MALARIA MATTERS

Featuring Netting News

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Reduced Efficacy of Insecticide Treated Nets and Indoor Residual Spraying for Malaria Control in Pyrethroid Resistance Areas, Benin

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Comparative trials of Indoor Residual Spraying (IRS) and Insecticide Treated Nets (ITNs) have shown that in areas with pyrethroid-susceptible *Anopheles gambiae*, there is no measurable difference between the effectiveness of the two methods in controlling malaria. The comparability may not hold true, however, for areas with pyrethroid-resistant populations. In southern Africa, for example, IRS with pyrethroid failed to control pyrethroid-resistant *An. funestus*, and necessitated a switch to an alternative class of insecticide to which there was no resistance. During the last decade, pyrethroid-resistance caused by the knockdown resistance (*kdr*) mechanism has become widespread in *An. gambiae* in West Africa, and is found at high frequency in some areas. It is unclear whether *kdr* undermines the effectiveness of ITNs in high prevalence areas. An early experimental hut trial of ITNs in Cote d'Ivoire demonstrated a homozygote survival advantage for *kdr* resistance, whereas subsequent hut trials in adjacent resistant and susceptible populations showed no apparent difference in the effectiveness of ITNs between the two localities. Village-level randomised trials in Cote d'Ivoire showed that ITNs continued to prevent malaria despite a vector population that was *kdr* resistant. It is unknown whether *kdr* would undermine the effectiveness of IRS in the same way as resistance due to oxidases did against *An. funestus* in southern Africa.

The Malanville field site with a row of experimental huts.

A trial to test the continuing efficacy of insecticide-treated nets and indoor residual spraying was undertaken in experimental huts at two sites in Benin, one where *kdr* is present at high frequency (Ladji), the other where *An. gambiae* is susceptible (Malanville). In both sites, the nets were deliberately holed to mimic older, worn nets and treated with lambdacyalothrin (SC) at 18mg/m^2. Lambdacyalothrin (WP) was applied at 30 mg/m^2 for the IRS. At each site, the trial ran for 50 nights over an 8–week period. Pyrethroid treatment of the holed net with 18mg/m^2 lambdacyhalothrin led to a 96% reduction in blood-feeding at the susceptible site (Malanville) but to no reduction in blood-feeding at the resistant site (Ladji). IRS led to limited inhibition of blood-feeding at both the resistant and susceptible sites. In Malanville, both modes of treatment were highly insecticidal, with the ITNs killing 98% and the IRS killing 72% of *An. gambiae* that entered the huts. At Ladji, however, the proportions of *An. gambiae* killed in either the ITN or IRS treated hut did not exceed 30%. There was higher oxidase and esterase activity in the Ladji mosquito population than in the susceptible strain, but this did not appear to contribute to resistance. The present study provides persuasive evidence that pyrethroid resistance in Benin is capable of undermining control measures based on ITNs. There is also no reassurance to be taken from IRS, and any attempt to switch vector control strategies may not be successful. The contribution of *kdr* to pyrethroid resistance in *An.*

gambiae needs to be reappraised, and there is an urgent need to focus current efforts on the development of alternative insecticides to replace or supplement pyrethroids on nets, in addition to the new antimalarial drugs and vaccines which have received far greater attention and resources in recent years.

Note: The full article is available at www.cdc.gov/eid *Emerging Infectious Diseases*: Vol.13, 2: 199-206.

FURTHER READING

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Correction

November 2006, Issue 16, *Update on Long-Lasting Insecticidal Nets:* the Interceptor® LLIN is manufactured by BASF and not Bayer as originally stated.

THE INNOVATIVE VECTOR CONTROL CONSORTIUM

Adapted by Manisha Kulkarni

The use of insecticide-treated nets is a cost-effective intervention that requires little vertical malaria control infrastructure. However, since pyrethroids are currently the only insecticides recommended for net treatment by the WHO Pesticide Evaluation Scheme (WHOPES), the emergence of pyrethroid resistance in many malaria-endemic countries now threatens the viability of this intervention. Fortunately, a network of academic and commercial partners is working together to provide solutions to overcome the increasing problems of insecticide resistance.

The Innovative Vector Control Consortium (IVCC) is a five-year programme established in November 2005 and funded by a $50.7 million grant from the Bill and Melinda Gates Foundation. It is a new public–private partnership designed to improve the tools and technologies currently available for malaria and dengue vector control. Its ultimate goal is to reduce the transmission of mosquito-borne pathogens around the home through improved control of adult household vectors. Although the vector control tools that the IVCC will produce are aimed at controlling malaria and dengue, they can ultimately be used for the control of all indoor transmitted vector-borne diseases. Five partner Institutions in Africa, Europe and the USA were instrumental in establishing the IVCC: the Liverpool School of Tropical Medicine, UK; the London School of Hygiene and Tropical Medicine, UK; Colorado State University, USA; University of California at Davis, USA; and Medical Research Council, South Africa.

The mission statement of the IVCC is "to improve health by enabling partnerships for the accelerated development and delivery of new products and tools that increase the effectiveness and efficiency of the control of insects which transmit disease" (http://www.ivcc.com/).

