

REVIEW ARTICLE

Present use of pesticides for vector and allergen control and future requirements

C. F. CURTIS and C. R. DAVIES

London School of Hygiene & Tropical Medicine, London, U.K.

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The number of Disability Adjusted Life Years (DALYs) lost gives a measure of the human impact of a disease via both death and disablement (World Bank, 1993; Murray, 1994). The rating of each disease on this scale gives some idea of where it is most worthwhile to apply control efforts, but these ratings need to be considered in the light of the likelihood of success per unit of resource applied. Table 1 shows estimates by the World Health Organization (WHO, 2000) of the percentage of the total DALYs lost by the world's population in 1999 attributable to (i) communicable diseases as a whole, (ii) three of the major non-vector borne communicable diseases or disease groups (acute respiratory infections [ARI], HIV/AIDS and tuberculosis [TB]) and (iii) the most significant diseases associated with arthropods. For the latter, estimates are also given of the percentage of total incidence that could be prevented if perfect vector or allergen control could be instituted. On this basis, an estimate is made of the reduction in disease burden (as a percentage of the global total) that could ideally be achieved by vector or allergen control. The total for this potential saving is comparable to the impacts of ARI and of AIDS and exceeds that of TB. The largest contributor to the possible impact of vector and allergen control is, as would be expected, malaria. However, those brought up on conventional medical entomology textbooks will be surprised to see that two of the next three items are diarrhoeal diseases and asthma. It has recently been shown in both Pakistan and The Gambia that the incidence of the former can be reduced by about 24% as a result of concerted space spraying with deltamethrin to control houseflies, *Musca domestica* L. (Chavasse *et al.*, 1999; Emerson *et al.*, 1999). Asthma is a rapidly increasing cause of disablement and death in developed countries. The causation is complex, but the severity of asthma symptoms (and incidence of asthma attacks) is certainly significantly exacerbated as the result of sensitization and triggering by allergens in the faeces of

house dust mites, *Dermatophagoides* spp. (Platts-Mills *et al.*, 1997); and mite populations in mattresses can be sustainably reduced with the use of permethrin-treated mattress covers (Cameron & Hill, 2001). Trachoma caused by eye infection with the bacterium *Chlamydia trachomatis*, the largest preventable cause of blindness, has long been said to be transmitted by muscid flies, but it has only recently been proved (in The Gambia by Emerson *et al.*, 1999), that housefly control by space-spraying can have an even more marked effect against the incidence of this disease than against diarrhoea.

The last columns of Table 1 could be fairly said to be a 'wish-list' because:

1. In tropical Africa, where 90% of the world's malaria occurs, there is very little vector control apart from an increasing number of small projects with treated bednets (Chavasse *et al.*, 1999).
2. The demonstrations that fly control can have a real impact on two very important classes of disease do not yet seem to have been acted upon by more extensive adoption of space spraying and/or use of fly traps (Cohen *et al.*, 1991; Meegan *et al.*, 2000).
3. Lymphatic filariasis causes the second largest burden of disablement after mental illness. The WHO programme to eliminate this disease is almost wholly based on annual antimicrofilarial mass drug treatment of human populations, which, it is assumed, will reduce the infectivity of mosquito populations sufficiently to interrupt transmission. Mention is made of integrating drug treatment with vector control but in only a few cases has this been done, e.g. with mass DEC treatment of people plus polystyrene beads in breeding places of *Culex quinquefasciatus* Say, the vector in Zanzibar (Maxwell *et al.*, 1999).
4. In the case of onchocerciasis the highly successful aerial application of larvicides against the *Simulium* vector is being wound down in favour of treatment of humans with the same types of drug as for lymphatic filariasis.
5. Where the great epidemics of African sleeping sickness are now raging in countries long affected by civil war, there is

Correspondence: Professor C. F. Curtis, Department of Infectious & Tropical Diseases, London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT, U.K. E-mail: chris.curtis@lshtm.ac.uk

Table 1 Percentage of the total global burden of disease (in disability adjusted life years, DALYs) lost due to particular communicable diseases (WHO, 2000) and estimates of percentage of total DALYs lost which could be prevented by achieving perfect control of relevant vectors or allergens

		% of total (all causes) DALYs lost		
All communicable and maternal and nutritional deficiencies		42.77		
of which:				
Acute respiratory infections		7.03		
HIV/AIDS		6.25		
TB		2.31		
wholly or partly vector-borne or caused by arthropod allergens:		9.96		
		% of total (all causes) DALYs lost	Given perfect vector/allergen control:	
Vector/allergen			% of incidence preventable	% of total DALYs lost that could be prevented
Malaria	<i>Anopheles</i>	3.12	100	3.12
Diarrhoeal diseases	Flies and cockroaches	5.01	≈ 24 ^{a,b}	1.20
Lymphatic filariasis	Mosquitoes	0.34	100	0.34
Asthma	House dust mites, etc.	0.90	≈ 33 ^c	0.30
African trypanosomiasis	<i>Glossina</i>	0.14	100	0.14
Leishmaniasis	Phlebotominae	0.14	100	0.14
Onchocerciasis	<i>Simulium</i>	0.07	100	0.07
Japanese encephalitis	Mosquitoes	0.07	100	0.07
Trachoma	Muscidae	0.09	≈ 70 ^b	0.06
Chagas disease	Triatominae	0.05	95 ^d	0.05
Dengue	<i>Aedes (Stegomyia)</i>	0.04 ^e	100	0.04
Total percentage of DALYs lost from all causes which could be prevented by perfect vector/allergen control				5.53

