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RESISTANCE TO INSECTICIDES USED IN PUBLIC HEALTH AND AGRICULTURE



PROCEEDINGS

OF AN INTERNATIONAL WORKSHOP

22 - 26 February 1982



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NATIONAL SCIENCE COUNCIL OF SRI LANKA

RESISTANCE TO INSECTICIDES USED IN
PUBLIC HEALTH AND AGRICULTURE

Proceedings of an International Workshop
held at the Sri Lanka Foundation Institute,
Colombo, from 22 - 26 February, 1982

*Organised by the National Science Council of Sri Lanka
together with the,*

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PREFACE

The possible selection for resistance in insect vectors of disease, through the use of pesticides in Agriculture, has been a cause for concern among national health authorities. In Sri Lanka pesticides, such as malathion and fenitrothion, were used in Agricultural pest control work, and also in the public health programmes particularly for the control of the mosquito. In India the development of vector resistance to malathion has been known to be widespread. Aware of this danger the Government of Sri Lanka in 1976 restricted the use of malathion and fenitrothion to the control of public health disease-carrying vectors. Thus a review of this problem involves not only the Agricultural and Health Sectors of a country, but also many other policy making and executing agencies.

The National Science Council of Sri Lanka consented to a suggestion by Dr. P.T. Haskell, Director of the Centre for Overseas Pest Research (COPR) in London, to convene a meeting of all agencies and persons concerned to discuss this problem.

In view of its global significance, the meeting was organized as an international forum with sponsorship from the World Health Organization and the Food and Agriculture Organization. The Advisory Committee consisting of Dr. R.P. Jayewardene (NSC), Dr. P.T. Haskell (COPR), Dr. N.G. Gratz (WHO) and Dr. L. Brader (FAO), formulated the action programme for an international workshop, the objectives of which are spelt out in Part II (para 2.0.6) of this Report.

The WHO and FAO agreed to sponsor consultants as well as national representatives from countries in the Region and the Australian Development Assistance Bureau sponsored additional representatives from countries in

the Region. The generous funding by agencies enabled many countries in the Region to participate, and also to have more than one participant at this Workshop. The countries represented were Bangladesh, Burma, China, India, Pakistan, Philippines, Sri Lanka and Thailand.

At the National level, on the invitation of the National Science Council, the Ministry of Health and the Ministry of Agricultural Development and Research supported the Workshop.

The Workshop programme included a visit to sites where public health vector control measures were being implemented.

Acknowledgement

The success of the Workshop was due to the untiring efforts of a number of persons and we take this opportunity to express our gratitude to all of them. In particular we would like to express our sincere thanks to Drs. P.T. Haskell (COPR), NG. Gratz (WHO) and L. Brader (FAO) for advice and assistance given to us throughout the preparatory phases, and also during the Workshop. In addition to his voluntary role as the moderator, Dr. Haskell was responsible for the preparation of the draft proceedings. Our thanks are also due to WHO, FAO, COPR and the Australian Development Assistance Bureau for sponsoring consultants and country representatives from the Region.

The National Science Council also acknowledges with thanks the support given by the Ministries of Health, and Agricultural Development and Research, and the following organizations:

- a. Sri Lanka Foundation Institute (for providing conference facilities)

- b. Ceylon Petroleum Corporation)
- c. Chemical Industries (Colombo) Ltd.)
- d. Haychem Ltd.) (For hosting participants
and observers for working
lunches)
- e. Lankem Ceylon Ltd.)
- f. J.L. Morrison Son & Jones (Cey)Ltd. (For providing the folders)

Our thanks are also due to Dr.(Mrs.) Nallini Wickremasinghe, Dr.(Miss) P.R.J. Herath, Dr. P. Sivapalan, Dr. N. Ranaweera and Y. Elikawela, who constituted the organizing Committee with staff members of the NSC.

Finally we wish to thank all participants and observers for the valuable contributions made to the Workshop.

NATIONAL SCIENCE COUNCIL OF SRI LANKA.

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1-0 ADDRESS OF WELCOME

by Hon. E.L. Senanayake

Minister of Agricultural Development and Research

I wish to thank the National Science Council for inviting me to deliver the address of welcome today at this international Workshop on Resistance to Insecticides used in Public Health and Agriculture.

The Problems of resistance to insecticides that are commonly used in public health and agriculture are of special significance to Sri Lanka for several reasons. As far as Agriculture is concerned our philosophy has been to minimise the use of pesticides, and use these only where it is absolutely necessary. This is essentially in keeping with our Buddhist traditions.

Our Agriculture Research Scientists have made very significant advances in the breeding of rice varieties with acceptable levels of tolerance to most of the common diseases of rice; and they have been able in recent times to incorporate resistance to some of the major pests such as the Brown Plant Hopper into our rice varieties.

I am indeed very proud that the efforts of the Plant Breeders in the Department of Agriculture who by their efforts have helped to achieve some of the chief objectives of today's workshop.

I also wish to pay a tribute to the Biological Scientists of this Department who have been able to develop the basic scientific knowledge on the life cycles and behaviours of the pests and diseases, which in turn, has enabled the Plant Breeders to develop varieties that possess various degrees of tolerance to the more commonly prevalent pests and diseases in this country.

You will therefore observe ladies, and gentlemen, that my Ministry gives every support to the Research Programmes that help us to obtain a better understanding of the basic Biological relationships that are so essential to develop the proper strategies for minimising the use of pesticides.

In the domestic Agricultural Sector which deals with rice and other

basic food commodities, it is observed, that Sri Lanka uses the lowest amount of pesticides per acre compared with other Asian countries in this region. At the same time, our rice yields are in the region of nearly 60 bushels per acre with 110 day varieties, which in terms of yield per acre per day compares well with even a country like South Korea.

Many factors have contributed to this happy situation. But I am glad that we have not come to the situation where our Agriculture has got entrapped or enslaved in the indiscriminate and haphazard use of pesticides.

When I was the Minister of Health during the latter half of 1960's we had a serious resurgence of Malaria in the dry zone of this country.

We were able to use well known insecticidal sprays to bring the Malaria transmitting mosquitoes under control.

Here is an example where we were compelled to use a well known pesticide to bring under control a dreadful disease that would have sapped the vigour of our farmers and thereby impede Agricultural production.

So you can therefore observe that in certain situations where we have to use insecticides we are faced with little or no alternative.

However, the policy in my Ministry at present is to permit only a selective use of pesticides, as and when, it is necessary according to the advise and recommendations given by the Research, Extension and Plant Protection services of the Department of Agriculture.

We have accordingly implemented legislation by the 'Control of Pesticide Act, No. 33' of September, 1980 which aims at further control and use of pesticides and also prevents misuse or overuse of pesticides in this country.

This Workshop, as you may know, has been organised by the National Science Council in collaboration with my Ministry and the Ministry of Health.

It has also received the co-operation and support of the major Agro-chemical Establishment in the country.

The World Health Organization, the Food & Agricultural Organization and the Centre for Overseas Pest Research in London, have come in a big way to assist this Workshop by sponsoring consultants and delegates. I would also like to make special reference to the Australian Development Assistance Bureau, which made a substantial contribution to support the participation of countries outside the Region, thus making the Workshop an important International event.

We have in our midst today several internationally known specialists in the field, together with distinguished delegates representing Burma, China, Indonesia, India, Pakistan, Philippines and Thailand.

On behalf of the Government of Sri Lanka, I wish to welcome them all to our country and hope that their short stay here will be most enjoyable and fruitful.

It is also my pleasure to welcome the many distinguished guests and invitees present here to participate in the inaugural session of this important International Seminar.

I wish the Workshop all success.

1.1 INAUGURAL ADDRESS

by Hon. Camini Jayasuriya
Minister of Health

Hon. Minister of Agricultural Development & Research, Secretary-General,
National Science Council, Ladies and Gentlemen.

I am extremely happy to be with you this morning at the inauguration of the International Workshop on Resistance to Insecticides used in Public Health and Agriculture organised by the National Science Council of Sri Lanka with the Department of Agriculture and my Ministry. I have seen the programme of work of the Workshop and I find that a number of very important issues relating to the use of insecticides and pesticides, in agriculture and public health will be examined in depth.

We are aware, that insecticides are used extensively in the control of pests in agriculture as well as in the control of vectors in public health in our countries. Although, a number of alternative control measures such as the use of biological control agents environmental management approaches are being currently emphasised, investigated or practiced in certain limited situations, these methods are far from being able to replace the use of pesticides at the present time. It is therefore apparent that this method of pest control, i.e. the use of insecticides will continue to remain the method of choice in the foreseeable future, and is in fact the only measure available for large scale application.

The number of insecticides available particularly for public health purposes is extremely limited. In the recent past there has been continuing reports of increasing trends in resistance development in geographical extent, the number of species and types of insecticides. This is of great significance particularly where disease vectors are concerned in view of the extremely limited number of candidate insecticides available for public health. Many of the disease vectors such as those of malaria, filariasis have developed resistance to insecticides used for their control. In addition resistance development

has also been reported even towards some of the candidate insecticides which are considered reserved for future use, despite their not being used for the control of the vectors concerned

While continued use of pesticides is known to be the obvious reason for selection of resistance, in the target population, towards the insecticide concerned, the use of pesticides for other purposes such as agricultural and technical considerations such as the phenomenon of 'cross resistance' are considered contributory factors for resistance development towards other insecticides.

There are reports of instances where large scale use of agricultural pesticides has been attributed to development of resistance on disease vectors. In Sri Lanka we have so far no direct evidence on this aspect. However, there is indirect evidence to suggest that resistance to DDT, which was the most economically feasible insecticide for malaria control was considered to have been enhanced to a certain extent, by DDT usage for agricultural purposes, although the major contributant was no doubt its many years of usage for malaria control itself.

We are all aware of the implication of DDT resistance on malaria vectors, not only in Sri Lanka but also in other countries in the developing world. DDT resistance leading to control failures necessitated changing in control strategies. DDT had to be replaced by an alternative insecticide, malathion, the economic consequence of which to the national budget is clearly obvious.

At present the Government of Sri Lanka incurs an annual expenditure of Rs. 90 million on insecticides which amounts to almost 10% of the health budget. We are fortunate so far in that the malaria vector remains susceptible to malathion. However, it is understood that a number of malaria vectors in other countries, including the same species as ours, in India have already developed resistance not only to malathion but in certain instances even towards most or all of the candidate insecticides available for public health.

While scientists all over the world are busily engaged in improving and developing alternative methods of control developing new insecticides we on our part should take them into consideration and attempt all possible methods to prolong the operational life of the limited insecticides available for public health by avoiding/minimising/delaying development of resistance towards these, through their rational use whether it is public health, agriculture, forestry or control of nuisance pests.

We have in our midst today several internationally known specialists in the field, together with distinguished delegates representing Burma, China, Indonesia, India, Pakistan, Philippines and Thailand.

On behalf of the Government of Sri Lanka, I wish to welcome them all to our country and hope that their short stay here will be most enjoyable and fruitful.

It is also my pleasure to welcome the many distinguished guests and invitees present here to participate in the inaugural session of this important International Seminar.

I wish the Workshop all success.

1-2 BACKGROUND TO AND OBJECTIVES OF THE WORKSHOP

by P.T. Haskell

(Centre for Overseas Pest Research, London)

I have been asked by the organisers of this workshop to say a few words on the background to and objectives of this international workshop by way of introduction to the sessions to come.

I suspect that there were two reasons why I was asked to undertake this task. The first is that I have been for some time now advocating the need for increased co-operation and co-ordination, at every level, between all institutions and individuals who have any responsibility for international or national programmes for the control of pests of agriculture and the control of vectors of human disease.

The second reason is that I am not an expert on insecticide resistance and I am therefore unlikely to steal the thunder of, or otherwise upset, at this early stage of our proceedings, the eminent experts in that subject who will be talking to you during the next few days.

But to go back to my first point, about collaboration - or rather, the lack of it - between those responsible for agricultural pest and disease vector control. Despite the very great importance of the phenomenon of resistance to the development and execution of pest control campaigns in agriculture and disease control, despite the fact that resistance has been spreading rapidly during the past thirty five years, despite the fact that it has now reached a level where it has during the last fifteen years, interrupted, stopped or rendered ineffectual a number of major control campaigns in agriculture and public health, it is an unfortunate fact that there has been little real liaison and co-operation between those responsible, both at international and national level, until quite recently.

For example, although both WHO and FAO have had for many years, the former from 1956 and the latter from 1963, expert committees reviewing the problems of resistance as it affected their particular area of concern, it was not until 1976, in the 22nd Report of the WHO Expert Committee, that attention was drawn to the probable interaction between agricultural and public health use of pesticides and a recommendation made to augment FAO/WHO collaboration in this field.

Although you will be hearing in more detail later on about the development of the resistance problem I think I should point out here, to put things in perspective, that at the time of which I am talking, that is the late 1970's, the actual situation was that some 100 species of insects of medical importance and some 220 agricultural pests had been reported as resistant, but by 1980, these numbers had risen to 152 and 262 respectively, that is a total of more than 400 species. Because of these figures organisations other than FAO and WHO were becoming alarmed about pesticide resistance and in 1979 UNEP presented a paper on the subject to their Seventh Governing Council.

These initiatives by the agencies were useful in providing publicity and in focussing attention on the growing problem but although by this time very severe constraints on use of various pesticides were evident in both international and national campaigns no specific joint efforts were focussed on what seemed a critical aspect of the problem, the interaction between agriculture and public health use of pesticides.

In fact, as far as I know, this workshop is the first international meeting ever to be held on this particular subject and it is therefore something of an historic occasion.

It is the more important because two of the sponsoring bodies are FAO and WHO with international responsibility for agricultural pest and disease vector control respectively; they both reacted positively when this meeting was suggested and I know that their representatives, who will be speaking later on today about their programmes on resistance, are very interested in

developing a collaborative approach.

I have mentioned two of the sponsoring organisations; the remaining two are the National Science Council of Sri Lanka and my own institute, the Centre for Overseas Pest Research, and it is certainly relevant as background to this meeting to explain how Dr. Jayawardena, the Secretary-General of the National Science Council, and I became involved in initiating the workshop. We were members of a WHO committee concerned with the WHO Special Programme on Tropical Diseases and at our meeting in 1980 the subject of pesticide resistance in insect vectors of tropical diseases was discussed. Talking about this afterwards, Dr. Jayawardena told me of the problems in Sri Lanka, where, as you will here in detail later, cross resistance problems between pesticides needed for both agricultural and malaria vector control had reached the point where regulations had to be imposed reserving certain compounds for vector control only. It so happened that I knew that on my return to the UK COPR was going to be visited by Dr. Wickremasinghe, of the Sri Lanka Department of Agriculture (who is one of the speakers in this workshop) and I said I would discuss this matter with her. In fact, when she came to the Centre this was one of the problems she wanted to discuss and during our conversation we reached the conclusion that it would be scientifically interesting, and important from the practical point of view, if we could arrange a meeting using the Sri Lanka problem as an example of the effect of resistance in both agriculture and vector control and I asked her to discuss this with her colleagues on her return to Sri Lanka. I also wrote to Dr. Jayawardena about this meeting; he discussed it in the National Science Council and their very positive reaction made him decide that the NSC would sponsor a workshop on this subject. We jointly approached FAO and WHO and as their response was also positive, the four organisations joined forces to initiate this workshop.

But I tell you this little bit of background not only to give credit to our colleagues here in Sri Lanka for their co-operative reaction but to stress one of the most important objectives of

this meeting - that it is concerned not with the theoretical and abstract problem of population dynamics and genetics in relation to resistance but with practical problems on the ground, which are today hindering pest control in agriculture and in public health here in this island.

It is important that we all bear in mind during this workshop that while naturally we shall be considering the scientific background to the development and spread of pesticide resistance, what we really have to face up to are the practical problems, now confronting almost every country in the world, of what to do about preventing or delaying pesticide resistance.

The need to concentrate on practical problems in this workshop was stressed by the planning committee and it accounts for the very welcome presence here of representatives from many countries - Bangladesh, Burma, China, India, Pakistan, Philippines, Thailand - who have been invited for the specific purpose of describing the practical problems they face at home due to pesticide resistance. You will see also that the programme is structured so that we first get an overview of the resistance problem and then concentrate on the situation in various countries.

Of course we will be discussing what possibilities there are for actually doing anything about resistance and I want to say something on that. As you will hear during the course of this meeting one of the most important advances in recent years in agricultural pest control, and to a lesser extent public health vector control, has been the development of the Integrated Pest Management approach. The unifying concept in this approach is the employment, in one integrated programme, of all techniques relevant to the control of the particular pest in question. Thus in the case of an agricultural pest the overall system might include the use of varieties of the crop resistant to the particular pest species, the use of cultural controls such as dates of planting and harvesting, spacing of plants and use of trap crops, the

employment of biological control to enhance the effect of the natural enemies of the pest, and the use of insecticides. IPM systems have been worked out for a variety of major pests on major crops and are now being widely and increasingly utilised in many developed and developing countries. One of the main factors which led to the development of IPM was infact the resistance problem, because in agriculture the misuse and overuse of pesticides had resulted in a situation for many crops in many countries where pest control was impossible or uneconomic.

From the point of view of this workshop, the important thing about the use of IPM is that it does offer a chance to reduce the use of pesticides in a given situation and hence to reduce the selection pressures that cause resistance, and we shall be hearing about that in more detail later. But IPM systems in agriculture still require in most cases some use of pesticides; also, as I said above, and again the detailed reasons for this will be given by later speakers, the concept of IPM is difficult to apply to the control of vectors, although a start has been made, but here chemical control will be the most important weapon for some years yet.

Thus despite the development of the IPM approach, the practical position at the moment is that, for the foreseeable future, the use of pesticides must continue to be a major weapon in the control of pests in both agriculture and public health. That is why the planning committee invited representatives of two other world bodies, UNEP and GIFAP, to this workshop because they are concerned with pesticide ueage. UNEP, the United Nations Environment Programme, has been concerned with problems of pesticides from the environmental point of view since its inception, and it has supported relevant research in this field for many years. One of its most important activities has been its joint sponsoring and financing, with FAO, of the UNEP/FAO Global Programme on Integrated Pest Control, which has done so much during the last ten years to develop and help put into practice in developing countries, programmes of integrated control. The

other body I mentioned is GIFAP - the Groupment Internationale des Associations Nationales de Fabricants de Produits Agrochimiques - in other words, the body which represents the world agro-chemical industry which develops and produces pesticides. GIFAP, and the industry it represents, is regarded by many people and organisations concerned with pesticides and their use as the villains of the piece, who in their sordid search for profit has covered the world with chemicals which kill man and his domestic animals, endanger wild life and wreak untold havoc in the environment as a whole.

I do not have to tell this audience that this extreme view is nonsensical and irrelevant to our purpose. What is relevant however, is that by definition pesticides are toxic compounds - they would be useless if they were not - they do present certain hazards under certain conditions to man and his environment, but it is necessary, and will be for at least the next decade, to use them in the control of agricultural pests and disease vectors. But clearly the use and usefulness of these compounds is threatened by the increase in resistance and the manufacturers are just as concerned as the rest of us about this problem. The cost of developing a new pesticide today, from initial discovery to marketing, is of the order of 20-25 million dollars. To recoup this expenditure and make a profit, the chemical has to continue to sell for a number of years - four to five at least; if its useful life span is reduced by resistance, these costs will not be covered and this is one reason why fewer new compounds are coming onto the market today, the economic risk being too great. This is a serious problem in relation to the strategies to be developed to delay the onset of resistance, because one of these, as you will hear later, is to rotate the use of several compounds in a given situation so as to minimise the overall selection pressure due to a particular compound. But if sufficient alternative compounds are not available then this strategy cannot be used. It is precisely this situation which faces the WHO Onchocerciasis Control Programme in West Africa, probably the largest single campaign against a human disease vector, the

blackfly Simulium damnosum, ever to be undertaken. I only need say here that resistance has appeared in one of the vector subspecies and alternative insecticides have had to be used; if resistance appears to the present compound, then it is unlikely that the programme can continue because further suitable alternatives are not available. So the difficulties of industry, in maintaining a flow of new compounds, are also part of the overall problem.

There are other tactics to delay the onset of resistance, which include the development of more selective compounds, the development of more efficient application methods which allow the amount of active ingredient applied to be reduced, and the formulation of compounds in a way which minimises damage to natural enemies; but all these require the active co operation of industry and we therefore welcome the GIFAP representative here as an important partner in the collanorative effort we are seeking to develop.

Before going on to sum up the objectives of this workshop I want to mention one more point. In our programme we are dealing exclusively with the problems of animal pests - insects and rodents for example, which are pests of agriculture and vectors of human disease. But it is worth remembering that resistance has now also appeared both to fungicides and herbicides and the instances of these are also increasing. Indeed, considering the biological basis of resistance, it seems likely that whenever any control measure is applied at such a level and over a long enough period to apply sufficient selection pressure to a pest population then resistance will appear. This means that even in the case of biological control, or the use of semio-chemicals which control pests by modifying their behaviour, it is possible that resistance, in this case in the form of altered behaviour patterns, could appear.

Pesticide resistance therefore poses a very dangerous and widespread threat to pest control as a whole and it is essential that practical steps be taken now to delay its onset and limit

its growth on a global basis. It is no exaggeration to say that if this cannot be done, and done fairly quickly, there will be very serious consequences in the not too distant future in the form of higher losses in world food production and higher rates of mortality and morbidity due to vector borne diseases.

I have explained already the need to concentrate on a practical approach and I have therefore formulated a series of objectives for the workshop which I hope will be useful in orienting our discussions, particularly in relation to the work of the drafting groups.

The objectives are as follows:-

- (a) To consider the relationship between the use of pesticides for agricultural pest and disease vector control in relation to the problems of the development of pesticide resistance;
- (b) To consider the techniques and strategies available to limit or reduce pesticide resistance in the future;
- (c) To make recommendations for action including further research and demonstration as regards policy and practice, to implement these strategies in international and national operations;
- (d) To publish these recommendations and bring them to the attention of governments, international agencies and the agro-chemical industry for consideration and appropriate action.

This is a formidable task and it can only be done with political support in the countries concerned, but, as I have tried to show, it is a very important one. If we can together develop this week the outline of a practical collaborative programme to combat resistance this would be of major importance to the future of pest control in agriculture and public health.

2-0 PROCEEDINGS OF THE WORKSHOP ON RESISTANCE TO
INSECTICIDES USED IN PUBLIC HEALTH AND AGRICULTURE

2.0 INTRODUCTION

2.0.1 The development of resistance to insecticides in agricultural pests and public health disease vectors is not a new phenomenon. It was first recorded as far back as 1908 but began to be a serious problem from the late 1940's onwards, and by the early 1980's resistance had been reported in 260 agricultural pests and 168 species of insects of public health importance.

2.0.2 Because the appearance of resistance can cause considerable economic losses and can impede or bring to a halt national and international campaigns in plant protection and public health, both WHO and FAO became concerned, and in 1956 and 1963 respectively these organisations set up standing bodies to collect information on a global scale on the occurrence and spread of the problem, and to encourage and foster research both on the mechanisms involved and on the development of strategies and techniques to detect and overcome resistance.

