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A Review of Control Methods for African Malaria Vectors

by

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Abbreviations

API	annual parasite index
Bs	*Bacillus sphaericus,* a bacterial pathogen
Bti	*Bacillus thuringiensis israelensis,* a bacterial pathogen
EHP	Environmental Health Project, sponsored by USAID
EIR	entomological inoculation rate
EM	environmental management
EPS	expanded polystyrene beads
FCCMC	Florida Coordinating Council on Mosquito Control
GIS	geographic information system
ha	hectare
IGR	insect growth regulator
IRS	indoor residual (house) spraying
ITM	insecticide-treated material
IVM	integrated vector management
km	kilometer
m^2	square meter
UNEP	UN Environment Program
USAID	U.S. Agency for International Development
WHO	World Health Organization
WHOPES	WHO Pesticide Evaluation Scheme

Foreword

Our understanding of the ecology and epidemiology of malaria and the availability of tools to combat it have changed dramatically in recent years. In Africa especially, the rapid spread of resistance first to chloroquine and now to sulfadoxine-pyremethamine has greatly increased the cost and difficulty of malaria case management. At the same time, it appears that reducing transmission may be more important and more useful than was previously thought. Two recent insights and two technical advances have generated renewed interest in vector control in general and larvae control in particular.

The first insight is the relation of vectorial capacity (or entomological inoculation rate, EIR) to parasite prevalence in the affected population and to morbidity and mortality rates for specific age groups. Malaria control programs during the "eradication era" focused on reducing parasite prevalence, preferably to zero. However, mathematical models and empirical data indicated that in much of Africa, where there are such efficient, long-lived, and anthropophilic vectors, vectorial capacity (or EIR) had to be reduced to an extremely low level to see a significant decrease in parasite prevalence. For example, in a review of 31 study sites, Beier et al. (1999) determined there were no sites with less than 50% prevalence when the EIR exceeded 15 infective bites per year. It was this focus on parasite prevalence and perception of the difficulties of achieving such low EIRs that led many to discount the value of vector control in much of Africa.

Field trials of insecticide-treated materials (ITMs) conducted in the 1990s brought a new understanding of disease control (as opposed to malaria parasite eradication) and its relation to EIR. A recent review by Smith et al. (2001) shows that severe disease and death are significantly reduced at lower EIRs. Thus, even though an incremental reduction in EIR may not substantially reduce parasite prevalence, it may produce a significant improvement in health outcomes for pregnant women and children under two years old. This realization, coupled with the increasing spread of drug resistance, has renewed interest in vector control as a vital component of malaria control programs.

The geographic focus of most malaria vector control programs is in areas of highest transmission and most morbidity and mortality: rural, tropical Africa. Because of the large vector populations and the ubiquity of the breeding sites in these areas, there is little justification for larvae control and most programs invest in ITMs and, in some areas, indoor residual spraying (IRS).

Although there is general consensus that larvae control has a limited role in rural, tropical Africa, there is a growing appreciation for the importance of malaria in areas of less intense transmission, particularly areas of seasonal transmission and periurban areas, where the breeding sites may be few, easily identifiable, and amenable to control. Though vector control in these areas may not have the dramatic and very visible impact of directly saving children who would otherwise die of malaria, it may quietly reduce the insidious *economic* burden of malaria in the vital urban and industrial areas of Africa (Sachs & Malaney 2002).

Coupled with these two realizations, advances in geographical information system (GIS) technology have allowed more precise mapping and modeling of the ecoepidemiological strata where larvae control may be a feasible adjunct to malaria control (D. Le Sueur, unpublished data). Additional developments of bacterial larvicides, insect growth regulators, and monomolecular films, along with a rediscovery of environmental management successes in the pre-DDT era (Utzinger et al. 2001), have brought a renewed interest to larvae control.

Thus, it is an opportune time to look back and review the vast literature on malaria vector control techniques, and particularly larvae control, as a foundation for developing integrated vector management (IVM) approaches that make use of a variety of control methods, each in its most appropriate settings. The Environmental Health Project (EHP), sponsored by the U.S. Agency for International Development (USAID), is working closely with the World Health Organization, Roll Back Malaria, and several key international institutions to develop practical guidelines and training for IVM and to support the development of vector biology and control programs in African ministries of health that are capable of using such approaches to improve malaria control and prevention.

Readers will notice a substantial literature on the ecology of mosquito breeding sites and the entomological impact of vector control methods. There is far less evidence of the epidemiological impact of vector control methods, even in experimental and trial conditions, much less in normal programmatic settings. Developing such evidence, through the coordinated efforts of many research groups and control programs, is the challenge before us. It will be a difficult task, but the following review shows us the foundation of a vast literature from which to begin.

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Executive Summary

This report reviews published information on selected control methods for anopheline mosquitoes and provides readers with a relatively brief introduction to options for malaria vector control. The review describes most of the physical, chemical, and biological methods that have been used in malaria vector control programs and summarizes information on factors that influence the efficacy of each method. Because of the programmatic focus of the Environmental Health Project (EHP) on community-based actions to prevent disease transmission, the review pays greatest attention to environmental management and other vector control methods that may be implemented by community-based organizations. The report is organized in accordance with the suggested groupings of the World Health Organization (WHO) *Manual on Environmental Management for Mosquito Control with Special Emphasis on Malaria Vectors* (WHO 1982).

1. **Environmental Management:** Environmental management is typically applied to reduce the burden of malaria over the long term. These interventions focus on avoiding creation of vector breeding areas, changing natural habitats, or improving human habitation to reduce the abundance of a target vector while creating minimal adverse environmental and social impacts. Examples include the following:

   - Marsh alteration
   - Filling, grading, and drainage
   - Vegetative plantings
   - House screening

2. **Chemical Application:** Chemical methods of malaria vector management can be organized quickly, are effective, and can produce results at relatively low cost if used efficiently. They have a special role in control programs for mosquito-borne diseases, particularly at the early stages of intervention to allow other control measures to develop and play effective roles in an integrated strategy. Examples of chemical application methods include the following:

   - Targeted residual spraying
   - Larviciding
   - Space spraying

   Because this is such a broad topic, EHP is focusing on the methods of chemical application that lend themselves to implementation at the community or household level rather than on analysis or comparison of available chemicals.

3. **Biological Control:** Biological methods consist of the utilization of natural enemies of targeted mosquitoes and of biological toxins to achieve effective vector management. They are typically most feasible with easily identifiable breeding places. Alternatives under this category include the following:

   - Larvivorous fish
   - Invertebrate predators
   - Nematodes
   - Protozoa and fungi
   - Bacteria

   EHP's focus in this area is particularly on methods that are applicable in urban and periurban areas.

This report does not include information on insecticide-treated bednets, which have been reviewed extensively in the published literature, or on natural or synthetic chemical repellants. The review includes an extensive bibliography of original research articles and guidance documents available from WHO and other institutions.

One of the purposes of the literature review was to summarize available information on the effectiveness of alternative vector control methods, specifically, documentation demonstrating that programs using such methods have achieved reductions in malaria morbidity or mortality rates. One conclusion of this review is that such information is not available for most vector control methods.

1

Introduction

The Environmental Health Project (EHP) provides technical assistance to ministries of health in developing countries to strengthen malaria surveillance systems, vector control programs, and related operational research. Under the Integrated Vector Management (IVM) program, EHP is working with international partners to achieve three results:

1. Determine the effectiveness of selected vector control interventions and identify the settings in which each intervention is likely to be effective;

2. Develop IVM approaches appropriate for malaria in urban and rural settings in Africa.

3. Promote the use of IVM approaches as part of official national malaria control plans and procedures.

In July 2000, EHP convened a Technical Working Group on Community-Based Malaria Vector Management to consider ways of increasing community participation in vector control programs and to identify particular methods that are amenable to use by community-based organizations. This review was prepared as background information for the group members.

1.1. Purpose and Scope

This literature review summarizes published information on selected control methods for anopheline mosquitoes and provides readers with a relatively brief introduction to options for malaria vector control. The review describes most of the physical, chemical, and biological methods that have been used in malaria vector control programs. It also summarizes information on factors that influence the efficacy of each method and the demonstrated effectiveness of each method for producing public health benefits (reductions in morbidity and mortality rates), to the extent such information is available. The review includes an extensive bibliography of original research articles and guidance documents available from the World Health Organization (WHO) and other institutions. This report does not include information on insecticide-treated bednets, which have been reviewed extensively in the published literature, or on natural or synthetic chemical repellants.

