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EPIDEMIOLOGICAL BASIS OF MALARIA CONTROL

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SYNOPSIS

The epidemiology of malaria is discussed with special reference to the pattern observed in equatorial Africa, where the disease is very stable and where certain features, such as severe epidemic tendencies and ready amenability to control, commonly found in other malarious regions, are lacking. The particular conditions giving rise to stability are described in detail, and the ways in which they can be modified to bring about control of the disease in its stable form are outlined. The importance of measuring certain rates—for example, the basic reproduction rate, the index of stability, and the actual reproduction rate—when making any major malaria survey is emphasized, and formulae by means of which such rates can be readily calculated are included in an annex.

Introduction

There has long been difficulty in understanding certain aspects of the epidemiology of malaria in Africa, and it has not been lessened by the recognition of the fact that, while in some respects the conditions in Africa resemble those in other countries, certain features which are characteristic of the disease in most malarious regions—for example, severe epidemic tendencies and ready amenability to control—are not as a rule found in Africa. In an attempt to resolve this difficulty, the author and some of his colleagues, at the time of the Kampala Conference in 1950, set out to explore some fundamental aspects of epidemiology, using both the theoretical and the practical approach. The theoretical approach was necessarily a mathematical one, for all propagation of disease is a numerical process involving many factors of which the relationships can be studied only in this way. The findings were published in a series of papers by Macdonald.[10-15] The corresponding field observations, made by Draper and Davidson,[2-7] were concerned with many of the problems brought to light by the mathematical studies, especially the measurement of mosquito longevity and the infectivity of man. Two of these studies [4, 5] consisted of complete field surveys in which an effort was made to measure all the factors involved in malaria transmission and to relate them to each other in accordance with the original theoretical work.

The object of mathematical analysis in epidemiology is to reach an understanding of the fundamental factors involved, but it is realized that the technique is a foreign one to many malaria workers and that it will, to some extent, fail in its purpose unless it is explained in ordinary words. Therefore, at the expense of precision of statement, which is invariably lost in such a process, much of the material presented here has been translated into non-technical language, in an effort to describe the events taking place in a typical part of equatorial Africa such as that covered in the special surveys. Some comparison has been made with conditions in Madras, which was selected for the purpose because very detailed analyses are available in the works of Russell, Menon & Rao [16] and Russell & Rao.[17-20] In the interests of clarity, the account has been kept free of references, except where it has been considered especially necessary to include them, but all the points made in it have been substantiated by observation. Reliance has not been placed solely on the papers cited, and due acknowledgement must be given to the very substantial collection of factual knowledge, built up by many workers, which served as a background for the studies to which specific reference is made.

Epidemiology

In most parts of equatorial Africa, the period of extrinsic development of *Plasmodium falciparum* and *P. vivax* is brief, usually being of the order of 10-12 days throughout the year. Several species of mosquito provide excellent hosts for the parasites: two of them—*Anopheles gambiae* and *A. funestus*—have been shown, under typical conditions, to enjoy the considerable longevity consequent on a daily death-rate of about 5% or even less, and to bite man almost regularly every second day. These features, which are commonplace to every malariologist in Africa, are not universally so; indeed, they are the factors which together differentiate malaria in Africa from that in most other countries and give it its special characteristics—intensity and stability. The former characteristic is not uniquely associated with these special features, but the latter is. When a mosquito subject to the above mortality rate bites an infective person, it has at least a fifty-fifty chance of surviving until sporozoites appear in its glands, and if it does so survive it then has a further expectation of life of about 20 days, so that its chances of conveying the infection to another may be as great as 5 to 1, which is over a thousand times greater than those of *A. culicifacies* in Madras. The perpetuation of malaria is therefore secure even when anophelines are very scarce. Anophelism without malaria is unknown in Africa (though it is common in Madras) and transmission becomes intense when the anophelines are numerous.

