

that programs must be directed at goals established jointly by health professionals and the community that are within the scope of available resources. They also asserted that the success of community development programs would be enhanced by establishing multisectoral units responsible for overseeing integration of the programs under the auspices of a government agency. This latter measure, it was felt, would allow the government, the private sector, and the community to be represented at all levels of program planning, implementation, and evaluation, and would also help to ensure program continuity. Special emphasis was placed on the need for periodic evaluation of health activities.

With respect to international technical cooperation, it was recommended that dif-

ferent countries share their information, experience, and methodologies relating to community health education. It was also stated that information systems must be established to facilitate collection of data about effective programs. With regard to international organizations, the participants felt that their proper role in community health education is to support the development of effective educational activities, materials, and models—and that through their work, programs between countries can be developed, facilitated, and improved.

*More detailed information about the Technical Discussions, including the final report of those discussions, is contained in PAHO documents CD27/DT/1, 2, and 3 issued in August and September 1980.*

## BIOLOGICAL INSECTICIDES: NEW WEAPONS AGAINST VECTOR-BORNE DISEASES

Modern chemical insecticides have revolutionized the fight against vector-borne diseases since the end of the Second World War. Despite certain limitations, they are likely to continue being used extensively for that purpose in the foreseeable future.

Most of these insecticides have a broad spectrum of effectiveness, and some are effective for long periods of time. These two features ensure the sizable markets that make industrial production profitable. On the other hand, these products' broad and widespread use also means that their careless large-scale application can have undesirable environmental effects.

Use of these insecticides for public health purposes has not been abusive. However, supervision of their use for crop protection has been poorer, and cause for concern about their use in that area is greater. In addition, environmentalist campaigns have resulted in increasingly restrictive regulations governing the production and application of chemical insecticides. Consequently, the use of some of

the leading public health insecticides has been so restricted as to dramatically reduce their availability; research and development costs have increased sharply; and all this has reduced the number of new insecticides that can be used for public health.

Another consequence of the massive use of chemical insecticides has been the steady development of resistance to them among disease vectors and crop pests. Attempts to overcome this have resulted in a use of larger dosages more often and a shifting from one insecticide group to another until, in some instances, no commercially available chemical can ensure the safe and effective control of the particular vectors or pests involved at a cost that the people concerned can afford.

This situation has been made worse by the recent deterioration of the world economic situation. Many countries now lack the resources, especially the hard currencies, needed to purchase the insecticides that can combat the local disease agents or vectors.

Thus, while it should be technically possible

to effectively control the transmission of vector-borne diseases in most endemic countries by the sound use of chemical insecticides, in fact, financial constraints make it increasingly rare for this to be accomplished. This means that alternative vector control methods are essential.

The World Health Organization considered the problem some years ago and began to encourage the evaluation of biological control agents. However, resource limitations retarded research efforts, and progress was very slow. This situation changed when the Special Program for Research and Training in Tropical Diseases—launched in 1976 and cosponsored by the United Nations Development Program (UNDP), the World Bank, and the World Health Organization—decided to include research and development of biological control agents among its activities.

### The Basis for Biological Control

Natural vector populations usually fluctuate within certain limits under the influence of climatic and biological factors. Vector pathogens, parasites, and predators all play leading roles in this natural population regulation which, on a long-term basis, implies an equilibrium between these biological vectors and their hosts. But this equilibrium rarely prevents the transmission of vector-borne diseases. The development of biological control tools and methods therefore requires the manipulation of the vector pathogens, parasites, and predators in such a way as to directly or indirectly reduce the abundance or longevity of the vectors below the level at which disease transmission is likely to occur.

Many living organisms contribute to the natural equilibrium of vector populations, but only some of these can be efficiently manipulated by man for vector control purposes. Biological agents need to be very specific, so that they do not endanger any living organism except the target vector or group of vectors. They should also be easy and inexpensive to mass-produce, store, and apply. And finally,

once introduced into an area, they should persist for long periods at a level preventing vector survival or reproduction. Unfortunately, these requirements are to a large extent conflicting. The development of biological control agents is therefore a slow and often costly process involving a number of screening stages not very different from those used for conventional chemical insecticides. The WHO screening procedure includes the following steps:

- a search for new and promising agents;
- assessment of the agents' potential for controlling key vector groups and of their safety for mammals and the environment;
- studies on the possibilities for mass production, the stability of the formulated product in storage, and application methods;
- eventual epidemiologic evaluation of the effect of the biological agent in disease control operations.

### Achievements and Prospects

Under the Special Program a broad plan of research and development began in 1978 with special emphasis on about a dozen species or strains of bacteria, fungi, protozoa, and parasitic nematodes that can infect and kill a variety of insect vectors. Vector predators were added to the list of priority agents by late 1979. While some important results have already been achieved, the work has also encountered some unexpected obstacles that have necessitated further research.

