



EDITORIAL

SENTINEL MALARIA SURVEILLANCE — MORE THAN A RESEARCH TOOL

The monotonic increase in South African malaria cases, with an over 100-fold increase in notifications during the past three decades, from 364 notified cases in 1971 to 51 433 cases in 1999, has elicited consternation throughout the public health sector.¹ Although this dramatic increase is clearly multifactorial, resulting from the effects of meteorological changes, human parasite-carrier migratory patterns, resistance of a mosquito vector (*Anopheles arabiensis*) to synthetic pyrethroid insecticides and an inconsistent notification system, the contribution of ineffective first-line malaria therapy should not be underestimated. The situation in KwaZulu-Natal (KZN) deserves particular mention, given this province's increasing proportional contribution to the national malaria burden. A recent dramatic increase in case numbers in KZN and anecdotal reports from clinic staff of patients returning with recurrence of symptoms within 2 weeks of treatment with sulfadoxine-pyrimethamine (SP) raised the alarm that the province might be in the grip of high-grade malaria parasite (*Plasmodium falciparum*) resistance to SP. Earlier results of a small 1996 hospital-based study found a 23.5% RI/RII/RIII parasitological failure rate on SP therapy (Medical Research Council — unpublished data). Although this finding was inconclusive because of the possibility of referral selection bias, it should have prompted an urgent, thorough evaluation of the effectiveness of SP therapy. The establishment of a sentinel surveillance site in KZN could have addressed this need.

Resistance of *P. falciparum* to antimalarial drugs is a serious impediment to controlling malaria.²⁻⁴ *P. falciparum* resistance to chloroquine was first reported in Africa in 1979, while clinical evidence of *P. falciparum* resistance to chloroquine emerged in South Africa during the mid-1980s.⁵⁻⁸ Despite resistance, chloroquine is often still used in areas of stable malaria because of the additive effect of host immune factors resulting in clinical but not parasitological cure. In South Africa, however, where the majority of the population resident in malaria areas are unlikely to enjoy any immunity, the risk of rapid progression to severe disease and even death necessitates effective first-line therapy that will rapidly eliminate *P. falciparum* and effect a parasitological cure. Thus the findings of *in vitro* tests demonstrating high levels of chloroquine resistance in KZN and Mpumalanga, and a striking increase in positive follow-up smears after chloroquine therapy in Mpumalanga, from 1.7% in 1990 to 16.7% in 1995, demanded confirmation by a carefully conducted *in vivo* evaluation.⁹⁻¹³

Following examples in other countries, Mpumalanga established sentinel site at Naas and Mangweni health centres in their most affected malaria districts for collecting *in vivo* resistance data. A standardised chloroquine *in vivo* study, based on the World Health Organisation (WHO) protocol, with 28-day follow-up, was conducted at these health centres during 1997.¹⁴ Unacceptable levels of RII/RIII (moderate to high level) parasitological failure (17.9%) and clinical failure (24%) were documented in Mpumalanga, with the total RI/RII/RIII parasitological failure rate being 48.4% (Freese J A, Report to the Department of Health). Similar patterns were found in Northern Province (RI/RII/RIII of 40%) and KZN (RI/RII/RIII of 62.5%) during surveys of smaller numbers of patients. This catalysed a national policy change from chloroquine to SP for first-line malaria treatment, although KZN had already made this change a decade earlier in 1988.

The same sentinel sites in Mpumalanga were used to conduct an informative baseline *in vivo* SP resistance survey on introduction of the change in first-line treatment.¹⁵ This evaluation, with 42-day follow-up, confirmed the efficacy of SP first-line therapy and demonstrated slower resolution of clinical symptoms than parasite clearance. In addition, it raised important questions about the adequacy of the recommended SP dosage for adults exceeding 60 kg, and the viability of gametocytes found to peak 7 - 14 days after therapy. The results of the most recent evaluation conducted 2 years after SP introduction at the same site in Mpumalanga (in this issue of the journal) confirm the continued efficacy of SP.¹⁶ This finding raises the possibility that SP usefulness may be extended through combination with artesunate, thus sustaining affordable therapy in Mpumalanga.¹⁷ This is necessary, since when used as monotherapy, resistance to SP has been shown to emerge more rapidly than resistance to chloroquine. Once high levels of SP resistance exist, few affordable treatment options remain.

