Review TRENDS in Parasitology Vol.21 No.11 November 2005
Full text provided by www.sciencedirect.com

Insecticide-treated nets against malaria vectors and polystyrene beads against *Culex* larvae

Chris Curtis

London School of Hygiene and Tropical Medicine, London, UK, WC1E 7HT

In *Parasitology Today* in 1985, Curtis and Lines, and Curtis and Minjas presented the ideas of insecticide-treated nets and polystyrene beads for mosquito control. The former idea has grown to be a major component of the strategy for malaria prevention, especially in Africa. However, although polystyrene beads have been demonstrated to work extremely well, they have yet to be taken up on a major scale.

Impact of insecticide-treated nets

At the time of the 1985 publication by Curtis and Lines [1] in *Parasitology Today,* there was already published evidence of the effectiveness against mosquitoes and ticks of the mosquito repellent DEET (N,N-diethyl-meta-toluamide) and the pyrethroid insecticide permethrin impregnated into clothing. Furthermore, three trials of insecticide-treated nets (ITNs) had been carried out by J.S. Hervey and J. Sales, and F. Darriet and P. Ranque in Burkina Faso and Mali. Two of these trials had been written up only in institutional or World Health Organization (http://www.who.int/en/) reports, but there was a publication by Ranque *et al.* [2] dated 1984. Curtis and Lines [1] pointed out that, although bednets would be expected to protect against malaria mosquitoes that bite in the middle of the night (such as *Anopheles gambiae*), medical entomologists knew that, if they needed bloodfed mosquitoes for their work, a good place to look was inside torn and untreated nets, as are most nets in African villages today [including at least one area in Tanzania, despite its ITN social marketing programme (C.A. Maxwell, unpublished)]. The first few days of a trial in Tanzania were summarized in the Curtis and Lines article [1], and the full results of this [3] showed that levels of biting were not reduced by untreated nets with large holes cut in them compared with levels in the same huts without nets. This has been confirmed with untreated nets that had more-moderate-sized holes (six holes sized 4×4 cm) [4]. More recently, Mwangi *et al.* [5] showed that, whereas untreated intact nets provide moderate protection against malaria, untreated holed nets do not. Lines *et al.* [3] also highlighted another drawback with untreated nets – they divert extra biting to people in the same room who are not protected by nets. If the net user were a malaria-immune adult and the non-user were a malaria-vulnerable child, the overall effect of the net would be counter-productive.

In 1985, it was hoped that, by adding a pyrethroid insecticide barrier to the inadequate physical barrier provided by the net, the chemical would kill many mosquitoes before they found the holes in a net, bit through the net or were diverted to an unprotected person. This has been abundantly confirmed by counting the numbers of bloodfed mosquitoes in the morning in rooms with or without ITNs and in exit traps covering the windows and eaves [3,4]. It was conjectured that the few bloodfed mosquitoes in rooms with ITNs might all have entered after feeding elsewhere. However, a study [6] in which the 'DNA fingerprints' (microsatellites) in blood meals were cross-compared with those of the people sleeping under the ITNs in rooms in which the mosquitoes were caught showed that the microsatellites matched in 85% of cases. It can be concluded that, although ITNs give good personal protection, the protection is not perfect.

Curtis and Lines [1] suggested that the killing power of many ITNs in a community, in which mosquitoes are attracted by the odour of the net occupant, might be sufficient to lower appreciably the population of mosquitoes living long enough for *Plasmodium* sporozoites to mature inside them. This was confirmed by Tony Wilkes' skilful dissections and ovarian age-grading, coupled with examination of the salivary glands for sporozoites [7]. Further confirmation of the important impact of community-wide use of ITNs has come from Carnevale *et al.* [8], Maxwell *et al.* [9] and Hawley *et al.* [10]. Unfortunately, many administrators seem to be unaware of this potential bonus of ensuring comprehensive ITN coverage. Therefore, targets for coverage with ITNs (including those in the Abuja Declaration by African Heads of State) have been expressed only in terms of malaria-vulnerable children and pregnant women. Free or subsidized provision is, therefore, generally directed only at providing personal protection for these vulnerable groups. It is far better that this should be done than ITN provision as a whole be left to the private-sector market. However, the entomological data mentioned earlier (in addition to the data of Maxwell *et al.* [11] about malaria morbidity in children, with or without their own ITNs, in villages with high but incomplete ITN coverage) suggest that the children's health would be markedly improved by providing the extra ITNs to gain the bonus of maximal