The work of these bodies has been published in a number of WHO and FAO reports and there is in addition a considerable body of scientific literature on the subject. (See Appendices 4 and 5).

2.0.3 From information which has become available there are indications that the widespread use of insecticides in agriculture has in some circumstances induced resistance in certain insect

vectors of disease. From 1976 onwards FAO and WHO augmented their collaboration in an attempt to codify the data available on this point. It soon became evident that there were indeed severe **problems** which necessitated close cooperation between national ministries of Health and Agriculture; in general the need for this cooperation has been ignored and the problems arising in several countries were dealt with on an ad hoc basis by the two sets of ministries.

2.0.4 By the early 1980's the difficulties had reached a level in certain countries where decisions on the use of various insecticides in agriculture and public health required urgent attention. One of these countries was Sri Lanka, where in 1977 a governmental decision was taken to restrict the use of malathion to public health vector control only. This decision had repercussions on agricultural pest control in that country and it is also of interest to several other countries, both developed and developing, which faced similar problems.

2.0.5 In 1980, following meetings in Geneva and London between representatives of the National Science Council of Sri Lanka, the Centre for Overseas Pest Research in the UK and FAO and WHO, these organisations decided to sponsor an international workshop to bring together experts in agricultural pest control and public health vector control, both from Sri Lanka and other countries in the region, to discuss all aspects of the problem.

2.0.6 This workshop was held in Sri Lanka from 22 - 26 February 1982 and brought together international experts and national representatives from Sri Lanka itself and from Bangladesh, Burma,

China, India, Pakistan, the Philippines and Thailand. The list of participants and the programme of the workshop are given in Appendices 2 & 3. The objectives of the Workshop were :

- (a) To consider the relationship between the use of pesticides for agricultural pest and disease vector control in relation to the problems of the development of pesticide resistance;
- (b) To consider the techniques and strategies available to limit or reduce pesticide resistance in the future;
- (c) To make recommendations for action, including further research and demonstration, as regards policy and practice, to implement these strategies in international and national operations;
- (d) To publish these recommendations and bring them to the attention of governments, international agencies and the agro-chemical industry for consideration and appropriate action.

2.1 BACKGROUND TO THE RESISTANCE PROBLEM

2.1.1 As stated above, the occurrence of resistance to pesticides in agricultural pests was first recognised as far back as 1908 and became a serious problem in both agriculture and public health in the late 1940's. The spread of resistance and information on the mechanisms concerned has been documented for agricultural pests in the reports of the FAO Panel of Experts on Resistance and for public health vectors by the reports of the WHO Expert Committee on Vector Biology and Control.

2.1.2 At the time of this workshop a total of 432 species of arthropods had been reported as resistant to one or more classes of pesticide. As regards agricultural pest control, more than 260 species of pest insects and mites were resistant, and to these must be added a growing number of plant pathogens, rodents, snails, slugs and weeds. The situation as regards the relatively new systemic fungicides is that there are 81 known cases of pathogen resistance and the usefulness of these chemicals is now greatly impaired. There are already several cases of resistance to herbicides and it is probable that more will develop in time.

2.1.3 The FAO Panel has made a special study of resistance to pests of stored products and this showed an alarming situation. Using as test species eight genera of the most economically important insect species infesting stored products, the survey showed that in 92% of the 86 countries where sampling was done there was resistance to malathion, in 96% there was resistance to lindane, and in 41% resistance to phosphine. This widespread occurrence of resistance, and the consequent obstacle to control of infestation, accounts no doubt for the very high losses due to insect infestation in stored products worldwide.

2.1.4 The result of the rapid spread of resistance in agricultural pests has had a deleterious effect, both internationally and nationally, on plant protection programmes. At a time when a global effort is being made to increase world agricultural production the fact that some 30-40% of total production is lost due to pests and diseases is particularly serious, and the spread of pesticide resistance constitutes a severe obstacle to efficient pest control.

2.1.5 A similar situation obtains in relation to control of vectors of public health importance. Some 168 arthropods of public health importance are resistant to insecticides and the 22nd report of the WHO Expert Committee on Insecticides in 1976 stated that "the extension of .. resistance is steadily diminishing the choice of effective and economically feasible insecticides available for vector control. The current survey has revealed various degrees of practical difficulty ranging from inconvenience and added cost (not a negligible factor in many countries) to severe difficulties in maintaining control, which in some cases had led to recrudescence and disease. It should be emphasised that the situation is steadily worsening and that no obvious single solution is in sight".

This state of affairs is particularly unfortunate in relation to the malaria problem, where there has been a large global increase in both the number of cases and the areas affected. This is due to a number of factors, but two important ones are the development of resistance to insecticides by 51 species of anopheline mosquito and the resistance of the malaria parasite itself to anti-malaria drugs.

2.1.6 Economic consequences of resistance

The consequences of the development of resistance in agriculture and public health costs a great deal of money. This is made up of direct losses of agricultural produce due to the reduced efficiency of pest control, indirect losses due to increased morbidity of agricultural workers due to the impairment of disease control, and other expenditure such as the use of higher dosages of pesticides in an attempt to delay the onset of resistance.

Total losses vary, of course, from country to country, but it has been calculated, for example, that these costs in the USA amount to 133 million dollars annually.

2.1.7 But there are other costs which affect different sections of the community. The world agro-chemical industry invests millions of dollars in producing pesticides and the cost of research, development and marketing is typically recouped over a period averaging eight years; if resistance renders the compound useless after less than this period then the company takes a loss. This has the effect of decreasing the total resources available for investment in R & D to produce new pesticides, which means that the supply of alternative compounds, essential to the strategy of resistance prevention outlined later in this report, will not be available.

This situation was put very clearly to the Committee for Agriculture of the US House of Representatives during a review of resistance problems in USA in 1981. "The loss of effectiveness of these chemicals is not being fully replaced by new materials, nor by alternative means of crop and livestock protection. Where for all major pests we once had a reserve of new chemicals to fall back on as resistance expanded, the lines of defence have now thinned in some cases to a single compound of declining effectiveness".

It will become clear in subsequent sections of these Proceedings that this situation has already been reached in several countries, with serious consequences.

2.1.8 It is clearly important therefore, from an overall economic viewpoint, to exert all possible efforts to delay or reduce the onset of pesticide resistance.

2.1.9 Benefits of pesticides

Pesticides remain one of the most powerful and dependable tools available for the control of pests. Indeed, they are in general the most effective and economical measure to reduce pest populations below damage thresholds. Their relative simplicity as a pest control technique for inclusion in crop production systems enhances their value. However the problems related to the use of pesticides, dealt with in later sections of these proceedings, has prompted the development of integrated pest control programmes, which permit the safest and most efficient use of pesticides.

2.1.10 The development of the synthetic organic persistent insecticides in the mid-1940's and their subsequent widespread use in public health campaigns were an immense benefit to human health and wellbeing. The use of DDT and other organochlorines enabled a number of countries to eradicate malaria from within their boundaries through residual applications to houses to control the anopheline vectors of that disease. Body louse vectors of typhus, flea vectors of plague and murine typhus and many other vectors were the targets of extremely successful control campaigns. The appearance and subsequent spread of insecticide resistance has for certain species necessitated a shift to OPs and eventually carbamates and pyrethroids, and finally increasing attention to integrated control, but the use of pesticides has greatly reduced the transmission of many of the vector-borne diseases including, as stated above, malaria, typhus, plague, onchocerciasis, filariasis, etc., and greatly contributed

to the wellbeing of human populations.

2.2 INTERACTION OF AGRICULTURAL PEST AND PUBLIC HEALTH VECTOR CONTROL

2.2.1 As mentioned in 2.0.3 above, as the resistance problem was studied in more detail by FAO and WHO and by independent scientists, the hypothesis was raised that the overuse or misuse of agricultural pesticides had contributed to the development of resistance in some disease vectors. The reason for this is that many different species of mosquito vectors of disease breed either in irrigation water or run-off water from fields. Contamination of this water with pesticides applied for agricultural pest control selects for resistance in mosquito populations. This led to closer cooperation between FAO and WHO in relation to the above hypothesis, but no special effort was made to collect evidence to prove or disprove the contention.

2.2.2 It was this situation that led to the initiation of the present workshop, the first objective of which was, (see para 2.0.6 above) "to consider the relationship between the use of pesticides for agricultural pest and disease vector control in relation to the problem of the development of pesticide resistance". The sponsoring bodies therefore arranged for a series of consultants to bring together the evidence available as regards this relationship, and the details of that evidence are given in Part IV of these Proceedings.

2.2.3 The evidence is marshalled under several headings as follows:

(a) appearance of resistance in a public health vector prior to application of a given chemical for the control of that vector

- (b) higher resistance in vector populations in agricultural than in non-agricultural areas
- (c) correlation between intensity of insecticide usage in agriculture and degree of resistance in an associated vector
- (d) fluctuation of the degrees of resistance in a vector in parallel with fluctuations in use of agricultural chemicals
- (e) correspondence between compounds to which vectors showed resistance and the compounds used in agriculture
- (f) temporary suppression of vector population densities in areas subjected to agricultural spraying.

2.2.4 Reviewing under these headings all the evidence available, including the reports of the situations in the various countries represented at the Workshop, as well as evidence from other countries produced by the consultants of FAO and WHO, *participants of the Workshop were unanimous in declaring that this evidence showed beyond reasonable doubt that in certain areas of the world the use of agricultural pesticides had induced resistance in a number of public health vectors.*

2.2.5 In making this important declaration, the participants emphasised that it did not apply to all disease vectors that had developed resistance, since many of these existed in ecological situations, such as domestic water containers or sewage pits, unaffected by agricultural pesticides. They pointed out, however, that the main danger zones were those in which large areas of crops were grown, such as cotton and rice, which required pesticide application to give economic yields, and which were also contiguous to vector breeding areas. Examples in which these areas are identical are irrigated cotton fields and rice paddys, in which several species

of vectors breed, particularly mosquitoes, and which are subject to several applications of pesticides to ensure high yields.

2.2.6 The Workshop also examined the data to see if there was evidence that application of vector control insecticides had induced resistance in agricultural pests, but only one minor case, possible induction of resistance in scale insects in an urban area by mosquito fogging application, was found.

2.2.7 Cooperation between Ministries of Health and Agriculture

The implication of the conclusion in para 2.2.4 above, confirming the interaction between agricultural pest and public health vector control in relation to the development and spread of resistance, is that it is essential to increase coordination in all countries between the government departments responsible for these pest control activities, usually the Ministries of Health and Agriculture.

How this is done is obviously a matter for the governments themselves to decide but the workshop felt that the minimal requirement was some mechanism, such as a joint committee, comprising administrators and technical representatives from the two ministries, which would discuss and agree on a pesticide management policy which would offer maximum opportunity for effective pest and vector control while at the same time minimising the development and speed of resistance. Such a body must have the necessary power to control the import and use of pesticides and regulate their employment in relation to agricultural pest and vector control.

Further details of the various courses of action desirable in this connection are given in Section 2.4 below.

2.2.8 Resistance monitoring surveys

In order that the coordination mechanism set up by the Ministries of Health and Agriculture can work properly, and without undue interference with the control requirements of both bodies, the Workshop pointed out that it was essential that all countries set up resistance monitoring surveys.

2.2.9 The importance of a continuous programme of resistance monitoring, not only for public health pests and vectors, but also for agricultural pests, cannot be too strongly emphasised. It is equally important, particularly in the public health field, that the laboratory and field evaluation of alternative insecticides should begin well before the onset of resistance makes currently used materials no longer effective. Field evaluation must be conducted in the locality or ecological zone where the main control operations are eventually to be carried out, as vectors can show considerable variation in their susceptibility to insecticides over their distribution range. Without a continuous flow of accurate information on the susceptibility of agricultural pests and public health vectors to the control chemicals in current use, the government departments concerned will be unable to plan for optimum pesticide usage and will not be able to put into practice strategies for preventing or delaying the onset of resistance which are outlined in Section 2.4 of these Proceedings.

2.2.10 Such a survey requires:

(a) an agreed programme stating the species to be tested, the

areas in which the tests are to be carried out and the frequency with which they have to be made

- (b) an appropriate national centre to be appointed as the insecticide resistance reference laboratory, whose function would be to confirm suspected cases of resistance, house standard susceptible strains for comparison testing, provide all necessary apparatus, equipment and standardised chemicals for the field surveys, register all tests carried out, and store, analyse and make available to the joint coordinating committee the data resulting from the tests.

These requirements can only be carried out if properly trained staff are available and all relevant information on insecticide resistance is centralised in the national centre; the following section deals with these requirements.

2.3 INFORMATION AND TRAINING

- 2.3.1 A large amount of information has been published by FAO, WHO and various national laboratories in both developed and developing countries on the protocols for field resistance surveys, the detailed conduct of resistance tests on particular species, the technical requirements for the necessary apparatus and chemicals, the storage and analysis of the data, the mechanisms of resistance and the strategies which can be employed to prevent or delay its onset.

- 2.3.2 Much information on all these matters is provided in the reports of the FAO and WHO statutory bodies dealing with resistance and a list of these publications is given in Appendix 1 to these Proceedings.

While all member countries of FAO and WHO are entitled to receive copies of such reports, the Workshop recognised that it was not possible for these organisations, partly for reasons of finance and partly because of protocol in certain countries, to provide copies for all personnel engaged in resistance work. The workshop therefore urged that member countries should take measures to equip their national resistance reference centre with all necessary documentation and should apply to FAO and WHO for information and assistance in this connection where necessary.

2.3.3 WHO has developed resistance testing kits for field use and a number of these have been distributed to various national laboratories to assist in the development of resistance surveys. However, it is not possible for WHO to provide kits free of charge to all national reference centres, but it would be prepared to give advice on the use and contents of such kits.

One major problem concerning resistance tests was the need for standardised chemicals and reagents, and the supply of technical grade pesticides and impregnated papers for the basic tests. While much of this could be provided by national laboratories, the question of quality control was crucial to accurate testing and WHO agreed to investigate the needs and problems of the supply of the necessary materials and consult with the agro-chemical industry to see if they could help.

2.3.4 In relation to the carrying out of resistance surveys, and the necessary cooperation of farmers and growers, it was suggested that the responsible government departments consider the need for supplying information through appropriate mass media - the press,

radio, TV and via technical advisory leaflets made available to farmers, on the importance of resistance testing and the need for cooperation with the relevant ministries. As mentioned above, resistance can cause severe economic problems and if this is explained it is likely to enhance cooperation and collaboration.

2.3.5 The conduct of resistance surveys requires adequately trained staff, and the Workshop felt it was of great importance to ensure that adequate training facilities were available both on a regional and a country basis. To this end, FAO and WHO agreed to investigate the possibility of their providing jointly regional training courses in all aspects of the resistance problem for personnel who would then return to their own country and set up in-country training programmes for all grades of local staff. FAO and WHO would consider providing expert assistance for these in-country training courses.

2.4 PRACTICAL MEASURES WHICH CAN BE ADOPTED NOW

2.4.1 The preceding section stressed the importance of setting up resistance surveys as a basis for development of measures to prevent or delay the onset of resistance, but the workshop stressed that this is only one basic approach open to governments.

The resistance phenomenon is only one aspect of the problems facing those responsible for agricultural pest and vector control, which involves the usage of pesticides in every sense - economic, ecological and environmental. In this section therefore the workshop outlined both policies and practical measures which they urge governments to consider in relation to their particular problems.

2.4.2 Pesticide management policy

It is essential that governments develop rationally-based pesticide management policies covering the use of pesticides in agriculture and public health. This should have the objective of promoting the economic, safe and effective use of pesticides, minimising their adverse effects and, most important in the context of resistance management, prolonging their effective working life. Sound pesticide management will require the close collaboration of official bodies concerned with agriculture and public health, as well as research institutions and commercial organisations. Pesticide management policies should be implemented through pesticide registration legislation, pesticide regulation, import policies and recommendations for pesticide usage. In addition to the management of resistance other aspects such as spray operator safety, pesticide residues and environmental contamination should be covered by pesticide management policies.

It is now evident that in a number of instances the use of particular insecticides in agriculture has resulted in vector resistance. There is little or no evidence of the reverse occurring. There is therefore a need, in formulating pesticide management policies, to consider whether, in the agricultural system, usage could lead to development of vector resistance. Situations where mosquitoes breed in irrigation or water run-off canals are particularly likely to favour development of resistance. Where agricultural usage of a chemical may give rise to vector resistance, it may be necessary to remove certain insecticides from agricultural usage and restrict them to the public health sector.

2.4.3 Pesticide usage in public health and agriculture

There are important differences in the way pesticides are used in public health and agriculture which need to be taken into consideration in formulating pesticide management policies. In public health vector control the target species are usually limited in number and the pesticides used are similarly limited. The procurement and usage of pesticides is usually centrally organised and supervised in public health operations and pesticide residues are not left, as is sometimes the case in agriculture, on export commodities. In agriculture, by contrast, target species are numerous, as are the crops on which they occur, and pesticide purchase and usage is usually the responsibility of private firms or groups of farmers. This leads to considerable variation in the types and qualities of pesticides used and their frequency of application.

2.4.4 Importance of integrated pest management in agriculture

The most effective way of delaying the onset of resistance is to reduce the selection pressure on the pest population. In the agricultural context the more rational use of pesticides can be brought about by the introduction of integrated pest management systems in which all possible non-insecticidal control factors are maximised and the application of pesticides is minimised.

2.4.5 Damage thresholds in agriculture and public health

The concept of the economic damage threshold is now more and more accepted in agriculture as a criterion for decision-taking in pesticide usage. Central to the concept is the fact that damage up to a certain level can be accepted on crop plants, indeed in

many instances control would otherwise not be economic, and in other cases the crop itself can compensate for some losses. In the public health field these concepts are irrelevant as no level of disease transmission or mortality above zero is readily acceptable. However, as it is rarely possible to achieve extremely high levels of vector control, let alone eradication of a disease, the objective must be to establish targets for the achievement of a given percentage reduction in transmission over a certain period of time and to plan the control campaign accordingly in line with funds and personnel available.

2.4.6 Pesticide management policy in practice

It is not possible to generalise about most aspects of pesticide management policy as variations in local circumstances will necessitate a national approach, and in many cases further research is required before rational decisions can be taken. However on the basis of present knowledge, it is possible to make positive statements about alternatives to pesticides, about the use of DDT, BHC and certain organophosphates and also about the best policy on larviciding and adulticiding.

2.4.7 Alternatives to pesticides

The Workshop discussed various aspects of pesticide use in public health and agriculture in South and South East Asia and it emphasised the following points:

- (a) there is an increased need for agricultural production in the area and in particular for rice growing, and this will lead to the further planting of high yielding varieties; this will be accompanied by an increased use of various inputs including pesticides;

- (b) many small farmers in the area use rather large amounts of a variety of pesticides, often under poorly controlled conditions;
- (c) for the control of malaria there has been a shift from eradication campaigns to control programmes. The latter requires the continuing application of control measures.

Because of the above, in the future there will be an increased use of control measures, especially pesticides, and this will increase the potential for the development of pesticide resistant disease vectors and agricultural pests. Moreover the increased use of agricultural insecticides may further enhance the development of resistance to insecticides in disease vectors.

2.4.8 The Workshop reiterated the earlier conclusions of research workers and expert meetings that reduction in selection pressure ie. reduced and/or selective pesticide usage, is the key factor to avoid or retard insecticide resistance development. Consequently, it strongly recommended that both in public health and agriculture increased efforts are made for the development and application of integrated pest control programmes. It discussed in detail various elements of such programmes and emphasised that the principle of economic damage threshold could not be applied to vector control. So far as malaria programmes are concerned, countries may adopt recognised tactical variants involving progressive reduction in mortality and incidence, with the final goal of eradication.

2.4.9 The Workshop discussed various elements of integrated pest control programmes and identified various priority areas for further action. It noted that in a serious effort to reduce our dependence on pesticides with all their attendant environmental complications,

more attention is now being paid to alternative methods of pest management. The workshop discussed the alternatives under the three major headings of environmental management, biological control and genetic control.

- 2.4.10 The development and application of alternative methods within the framework of integrated pest control programmes requires in the first place the adoption of a national policy aimed at the promotion of such activities. Adequate resources should be made available and where possible international collaboration and funding should be sought for support.

For agricultural pest control special efforts are needed for the elaboration of economic damage thresholds for major pest species, for the development of rather simple but reliable sampling methods and for the provision of adequate advice to farmers to monitor and evaluate pest populations.

2.4.11 Environmental management

As far as public health practices are concerned environmental management entails the avoidance of the creation of pest breeding grounds by good sanitation practices and water management. The first includes the proper disposal of waste food and excreta and the creation of proper, closed sewage systems. Water management involves the removal by disposal, drainage or filling-in of unnecessary water collections or by rendering of them unsuitable as breeding habitats for such pests as mosquitoes, by the removal where appropriate of marginal and floating vegetation. Other water management methods exist such as flushing, salinity changes, etc and may be locally appropriate. These methods may vary from species to species and one geographical area to another.

2.4.12 Environmental management for agricultural pest control ie: various cultural practices, have proven their effectiveness in reducing overall pest incidence. This includes practices such as stubble destruction at the end of the growing season, uniform sowing dates, crop rotation, limitation of crop growth to certain periods of the year etc. The usefulness of such practices depends in the first place on their application over relatively large areas and this requires therefore well organised community action.

2.4.13 Breeding for pest and disease resistant crop varieties has given excellent results. The introduction of such varieties within integrated pest control programmes can be a very effective means in reducing the need for pesticide applications. Moreover the distribution of seed of resistant varieties requires very little special effort and is readily acceptable to small farmers. But these varieties should of course possess identical or better characteristics compared to those normally grown in particular with respect to yield level, nutritional quality and taste.

2.4.14 Biological control

Cultural practices and resistant varieties are part of the efforts to decrease the overall level of pest incidence. In the same context classical biological control (the introduction of exotic parasites and predators) should be considered as well as the safeguarding of the naturally occurring parasites and predators. For example in rice growing it has been clearly proven that natural biological control is extremely important for keeping certain pest species below the economic damage threshold eg. plant and leafhoppers and rice whorl maggot. Thus, when applying insecticides every effort should be made to avoid disruptive action in relation to the existing natural enemy complex.

The deliberate application of microbial control organisms has been studied extensively during the last two decades, and in certain areas considerable progress has been made. However, successes have been limited mainly to lepidopterous pests (which are among the major pests in agriculture) and concern the use of *Bacillus thuringiensis*, certain nuclear polyhedrosis and granulosis viruses and the egg parasite, *Trichogramma* spp. Further research and development work is needed to augment the number of positive results and to make them applicable to small farmer conditions.

