Chapter Eleven

PRACTICAL CONCLUSIONS FOR THE FUTURE OF MALARIA CONTROL

This chapter draws the practical conclusions from the field observations made in Garki and the theoretical work involved in making a coherent interpretation of these observations, both the observations and the interpretation being viewed in the light of the results obtained by previous workers.

The first group of conclusions (pp. 290-294) refers to the importance of malaria as a public health problem and to its control in a specific ecological area of Africa, the Sudan savanna. The results obtained in the Garki project can confidently be extrapolated to the rural areas of the whole Sudan savanna, which cuts across the African continent and has a numerous population (see Fig. 2 for West Africa; the Sudan savanna extends further east across the United Republic of Cameroon, Chad, the Central African Republic and Sudan). The main vectors (***A. gambiae, A. arabiensis*** and A.funestus) are the same throughout that zone, and so are the ecological and climatic factors. The surveys carried out so far, as well as the epidemiological studies and control trials, have shown remarkable similarities in parasite rates, vectorial capacity and type of response to residual insecticides, drugs, or both. The results may probably be extrapolated also to the Guinea savanna, which extends between the Sudan savanna and the forest and which also has a numerous population; since the Guinea savanna is wetter, ***A. arabiensis*** is probably absent from the rural areas of its southern half. The area of Bobo-Dioulasso, Upper Volta, with which certain comparisons are made below, lies at the limit between the Sudan and Guinea savanna vegetation zones. The findings made in Garki relate to a community which did not yet have the benefit of modern medical care in the area, where practically nothing was being done to reduce the contact between malaria vectors and man, and where antimalarial drugs were practically not available either from the health services or through commerce.

The prevalence of malaria, the risk of transmission and the actual incidence of new infections in the Garki area were all among the highest

documented from any area of endemic malaria. In the dry season, transmission was very limited in most of the study area but remained easily measurable where some surface water persisted, as around the village of Sugungum; this suggests that the development of irrigation will prolong the season of significant malaria transmission, unless appropriate measures are taken.

The second group of conclusions (pp. 294-296) refers to the planning and to the evaluation of malaria control in general, i.e., outside the particular situation and environment directly investigated in Garki.

The Control of Malaria in the Sudan Savanna of Africa

Residual insecticides

The domiciliary spraying of propoxur alone had a very limited impact on malaria. The vectorial capacity (i.e., the risk of transmission) was reduced by about 90%, but the prevalence of ***P.falciparum*** was reduced only by about 25% on the average and in the villages with the highest baseline transmission, a new equilibrium already had been reached after 2 years (i.e., further spraying would not improve the result). These findings confirm the poor results obtained previously by others with the application of various residual insecticides in the Sudan savanna of Africa, in particular in Western Sokoto (19, 47), in northern Cameroon (23,24) and in the area of Bobo-Dioulasso, Upper Volta (26).

The possible causes for these poor results obtained in the past have been reviewed and discussed by several authors ***(see inter alia 16, 78, 80,*** 122, 169). The following have been considered as causes for failure: (1) operational inadequacies (in particular incomplete coverage) and the underlying administrative difficulties (16, 99); (2) ineffectiveness of the insecticide, because of resistance, in particular to dieldrin (19, 24), irritation of the vector limiting its exposure ***(see inter alia 89, 123, 124),*** or insufficient vector mortality (related to the dosage applied, to the interval between successive applications and to the high mortality required when the baseline level of transmission is high (see Ref. 99, 144, and the text below); (3) loss of insecticide through sorption into mud walls (99), wearing off and decay of straw or thatch walls and roofs (24) and replastering of walls; (4) immigration of infected people, of vectors, or of both from unsprayed into sprayed areas, a source of failure caused by the limited extent of the treated areas (167); (5) the very high baseline level of transmission and the relative exophily of the vector (26).

In Garki, the resources invested in the control operations and in the evaluation allow a firm and exhaustive interpretation of the incomplete-

ness of malaria control achieved by propoxur alone. Geographical reconnaissance was thorough and regularly updated; propoxur was sprayed at short intervals and under strict supervision, and the coverage achieved in time and space was probably as nearly complete as possible. The extremely low catches by pyrethrum spray collection and exit-trap collection, and the high mortality observed in the wall and air bioassays, demonstrated that residual spraying with propoxur was very effective in killing the exposed vectors. Thus categories 1 to 3 of those listed above can be ruled out. This does not imply that in other situations they are not important factors of failure. Category 4, the limited size of the sprayed area, was not a significant factor. This was because the entomological effect of propoxur was about the same in the main trial (covering 165 villages) as in the preliminary village-scale trial; because the variation in the entomological effect of propoxur was not related to distance from unsprayed villages; and because the parasitological comparison between the stable and mobile parts of the human population demonstrated that mobility did not cause a significant increase in the parasite reservoir. This leaves only the fifth category of causes of failure. The baseline vectorial capacity (i.e., the risk of transmission) was very high indeed, and the local ***A. gambiae*** s.l. rested outdoors to a significant degree; this applies both to ***A. gambiae*** s.s. (species A) and to ***A. arabiensis*** (species B), the two members of the ***gambiae*** complex present in the area. This exophilic behaviour is probably genetically determined, at least in part. Hence a significant fraction of the vector populations avoids exposure altogether and has a normal longevity. This has the following consequences: (1) transmission may continue, even if the insecticide is 100% effective at a single exposure; (2) the actual reduction in vectorial capacity (risk of transmission), corresponding to a given reduction in density and average age of a vector population, is smaller than the reduction calculated in the usual way, which implicitly assumes a uniform exposure of the vectors to the insecticide.