Corresponding author: Curtis, C. (chris.curtis@lshtm.ac.uk).
Available online 8 September 2005

www.sciencedirect.com 1471-4922/$ - see front matter doi:10.1016/j.pt.2005.08.025

suppression of the infective vector population. It is hoped that this can be checked by a direct study of malaria incidence in children with ITNs that are targeted only at them or at whole communities.

There is now abundant evidence from randomized controlled trials of reductions in levels of malaria morbidity and mortality because of community-wide provision of ITNs [11–13]. In summary, approximately six child deaths are prevented each year per 1000 children provided for [12]. It is hoped that ITNs will become a major component in the attempt to bring malaria under control, especially in its heartland in tropical Africa [14,15].

Biological factors in the sustainability of the effects of ITNs

There has been concern that major reduction (but not elimination) of malaria transmission might lead to inadequate build-up of anti-malaria immunity as a child grows up and that this might lead only to a postponement, not a lifetime reduction, in the amount of morbidity or threat of mortality. However, studies extending three to six years have shown that very young children (who are, by far, the most vulnerable to malaria) continue to benefit from the presence of ITNs and that older children are not much better off but, importantly, are not worse off because of the presence of ITNs [11,16–18]. There is evidence of a reduction in mean levels of two antibodies as a result of prolonged use of ITNs [19,20]. However, if a vaccine [21] could replace the immunity lost by long-term reduction in transmission, deployment of the vaccine could usefully synergize the effect of ITNs.

At present, only pyrethroid insecticides are used on nets. Therefore, there has been concern about the threat of resistance in vectors to this insecticide class. It is important that studies are pursued to identify alternative insecticides with low mammalian toxicity and with little prospect that a gene for pyrethroid resistance would confer cross-resistance to the alternative insecticide, so that an effective switch to it could be made quickly [22]. There is already a high frequency of the *kdr* resistance gene in *A. gambiae* in Côte d'Ivoire but there is clear evidence that, nevertheless, mosquitoes are at high risk of being killed if they enter huts containing ITNs [23,24] and that ITNs used by village communities lower both the infective biting rate per person and the malaria incidence [25]. Pyrethroid resistance in *Culex quinquefasciatus* in Tanzania has led to complaints by households that ITNs are not effective against nuisance mosquitoes, although they do provide considerable protection against bites. The mortality of *Culex* mosquitoes when ITNs are tested in experimental huts in Tanzania is low [4] and there is a marked absence, for these mosquitoes, of the community-wide impact of ITNs that is commonly seen with *Anopheles* [9].

Studies of *Anopheles* to determine whether prolonged use of ITNs will lead to evolution of behavioural resistance in the form of early and/or outdoor biting must be continued [26,27].

Political factors in the sustainability of ITNs

The importance of the community-wide use of effective insecticidal nets has already been emphasized, and Figure 1 shows the simple process of annual retreatment of nets. However, only the Vietnamese and Eritrean Governments have so far set up extensive systems for free annual retreatment of the nets of millions of people. The existence of these systems has been associated with remarkable reductions in national malaria burdens (see data reported by Tran Duc Hinh from Vietnam reproduced in Ref. [28] and the Tesseney declaration from Eritrea). The frequency of retreatment should decline, or the need for it might be eliminated, with the increasing availability of manufactured long-lasting insecticidal nets or the use of a net-dipping mixture that combines a pyrethroid and a resin to increase substantially the wash resistance of the insecticide deposit on nets.