2.4.15 A number of potential biological control agents for the suppression of arthropods of medical importance exist. The control of mosquito larvae by predatory fish has long been practised and may be useful where water collections are of limited area and discreet. However the fish themselves have their own habitat preferences and cannot breed in all kinds of water. They are also subject to diseases themselves and can contribute to environmental damage in upsetting natural food chains. Pathogenic viruses, bacteria, fungi, protozoa and nematodes are under continuous investigation as biological control agents and some have reached the field trial stage. Most of them are larvicides however with their consequent limitations for the control of human diseases borne by the adults. Serotype H-14 of *Bacillus thuringiensis israelensis* is proving a boon however as a substitute for conventional insecticides in the control of *Simulium damonsum*, the vector of onchocerciasis in Africa. Here larval resistance to temephos and chlorphoxim has necessitated such a change. *Bacillus thuringiensis* is already commercially available and in use against mosquito larvae in America and southern Europe.

2.4.16 Genetic control

Control of some pests, eg. the screwworm, has been achieved in some areas by the release of sterilised flies but such a population suppression technique is difficult to apply to pests with high reproductive potential and in the field of public health might be limited to such insects as tsetse flies.

Genetic control research activities are still at a preliminary stage and enormous logistical problems remain to be solved before its large-scale application becomes practical; in general, genetic control seems to offer more promise for agricultural pest control than for public health vectors.

Population replacement techniques have potential for the re-introduction of genes for susceptibility to economic and efficient insecticides like DDT and HCH, and for the introduction of genes rendering vectors incapable of supporting the development of the pathogens of human, animal and plant diseases. Impetus to the approach comes from the recent discovery of genetic sexing techniques which will enable the mass production of the harmless sex (the male in the case of the mosquito for example). One present technique involves the translocation of an autosomal insecticide resistance gene on to the Y-chromosome; this makes the male mosquito resistant to the insecticide but his daughters susceptible.

2.4.17 Utilisation of DDT, BHC and certain organophosphates

DDT: Where it can be established that there is no resistance to DDT in the target vector population, then this compound should continue to be first choice in indoor situations. It should not be replaced with alternative compounds until resistance is

established in the laboratory, and field entomological and epidemiological experience show it is no longer effective. Where DDT is being used in public health programmes consideration should be given to withdrawing it from agricultural use, providing acceptable alternative compounds are available. The basis of this proposal is that until alternative environmentally acceptable compounds become available DDT remains the cheapest, safest and most effective compound for vector control for indoor use.

- 2.4.18 BHC: The same situation applies with BHC, which continues to have considerable potential for public health usage. In both cases adequate safeguards are necessary to avoid environmental contamination.

As regards the use of DDT and BHC in agriculture this must be regulated according to the pesticide legislation in each country.

2.4.19 Malathion and other organophosphates

Where DDT and BHC resistance has the effect of reducing the epidemiological impact of spraying operations in vector control operations to such an extent that a change of insecticide is strongly indicated then malathion should be the next insecticide of choice provided adequate field trials have confirmed the effectiveness of the compound. Malathion pressure is likely to select only Malathion resistance attributable to a carboxylesterase enzyme detoxifying mechanism and no cross resistance to other organophosphates, carbamates etc.

Where malathion has been the first organophosphate to be used for vector control, and where there has been no exposure of the mosquito population to other organophosphates as a result of agricultural usage, then the type of resistance that evolves is usually specific to malathion.

2.4.20 Where other organophosphates were first used against the mosquitoes, either directly through public health programmes, or indirectly through agricultural usage, then a broader type of OP resistance appears to emerge which includes a number of organophosphate compounds at various levels of resistance, and, in some cases but not all, malathion resistance is included in this spectrum of multiple resistance.

Therefore, because of the uniqueness of the type of malathion resistance that occurs when the compound is the first organophosphate to be used, it would be logical to give it first preference among compounds of this class in vector control programmes, assuming levels of resistance preventing effective use have not been established in laboratory and field programmes.

2.4.21 Larviciding and Adulticiding

Only a limited number of malaria vectors are subject to larvicidal control. This is carried out where circumscribed breeding sites allow a high level of control to be obtained by larviciding (eg. *Anopheles stephensi* where it breeds in wells, *An. annularis*, which breeds in stagnant water in cities and on city margins).

Generally, malaria control programmes should concentrate on adults since it is well established that selection pressure on larvae is more likely to result in resistance. However, where larval control is feasible, priority should be given to non-chemical methods eg. fish, *Bacillus thuringiensis* H-14, and environmental manipulation, but where a larvicide chemical must be used it is important that it should be a chemical not known to have any resistance to the original adult population.

2.5 AREAS REQUIRING FURTHER RESEARCH

2.5.1 During the Workshop discussions it became obvious that further knowledge was urgently required in certain areas in order to improve the present capability for rational design of control programmes both in agriculture and public health, especially if progress is to be made in coordination and formulation of a mutually acceptable pest control policy aimed at resistance limitation.

2.5.2 The three main areas requiring increased research effort can be classified under the following headings:

- (a) Further understanding of the background and mechanisms of resistance development, both in agricultural pests and human disease vectors, especially with regard to the impact of agricultural pesticide usage on resistance development in vectors.
- (b) Improvement of the susceptibility testing and resistance monitoring process by further development of standardised test methods in general and for agricultural pests in particular.

- (c) Development of new control strategies and materials aimed at limitation of exposure to selection pressure by each selecting agent, and hence also facilitating improvement in integrated control design.
- (d) Further developments of biological control techniques and agents.

2.5.3 The following particular items were identified under each of the above headings:

Under 2.5.2 (a)

- (i) Further investigation of comparative behaviour patterns, physiology, biochemistry and ecology of pest/vector species showing differential resistance development in the same area.
- (ii) Clarification of the implications of agricultural pesticide usage for resistance in disease vectors, with emphasis on those pesticides which are used only in agriculture. This would include the analysis and bioassay of water in mosquito habitats in agricultural areas.
- (iii) Investigation of the effect of continued use of pesticides on the succession of pest and vector species in particular ecosystems.
- (iv) Further clarification of the possible effects of low and sublethal dosages on evaluation of resistance.

Under 2.5.2 (b)

- (i) Continued improvement of standardised test methods both in agriculture and public health including the further development of simple diagnostic tests.
- (ii) Development of improved sampling techniques possibly involving semio-chemicals.

Under 2.5.2 (c)

- (i) Trials of promising resistance-limiting treatment sequences, with appropriate evaluation procedures, should be carried out in selected control programmes, primarily of disease vectors.
- (ii) Investigation of the effects of various cultural practices such as crop rotation and/or closed season in minimising resistance development in agricultural pests.
- (iii) Further investigations of the feasibility of genetic control techniques.
- (iv) Further research on the efficiency of larvicide formulations of all types for mosquito control, including the use of chitin inhibitors.
- (v) The assembly of ecological data on major pests of important crops, together with estimates of their economic threshold level, in order to facilitate the rational design of integrated pest management systems.
- (vi) Further work is urgently required on the development of ovicides for the agricultural sector.
- (vii) Further research on synergists incorporated in pesticide formulations for reducing the impact of resistance.
- (viii) Continued investigation of the potential of mixtures of pesticides in resistance limitation.
- (ix) Continued improvement in application technology and pesticide formulation.
- (x) To provide early guidance in the planning of continued pest and vector control strategies, trials with potential replacement insecticides are recommended to assess the efficiency, applicability and methods of application under local conditions. However, realising that the feasibility of using such alternatives

is dependent on the nature of resistance developed in the populations, there is a need to establish early on the cross resistance spectrum of the resistant populations detected. Where feasible an attempt is needed to characterise early on the resistant population encountered.

Under 2.5.2 (d)

- (i) Further research on biological control agents and systems is essential, as described in Section 2.4.14 and 2.4.15 above.

2.6 PAPERS AND REPORTS PRESENTED TO THE WORKSHOP

2.6.1 The information presented to the Workshop varied from detailed research reports on several aspects of the resistance problem prepared by the consultants to country position papers. There was inevitably much duplication of information in the latter in, for example, the reporting of resistance to various insecticides in pests and vectors which had a wide geographical distribution, and hence it was agreed that in these Proceedings the country papers would be reduced to a precis of the relevant information.

An exception to this was made in respect of the contribution from Sri Lanka because these papers constitute an important case study of the interaction between agricultural pest and public health vector control.

2.7 RECOMMENDATIONS

2.7.1 The Workshop, although focussed on the interaction between agricultural pest and public health vector control, covered a large number of subjects relevant to this, ranging from requirements for government action to detailed proposals for further

research.

Many of the proposals made were too detailed to be put down in the form of recommendations, particularly as in any case for action to be taken the prior agreement and support of government departments will be required.

2.7.2 Since the majority of these detailed recommendations are dealt with in the text of the Proceedings in Sections 2.2 - 2.5 above, the Workshop placed particular emphasis on the following four recommendations dealing with the major areas in which action is urgently needed. These are:

- (a) Government action and coordination
- (b) Resistance monitoring surveys
- (c) Research requirements
- (d) Information and training

2.7.3 Government action and coordination

The Workshop, in light of its unanimous opinion that in certain areas and circumstances the use of agricultural pesticides had induced resistance in some public health vectors, strongly emphasised the need for increased collaboration between government departments concerned with agriculture and public health particularly in relation to:

- (a) the formulation and application of overall pesticide management policies designed to reduce resistance to pesticides
- (b) the development, application and enforcement of legislation governing pesticide usage in line with the agreed pesticide management policy.

2.7.4 Resistance surveys

The Workshop, pointing out that effective pesticide management policies could only be developed on a basis of accurate information on all aspects of the resistance problem, emphasised the need for continuous careful, standardised monitoring of the susceptibility status of insect pests to pesticides and recommended that -

- (a) appropriate national centres be appointed as insecticide resistance reference laboratories whose function would be to confirm suspected cases of resistance, house standard susceptible strains of the insects concerned, where possible, and provide standard solutions and impregnated papers of those pesticides not readily available to the field tester. They would also act as the national register of all susceptibility tests carried out and could be the venue for national training courses in monitoring techniques.
- (b) a mechanism be developed through which support can be provided to national centres and institutes for the monitoring of pesticide resistance, eg. through the provision of technical grade samples of insecticides. FAO and WHO are requested to study the setting up of such a mechanism and explore the possible cooperation with the pesticide industry.

2.7.5 Research requirements

The Workshop, recognising the gravity of the situation now faced by agricultural pest and disease vector control services in relation to the development of resistance to pesticide, and aware of the imminent serious consequences for agricultural production

and public health should the situation be allowed to deteriorate further, emphasised the essential need for close coordination of agricultural pest and disease vector control strategies.

There are many gaps in the knowledge required for rational operational design, especially in the areas of (a) understanding of the background and mechanisms of resistance development; (b) improvement of susceptibility testing and resistance monitoring services, and (c) development of new control strategies and materials aimed at resistance limitation.

The Workshop therefore recommended strongly that urgent attention be paid by international agencies and governments to the research and development needs detailed in Section 6 above.

2.7.6 Information and Training

The Workshop, recognising the great importance of adequate information on the resistance problem in general and on methods of survey and testing in particular, urged FAO and WHO and national governments to implement as far as is practicable the proposals made in Section 2.3 above, and particularly in respect of training noted with satisfaction the agreement by FAO and WHO to investigate the possibility of developing regional training courses linked to national in-country training courses.

[This Report was prepared by Dr. P.T. Haskell in consultation with members of the International Advisory Committee of the Workshop]

3-0 THE SURVEILLANCE OF PEST RESISTANCE TO INSECTICIDES
IN AGRICULTURE

by **George P. Georghiou**
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Since the first case was reported 67 years ago (Melander 1914), the phenomenon of resistance to pesticides has been the focus of much concern in both agriculture and public health. Cases of resistance in arthropod pests of crops, animals and man proliferated almost exponentially in the decades following the introduction of synthetic organic insecticides, leading to the current situation of at least 428 species that have developed strains resistant to one or more pesticides in areas where chemical control has been practiced intensively (Fig. 1). The

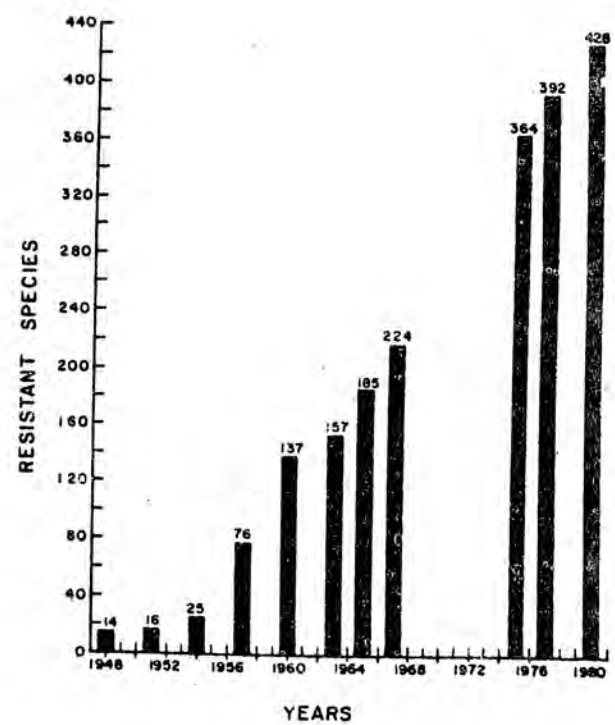


Fig. 1. Chronological increase in number of species of insects and mites that have developed strains resistant to one or more insecticides.

consequences of resistance have been primarily economic: Elevated crop losses are incurred before resistance is detected, and an increase in dosage or in the number of applications entails higher direct costs. Not only are the newer insecticides usually more expensive, but the prospect of resistance has discouraged more substantial investment in research and development of alternative chemical compounds. In several cases, multiple resistance (the ability of a pest population to resist

several unrelated chemicals) has raised the specter of depletion of choices from among the currently available effective chemicals.

In addition to its frequent occurrence in insects and mites, the problem of resistance is also encountered in plant pathogenic bacteria and fungi. It has especially affected the performance of systemically acting fungicides and bactericides (review by Ogawa et al. 1982). More recently, cases of resistance have appeared in a small number of weed species toward triazine herbicides (review by Gressel 1979). There are also early indications suggestive of some resistance in plant parasitic nematodes toward residual carbamate nematocides (Smolik 1978). Thus, resistance has emerged as a problem of actual or potential significance in all areas of pest control.

FAO PANEL OF EXPERTS ON PEST RESISTANCE TO PESTICIDES

The economic significance of resistance prompted FAO to establish a Working Party (subsequently, a Panel of Experts) on Pest Resistance to Pesticides, which has met periodically since 1965 to assess the extent of occurrence of resistance, to evaluate its significance, and to discuss measures for its avoidance or suppression. Lists of cases of resistance reported to FAO through surveys initiated by the Working Party were published in the 1967, 1969 and 1977 Reports of the Working Party (Table 1).

Table 1

MEETINGS AND REPORTS OF FAO PANEL OF EXPERTS ON PEST RESISTANCE TO PESTICIDES

	<u>Meetings</u>	<u>Reports</u>	<u>Reference</u>
1.	1965	1967a*	PL/1965/18 (106 p)
2.	1966	1967b	PL/1966/M/13 (8 p)
3.	1967	1968	PL/1967/M/8 (20 p)
4.	1968	1969*	PL/1968/M/10 (45 p)
5.	1969	1970	PL/1969/M/7 (5 p)
6.	1970	1971a	AGP:1970/M/9 (10 p)
7.	1971	1971b	AGP:1971/M/7 (19 p)
8.	1972	1973a	FAO Ag. Studies 91
9.	1973	1973b	AGP:1973/M/10 (17 p)
10.	1974	1974	AGP:1974/M/9 (28 p)
11.	1976	1977*	AGP:1976/M/10 (42 p)
12.	1978	1979	AGP:1979/M/2 (41 p)
13.	1980	1981	AGP:M/1981/2 (35 p)

*Contains lists of resistance cases.

A brief publication on "Pest Resistance to Pesticides in Agriculture: Importance, Recognition and Countermeasures" was prepared in 1970 (AGP:CP/26, 32 pp.). Subsequent publications sponsored by the Working Party include the results of a global survey of pesticide susceptibility of stored grain pests (Champ and Dyte 1976), a model extension leaflet on resistance of plant pathogens (Ogawa et al. 1979), and a consolidation of recommended methods for measurement of pest resistance (Busvine 1980). The latter contains detailed instructions for the determination of resistance in some major pest species and is proving of practical value to researchers in many countries (Table 2). A detailed account of the history and activities of the FAO Panel has been provided by D. F. Waterhouse, Chairman of the Panel since its establishment in 1963 (Waterhouse 1977).

Table 2

FAO RECOMMENDED METHODS FOR MEASUREMENT OF RESISTANCE
IN AGRICULTURAL PESTS TO PESTICIDES*

Acarina:	<i>Acarus</i> (19), <i>Boophilus</i> (7), <i>Panonychus</i> (10), <i>Tetranychus</i> (10)
Coleoptera:	<i>Leptinotarsa</i> (12), <i>Oryzaephilus</i> (15,16), <i>Rhyzopertha</i> (15,16), <i>Sitophilus</i> (15,16), <i>Tribolium</i> (15,16)
Diptera:	<i>Ceratitis</i> (20), <i>Dacus</i> (20), <i>Hylemya</i> (2), <i>Lucilia</i> (14), <i>Psila</i> (2), <i>Rhagoletis</i> (20)
Heteroptera:	<i>Distantiella</i> (9), <i>Lygus</i> (18), <i>Sahlbergella</i> (9)
Homoptera:	<i>Aphis</i> (17), <i>Myzus</i> (17), <i>Nephotettix</i> (5), <i>Phorodon</i> (17), <i>Therioaphis</i> (17), <i>Trialeurodes</i> (23)
Lepidoptera:	<i>Chilo</i> (3), <i>Ephestia</i> (22), <i>Laspeyresia</i> (11), <i>Plodia</i> (22), <i>Plutella</i> (21), <i>Spodoptera</i> (8)
Orthoptera:	<i>Locusta</i> (13), <i>Nomadaeris</i> (13), <i>Schistocerca</i> (13)

*Details in Busvine (1980), FAO Plant Production & Protection
Paper 21.

(Test number in parenthesis.)

DOCUMENTATION OF CASES OF RESISTANCE

The proliferation of information on resistance, both in terms of research findings on its mechanisms, genetics and dynamics, and on the specifics of its occurrence in pest species on various crops, has prompted the Panel of Experts to recommend that an advanced, comprehensive monograph on the subject be prepared. The writer and H. T. Reynolds at the University of California are currently in the process of preparing such a monograph with the collaboration of several experts in various pest groups. As a first contribution of this effort, an "Index" of all documented cases of resistance worldwide has been completed (Georghiou 1982). The statistics on the occurrence of resistance given in the present paper are derived largely from that publication.

The sources of information for the Index have been many and varied. Most helpful have been the three worldwide surveys of resistance conducted by the FAO Panel of Experts in 1965, 1968 and 1974, but several reviews were consulted extensively. Of considerable value were those by Brown (1958, 1971), Brown and Pal (1971), and Metcalf (1980), the survey of resistance in stored grain by Champ and Dyte (1976), and several reports by WHO committees on the occurrence of resistance in arthropods of medical importance (WHO 1970, 1976, 1980). Regional reviews on the presence of resistance, i.e., for Australia (Kerr 1977) and Japan (Asakawa 1975), and reviews dealing with specific groups of arthropods, e.g., acarina (Dittrich 1975) and beneficial species (Croft and Strickler 1982), were also valuable. In as far as it was possible, original reports and published papers were examined, especially those of more recent date. Included also were several personal communications and information from manuscripts in press provided by the authors.

It is realized that certain old cases of resistance involving obsolete chemicals, e.g., arsenicals, HCN, selenium, lime sulfur, etc., are no longer of practical significance. They have been retained, however, as evidence of the ability of arthropods to develop resistance to these toxicants as well. Likewise, low-level resistance in populations that have not remained under continued selection by the same or related chemicals may have regressed to non-detectable levels. However, in view of the known tendency of regressed resistance to be rapidly

re-selected, it was considered essential to retain all cases regardless of their present status.

It must be stressed that the inclusion of a case of resistance in these records does not imply that the chemical in question is no longer effective against that pest throughout the indicated country. There are numerous examples of continued effectiveness of a listed chemical in areas where selection pressure has been less severe. For example, organophosphate-resistant *Aonidiella aurantii* is found in a limited area of South Africa although good control continues to be obtained elsewhere in that country (Nel et al. 1979). Carbamate-resistant *Leptinotarsa decemlineata* is found on Long Island, New York (Semel 1980), and in Sherbrooke, Quebec, but not in London, Ontario (Harris and Svec 1981), and propoxur, fenitrothion and malathion resistance is common in populations of *Anopheles albimanus* along the Pacific coast of certain Central American countries but not on their Atlantic coast. In contrast, some species have developed resistance to certain insecticides almost throughout the world, as is the case with the house fly and DDT (WHO 1980) and with *Sitophilus oryzae* and lindane (Champ and Dyte 1976). Reports of the development of resistance in a species toward a certain chemical should be considered as a forewarning of the possibility of similar developments elsewhere. They also indicate conditions under which the species in question can develop resistance and may thus provide clues for the application of suitable resistance-delaying tactics.

The information in the Index is computerized and it is our intention to continue adding all newly reported cases to it so that supplements or updated editions could be issued periodically.

STATUS OF RESISTANCE

The present status of resistance in terms of numbers of species involved and classes of chemicals concerned is summarized in Table 3. The total number of species in which resistant strains appeared by the end of 1980 reached 428, of which 260 are of agricultural importance and 168 of medical or veterinary importance (Fig. 2). The largest number of resistant species of any class is found in the Diptera (153 species, i.e., 35.7%) (Table 3), reflecting the strong chemical selection pressure

Table 3

NUMBER OF SPECIES OF ARTHROPODA WITH REPORTED CASES OF RESISTANCE THROUGH 1980.

Order	Pesticide group						Importance		Total	(%)
	Dieldrin/ BHC	DDT	OP	Carb.	Pyr.	Other	Med./ Vet.	Agr.		
Diptera	107	106	60	11	6	1	130	23	153	(35.7)
Lepidoptera	40	40	31	14	8	2	-	64	64	(14.9)
Coleoptera	55	24	26	9	3	19	-	64	64	(14.9)
Homoptera	13	13	28	9	3	4	-	42	42	(9.8)
Heteroptera	16	8	6	-	-	-	4	16	20	(4.7)
Other Insecta	23	21	7	2	1	2	19	13	32	(7.5)
Acarina	15	17	42	6	1	30	15	38	53	(12.3)
Total (%)	<u>269</u> (62.9)	<u>229</u> (53.5)	<u>200</u> (46.7)	<u>51</u> (11.9)	<u>22</u> (5.1)	<u>58</u> (13.5)	<u>168</u> (39.3)	<u>260</u> (60.7)	<u>428</u>	(100.)

