Malaria in South Africa: no grounds for complacency

The huge global burden of malaria is repeatedly stated, to the point of triteness, yet the depressing fact remains that each year, world-wide, half-a-billion acute malaria episodes occur, and up to 3 million people – mainly African children – die in consequence.[1] There is currently some renewed interest in the possibility of substantially improved control of malaria in some regions. The primary reason for this has been the widespread introduction of more effective malaria treatment, i.e. artemisinin-based combination therapy (ACT).[2] Improved primary care level diagnosis through the use of rapid malaria tests is another recent development. Vector control, including use of insecticide-impregnated bed-nets, has much added potential. The inevitable emergence of antimalarial and insecticide resistance has to temper any overconfidence, however. Another, more long-term, hope for malaria control has been sparked by the recent moderate successes of the RTS,S/AS02 malaria vaccine trials.[3-5] Briefly, these phase 2 studies showed short-term efficacy against malaria infection in children of around 40% in Mozambique,[3] 65% in Tanzania,[4] and 53% in Kenya and Tanzania.[5] While immunisation may ultimately rescue mankind from malaria, or at least reduce the extent of its effects, the road towards an effective vaccine being available and used on a large scale will, in the words of commentators in the *Lancet*, be 'long and chaotic'.[6] With these developments in mind, a brief look at the recent South African experience with malaria as a public health problem will be instructive.

Historically, malaria control in South Africa has relied mainly on indoor residual insecticide spraying (IRS) of houses, which utilises the feeding and resting behaviour of vectors, and relies on the assumption that the vectors bite humans indoors and then rest on the walls. This is true of the two major African vectors, *Anopheles gambiae* and *A. funestus*. However, *A. arabiensis*, which is the more important vector in southern Africa with its wider range of behaviours, can be controlled but not eliminated by residual spraying of houses. IRS is labour-intensive and expensive, and requires a strong vertical programme to maintain efficacy. It has been highly successful in South Africa[7] but has not been sustainable on a wide scale elsewhere in Africa. *A. arabiensis* breeds in small, sunlit temporary pools, such as cattle hoofprints, and is not amenable to larval control, unlike *A. funestus*, which prefers more permanent water.[8] This latter vector, which is highly susceptible to IRS, was eliminated from the malaria transmission area in KwaZulu-Natal many years ago. In 1996, bowing to environmentalist pressure, the South African malaria control programme replaced DDT with synthetic pyrethroid insecticides. The incidence of malaria in the area rapidly increased by 500% to around 60 000 cases per year (Fig. 1); a contributing factor was widespread resistance of the parasite to sulphadoxine-pyrimethamine (SP) (Fansidar), which had been used as first-line treatment for the previous decade.[7] In 1999, pyrethroid-resistant *A. funestus* was found resting indoors in sprayed houses: an invasion from neighbouring Mozambique.[7] A change in first-line treatment from SP to artemether-lumefantrine (Coartem) and reversion to DDT house-spraying brought the malaria incidence to historically normal levels (Fig. 1), which illustrates the great importance of clinical and laboratory monitoring of antimalarial drug resistance in the parasite, and the entomological monitoring of vectors and insecticide resistance. The Lubombo Spatial

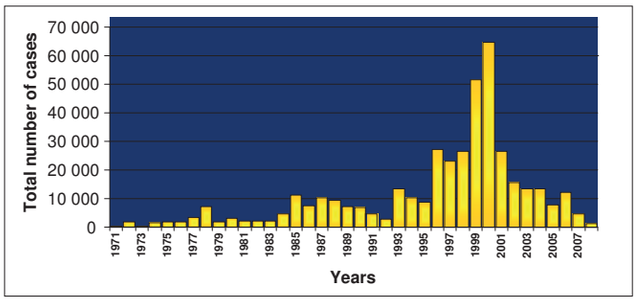

Fig. 1. Malaria notifications, 1971 - 2007 (source: National Department of Health). Because of probable substantial under-notification, these should be regarded as minimum estimates.