With their combination of personal protection and community-wide bonus, ITNs resemble vaccination against measles. Recently, several countries have had remarkable success in linking ITN distribution to measles-vaccination campaigns. Delivery costs per net of US$0.32 in Ghana [29] were far lower than for delivery by social marketing. In Mali, the linking of these two disease-prevention measures led to improved coverage of both of them.

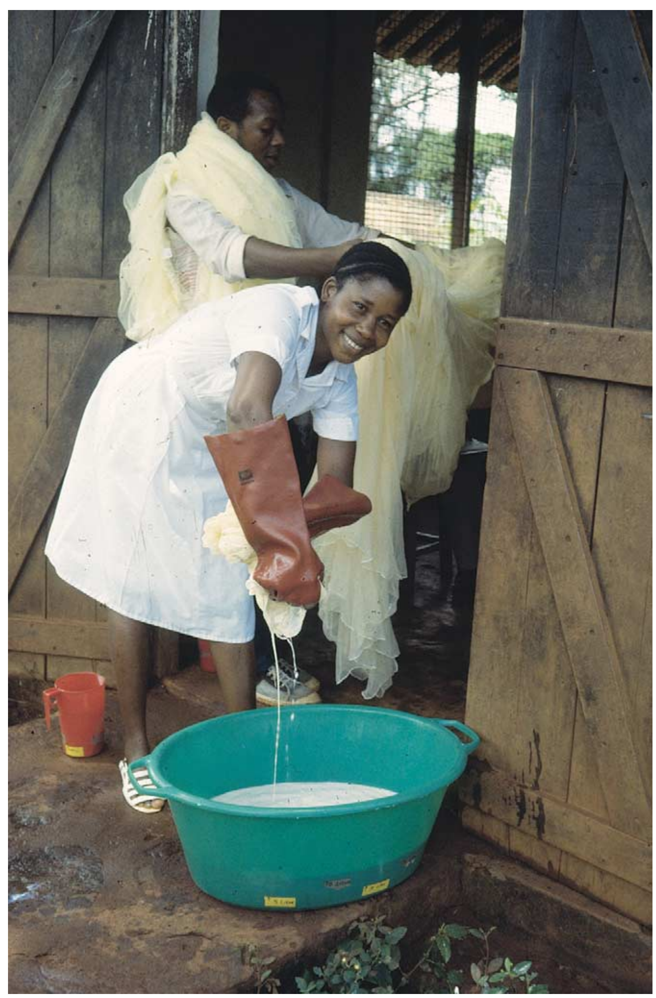

Figure 1. The nets from all houses in a Tanzanian village are given their annual retreatment free of charge by a nurse from the health centre. Photograph taken by T.J. Wilkes.

There is much emphasis on social marketing of nets [30] and on the view that African subsistence farmers must be educated by social marketing to become used to paying for ITNs for their families because donors in developed countries cannot be relied on to continue providing them. However, the costing of current systems of social marketing [31], including provision of highly subsidized (but not free) nets to pregnant women and children, shows that such systems are at least as dependent on continued funding from donors as are high-productivity systems for mass provision of free ITNs [29,32]. Furthermore, in view of the strong link between African poverty and malaria [33], it is in everyone's interest in a globalized world to break into the vicious circle of African poverty and malaria. It has been estimated [32] that it would cost approximately US$358 million per year to provide ITNs for all lowland tropical African villages (leaving a market in nets to flourish in towns, where many people already buy nets against the *Culex* nuisance and where malaria transmission is much less intense compared with rural areas). US$358 million per year to establish a large measure of control over the world malaria burden would be a readily affordable and sensible long-term investment by the world's affluent – it is ~17% of the amount that European and American owners of cats and dogs pay for flea control [34].

Polystyrene bead layers against larvae of the *Culex pipiens* complex

Mosquito larvae must penetrate the water surface to breathe air. Oil has long been used to obstruct this but oil layers are not fully mosquito-proof and they are destroyed fairly rapidly by bacterial action [35]. Curtis and Minjas [36] cited the alternative idea of Reiter [37] to use floating layers of non-biodegradable expanded polystyrene beads at sites of mosquito breeding that are confined between walls: for example, wet pit latrines, cess pits and flooded cellars. These beads are not toxic or environmentally harmful and they need replacing only when lost because of flooding The effectiveness of the layers at permanently stopping mosquito emergence from treated pits was reported by Curtis and Minjas [36], who looked forward to community-wide trials of the control of adult *Culex* populations and the filariasis that they transmit. Such trials have now been conducted in Zanzibar and South India [38].