1.2. Background

1.2.1. Malaria

Malaria is a serious health problem in many developing countries, infecting between 300 and 500 million people annually, and the disease is a leading cause of infant and child mortality in sub-Saharan Africa (WHO 1995). It is also a highly complex disease caused by four different pathogens and vectored by many different mosquito species. Table 1 summarizes the malaria situation in the five WHO-designated regions.

Table 1. Breakdown by Region of Malaria Incidence, Primary Vector, and Control Activities

	Africa (sub-Saharan)	Southeast Asia	The Americas	Eastern Mediterranean (including N. Africa)	Western Pacific
Millions of people at moderate to high risk	512	398	280	240	150
Malaria cases/ deaths[a]	237,647,000/ 961,000	15,791,000/ 73,000	2,043,000/ 4,000	13,693,000/ 53,000	3,751,000/ 20,000
Primary vector[b] species	*An. gambiae complex, funestus, pharoensis*	*An. culicifacies, dirus, fluviatilis, minimus, stephensi*	*An. albimanus, aquasalis, darlingi, nuneztovari, pseudo-punctipennis, punctimacula, vestipennis*	*An. pharoensis* (N. Africa), *sacharovi, sargentii, stephensi*	*An. aconitus, anthropo-phagus dirus farauti* s.l., *minimus, sinensis, sundaicus*
Main forms of vector control[c]	• Few organized programs (stable transmission areas) • Indoor spraying and outdoor larviciding (epidemics)	Indoor spraying	• Indoor spraying, larviciding (chemical and biological) • Environ-mental management (in some areas)	Indoor spraying	Impregnated bednets, indoor spraying

[a] Estimated number of malaria cases and deaths for 1998—source, WHO 1999a.

[b] Lists of primary vector species derived from Bruce-Chwatt 1985; AAAS 1991; Kondrashin 1992; Pan American Health Organization 1997.

[c] Information source—WHO 1995.

Given the variable nature of the disease, its vectors, and the vulnerability of particular human populations, WHO stresses the need for a range of malaria control approaches in its Global Malaria Control Strategy (WHO 1993). WHO recommends an integrated approach that relies on early case identification and treatment as well as selective and sustainable prevention measures, including vector control.

Options for vector control include environmental management, chemical control, biological control, and personal protection. An integrated vector control program would incorporate local information about vector distribution and behavior to identify one or more control techniques that would be effective, affordable, and acceptable to local communities. This review examines recent literature on the field effectiveness and, where available, impacts on malaria transmission of the first three types of vector control. Although personal protection , such as use of impregnated bednets or repellants, is clearly important in community-based malaria control programs, these approaches have already been extensively reviewed elsewhere.

1.2.2. Vector Biology

Adult females of many mosquito species will bite humans, using the blood meals for egg production. However, only about 60 species of the genus *Anopheles* can transmit malaria. Anophelines generally bite at night and usually rest on a surface (such as the wall of a house) before or after feeding. As with all mosquitoes, the immature stages are aquatic, and they prefer slow-moving or still water in which they can stay close to the water surface with their breathing orifices open to the air. Unlike some other mosquito genera, anophelines require relatively clean water for larval development, which is why malaria transmission frequently declines with urbanization and concomitant water pollution.

Although malaria is transmitted exclusively by anophelines, only certain species are important vectors of the disease. Several factors determine both the importance of each species as a vector of malaria (or other diseases) and the options for control. A good understanding of the biology and ecology of the principal vectors is essential to the development of an integrated vector control approach. These factors include the following:

- Time of biting (evening, dawn, night)
- Flight range of the vector (usually 3 kilometers [km])
- Feeding preferences of adult female mosquitoes (humans or animals)
- Adult behavior—particularly, preference for biting and resting indoors (endophagic, endophilic) or outdoors (exophagic, exophilic)
- Larval habitat preferences (e.g., pools vs. containers, brackish vs. fresh water, full sun vs. shade)
- Resistance to insecticides

The following sections review recent literature on the effects of three types of malaria vector control interventions—environmental management, biological control, and chemical control—as tested at the field level. As vector control focuses on the mosquito, many researchers have used only entomological indicators of effectiveness, without addressing the impacts of the interventions on the incidence or prevalence of the disease itself. Conversely, some studies have examined the overall effects on malaria of field programs incorporating several different vector control interventions at once. In these cases, though data are available on the incidence and prevalence of malaria, the role of any one of the interventions in producing changes in the disease burden is less clear.

2

Technical Review of Vector Control Techniques

2.1. Environmental Management of Malaria Vectors

Since the discovery of the role of *Anopheles* mosquitoes in malaria transmission over one hundred years ago, malaria control experts have recognized the value of changing mosquito larval habitats to reduce or eliminate malaria transmission. Habitat elimination or modification efforts have included general programs to reduce the abundance of all mosquitoes as well as more targeted projects of "species sanitation" directed at the principal malaria vectors (Bruce-Chwatt 1985). The concept of modifying vector habitat to discourage larval development or human vector contact is generally referred to as environmental management (EM). The WHO Expert Committee on Vector Biology and Control (1980) defined environmental management as the following:

> The planning, organization, carrying out and monitoring of activities for the modification and/or manipulation of environmental factors or their interaction with man with a view to preventing or minimizing vector propagation and reducing man-vector-pathogen contact. This approach, which should be carried out prudently and skillfully, is naturalistic and involves an attempt to extend and intensify natural factors which limit vector breeding, survival and contact with man.

The specific techniques of EM are generally grouped into three main categories: (1) environmental modification, (2) environmental manipulation, and (3) modification of human habitations and behaviors (WHO 1982). A number of manuals and reviews explain specific EM techniques in detail (WHO 1982; Rafatjah 1988; Rozendaal 1997; Florida Coordinating Council on Mosquito Control [FCCMC] 1997). These sources include extensive technical information on major engineering projects, such as large-scale dams. EM has proven valuable in preventing or mitigating malaria and other vector-borne diseases sometimes exacerbated by large-scale water projects (Lim et al. 1987; Hunter et al. 1993). However, this review focuses on community-level interventions to address existing malaria problems.

2.1.1. Environmental Modification

2.1.1.1. Techniques

Environmental modification involves a physical change (often long term) to potential mosquito breeding areas designed to prevent, eliminate, or reduce vector habitat. The principal methods of achieving these changes include drainage, land leveling, and filling (WHO 1982). Draining operations include the creation of ditches or drains to keep water moving and to carry the water used as breeding sites away in a managed way. Drains may be lined or unlined and located at the surface or subsoil level. In some instances, marshes have been drained through pumping (Takken et al. 1990).

As an alternative to complete elimination of wetlands, modification projects could involve the creation of channels to improve water flow in areas of standing water, filling small ponds or water-collecting depressions, or changing the banks of water impoundments to reduce mosquito populations. As rivers and streams can create anopheline larval breeding sites, particularly in slow-moving pools with heavy vegetation, regrading streams and even straightening riverbanks may reduce vector populations (Thevasagayam 1985). Some of these activities require regular maintenance, whereas others represent permanent changes to the landscape (which may require substantial initial effort and expense). An important component to environmental modification addresses problems of man-made vector breeding sites associated with water-holding structures in mini-dams and small-scale irrigation projects. The creation of favorable vector habitat can often be avoided through careful design (WHO 1982).

Large-scale environmental modification projects as part of broad-based programs to control and eventually eradicate malaria were implemented successfully prior to the 1940s in Italy, the Tennessee Valley in the United States (Kitron and Spielman 1989), and Indonesia (then the Dutch East Indies) (Takken et al. 1990). In Italy, modification efforts involved substantial investment of money and time to achieve major engineering feats including the 16 km diversion of the Ombrone River into a canal and draining the almost 100,000-hectare (ha) Pontine marshes, using an elaborate series of ditches and canals. In Indonesia, many smaller-scale modification projects focused on eliminating coastal habitat for *An. sundaicus*. Methods included draining or filling brackish water swamps, lagoons, and fishponds and raising, diking, and improving tidal drainage to coastal zones near towns and ports. Interest in environmental modification faded with the rise of DDT use and hopes of chemical-based eradication of malaria, but the practice may be reexamined as countries look for more sustainable approaches to vector control (Rafatjah 1988).

More recently, a saltwater marsh drainage project was initiated along with larviciding and drug treatment to contain a malaria epidemic in Haiti (Schliessmann et al. 1973, cited in Ault 1994). In Kitwe, Zambia, a project was begun in the 1950s to use lined drains, filling and leveling, and planting eucalyptus and other water-intensive vegetation to convert a large periurban wetland into a public park (Baer et al. 1999). New environmental modification projects modeled after this earlier success were begun in 1998, and initial entomological data suggest that this effort reduced adult mosquito densities (Baer et al. 1999). At two industrial sites in India, integrated bioenvironmental malaria control projects included small-scale filling of construction borrow sites, unused ditches, and low-lying areas with fly ash (Dua et al. 1991; Dua et al. 1997). In both areas, incidence of malaria declined significantly, although the impact of any one of the many control techniques would be difficult to assess.