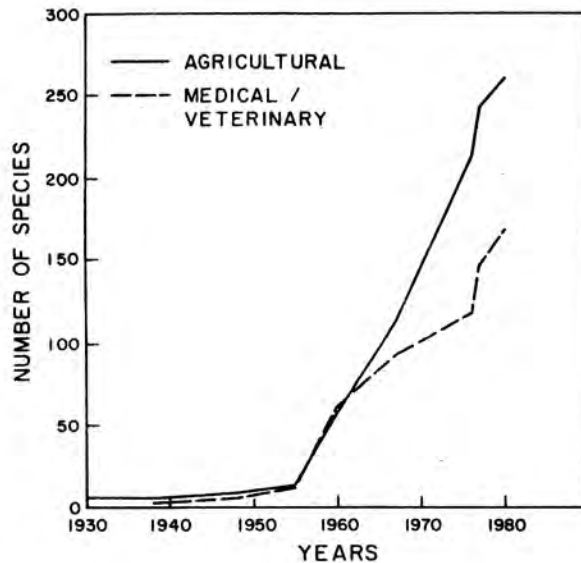


Fig. 2. Chronological increase in number of resistant species of arthropods of agricultural (—) or medical/veterinary (-----) importance.

that has been applied directly or indirectly against mosquitoes throughout the world. Substantial numbers of resistant species are also evident in such agriculturally important Orders as the Lepidoptera and Coleoptera (64 species each, 14.9%), Acarina (53, 12.3%), Homoptera (42, 9.8%), and Heteroptera (20, 4.7%). These species include many of the major pests, since it is against these that chemical control is mainly directed.

Viewed on the basis of the extent to which insecticide classes are affected, it is of interest to note that 62.9% of the resistant species can resist compounds of the cyclodiene group (dieldrin/BHC), but only 11.9% can resist carbamates and still less, 5.1%, can resist insecticides of the pyrethroid class (Table 3). As might be expected, during the decade 1971-80 greater percentage increases in resistance cases have occurred toward the relatively "new" classes of chemicals, i.e., carbamates (17-fold) and pyrethroids (7.33-fold), compared to organophosphates (3.7-fold), DDT (2.34-fold) and cyclodienes (1.92-fold) (Table 4).

Table 4

INCREASES IN CASES OF RESISTANCE DURING THE DECADE 1971-80

	1970 ^{a/}	1980	Fold increase '70-'80
Species with reported resistance	224	428	1.91
Cases ^{b/} of resistance by pesticide group			
DDT	98	229	2.34
Cyclodiene	140	269	1.92
Organophosphate	54	200	3.70
Carbamate	3	51	17.00
Pyrethroid	3	22	7.33
Fumigant	3	17	5.67
Other	12	41	3.42
Total for all pesticide groups	313	829	2.65

^{a/} Calculated from data in Brown (1971).

^{b/} Denotes number of species.

However, assessment of the growth of resistance merely in terms of the numbers of species involved strongly understates the problem in as much as these numbers do not reflect the extent of multiple resistance in a species, or other significant information such as increases in the frequency of resistance genes and geographic expansion of resistant populations. Multiple resistance is discussed in a later paper of this workshop in terms of the roles of the different mechanisms that are involved. Suffice to point out that of the 428 species that are resistant, 183 species can resist insecticides of more than one class, and 10 species can resist insecticides in all five available classes (i.e., DDT, cyclodiene, organophosphate, carbamate and pyrethroid) (Table 5).

Table 5

DEVELOPMENT OF MULTIPLE RESISTANCE TO INSECTICIDES

Year	All Resistant Species	Stages of multiple resistance*				
		I	II	III	IV	V
1948	14	13	1	0	-	-
1955	25	4	18	3	0	-
1969	224	155	42	23	4	0
1976	364	221	70	44	22	7
1980	428	245	95	53	25	10

*Species in stage I-V can resist insecticides belonging to 1,2,3,4, and 5 chemical classes, respectively (DDT, cyclodienes, organophosphates, carbamates and pyrethroids).

Data on the geographic extent of resistant populations and on the frequency of resistant genes often reveal some surprising situations. For example, resistance to dimethoate in the aphid *Myzus persicae* in Britain was found to be so generally distributed that of 258 collections that were examined, only three did not contain resistant individuals. With 196 collections, more than 76% of the aphids were resistant (Sawicki et al. 1978). Strains of the cattle tick *Boophilus microplus* that are multi-resistant to acaricides are widely distributed in Queensland (Roulston et al. 1981); the house fly is almost universally resistant to

DDT, and the green rice leafhopper (*Nephotettix cincticeps*) is resistant to several organophosphates and carbamates nearly throughout the area of its distribution in Japan (K. Ozaki 1981, personal communication).

The frequency of DDT-resistance genes in *Anopheles culicifacies* in India during 1970-71 was calculated to have been 0.34. In *Anopheles albimanus* in certain areas of El Salvador, the frequency of DDT- and propoxur-resistance genes during 1970-72 was found to be 0.80 and 0.48, respectively (Georghiou and Taylor 1976). Nearly complete homozygosity for esterases responsible for organophosphate resistance was noted in populations of the green rice leafhopper in Hiroshima Prefecture in 1968 (Kimura and Nakazawa 1973), in *Culex pipiens* on the south coast of France (Pasteur et al. 1980) and in *Culex quinquefasciatus* in areas of California (Georghiou 1982, unpublished).

Since this workshop will be concerned primarily with resistance problems in tropical and subtropical crops, the status of resistance in pests of cotton and rice is reviewed briefly below. These crops constitute the most important markets for insecticides, as shown in 1979 estimates of end-user dollar value of the leading crop pesticide sectors (Table 6).

Table 6

ESTIMATED END-USER DOLLAR VALUE OF THE LEADING
CROP PESTICIDE SECTORS --1979*

	- million dollars -
Maize herbicides	1,050
Cotton insecticides	975
Fruit and vegetable insecticides	900
Fruit and vegetable fungicides	860
Soybean herbicides	760
Rice insecticides	420
Maize insecticides	360
Cotton herbicides	350

*Braunholtz, 1981

Resistance in pests of cotton

In no other crop is pest resistance to pesticides as widespread as it is in cotton. Serious control difficulties are being experienced in Central and South American countries, in the U.S., Mexico, Turkey, Egypt, the Sudan, and elsewhere. Partly for economic reasons but undoubtedly also because of resistance problems, cotton crops were treated frequently with a large variety of pesticides over the relatively long growing season of four to six months. In many cases, insecticides are applied weekly, or more frequently, so that as many as 30 applications are not unusual. In Central American countries where cotton is grown during the wet season, repeat applications are often necessitated by rain. Indicative of the high degree of selection pressure that is exerted on pests of cotton are statistics which show that 40% of the insecticide used in the U.S. in 1980 was applied on cotton (Table 7). Worldwide, the value of insecticides applied on cotton in 1973 was estimated at \$975 million, the highest of any crop (Braunholtz 1981) (Table 6). Equally revealing are the records on the types and quantities

TABLE 7

CROPS' SHARE OF TOTAL PESTICIDES
USED IN THE U.S. IN 1980

Crop	Share of pesticides used	
	Insecticides	Herbicides
	- percent -	
Cotton	40	5
Corn	20	53
Soybeans	5	21
Wheat	5	6
Combined	70	85

Source: USDA 1981

of insecticides applied. In the area of Tapachula, Mexico, during the 1979/80 and 1980/81 growing seasons, 24 different insecticides were used to treat 28,000 hectares of cotton at an average rate of some 29 liters active ingredient per hectare (Table 8). Although methyl parathion and toxaphene were employed in the largest quantities, substantial amounts of parathion, monocrotophos, profenofos, methamidophos, mevinphos, sulprofos, mephospholan, DDT, chlordimeform and smaller amounts of carbamates and pyrethroids were also used.

TABLE 8

INSECTICIDES APPLIED ON COTTON IN TAPACHULA, MEXICO, 1979-81

Insecticide class	Compound	1979/80 (Liters, a.i.)	1980/81 (Liters, a.i.)
OPs	methyl parathion	369,626	340,800
	parathion	60,091	50,000
	monocrotophos	35,771	30,350
	profenofos	30,344	30,000
	methamidophos	14,441	21,880
	mevinphos	7,380	15,000
	sulprofos	7,589	14,400
	mephosfolan	1,773	10,000
	azinhosmethyl	2,595	4,000
	EPN	1,441	4,500
	dicrotophos	1,687	3,496
	dimethoate	684	
	omethoate		500
	Total	533,422	524,926
Cyclodienes	toxaphene	209,009	153,300
	endrin	4,896	3,797
	endosulfan	232	
	Total	214,137	157,097
Carbamates*	carbaryl	7,420	15,560
	bufencarb	688	
	Total	8,108	15,560
Pyrethroids	permethrin	2,314	5,200
	cypermethrin	660	1,300
	fenvaterate	529	690
	deltamethrin	60	50
	Total	3,563	7,240
DDT	DDT	44,388	60,000
Other	chlordimeform	24,450	25,000
GRAND TOTAL (liters)		828,068	789,823
Hectares treated		28,000	27,000
Liters a.i./HA		29.57	29.25

*Also methomyl, 7,740 Kg. 1979/80, 6,750 Kg. 1980/81.

The occurrence of resistance in pests of cotton is summarized in Table 9. At least 26 species are reported to be resistant, of which a high proportion (14 species) are Lepidoptera. Prominent among these are *Heliothis virescens*, *Spodoptera frugiperda* and *Spodoptera littoralis*, all displaying resistance to insecticides in the five principal classes (DDT, cyclodiene, organophosphate, carbamate and pyrethroid). Also notable is the high resistance to organophosphates in the cotton leaf perforator *Bucculatrix thurberiella* in the U.S. and the increasingly serious resistance to these insecticides in white flies (*Bremisia* and *Trialeurodes*) in a number of countries.

TABLE 9

INSECTICIDE RESISTANCE IN PESTS OF COTTON

Order	Species	Pesticide Group		Country
Acarina	<i>Tetranychus</i> spp.	DDT	OP	most countries
Coleoptera	<i>Anthonomus grandis</i>	DDT; Cyclod.		USA; Mexico; Venezuela
	<i>Eutinobothrus brasiliensis</i>	Cyclod.		Brazil
	<i>Graphognathus</i> spp.	Cyclod.		USA
Heteroptera	<i>Lygus hesperus</i>	DDT; Cyclod.;	OP	USA
	<i>Dysdercus peruvianus</i>	Cyclod.		Peru
Homoptera	<i>Bremisia tabaci</i>		OP	Sudan
	<i>Trialeurodes abutilonea</i>		OP	USA
	<i>Aphis craccivora</i>		OP	USSR
	<i>A. gossypii</i>	Cyclod.		Madagascar; USA; GDR; Peru
	" "		OP	China; Japan; USSR; Zambia
	<i>Empoasca biguttula</i>	DDT; Cyclod.	Carb.	French Polynesia Taiwan
Lepidoptera	<i>Estigmene acrea</i>	DDT; Cyclod.		USA
	<i>Pectinophora gossypiella</i>	DDT		USA; Mexico
	" "		OP; Carb.	Egypt
	<i>Bucculatrix thurberiella</i>	DDT		USA; Peru
	" "	Cyclod.		USA
	" "		OP	USA; Mexico; Peru
	" "		Carb.	USA
	<i>Alabama argillacea</i>	DDT		USA
	" "	Cyclod.		USA; Colombia; Venezuela
	<i>Anomis texana</i>	Cyclod.		Peru
<i>Cosmophila flava</i>	DDT; Cyclod.		Ivory Coast; Mali; Niger; Upper Volta	
<i>Earias biplaga</i>	DDT; Cyclod.		Madagascar	
<i>E. insulana</i>	DDT		Madagascar	
" "	Cyclod.		Israel; Madagascar; Spain (continued)	
Lepidoptera	<i>Heliothis armigera</i>	DDT		Australia; USSR; Thailand
	" "	Cyclod.		Australia; Portugal; Thailand
	" "		OP	Canada; Portugal; Australia
	" "		Carb.	Canada; USSR
	<i>H. virescens</i>	DDT; Cyclod.		USA; Colombia; Mexico; Peru
	" "		OP	USA; Mexico; Colombia
	" "		Carb.; Pyr.	USA
	<i>Plusia brassicae</i>	DDT;	Carb.	Barbados
	<i>Spodoptera exigua</i>	DDT; Cyclod.; OP		USA
	" "		Pyr.	El Salvador; Guatemala; Nicaragua
	<i>S. frugiperda</i>	DDT		Bolivia; USA; Venezuela
	" "	Cyclod.		Bolivia; Paraguay
	" "		OP; Carb.; Pyr.	USA
	<i>S. littoralis</i>	DDT		Egypt; Taiwan
" "	Cyclod.		Egypt; India; Turkey	
" "		OP	Japan; Egypt; Cyprus; Turkey; Israel	
" "		Carb.	Egypt; Japan	
" "		Pyr.	Egypt	
Thysanoptera	<i>Frankliniella occidentalis</i>	Cyclod.		USA

Resistance in pests of rice

The available records indicate that at least 12 species of insects attacking rice have developed strains resistant to insecticides (Table 10).

TABLE 10
INSECTICIDE RESISTANCE IN PESTS OF RICE

Order	Species	Pesticide Group	Country
Diptera	<i>Agromyza oryzae</i>	DDT; Cyclod.	Japan
Heteroptera	<i>Leptocorisa acuta</i>	Cyclod.; OP	Thailand
	<i>L. varicornis</i>	Cyclod.	Sri Lanka; Thailand
	" "	OP	Thailand
	<i>Scotinophora lurida</i>	Cyclod.	Taiwan
Homoptera	<i>Delphacodes striatella</i>	Cyclod.	Japan
	<i>Inazuma dorsalis</i>	DDT	Taiwan
	<i>Laodelphax striatellus</i>	Cyclod.	Japan
	" "	OP	Japan; Korea
	<i>Nephotettix bipunctatus</i>	DDT	Viet Nam
	<i>N. cincticeps</i>	OP	Japan; Korea; China; Taiwan
	" "	Carb.	Japan; Taiwan
	<i>Nilaparvata lugens</i>	DDT	Viet Nam
	" "	Cyclod.	Fiji; Taiwan; Japan
	" "	OP	Philippines; Viet Nam
	<i>Chilo suppressalis</i>	OP; Carb.	Japan; Taiwan
	" "	Cyclod.	Japan; Taiwan
	" "	OP	Japan; Taiwan; Korea
Lepidoptera	<i>Tryporyza incertula</i>	Cyclod.	China
	" "	OP	China; Taiwan

All such records concern countries of the Far East, but it is likely that resistance in rice pests occurs also in Central America but has not been investigated. Homoptera are by far the most important pests of rice and have been the target of intensive chemical control. The most serious resistance problems are found in the green rice leafhopper *Nephotettix cincticeps*, involving organophosphates (Japan, Korea, China, Taiwan) and carbamates (Japan, Taiwan). In Japan, where resistance in rice pests has been studied in considerable detail, field populations of *N. cincticeps* show resistance to parathion, methyl parathion, EPN, fenitrothion, diazinon, dimethoate, malathion, carbaryl and propoxur (Ozaki and Kassai 1971; Iwata and Hama 1971). Somewhat lower resistance to organophosphates is found in the smaller brown planthopper, *Laodelphax striatellus* in Japan and Korea. Another important pest of rice, the brown planthopper, *Nilaparvata lugens*, occurs in China and southeast Asia, but migrants reach Japan annually where they reproduce and cause economic losses. Organophosphate- and carbamate-resistant populations of this species were detected in Japan in 1977 (Ozaki 1978) following

the appearance of such resistance in Taiwan (Ku et al. 1977; Lin et al. 1979) and the Philippines (Heinricks and Valencia 1978). Since then, increasingly higher levels of resistance have been noted in the migrant population in Japan (Kilin et al. 1981).

Of much concern is the fact that a large part of the resistance to organophosphates and carbamates in *N. cincticeps* is due to reduced sensitivity of the target enzyme, acetylcholinesterase. This and other types of resistance that are based on reduced sensitivity of the site of action are often considered to be the result of selection pressure of a magnitude that exceeds the capacity of metabolic defenses in the insect.

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3-1 RESISTANCE PROBLEMS IN PUBLIC HEALTH VECTOR CONTROL, ON A GLOBAL BASIS, AND ARRANGEMENTS MADE FOR RESISTANCE SURVEY WORK

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Introduction

The development of resistance to pesticides in vectors of disease is now recognized as a major problem facing the control of vector borne diseases. The number of vector species resistant to insecticides and the size of the endemic areas affected by resistance continue to increase while new types of resistance and cross-resistance are also observed.

Although this situation has affected mainly malaria vectors, development of resistance in other vector species and rodent reservoirs of disease has also seriously impeded control campaigns and greatly added to their cost.

Present status of resistance

Although tabular recording serves as a useful indication of trends, the limitations to the information provided need to be recognised. Resistance is a dynamic phenomenon, developing at widely different rates in different species, and in the same species subjected to different conditions of insecticidal pressure.

Nevertheless the trends are clear with the development of multiresistance in several important vectors.

With the finding of DDT resistance in the sandfly Phlebotomus papatasi in Bihar State, India, the Tsetse fly remains the only important vector species in which resistance has not been reported.

The seriousness of the technical and financial problems faced in some malaria control programmes, due in part to the emergence of further spread of organophosphate resistance in Anopheles sacharovi, A.culicifacies, A. arabiensis, A.stephensi, and A.albimanus cannot be overemphasized. Similarly, organophosphate resistance in Aedes aegypti raises potential problems for the control of arbovirus disease outbreaks. In this regard, the cross-resistance to synthetic pyrethroids in several DDT-resistant arthropods, including A.aegypti, some strains of Musca domestica and the cattle tick Boophilus microplus, is an indication of the care that must be taken in the assessment and development of new insecticidal chemicals.

a) Anopheline mosquitos (Annex 1, Table 1)

Altogether, 51 species have been reported to be resistant to one or more insecticides: 34 are resistant to DDT, 47 to dieldrin and 30 to both DDT and dieldrin. Organophosphate resistance has been recorded in 10 species and resistance to carbamates in 4 species. In view of the importance of anopheline mosquitos and the implications for malaria control, organophosphate resistance has been characterized, where possible, by indicating, in Table 1 of Annex 1, the insecticides involved.

There have been many records of change in resistance status, of which the following appear to be of greatest significance.

A.sacharovi is now resistant to several organophosphate and carbamate insecticides in certain areas of Greece and Turkey, and to fenitrothion in some areas of Lebanon and the Syrian Arab Republic. Malathion, however, continued to be operationally effective in Turkey.

DDT resistance in this species has recently been discovered in the USSR.

A.culicifacies in Gujarat and Maharashtra States, India, is resistant to malathion, DDT and HCH, and in some instances also to fenithrothion. However, in Sri Lanka it remains susceptible to dieldrin/HCH and to malathion.

A.stephensi in India, Iran, Iraq and Pakistan has shown resistance to malathion.

A.arabiensis in Sudan has also been reported to be resistant to malathion. Resistance to permethrin has been selected out in the laboratory in A.stephensi, A.arabiensis and A.gambiae. Organophosphate and carbamate resistance in A.albimanus continues to spread in Central American countries and now affects parts of Mexico. A.sinensis has been found to be resistant to DDT, dieldrin/HCH and malathion in China. In Viet Nam it is reported to be resistant on DDT. A.superpictus has shown resistance to DDT in areas of the USSR from which malaria has been eradicated.

So far, the following vector species have not been reported to have developed resistance: A.darlingi, A.claviger, A.campestris, A.gambiae D, A.merus, A.moucheti, A.punctulatus, and A.koliensis.

In the case of several of the anopheline species which have been listed as resistant, confirmation of such status is required. This applies both to old records from areas in which no tests have recently been carried out, and to records from areas in which recent tests suggest the presence of resistance according to existing criteria but in which resistance has not yet been conclusively confirmed.

Such records, referring to some of the more important malaria vectors, include the following:

(1) Resistance to DDT:

A.balabacensis (Burma, Malaysia, Thailand): A.maculatus

(Malaysia, Thailand); A.minimus (Thailand); A.sergentii (Jordan);
A.sundaicus (Thailand); A.melas (Angola, Zaire).

(2) Resistance to dieldrin:

A.maculatus (Malaysia); A.minimus (Indonesia, Thailand).

(3) Resistance to organophosphates:

A.sergentii (Jordan); A.culicifacies (Oman, United Arab
Emirates); A.multicolor (Jordan); A.d'thali (Jordan); A.maculipennis
(Greece).

(4) Resistance to carbamates:

A.stephensi (India); A.maculipennis (Greece).

(5) Resistance to pyrethroids:

A.sacharovi (Turkey).

b) Culicine mosquitos (Annex 1, Table 2).

Altogether 42 species have been reported to be resistant to one or more insecticides, of these 37 are resistant to DDT, 27 to dieldrin/HCH and 23 to organophosphate insecticides. There have been several new territorial records of the spread of resistance. Table 2 of Annex 1 summarizes the available information. In view of the implications for control, organophosphate resistance has been characterized, where possible, by indicating the insecticides involved.

A.aegypti in many parts of Africa and Asia has developed resistance to organochlorine insecticides. In Malaysia and Viet Nam resistance to organophosphate insecticides is suspected but requires

confirmation. In Central America, resistance to DDT and HCH/dieldrin has been confirmed in almost all the areas of which A.aegypti eradication programmes have been operating. Low-level resistance to certain organophosphates has been observed in some Garibbean countries, but its operational importance needs confirmation. Cross-resistance to synthetic pyrethroids in DDT-resistant A.aegypti has been recorded in Thailand and suspected in Indonesia.

Culex quinquefasciatus, a major vector of bancroftian filariasis, is generally resistant to organochlorine insecticides and resistance to organophosphate insecticides is appearing in different parts of the world. Recently, resistance to organophosphate compounds has been recorded in India, Kenya and the United Republic of Tanzania, where it extends to chlorpyrifos, fenthion and temephos, which are the larvicides most commonly used against this vector. Low levels of resistance to chlorpyrifos have also been recorded in laboratory colonies from other countries - e.g., Brazil, Liberia and Sri Lanka. Resistance to synthetic pyrethroids has been selected in the laboratory in the USA. In Maldives, organophosphate resistance is suspected.

C.pipiens has been discovered to be multiresistant in many countries. In the laboratory this species has been shown to develop resistance to methoprene, the insect growth inhibitor. C.tritaeniorhynchus and C.gelidus, the major vectors of Japanese encephalitis, have now been shown to be resistant to DDT in Bangladesh; the former species is resistant to DDT, dieldrin/HCH and temephos in China. C.tarsalis, which was already multiresistant in the USA has been shown in the laboratory to develop resistance to methoprene.

c) Other arthropods of public health or veterinary importance (Annex 1, Table 3)

Among the records of resistance in other arthropods of

public health or veterinary importance, the most notable is the evidence of DDT resistance in Phlebotomus papatasi, in northern Bihar, India, which was under DDT spray for malaria control during 1953-62.

