THE EPIDEMIOLOGICAL EFFECT OF INSECTICIDE RESISTANCE ON MALARIA INCIDENCE – THE SOUTH AFRICAN EXPERIENCE

Basil Brooke

Centre for Opportunistic, Tropical & Hospital Infections, NICD

Resistance to insecticides is postulated to have a dramatic effect on the efficacy of insecticide-based malaria control interventions. This effect can usefully be measured using entomological indicators as a proxy[1], but is probably best measured in terms of epidemiological outcomes. However, natural cycles of disease transmission, bionomic factors including changes in malaria vector species composition and abundance, climatic and environmental factors, migration, changing land use patterns and other control interventions are likely to confound evaluations of the actual effect of insecticide resistance on disease incidence.

To date, the effect of insecticide resistance on malaria transmission and incidence in South Africa stands as a primary example of the epidemiological effect that insecticide resistance can exert. This is because resistance to pyrethroids was at last partially responsible for the malaria epidemic experienced in South Africa during the period 1996 to 2000. Prior to 1996, South Africa's insecticide-based indoor residual spraying (IRS) vector control programme was dependent on DDT. While this regimen was generally sufficient for control (malaria incidence seldom exceeded 4000 cases per annum), sporadic outbreaks and more severe epidemics did occur, such as the 1971-1972 epidemic followed by the 1978 epidemic both of which were congruent with widespread rains.[2] In 1995 a policy to move away from the use of DDT for IRS in favor of pyrethroids was adopted, largely because of mounting pressure against the use of DDT. Furthermore, an upsurge in cross-border migration from Mozambique coupled with good rainfall during this period coincided with a sharp rise in malaria incidence within South Africa, in which the number of cases rose from 8750 in 1995 to 27 035 in 1996 and peaked at 64 622 in 2000.[3] A primary cause of this epidemic was the resurgence of pyrethroid resistant *An. funestus* following the introduction of pyrethroids for IRS.[4] Although the link between insecticide resistance and increased malaria incidence may seem tenuous based on these events alone, the re-introduction of DDT for IRS in South Africa post 2000 and the resultant substantial decline in malaria incidence to fewer than 10 000 cases per annum during much of the subsequent period shows that pyrethroid efficacy was severely undermined by the development of pyrethroid resistance in *An. funestus* and that DDT use, in conjunction with pyrethroids, was necessary to re-establish control.[2] However, the re-introduction of DDT for IRS also coincided with a change in anti-malarial drug regimen from sulfadoxine-pyrimethamine (SP) to artemisinin-containing combination therapy (ACT) (Maharaj et al., 2013).[3] Although it is almost impossible to quantify the actual contribution of each intervention to the decrease in malaria incidence post 2000, the use of DDT dramatically decreased the abundance of *An. funestus* in South Africa to undetectable levels, leaving the less efficient vector *An. arabiensis* to maintain lower level residual transmission as a consequence of this species' behavioural plasticity and lower susceptibility to IRS.[5]

Currently, DDT is used for spraying traditional structures and pyrethroids are used for modern structures in South Africa's provincial IRS programmes, which conveniently amounts to a mosaic resistance management strategy as described in the Global Plan for Insecticide Resistance Management (GPIRM).[6] South Africa's low incidence of malaria post 2007 has led to the adoption of a malaria elimination agenda according to which South Africa's national malaria control programme aims to eliminate malaria with the country's borders by 2018 (National Malaria Elimination Strategy for malaria 2012-2018). Part of this strategy involves the scaling up of vector control interventions including enhanced vector surveillance in transmission foci. Recent surveillance data from the Mamfene region of northern KwaZulu-Natal show that the extent of insecticide resistance in the malaria vector *An. arabiensis* is worsening[7] although the actual epidemiological implications of these data remain to be determined.

In conclusion, the data available indicate that insecticide resistance can lead to vector control failure and thereby induce an epidemiologically significant effect on malaria incidence, as witnessed in South Africa during the 1996 – 2000 epidemic. Case studies further indicate that the effect of insecticide resistance is most pronounced in an IRS control setting, as compared to programmes based on the distribution of insecticide treated nets (ITNs)[1], primarily because ITNs still offer a measure of personal protection despite insecticide resistance. Nevertheless, IRS is currently the only vector control method that allows for adequate insecticide resistance management and therefore offers the greater protection to affected communities in the longer term.

Disclaimer:

Parts of this article are excerpted from: Paine P & Brooke BD. 2016. Insecticide resistance and its impact on vector control. Chapter 16 in *Advances in Insect Control and in Resistance Management* eds: A. Rami Horowitz & Isaac Ishaaya, Springer Science + Business Media B.V., Dordrecht, The Netherlands (in press).

Acknowledgements

Prof Maureen Coetzee and Dr Mark Paine are thanked for their comments on the manuscript.

References

1. Strode C, Donegan S, Garner P, Enayati AA, Hemingway J. 2014. The impact of pyrethroid resistance on the efficacy of insecticide-treated bed nets against African anopheline mosquitoes: systematic review and meta-analysis. *PLoS Med* 11(3):e1001619. doi: 10.1371/journal.pmed.1001619. eCollection 2014.
2. Coetzee M, Kruger P, Hunt RH, Durrheim DN, Urbach J, Hansford CF. 2013. Malaria in South Africa:110 years of learning to control the disease. *S Afr Med J* 103: No. 10 (Suppl 2): 770-778.
3. Maharaj R, Raman J, Morris N, Moonasar D, Durrheim D, Seocharan I, Kruger P, Shandukani B, Kleinschmidt I. 2013. Epidemiology of malaria in South Africa: from control to elimination. *S Afr Med J* 103: No. 10 (Suppl 2): 779-783.
4. Hargreaves K, Koekemoer LL, Brooke BD, Hunt RH, Mthembu J, Coetzee M. 2000. *Anopheles funestus* resistant to pyrethroids in South Africa. *Med Vet Entomol* 14: 181-189.
5. Hargreaves K, Hunt RH, Brooke BD, Mthembu J, Weeto MM, Awolola TS, Coetzee M. 2003. *Anopheles arabiensis* and *An. quadriannulatus* resistance to DDT in South Africa. *Med Vet Entomol* 17: 417-422.
6. WHO. *Global plan for insecticide resistance management in malaria vectors (GPIRM)*. World Health Organisation, Geneva; 2012.
7. Brooke BD, Robertson L, Kaiser ML, Raswiswi E, Munhenga G, Venter N, Wood OR, Koekemoer LL. Insecticide resistance in the malaria vector *Anopheles arabiensis* in Mamfene, KwaZulu-Natal. *S Afr J Sci* 2015; 111(11/12), Art. #2015-0261, 3 pages. http://dx.doi.org/10.17159/sajs.2015/20150261