2.1.1.2. Factors Influencing the Efficacy of Environmental Modification

Many modification projects require regular maintenance, as they are designed to make permanent changes in the environment. In fact, poorly maintained drainage projects may actually increase larval breeding habitat (Takken et al. 1990). As modification projects tend to require significant initial investments in construction, such a method may be feasible only where the water body or wetland under consideration is clearly the main larval breeding site for the malaria vector species.

2.1.2. Environmental Manipulation

2.1.2.1. Techniques

Environmental manipulation refers to activities that reduce larval breeding sites of the vector mosquito through temporary changes to the aquatic environment in which larvae develop. Water management activities include changing water levels in reservoirs, flushing streams or canals, providing intermittent irrigation to agricultural fields (particularly rice), flooding or temporarily dewatering man-made or (where feasible) natural wetlands, and changing water salinity. Manipulation of vegetation may also be useful. Planting water-intensive tree species, such as *Eucalyptus robusta,* can reduce standing water in marshy areas (WHO 1982; Sharma et al. 1986a; Sharma & Sharma 1989). Planting shade trees near potential larval habitats may help reduce the abundance of vectors, such as *An. gambiae, An. funestus, An. minimus,* and *An. sundaicus,* that prefer sunny conditions for larval development (Rafatjah 1988).

The feasibility of flushing streams to control *An. culicifacies* was recently examined in rural Sri Lanka (Konradsen et al. 1998). The seasonal nature of vector activity and the species' preference for breeding in drying stream beds led the researchers to conclude that periodic flushing of a natural stream whose water flow was already controlled for irrigation could reduce malaria cases and reduce the need for larviciding. However, further field testing would be needed to demonstrate the efficacy of flushing and to indicate the level of intersectoral collaboration required for successful implementation. Flushing has also been used successfully in Mexico to remove *An. pseudopunctipennis* larvae associated with rice fields (Rafatjah 1988).

Intermittent irrigation has been suggested to remedy the problem of increased malaria vector abundance associated with irrigated agriculture. Common farming practices associated with wet rice cultivation in particular have been clearly linked to increased malaria transmission in some areas (Surtees 1970). Intermittent irrigation involves the periodic draining of the fields timed to occur at a frequency that prevents the mosquito larvae from completing their development cycle. This method has proven successful in rice-growing regions in India, China, and other parts of Asia (Lacey & Lacey 1990). In China, vector control has also been accomplished by simply letting fields dry up naturally (Pal 1982). The combined use of the natural insecticide neem *(Azadirachta indica)* and intermittent irrigation in Indian rice fields achieved substantial reductions in culicine larvae as well as smaller but still significant reductions in anophelines (Rao et al. 1995). Initial experiments with the intermittent irrigation method in African rice showed a high level of *An. arabiensis* larval mortality, but the preferential oviposition by adult vectors in the fields under the intermittent treatment caused overall vector abundance to remain the same (Mutero et al. 2000). Further research is needed to assess the utility of this technique in Africa.

Tree planting to help drain marshy land was included both as part of an integrated vector control program and to address other environmental problems associated with deforestation in the Kheda District in Gujarat, India (Sharma et al. 1986a; Sharma & Sharma 1989). The impact of the tree planting itself on vector abundance could not be assessed, but the researchers predict that the economic value of the 2 million trees could provide financial benefits.

Although more widely used to control *Culex quinquefasciatus* breeding in pit latrines, expanded polystyrene (EPS) beads have also been applied to control anopheline larvae in water tanks and abandoned wells, particularly in India (Sharma et al. 1985; Dua et al. 1989; Sharma & Sharma 1989; Dua et al. 1997). EPS beads form a floating layer on the water surface, blocking mosquito oviposition and causing high larval mortality. The advantages of the EPS method are its simplicity, safety, low cost, and persistence. In shallow water, however, EPS beads exposed to wind are easily blown off, and in one instance, local people collected the beads to make jewelry (Singh et al. 1989).

2.1.2.2. Factors Influencing the Efficacy of Environmental Manipulation

The efficacy of all environmental manipulations depends on how well the intervention is matched to the specific ecological requirements of local populations of the vector mosquito. Information on the distribution of breeding sites is also essential. Furthermore, different environmental conditions, including humidity, rainfall, and soil composition, may also affect particular interventions on the malaria vector and disease transmission. Finally, as environmental manipulations are aimed at reducing overall vector population density, good coordination of activities at a local level is needed.

In the case of intermittent irrigation, poor soil drainage may result in standing pools that permit vector larvae to complete development, which may have reduced the impact of this method in the Mwea irrigation scheme in Kenya (Mutero et al. 2000). At the same time, the soil and crop varieties must be such that temporary removal of water does not effect yield negatively (Lacey & Lacey 1990).

2.1.3. Modification of Human Habitations or Behaviors

2.1.3.1. Techniques

Changes in placement and structure of human habitations as well as changes in behavior may reduce human-vector contact (Rozendaal 1997; Ault 1994; WHO 1982). Humans have long practiced a simple form of malaria prevention by locating houses away from breeding sites, although settlements must be near enough to a water source to supply domestic needs. Even though many anopheline adults can fly as far as 3 km from their larval habitat, locating settlements 1.5 to 2 km away from major breeding sites may significantly reduce transmission (WHO 1982). Preferred housing sites should also be on well drained, high ground, upwind (rather than downwind) of probable breeding sites (Rozendaal 1997). Raising houses on poles may also reduce transmission, as many vector species tend to fly fairly low (Charlwood et al. 1984). Although it has often been suggested that removing vegetation from around houses may control mosquitoes by removing resting sites, one of the few studies evaluating this practice found it had no effect on anophelines (Ribbands 1946, cited in Stephens et al. 1995).

Mosquito-proofing dwellings by covering windows, eaves, and doors with screening and repairing cracks and holes by which mosquitoes enter may reduce transmission both by protecting people from bites and by preventing the spread of the disease from infected human reservoirs. It is important, however, that such improvements not impede ventilation unless the house is air-conditioned. Screening materials include cotton netting (which is inexpensive but reduces ventilation up to 70% and is easily damaged), plastic mesh (which is inexpensive and allows ventilation, but is variable in its durability), and metal mesh (which is durable and allows ventilation but is often expensive) (Rozendaal 1997).

Screening and general housing improvements may reduce malaria transmission while raising overall living conditions. Improved house construction played a role in controlling malaria in the United States in the early 20th century (Boyd 1926; Fullerton & Bishop 1933). In the early 1940s, residents of several Jewish settlements in northern Palestine employed a range of measures to protect themselves from malaria, including careful screening of rooms and the restriction of human activity to screened areas between sunset and sunrise (Kitron & Spielman 1989). More recent research in Sri Lanka indicated that residents of poorly constructed houses were as much as 2.5 times more likely to contract malaria than neighbors in houses of good construction (Gamage-Mendis et al. 1991; Gunawardena et al. 1998). Economic calculations suggested that government investments to improve the most vulnerable houses would be offset within 7.2 years by savings in malaria treatment (Gunawardena et al. 1998). In rural Gambia, Lindsay and Snow (1988) found that children sleeping in houses with closed eaves and metal roofs experienced fewer malaria infections than children sleeping in houses with open eaves. Not all forms of housing improvement will reduce malaria transmission, however. Compulsory house improvements to reduce rat-vectored plague epidemics implemented in Java in the 1930s resulted in a dramatic increase in malaria transmission (Takken et al. 1990).

In areas where wet rice or other heavily irrigated crops are implicated in providing larval habitat for malaria vectors, the practice of dry-belting is recommended (WHO 1982; Thevasagayam 1985; Rafatjah 1988). Dry-belting involves maintaining a band of pasture or other dry crop around a village or town that would otherwise be bordered or even surrounded by wet fields. Information on whether this method is feasible or widely practiced was not available in the recent literature.

One strategy that has not yet been widely tested is zooprophylaxis—the diversion of vectors away from humans, using nonreservoir domestic or wild animals. Vector diversion to livestock associated with reduced malaria transmission has been observed in Indonesia (Kirnowordoyo & Supalin 1986), the Philippines (Schultz 1989), and Sri Lanka (Van der Hoek et al. 1998). In the United States, Nasci et al. (1990) found that treating cattle with topical applications of permethrin reduced abundance of the nuisance mosquito *Psorophora columbiae* and suggested that livestock treated with insecticides might be useful for controlling zoophilic anopheline species. Some malaria vectors, such as *An. annularis* and *An. sinensis,* already exhibit strong preferences for feeding on nonhuman hosts and may be appropriate targets for such an intervention. In contrast, strongly anthropophilic species, such as *An. sundaicus* and *An. darlingi,* may not be appropriate targets (WHO 1982).