Resistance to DDT in the Simulium damnosum complex, members of which are the principal vectors of onchocerciasis in Africa, has been confirmed, using a new method of testing, in Benin, the Ivory Coast, Mali and Togo. The level of resistance varies from one locality to another, and a probable relationship between high-level resistance and intensive local agricultural practice or the treatment of rivers has been established. Reduction in susceptibility to temephos, the insecticide used in the Onchocerciasis Control Programme in West Africa has recently been detected. Resistance to DDT in S.hargreavesi, a nonvector species in Mali and Upper Volta, has also been reported.

The body louse (Pediculus humanus humanus) has developed resistance to DDT in virtually every area in which the compound has been used for control for any length of time. Resistance to HCH also occurs widely, and resistance to malathion has been found in Burundi and Ethiopia. A similar report of malathion resistance from Egypt has not been confirmed. Resistance of the head louse (P.h. capitis) is less widespread but organochlorine resistance has been reported from European as well as North American countries and South Africa.

Xenopsylla cheopis and X.astia have been shown to be resistant to DDT and, to a lesser extent, to dieldrin in Burma. In Indonesia, X.cheopis has been recorded as DDT-resistant in the Boyolali plague zone and elsewhere. In the United Republic of Tanzania, resistance to DDT in X. brasiliensis was observed in the field and it was subsequently selected to a high level in the laboratory. Stivalius cognatus, the field-rat flea, has been reported to be resistant to malathion in a limited area in Central Java, Indonesia.

In the housefly (*Musca domestica*), DDT and dieldrin resistance are generally widespread. Multiresistance, extending to several organophosphate insecticides with cross-resistance to carbamates, has been found in many countries. High-level pyrethroid resistance has been reported from several European countries, and it has been selected in the laboratory in the USA. Resistance to diflubenzuron, the insect growth regulator, also has been selected in the laboratory, and a wild organophosphate-resistant strain has been shown to be cross-resistant to methoprene, the juvenile hormone analogue.

Cimex hemipterus, which earlier developed resistance to DDT, has been shown to be also resistant to malathion in India and Sri Lanka. In both countries residual malathion spraying has been carried out for the control of malaria.

Resistance of Rhodnius prolixus to dieldrin has been confirmed only in Trujillo State in Venezuela, where low levels of tolerance to fenthion and propoxur have also been noted, but the species continues to be susceptible to fenitrothion. Earlier suspicions of resistance to dieldrin in Triatoma maculata in Venezuela have not been confirmed.

Resistance to malathion and propoxur in Blattella germanica has been found in the USA, and to chlordane, propoxur and malathion in Canada, where, however, the species continues to be susceptible to chlorpyrifos and diazinon. Recently, field strains of B.germanica were found to be resistant to bendiocarb in the United Kingdom but continued to be susceptible to fenitrothion. In the USSR, decreased susceptibility to pyrethroids has been observed, probably as a result of the regular use of these compounds in disinsection in recent years.

Resistance in the two- and three-host ticks Rhipicephalus evertsi and R.appendiculatus has become of increasing importance in southern and eastern African countries following the earlier

development of resistance to arsenic, organochlorine and organophosphates in the one-host tick Boophilus decoloratus. A serious resistance problem with B.microplus in Australia and southern American countries, but has been alleviated by the introduction of amidine compounds, to which no resistance has developed. Cross-resistance to the synthetic pyrethroids has been recognized in DDT-resistant B.microplus in Australia.

Earlier records of resistance to DDT and dieldrin in Amblyomma americanum and Dermacentor variabilis are now considered of doubtful significance. In the dog-tick, Rhipicephalus sanguineus, resistance to dioxathion has recently been reported from Kenya.

d) Nontarget organisms

Selective pressures from agricultural contamination have resulted in the development of a population of the mosquito fish (Gambusia affinis) resistant to organochlorine insecticides in the Mississippi delta area in the USA, which has a long history of insecticide use.

There seems to be no further addition of our knowledge concerning such nontarget organisms as cladocerans (Daphnia and Moina), copepods (Cyclops), mayflies, damselflies, notonectids and dytiscids.

e) Resistance in reservoirs and intermediate hosts of disease

Rodents. Anticoagulant resistance in the Norway rat (Rattus norvegicus) has now spread in the USA to more than 40 cities in 20 states, and in the roof rat (R.rattus) in 9 cities in 4 states. In France, near Marseilles, it has been discovered that R.rattus is resistant to coumafene, a hyseoxycoumarin anticoagulant. Resistance to warfarin in R.norvegicus, R.rattus

and the house mouse (Mus musculus) has been well documented in Canada and the United Kingdom, resistance to the anticoagulant difenacoum (one of a new series of 4-hydroxycoumarin anticoagulants) has been recorded in the laboratory in the warfarin-resistant Norway rat.

Snail hosts of schistosomiasis. Recently, some preliminary and possibly debatable evidence has pointed to decreased susceptibility of Bulinus truncatus from foci in Iran, which had been subjected to an annual treatment of niclosamide for about 10 years at a concentration of 1.0 mg/l. Moreover, field populations of B. truncatus exposed to trifenmorph in the Sudan have been shown to be more tolerant and take up the chemical more slowly than snails from untreated areas.

With regard to Oncomelania snail hosts, several studies have been undertaken by Japanese workers on resistance to molluscicides, mainly sodium pentachlorophenate (NaPCP). The results have been variable: some provide evidence of resistance, while others - even those relating to snail populations treated with NaPCP twice a year for more than 18 years - show no such evidence.

Fortunately, from the practical viewpoint there is still no definite evidence that snail hosts can develop serious resistance to molluscicides, nor have snail control operations yet been hampered by this phenomenon.

Impact of pesticide resistance on vector-borne disease control programmes

For the foreseeable future insecticides will likely remain the main (and in some cases the only) weapon in most vector-borne disease control programmes. The appearance of insecticide resistance to an increasing number of insecticides in an increasing number of vector species over geographically spreading areas has already had serious consequences to many

vector-control programmes. As emphasized in the WHO Expert Committee report (ibid) the change over has usually been from organochlorines to organophosphates and carbamates, or, in the case of larviciding programmes to insect growth inhibitors or biological control agents. The consequences of such a change over in the case of chemicals may include greater expense for the purchase of the more expensive alternative compounds, the necessity to apply them more frequently as well as increased risk to man and domestic animals due to higher mammalian toxicity. All of the above can result in considerably increased costs to governments for materials, transport, labour and increased precautionary measures.

Impact on malaria vectors in the South-East Asia Region

In the South-East Asia Region, An. culicifacies, the major vector of malaria in India, is broadly resistant to DDT in 114 districts, to HCH in 33 and to malathion in 2, involving a human population of 250 million. It is of significance to note that malathion resistance in this species has been detected in two additional districts where the compound is used in agriculture but not in public health. The urban vector of malaria An. stephensi has shown resistance to DDT in urban areas in which 13.5 million people live of whom 2.7 million are in areas of dual resistance to DDT and HCH. In Assam and Orissa, An. annularis is resistant to DDT and in Orissa to dieldrin as well.

Despite the insecticide resistance malaria rates have remained more or less constant in sprayed areas of India except for Maharashtra and Gujarat States. In these States malathion was applied in 1980 and 1981 and although small foci of malathion resistance were present, control was effective. Nevertheless the change to malathion has resulted in higher operational costs.

An. aconitus resistance in Central Java to DDT where the species is the main malaria vector, is of considerable concern. Spraying with DDT is of limited effectiveness and several

studies have been undertaken involving field trials of alternative insecticides ranging from village to area wide scales, the latter including epidemiological investigations. Despite its susceptibility to malathion this insecticide has not proven successful against An. acontus under the conditions of Central Java.

In parts of Nepal where An. annularis is the vector of malaria both that species and a suspected vector An. culicifacies are resistant to DDT and dieldrin. Transmission in the areas of resistance has more than trebled and a shift has been made to malathion on a selective basis.

DDT resistance in An. culicifacies in Sri Lanka led to the use of malathion and fenitrothion which were effective in reducing the incidence of P. falciparum malaria. As is well-known the use of malathion for agricultural pest control has been banned at the request of the anti-malaria campaign.

Despite the pressure of DDT-resistant populations of An. annularis in Akyab and An. balabacensis in Moulmein DDT continues to be used for residual spraying in both areas of Burma at one round a year.

Impact on malaria vectors in the Western Pacific Region

In the Western Pacific Region the primary vectors of malaria are still susceptible to DDT with the exception of An. sinensis - a major vector in China. This species is resistant to organochlorine and organophosphate compounds in rice-growing areas where considerable use is made of agricultural pesticides.

There are reports of secondary vectors of malaria being resistant to DDT in Viet Nam, but few details are available.

The impact on other mosquito vectors of disease

In the Western Pacific Region the vectors of Japanese Encephalitis, Cx. tritaeniorhynchus and Cx. gelidus, although resistant to organochlorines and some organophosphates in Japan and the Republic of Korea can still be controlled by ULV applications of pesticides. Chemical control of this species is, in any event, difficult and environmental and biological methods should be given high priority with the highest being given to investigations on the efficacy of intermittent irrigation against vector populations and its effect on rice production.

As shown above, organochlorine resistance is very widespread throughout both the Western Pacific and S.E. Asian Regions in two of the most important vectors of disease - Ae. aegypti and Cx. quinquefasciatus. For the time being it is still possible to effectively control Ae. aegypti with temephos sand granules against the larvae and malathion and other organophosphate space sprays against the adults - the latter method is increasingly used during outbreaks of DHF. Due to cross-resistance with DDT it appears that it will be unlikely that the pyrethroids could be considered as an alternative group should broad resistance to the OPs evolve.

The high potential for resistance in Cx. quinquefasciatus populations make it imperative that routine susceptibility testing be an active component of any chemical control programme. It is, however, almost inevitable that in the long-run resistance will develop in any population of this species to most larvicides being used against them. Since any filariasis vector control programme must be carried out for well over 10 years so as to allow for the death of the adult worms in the human population, long range planning of a likely sequence of insecticides should be carried out at a very early stage of the programme.

The recent recrudescence of visceral leishmaniasis (Kala-azar) in India is, no doubt, related to the earlier reduction of malaria

control sprayings in the same area and the recovery of the vector populations. Unfortunately, the fact that the main vector, Phlebotomus papatasi has now developed resistance to DDT has very serious consequences for any future control campaign which may be aimed against this vector. It was possible to contemplate a limited DDT residual spray programme aimed solely against sandflies in view of the low cost, high margin of safety and long persistence of this compound. Should it prove necessary to replace the organochlorines with an OP or carbamate the cost may prove to be prohibitive unless the concentration of cases is such that only a limited geographical area need be sprayed.

No louse-borne typhus or louse-borne relapsing fever has been reported for some time from any country in the Western Pacific or South East Asia regions; should such an outbreak occur there is no question that its control would be impeded by the widespread resistance of human body lice to the organochlorines in the two regions. Appropriate formulations of OP and carbamates have a mammalian toxicity as low as that of DDT in dusting formulations.

The occurrence of organochlorine insecticide resistance in flea vector population X. cheopis and X. astia has already impeded plague control operations in Viet Nam and elsewhere. The presence of malathion resistance in a population of S. cognatus in Indonesia in an area where this insecticide has not been applied for public health vector control is doubtless associated with contact of field flea populations and their sylvatic rodent hosts with agricultural pesticides. Relatively few tests have been carried out on rat flea susceptibility to insecticides and it seems likely that resistance is probably more widespread than has been reported.

Resistance survey activities

For over 20 years WHO has had a programme of monitoring the

spread of resistance based on the use of standard methods of measuring the susceptibility of vector species. Ways are continually being sought of streamlining the monitoring process so that the present strategies for the control of vectors and the diseases they transmit can be quickly adapted where required, to deal with new situations. The aim is to assist developing countries in forward programme planning, in making optimum use of current methods of vector control, and, where possible in adopting operational approaches which would tend to inhibit the emergence, growth, or further geographical spread of resistance.

With the provision of new reporting forms (Annex 2) together with the current codes for pesticides, insect species, and countries, and the introduction of map co-ordinates, attempts are being made to obtain more accurate information on detection, monitoring, extent and spread of resistance. Regional offices are being encouraged to carefully scrutinize all test reports coming from countries in their Region before despatching them to Headquarters.

Upon receipt of the reporting forms at Headquarters, and after checking the data, the reports are processed by computer, and a six-monthly feed-back will now be provided for Regional and country use.

In support of the above activity a new system of ordering and supply of test material has been introduced and appears to be working satisfactorily (Annex 3).

Instructions for the conduct of tests have been thoroughly revised, and are included in all test kits.

Annex 1

**INSECTICIDE RESISTANCE IN ANOPHELINE MOSQUITOS,
CULICINE MOSQUITOS,
AND OTHER ARTHROPOD VECTORS**

It should be noted that the following series of tables are based on data submitted to WHO or on other available evidence, which should not be taken as reflecting all-encompassing, worldwide information on insecticide resistance. The intensity of resistance may vary with season and year and may be strictly localized or widespread. For details, the reader should refer to published documents.

In view of the existence of subgroup cross-resistance within the organophosphates, the present records do not imply that all organophosphate compounds are ineffective against the species listed. In the column entitled "Organophosphates" in Tables 1 and 2, the common compounds affected are indicated as follows:

<i>x</i>	no precise knowledge
<i>a</i>	malathion
<i>b</i>	fenitrothion
<i>c</i>	parathion methyl
<i>d</i>	pirimiphos methyl
<i>e</i>	temephos
<i>f</i>	fenthion
<i>g</i>	jodfenphos
<i>h</i>	chlorpyrifos
<i>i</i>	chlorphoxim
<i>j</i>	phoxim
<i>k</i>	parathion

For the sake of convenience, a similar procedure has been adopted in the column "Other insecticides" in Tables 1, 2 and 3 to indicate the substances to which resistance has developed:

<i>l</i>	propoxur
<i>m</i>	pyrethroids
<i>n</i>	bioresmethrin
<i>o</i>	methoprene
<i>p</i>	carbamates
<i>q</i>	juvenoids

Table 1. Insecticide resistance in anopheline mosquitos in countries or areas

Species	DDT	Dieldrin/HCH	Organophosphates	Other insecticides
<i>Anopheles aconitus</i>	Indonesia	Indonesia	—	—
<i>A. albimanus</i>	Colombia, Costa Rica, Cuba, Dominican Republic, El Salvador, Guatemala, Haiti, Honduras, Mexico, Nicaragua, Panama	Belize, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, El Salvador, Guatemala, Haiti, Honduras, Jamaica, Mexico, Nicaragua	El Salvador (a, b, g, h, i, j, k), Guatemala (b, c, i, k), Honduras (a), Mexico (a, b), Nicaragua (a, b, i)	Costa Rica (l), El Salvador (l), Guatemala (l), Honduras (l), Nicaragua (l), Mexico (l)
<i>A. albivittatus</i>	Colombia, Brazil	Venezuela	—	—
<i>A. annularis</i>	Bangladesh, Burma, India, Nepal, Pakistan, Thailand	India, Indonesia, Nepal, Pakistan	—	—
<i>A. aquasalis</i>	—	Brazil, Trinidad, Venezuela	—	—
<i>A. arabiensis</i>	Senegal, Sudan, Swaziland	Chad, Ethiopia, Kenya, Nigeria, Madagascar, Mauritania, Mozambique, Senegal, Sudan, Swaziland, Upper Volta, Zimbabwe	Sudan (a)	Sudan (m)
<i>A. atroparvus</i>	Romania, Spain, USSR, United Kingdom	Bulgaria, Romania, Spain	Spain (a, b)	Spain (l)
<i>A. barbirostris</i>	Indonesia	Indonesia	—	—
<i>A. coustani</i>	—	Saudi Arabia	—	—
<i>A. crucians</i>	—	Dominican Republic, USA	—	—
<i>A. culicifacies</i>	Afghanistan, Burma, India, Iran, Nepal, Pakistan, Sri Lanka	Afghanistan, India, Nepal, Oman, Pakistan	India (a, b)	—
<i>A. c. adenensis</i>	Oman	—	—	—
<i>A. donaldi</i>	Malaysia	Malaysia	—	—
<i>A. d'thali</i>	—	Iran	—	—
<i>A. farauti</i> , sp. No. 1	—	Solomon Islands	—	—
<i>A. farauti</i> , sp. No. 2	—	Australia	—	—
<i>A. filipinae</i>	—	Philippines	—	—
<i>A. flavirostris</i>	—	Philippines	—	—
<i>A. fluviatilis</i>	India	Saudi Arabia	—	—
<i>A. funestus</i>	—	Benin, Central African Republic, Ghana, Kenya, Mali, Nigeria, United Republic of Cameroon, Upper Volta	—	—
<i>A. gambiae</i>	Benin, Central African Republic, Liberia, Niger, Nigeria, South Africa, Togo, United Republic of Cameroon, Upper Volta, Zaire	Benin, Central African Republic, Congo, Equatorial Guinea, Gambia, Ghana, Guinea, Ivory Coast, Kenya, Liberia, Madagascar, Mali, Mauritania, Nigeria, Senegal, Togo, United Republic of Cameroon, Upper Volta, Zaire	—	Nigeria (m—laboratory)
<i>A. hyrcanus</i>	Afghanistan, Turkey	Afghanistan, Turkey	Turkey (b, f, g, i, j)	—
<i>A. labranchiae</i>	Algeria, Morocco, Tunisia	Algeria, Morocco	—	—
<i>A. maculipennis</i>	Greece, Iran, Turkey, USSR	Greece, Turkey	Turkey (b, g)	Turkey (l)
<i>A. messeae</i>	Bulgaria, Romania, USSR	Bulgaria, Romania	Romania (a, f)	—
<i>A. minimus</i>	—	Indonesia	—	—
<i>A. multicolor</i>	Saudi Arabia	Saudi Arabia	—	—
<i>A. neomaculipalpis</i>	—	Colombia, Trinidad and Tobago	—	—
<i>A. nigerrimus</i>	Burma, India, Indonesia, Pakistan, Sri Lanka	Burma, Pakistan	—	—
<i>A. nili</i>	—	Ghana	—	—
<i>A. pedataeniatus</i>	Indonesia, Viet Nam	—	—	—
<i>A. pharoensis</i>	Egypt, Ethiopia, Sudan	Egypt, Israel, Sudan	—	—
<i>A. philippinensis</i>	India	Malaysia	—	—
<i>A. pseudopunctipennis</i>	Mexico, Peru	Ecuador, Guatemala, Mexico, Nicaragua, Peru, Venezuela	—	—

Table 1 (continued)

Species	DDT	Dieldrin/HCH	Organophosphates	Other insecticides
<i>A. pulcherrimus</i>	Afghanistan, Iraq	Pakistan, Saudi Arabia, Syrian Arab Republic	—	—
<i>A. quadrimaculatus</i>	Mexico, USA	Mexico, USA	—	—
<i>A. rangeli</i>	—	Venezuela	—	—
<i>A. rulipes</i>	—	Mali	—	—
<i>A. sacharovi</i>	Greece, Iran, Iraq, Lebanon, Syrian Arab Republic, Turkey, USSR	Greece, Iraq, Lebanon, Syrian Arab Republic, Turkey	Greece (b), Lebanon (b), Syrian Arab Republic (b), Turkey (b, f, g, h, i, j, k)	Greece (l), Turkey (l)
<i>A. sergenti</i>	—	Jordan	—	—
<i>A. sinensis</i>	China, Japan, Viet Nam	Republic of Korea	China (a), Hong Kong (a, b), Japan (a, f), Republic of Korea (b, f)	—
<i>A. splendidus</i>	—	Pakistan	—	—
<i>A. stephensi</i>	Afghanistan, Arabia, India, Iran, Iraq, Oman, Pakistan, Sudan	Afghanistan, India, Iran, Iraq, Oman, Pakistan, Saudi Arabia	India (a, b, g), Iran (a, b, g, i, j), Iraq (a, b), Pakistan (a)	Pakistan (m)
<i>A. strodei</i>	—	Venezuela	—	—
<i>A. subpictus</i>	Afghanistan, India, Indonesia, Nepal, Pakistan, Viet Nam	Afghanistan, Bangladesh, India, Indonesia, Pakistan, Sri Lanka	—	—
<i>A. sundaicus</i>	Indonesia, Malaysia	Indonesia, Malaysia	—	—
<i>A. superpictus</i>	USSR	—	—	—
<i>A. tessellatus</i>	Sri Lanka	India	—	—
<i>A. triannulatus</i>	Bolivia	Colombia, Venezuela	—	—
<i>A. turkhudi</i>	Afghanistan	—	—	—
<i>A. vagus</i>	Bangladesh, Malaysia, Nepal, Thailand, Viet Nam	Indonesia, Malaysia, Nepal, Philippines, Thailand, Viet Nam	—	—

Table 2. Insecticide resistance in culicine mosquitos in countries or areas

Species	DDT	Dieldrin/HCH	Organophosphates	Other insecticides
<i>Aedes aegypti</i>	In almost every part of the world in which this species is present, except certain African countries	—	Widespread in the Caribbean and neighbouring countries (a, b, e, f); India (a), Malaysia (a), New Caledonia (e), Solomon Islands (x), Thailand (e), Viet Nam (e)	Thailand (n)
<i>A. albopictus</i>	Democratic Kampuchea, India, Indonesia, Japan, Malaysia, Philippines, Singapore, Thailand, Viet Nam	India, Indonesia, Japan, Malaysia, Philippines, Thailand, Viet Nam	Madagascar (b, f), Malaysia (f), Viet Nam (e)	—
<i>A. atropalpus</i>	USA	—	—	—
<i>A. canadensis</i>	—	—	USA (h)	—
<i>A. cantans</i>	Czechoslovakia, Federal Republic of Germany	Czechoslovakia	—	—
<i>A. cantator</i>	Canada	Canada	—	—
<i>A. caspius</i>	Sudan	—	France (e)	—
<i>A. detritus</i>	France	France	France (e)	—
<i>A. dorsalis</i>	—	—	USA (a, f)	—
<i>A. lijiensis</i>	Fiji	—	—	—
<i>A. melanimon</i>	USA	USA	USA (a, f)	—
<i>A. nigromaculis</i>	USA	USA	USA (a, b, e, f, h)	—
<i>A. polynesiensis</i>	Tahiti and other parts of French Polynesia	—	—	—
<i>A. pseudoscutellaris</i>	Fiji	—	—	—
<i>A. sierrensis</i>	USA	—	—	—

Table 2 (continued)