#### *Spore-forming Bacteria*

About five years ago strains of a microorganism called *Bacillus sphaericus* were shown to be mildly pathogenic for mosquito larvae. A specific search for more potent strains resulted in the discovery of a few suspected of being potentially as effective as chemical larvicides. At present the most nearly developed candidate is a strain known as "1593," which has been produced industrially on an experimental basis and evaluated in the field.

Several more recently discovered strains of this bacillus seem equally promising. For many years *Bacillus thuringiensis* has been used for destroying certain crop and forest pests. Until 1977 all known strains of this bacillus were specific only for caterpillars, so it came as a great surprise when in that year de Barjac identified a new bacterial strain highly pathogenic to mosquito larvae. This strain had been found in Israel a few months before by Goldberg and Margalit. Dr. de Barjac, head of the International Reference Center for *B. thuringiensis*, described her findings in the following words at a meeting hosted by the Pasteur Institute in Paris:

"WHO had sent me a strain of bacillus with promising larvicide properties for complementary study. It was not yet identified. I examined it and determined it was a new type of *B. thuringiensis*, which I designated as serotype H-14 because 13 other different serotypes were already known. I then tried to check its larvicidal power against larvae of *Aedes aegypti*, the mosquito vector of yellow fever and dengue hemorrhagic fever. At first I could not believe my eyes. Within 15 minutes serotype H-14 had killed the larvae.

"I thought I must have made a mistake, and I repeated these investigations several times, always with the same result. There could be no doubt, the larvicide acted with dramatic effect within half an hour after application. What is more, *B. thuringiensis* proved to be effective against the larvae of at least six species of mosquito including *Anopheles stephensis*, one important vector of malaria. It also has the great advantage of being specific, which means that serotype H-14 does not affect any other aspect of the environment and is not harmful to humans."

Further investigation of serotype H-14 showed that its spectrum of effectiveness encompassed not only all mosquito species (including the vectors of lymphatic filariasis) but also blackflies, the vectors of river blindness.

Extensive mammalian environmental safety studies have shown that these promising strains of *B. sphaericus* and *B. thuringiensis* are entirely innocuous for vertebrates and non-target invertebrates; they would therefore appear to be even more environmentally acceptable than the safest chemical larvicides in use for mosquito and blackfly control.

*B. thuringiensis* serotype H-14 will soon be marketed, but this does not imply that all the problems involving its use are solved. The effectiveness of this agent, as well as that of *B. sphaericus* strain 1593, could be further improved if an adequate concentration of the material produced by the bacteria could be maintained for longer periods in the same water layer as mosquito and blackfly larvae. Formulation research will help to resolve such problems. One of the advantages of *B. thuringiensis* is that it is possible for local "cottage" or small-scale industries to produce it easily and cheaply. Such production could provide an important example of appropriate technology applied to disease control. However, realization of this goal must depend on further work needed to develop suitable quality control methods.

#### Fungi

Although research on fungi pathogenic to mosquito larvae has not progressed at the same rapid pace as the *B. sphaericus* and *B. thuringiensis* investigations, steady advances relating to the use of several fungal species have nevertheless been made. One such species is an Australian fungus named *Culicinomyces* that can be mass-produced industrially. It has been shown safe enough for man and the environment to justify its large-scale evaluation against vectors of arboviral diseases in Australia. North American strains of *Lagenidium giganteum* (isolated from mosquitoes) affect a large number of mosquito species, including some important pests and vectors. Progress has also been made at a more modest level in evaluating the potential of several species of *Coelomomyces*, one species of *Leptolegnia*, and several strains of *Metarhizium anisopliae*.

In general, these fungal agents have shown a lower degree of effectiveness and a shorter shelf life than *B. sphaericus* or *B. thuringiensis*. However, they might have the great advantage of being able to sharply decrease mosquito production for long periods following their introduction into vector breeding sites.

### Protozoa

Only two species affecting mosquitoes, *Vavraia culicis* and *Nosema algerae*, have been actively considered in research supported by the Special Program. These can be mass-produced only inside living hosts such as caterpillars or mosquito larvae, and this limits their production to areas where skilled labor is relatively cheap. The two agents have the advantage of being disseminated by the vectors themselves, and both seem safe for man and the environment.

### Nematodes

For about 10 years a North American nematode named *Romanomermis culicivorax* has received great attention because of its potential for mosquito control. It parasitizes only mosquitoes. Simple methods have been developed for mass production using the easily colonized house mosquito *Culex quinquefasciatus*. The worm has been subjected to large-scale field evaluation in the United States and has been tested against an important mosquito vector of malaria in El Salvador.

