

Experience and results in control programmes heavily underscore the old adage that prevention is better than cure. In this regard it is the broad experience of WHO that 'malaria eradication programmes depend for their success on a well-established and efficient network of basic health services, especially in rural areas. In fact, successful eradication is possible only in areas where health service coverage is sufficiently extensive to permit appropriate surveillance activities at the end of the attack phase and throughout the consolidation and maintenance phases.' It is therefore not surprising that a number of the recommendations on malaria published in the Technical Report Series I referred to, have been directly concerned with the development of health services. The expert committee reports have emphasised the need for careful planning to obtain the highest possible coverage of the population, with at least a minimum of preventive and curative services. The reports have also stressed the need for training health staff to undertake a wide range of basic tasks consistent with the epidemiological and socio-economic conditions in the country. Another aspect that has been stressed is the need for the systematic and continuing collection of information and data on a country's health situation and health services as a prerequisite for the planning and management of health programmes.

Experience shows that the defects in such programmes are 75% in management and 25% in operation. So often the problems may be administrative and, as the wag said, 'Look for bottlenecks, and as in bottles, you will always find them at the top.'

CURATIVE MEASURES

With regard to treatment and medicinal protection, the 4-aminoquinolines have indeed been a boon to mankind and a major asset as a schizonticide. The primary compound chloroquine sulphate, synthesised by Andersag in Germany in 1934, has been the starting point for many variations. Owing to the grave threat of medicinal resistance which developed in parasites in the Far East, the USA army programme has screened some 140 000 compounds over the past 7 years.

With regard to Africa, it has not been possible as yet to substantiate observations on resistant strains of *P. falciparum*. I agree with Bruce-Chwatt that it would be wrong to undermine, without factual evidence, the well-founded 'therapeutic credit' that chloroquine and amodiaquin have built up in Africa over the past 20 years.

To return to my opening remarks, while on the agricultural front we may rejoice in good seasonal rains for bountiful crops, and we certainly all rejoice in that, the health sector on the other hand needs to be all the more vigilant with the concomitantly greater opportunity for breeding sites for the vector mosquitoes. This is also particularly pertinent where our chief vector, *A. gambiae*, is satisfied at times with so little, even the little puddle of a deep cattle spoor in the rainy season. This ever-present possibility, coupled with the growing tourist traffic through Nelspruit, as the chief north-eastern portal, makes it imperative that both the public and the health services, and that means all of us, be aware and vigilant at all times. Whereas routine measures may cope adequately in most circumstances, we must realise that a relatively minor upset in the whole ecological system could lead to grave health destruction. As Lao Tse, the wise Chinese of 2 500 years ago, has already said: 'Solve the small problem before it becomes a big one.'

This symposium is to be welcomed as an active step in promoting our preparedness and vigilance in a never-ending programme of guarding and protecting our exposed frontiers against malaria. I am sure that the combined experience available here will bring valuable advice both on short-term and long-term issues, both on the preventive and curative aspects. An old enemy of mankind which in the past has destroyed whole civilisations, lies but partly leashed and subdued. It needs man's vigilance and discipline to maintain and extend the achievement and thus make the fair face of our earth free from malaria.