Species	DDT	Dieldrin/HCH	Organophosphates	Other insecticides
<i>A. sollicitans</i>	USA	USA	USA (a, e)	—
<i>A. taeniorhynchus</i>	Grand Cayman, USA	Grand Cayman, USA	USA (a)	—
<i>A. togoi</i>	Republic of Korea	—	Republic of Korea (f, h)	—
<i>A. vexans</i>	Canada	—	USA (f)	—
<i>Armigeres subalbatus</i>	Japan, Malaysia, Sri Lanka	Japan, Sri Lanka	Japan (a), Sri Lanka (a, f)	—
<i>Culex coronator</i>	Panama	—	—	—
<i>C. erythrothorax</i>	USA	—	—	—
<i>C. fuscocephalus</i>	China (Province of Taiwan)	China (Province of Taiwan)	China (Province of Taiwan) (a, b, e, f, h)	—
<i>C. gelidus</i>	Bangladesh, India, Thailand	India, Thailand	—	—
<i>C. nebulosus</i>	—	Benin	—	—
<i>C. nigripalpus</i>	USA	—	USA (x)	—
<i>C. peus</i>	USA	USA	USA (a, e, f)	—
<i>C. pipiens pallens</i>	China, Japan, Republic of Korea	China, Japan, Republic of Korea	China (a), Japan (a, b, e, h), Republic of Korea (a, b)	—
<i>C. p. pipiens</i>	Albania, Bulgaria, Egypt, France, Greece, Iran, Iraq, Israel, Italy, Japan, Lebanon, Morocco, Republic of Korea, Turkey, USSR	Czechoslovakia, Egypt, France, Greece, Iran, Israel, Italy, Japan, Lebanon, Morocco, Republic of Korea, Tunisia, USSR, USA	Egypt (a, e, f, h), France (a, b, e, f, h), Israel (e, f, h), USA (a, e)	Iraq (f; o—laboratory)
<i>C. poicilipes</i>	Benin	—	—	—
<i>C. quinquefasciatus</i>	General	General	China (Province of Taiwan) (a), Guinea (a, b), India (x), Japan (a, e, h), Kenya (a, b, f, h), Madagascar (a, b, f), Maldives (x), Sri Lanka (x), United Republic of Cameroon (a, b), United Republic of Tanzania (x), USA (a, b, e, f, h), Viet Nam (a)	Kenya, Madagascar, United Republic of Cameroon, and USA (f); General (m, o—laboratory)
<i>C. restuans</i>	USA	USA	—	—
<i>C. salinarius</i>	USA	USA	—	—
<i>C. tarsalis</i>	USA	USA	USA (a, b, e, f, h)	USA (o—laboratory)
<i>C. tritaeniorhynchus</i>	Bangladesh, Benin, China (incl. Province of Taiwan), Japan, Nigeria, Republic of Korea	Benin, China (incl. Province of Taiwan), Japan, Nigeria, Republic of Korea	China (incl. Province of Taiwan) (e), Japan (a, f, h), Republic of Korea (a, b, f)	—
<i>C. vishnui</i>	China (Province of Taiwan)	China (Province of Taiwan)	China (Province of Taiwan) (a, e)	—
<i>Culiseta inornata</i>	USA	USA	USA (a, e, f, h)	—
<i>Mansonia annulifera</i>	Thailand	Thailand	—	—
<i>M. indiana</i>	Thailand	—	—	—
<i>M. uniformis</i>	—	Thailand	—	—
<i>Psorophora confinnis</i>	USA	USA	—	—
<i>P. discolor</i>	—	USA	—	—

Table 3. Insecticide resistance in other arthropods of public health or veterinary importance in countries or areas

Species	DDT	Dieldrin/HCH	Organophosphates	Other insecticides
Flies				
<i>Chrysomya putoria</i>	—	Madagascar, United Republic of Tanzania, Zaire	Zaire	—
<i>Culicoides furens</i>	—	Panama, USA	—	—
<i>Fannia canicularis</i>	Japan, Scandinavia, Spain, United Kingdom, USA	USA	USA	—
<i>F. femoralis</i>	USA	USA	USA	—
<i>Haematobia irritans</i>	—	USA	—	—
<i>Hippelates colusor</i>	—	USA	—	—
<i>Leptoconops kerteszi</i>	USA	USA	—	—
<i>Lucilia cuprina</i>	—	Australia	Australia	—
<i>L. sericata</i>	—	Lebanon, New Zealand, South Africa	—	—
<i>Musca domestica</i>	Generally widespread	Generally widespread	Malathion resistance is widespread. Resistance to other compounds is common in Australia (diazinon), China, (diazinon), Fiji, France (all compounds), Hong Kong (diazinon), India, Japan, Kuwait, Lebanon, Malaysia, New Hebrides, Northern Europe, Papua New Guinea, Senegal, Solomon Islands, Tunisia, USA	Czechoslovakia (p), Denmark (m), Finland (m), France (m), Federal Republic of Germany (m), Sweden (m), Switzerland (p), United Kingdom (q), USA (q)
<i>Phlebotomus papatasi</i>	India	—	—	—
<i>Protophormia terranova</i>	USSR	USA	USA	—
<i>Simulium aokii</i>	Japan	—	—	—
<i>S. damnosum sensu lato*</i>	Benin, Ghana, Ivory Coast, Mali, Nigeria, Togo	—	—	—
<i>S. fuscum</i>	USA	—	—	—
<i>S. hargreavesi</i>	Mali, Upper Volta	—	—	—
<i>S. ornatum</i>	Japan	—	Japan	—
<i>S. venustum</i>	Canada, USA	—	—	—
<i>Stomoxys calcitrans</i>	Federal Republic of Germany, Italy	Federal Republic of Germany, Norway, USA	—	—
Lice				
<i>Pediculus humanus capitis</i>	Canada, Denmark, France, Netherlands, South America, United Kingdom, USA	United Kingdom	—	—
<i>P. h. humanus</i>	Afghanistan, Burundi, Chile, Egypt, Ethiopia, France, Gaza Strip, Hong Kong, India, Iran, Japan, Libyan Arab Jamahiriya, Mexico, Peru, Republic of Korea, Romania, Sudan, Syrian Arab Republic, Turkey, Uganda, West Africa, Yugoslavia	Egypt, France, Hong Kong, India, Iran, Japan, Nigeria, Republic of Korea, Senegal, Sierra Leone, South Africa, Sudan, Syrian Arab Republic, United Republic of Tanzania, West Africa, Yugoslavia	Burundi, Ethiopia, Egypt (malathion)	—
Bedbugs				
<i>Cimex hemipterus</i>	China (Province of Taiwan), Gambia, India, Kenya, Madagascar, Malaysia, Singapore, Somalia, Sri Lanka, Thailand, Upper Volta	Benin, Gambia, India, Kenya, Madagascar, Malaysia, United Republic of Tanzania, Upper Volta	—	—
<i>C. lectularius</i>	Almost everywhere	Almost everywhere	Israel, USSR	—

Table 3 (continued)

Species	DDT	Dieldrin/HCH	Organophosphates	Other insecticides
Fleas				
<i>Ceratophyllus fasciatus</i>	USSR	—	—	—
<i>Ctenocephalides felis</i>	Colombia, Guyana, USA	Hong Kong, Japan, USA	—	—
<i>Pulex irritans</i>	Brazil, Czechoslovakia, Ecuador, Egypt, Greece, Peru, Turkey	Brazil, Czechoslovakia, Egypt, Turkey, United Republic of Tanzania	—	—
<i>Stivalius cognatus</i>	—	—	Indonesia	—
<i>Xenopsylla astia</i>	Burma, India	Burma, India	—	—
<i>X. brasiliensis</i>	United Republic of Tanzania	—	—	—
<i>X. cheopis</i>	Brazil, Burma, China, Egypt, India, Indonesia, Madagascar, Philippines, Thailand, Viet Nam	Brazil, Burma, Ecuador, India, Thailand, Viet Nam	—	—
Cockroaches				
<i>Blatta orientalis</i>	Czechoslovakia	Czechoslovakia, Federal Republic of Germany	—	—
<i>Blatella germanica</i>	Widespread	Widespread	Canada, USA	Canada (m**), USSR (m**), USA (m**)
Reduviid bugs				
<i>Rhodnius prolixus</i>	—	Venezuela	—	—
Ticks				
<i>Amblyomma hebraeum</i>	—	South Africa	South Africa	—
<i>A. variegatum</i>	—	Kenya, Uganda, United Republic of Tanzania, Zambia	—	—
<i>Boophilus decoloratus</i>	South Africa, Zimbabwe	Kenya, South Africa, Uganda, Zambia, Zimbabwe	South Africa, Zimbabwe	—
<i>B. microplus</i>	Argentina, Australia, Brazil, Venezuela	Argentina, Australia, Brazil, India, Malaysia, Trinidad and Tobago, Venezuela	Argentina, Australia, Brazil, Colombia, Venezuela	—
<i>Hyalomma marginatum</i>	—	Spain	—	—
<i>Rhipicephalus appendiculatus</i>	—	Kenya, South Africa, Uganda, United Republic of Tanzania, Zambia, Zimbabwe	South Africa	—
<i>R. evertsi</i>	—	Kenya, South Africa, Uganda, United Republic of Tanzania, Zambia, Zimbabwe	South Africa	—
<i>R. sanguineus</i>	—	Democratic Yemen, Kenya, Madagascar, Puerto Rico, Singapore, USA	Kenya	—

* See footnote 2 on page 12.

** Reduced susceptibility.

WHO TEST FOR INSECTICIDE RESISTANCE IN ADULT INSECTS
REPORT FORM FOR DETERMINATION OF LT₅₀

1-3 Study number:

4-8 Record number

*The boxes for the record number should be left blank, they will be filled in by VBC/WHO/HQ

9-32 Investigator:

33-35 Country:

Code:

36-47 Area:

48-59 Locality:

Map coordinates: 60-66 Longitude
Box 60 E or W

67-72 Latitude
Box 67 N or S

73-96 History of insecticide use

97-102 Date of test

Day

Month

Year

103-110 Insecticide tested:

Code:

Date of impregnation:

Date of removal from

No. of times

packet:

paper used:

111-119 Species:

Code:

120 Sex:

- Male: 1
- Female: 2
- Unsexed: 3

101 Where Collected:

- Sprayed shelters: 1
- Unsprayed shelters: 2
- Field: 3
- Laboratory reared: 4
- F₁ progeny: 5
- Other: 6

102 Condition of insect:

- Unfed: 1
- Blood fed: 2
- Sugar fed: 3
- Gravid: 4
- Unspecified: 5

123-125 Temperature* (°C)

126-128 Relative humidity* (%)

*The temperature and relative humidity should be recorded for the exposure period only.

129-133 Concentration of insecticide used

Exposure period

days

hours

mins.

no. dead

Total no. tested

% Mortality corrected

Control 134-144

145-155

156-166

167-177

178-188

189-199

200 Probable Insecticide Resistance Status

Criteria for diagnostic dosages

S: Susceptible

Mort. 98-100%

V: Verification required

Mort. 80-97%

R: Resistant

Below 80%

WORLD HEALTH ORGANIZATION



REQUISITION FOR ENTOMOLOGICAL SUPPLIES

Requisition No: _____
 Regional office: _____
 Authorized Signatory: _____
 Date: _____
 Debit Allotment No: _____

PLEASE READ THE INSTRUCTIONS BELOW BEFORE COMPLETING FORM

To: MSO or SSO (for checking correctness of address and allot. etc.)

Signature: _____
 Attention: HQ - VBC/PDS
 Approved by: _____ Prepared by: _____

To be sent to: (full address)

Delivery Ref. No: _____ (For HQ use)
 Date: _____
 Despatch by: _____
 Credit Allotment No: _____

Despatch by: Surface mail Air mail Pouch Air freight

Code Test Kit	Qty	Description	Est. value in Sw Fr. according to price list	Sw. Fr. Amount
(For HQ use) Total parcels: _____ Total weight kg: _____			Shipping cost	
			Total value Sw Fr	

IMPORTANT INSTRUCTIONS FOR COMPLETING FORM

THIS FORM MUST BE TYPEWRITTEN

- Please do not type anything in the spaces heavily outlined in black.
 - A form must be completed for each consignment.
 - Your requisition No. is essential as a reference.
 - The allotment No. must be clearly indicated. Its omission will result in the return of the requisition.
 - MSO or SSO who must clear each requisition should carefully check the allotment number and the address to which the goods are to be sent.
 - All shipments which include volatile solvents (alcohol, acetone, butanone) are automatically airfreighted. For other shipments, please indicate the despatch route.
 - The code of each test kit is specified in the price list.
 - Descriptions must indicate the name, of insecticide, the concentration and the number of packages or bottles of impregnated papers and solutions. One consignment cannot include more than 21 (50 ml) bottles due to restrictions on the transport of solvents.
- The estimation must conform with the price list. It will be corrected as necessary and the cost of shipping added.

WHO/VBC/81.8.29

CATALOGUE OF TEST KIT MATERIALS FOR DETERMINING
THE SUSCEPTIBILITY OF VECTORS TO PESTICIDES

PRICE LIST No 1
October 1981

IMPORTANT

Note 1. WHO Regional Offices and projects should order materials on form WHO 5397. Orders by telex or memorandum can only be accepted under exceptional circumstances.

Note 2. Equipment and/or insecticides may be ordered separately. Dichlorvos and other persistent fumigants, rodents kits are however only issued complete. The order should specify the concentrations and the number of boxes, sets of boxes, solutions or sets of solutions.

Note 3. Solutions containing volatile solvents are normally air freighted and in accordance with air transport regulations, the maximum volume of solvents allowed per parcel is 1 litre (i.e. twenty 50 ml bottles). The minimum air freight charge to be expected is S. Frs. 125.

WHO/VBC/75.593

COCKROACHES

Equipment as described in the instruction sheet

Complete Test Kit (including one bottle of each insecticide)

Insecticides in acetone (glass bottle 50 ml)

dieldrin 0.5% malathion 1.0% diazinon 5%
Control acetone only

VOLATILE SOLVENT. SEE NOTE 3 ON FRONT PAGE

DICHLORVOS AND OTHER PERSISTENT FUMIGANTS

WHO/VBC/75.594

Complete Test Kit as described in the instruction sheet
(including dichlorvos solution in butanone)

RODENTS

WHO/VBC/75.595

Complete Test Kit as described in the in the instruction sheet

ADULT MOSQUITOS ESTABLISHMENT OF THE BASE-LINE WHO/VBC/81.805

Equipment as described in the instruction sheet

Insecticides

OC papers impregnated with :

DDT 0.25% 0.5% 1% 2% 4%

deildrin 0.05% 0.1% 0.2% 0.4% 0.8% 4%

OC control papers

OP - carbamate papers impregnated with:
malathion 5% fenitrothion 1% propoxur 0.1%
OP - carbamate control papers

On special request with delivery time of at least two months,
papers impregnated with: bendiocarb 0.1% chlorphoxim 5%,
deltamethrin 0.025%, permethrin 0.25%, can be supplied for
research purposes.

Remark

Pirimiphos methyl impregnated papers have given variable results
and should test with this insecticide be necessary, WHO can
provide technical pirimiphos methyl, filter papers and a method
to prepare the impregnated papers locally.

ADULT MOSQUITOS-DIAGNOSTIC TEST

WHO/VBC/81.806

Equipment as described in the instruction sheet

Insecticides

OC papers impregnated with: DDT 4% dieldrin 0.4%

OC control papers

OP - carbamate control papers impregnated with: malathion 5%
fenitrothion 1% propoxur 0.1%

OP - carbamate control papers

On special request with delivery time of at least two months,
papers impregnated with: bendiocarb 0.1% chlorphoxim 5% deltamethrin
0.025% permethrin 0.25%, can be supplied for research purposes.

Remarks

Pirimiphos methyl impregnated papers have given variable results and
should test with this insecticide be necessary, WHO can provide
technical pirimiphos methyl, filter paper and a method to
prepare the impregnated papers locally.

MOSQUITO LARVAE

WHO/VBC/81.807

Equipment as described in the instruction sheet

Test Kit including 1 complete set of solution
2 complete sets of solution
3 complete sets of solution
4 complete sets

(Maximum allowed per Kit: five) 5 complete sets of solutions

Insecticides (alcohol used has been denatured by add:-
of 2% butanone)

malathion	781.25 mg/l	156.25mg/l	31.25mg/l	6.25mg/l
temephos	156.25mg/l	31.25mg/l	6.25mg/l	1.25mg/l
bromophos	31.25mg/l	6.25mg/l	1.25mg/l	0.25mg/l
fenitrothion	31.25mg/l	6.25mg/l	1.25mg/l	0.25mg/l
fenthion	31.25mg/l	6.25mg/l	1.25mg/l	0.25mg/l
chlorpyrifos	6.25mg/l	1.25mg/l	0.25mg/l	0.05mg/l

Control alcohol only

VOLATILE SOLVENT. SEE NOTE 3 ON FRONT PAGE

BODY LICE AND HEAD LICE

WHO/VBC/81.808

Equipment as described in the instruction sheet

Insecticides

OC papers impregnated with : DDT 4%, dieldrin 0.1%
OC control papers
OP papers impregnated with : malathion 5%
OP control papers

On special request with delivery time of at least two months papers impregnated with : deltamethrin 0.025% permethrin 0.25% propoxur 0.8% trichlorfon 1%, can be supplied for research purposes.

ADULT BED-BUGS

WHO/VBC/81.809

Equipment as described in the instruction sheet

Insecticides

OC papers impregnated with : DDT 4% dieldrin 0.8%

OC control papers

OP papers impregnated with : malathion 5% fenitrothion 1%

OP control papers

On special request with delivery time of at least two months papers impregnated with : deltamethrin 0.025% permethrin 0.25% propoxur 0.8% trichlorfon 1%, can be supplied for research purposes.

ADULT BLACKFLIES, SANDFLIES AND BITING MIDGES

WHO/VBC/81.810

Equipment as described in the instruction sheet

Insecticides

OC papers impregnated with :

DDT 0.25% 0.5% 1% 2% 4%

dieldrin 0.05% 0.1% 0.2% 0.4% 0.8% 1.6%

OC control papers

On special request

dieldrin 4%

on request

BLACKFLY LARVAE

WHO/VBC/81.811

Equipment as described in the instruction sheet

Test Kit including suitable equipment for 1 insecticide
2 insecticides
3 insecticides
4 insecticides
(Maximum allowed per parcel : four)

Insecticides (alcohol) used has been denatured by addition of 2% butanone)

DDT	625mg/1	125mg/1	25mg/1	5mg/1	1mg/1
methoxychlor	625mg/1	125mg/1	25mg/1	5mg/1	1mg/1
chlorphoxim	312.5mg/1	62.5mg/1	12.5mg/1	2.5mg/1	0.5mg/1
chloropyri-fos-					
methyl	"	"	"	"	"
pirimiphos-					
methyl	"	"	"	"	"
temephos	"	"	"	"	"

Control alcohol only

VOLATILE SOLVENT, SEE NOTE 3 ON FRONT PAGE

MOSQUITO LARVAE TO INSECT DEVELOPMENT INHIBITORS WHO/VBC/81.812

Equipment as described in the instruction sheet

Complete Test Kit (including one bottle of each insecticide

Insecticides (alcohol) used has been denatured by addition of 2% butanone)

methoprene	20mg/1	4mg/1	0.8mg/1	0.16mg/1	0.032mg/1
diflubenzuron	20mg/1	4mg/1	0.8mg/1	0.16mg/1	0.032mg/1

Control alcohol only

VOLATILE SOLVENT, SEE NOTE 3 ON FRONT PAGE

HOUSEFLIES, TSETSE, STABLEFLIES, BLOWFLIES ETC WHO/VBC/81.813

Equipment as described in the instruction sheet

Test Kit including suitable equipment for

1 insectide
2 insecticides
3 insecticides
4 insecticides
5 insecticides
6 insecticides
7 insecticides
8 insecticides
9 insecticides
10 insecticides

The composition of equipment depends
on the number of insecticides requested

(Maximum allowed per Kit : ten)

Insecticides in butanone (in glass bottle of 50ml) DDT 4%
lindane 2% malathion 8% fenclorophos 2% bromophos 2%
carbaryl 5% diazinon 1% dieldrin 1% propoxur 16% tetrachlorvinphos
2% dichlorvos 0.5% dimethoate 0.5% fenthion 1%
endosulfan 1.5% trichlorfon 5% permethrin 0.5%
deltamethrin 0.05%
Control butanone only

VOLATILE SOLVENT, SEE NOTE 3 ON FRONT PAGE

ADULT TICKS

WHO/VBC/81.814

Equipment as described in the instruction sheet

Test Kit including suitable equipment for : 1 solution
2 solutions
The composition of equipment depends on 3 solutions
the number of various insecticides requested 4 solutions

Insecticides in butanone (in glass bottle of 50ml)

DDT 10%	dieldrin 5%
malathion 10%	fenthion 5%

Control butanone only

VOLATILE SOLVENT, SEE NOTE 3 ON FRONT PAGE

FLEAS

WHO/VBC/81.815

Equipment as described in the instruction sheet

Insecticides

OC papers impregnated with : DDT 1% dieldrin 0.2%
OC control papers
OP carbamate papers impregnated with malathion 0.5%
fentrothion 1% propoxur 0.1% of carbamate control papers

On special request with delivery time of at least two
months papers impregnated with : trichlorfon 1% can be supplied
for research purposes.

Bio Assay on wall surfaces

VBC/81.5

Equipment as described in the instruction sheet.

Spare Equipment

Plastic tubes, comprising : 1 tube with a red dot (exposure)
1 tube with a green dot (holding) 1 slide

Aspirator comprising : 1 glass tube 1 rubber tubing
1 mouthpiece.

Conical chamber.

4-0

THE IMPLICATION OF AGRICULTURAL INSECTICIDES
IN THE DEVELOPMENT OF RESISTANCE BY MOSQUITOES
WITH EMPHASIS ON CENTRAL AMERICA

by George P. Georghiou

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ABSTRACT

Reports implicating agricultural insecticides in the development or intensification of resistance in mosquitoes are available from different areas of the world, especially where large acreage is devoted to the cultivation of cotton or rice. The problem is discussed with emphasis on the situation prevailing in the Pacific coast zone of Central America where multiple resistance in the vector *Anopheles albimanus* toward organochlorine, organophosphorus and carbamate insecticides has impeded malaria eradication efforts.

Evidence of the implication of agricultural insecticides consists of (1) appearance of mosquito resistance prior to application of chemicals against vectors, (2) higher mosquito resistance in agricultural than non-agricultural areas, (3) correlation between intensity of insecticide use on crops and degree of resistance in mosquitoes, (4) fluctuations of mosquito resistance in parallel with periods of agricultural spraying, (5) correspondence between spectrum of mosquito resistance and types of insecticides applied to crops, and (6) temporary suppression of mosquito population densities in sprayed areas.

Measures proposed for coping with the problem are (1) collaboration between appropriate international agencies and governments for the purpose of identifying and reserving certain insecticides for use exclusively in public health, (2) introduction of comprehensive pest management practices in agriculture, and (3) greater emphasis on supplemental mosquito control measures.

INTRODUCTION

Insects affect not only the health of man but also his many crops, animals and stored products. Crop losses due to insect pests worldwide have been estimated to amount from as low as 12% of potential production (Anonymous 1974) to several times that much (Pimentel et al. 1978). Since insecticides constitute the most practical means of reducing these losses, they are being used extensively throughout the world. The 1980 world market for insecticides is estimated at \$3,083,000,000 (Table 1).