In Zanzibar, a 1-cm-thick layer of polystyrene beads of 2-mm diameter was applied to all 500 wet pit latrines in a community of 12 000 people (omitting the 1500 pits that were never seen to contain free water in which *Culex* could breed) [39]. The treatment reduced the number of adult *Culex* that entered bedrooms by ~98%. This was coupled with a single campaign of mass treatment of the community with diethylcarbamazine (DEC). In the short term, the latter campaign reduced the prevalence of microfilarial infection from 49% to 10%. During the next four years, the continued near-elimination of *Culex* prevented cured people from being reinfected and prevalence declined to 3% [40]. Another Zanzibari community – with a DEC campaign but no mosquito control – showed similar short-term reduction but, in the longer term, there was resurgence towards the original level of prevalence.

Comparable results were obtained in a two-year campaign using DEC and ivermectin mass treatment of two South Indian communities with or without polystyrene treatment of breeding sites of *Culex* in bathroom water soakage-pits [41]. Again, the short-term results, for as long as the drug treatment continued, were similar in the two communities. However, when drug treatment was stopped, without any measures to suppress the *Culex* population, filaria-infective *Culex* reappeared the next year. By contrast, no infective *Culex* were found where the polystyrene had suppressed the mosquito population to a low level.

Integrated control

There is much talk of the integrated control of vector-borne diseases but there are few cases in which the combination of two methods has proven to be better than the best of the individual methods. However, the trials in Zanzibar and India are such cases.

It is hoped that, where *Culex* vectors breed mainly in pits and cellars rather than in open drains, the integrated method will be incorporated into current efforts to eliminate filariasis as a public-health problem. Mosquito control has been criticized as being too expensive compared with the annually repeated administration of drugs provided free of charge by the manufacturers. However, mosquito control should provide backup to projects in which it is difficult to achieve a high enough coverage with drugs to interrupt transmission. Also, elimination of the nuisance of the nightly emergence of thousands of biting *Culex* from backyard latrines adds greatly to the prestige and public acceptance of an anti-filariasis project.

In several European countries, the problem of leaking sewer pipes in cellars leading to indoor breeding of human-biting *Culex pipiens molestus* mosquitoes has been reported. These mosquitoes are likely to be the main vectors of West Nile virus. Polystyrene beads work well in flooded cellars (Figure 2) and might have a role in the control of this newly emerging disease [42].

Figure 2. A flooded cellar in a residential block in Zanzibar Town (Tanzania) treated with polystyrene beads to eliminate the previously profuse breeding of *Culex* mosquitoes. Photograph taken by C.F. Curtis.

Concluding remarks

In light of the demonstrated effectiveness of ITNs and polystyrene beads at controlling transmission of two extremely important tropical diseases, one might have hoped that more energy and funding would have been put into scaling up their use from the current levels, which are far from adequate. However, now that the evidence base exists and innumerable statements have been made by politicians about the need to control the diseases of poverty, perhaps we can hope that, in the next 20 years, real progress will be made in the anti-vector route towards making malaria and filariasis history.

Acknowledgements

I thank my colleagues and their field teams over many years for carrying out much of the work alluded to in this short article, especially Caroline Maxwell, Tony Wilkes, Jo Lines and Rachel Reuben.