^a Data from Chavasse *et al.* (1999)^b Data from Emerson *et al.* (1999)^c Estimate, as sensitization and 'triggering' of asthma by dust mite allergens is difficult to quantify^d Excludes transmission via blood transfusion^e Estimate from Gubler & Meltzer (1999), which is slightly greater than that indicated by WHO.

only very localized control of the vector *Glossina*, tsetse flies, although in Angola the charity Caritas is making available tsetse traps, which can be highly effective (Laveissière *et al.*, 1991).

The diseases for which vector control is most extensively applied are at the bottom of the list in Table 1: Chagas disease and dengue. From 1990 to 1999 the WHO estimates of the annual burden of disease attributable to Chagas disease have dropped by about 75%, while the estimated burden of other vector-borne diseases have either remained stable (e.g. leishmaniasis) or increased significantly (e.g. onchocerciasis). The reduction in the burden of Chagas disease is the result of an extremely successful house-spraying programme with residual pyrethroid insecticides against the domestic vector, *Triatoma infestans* (Klug) in countries of the 'southern cone' of South America (Schofield & Dias, 1999).

In the absence of a vaccine or drug to treat dengue viruses transmitted mainly by *Aedes (Stegomyia)* mosquitoes, vector control is the only option for reducing the burden of disease from dengue. The most successful programmes are those that take account of the highly domesticated nature of the *Aedes* vectors and put the onus on householders by legal enforcement (Cuba and Singapore) or community action (Vietnam) to eliminate domestic breeding or distribute *Mesocyclops* predators (Nam *et al.*, 1998).

Most progress due to vector control can probably be expected by reviving the enthusiasm for malaria vector control that existed in the 1950s and 1960s. In India the annual consumption of DDT has dropped from about 18 000 to about 7000 tonnes since then (Lal, 1999). A correlation has been found between the extent of recent reduction in spray coverage in different districts with increase in *P. falciparum* incidence

(M. Bouma, unpublished data). With decline in spray coverage, visceral leishmaniasis (due to *Leishmania donovani* transmitted by *Phlebotomus* sandflies), which was virtually eradicated as an unplanned side-effect of antimalaria spraying, has now returned and, according to WHO figures, is now a more important cause of lost DALYs in India than is malaria. Sudan is the other country primarily responsible for the global burden of disease due to leishmaniasis (WHO, 1990, 2000). Current efforts by Médecins Sans Frontières and Sudan authorities to reduce the incidence of visceral leishmaniasis in this region are focusing on the provision of insecticide impregnated bednets (Elnaiem *et al.*, 1999; Keus, 2000), but the effectiveness of this strategy has yet to be fully quantified. In other countries where the sandfly vector is significantly endophilic, vector control for leishmaniasis has traditionally been based on residual insecticide house-spraying – with great effectiveness in China (Li-ren, 1991) but less so in Brazil (Vieira & Coelho, 1998). Comparative studies in Afghanistan (Reyburn *et al.*, 2000) suggest that house-spraying may have less effect on leishmaniasis incidence than impregnated bednets (which are also cheaper).

In South America since the 1970s there has been a steady rise in malaria incidence as DDT consumption declined for antimalaria house-spraying against the *Anopheles* vectors (Roberts *et al.*, 1997). Some emphasize other factors, such as colonization of the Amazon basin, which have no doubt contributed to the resurgence of malaria. However, it seems clear that reduction in vector control efforts is the main factor. There is a prejudice against DDT despite its inexpensiveness (Walker, 2000); given the political will, these countries are not so poor as to be unable to replace the successful DDT with alternative residual insecticides for house-spraying.

In South Africa 50 years of successful use of DDT eradicated one of the vectors, *Anopheles funestus* Giles, and drove malaria back to the northern frontier. A switch was made to deltamethrin house-spraying in 1996 and, since that time, numbers of malaria cases have greatly increased. *Anopheles funestus* re-appeared and is now pyrethroid-resistant but DDT-susceptible (Hargreaves *et al.*, 2000), so DDT spraying has recommenced. In the UNEP treaty on Persistent Organic Pollutants (www.chems.unep.ch), an amendment, which was introduced by the South African government, now exempts DDT from being banned for malaria vector control.

In tropical Africa, where malaria vector control is most needed, there were remarkable demonstrations in the 1950s, 1960s and 1970s of the possibility of having a major impact on malaria by house-spraying (see reviews by Kouznetzov, 1977; Curtis & Mnzava, 2000). For example, there was a halving of all-cause mortality in the Pare-Taveta scheme by dieltrin spraying, a reduction of holoendemic malaria to a prevalence of parasites of less than 5% in Zanzibar by DDT spraying, and a reduction of all-cause mortality by 47% near Kisumu by fenitrothion spraying.