Table 1
U.S. and World Market for Pesticides -- 1980 Estimates

	U.S. Market	World Market	U.S.% of World Market
- Thousand dollars -			
Herbicides	1,785,000	3,965,000	45
Insecticides	925,000	3,083,000	30
Fungicides	330,000	2,200,000	15
Other	265,000	530,000	50
Total	3,305,000	9,778,000	34

Note: Values at basic producer level.
Source: EPA. (Pesticide Pipeline 14(6):1, June 1981.)

Of this, 30% is sold in the United States. It may be expected that worldwide demand for insecticides and other pesticides will increase substantially as developing countries strive to reap the benefits of new high-yielding varieties and to improve their economic, nutritional and health standards. In the absence of strong economic or policy constraints, a five-fold increase in worldwide use of pesticides is projected by the year 2000 (Anonymous 1974).

Strange as it may seem, intensive efforts to control pests of crops by insecticides have diminished in a number of cases man's ability to control adequately mosquito vectors of human disease in the same environment. The ready availability of pesticides, often unaccompanied by adequate controls, has led to excesses in the frequency of their use and in the quantities applied, especially on non-food crops. These abuses have not only complicated agricultural pest control by the selection of

resistant strains of pests and suppression of biological controls, but have also altered, in some cases profoundly, the susceptibility levels of insect vectors of human diseases.

Insects of medical importance, especially mosquitoes, are often found breeding in agricultural habitats and are hence exposed to the insecticides employed in agriculture. Aerial application of insecticides, especially by ultra low volume, is known to result in some drift into surrounding areas, even under optimal meteorological conditions (Yates et al. 1978). These treatments may be expected to have a suppressive effect on adult mosquitoes in that environment (Hobbs 1973). Contamination of breeding sites in the vicinity of treated fields, due to drift or water run-off, can also exert strong lethal action on larvae. Such suppression of the mosquito population, when occurring repeatedly, could lead to accelerated development of resistance to insecticides.

During the last several years, reports from various parts of the world have indicated that mosquito control has become more difficult in areas of intensive agriculture due to decreased susceptibility of the mosquito (Busvine and Pal 1969; WHO 1976). It has also been observed that mosquito resistance has been most severe in areas where crops are treated frequently with insecticides. Although some of the evidence is circumstantial, an increasing body of information points to a direct cause-effect relationship between the use of insecticides in agriculture and serious problems in mosquito control. The dilemma arising from this conflict has been discussed in historical perspective by Garcia Martin and Najera-Morrondo (1972) and more recently by Chapin and Wasserstrom (1981).

REPORTED CASES

A list of cases of resistance in mosquitoes alleged to have been caused or aggravated by agricultural insecticides is given in Table 2. The large number of *Anopheles* species involved may be due to the fact that the susceptibility of anophelines has been followed more closely in connection with malaria eradication. It is suspected that many other cases also exist, especially in *Culex* and *Aedes*, which remain unexamined. It is of interest to note that the majority of cases on record involve dieldrin and DDT, undoubtedly because resistance to dieldrin is known to

Table 2

Cases of resistance to insecticides in mosquitoes presumed to have been caused or aggravated by indirect selection pressure by agricultural insecticides.

Species	Country	Crop	Insecticide Resistance	Reference
<i>Anopheles aconitius</i>	Java	various, rice	dieldrin	11
			DDT	32
<i>An. albimanus</i>	El Salvador, Nicaragua	cotton, rice	parathion	16, 18-19
			methyl parathion, malathion, fenitrothion, propoxur, carbaryl	
<i>An. culicifacies</i>	El Salvador	cotton	DDT	34
	Mexico, Guatemala, El Salvador, Honduras, Nicaragua	cotton	DDT, dieldrin	various (in 11)
	India (Andhra Pradesh, Madhya Pradesh)	various	malathion	40, 41
<i>An. gambiae</i> s.l.	India (Haryana, Punjab)	various	BHC	40
	Ivory Coast	coffee, cocoa	dieldrin	22
	Nigeria	ground nuts	dieldrin	14
	Ghana	cocoa	dieldrin	Coker 1956 (in 22)
	Mali	cotton	dieldrin	6
Upper Volta	cotton	DDT	Hamon <i>et al.</i> , 1968* (in 11)	

Table 2 (con't)

Species	Country	Crop	Insecticide Resistance	Reference
<i>An. gambiae</i> (con't)	Sudan, Ethiopia, Togo, Senegal	various	DDT	41
<i>An. maculipennis</i>	Romania, Turkey	various	dieldrin	Duport, 1965* (in 11,8), 35,36
<i>An. melanoon subalpinus</i>	Turkey	various	dieldrin	35
<i>An. melas</i>	Zaire	bananas	DDT	23
<i>An. pharoensis</i>	Egypt	cotton	dieldrin	Zahar & Thymakis, 1962* (in 11)
			DDT	Zahar, 1965* (in 11)
	Sudan	various	dieldrin, DDT	25
<i>An. quadrimaculatus</i>	USA	cotton	dieldrin	29
	Mexico	cotton	DDT, dieldrin	28
<i>An. rufipes</i>	Mali	cotton	dieldrin	Hamon, 1968* (in 11)
<i>An. sacharovi</i>	Greece, Turkey	cotton, rice	DDT, dieldrin	10,35,36,48
<i>An. sinensis</i>	China	rice	DDT, malathion	3

Table 2 (con't)

Species	Country	Crop	Insecticide Resistance	Reference
<i>Aedes aegypti</i>	Tahiti	coconut	dieldrin	30
<i>Ae. nigromaculis</i>	USA	various	DDT, dieldrin, OP	various (in 11)
<i>Culex quinquefasciatus</i>	USA	various	OP	21

*Communications to WHO.

develop readily and is easily detectable in heterozygotes and because DDT has enjoyed wider and longer use than other classes of insecticides. However, selection by organophosphates (OP), carbamates or both has also occurred, as is evident in *Anopheles albimanus* in the cotton-growing areas of the Pacific coast of Central America, in *An. sinensis* in rice-growing areas of central China, and in *Aedes nigromaculis* and *Cx. quinquefasciatus* in the heavily agricultural areas of California.

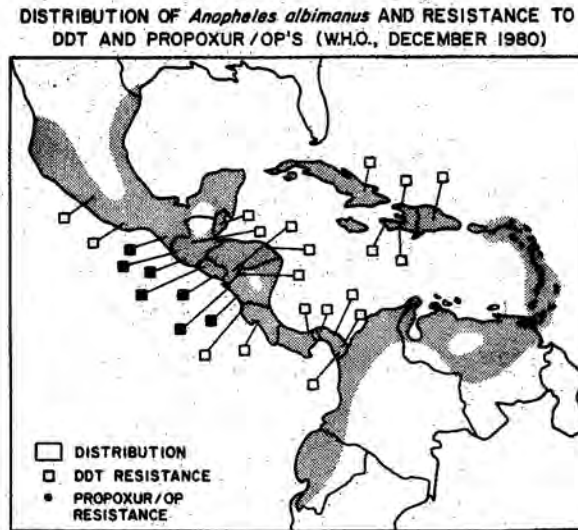
No attempt will be made to recount the specific details of every reported case since these can be found in the available literature. Reference to individual cases will be made only as evidence for the criteria of implication discussed below.

EVIDENCE OF IMPLICATION

Many of the available reports are limited to merely pointing out either that the problem exists in an agricultural area that is heavily treated with insecticides or that mosquito populations are more resistant in agricultural than non-agricultural areas even when both areas have received an equal number of treatments by public health authorities. While much of this information may be convincing enough, definitive evidence comes primarily from the more comprehensive studies on *An. albimanus* (Georghiou et al. 1971, 1973, 1974; Georghiou 1972; Hobbs 1973; Ariaratnam and Georghiou 1974, 1975; Ayad and Georghiou 1975, 1979; Bailey et al. 1981). Much of the relevant evidence was obtained from 1970 to 1973, i.e., during the early stages of emergence of OP and carbamate resistance and before its spread beyond "focal" areas had masked the contribution of the precipitating factors. The geographical distribution of *An. albimanus* and resistance to DDT, organophosphates, and carbamates in 1980 are shown in Figure 1.

The available evidence of the implication of agricultural insecticides is discussed under the following categories: (1) appearance of mosquito resistance prior to application of chemicals against vectors, (2) higher mosquito resistance in agricultural than non-agricultural areas, (3) correlation between intensity of insecticide use on crops and degree of resistance in mosquitoes, (4) fluctuations of mosquito resistance in parallel with periods of agricultural spraying, (5) correspondence

Figure 1



between spectrum of mosquito resistance and types of insecticides applied to crops and (6) temporary suppression of mosquito population densities in sprayed areas.

1. Appearance of mosquito resistance prior to application of chemicals against vectors.

In Turkey, Ramsdale (1973) reported that dieldrin resistance was present in *An. sacharovi*, *An. maculipennis* and *An. melanoon subalpinus* in many agricultural areas where neither BHC nor dieldrin had been used to spray buildings. In the delta area of Egypt, where cotton was treated extensively with toxaphene and DDT, marked resistance to dieldrin and incipient resistance to DDT were noted in *An. pharoensis* in 1959 prior to commencement of residual house spraying (A. R. Zahar and Thymakis, unpublished report to WHO, 1962). Between 1959 and 1962 this DDT resistance was reported to have increased greatly in non-treated areas as well as in those that had received residual house treatments, a situation that was likewise attributed to the effect of agricultural insecticides (A. R. Zahar et al., unpublished report to WHO, 1965). Similar occurrences of resistance in areas that received only agricultural sprays were reported for dieldrin in *An. maculipennis* in the Spineni

region of Romania (M. Duport, unpublished report to WHO, 1965), in *An. aconitus* in the Malang district of East Java in 1961 (Brown and Pal 1971), and in *An. gambiae* at Bougouni, Mali (Hamon et al. 1961) and in the lower Volta region of Ghana (W. Z. Coker, cited in Hamon and Garrett-Jones 1963).

2. *Higher mosquito resistance in agricultural than non-agricultural areas.*

Frequently cited are reports of mosquito resistance or higher levels of resistance in agricultural than non-agricultural areas, although both had received residual house spraying. Thus, in Greece, Belios (unpublished reports to WHO, 1961) found higher dieldrin and DDT resistance in *An. sacharovi* in the cotton- and rice-growing area of Laconia than in Etolia and Euboea, a fact that he attributed to strong selection pressure on the larvae by agricultural insecticides.

In Turkey, Ramsdale (1973, 1975) pointed out that although DDT had been widely used for more than 20 years in public health and agriculture, the incidence of DDT resistance was not related to the duration of DDT house spraying operations: More than ten years of regular house treatment had not affected the susceptibility of *An. sacharovi* or *An. maculipennis* in the southeastern part of the country. However, remarkable DDT resistance had developed in *An. sacharovi* in the cotton-growing district of Manan, Adana (M. H. Holstein, cited by Brown and Pal 1971).

A considerable difference in susceptibility to OP and carbamate insecticides occurs in field strains of *An. albimanus* from different areas: Strains from Haiti, where agricultural use of these insecticides is minimal, are of "normal" susceptibility (generally equalling that of the long-established Gorgas reference strain from Panama) whereas strains from the cotton- and rice-growing areas of El Salvador show remarkable levels of resistance to insecticides within these groups (Georghiou et al. 1971). Such differences are apparently not due to the extreme geographical separation of the populations since a strain from the isolated area of Texistipeque, Santa Ana, El Salvador, which had not experienced commercial use of OP or carbamate insecticides, was equally susceptible to propoxur and DDT as was the strain from Haiti (Georghiou et al. 1972).

3. Correlation between intensity of insecticide use on crops and degree of resistance in mosquitoes.

The implication of agricultural insecticides in the development of resistance by mosquitoes was enhanced by the demonstration in 1971 of correlations between the intensity of pest control operations on cotton and rice in areas of El Salvador and Nicaragua and the degree of OP and carbamate resistance in *An. albimanus* (Georghiou 1972). Cotton has been grown in the Pacific coastal zone of Central America on a large scale since the mid-1950s. This crop is treated with insecticides at frequent intervals, as many as 30 applications during the six-month growing season not being unusual (Fig. 2).

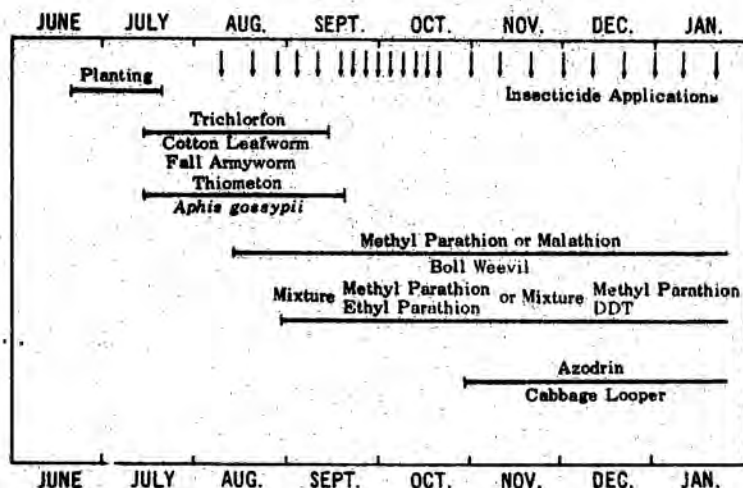


Fig. 2. Summary of insecticide use against pests of cotton in El Salvador, 1971. (Data from Programa del Algodon, Direccion General de Investigacion y Extension Agricola, Ministerio de Agricultura y Ganaderia, Santa Tecla, El Salvador.)

These treatments have led to development of resistance in cotton pests, especially bollworms (*Heliothis* spp.), and changes in the composition of the cotton pest complex (Bareket and Brito 1968, Wolfenbarger et al. 1971). According to Smith (1968) problems of resistance to insecticides in Central America cotton insects "have usually started first in El Salvador."

In the course of an extensive field survey of susceptibility of *An. albimanus* in Nicaragua, Honduras, El Salvador and Guatemala in 1971, the writer obtained evidence of significant resistance to carbamates (propoxur) and to OP's (malathion and parathion) in the Department of La Paz in the center of the coastal zone of El Salvador and in the Sebaco Valley of Nicaragua. Lower resistance levels or an absence of resistance was obtained elsewhere in these countries (Georghiou 1972). Examination of the available agronomic and pest control information of El Salvador indicated that the higher resistance in La Paz was in agreement with the more intensive chemical pest control that was practiced on cotton and rice in this Department than elsewhere in the country. No information could be obtained on the quantities of insecticides used per acre in each Department. However, calculations from data provided by the Ministry of Agriculture indicated that 26% of the country's cotton acreage was found in the Department of La Paz. Here, the average holding per cotton grower was 111.48 manzanas (1 manzana = 1.73 acres), as compared to 34.71 manzanas per grower in the remainder of the country. There were indications that the larger the holding the greater the tendency to apply insecticide treatments on a fixed schedule rather than discriminately when and where needed. Eighty-seven percent of the cotton acreage in El Salvador was treated by aircraft, a practice that may be expected to result frequently in contamination of mosquito breeding habitats. In the Department of La Paz it was pointed out that 95% of the acreage was treated by air, and approximately one-fifth of this was treated by ultra low-volume sprays (Georghiou 1972).

As in the case of cotton, rice cultivation is also more intensive in the Department of La Paz than elsewhere in the country. During 1969 to 1970, 53.6% of the rice acreage of the country was in the central part of the coastal plain, including La Paz, as compared to 25.5% in the western and 20.9% in the eastern parts.

Intensive use of chemicals on crops, especially rice, was also found to be practiced in Nicaragua. As in the case of cotton, complete reliance on chemical control of rice pests lead to a spiraling number of insecticide applications. On one large farm at La Concepcion on which rice growing began in 1963, the following treatments were applied up to 1971 according to information provided by the owner:

<u>Year</u>	<u>Insecticide applications</u>	<u>Total</u>
1963	none	0
1964	carbaryl (4)	4
1965	carbaryl (6)	6
1966	carbaryl (3); carbaryl + methyl parathion (4)	7
1967	monocrotophos (2); carbaryl + methyl parathion (7)	9
1968	monocrotophos (3); endrin (2); disulfoton (1); ethyl/methyl parathion (2)	8
1969	perthane (1); monocrotophos (2); endrin (2); naled (3)	8
1970	perthane (1); naled (2); benfucarb (3); methamidophos (2)	8
1971	naled (3); benfucarb (3); methamidophos (3); diazinon (1)	10
1972	changed to sorghum	

As in the case of OP and carbamate resistance, DDT resistance also occurred at higher levels in the cotton-growing area of Nicaragua, as indicated in Figure 3.

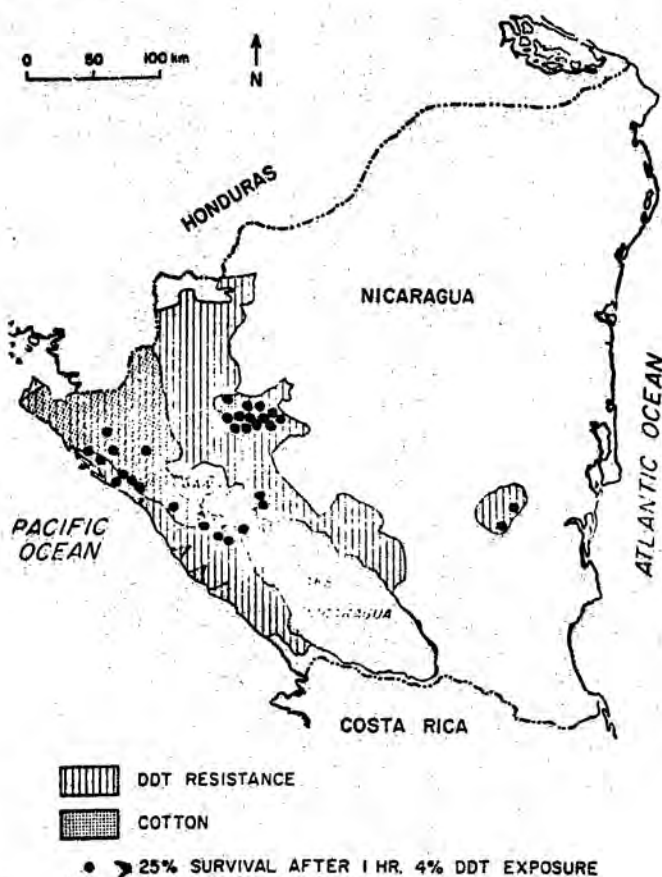


Fig. 3. Map of Nicaragua indicating geographical distribution of DDT resistance in *Anopheles albimanus* and cotton cultivation, 1970.

Additional evidence of the impact of agricultural insecticides is revealed by a study of OP multiresistance in populations of *Cx. quinquefasciatus* in California (Georghiou et al. 1975). Strains collected from dairy waste drains of two farms located six miles apart in the intensely agricultural San Joaquin Valley revealed significantly different levels of OP resistance. Both breeding sites had experienced similar larvicidal treatments applied by the local mosquito abatement district, the 1973 and 1974 treatments consisting exclusively of chlorpyrifos. However, examination of official records of agricultural insecticide applications within a three-mile radius of each farm indicated that during 1971-74 approximately twice as large a quantity of OP and carbamate insecticides had been applied to crops in the area of the more resistant population.

4. *Fluctuations of mosquito resistance in parallel with periods of agricultural spraying.*

A study conducted over a two-year period (1970-72) in the cotton-growing area of El Salvador indicated that the susceptibility levels of *An. albimanus* show seasonal fluctuations in parallel with the period of spray applications on cotton. Sampling was done in June and February of each year, i.e., at the beginning and end of the cotton-spraying season (Fig. 4).

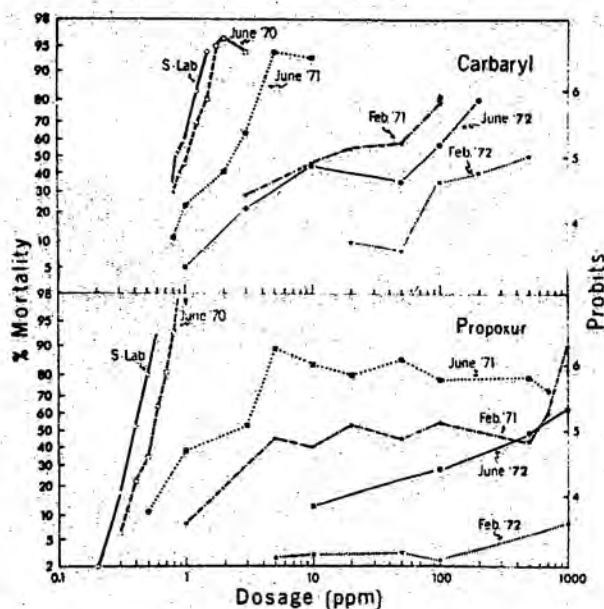


Fig. 4. Dose-response lines for carbaryl and propoxur showing season fluctuations in susceptibility of a field population of *An. albimanus* at Hacienda Melara, La Libertad, El Salvador (from Georghiou et al. 1973).

Resistance to parathion, methyl parathion, malathion, fenitrothion, carbaryl and propoxur was found to rise during the spray period and to decline somewhat during the non-spray period. This escalatory pattern led to remarkably high levels of resistance by February 1972, when the study was terminated. With reference to a susceptible strain, the resistance levels observed (at the LC_{50}) were: malathion 117x; parathion 158x; methyl parathion 144x; fenitrothion 45x; propoxur >1000x, and carbaryl 443x (Georghiou et al. 1973) (Figures 5-6).

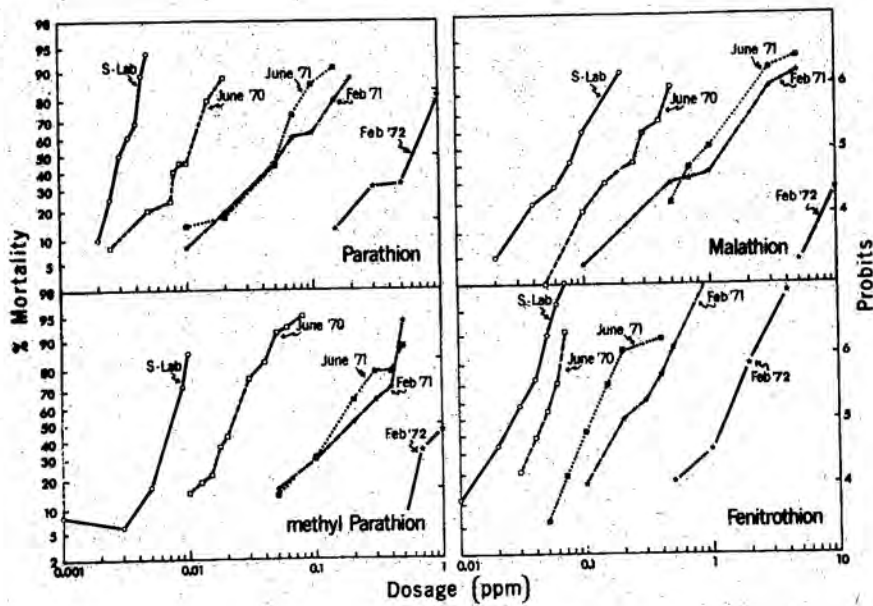


Fig. 5. Dose-response lines for parathion, malathion, methyl parathion and fenitrothion showing seasonal fluctuations in susceptibility of a field population of *An. albimanus* at Hacienda Melara, La Libertad, El Salvador (from Georghiou et al. 1973).