In all likelihood other and cheaper insecticides would have given results inferior to those obtained with propoxur, which has a very high and rapid knock-down effect and also a fumigant toxicity. It is likely that the much greater impact achieved by fenitrothion on malaria transmission by ***A. gambiae*** s.l. in Kisumu, Kenya (64), than by propoxur in Garki is in fact due to the greater endophily of the vector in Kisumu, rather than to a greater effectiveness of fenitrothion against the exposed vectors.

Even the modest gains due to propoxur may be nullified by the development of mosquito resistance to propoxur after a few years. It may be concluded that in the rural areas of the Sudan savanna of Africa residual spraying is not to be recommended as a malaria control method. Its possible combination with mass drug administration is discussed in the

next section.

The outdoor resting places of ***A.gambiae*** s.l. are little known, and therefore the possibility of controlling the vector by outdoor spraying at an acceptable cost and without selecting resistant genotypes appears remote.

The combination of mass drug administration with residual insecticides

The combination of mass administration of sulfalene-pyrimethamine with residual spraying of propoxur failed to interrupt transmission for any length of time. This was true even when drugs were given every 2 weeks in the wet season and every 10 weeks in the dry season with a coverage of 85%. A high level of control was, however, achieved at that frequency of MDA: the prevalence of parasitaemia decreased very rapidly and varied in the 1-5% range, according to season. When drugs were given every 10 weeks throughout the year, the prevalence was also considerably reduced but rose to 30% in the wet season of the second year, when conditions were favourable for vector breeding. MDA probably reduced infant and childhood mortality; temperature and nutritional anthropometric surveys, conducted in the population treated at high frequency, demonstrated a decrease in morbidity in children. In the first wet season after the period of intervention of 1½ years with high-frequency MDA, the prevalence of ***P. falciparum*** rose temporarily above the baseline or comparison levels, demonstrating a loss of parasitological immunity without a corresponding increase in the point-prevalence of fever in the middle of the wet season. This suggests that there was no significant loss of clinical immunity. However, one cannot state what would have happened if the period of effective control had been prolonged further.

Previous trials using the combination of MDA and residual spraying in the Sudan savanna of Africa had achieved variable degrees of control, but all had failed to interrupt transmission (24,53,54,80, 126,169). A failure to interrupt transmission by the addition of MDA to residual spraying could be due to many causes: resistance to the drug, inadequate coverage, dosage or frequency, immigration of infected persons. As was the case for the effect of residual spraying, the resources invested in the implementation and evaluation of the Garki project allow a definite interpretation of the results. The local parasites were fully susceptible and the dosage used was adequate, as demonstrated by a special trial. The coverage was probably about as high as is possible in favourable circumstances (well qualified and motivated staff, good supervision), and it is

unlikely that at a higher frequency good coverage could be maintained for a long time. Immigration of infected persons contributed to transmission but was not necessary to maintain it. This is fairly certain at the lower frequency of MDA and probably also at the higher frequency. The most likely explanation of the persistence of local transmission is that effective coverage is never total while the vectorial capacity (risk of transmission) remains relatively high, even after the application of propoxur. Coverage was nonrandom, i.e., certain persons were consistently missed by the MDA. From the point of view of reducing transmission, nonrandom coverage is much worse than random coverage. Actual coverage is probably always nonrandom, in contrast to the random coverage implicitly assumed in computing the expected effect of MDA in a previous trial (100).

The combination of propoxur and MDA, which achieved a high level of control by means of adequate planning, staff and supervision, is, however, too expensive to be used on a large scale or for a long period. In addition, its prolonged use could lead to the selection of resistant parasites or to a loss of immunity in older children and adults, with dangerous consequences in case of interruption of the programme of MDA. The use of such methods was justified in a research project limited in time and space, for the sake of measuring what can and what cannot be achieved by presently available control methods and in order to study the effect of a drastic reduction in antigenic stimulus on the immune response.

In conclusion, MDA either alone or in combination with residual insecticides, is not recommended in the rural areas of the Sudan savanna of Africa.