When this nematode can be introduced and permanently established in an appropriate environment, it may provide a very useful measure of mosquito control. Conceivably, the same could be achieved with similar nematode species naturally occurring in tropical environments—in particular *Romanomermis iyengari*, which has already been subjected to successful laboratory mass production in India.

### Other Agents

Less progress has been achieved with other potential biological control agents such as viruses that attack insects and insect predators. Too little is understood about the dynamics of insect viruses to make any effective use of them against insects of public health importance, and investigations on how insect predators might be used have not advanced sufficiently.

Before any use can be made of viruses against mosquitoes and other disease-spreading insects, more must be learned about how to produce and store those viruses and about their specificity for insects—and their safety for man.

In some instances, very successful use has already been made of fish predators against mosquito larvae, and in fact some species of fish have been used for this purpose for many decades. Some studies are now being started on how fish can be used more efficiently against mosquito larvae.

### Future Progress and Constraints

Overall, research on biological control of vectors has taken a large step forward since 1977 under the aegis of the Special Program. Bacterial larvicides are on the verge of operational use; fungal larvicides are under development; protozoal larvicides are being studied; and nematode larvicides could be applied operationally once a way of producing them cheaply enough becomes available.

But although progress has been faster than expected, there are still major limitations. All the promising agents are biological larvicides; and, with the exception of *B. thuringiensis* serotype H-14, their effectiveness is limited to mosquito larvae.

Right now, chemical larvicides are extensively used against mosquitoes in urban and other densely populated areas; they also represent the best tool for controlling vectors of river blindness. However, their impact in malaria control is constrained because the resources required for their frequent and effective application against malaria vectors in rural areas far exceed those locally available for malaria control. Biological control agents might provide an effective tool for overcoming some of these constraints.

The considerable task ahead is two-fold: to find and develop a greater variety of biological agents that can be used against a larger spectrum of vector groups, and to facilitate the local production of these agents in endemic areas where their use is contemplated. The

latter goal should be relatively easy to achieve, because in most instances the production of these agents does not require the costly infrastructures associated with production of conventional insecticides. Furthermore, the production of many of these promising agents is much more labor-intensive than capital-intensive, and should thus be quite suitable for the many countries of the tropical zone where labor-intensive methods are still economically feasible.

To pave the way for such developments, the

research on biological control of vectors is being closely associated with special efforts to develop national expertise within endemic countries and to disseminate relevant information among those countries so that they can ultimately achieve a measure of regional or national self-reliance in controlling the vector-borne diseases that continue to plague them.

*Source:* World Health Organization document TDR/PK/VEC/80, 1980.

## ANTIBIOTIC TREATMENT OF DIARRHEA

*The use of antibiotics for the treatment of diarrheal disease is controversial. The Australian National Health and Medical Research Council has recently recommended the following policies in an attempt to rationalize the attitude of medical practitioners on this issue.<sup>1</sup>*

### Introduction

Diarrhea is a common symptom of many noninfective diseases, and sometimes it may be prominent in infections which do not primarily affect the bowel, e.g., malaria. It is also a frequent side-effect of drug administration, including the administration of antibiotics. In fact, antibiotic-induced diarrhea is occasionally very severe and many even cause death.

Many infective diarrheal diseases, such as rotavirus gastroenteritis and staphylococcal toxin food-poisoning, do not benefit from antibiotics. In addition, some bacterial gastrointestinal infections such as salmonellosis are not improved by antibiotic treatment despite the *in vitro* sensitivity of the salmonella species strain concerned. For these reasons, antimicrobial agents should only be prescribed for certain selected gastrointestinal infections that

have been shown to benefit clinically from specific chemotherapy. Accurate diagnosis of the diarrheal disease is a prerequisite for this.

### Acute Diarrhea, Diagnosis Pending

Chemotherapy is rarely necessary in these circumstances. Rehydration, if necessary, is the essential measure for acutely ill patients. Immediate chemotherapy, after the collection of appropriate culture specimens, may be considered for selected patients if the epidemiology strongly favors a particular etiology such as giardiasis or cholera. If salmonella food poisoning is suspected, empirical chemotherapy may be considered for patients who are prone to septicemia because of impaired defense mechanisms, e.g., immunosuppression.

### Salmonella Gastroenteritis

Antibiotics are of no value in cases of uncomplicated salmonella gastroenteritis, either for treatment of the disease or for treatment of the resultant asymptomatic sal-

<sup>1</sup>A comprehensive list of references on which the above note has been based are available from the Editor, Communicable Diseases Intelligence, P.O. Box 100, Woden, A.C.T. 2606, Australia.