If gametocyte carriers are few in the community, the proportion of mosquitos infected will be small, and at first will rise roughly in proportion

to any increase in gametocyte carriers. The sporozoite rate, however, will become high when the carriers are present in moderate numbers only, and this means that a further increase in the carrier rate must progressively produce less and less increase in the sporozoite rate, and so restrict the multiplication of cases which would otherwise occur. That some such restrictive mechanism must come into play sooner or later in any circumstances is obvious, but its particular importance in Africa is not well understood. In other places, the immediate effect of the restriction is moderate; for example, a rise in the infective gametocyte carrier rate from 1% to 100% would, under the typical African conditions used here for illustration, increase the sporozoite rate to about 6 times its original level, whereas in Madras the corresponding increase would be about 25 times. However, this represents only a small part of the influence exerted by the restrictive mechanism, for the effect is cumulative, a rise in the gametocyte rate increasing the sporozoite rate, which in turn increases the gametocyte rate, and so on, though in diminishing degree. The total effect is such that if some change in environment starts off an increase in transmission, the response in the parasite rate is some 200 times as great in Madras as in Africa. Thus, the epidemiological factors provide a governing mechanism in Africa which makes stability or lack of variation the most notable feature of typical African malaria, but do not do so in areas such as Madras, where *A. culicifacies* is the principal vector and instability is the rule, recession, recurrence, epidemics, and good and bad years following each other in irregular order. It is notable that all grades of malaria severity are experienced in both sets of circumstances, the distinction between African and Madras malaria lying in the regularity with which any degree of severity is maintained over the years, rather than in the degree attained at any particular time.

The greatest degree of stability is attained when the time of extrinsic development of the parasite is short, and when the anopheline is highly susceptible to infection by the local parasites, its mortality is low, and it bites man regularly. The stability decreases when any one of these conditions is lacking and especially when more than one are absent. Though the picture of stability is generally true of equatorial Africa, a review of conditions in the continent as a whole will reveal many exceptions, and will usually also provide the explanation for them. Epidemics and other manifestations of instability are well known on the northern desert edge of equatorial Africa and in Somaliland; in the mountains of Kenya; and in the Rhodesias, which form the southern fringe of the malaria zone. In the first case, the instability is due to increased mosquito mortality under arid conditions; in the second, to prolongation of the period of extrinsic development of the parasite under cool conditions; and in the third, probably to a combination of both these factors and possibly also to the zoophilism which is thought to be common in the *A. gambiae* of those

regions. In contrast to the position in Africa, some degree of instability is very common in other parts of the world. Over great tracts, almost continental in extent, truly stable malaria such as that seen in Africa is unknown, and possibly the only large areas in which conditions are really comparable with those in much of Africa are the stretches of hilly land infested by *A. minimus minimus* in north-east India, Burma, Thailand and Indochina. In most of India, Ceylon, Malaya and Indonesia, and in almost all the malarious zones of the Americas, the typical picture is of marked instability, often with a cyclically recurring tendency to severe epidemics. The epidemiological characteristics of the disease are so closely related to its stability that it seems preferable to use this feature as the primary basis for classification and severity as the secondary, rather than to base the classification on severity alone, as is commonly done at present. Admittedly, stability is less readily measured, but this is due as much to lack of practice as to unfeasibility. The first precise measurement of stability, as of so many other aspects of malaria, was made by Christophers [1] in the form of the " epidemic potential ", but this was suitable more for differentiating the degrees of marked instability than for examining the entire range. Gabaldon [8] has for a long time insisted on the importance of a direct measure of the " condition " of malaria, obtained by examining the range of variation of the spleen rate over a period of years. Through adaptation of the principles of these two workers, a system of measurement as good and as generally applicable as that now used for severity could readily be provided. The anopheline characteristics determining stability are measurable in the form of the mean number of times an anopheline bites man during its expectation of life—a figure which can be determined by the precipitin test, analysis of the feeding cycle, and measures of longevity such as those developed by Davidson and Draper.[2-5] This composite figure is a direct index of stability and is of the order of 10 in Africa, under typical conditions, and of 0.05 in Madras.