The discovery of high-level failure of SP in the treatment of uncomplicated malaria in KZN, found in the standardised *in vivo* study conducted at clinic level in KZN in this issue of the journal), confirms concerns regarding the effectiveness of SP in this province.¹⁸ More alarmingly, this has precluded the use of the SP-artesunate combination in KZN. Although the true impact of persistent use of failed SP first-line therapy during the recent past in KZN on morbidity, mortality, economic losses, malaria transmission and resultant public health expenditure cannot be accurately determined, the resulting crisis could have been circumvented had regular clinic-level sentinel surveillance been conducted.

Public health surveillance has many uses, the most well known being detection of epidemics, evaluation of control and prevention activities, detection of changes in health practice, quantitative estimates of the magnitude of health problems, and monitoring of changes in infectious agents, particularly the



evolution of drug resistance.¹⁹ Although the term 'surveillance' was initially restricted to the collection, analysis and dissemination of data and did not encompass direct responsibility for responding to findings, more recently the quality of surveillance has been judged by its capacity to provide 'data for action'.²⁰⁻²²

Sentinel surveillance encompasses those activities focused on monitoring key health indicators in the general population subgroups. The term sentinel is applied to health events, including cholera, malaria or maternal deaths, which provide a warning signal that the quality of preventive or therapeutic health services merits investigation.^{23,24} Sentinel surveillance also refers to specifically chosen sites, whether health facilities or health providers, where data that are not routinely available are collected.²⁵ Careful selection of sites allows for adequate resources, including experienced and dedicated personnel, for collecting detailed information on each case and providing careful follow-up. As the collection of data is the most costly and difficult component of any surveillance system, it is essential that all elements to assure quality, reliability and uniformity of data are in place.²⁶ These include the ease of data collection facilitated by clarity, simplicity and lack of ambiguity of standardised forms and flow charts; well-defined case definitions; timeliness; mechanisms for preventing loss to follow-up; and measures to motivate data collectors, including feedback, participation in planning and review, recognition and other incentives.

In selecting a sentinel surveillance site, consideration must be given to a number of issues. These include the particular purpose of surveillance, frequency of the health event (accuracy of sample estimate), available resources, feasibility, the need to generalise findings (external validity), duration (trends) and likely quality of data (internal validity). Use of hospitals or other sophisticated facilities may pose problems because of the selection bias that usually operates.²⁷ However, hospitals are particularly valuable sites for tracking mortality trends or for detecting severe diseases that are almost inevitably admitted.^{28,29}

South Africa has been tardy in recognising the potential value of sentinel sites. A number of malaria control programmes in other African and South-East Asian countries have an established tradition of assessing the efficacy of their first-line malaria therapeutic regimens at sentinel surveillance sites to guide public health policy. In recent years both Zambia and Malawi have altered their national malaria treatment policies on the basis of results from standardised *in vivo* studies conducted at sentinel clinics.^{30,31}

Malaria sentinel sites may serve additional valuable functions. In particular, their usefulness as an epidemiological early warning system for malaria epidemics is being increasingly realised. The alarm is triggered when monthly morbidity thresholds set for particular clinics are exceeded.³²⁻³⁴

Mpumalanga has also harnessed the capacity developed at its sentinel sites to field test the accuracy and utility of rapid malaria diagnostic tests.^{35,36} The seasonal nature of malaria transmission in South Africa creates the opportunity for using the capacity developed at these sites to the benefit of other public health programmes.

The need for a sentinel surveillance network as a prerequisite for epidemiological research and health planning in South Africa was mooted more than 60 years ago.³⁷ This plea appears to have been vindicated by the high-quality drug efficacy information and data on the accuracy of diagnostic tests already collected at the malaria sentinel sites in South Africa that have facilitated major policy changes. The proposed plan to establish similar sites in KZN, Northern Province, Swaziland and Mozambique should therefore be vigorously pursued. However, the true value of these sites will not be measured by the volume of information they generate, but by the public health actions triggered.

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