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Monitoring of drug-resistant malaria in Africa

Sir—Charles Wendo, in his March 2 news item,[1] would have us believe that there is no effective programme for monitoring of drug-resistant malaria in East Africa. He suggests that African scientists are just beginning to come together to harmonise their protocols, and that molecular markers should form the basis of the monitoring exercise. This picture is incorrect.

The National Malaria Control Programmes (NMCPs) of Kenya, Tanzania, and Uganda have been actively collaborating to monitor antimalarial drug resistance with a standard in-vivo test since 1998. Rwanda joined the network (the East African Network for Monitoring Antimalarial Treatment [EANMAT]) in 1999, and Burundi will join soon.

Individual NMCPs and the EANMAT Secretariat opted for the WHO in-vivo test[2] for good reasons—it is a practicable test that provides data meaningful to policy makers. Although molecular markers provide useful ancillary information on the epidemiology of drug-resistant malaria, there is as yet no validated molecular test that can be used as a basic surveillance tool. Furthermore, the clinical nature of the in-vivo test, with its emphasis on response to treatment, has proved instrumental in convincing policy makers of the need for change. The impact of this test, within the EANMAT monitoring framework, on antimalarial-drug policy change in the subregion has been documented.[3]

All NMCPs with active monitoring programmes are aware of the potential benefits to be gained by replacing the time-consuming and expensive in-vivo test by a quick, accurate, and specific molecular test. For drugs such as chloroquine and sulfadoxine-pyrimethamine, but not others, such a test seems to be just round the corner. However, thorough validation of the molecular test against the clinical test is essential if the new method is to have the same impact on policy as the old test. Without this important step, we risk a return to the days when Ministry of Health policy makers, confused and unconvinced by a wealth of scientific data, delayed the change to more effective malaria treatment.

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Sir—After reading Charles Wendo's news item,[1] we would like to bring to your attention some endeavours at malaria control that are underway.

The Roll Back Malaria initiative aims to support countries in Africa and elsewhere in the world in the obtaining of the necessary information to enable them to update their antimalarial drug policies. Much emphasis has been placed on the need for strengthening national and regional networks of sentinel sites and for increased collaboration between the public health sector and research institutions. To date, 37 countries have set up a total of 122 sentinel sites to monitor the efficacy of chloroquine and sulfadoxine-pyrimethamine for the treatment of uncomplicated falciparum malaria in Africa alone. On the basis of their data, 13 countries have changed their drug policies, four have started the process, and 20 are still collecting data.

All studies supported by WHO use the standard and simplified 14-day in-vivo protocol developed in 1996 (updated December, 2001).[2] This protocol assesses parasitological and clinical treatment outcomes only in symptomatic children younger than 5 years. The previous protocol, developed in 1973, was abandoned because of difficulties in obtaining daily blood smears during the first 7 days after starting treatment. The number of required blood smears has been reduced, and particular attention has been paid to quality assurance, training, drug quality, microscopy, data entry, and analysis. In addition, efforts have been made to lower the number of patients lost to follow-up, which is now generally less than 8%.

The in-vivo test for therapeutic efficacy is the major determinant for antimalarial drug policy. Laboratory tools, such as in-vitro drug sensitivity assays and molecular markers, can, however, clarify or complete epidemiological observations and provide an early warning system for orienting therapeutic efficacy studies, although models for implementing molecular surveillance in different epidemiological settings need validation.

Such a system has been assessed in Mali.[3] Some advantages associated with molecular markers are ease of handling large numbers of samples, transportation, and storage. Although advances have been made in molecular-marker analysis, the relation between the presence of mutations and clinical outcome remains unclear and needs further validation before they can be used with any certainty as surveillance tools.[4,5] So far, mutations associated with resistance have been identified for a small number of drugs (chloroquine, pyrimethamime, sulfadoxine, atovaquone), but the genetic basis for resistance to other widely used drugs (quinine, mefloquine, halofantrine, artemisinin derivatives) has not been clearly established.

Although there is still no pan-African consensus on the choice of alternative drugs after first-line drug failure, new therapeutic options and general framework for the implementation of novel antimalarial treatment policy in Africa are being proposed by the Roll Back Malaria Initiative. It is through well-devised and standardised protocols and guidelines that a consensus on treatment strategies can be achieved.

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