The causes of stability have been stated. Its primary features are that the disease is perpetuated by very small numbers of anophelines and that the endemic level is relatively insensitive to minor changes in the environment. Secondary characteristics include a commonly intense endemicity, a regular and therefore potent stimulation of immunity in the population, a greater incidence of *P. falciparum* and a lesser incidence of *P. vivax* than in most areas of instability, and a resistance of the disease to artificial control. The manner in which these factors operate is as follows.

The average mosquito ingesting an ample number of fully infective gametocytes may later distribute the infection to about five people. The normal prevalence of anophelines and the long duration of gametocytaemia in an untreated person, combined with this vector capacity, make the potential infectivity of a single case surrounded by susceptible people fantastically high, as many as 5000 secondary infections resulting from one

case in some instances. The author has called the estimated number of secondary infections the " basic reproduction rate ". This is only a concept and not an actual event in nature, where reproduction is enormously reduced by immunity, but it is an important concept because, in the final analysis, control must be concerned with non-immune persons, and the basic rate gives a measure of the intensity of transmission, which must be reduced to 1 or less if control is to succeed.

Whether the basic reproduction rate is of this extreme order or not, it is usually high. Moreover, transmission is regular and often continuous; infants and non-immunes quickly and repeatedly become infected, and a reaction of immunity is stimulated in them. The antiparasitic and antitoxic features of this immunity which protect the individual have received much attention at the expense of what is probably immunity's most important manifestation—namely, restriction of gametocyte output, a mechanism which protects the community. This restriction of gametocytes may occur very early, before any restriction of asexual parasites; in one series it was recorded in infants four months old before asexual parasitaemia had even reached its height. It is manifest first as a reduced gametocyte count and only much later as a reduced gametocyte rate. The combined effect is that the gametocyte carriers are relatively rare, and that all but a very small minority have very few gametocytes in their blood. All relevant experimental evidence shows that very low gametocyte counts are associated both with low infectivity to anophelines feeding on the carriers and with low-grade infections in the anophelines, which often fail to establish infections in the persons on whom they feed. Field observations have fully supported these findings. The gametocyte rate in one group surveyed was low (7.7%), and only 0.4% had over 100 gametocytes per mm^3 of blood. Direct trials on a comparable population suggested that only 1.7% of anophelines feeding on such a group would become infected, and very strong indirect evidence, probably more reliable than the direct, showed that only 1.6% of feeds resulted in infection of the mosquito. There is also evidence, which appears conclusive to the writer, that in this area only about 1 in every 100 bites inflicted on infants by sporozoite-infected mosquitos resulted in establishment of infection, and in another area only 1 in 20 did so. There may be many causes for this failure, and their relative importance cannot at present be assessed, but among them some considerable weight must be given to the very small numbers of oocysts and sporozoites typically found in mosquitos in such places, numbers which are almost negligible when compared with those commonly seen in experimental infections.

The combined effect of a reduced gametocyte rate and gametocyte count —particularly the latter—in lessening the infectivity of man to the mosquito and of the mosquito to man is enormous, and sufficient to reduce the basic reproduction rate to an actual reproduction rate which is very low indeed; in the two surveys carried out with the express intention of measuring

it, values of only 1.15 and 1.25 were obtained. Date from several other surveys carried out by different workers in equatorial Africa have also been used for computing the actual reproduction rate, and in all cases the rate was found to lie between 1.05 and 1.2. Both the similarity and the nature of the figures are remarkable. The factors which come together to form the rate are widely different in the various surveys, but in each case they combine to give it approximately the same actual value. The resultant rate is just a fraction over the critical level of 1.0, values below which indicate a disappearing disease and values above, a persistent one. The implication is quite definite: the stimulus of infection of all the individuals in a community produces a reaction of immunity, which limits the amount of transmission by reducing gametocytogenesis. This reaction is in almost perfect balance with the amount of transmission, and results in the average infection's rarely producing more than one secondary infection in another person. The actual complete transmission of the disease is reduced to a level which, though it may seem high to the non-immune observer, is in fact low to the indigenous people and well within the community's capacity to bear without danger of extinction. It is for this reason that infections in infants are often delayed for months, when entomological study would suggest their inevitability about a fortnight after birth, and that malaria at its most severe, provided the incidence is stable, does not depopulate the countryside. Variations in the basic reproduction rate, if sufficiently lasting, appear only to modify the immune response in such a way as to keep the actual reproduction rate at almost the same level, chiefly by modifying the age at which gametocyte production is first limited.