2.1.3.2. Factors Influencing the Efficacy of House Improvement and Other Interventions

In poor rural areas of many tropical countries, traditional house design or construction materials may not be suitable for mosquito proofing (WHO 1982). This is especially true where houses lack walls on all four sides or are made of thatch or other materials that are full of cracks and holes. House improvements may also be ineffective for malaria control where people frequently sleep outdoors. In these situations, personal protection, such as impregnated bednets, may be more appropriate.

Zooprophylaxis may fail in some instances when the presence of livestock actually increases the vector population to the point of increasing mosquito biting on humans. For example, Bouma and Rowland (1995) found that the prevalence of malaria infection in villages in Pakistan increased in proportion to the number of families owning cattle.

2.1.4. Secondary and Unintended Effects of Environmental Management

The impact of environmental management depends in part on the scale of the operation. Clearly, some of the large-scale, permanent draining projects, particularly of natural wetlands, must have significant impact on local ecosystems. Zimmerman and Berti (1994) pointed out that natural wetlands are in decline worldwide and strongly suggested that modification of natural ecosystems be avoided. Conversely, one of the benefits of large-scale draining operations, particularly in urban and periurban areas, has been the creation or renovation land for agriculture or building construction (Panel of Experts on Environmental Management for Vector Control 1986; Takken et al. 1990).

Environmental manipulation through water management can affect access to water for other uses. For interventions associated with agriculture to be practical, methods such as intermittent irrigation should have a minimal or, preferably, positive impact on crop yields. Activities that involve flooding or flushing of streams with high volumes of water could create drowning hazards to people in nearby communities, so safety measures would need to be developed (WHO 1982). Finally, although temporary manipulation activities are not expected to be as disruptive to local ecosystems as permanent modification, dramatic changes in water levels are likely to impact some nontarget aquatic organisms.

House screening and other home improvements to prevent human-vector contact for malaria control may indeed reduce problems with other vectors and nuisance pests (Rozendaal 1997). In fact, improved house construction may be seen as raising the quality of life overall and may be driven by broader development goals than disease prevention. On the other hand, zooprophylaxis may cause unintended health problems if the placement of livestock near homes increases transmission of other diseases.

2.1.5. Community Participation

The early large-scale environmental modification projects required significant inputs of labor both by paid workers and sometimes by voluntary or obligatory labor contributions by communities (Takken et al. 1990). In some areas under colonial rule, such as Palestine and the Dutch East Indies, measures to reduce larval habitat, including sealing water sources and the removal of fishponds, were forcibly imposed on communities (Kitron & Spielman 1989; Takken et al. 1990). Failure to properly seal a well or cistern in urban Palestine was, in fact, a criminal offense; homeowners in violation were subject to prosecution (Kitron & Spielman 1989).

More recent efforts to control malaria vectors through environmental methods have focused more on voluntary community participation. In Sri Lanka, an experiment in community-based malaria vector control involving filling small breeding sites and repairing irrigation canals used a traditional practice of community donation of labor (Silva 1988, cited in Ault 1994). High levels of community involvement were considered critical to the success of two bioenvironmental malaria control programs initiated in rural India (Sharma & Sharma 1989; Singh et al. 1989). Although environmental management projects to control malaria should be aimed at reducing anopheline density, research by Fletcher et al. (1992) suggested that the control of nuisance-biting species is also important for fostering community support and satisfaction.

Malaria programs that include screening or other home construction improvements clearly require the direct involvement of the residents. Active participation by householders or community groups is essential for planning, installing, and maintaining the improvements. Experience in community-based programs to control Chagas' disease through housing improvements in Brazil, Venezuela, and Bolivia suggests that developing a local organizational structure may have many benefits (Bryan et al. 1994). The researchers found that the active participation of community members made the interventions more cost-effective than the traditional vertically organized program and also fostered community pride and solidarity.

2.2. Larviciding—Biological and Chemical Methods

Environmental management involves physical changes to the mosquito larval breeding habitat, but mosquito suppression can also be achieved through treating the breeding sites directly with chemical or biological agents that kill the larvae. Chemical larviciding and biological control, particularly using larvivorous fish, were important to malaria control programs in the early part of the 20th century, particularly in urban and periurban areas (Gratz & Pal 1988). However, with several notable exceptions, such as the eradication of *An. gambiae* in Brazil (Soper & Wilson 1943, cited in Gratz & Pal 1988) and Egypt (Shousha 1948), larviciding did not play an important role in most eradication efforts.

Chemical or biological larviciding for the control of malaria vectors is feasible and effective only when breeding sites are relatively few or are easily identified and treated. That is, it must be possible to treat enough of the sites to have a significant impact on the adult mosquito population and on subsequent malaria transmission. Therefore, some vector species—such as *An. stephensi,* whose larvae are generally restricted to man-made water containers in urban areas—may be good targets for such control methods. Larval control appears promising in urban areas generally, given the high density of humans needing protection and the limited number of breeding sites. For example, the vector *An. gambiae* is capable of breeding in small puddles of rainwater and may not be controllable in rural areas, where the number of potential breeding sites is enormous. However, under certain circumstances, populations of this species may concentrate in a few sites (e.g., construction borrow pits) in urban areas, in which case larviciding may be feasible (Gratz & Pal 1988).

2.2.1. Biological Control

A wide range of organisms help to regulate *Anopheles* populations naturally through predation, parasitism, and competition. *Biological control* refers to the introduction or manipulation of these organisms to suppress vector populations. At present, the principal biological control agents that have been successfully employed against *Anopheles* are predators, particularly fish, and the bacterial pathogens *Bacillus thuringiensis israelensis* (Bti) and *Bacillus sphaericus* (Bs) that attack the larval stages of the mosquito (Das & Amalraj 1997). Other organisms showing promise include a number of fungal pathogens, the nematode *Romanomermis culcivorax*, and the aquatic plant *Azolla* (Lacey & Lacey 1990).

The advantages of biological larval control agents in comparison with chemical controls can include their effectiveness at relatively low doses, safety to humans and nontarget wildlife, low cost of production in some cases, and the lower risk of resistance development (Yap 1985). However, biological control agents against malaria vectors can be more difficult to use than chemicals. Agents that effectively suppress larval populations under laboratory conditions often fail under less favorable field conditions. Furthermore, biological control agents tend to be more specific in terms of which mosquitoes they can control and which habitats they will work in (Das & Amalraj 1997).

2.2.2. Larvivorous Fish

2.2.2.1. Technique

Predatory fish that eat mosquito larvae, particularly in the family *Cyprinodontidae*, have been used for mosquito control for at least 100 years (Meisch 1985). Prior to the 1970s, the most commonly used species was the mosquitofish *Gambusia affinis*, a freshwater species native to the southeastern United States. This species was introduced widely around the world. The practice has since been discouraged as the efficacy is highly variable and the negative impacts on native fauna of this voracious and aggressive fish have been quite significant (WHO 1982). The introduction of *Gambusia* has actually led to the elimination of native fish from certain habitats (Rupp 1996). More recently, researchers have evaluated native fish species to identify appropriate local biological control agents. In spite of widespread recommendations for the use of fish and extensive laboratory data, reports of controlled field experiments evaluating the effectiveness of larvivorous fish in reducing malaria transmission are fairly limited.

In rural areas, fish may be appropriate components of malaria control if breeding sites are well known and limited in number, but use of fish may be less feasible where natural breeding sites are extremely numerous. Fish may be particularly useful in controlling malaria vectors associated with rice fields (Lacey & Lacey 1990). This practice has proved effective under certain conditions in California (Blaustein & Karban 1985; Kramer et al. 1988). In Asia, introduction or management of larvivorous fish has been effective where pisciculture can provide additional economic, agricultural, and nutritional benefits (Gupta et al. 1989; Wu et al. 1991; Victor et al. 1994). In China, Wu et al. (1991) found that stocking rice paddies with edible fish, such as carp, improved rice yield, supported significant fish production, and greatly reduced the number of malaria cases (see Table 2).