Development Initiative (LSDI) Malaria Control Programme, which involves co-ordinated vector control programmes in South Africa, Swaziland and Mozambique, had a rapid and dramatic effect on reducing malaria transmission in southern Mozambique and the adjoining areas of the LSDI partners.[7] One of the consequences of reduced malaria incidence is less clinical exposure of doctors to the condition.

Confidential reviews of deaths from malaria have shown that clinical assessment and treatment of malaria is frequently sub-optimal in South Africa.[9] Malaria cases often present outside the traditional transmission areas, and all clinicians should be familiar with prevention, diagnosis and treatment of this dangerous disease. The introduction of rapid diagnostic ('dipstick') tests for malaria at primary health level has the potential to expedite early diagnosis and treatment, but test performance and usage requires careful quality control.[10]

Compared with most of sub-Saharan Africa, South Africa is fortunate in several ways regarding malaria: it is at the southern extreme of malaria distribution on the continent, and relatively small areas experience seasonal transmission; it has a well-organised national malaria control programme; and it has a relatively well-developed scientific, economic and health infrastructure. However, problems with importation of malaria cases from neighbouring countries, antimalarial drug resistance, vector insecticide resistance, climatic events, distractions by other major public health problems such as HIV and tuberculosis, and deteriorating preventive and curative health services, provide no grounds for complacency about malaria in South Africa.

John Frean
National Institute for Communicable Diseases and University of the Witwatersrand, Johannesburg

References

1. Hay SI, Guerra CA, Tatem AJ, Noor AM, Snow RW. The global distribution and population at risk of malaria: past, present, and future. *Lancet Infect Dis* 2004; 4: 327-336.
2. Ogbonna A, Uneke CJ. Artemisinin-based combination therapy for uncomplicated malaria in sub-Saharan Africa: the efficacy, safety, resistance and policy implementation since Abuja 2000. *Trans R Soc Trop Med Hyg* 2008; 102: 621-627.
3. Alonso PL, Sacarlal J, Aponte JJ, *et al*. Efficacy of the RTS,S/AS02A vaccine against *Plasmodium falciparum* infection and disease in young African children: randomized controlled trial. *Lancet* 2004; 364: 1411-20.

4. Abdulla S, Oberholzer R, Juma O, *et al*. Safety and immunogenicity of RTS,S/AS02D malaria vaccine in infants. *N Engl J Med* 2008; 359: 2533-2544.
5. Bejon P, Lusingu J, Olotu A, *et al*. Efficacy of RTS,S/AS01E vaccine against malaria in children 5 to 7 months of age. *N Engl J Med* 2008; 359: 2521-2532.
6. Van de Perre P, Dedet J-P. Vaccine efficacy: winning a battle (not war) against malaria (editorial). *Lancet* 2004; 364; 1380-1383.
7. Mabaso MLH, Sharp B, Lengeler C. Historical review of malarial control in southern Africa with emphasis on the use of indoor residual house-spraying. *Trop Med Int Health* 2004; 9: 846-856.
8. Coetzee M, Horne DWK, Hunt RH, Koekemoer LL, Segerman J. *Handbook of Medical Entomology and Vector-Borne Diseases*. Johannesburg: Vector Control Reference Unit, National Institute for Communicable Diseases.
9. Mehta U, Durrheim DN, Blumberg L, *et al*. Malaria deaths as sentinel events to monitor healthcare delivery and antimalarial drug safety. *Trop Med Int Health* 2007; 12; 617-628.
10. Moonasar D, Goga AE, Frean J, Kruger P, Chandramohan D. An exploratory study of factors that affect the performance and usage of rapid diagnostic tests for malaria in the Limpopo Province, South Africa. *Malar J* 2007; 6: 74.

LETTER

Neonatal cholinergic syndrome – organophosphate poisoning or herbal medicine intoxication?