The greater relative frequency of *P. falciparum* in Africa is also probably attributable to the stability of the disease. The essential differences between this parasite and *P. vivax* are its lesser stimulation of immune response and its longer cycle of multiplication, due to the delayed appearance of gametocytes after the first infection and to the slightly longer period of extrinsic development. These features result in its slower multiplication at the start of transmission, a fact well acknowledged in all epidemic surveys, and in its persistence for a longer time when once established. Brief periods of transmission, such as are common in regions where the disease is unstable, therefore favour the multiplication of *P. vivax*, whereas long periods, common in stable areas, favour *P. falciparum*.

In areas where the disease is unstable, the epidemiological situation is quite different. Instability is attributable to zoophilism, high mosquito mortality, or a long period of extrinsic development of the parasite, or to more than one of these factors. The probability of a mosquito's passing on an infection once it has swallowed gametocytes is very small, and in consequence the disease can be perpetuated only where mosquitos are very numerous. Anophelism without malaria is therefore common. If the mosquitos are sufficiently numerous to perpetuate transmission, however,

the sporozoite rate varies much more nearly in proportion to the gametocyte rate than it does under stable conditions, and the endemic level is infinitely more sensitive to minor changes—whether for better or for worse—in environment. Interruptions of transmission are therefore common and at times prolonged, and tend to be succeeded by epidemics, the inevitable severity of which is often aggravated by the size of the non-immune population which has grown up in the meantime. This provides a gametocyte reservoir which is not controlled by the mechanism already described until too late. In these epidemics *P. vivax* always precedes *P. falciparum* and may often continue to preponderate. The fact that communal immunity, which restricts transmission, is delayed permits intense transmission to take place, and this results in a correspondingly marked immune response after the epidemic—a response which may be sufficient to stop transmission entirely and bring about local elimination of the disease or may result in cyclically recurring outbreaks. Both of these consequences are well known: local elimination following epidemics has occurred recently—and probably many times before—in the Canary Islands and in many parts of Europe, while periodic outbreaks are well known in India, Ceylon, the Caribbean area, South America and the Netherlands. Even in the last-mentioned areas, however, local elimination of the disease seems to be effected to a considerable extent; the best example is the Netherlands, where it has been shown that the disease becomes restricted to small foci, which remain malarious in a non-malarious terrain for some years until the disease again extends over the countryside, presumably with the lowering of communal immunity by births, immigration and the passage of time. It seems probable that any approach to elimination must take this form, and that, consequently, such foci should be deliberately sought out and subjected to intensive action.

Control

The object of control is to reduce the actual reproduction rate to less than 1.0 and to keep it at that level, so that the number of cases will eventually diminish to zero, even if complete control is not immediately achieved. In practice, this means that the basic reproduction rate must be reduced to below this level. When control is started, the actual rate inevitably begins to decrease, and even mild measures could bring it down below 1.0. However, the improvement would only be balanced by a decrease of communal immunity in the form of prolongation of the period of gametocyte production in infants and a restoration of the previous position. Some advantage would probably be gained, in that the stress of infection without immunity would be distributed over a longer age-period, but it would, in total, amount to much the same as before. As control becomes more effective, the basic rate decreases towards the actual, and when it sinks

below 1.0 no further aid is demanded from immunity. If rapidly and effectively utilized, the immunity retained by older people would, of course, be of some considerable help, and the full measure of reduction of the basic rate might not be necessary.