Table 2. Larvivorous Fish Used to Control Mosquito Larvae in Rice Fields

Fish species	Anopheles species targeted	No. of fish/m² of water surface	% reduction in anopheline larval density	Duration of control	Reference (location)
Combination: *Cyprinus carpio, Ctenopharyngodon idella, Tilapia* spp	*An. sinensis*	1	Significant reductions, reported graphically	150–170 days (length of observation period)	Wu et al. 1991 (China)
Gambusia affinis	*An. subpictus, culicifacies, annularis, nigerrimus*	5		42 days (length of observation period)	Das & Prasad 1991 (Uttar Pradesh, India)
Combination: *Cyprinus carpio, Ctenopharyngodon idella, Catla catla, Labeo rohita, Cirrhinus mrigala*			81.0 (anopheline) 83.5 (culicines)		Victor et al. 1994 (southern India)

Larvivorous fish also show promise in controlling malaria vectors under certain conditions in urban areas. Fish have been used in both African and Indian urban and periurban areas to control vectors that breed in man-made water-holding structures, such as wells, cisterns, and barrels (Table 3).

Table 3. Larvivorous Fish Used to Control Malaria Vectors in Man-Made Containers, Particularly in Urban Areas

Fish species	***Anopheles* species targeted (and culicine species)**	**No. of fish/m^2 of water surface**	**% reduction in anopheline larval density[a] (all mosquito species)**	**Duration of control**	**Release habitat/ region**	**Reference**
Aphanius dispar (native)	*An. culicifacies adanesis*	Variable, depending on water container	97 (95)	2–4 weeks	Cisterns, wells and barrels/ city of Assab, Ethiopia	Fletcher et al. 1992
	An. arabiensis, gambiae complex				Djibouti	Louis & Albert 1988
Gambusia affinis (introduced)	*An. stephensi (C. fatigans)*	?	98 (86)	4 weeks 4 weeks	Wells/ Pondicherry town, India	Menon & Rajagopalan 1978
Aplocheilus blocki (native)	*An. stephensi*	5	75[b]	Single intro.— 18 months	Wells, tanks/ coastal urban areas in Goa, India	Kumar et al. 1998
Poecilia reticulata	*An. gambiae* s.s.	3–5	85	Single intro.— 1 year	Washbasins, cisterns/ Gr. Comore Is.	Sabatinelli et al. 1991
	An. stephensi & subpictus	5–10 per container	(81–86)	Variable	Containers/ India	Gupta et al. 1992
	An. stephensi	5–10	(78)	Variable	Wells/ India	Rajnikant et al. 1993

[a] Percentage decline measured by the change in percentage of possible breeding sites infested with anopheline larvae after fish were introduced.

[b] Compared average percentage of breeding sites with *An. stephensi* larvae during the 6-month period prior to fish release with the average percentage of infested breeding during the same 6-month period in year following release.

In an urban area in Ethiopia, Fletcher et al. (1992) found that the indigenous fish, *Aphanius dispar*, effectively suppressed *An. culicifacies adanensis* breeding in wells and containers although the experimental design did not allow the researchers to assess the impact on malaria transmission. Near the Ethiopia-Somalia border, the same researchers observed a locally developed initiative to control container-breeding malaria vectors, using the indigenous fish *Oreochromis spilurus spilurus* (Teklehaimanot et al. 1993). On Grande Comore Island, where the vector *An. gambiae* s.s. breeds only in man-made reservoirs, the introduced fish, *Poecilia reticulata*, provided yearlong suppression of larval and adult mosquito populations and significantly reduced malaria incidence (Sabatinelli et al. 1991). In the majority of breeding sites the fish reproduced successfully, thus reducing the need to restock.

In parts of India *An. stephensi*, a very efficient malaria vector even at low densities, is the major urban vector. It can breed in clean water containers and other habitats common in urban and periurban areas. Interest in the use of fish is rising as high levels of resistance to DDT have been documented in *An. stephensi* populations in Panaji, Goa, India (Thavaselvam et al. 1993). A number of studies have found both the introduced fish species, *Gambusia affinis* and *Poecilia reticulata,* and indigenous species to be effective at suppressing *An. stephensi* populations breeding in containers (Menon & Rajagopalan 1978; Gupta et al. 1992; Rajnikant et al. 1993). One study (Kumar et al. 1998) combined the use of the native fish *Aplocheilus blocki* in large breeding sites (wells and water tanks) and Bti in smaller habitats. The experimental design did not allow a direct comparison of *Anopheles* larval densities in treated versus untreated sites, but the study is very interesting in that it examined the impact of these interventions on the incidence of malaria, comparing the annual parasite index (API) in the area receiving the large-scale field trials of the fish and microbial biological control agents with neighboring areas that received the conventional vector controls of indoor residual house spraying (IRS) with DDT and pyrethrum fogging. Overall, the interventions including biological control were more effective at reducing API than conventional insecticide spraying.

2.2.2.2. Factors Influencing the Efficacy of Larvivorous Fish

The two main factors determining the efficacy of the fish are the suitability of the fish species to the water bodies where the vector species breed and the ability of the fish to eat enough larvae to significantly reduce the number of infective bites that people receive. The first factor is best addressed by finding a native fish species that thrives under the conditions present in breeding sites rather than to change breeding sites to suit the fish, although Wu et al. (1991) recommended a ditch-ridge system for rice fields to better accommodate the fish. Also, the use of pesticides and fertilizers can negatively impact fish stocked in irrigated fields (Lacey & Lacey 1990). The second factor may be strongly influenced by aquatic vegetation, which can interfere with fish feeding and can also provide refuge for the mosquito larvae. Periodic vegetation removal may be needed to facilitate the activity of the fish (Dua & Sharma 1994).

When fish are used in man-made breeding sites in urban areas, there is a clear need to restock the fish periodically to maintain populations sufficient to suppress the mosquito larvae. Fletcher et al. (1992) found that restocking of fish was necessary due to a number of factors, including loss of fish during cleaning or accidental contamination of the container with hot or chlorinated water. Furthermore, another larvicidal agent (e.g., one of the bacilli products) may be needed in sites where fish cannot survive (Kramer et al. 1988; Louis & Albert 1988; Kumar et al. 1998).

2.2.3. Microbial Control

2.2.3.1. Techniques

Two different species of bacteria of the genus *Bacillus, B. thuringiensis israelensis* (Bti) and *B. sphaericus* (Bs), have been widely demonstrated to be effective larvicides against both anopheline and other mosquito species. Both Bti and Bs function as stomach poisons in the mosquito larva midgut. Since the discovery of the mosquito larvicidal activity of Bti spores (serotype H-14) in 1977, different formulations of Bti have been found effective against larvae of many mosquito species, including the malaria vectors *An. albimanus, An. sinensis, An. culcifacies, An. sundaicus, An. stephensi, An. gambiae, An. arabiensis,* and *An. maculatus* (Das & Amalraj 1997; Becker & Margalit 1993; Lacey & Lacey 1990). The lethal effect of Bti on mosquito larvae is actually caused by toxins on the bacterial spore coat rather than an infection. Most formulations use dead spores and therefore do not persist or reproduce in the field. In contrast, Bs (serotype H 5a 5b) formulations tend to use live spores and have some capacity to persist and recycle in the field (Des Rochers & Garcia 1984; Karch et al. 1992). The recycling capacity of Bs may help to explain the longer duration of its larvicidal activity sometimes observed in the field (two to eight weeks). Bti is usually active for one to two weeks at most (Lacey & Lacey 1990). Bs is generally considered even more selective in its host range, affecting only mosquito larvae. Bti and Bs also differ in their response to water quality: Bti generally requires fairly clean water to be effective, whereas Bs can be used successfully in water with some organic pollution (Rishikesh et al. 1988).

Several recent field trials and pilot control programs using Bti for malaria vector control are summarized in Table 4.

Table 4. Field Tests of *Bacillus thuringiensis israelensis* (H-14) against Malaria Vectors

Target malaria vector (other mosquitoes targeted)	Habitat (country)	Product used—formulations	Effective application rate—unit/ha of water surface	Duration of control[a] (days to retreatment)	References—country
An. gambiae, (C. quinquefasciatus)	Irrigation ponds *(Anopheles),* sewage ponds, gutters *(Culex)*—Kinshasa, Zaire	Vectobac 12AS flow conc.	2–8 L/ha	Less than 2 days	Karch et al. 1991
		Vectobac-G granule	10–20 kg/ha	Less than 5 days	
An. arabiensis	Natural pools, rice fields, man-made ditches—highlands, Madagascar	Vectobac 12AS	0.6–1 L/ha	Less than 5 days	Romi et al. 1993
		Vectobac GR granule	2–10 kg/ha		
An. stephensi	Construction sites and tanks—Goa, India	Bacto-culicide suspension	10 kg/ha	3–7 days	Kumar et al. 1995
	Man-made wells and tanks—Goa, India	Powder	10 kg/ha		Kumar et al. 1998
An. albimanus	Rice fields and ponds—rural Peru & Ecuador	Vectobac TP	1 kg/ha	7–10 days	Kroeger et al. 1995
		Bactimos WP	2 kg/ha		
An. albimanus	Irrigation ditches, rice fields, ponds, streams—periurban Comayagua, Honduras	Teknar (alone and with chemical larvicides)	1.17 L/ha (Teknar alone)	10 days	Perich et al. 1990

[a] All field trials listed achieved 90% to 100% larval mortality within 48 hours after treatment.