To the Editor: May I commend Van Wyk and Els on their successful management of a 10-day-old baby with organophosphate poisoning?[1] A low plasma pseudocholinesterase (butyrylcholinesterase) level as reported in the patient is a confirmation of organophosphate poisoning irrespective of the source of the poison or the mode of exposure. Perhaps 'Organophosphate poisoning in a newborn' would have been a more appropriate title. I would like to raise a few points relating to the potential source of poisoning and management of the patient.

A history of organophosphate exposure may not be evident in neonates presenting with cholinergic symptoms;[2,3] the effects depend on the type of chemical, its concentration and length of exposure. Exposure can occur in various ways, such as inhalation or absorption through intact skin from contact with contaminated work clothes of an adult, which can explain cases where no pesticides were used in the home. Clothes may remain contaminated even after being laundered,[4] at which stage the dose may not be toxic to adults but enough to cause symptoms in babies. Sudden onset of feeding difficulties, fever, cough, respiratory distress and lethargy, as initially presented by Van Wyk and Els's patient, are similar to symptoms reported for early severe organophosphate poisoning,[3] suggesting that exposure might have occurred before the baby was taken to the traditional healer.

A possible differential diagnosis not considered in this patient was cyanide poisoning. Herbal products can contain high levels of heavy metals and cyanide.[5] It might have been useful to analyse heavy metals and cyanide, in addition to organophosphate, in the samples sent for toxicological studies.

The authors did not report the baby's blood glucose level, and yet 5% dextrose saline was infused. Moderate to severe hyperglycaemia has been reported in patients with organophosphate poisoning,[6] which is believed to be due to secondary release of catecholamines from the adrenal medulla[7] and may require insulin. The relative risk of dying from hyperglycaemia has been reported to be increased when the maximum glucose level is over 150 mg/dl on admission.[8]

Atropine has been successfully used in the treatment of children, but is not without adverse effects.[9] Combination with an oximine may reduce atropine toxicity. Oximine is more useful early in the presentation (36 - 48 hours),[10] and is recommended when the plasma pseudocholinesterase level is below 25% of normal and the cholinergic poison is unknown;[11] it might have been worth a trial in this patient.

Kazeem A Oshikoya

Department of Pharmacology
Lagos State University College of Medicine, and
Department of Paediatrics
Lagos State University Teaching Hospital
Ikeja, Lagos
Nigeria

1. Van Wyk LV, Els I. Neonatal cholinergic syndrome – organophosphate poisoning or herbal medicine intoxication? *South African Journal of Child Health* 2008; 2: 26-27.
2. Zweiner RJ, Ginsburg MC. Organophosphate and carbamate poisoning in infants and children. *Pediatrics* 1988; 81: 121-126.
3. Kaur I, Jayashree K, Hiranandani M, Singhi SC. Severe organophosphate poisoning in a neonate. *Indian Pediatr* 1996; 33: 517-518.
4. Clifford NJ, Nies AS. Organophosphate poisoning from wearing a laundered uniform previously contaminated with parathion. *JAMA* 1989; 262: 3035-3036.
5. Obi E, Akunyili DN, Ekpo B, Orisakwe OE. Heavy metal hazards of Nigerian herbal remedies. *Sci Total Environ* 2006; 369: 35-41.
6. Sungur M, Guven M. Intensive care management of organophosphate insecticide poisoning. *Critical Care* 2001; 5: 211-215.
7. Mack R. Toxic encounters of various kind. *N C Med J* 1983; 44: 103-105.
8. Di Carlo JN. Nutritional stabilization: hyperglycemia and glucose control. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF, eds. *Nelson Textbook of Paediatrics*. 18th ed. Philadelphia: Saunders Elsevier, 2007: 437.
9. Dippenaar R, Diedericks RJ. Paediatric organophosphate poisoning – a rural hospital experience. *S Afr Med J* 2005; 95: 678-681.
10. Wadia RS. Treatment of organophosphate poisoning. *Indian J Crit Care Med* 2003; 7: 85-87.
11. Nair PMC, Javad H, Al-Mandhiry ZA. Organophosphate poisoning in children – atropine, pralidoxime or both? *Saudi Med J* 2001; 22: 814-815.