The reproduction rate can be reduced by modifying any of its component factors—mosquito numbers, longevity and biting habit, and the recovery rate of the people affected—and, hypothetically only, by changing the length of the extrinsic cycle of the parasite. These factors, however, have very different influences on the rate. The one with the least influence is the size of the mosquito population, upon which the traditional attack has always been made in the form of prevention of breeding. Its influence is direct: reduction of mosquitos to, say, a tenth of their previous number reduces the basic rate to a tenth of its previous value. Consequently, if reduction of the rate to a thousandth or a five-thousandth of its value is required, the hopelessness of anything except total mosquito elimination can be appreciated, and thus a ready explanation is provided for the many failures of larval control in Africa, despite its many successes elsewhere. An unaided attack on the recovery rate by treatment of cases suffers from a similar disadvantage, in that omission of even the occasional carrier leaves persistent transmission. Modification of the biting habit has been brought about unintentionally in northern Europe and North America by changes in the pattern of husbandry, and the excellent results obtained by chance have given rise to a few preliminary experiments in the shape of deliberate zooprophylaxis. The success of this method of control in some areas, where the local anopheline readily accepts deviation to cattle, is attributable to the greater influence of the man-biting habit than of the size of the mosquito population on the reproduction rate. The influence is squared, reduction of the anthropophilic index to one-tenth of its original value reducing the reproduction rate to one-hundredth, as the latter is associated with the mosquito's necessity to bite twice—once to acquire and once to convey infection. In Africa, the change required in the habit would be great; it would probably be necessary to reduce the anthropophilic index of *A. gambiae* to less than 2%, and our present entomological knowledge does not suggest that this would be possible. With some other species, however, it does seem possible; and zooprophylaxis, within the agricultural pattern, may well become the backbone of malaria control in the Philippines and Malaya, where *A. minimus flavirostris* and *A. maculatus* are readily deviated.

The influence of mosquito mortality on the reproduction rate is very strong; a rise in the mortality acts by reducing mosquito numbers, reducing the probability of a mosquito's surviving through the extrinsic cycle, and reducing its subsequent expectation of life should it do so. The sum of these effects is such that an increase of 10% in the daily mortality decreases the basic reproduction rate to roughly one-tenth of its original value;

a 20% increase reduces it to one-hundredth; a 30% increase to one-thousandth; and so on. The worst conditions known in Africa could therefore be overcome by an increase in the daily mortality of the vector from about 5% to about 45%.

Experiments have been made to determine the mortality achieved by different insecticides, with results which are well known. In these experiments, however, what has in fact been determined is the mortality among the mosquitos actually entering treated houses, and this will be truly representative of the mortality among the entire local mosquito population only in the case of wholly endophilic species. Our knowledge of the endophilism or exophilism of *A. gambiae* and *A. funestus* is largely derived from this type of work and cannot therefore throw much light on the subject, but it appears that *A. funestus* is largely endophilic and *A. gambiae* only partly so. Transmission by the first species may be stopped by insecticides producing little more than the theoretical mortality of 45%, whereas control of transmission by the latter probably requires an insecticide producing a mortality of the order of 65%. Certainly the prospect of anopheline eradication by imagicidal methods turns largely on the question of endophilism. Theory suggests that an actual daily mortality of about 65% to 75% should result in eradication, and such a rate is readily attainable in the case of mosquitos which enter houses. The widespread eradication of *A. darlingi* in South America and the local examples of eradication of *A. funestus* in Africa probably reflect more the endophilism of the two species than any special susceptibility to the action of insecticides.

The powerful influence exerted by changes in the mosquito mortality rate on the transmission of the disease is the explanation for the brilliant success of residual insecticides. The first trials were, by chance, made in the favourable circumstances of unstable malaria (which is much more widely distributed than the truly stable form), some of them, in fact, being held under what are now known to be peculiarly favourable conditions. In many of these cases the basic reproduction rate was probably initially quite low and needed little reduction to secure elimination of the disease, such as might be attainable by a 10% or 20% increase in daily mosquito mortality. The almost universal attainment of such mortalities by even small doses of DDT or any other accepted residual insecticide explains the miraculous initial results of residual spraying. The first failures occurred in trials against *A. gambiae* and *A. funestus* in Uganda and elsewhere, but present knowledge of the requisite order of mosquito mortality, and the common failure of DDT to secure it, explain them adequately. It now seems that only the more potent insecticides, producing a mortality higher than 65%, should be used under typical African conditions, and that wherever possible the control requirements should be checked by survey methods adapted to modern concepts and needs. There is no reason to

suspect that the adequate use of potent insecticides, if properly checked, should not result in the elimination of African malaria in its most stable form, but the cost in insecticide and labour is bound to be higher than for the elimination of the unstable, and readily controlled, disease. Economy is to be sought by the combination of insecticidal attack with such methods as effective mass treatment to reduce the period of operation, and by improved survey and checking mechanisms to avoid waste without sacrificing effect.