Bti is an important part of mosquito control in the United States (FCCMC 1997; Lacey & Lacey 1990), but it is not part of large-scale routine malaria control operations in other countries. Fields trials of Bti in rural and periurban areas of Latin America have shown promise in reducing larval densities of *An. albimanus* and *Aedes aegypti* (Perich et al. 1990; Chiu-Garcia & Fernandez-Salas 1999; Castillo & Scorza 1999). Pilot projects in rural Ecuador and Peru found that weekly applications of Bti reduced the anopheline biting rate by as much as 70%, although the impact of this reduction on malaria transmission was not measured (Kroeger et al. 1995). In rural Madagascar, Bti granule formulation effectively controlled *An. arabiensis* larvae in ditches and rice fields, although, again, larger-scale trials are needed to assess impact on malaria transmission (Romi et al. 1993). Bti exhibited an extremely short duration of activity against *An. gambiae* in irrigation ponds in periurban Kinshasa, Zaire (Democratic Republic of the Congo), and was therefore not considered promising

(Karch et al. 1991). Large-scale field trials of Bti in urban areas have produced mixed results. As discussed above, a combination of larvivorous fish and Bti successfully controlled malaria in coastal villages of Goa, India (Kumar et al. 1998). Experiments in irrigated rice fields in Kenya also showed promising though preliminary results with combinations of Bti and the larvivorous fish, *Tilapia zilli* and *Oreochromis niloticus* (Asimeng & Mutinga 1993).

A selection of recent field evaluations of Bs is summarized in Table 5 and includes several African studies.

Table 5. Field Tests of *Bacillus sphaericus* (Strain 2362) against Malaria Vectors

Mosquito species controlled	Habitat (country)	Product used	Effective application rate—unit/ha of water surface	Duration of control[a] (days to retreatment)	Reference
An. gambiae, (C. quinquefasciatus)	Irrigation ponds *(Anopheles),* sewage ponds, gutters *(Culex)*	Vectolex-G (ABG-6185) granule	10–30 kg/ha	5–7 days	Karch et al. 1991
	Swamps and rice fields in suburban village (Kinshasa, Zaire)	Same as above	10 kg/ha	7 days	Karch et al. 1992
An. gambiae s.l. *(C. quinquefasciatus*)	Ponds (village, Senegal)	Spherimos FC and locally produced granular form compared in both studies	30 L/ha for FC, 30 kg/ha for granules	15 days (granules), 5 days (FC) for Senegal study	Skovmand & Baudin 1997
	Rain puddles *(Anopheles),* cesspits *(Culex)* (Ouagadougou, Burkina Faso)			10 days for both forms for Burkina Faso study	Skovmand & Sanogo 1999
An. arabiensis	In natural pools, rice fields, man-made ditches—highlands, Madagascar	ABG 6185 granule	2.5–18 kg/ha	Less than 5 days	Romi et al. 1993
An. gambiae complex (main target, *C. quinquefasciatus*)	Ditches, puddles and naturally flooded areas in periurban Maroua, Cameroon	Suspension	10 kg/ha	Not measured (6 months)	Barbazan et al. 1998
An. albimanus, C. quinquefasciatus, Aedes taeniorhynchus	Ponds, dams, a river, and water pits— town of Santa Cruz del Norte, Cuba	Liquid formulation	100 L/ha (applied by backpack sprayer and by plane)	Up to 5 months in water without current	Montero Lago et al. 1991
An. albimanus and others	Rural Peru and Ecuador	Vectobac TP	1 kg/ha	7–10 days	Kroeger et al. 1995
		Bactimos WP	2 kg/ha		

[a] All field trials listed achieved 90 to 100% larval mortality within the first 48 hours after treatment.

Skovmand & Sanogo (1999) tested Bs granules against *An. gambiae* in rainwater puddles in urban and periurban Ouagadougou, Burkina Faso, and found that although the granules were effective in larger water bodies, the transient nature of the puddles, particularly during the rainy season, thwarted this effort. The Bs granules were found to remain active as long as 15 days in larger ponds outside a village in Senegal (Skovmand & Baudin 1997). In a periurban village near Kinshasa, Zaire, Karch et al. (1992) found that biweekly application of Bs granules to rice fields and swamps caused a 13.6% decrease in the average *An. gambiae* bites to humans. Although this reduction was too low to consider the Bs a successful control by itself, it suggests that Bs may be useful in some integrated control programs. In urban and periurban Maroua, Cameroon, Barbazan et al. (1998) found that a large-scale Bs spray program targeting *C. quinquefasciatus* delayed the onset of the seasonal malaria transmission period by two months.

The laboratory and field efficacy of Bs against *An. stephensi, An. culicifacies,* and other anophelines as well as *C. quinquefasciatus* has been extensively tested in India (Ansari et al. 1989; Mittal et al. 1993; Kumar et al. 1994; Shukla et al. 1997; Sharma et al. 1998). Bs formulations were found to be effective against *An. stephensi* and persisted two to four weeks under field conditions (Mittal et al. 1993). A large-scale trial of weekly applications of Bs in Panaji City achieved significant reductions in both *An. stephensi* density and malaria incidence (Kumar et al. 1994). Bs was less effective and persistent against *An. culifacies* (Ansari et al. 1989). Furthermore, the efficacy of Bs against *C. quinquefasciatus* appeared to decline after 15 application rounds (Sharma et al. 1998).

Several field studies compared the efficacy and persistence of Bti and Bs under African conditions (Karch et al. 1991 [Zaire]; Romi et al. 1993 [Madagascar]; Skovmand & Sanogo 1999 [Burkina Faso]). In Burkina Faso and Zaire, Bs granules were generally found more effective than Bti formulations against *An. gambiae* s.l., whereas in Madagascar Bti granules were effective against *An. arabiensis* in a wider range of larval habitats than Bs. A comparison study of the control of *An. culicifacies* and *An. fluviatilis* in man-made water containers in India found that Bs was superior to Bti in cement tanks (Bs activity lasted up to six weeks), but Bti was more persistent (one week) in ponds (Shukla et al. 1997).

Formulations of Bti and Bs are manufactured in the United States, Canada, Russia, India, and Cuba (and possibly other countries) and are commercially available. In addition to liquid and water-soluble powder formulations that are similar to many chemical insecticides, Bti and Bs products available or under development include slow-release granules and briquettes (Chavasse & Yap 1997). In Burkina Faso, researchers have experimented with local production of slow-release granular formulations, using imported bacilli (Skovmand & Baudin 1997; Skovmand & Sanogo 1999). The capacity to produce Bti and Bs locally and economically would make microbial control of larvae more widely feasible. In India, Balaraman and Hoti (1987) found that local production cost of Bti and Bs in briquette formulation was U.S.$11.02 per batch (enough to treat 0.2 ha) for Bti and U.S.$13.34 for Bs. If, as the authors assumed, the briquettes had low application costs and provided control for four weeks, the Bti and Bs treatments would cost the same or less than treatments with chemical larvicides. In Peru, communities in Piura State have used Bti cultured in coconuts to control malaria vectors breeding in fish farm ponds (Ventosilla et al. 1999).

2.2.4. Factors Influencing the Efficacy of Microbial Controls

Many environmental factors can reduce the efficacy or effective life span of Bti and Bs products. Natural breakdown or inactivation processes are accelerated by heat, ultraviolet light, and water with high organic matter (Consoli et al. 1995; Lacey & Lacey 1990). Bti and Bs products may also fail to control anopheline larvae due to the tendency of spores to sink below the surface level where larval feeding occurs (Kroeger et al. 1995; Orduz et al. 1995). At present, weekly applications are often recommended to deal with the problem of their short effective life spans, although such frequent applications may not be economically feasible in some circumstances (Kumar et al. 1995). Improved slow-release formulations may help to solve this problem, but researchers are also exploring the possibility of genetically modifying other bacteria common in mosquito breeding sites to produce Bti or Bs toxins (Orduz et al. 1995).