References

1 Curtis, C.F. and Lines, J.D. (1985) Impregnated fabrics against malaria mosquitoes. *Parasitol. Today* 1, 147
2 Ranque, P. *et al*. (1984) Etude expérimentale sur l'utilisation de moustiquaires imprégnées de deltaméthrine dans la lutte contre le paludisme. *Parassitologia* 26, 261–268
3 Lines, J.D. *et al*. (1987) Experimental hut trials of permethrin-impregnated mosquito nets and eave curtains against malaria vectors in Tanzania. *Med. Vet. Entomol.* 1, 37–51
4 Curtis, C.F. *et al*. (1996) Comparison of different insecticides and fabrics for anti-mosquito bednets and curtains. *Med. Vet. Entomol.* 10, 1–11
5 Mwangi, T.W. *et al*. (2003) The effects of untreated bednets on malaria infection and morbidity on the Kenyan coast. *Trans. R. Soc. Trop. Med. Hyg.* 97, 369–372
6 Soremekun, S. *et al*. (2004) Measuring the efficacy of insecticide treated bednets: the use of DNA fingerprinting to increase the accuracy of personal protection estimates in Tanzania. *Trop. Med. Int. Health* 9, 664–672
7 Magesa, S.M. *et al*. (1991) Trial of pyrethroid impregnated bednets in an area of Tanzania holoendemic for malaria. Part 2: effects on the malaria vector population. *Acta Trop.* 49, 97–108
8 Carnevale, P. *et al*. (1988) La lutte contre le paludisme par des moustiquaires imprégnées de pyrethrinoides au Burkina Faso. *Bull. Soc. Pathol. Exot.* 81, 832–838
9 Maxwell, C.A. *et al*. (1999) Comparisons of bednets impregnated with different pyrethroids for their impact on mosquitoes and on re-infection with malaria after clearance of existing infections with chlorprogaunail–dapsone. *Trans. R. Soc. Trop. Med. Hyg.* 93, 4–11
10 Hawley, W.A. *et al*. (2003) Community-wide effects of permethrin-treated bed nets and child mortality and malaria morbidity in western Kenya. *Am. J. Trop. Med. Hyg.* 68 (Suppl. 4), 121–127
11 Maxwell, C.A. *et al*. (2002) Effect on malaria morbidity of community-wide use in Tanzania of insecticide treated nets for 3–4 years. *Trop. Med. Int. Health* 7, 1003–1008
12 Lengeler, C. (2004) Insecticide-treated bed nets and curtains for preventing malaria. *Cochrane Database Syst Rev.* 2, CD000363
13 Phillips-Howard, P. *et al*. (2003) Efficacy of permethrin-treated bed nets in the prevention of mortality in young children in an area of high perennial malaria transmission. *Am. J. Trop. Med. Hyg.* 68 (Suppl. 4), 23–29
14 UN Millennium Project (2005) *Coming to Grips with Malaria in the New Millennium*, Earthscan
15 Monasch, R. *et al*. (2004) Child coverage with mosquito nets and malaria treatment from population-based surveys in African countries: a baseline for monitoring progress in Roll Back Malaria. *Am. J. Trop. Med. Hyg.* 71 (Suppl. 2), 232–238
16 Lindblade, K.A. *et al*. (2004) Sustainability of reductions in malaria transmission and infant morality in western Kenya with use of insecticide treated bednets. *J. Am. Med. Assoc.* 291, 2571–2580
17 Eisele, T.P. *et al*. (2005) Effect of sustained insecticide-treated bednet use on all-cause child mortality in an area of intense perennial malaria transmission in western Kenya. *Am. J. Trop. Med. Hyg.* 73, 149–156
18 Binka, F.N. *et al*. (2002) Mortality in a seven-and-a-half year follow-up of a trial of insecticide treated mosquito nets in Ghana. *Trans. R. Soc. Trop. Med. Hyg.* 96, 597–599
19 Metzger, W.G. *et al*. (1998) Anti-sporozoite immunity and impregnated bednets in Tanzanian villages. *Ann. Trop. Med. Parasitol.* 92, 727–729
20 Askjaer, N. *et al*. (2001) Insecticide-treated bed nets reduce antibody levels and limit the repertoire of antibodies to *Plasmodium falciparum* variant surface antigens. *Clin. Diagn. Lab. Immunol.* 8, 1289–1291