Survey

Any form of factual measurement or observation may add value to a survey and, when permitted and justified by circumstances, elaboration is an advantage. There is, however, no reason for the routine multiplication of techniques, rates and indices, which should normally be restricted to those of obviously direct value in the planning and guidance of a control programme. The writer has no doubt that the application of this criterion would result in many standard procedures being relegated to the research department or the museum.

Assuming that sufficient parasitological, entomological and statistical inquiries have been made to establish the presence of malaria parasites, their species, the vectors and their resting and biting habits, the season of malaria transmission and the incidence of the disease, the additional epidemiological information necessary for a major survey can then be gathered from relatively few measurements, which are best made in areas where transmission is most severe. These measurements are mosquito density, biting habit and longevity, the period of extrinsic development of the parasite, the sporozoite rate and total infection rate of the vectors, and the infant parasite-rate, preferably classified in three-monthly age-groups.

Estimates of mosquito density need not usually be precise, and indeed this apparently simple measure is by far the most difficult to make precise, but they should refer to the greatest densities occurring over any given period or area. Accuracy is only necessary when the figures are to be used in some research process and is not needed for routine purposes. The figure required is a density in relation to the density of man, and may be estimated from the number of mosquitos entering human dwellings. Alternatively, if it is possible to determine the number of bites received by an average person per night, an adjustment for the known frequency of biting can easily be made.

Assessment of the biting habit requires knowledge of the normal biting cycle and a study of the nature of blood meals by means of the precipitin test. African malariology suffers from the fact that this test is not carried out as often as it should be—as often as it has been, for instance, in India,

where our knowledge of epidemiology is much more elaborate—considering that the biting habit is one of the most important characteristics of a mosquito. It is true that for highly accurate diagnoses of large numbers of feeds, in which the possibility of even rare errors is excluded, sera and techniques beyond the reach of most field workers are required. There are, however, centres where exact work of this nature can be done on dried specimens of blood, and, moreover, it is not sufficiently widely known that a reasonable separation of specimens into human and non-human groups can be effected by simple techniques and with readily obtainable sera, the only risk entailed being the rather unlikely one of confusion of simian blood. The writer feels strongly that at least an approximate analysis should be made of blood meals in every survey that aims at completeness.

The measurement of longevity is a very new technique, but again the writer considers it very important. This characteristic influences transmission almost as much as the biting habit does, and it is by its modification that it is hoped to secure control. Two separate techniques of measurement have been tested by Davidson,[2-4] and Gillies [9] has made valuable observations on and criticisms of other techniques. Davidson's methods give results which are probably nearly correct, but the measurement of longevity is a recent innovation and experimentation in technique should be encouraged. The method involving measurement of the ampulla is probably more generally applicable than the comparison of immediate and delayed sporozoite rates, and may well prove the most appropriate technique of all.

The influence of minor variations in the length of the extrinsic cycle is small, and in the perennially hot equatorial region an estimate of 12 days for *P. falciparum* is all that is needed for most purposes. The technique for determining the sporozoite rate is standard, but specimens should be dissected as soon as possible after capture. Moreover, useful information is lost unless an equally careful search is also made for oocysts and the total infection rate as well as the sporozoite rate recorded, since the ratio between these two rates is closely related to the longevity of the mosquito, which can be easily calculated from it provided that sufficient dissections are made to ensure the accuracy of the rates. The technique for determining the infant parasite-rate is also standard, but it is desirable to record the ages of the infants and to classify the infection rates in three-monthly age-groups up to two years.