2.2.5. Chemical Larvicides

2.2.5.1. Techniques

As is the case with biological control of vectors, the goal of chemical larviciding is to eliminate or reduce the vector population by killing the larvae. Larviciding, particularly using petroleum oils to smother the larvae, was widely used before the commercialization of DDT, particularly for control of malaria in urban and periurban areas (Gratz & Pal 1988). In addition, larviciding has been widely practiced to control nuisance-biting mosquitoes, particularly in the United States (FCCMC 1997).

A range of chemicals have been used successfully as malaria vector larvicides. In addition to petroleum oils, one of the most widely used compounds before the 1940s was Paris green (copper acetoarsenite). Although insoluble in water, the compound was applied as a fine powder that floated on the water surface, where it was eaten by *Anopheles* larvae (Rozendaal 1997). Although inexpensive and highly effective, use of Paris green is no longer recommended due the risks posed by its high toxicity and the availability of safer alternatives (Coosemans & Carnevale 1995). DDT was an early replacement in the 1940s and 1950s, followed by several organophosphate insecticides in the 1960s. One of them, temephos (trade name Abate), which exhibits very low mammalian toxicity, is widely recommended (FCCMC 1997; Gratz & Pal 1988) and has been used for malaria control in India and Mauritius (Kumar et al. 1994; Gopaul 1995). Temephos has also been valuable in the Onchercerciasis Control Programme in West Africa (Rozendaal 1997). Synthetic pyrethroids are also effective but are problematic as larvicides due to their often high toxicity to aquatic nontarget organisms (Chavasse & Yap 1997). Insect growth regulators (IGRs), which are generally safer for nontargets, may become more useful in the future, particularly as larval resistance to older compounds develops. IGRs, however, have not been widely tested for malaria control (Graf 1993).

2.2.6. Factors Influencing Efficacy

The efficacy of chemical larvicides depends on several factors, including the formulation, the water quality, and the susceptibility of the targeted larvae. Larvicidal activity tends to be short for conventional fluid or wettable powder formulations (one to two weeks in the tropics) and can be improved through application of slow-release granules, briquettes, or microencapsulated forms (Rozendaal 1997). Activity tends to be longer in cooler, cleaner water (Chavasse & Yap 1997). Larval resistance to some of the more widely applied larvicides, such as temephos, is a growing concern (Majori et al. 1986).

2.2.7. Secondary and Unintended Effects of Biological and Chemical Larval Control

As chemical larval control involves application of insecticides to water bodies, contamination of aquatic ecosystems is a serious problem. Early chemical larviciding programs, using products such as petroleum oil, DDT, or Paris green, undoubtedly killed many aquatic organisms and may have caused profound changes in certain ecosystems. Even today, the organophosphate insecticide fenthion is still widely used in spite of its relatively high toxicity to nontarget fauna (Rozendaal 1997). Even temephos (trade name Abate), which is not acutely toxic to mammals (Ware 1989), has been found to harm crabs, shrimp, and zooplankton, leading to the recommendation in Florida that this chemical not be applied to environmentally sensitive areas (FCCMC 1997).

An important advantage to biological control is the (assumed) reduction in ecosystem disturbance. The microbial larvicides do not persist or accumulate in the environment or in body tissues and are not toxic to vertebrates and nontarget aquatic organisms (WHO 1999b). Therefore, these microbial products can be safely added to drinking water used for humans and livestock and in environmentally sensitive areas. Larvivorous fish have also been used in drinking water, although the issue of possible health impacts has not been widely addressed. The introduction of exotic fish species is associated with the disruption of native fish populations but has been addressed by the move to indigenous fish or fish introduced a long time ago. However, manipulating even native fish into different habitats may have some unintended ecological consequences.

A positive secondary effect of biological control using larvivorous fish, particularly edible fish or combinations of edible and larvivorous fish, is the improvements to income or diet. The use of edible fish in malaria control may also encourage community support and the long-term sustainability of the program. However, malaria control programs that include fish usually must develop fish hatchery and distribution programs, particularly for control of container-breeding vectors (Gupta et al. 1989).

2.2.8. Community Participation in Chemical and Biological Control of Larvae

In all control methods focusing on larvae, the community, at a minimum, may be involved in the identification and monitoring of permanent and transitory breeding sites of the malaria vector. In areas where the sites are relatively few and located on public land, participation in control activities may be limited. However, particularly in urban and periurban areas where the primary vectors breed in numerous water bodies or containers located in individual households, community understanding, interest, and involvement are critical to successful larval control programs (Rishikesh et al. 1988; Yap 1985). Use of some agents, such as chemicals perceived as toxic or oils that are messy, may be less appealing to residents than use of biological agents (Fletcher et al. 1992). In addition, public acceptance and involvement in household larval control programs may be influenced by the impact of malaria control interventions on general nuisance biting. In their study of community awareness and mosquito control programs in two Tanzanian cities, Stephens et al. (1995) found that the persistence of nuisance mosquitoes created dissatisfaction with existing insecticide spraying programs for malaria control.

Some biological control agents offer (and even require) much greater public involvement. Urban malaria control programs using fish must both determine whether the community will accept fish swimming in their drinking and bathing water and educate inhabitants to avoid killing the fish accidentally. Researchers have generally found public acceptance of fish to be high (Louis & Albert 1988; Fletcher et al. 1992; Gupta et al. 1992; Rajnikant et al. 1993; Kumar et al. 1998), but sometimes investigators have encountered individuals concerned about negative impacts of the fish (Sabatinelli et al. 1991). Programs including Bti or Bs may also benefit from increased community participation as certain formulations, such as granules and briquettes, do not require special equipment and may be safely dispersed into breeding sites by householders or community volunteers (WHO 1999b).

2.3. Chemical Control of Malaria Vectors—Adult Mosquitoes

2.3.1. Indoor Residual House Spraying

2.3.1.1. Techniques

Chemical control of adult female mosquitoes has been the most widely successful vector control method since the 1940s. The most common practice is indoor residual house spraying (IRS), in which the inside walls, the ceiling, and sometimes the outside eaves, porches, and nearby animal sheds are sprayed with a persistent insecticide. The rationale for IRS is based on the behavior of those *Anopheles* species that rest on walls before or after biting humans. Dramatic reductions in the annual parasite index (API) achieved by pilot IRS projects in many parts of the world inspired the World Health Assembly to adopt malaria eradication as a goal in 1955 (Pant 1988). However, the goal of eradication proved elusive in most malaria-endemic countries in the tropics.

The effectiveness of IRS is, nonetheless, well established (WHO 1995). Many different insecticides could be suitable for IRS. An appropriate insecticide should be highly toxic to the insect, safe for humans and nontarget organisms, persistent on the wall or ceiling surface, acceptable to the inhabitants of the house, easy to apply, and fairly inexpensive (Rozendaal 1997). House spraying programs are most likely to be effective when the principal vectors are endophilic and endophagic and where strong financial support can ensure timely chemical application by well-trained operators, using appropriate equipment and insecticides (Chavasse & Yap 1997).

DDT has been the most widely used insecticide for vector control since the 1940s. DDT spraying has been widely demonstrated as a valuable tool for the prevention of malaria transmission (Pant 1988). During the WHO-sponsored malaria eradication program of the 1950s and 1960s, global DDT use was high, but it has declined significantly over the past 30 years. According to a preliminary WHO inventory, DDT is still used or stockpiled for use in about 26 countries; however, several are planning to phase it out in the near future. One factor motivating countries to examine alternatives may be the global treaty on persistent organic pollutants, including DDT, currently being negotiated through the UN Environment Program (UNEP). The treaty is expected to allow countries to continue to use DDT for vector control, but UNEP will collaborate with WHO to provide technical and financial support to assist countries in safely phasing out DDT over time.

In some countries that still use indoor house spraying for vector control, other insecticides have been employed in place of DDT. Early replacements have included organophosphates (malathion, pirimiphos-methyl, and fenitrothion) and carbamates (bendiocarb, carbosulfan, and propoxur). More recently, light-stable pyrethroids—including permethrin, deltamethrin, cypermethrin, cyfluthrin, and lambda-cyhalothrin—and the pyrethroid mimic etofenprox have also been used (Chavasse & Yap 1997).

2.3.1.2. Factors Influencing the Efficacy of Indoor Residual Spraying

WHO has established a program, the Pesticide Evaluation Scheme (WHOPES), to test various insecticides used for vector control, including IRS, larviciding, and space spraying, to provide recommendations on the appropriate formulations and application doses (Chavasse & Yap 1997). WHO and other technical information sources stress the need to apply insecticides following the appropriate techniques to ensure effective control (Rozendaal 1997, Pant 1988). However, even when insecticides are applied as directed, other factors, such as the type of house structure and building material, can reduce the impact of IRS. Insecticides tend to last longest on wooden or painted walls and to break down quickly (especially pyrethroids) on mud walls with a high clay content (Rozendaal 1997). IRS may also be less effective where houses are not walled on all sides. As stated above, vector behavior is also important, as different species rest on different types of surfaces. Species that tend to bite outdoors are not easily controlled through IRS (Pant 1988; Loyola et al. 1991).