The numerous trials of pyrethroid treated nets have consistently shown 50–60% reduction in mild malaria fever and in anaemia and in four large trials there was significant reduction in all-cause child mortality (Lengeler, 1998). These reductions have not been as great as in the above-mentioned

spraying operations (Curtis & Mnzava, 2000). The explanation is not clear but may lie in the irritant effect of pyrethroids in driving mosquitoes away before they have picked up a lethal dose. In hut trials in Côte d'Ivoire, where the *An. gambiae* population has a high frequency of the *kdr* resistance gene, very high and sustainable mortality (as well as some reduction in biting of the sleeper under the net) was achieved with carbosulfan-treated nets (Kolaczinski *et al.*, 2000; Guillet *et al.*, 2001). Despite the pyrethroid resistance, a multivillage trial showed that a significant reduction was achieved in mosquito survival and sporozoite rate and in malaria incidence as a result of use of lambdacyhalothrin-treated nets (Dossou-Yovo *et al.*, 2000). It is thought that the resistant mosquitoes are not so readily irritated and therefore remain resting on treated nets long enough to be killed. However, the above mentioned example in South Africa warns against any complacent attitude that pyrethroid resistance is, after all, no real problem: tested non-pyrethroid alternatives of acceptably low human toxicity are urgently needed.

The most successful nation-wide or province-wide operations with treated nets are in Vietnam, China and Vanuatu, where major reductions in malaria incidence have occurred in the last 10–15 years (e.g. Cheng *et al.*, 1995; Verlé *et al.*, 1998; Ichimori *et al.*, 2000). In the case of Vietnam there was simultaneous improvement in antimalarial drug treatment, but it seems very probable that the treated nets contributed considerably to the encouraging trend. In all three countries, insecticide for net re-treatment has been supplied free of charge by government-organized programmes in the same manner as for house-spraying. This was also the case in the WHO-organized trials, which demonstrated reductions in child mortality in Africa (Lengeler, 1998). However, the trend now is to say that the poor should be made to pay for their own malaria protection. Several companies have therefore produced individual net treatment kits. These are relatively expensive for the amount of insecticide in them and considerable amounts of donor funds are being spent trying to market them. Despite all this effort, re-treatment rates in these operations are relatively low in contrast, for example, to our project in Tanzania (C. A. Maxwell *et al.*, unpublished data) where insecticide in 1 L bottles is provided free of charge and re-treatment rates of up to 90% are quickly and easily achieved and where sustainable reductions in numbers of infective vectors, prevalence of malaria infection, anaemia, etc. are observed compared with nearby villages without nets. There are now some published data (Abdulla *et al.*, 2001) showing lower prevalence of malaria infections and anaemia in babies of those who have responded to a Social Marketing campaign and bought nets and insecticide, compared with the babies of parents in the same villages who have not responded. However, it seems difficult to exclude the influence of factors other than the treated nets when comparing households who are more or less able and willing to pay.

One possible way of avoiding the problem of low re-treatment rates when people are asked to pay for insecticide is to use nets that are durably insecticidal despite repeated washing. It has been reported that so-called PermaNetsTM have this property, based on a simulated washing procedure in the

laboratory and bioassays with 3 min exposure plus 24 h holding. However, colleagues in Tanzania (Curtis, 2001) have recently found that, when green-dyed PermaNets were handwashed in a realistic way with detergent or soap, the median time for knockdown of mosquitoes in contact with the net rose steadily from about 400 s before any washes to 800–1200 s after 20 washes. They found similar results with bednets conventionally impregnated with pyrethroid by dipping. We have now started a multi-village malaria control trial of PermaNets in comparison with conventionally dipped nets.

In various recent conference presentations, such authorities as W. Kilama and J-F. Trape have drawn attention to the rapidly increasing urbanization of Africa (Warren *et al.*, 1999), so that in urban areas larviciding may be more appropriate than adulticidal mosquito control measures developed for humid rural areas, where breeding sites are so numerous and sporadic that it is not cost-effective to attempt to treat them. All the adulticides employed against vectors have been developed primarily for the much larger agricultural insecticide market. However, among larvicides are products specifically developed for anti-vector applications. The best known is the biopesticide *Bacillus thuringiensis* H-14. This is said to be an attractive option in India because its specificity ensures that there is no incentive for anti-mosquito spraymen to try to sell it to farmers. Regarding Insect Growth Regulators (IGRs), Yapabandara *et al.* (2001) in Sri Lanka showed very good results with pyriproxyfen in gem pits. Only three treatments per year at very low doses with a sand granule formulation were needed to prevent adult *Anopheles* emergence. Concerted treatment of all the numerous mapped pits in four villages produced clear reductions in adult vector populations and in malaria, as monitored by active and passive surveillance.

Enthusiasts for postgenomics believe that knowledge of the gene sequences of important mosquito species will soon allow the production of tailor-made insecticides directed against newly discovered targets. This may be technically possible, but it seems likely that such products would be marketed at prices geared to nuisance mosquito control operations in developed countries, so they may not be affordable for vector control operations in the tropics.

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