A very full epidemiological picture can be worked out from data collected in this way. Its most important components are the basic reproduction rate, the index of stability, the inoculation rate, and the actual reproduction rate. The numerical manipulation needed to obtain the first three is simple, though unavoidable if the rates are to be recorded as figures and made comparable with data from other sources. The mathematical expressions used for the more important rates and indices are given in the Annex

below. The immediate value of the infant parasite-rate in all surveys is to give a general picture of the scale of transmission, at present and in the immediate past, and this can be assessed accurately enough for most purposes from the age-classified infant parasite-rates.

Annex

GLOSSARY OF SYMBOLS AND MATHEMATICAL EXPRESSIONS USED FOR VARIOUS RATES AND INDICES

Symbols

m = the anopheline density in relation to man.

a = the average number of humans bitten by one mosquito in one day.

p = the probability of a mosquito's surviving through one whole day.

n = the time taken for the completion of the extrinsic cycle to the stage of sporozoite development.

r = the recovery rate, or proportion of affected people who have received one inoculum only who revert to the unaffected state in one day. (The symbol is used here only in expressing the basic reproduction rate, in which it is intended to refer exclusively to non-immunes; a value of 0.0125, or one-eightieth, may be appropriate when infectivity and not parasitaemia is considered.)

s = the sporozoite rate, expressed as a proportion and *not* as a percentage, i.e., 0.1, *not* 10%.

Expressions

1. The basic reproduction rate (somewhat simplified) is:

$$\frac{ma^2p^n}{r-(\log_e p)}$$

2. The index of stability, which is the symbolic expression of the number of bites on man taken by the average mosquito during its lifetime, is:

$$\frac{a}{-\log_e p}$$

3. The actual reproduction rate can be estimated under fairly static conditions from the following expression, which is simpler to use than the full expression:

$$\frac{p^n}{p^n-s}$$

4. A mosquito's expectation of life is: $\frac{1}{-\log_e p}$

5. A mosquito's probability of surviving through n days is: p^n

The following table, which gives the values of p^n and $-\log_e p$, should greatly simplify calculation, except in the case of the inoculation rate, which cannot be simplified in this way. However, calculation of the latter rate is not so necessary as calculation of the other rates.

Value of p	0.95	0.90	0.85	0.80	0.75	0.70	0.65	0.60	0.55	0.50
p^8	0.6634	0.4305	0.2725	0.1678	0.1001	0.0576	0.0319	0.0168	0.0084	0.0039
p^9	0.6302	0.3874	0.2316	0.1342	0.0751	0.0404	0.0207	0.0101	0.0046	0.0020
p^{10}	0.5987	0.3487	0.1969	0.1074	0.0563	0.0282	0.0135	0.0060	0.0025	0.0010
p^{11}	0.5688	0.3138	0.1673	0.0859	0.0422	0.0198	0.0088	0.0036	0.0014	0.0005
p^{12}	0.5404	0.2824	0.1422	0.0687	0.0317	0.0138	0.0057	0.0022	0.0008	0.0002
p^{13}	0.5133	0.2542	0.1209	0.0550	0.0238	0.0097	0.0037	0.0013	0.0004	0.0001
p^{14}	0.4877	0.2288	0.1028	0.0440	0.0178	0.0068	0.0024	0.0008	0.0002	
p^{15}	0.4633	0.2059	0.0874	0.0352	0.0134	0.0047	0.0016	0.0005	0.0001	
p^{16}	0.4401	0.1853	0.0743	0.0281	0.0100	0.0033	0.0010	0.0003		
p^{17}	0.4181	0.1668	0.0631	0.0225	0.0075	0.0023	0.0007	0.0002		
p^{18}	0.3972	0.1501	0.0536	0.0180	0.0056	0.0016	0.0004	0.0001		
p^{19}	0.3774	0.1351	0.0456	0.0144	0.0042	0.0011	0.0003			
p^{20}	0.3585	0.1216	0.0388	0.0115	0.0032	0.0008	0.0002			
$-\log_e p$	0.0513	0.1054	0.1625	0.2231	0.2877	0.3567	0.4308	0.5108	0.5978	0.6931

Note: It must be borne in mind that $-\log_e p$ is a *positive* number.