21 Alonso, P. *et al*. (2004) Efficacy of the RTS,S/AS02A vaccine against *Plasmodium falciparum* infection and disease in young African children: randomised controlled trial. *Lancet* 364, 1411–1420
22 Zaim, M. and Guillet, P. (2002) Alternative insecticides: an urgent need. *Trends Parasitol.* 18, 161–163
23 Darriet, F. *et al*. (2000) Impact de la résistance aux pyréthrinoides sur l'efficaité des moustiquaires impregnées dans la prevention du paludisme: résultats des essais en cases expérimentales avec déltaméthrine SC. *Bull. Soc. Path. Exot.* 95, 131–134
24 Asidi, A.N. *et al*. (2004) Experimental hut comparisons of nets treated with carbamate or pyrethroid insecticides, washed or unwashed, against pyrethroid resistant mosquitoes. *Med. Vet. Entomol.* 18, 134–140
25 Henry, M-C. *et al.* Protective efficacy of lambdacyhalothrin-treated nets in *Anopheles gambiae* pyrethroid resistant areas of Côte d'Ivoire. *Am. J. Trop. Med. Hyg.* (in press)
26 Pates, H.V. and Curtis, C.F. (2005) Mosquito behavior and vector control. *Annu. Rev. Entomol.* 50, 53–70
27 Braimah, N. *et al.* Tests of bednet traps (Mbita traps) for monitoring mosquito populations and time of biting in Tanzania. *Int. J. Trop. Insect Sci.* (in press)
28 Curtis, C.F. *et al*. (2003) Insecticide treated nets: impact on vector populations and relevance of initial intensity of transmission. *J. Vector Borne Dis.* 40, 1–8
29 Grabowsky, M. *et al*. (2005) Distributing insecticide-treated bednets during measles vaccination: low-cost means of achieving high and equitable coverage. *Bull. World Health Organ.* 83, 195–199
30 Schellenberg, J.R. *et al*. (2001) Effects of large scale social marketing of insecticide-treated nets on child survival in Tanzania. *Lancet* 347, 1241–1247
31 Stevens, W. *et al*. (2005) The costs and effects of a nationwide insecticide-treated net programme: the case of Malawi. *Malar. J.* 4, 22
32 Curtis, C.F. *et al.* Insecticide treated bednets. *J. Am. Mosq. Contr. Assoc.* (in press)
33 Sachs, J. and Malaney, P. (2002) The economic and social burden of malaria. *Nature* 415, 580–585
34 Rust, M.K. (2005) Advances in the control of *Ctenocephalides felis* (cat flea) on cats and dogs. *Trends Parasitol.* 21, 232–236
35 Beckeit, S.S. *et al*. (1991) Small scale field trials with polystyrene beads for the control of mosquito breeding. *J. Egypt. Soc. Parasitol.* 21, 179–182
36 Curtis, C.F. and Minjas, J. (1985) Expanded polystyrene beads for mosquito control. *Parasitol. Today* 1, 36
37 Reiter, P. (1978) Expanded polystyrene beads: an idea for mosquito control. *Trop. Med. Parasitol.* 72, 595–596
38 Curtis, C.F. *et al*. (2002) Use of floating layers of polystyrene beads to control populations of the filarial vector *Culex quinquefasciatus*. *Ann. Trop. Med. Parasitol.* 96 (Suppl. 2), S97–S104
39 Maxwell, C.A. *et al*. (1990) Control of bancroftian filariasis by integrating therapy with vector control using polystyrene beads in wet pit latrines. *Trans. R. Soc. Trop. Med. Hyg.* 84, 709–714
40 Maxwell, C.A. *et al*. (1999) Can vector control play a useful supplementary role against bancroftian filaraisis? *Bull. World Health Organ.* 77, 138–143
41 Reuben, R. *et al*. (2001) Annual single dose diethylcarbamazine plus ivermectin for control of filariasis: comparative efficacy with and without vector control. *Ann. Trop. Med. Parasitol.* 95, 361–378
42 Murgue, B. *et al*. (2002) The ecology and epidemiology of West Nile virus in Africa, Europe and Asia. *Curr. Top. Microbiol. Immunol.* 267, 195–221