The IVCC recognizes that effective optimal control of vector-borne diseases requires that communities have accurate information and access to insecticide-treated nets, indoor spraying technology, and improved insecticides, as well as integrated decision-support systems on which to base control applications. There are two distinct tracks within the IVCC; the first aims to develop new insecticides and formulations, while the second aims to improve vector control delivery through the development of new technological tools.

New insecticides and formulations

Although drug and vaccine developments for diseases such as malaria and dengue have received increased attention since 2000, there has been no major initiative to improve vector control. The result is that the number of public health insecticides available is dwindling and vector-borne disease transmission is increasing as insecticide-resistance expands.

To rectify the market's failure to produce new public health insecticides, the IVCC is using a portfolio approach to produce a pipeline of potential new products for disease vector control. New insecticides for insecticide-treated materials and indoor spraying applications will include alternative active ingredients, longer-lasting formulations, and new combinations of existing insecticides. Insecticide-based products will be put through the formal WHOPES phase I–III studies to ensure the acceptability and global accessibility of products before full-scale production.

Improved decision support tools for vector control

The second track of the IVCC aims to improve decision-making about the management of malaria and dengue vector control programs. The new tools will contribute to improved control through: (i) more directed and efficient monitoring of entomological and epidemiological parameters related to transmission; (ii) more effective control of vector mosquitoes, through prompt, timely, and focused application of insecticides, which will delay insecticide-resistance; (iii) more effective and efficient use of resources; and (iv) better design and development of new-generation pyrethroids through real-time interactions between the two consortium tracks. The expected outcomes of this track are reduced transmission of vector-borne diseases, reduced abundance of arthropod vectors, optimization of insecticide use whether sprayed or in nets, and increased empowerment of community-level public health officials and populations.

New technological tools will support improved decision making at the community level. The IVCC will develop an informatic tool that includes data, decision support software, and online access to one or more central databases of entomological, epidemiological, and related data in a GIS-based format, combined with improved models of dengue and malaria transmission. This will be complemented by the development and deployment of field-appropriate kits for monitoring essential characteristics (vector abundance, species composition, infection status, and insecticide-resistance status) of local vector populations and quantifying the amount of pyrethroid insecticide remaining on insecticide-treated materials.

The objectives of the Innovative Vector Control Consortium are to:

- Develop alternatives to existing pyrethroids for insecticide-treated materials and indoor residual (long-lasting) spray treatments.
- Develop longer-lasting insecticide formulations for such materials and sprays.
- Develop insecticide combinations, such as bi-treated nets and insecticide treated materials, which are useful in areas where insecticide resistance might otherwise be a problem.
- Refine and further develop an informatic tool for use at the community level that includes relevant literature, decision support software, and access to one or more central databases of entomological, epidemiological, and related data in a GIS-based format.
- Develop and extend simulation and analytical models that can be used to establish the threshold levels and various entomological end points that will need to be achieved for optimal vector control and disease prevention.
- Develop a field-appropriate kit for quantifying the amount of pyrethroid insecticide remaining on insecticide-treated materials.
- Develop one or more field-appropriate tools for monitoring essential characteristics of local vector populations (e.g. insecticide resistance).

Conclusions: the impact of the IVCC on disease reduction

A major strength of the IVCC is its direct links with existing disease prevention programs. All its interventions will be tested within the context of these real control programs; both the new insecticide formulations and the refinement of its informatics and decision support tools will therefore be informed continuously

and specifically by local control efforts. Effective implementation of the new innovative vector control tools, which will be based on rigorous evaluations in the context of disease-endemic country disease prevention programs, will contribute to: (i) more effective reduction of disease vector populations; (ii) major reduction in transmission of vector-borne disease; and (iii) more cost effective and efficient use of resources. This approach will translate into the most important attributable benefit, reduction of disease burden and numbers of deaths from vector-borne disease. Vector control alone can reduce malaria transmission in highly endemic areas by up to 50%. In combination with improved drug and vaccine initiatives, the potential exists to move towards local or regional elimination of one or more of these vector-borne diseases.

Note: Adapted from: Hemingway, J. *et al*. (2006) The Innovative Vector Control Consortium: improved control of mosquito-borne diseases. *Trends in Parasitology* 22(7): 309-312.

Further Reading

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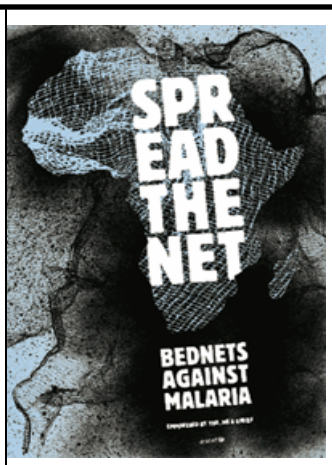

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Africa Malaria Day is commemorated on 25 April every year. This day has been set aside by African governments committed to rolling back malaria and meeting the United Nations malaria-related Millennium Development Goals.

The focus of this year's Africa Malaria Day will be on the need to work in partnership to reverse the progression of malaria and make a significant impact in endemic countries.

www.rollbackmalaria.org/amd2007

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