RÉSUMÉ

L'épidémiologie du paludisme en Afrique diffère sur des points fondamentaux de celle d'autres régions du monde. La lutte antipaludique doit être adaptée à ces conditions particulières. L'auteur analyse certaines d'entre elles sur le plan théorique et pratique et évalue leur rôle dans le succès de la lutte contre le paludisme en Afrique.

L'endémie paludéenne en Afrique se distingue principalement par sa stabilité. Celle-ci est maximum dans les cas où la période de développement extrinsèque du parasite est courte, quand l'anophèle est très sensible à l'infection par le parasite local, quand sa mortalité est faible et qu'il pique l'homme régulièrement. Ces conditions sont réalisées dans une grande partie du continent africain où *Anopheles gambiae* et *A. funestus*, qui sont d'excellents hôtes de *falciparum* et de *vivax*, n'accusent qu'une très faible mortalité (de l'ordre de 5% par jour) et piquent l'homme tous les deux jours. La probabilité pour un moustique qui pique un sujet infecté de transmettre l'infection est mille fois supérieure pour les principaux vecteurs du paludisme en Afrique que pour *A. culicifacies* à Madras, par exemple, où des études du même genre ont été faites. L'endémie n'est pas également stable dans tout le continent. Des épidémies et d'autres manifestations d'instabilité sont connues dans les confins désertiques de l'Afrique équatoriale, dans les montagnes du Kénya et en Rhodésie où les conditions climatiques modifient un ou plusieurs des facteurs déterminant la stabilité.

L'auteur désigne par « taux de reproduction de base » le nombre évalué d'infections secondaires possibles à partir d'un moustique infecté, nombre qui doit être réduit à

1 ou moins pour que la lutte antipaludique soit efficace. Dans les conditions optimums de stabilité qui viennent d'être mentionnées, ce nombre peut atteindre *théoriquement* 5000.

Le taux de mortalité quotidienne des moustiques est le facteur qui influe le plus sur ce nombre. Il suffit que la mortalité augmente de 10% pour que le taux de reproduction de base s'abaisse à un dixième de sa valeur initiale. Les succès enregistrés dans certaines régions à la suite de l'emploi des insecticides ont été probablement dus au fait qu'il s'agissait d'une endémie relativement instable, dans des conditions où une augmentation du taux de mortalité à 20% suffisait à éliminer la maladie. Là où l'endémie est stable et où les conditions sont les moins favorables, il faudrait que la mortalité quotidienne du vecteur passe de 5% à 45% pour que la lutte soit couronnée de succès. Et encore ces chiffres s'appliquent-ils à des espèces exclusivement endophiles. Il est possible qu'ils suffisent dans les cas où le vecteur est *A. funestus*, espèce essentiellement endophile. Mais ils sont insuffisants lorsqu'il s'agit de *A. gambiae* partiellement exophile. Dans ce dernier cas, il faudrait que la mortalité atteigne un pourcentage de 65-75. Il semble dès lors, à la lumière de ces faits, que seuls des insecticides puissants, pouvant assurer une telle mortalité, devraient être utilisés en Afrique. Il n'y a pas de raison de croire que l'éradication du paludisme, sous sa forme endémique la plus stable, soit impossible. Mais il est certain que le coût de l'opération sera plus élevé que dans les régions où l'endémie est moins stable.

Pour que la lutte soit menée avec le maximum de chances, les enquêtes sur l'endémie devraient comporter outre les données entomologiques, parasitologiques et statistiques classiques, un certain nombre d'informations complémentaires, dont les analyses épidémiologiques ont démontré l'importance: la densité anophélienne, le rythme de piqûre des vecteurs, leur durée de vie, la période de développement extrinsèque du parasite, l'indice sporozoïtique et l'indice d'infection du vecteur ainsi que l'indice parasitaire des nourrissons, par groupe d'âge de 3 mois.

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