The development of insecticide resistance by the vector species is a serious problem for IRS programs. Due to both its history of widespread use in agriculture and public health and its persistence in the environment, moderate to high levels of resistance to DDT have developed in many malaria vectors. In 1992, there were 56 species of *Anopheles* reported to have DDT-resistant populations (WHO 1992). Although DDT can still provide effective control in some areas with moderate levels of resistance in the target mosquito population (Roberts & Andre 1994; Sharma et al. 1986b), in areas where vectors exhibit high levels of DDT resistance, such as Guatemala, Sri Lanka, and parts of India, IRS programs have switched to other insecticides (Beach et al. 1989; Herath et al. 1988; Tyagi 1992, respectively). WHO has developed a global program to measure and document the problem of resistance in vector species (Shidrawi 1990).

The problem of insecticide resistance is by no means limited to DDT. Widespread use of malathion in parts of India (as a response to DDT resistance) has contributed to high levels of malathion resistance in target vectors (Tan & Yap 1986). Heavy agricultural use of a particular insecticide can reduce its subsequent efficacy for indoor vector control (Georghiou et al. 1973; Chapin & Wasserstrom 1981). In some cases, resistance created by previous use of DDT and other insecticides for house spraying as well as agricultural uses may also confer cross resistance to new insecticides or may stimulate the development of multiple-insecticide resistance within the vector population (Beach et al. 1989; Pant 1988). Research showing some cross-resistance between DDT and pyrethroids raises special concern (Chakravorthy & Kalyanasundaram 1992; WHO 1992). The increasing problems associated with resistance argue for resistance management through the use of multiple vector control methods, including nonchemical tactics (Roberts & Andre 1994).

2.3.2. Secondary and Unintended Effects of Chemical Control of Adult Mosquitoes

2.3.2.1. Human Health Effects

As insecticides are applied inside homes, there is significant chemical exposure for both the spray teams and the inhabitants. The various insecticides suitable for house spraying vary in the acute and chronic toxicity hazards they pose, particularly to sprayers. To protect themselves against acute intoxication, sprayers and people mixing or repackaging the concentrated pesticide formulations should wear protective clothing and receive proper training and supervision in safe pesticide handling (Chavasse & Yap 1997). DDT is not considered a serious acute poisoning hazard (Ware 1989). However, organophosphate and carbamate alternatives, which are acetylcholinesterase inhibitors, are more acutely toxic. Workers using organophosphates or carbamates should not be exposed for more than six hours per day. Regular tests of cholinesterase levels in the blood are recommended to monitor levels of exposure of spray workers using organophosphate insecticides, although such monitoring is not useful with carbamates (Plestina 1984). Sprayers accustomed to working with DDT may need further safety training, or serious poisoning accidents could happen. For example, isomalathion contaminants in poorly stored malathion caused a poisoning epidemic that affected 2,800 malaria program workers (of whom at least 5 died) in Pakistan in 1976 before improved safety procedures were implemented (Baker et al. 1978). Pyrethroid insecticides do not appear to present such severe hazards to sprayers, but the are associated with temporary facial burning or numbness, coughing, and eye irritation (He et al. 1989; Moretto 1991; Chester et al. 1992). The recommended safety precautions include protective clothing and bathing after work. Disposable face masks may also be helpful to reduce skin irritation (Chavasse & Yap 1997).

Although DDT is highly toxic to fish and invertebrates and moderately toxic to birds, the acute toxicity of DDT to mammals is low (Beyer et al. 1996), and DDT is considered not acutely toxic to humans (Oaks et al. 1991). However, the extraordinary persistence of DDT and its tendency to bioaccumulate in body fat (Barrie et al. 1992) raises concern regarding the chronic effects of exposure to DDT. Due to the carcinogenic activity of DDT in some lab animals, DDT, DDD, and DDE are classified by the U.S. Environmental Protection Agency as class B2 probable human carcinogens (Agency for Toxic Substances and Disease Registry 1994). Some research suggests that DDT and DDE may interfere with normal functioning of certain hormone-mediated processes (U.S. Environmental Protection Agency 1997; Fry & Toone 1981).

Indoor spraying with DDT is a significant source of exposure to DDT and its metabolites DDE and DDD (referred to henceforth simply as DDT) for house residents. In South Africa, researchers found that residents of houses sprayed with DDT have significantly higher body burdens and breast milk concentrations of DDT than residents of unsprayed houses (Bouwman et al. 1991; Bouwman et al. 1990). In India, where DDT has mainly been used for vector control rather than for agriculture, a comparison of DDT levels in human blood found that inhabitants of villages sprayed with DDT had body burdens of the chemical almost 10 times higher than inhabitants of nearby villages using bioenvironmental methods to control malaria (Dua et al. 1996). Similar elevations related to DDT spraying for malaria control were observed in human breast milk in Mexico (Waliszewski et al. 1996).

2.3.2.2. Environmental Effects

The heavy use of insecticides for either IRS or space spraying can be expected to have some impact on the environment, but there is little information in the literature documenting these impacts. In IRS, most of the chemical applications occur inside houses, so the environmental impacts should be considerably less than usually occur during agricultural applications. However, as the insecticides (almost all of which are harmful to aquatic organisms) must be mixed with water and the spraying equipment must be washed after use, there is some risk of contamination of streams and other aquatic ecosystems near areas of IRS.

Although most documented environmental damage is thought to be connected to agricultural use of DDT, the long persistence of DDT and its metabolites in soil may pose special threats to ecosystems where large-scale DDT spray programs operate over a long period. A “mass balance” model commissioned by the World Wildlife Fund estimated the fate of DDT applied for IRS (Feltmate et al. 1998). The model, based on the fugacity of DDT, calculated that about 60% to 82% of the DDT would be physically removed from the walls and released into the outside environment within six months after application. Empirical data are not available as yet to support or refute the model. However, analyses of DDT residues in soil and water in areas using DDT for vector control in India showed higher levels of DDT contamination than areas where the chemical was not used for IRS (Dua et al. 1996).

2.3.3. Community Participation in Indoor Residual House Spraying

In general, the community plays a passive role in IRS programs. The spraying is usually done by a team of workers paid and supervised by the government rather than by the residents or volunteer community groups. Community participation for IRS often consists of cooperating with the spray teams by removing food and covering surfaces prior to spraying and refraining from covering the treated surfaces with new paint or plaster. However, community or individual householder opposition to IRS due to the smell, mess, possible chemical exposure, or sheer bother has become a serious problem in some areas (Wu et al. 1993; Sharma & Sharma 1989). Compliance with IRS may be particularly low where nuisance pests, such as roaches or bedbugs, have become resistant to the sprays (Rafatjah 1971).

2.4. Summary

A wide range of chemical, biological, and environmental management techniques may be used to control malaria vectors. Nonchemical approaches generally require substantial information about vector ecology, distribution of larval habitats, and local environmental conditions. Furthermore, these interventions tend to be effective only under certain conditions, and successful control in one location may not be predictive of results elsewhere. Chemical control, particularly IRS, appears more consistently effective across a wide range of vectors and environmental conditions, although problems with insecticide resistance and concerns about pesticide exposure risks suggest that selective and limited applications of this technique may be desirable. Environmental management was successfully applied early in the 20th century to ensure that no water of the quality required by an identified local vector species was available. Its application is not, however, universally applicable, and its implementation must be designed with close attention to the local ecological, socioeconomic, political, and cultural setting.

This technical review indicates that within the broad field experience of the three techniques, there are gaps in the literature on malaria vector control. Extensive field research on various vector control methods has been conducted in some regions, particularly Asia, but research on malaria vector control in Africa is more limited and tends to focus mainly on urban areas. Published reports describing large-scale implementation of nonchemical techniques suggest that combinations of several interventions appropriate to local conditions and vectors may provide good control, but such reports are few. In addition, although the desirability of community participation in vector control program is often mentioned, detailed descriptions of the nature of that participation are frequently not included.

It is the task of EHP to examine both the existing literature and the gaps in that literature in order to identify operations research questions that can be addressed within the scope, capacity, and resources of the project. To begin this task, EHP has convened a meeting of experts with significant field experience in malaria vector control and other technical areas to do the following:

- Identify priority issues and gaps in knowledge related to malaria vector control to be addressed by community-based actions
- Elaborate research questions related to the priority issues
- Develop preliminary research designs and indicators to address the research questions

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