Selective chemotherapy and chemoprophylaxis

It may not be feasible at an acceptable cost at the present time to control malaria in the rural areas of the Sudan savanna by an attack on transmission. It should, however, be possible to reduce the morbidity and mortality due to malaria by the treatment of clinical cases. At the age-group-related dosages tried in Kano, a single dose of chloroquine can cure a *P. falciparum* infection that has not been allowed to develop into a pernicious form. When the aim is not a reduction of transmission, the addition of pyrimethamine or primaquine would be redundant. Although the reproduction rate and the parasite rate of malaria would remain unchanged, the number of early deaths and the duration of incapacitating morbidity could be greatly reduced, without affecting the build-up of immunological processes. For this the requirements are: (1) the making available and constant replenishment of 4-aminoquinolines in suitable form and at cost price in every village; (2) an intense and simple

health education campaign stating the effect of the drugs, the dosage required for each age-group, and the advantages of self-administration of the drug in case of fever.

This method does not exclude the use of chemoprophylaxis for the most vulnerable groups of population, wherever facilities exist, nor the use of other control methods where the prevailing conditions make their use profitable (e.g., antilarval operations in cities, combined operations in selected communities or development areas). The cost of the application of this method would be obviously very limited, especially if the drugs were sold at cost price to the people. The availability and replenishment of the drugs could greatly benefit from the support of the existing primary health services organization or from the assistance of local residents.

In Garki, chloroquine treatment of fever cases by a voluntary worker designated by the village and given very simple instruction was used in 1974-1975, i.e., after the end of the intervention phase of the project in the villages previously protected by propoxur and MDA. The itinerant workers employed at a small fee for the registration of births were also used to ensure the supply of chloroquine to the villages. The chloroquine itself was supplied free of charge. This modest programme was well received by the village population, but the project's resources in 1974-1975 did not allow for its adequate evaluation. The socioeconomic conditions of the success of such a programme and the actual results it can achieve in terms of morbidity and mortality are imperfectly known, but several trials have been in progress for a number of years (e.g., 44, 4.5).

Selective chemotherapy and chemoprophylaxis are unlikely to exert sufficient pressure for the selection of resistant strains of ***Plasmodium*** parasites.

The Use of the Malaria Transmission Model for the Planning of Malaria Control

The model simulates fairly realistically the epidemiology of ***P. falciparum.*** It can calculate the parasitological consequences of: (1) specified changes in the vectorial capacity (risk of transmission) or its component entomological factors (density, longevity, man-biting habit) and (2) MDA at a specified effective coverage and frequency, with a drug protecting the individual for a specified period. The model can be used to compare the outcomes of alternative plans of intervention, as follows: (1) a range of baseline situations is simulated; all that is required for this is

a range of vectorial capacities; the precise estimation of the vectorial capacity is complicated, expensive and subject to a large error; however, in many situations, a plausible range can be calculated on the basis of available entomological information; at low levels of endemicity, in the absence of the large-scale use of drugs, the vectorial capacity corresponding to a given endemic level may be read off the graph in Fig. 83; (2) the intervention strategies which are operationally and financially feasible are listed; (3) the range of expected effect of each single control method on its immediate target is specified (e.g., "larviciding will reduce emergence by 60-80%"; "residual spraying will reduce longevity of exposed vectors by 50-75%, but 5-10% of vectors avoid exposure altogether"; MDA will cover 60-80% of the participating population at each round, but 1-5% of the population are never reached"; etc.); (4) simulations are made, applying the various strategies (comprising one or more single control methods, with the above specified ranges of direct effects) to the range of baseline situations; (5) the outcomes of the simulations using the different strategies are compared; if one strategy gives a better outcome over the whole range of assumptions explored, it is obviously preferred; (6) if, within the range of assumptions explored, it is not always the same strategy that gives the best result, or if a threshold result (e.g., eradication) is reached under some assumptions only, more information is required to make the best decision; the simulations will have helped to identify the crucial missing information or to specify the minimum level of effectiveness to be reached by a given control method to achieve a specified result; (7) if none of the strategies gives an acceptable result, one may look for other strategies or new control methods, or additional resources, or one may devote the available resources to the solution of some other problem.

It is clear from the above that the predictions of the model are conditional and comparative. The possibility of predicting the future in absolute terms is limited by ignorance about spontaneous changes (e.g., in breeding conditions for the vector) and uncertainty about the precise impact of a control method on its direct target (e.g., the precise reduction in vectorial capacity that will follow from the use of a given insecticide by a given **team** in a given situation), or about the actual effective coverage that will be achieved by a control method (e.g., MDA). The aim of model simulations for planning, however, is not so much to predict the future as to choose the best line of action among a limited number of possible interventions. A major effort has, however, been made in this project to test the model against actual field observations, because it is likely that among different models the one which is capable of simulating the epidemiology of malaria most realistically will also be the safest guide for action, even in situations for which only limited information is available.

The model's output is in terms of ***P. falciparum*** parasitaemia. To simulate the epidemiology of other malaria parasites or to use other end-points than parasitaemia, e.g., morbidity and/or mortality, various adaptations would be required. Adequate data against which to test such adaptations may not be available, but this would not necessarily invalidate their use in planning.

Computer programmes representing the model have been written in FORTRAN IV (for IBM 370) and in interactive BASIC (for HP 9830). These programmes and the corresponding documentation may be requested from WHO. Requests will be satisfied according to their merits and as resources permit, at a fee to cover costs.