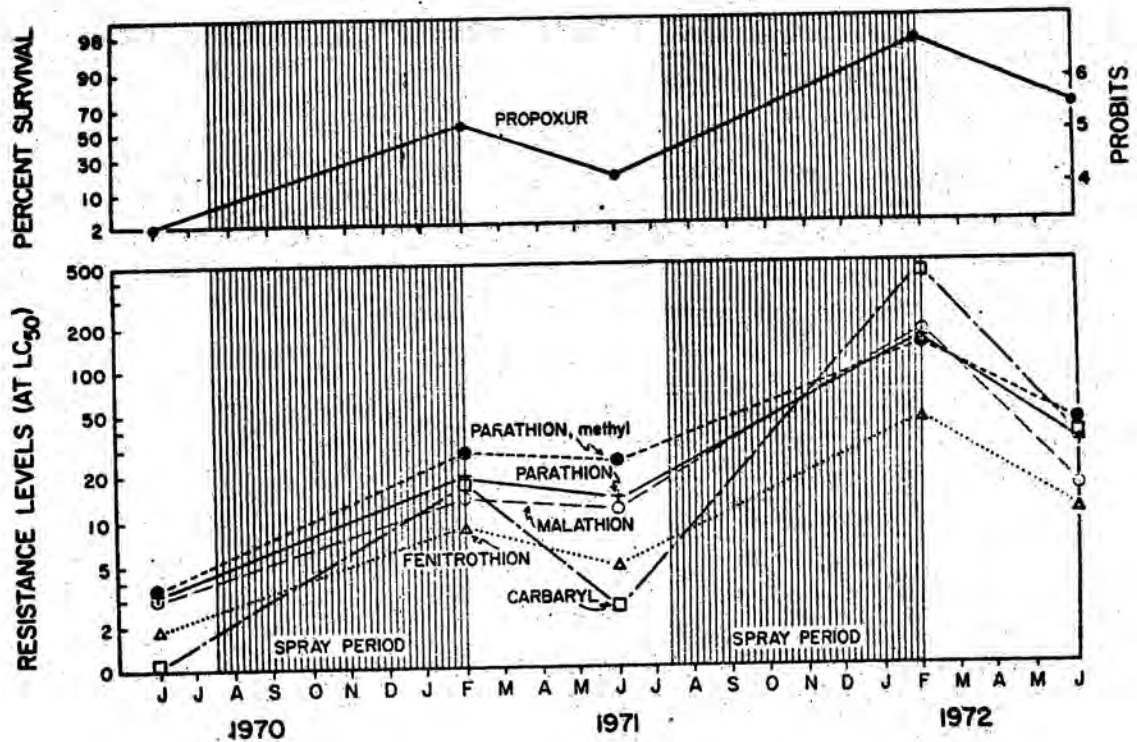


Fig. 6. Fluctuations in resistance levels toward organo-phosphates and carbamates in *An. albimanus* with reference to alternating agricultural spray and non-spray periods (after Georghiou et al. 1973).

5. Correspondence between spectrum of mosquito resistance and types of insecticides applied to crops.

The El Salvador studies of 1970-73 have also indicated that the spectrum of multiresistance in *An. albimanus* can be traced to the types of insecticides applied to cotton, by far the most common crop subject to insecticide treatments. Parathion and methyl parathion have been the principal insecticides used on this crop for over a decade. Other insecticides, including carbaryl, azinphosmethyl, trichlorphon, monocrotophos and malathion had been used to a lesser extent against specific pests. Since the geographical distribution of *An. albimanus* in this country coincides to a large extent with the agricultural area, data on insecticide imports into the country were used as an approximate indication of the degree of selection pressure contributed by each chemical. Calculations from official records during the 10-year period 1961-70 show that 51.22% of the insecticides imported were organophosphate,

46.37% organochlorine, and 2.41% carbamate. Methyl parathion and parathion constituted the bulk of the organophosphates (93.3%) while carbaryl was the most common among the carbamates (88.1%) (Georghiou 1972, Georghiou et al. 1973).

Table 3
Importation of insecticides in El Salvador
1961-70^{a/}

	Kilos ^b	% within group	% of total
Organophosphate			
Parathion, methyl	11,259,500	55.1	28.20
Parathion	7,808,500	38.2	19.56
Azinphosmethyl	409,200	2.0	1.02
Trichlorphon	310,100	1.5	0.78
Monocrotophos	278,000	1.4	0.70
Malathion	165,800	0.8	0.42
other	215,800	1.0	0.54
Total	20,446,900	100.0	51.22
Carbamate			
Carbaryl	850,200	88.1	2.13
Propoxur	61,800	6.4	0.15
other	53,200	5.5	0.13
Total	965,200	100.0	2.41
Organochlorine			
DDT	9,337,500	50.4	23.39
Toxaphene	8,374,800	45.2	20.97
other	801,700	4.4	2.01
Total	18,514,000	100.0	46.37
Grand total	39,926,100		100.00

^a Compiled from data in Georghiou (1972).
^b Active ingredient.

It is thus obvious that methyl parathion and parathion have had the greatest impact on *An. albimanus*, as reflected by the high resistance levels to these compounds. The elevated resistance to malathion may have resulted from the relatively limited malathion treatments, with additional selection of malathion-resistant genotypes by other organophosphates. Carbamate resistance may be the consequence of carbaryl applications and to a lesser extent of propoxur, such resistance being supported and enhanced further by organophosphate selection pressure. This suggestion was later validated by biochemical tests, which revealed that organophosphate (parathion) and carbamate (propoxur) resistance in this mosquito is due to the selection of a variant acetylcholinesterase that is far less sensitive than normal to inhibition by these chemicals (Ayad and Georghiou 1975). This property is due to a single gene which may also be responsible for the high resistance observed toward other organophosphates and carbamates (Georghiou et al. 1975).

6. Temporary suppression of mosquito population densities in sprayed areas.

That agricultural applications of insecticides do indeed suppress the density of mosquito populations was clearly demonstrated by Hobbs in El Salvador (Hobbs 1973). Adult density fluctuations of *An. albimanus* were measured weekly from February through December, 1972, within a 100-square-kilometer cotton-growing area and a comparable area well removed from cotton fields. Adult densities began to build up in May in both areas following the onset of the rainy season. However, whereas in the non-cotton area the density remained relatively high throughout the rainy season, in the cotton area the density declined abruptly in mid August and remained low or negative until December. This decline coincided with the increased application of insecticides to cotton fields as revealed by the data on the number of flights of pest control aircraft per week (Fig. 7). In the same study

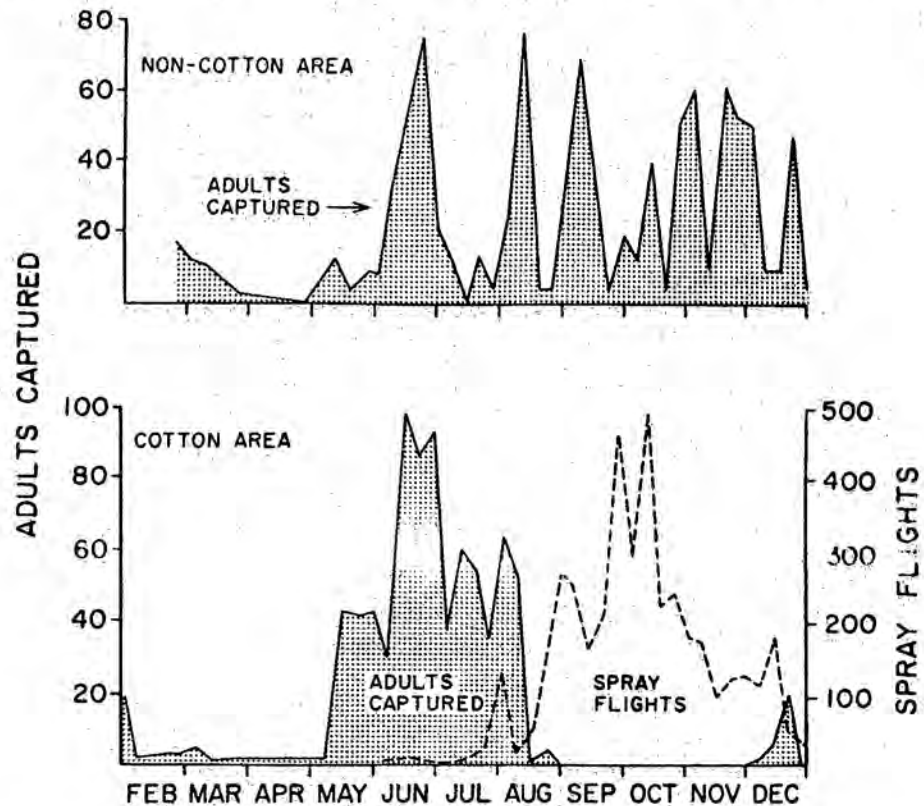


Fig. 7. Adult densities of *An. albimanus* at Melara (cotton area) and Santa Emilia (non-cotton area), El Salvador, with records of cotton spray flights by week, in 1972. (Data from Hobbs 1973)

study (Hobbs 1963), 16 larval breeding sites within the cotton area were found negative to the end of August and remained so until December. The single exception that remained continuously positive was a cattle watering pond, situated at the limit of the cotton district.

As might have been expected, such severe selection pressure gradually resulted in the evolution of a resistant population whose density was suppressed less severely by the agricultural sprays. This was documented by a study conducted five years later in the same area of El Salvador by Bailey et al. (1981). These investigators made standardized collections at weekly intervals from July 18, 1977 to March 25, 1979 at several sites within the cotton area as well as at sites located at least 1 Km away from cotton fields. Their data, illustrated in Figures 8 and 9, show that the adult mosquito population within the cotton area was suppressed only mildly by the first treatments and that its density recovered steadily so that by the end of the spraying season it had reached a level similar to that observed in the non-cotton area. Roughly similar results were obtained by the larval counts. It was thus concluded that through continued yearly selection and intermingling of the population of the sprayed and non-sprayed areas a uniformly resistant population had evolved whose density was no longer drastically suppressed by control treatments.

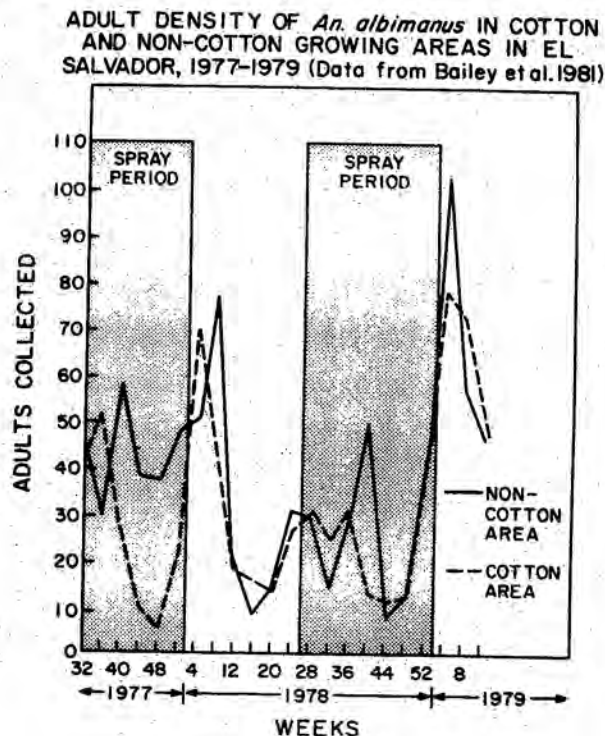


Figure 8

LARVAL DENSITY OF *An. albimanus* IN COTTON AND NON-COTTON GROWING AREAS IN EL SALVADOR, 1977-1979 (Data from Bailey et al. 1981)

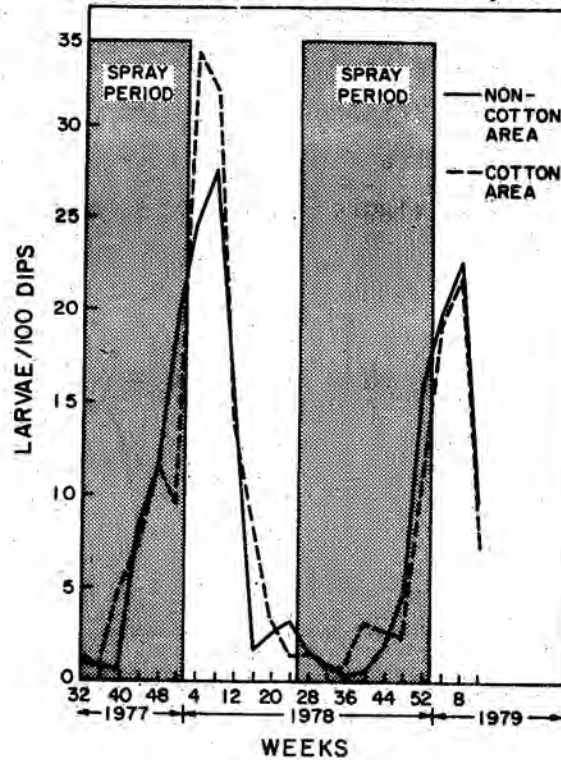


Figure 9

DISCUSSION AND RECOMMENDATIONS

The available evidence leaves little doubt that agricultural insecticides, especially when applied by aircraft, are capable of exerting strong selection pressure against mosquito populations. Such pressure could be the result of decimation of the flying adult population, suppression of larvae by contamination of breeding habitats, or both. The consequences of such selection have been shown to be commensurate with the extent and frequency with which such exposure occurs in a given area. In the most serious case studied, El Salvador (as well as in cases throughout the Pacific coast zone of Nicaragua, Honduras, Guatemala and southeastern Mexico), selection occurs with regularity from August through December, as shown by the large number of spray flights carried out and the nearly complete suppression of mosquito populations. Such selection was shown to result in the development of resistance, which rises annually to higher levels in concert with the

seasonal spray/non-spray periods. Resistance is quantitatively congruent with the intensity of agricultural operations in each area, and qualitatively involves those compounds that are employed in the largest quantities in agriculture. The resultant multi-resistance in the vector has considerably reduced the efficacy of residual applications of propoxur, malathion and fenitrothion with a concomitant resurgence of malaria transmission (WHO 1976, 1980; Figure 10).

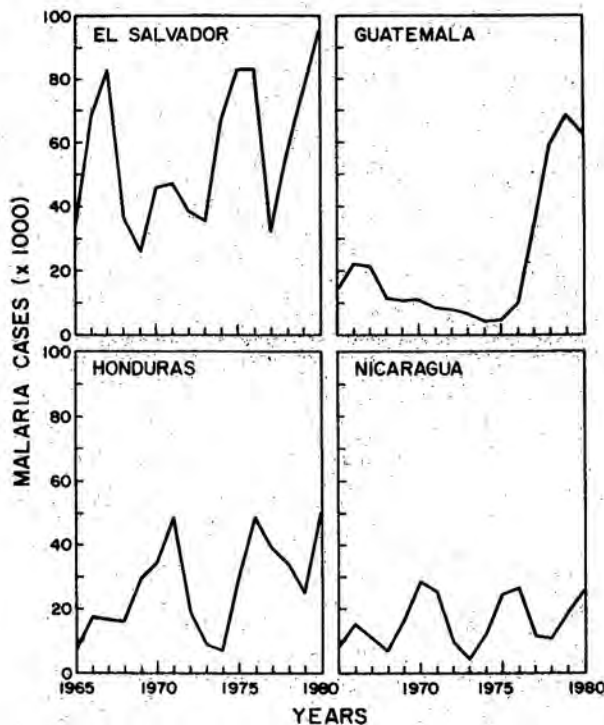


Fig. 10. Malaria cases detected in El Salvador, Guatemala, Honduras and Nicaragua from 1965 to 1980. (Data from PAHO Annual Reports)

Recently (1977-79), the El Salvador population of *An. albimanus* was found to be less suppressible by agricultural sprays than formerly, probably due to an increase in the frequency of the mechanism of decreased sensitivity of acetylcholinesterase. This development would tend to remove the initial advantage of agricultural sprays, e.g. that of temporarily suppressing *An. albimanus* and reducing the incidence of disease transmission.

The course of development of resistance in mosquitoes may be influenced also by the application of insecticides in public health

programs. However, residual house spraying alone, as applied for malaria control, exerts selection pressure on only about 50% of the population since mostly female mosquitoes enter houses. This proportion would be even smaller in rural, sparsely populated areas, and where the vector is partly exophagic, as in the case with *An. albimanus*. Under these conditions, the possibility of resistance due to these treatments alone must be minimal. Where larvicides are used, especially in combination with residual house spraying, a higher degree of selection pressure is exerted, particularly if related chemicals are involved. Exposure to both agricultural and public health treatments enhances further the prospects of resistance development. In the case of *Cx. fatigans* referred to earlier, it was concluded that the large variety of insecticides applied to crops had predisposed the population to respond readily to the specific selection pressure applied by chlorpyrifos at the breeding sites. The resultant multi-resistance thus involved not only chlorpyrifos, but also the compounds that had been applied directly or indirectly against the population and had thus exerted long-standing selection pressure.

In devising recommendations for alleviating this problem, two questions must be considered. Firstly, the introduction and use of insecticides in agriculture in most developing countries remains unrestricted and unregulated. New compounds are introduced before they have been fully tested and licensed in developed countries. In contrast, their use in public health, especially for residual house spraying, is preceded by exhaustive testing (e.g., WHO Testing Programme, Wright 1971) requiring several years for completion. Since the same compounds are usually candidates for both agriculture and public health, their earlier availability and use in agriculture jeopardizes their subsequent usefulness against mosquitoes as a result of previously developed resistance.

A second consideration is the general, non-specific selection effect exerted on mosquitoes by the multitude of insecticides applied in agriculture. Exposure to compounds of varied chemical nature appears to select in favor of several pathways of detoxication, thus preparing the population to respond more readily to specific selection subsequently

applied against mosquitoes. Extremely severe pressure may also lead to selection of strains possessing "insensitive" acetylcholinesterase, and thus "immunity" to certain insecticides. This has evidently occurred in *An. albimanus*.

In view of the above, the following actions are suggested as offering possible solutions:

1. Collaboration between agricultural and public health agencies and industry, on the broadest possible scale for the purpose of *identifying chemicals with unique modes of action that offer the greatest promise of effectiveness against mosquitoes, and reserving these exclusively for public health use*. To be effective, any agreement of this nature must be established at the highest level of authority, preferably among WHO, FAO and industry, and implemented by country governments. A standing joint committee could be appointed by these organizations to review periodically the available information and to provide guidelines for action. The discovery of *Bacillus thuringiensis* serotype H15 offers an opportunity for testing the feasibility of such measure. Certain countries have banned the use of DDT in agriculture while still allowing its use in public health programs. Where *Anopheles* continues to be susceptible to DDT, such a measure appears reasonable. The experience thus gained would serve as a model for other countries.
2. Reduction of indirect selection of mosquitoes by agricultural insecticides by the *introduction of comprehensive pest management practices*. It is realized that agricultural exports provide a considerable share of the foreign exchange earnings of developing countries. Thus a reduction in the extent of insecticide usage can be expected only when alternative effective measures have been demonstrated. Since specific research is necessary to provide comprehensive pest management programs for each crop, progress in this area may be expected to be slow. Nevertheless, it is believed that the present excesses in insecticide usage can be reduced by closer collaboration between the public health and agricultural services and by an intensive program of research in agricultural pest management.
3. *Greater emphasis must be placed on the use of comprehensive mosquito control measures*. The need for supplementing insecticide applications

with other measures designed to reduced mosquito populations has been discussed on a number of occasions (Garcia Martin and Najera-Morrondo 1972; Mulhern 1972; Schliessmann 1974). Such measures could contribute to reduction of mosquito density below threshold levels, at least during part of the season, thereby curtailing the number of insecticide applications needed. Since much mosquito breeding occurs in irrigation and runoff water, the cooperation of agriculture in effecting the necessary engineering improvements (Junkert and Townzen 1973) (e.g. drainage) and/or agronomic modifications (e.g., intermittent vs continuous irrigation of rice fields) will be required.

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4.1 THE AGRICULTURAL USAGE OF INSECTICIDES IN TURKEY
AND THE RESURGENCE OF MALARIA

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The most obviously positive benefit of the world-wide malaria eradication campaign initiated by the World Health Organization in 1957 was the rapid and complete eradication of the disease from the European shores of the Mediterranean, west of the Dardanelles (Bruce-Chwatt & de Zulueta, 1980). The programme in Asian Turkey, which started in earnest in 1960, looked as though it would achieve the same result as elsewhere and in fact Plasmodium falciparum was eradicated. However a pocket of transmission of P. vivax remained in south-east Anatolia and in 1973, 2 438 cases were detected in this area inhabited by less than 3 per cent of the population of the country (estimated to be of the order of 40 million). This proved to be the focus from which a major resurgence of the disease was to occur further west in the Chukurova Plain where extensive agricultural development had attracted migrant labour, mainly from Anatolia (Ramsdale & Haas, 1978). The disease was then to spread from the Atana area of the Chukurova plain to many other parts of Turkey. According to Postiglions (1980) the following numbers of positive blood slides were recorded in the years following 1975:-

<u>Year</u>	<u>Slides examined</u>	<u>Slides positive for P. vivax</u>
1976	2 284 121	37 320
1977	2 798 764	115 512
1978	3 134 455	87 867
1979	2 920 239	29 324
*1979	-	24 744
*1980	-	2 583

*in the first nine months of the year only

This author estimates that 50 per cent of the cases came from Chukurova in 1979 and 80 per cent in 1980. The persistence of this malaria presents a continuous threat to the rest of Europe where anti-malaria measures are no longer in force and where no specific quarantine regulations exist.

Since the malaria control activities started in Turkey, agricultural practice has changed from predominantly small-scale mixed farming to the large-scale cultivation of single crops like cotton and rice. This change has been accompanied by increased land irrigation with consequent increased mosquito production over a longer period of the year. The Chukurova Plain was the first such large-scale irrigation project and most of the area was devoted to growing cotton. Cotton (and rice) monoculture has brought its attendant pest problems and these have led to a massive outdoor use of a large number of different insecticides at frequent intervals. Detailed information on this agricultural usage of insecticides in Chukurova is only available from 1968 when organochlorines predominated, though organophosphates and carbamates were already being used in substantial amounts. Between 1968 and 1971 the main organochlorines in use (in quantities containing more than 14 tons of active ingredient) were DDT, toxaphene, endrin, aldrin and HCH, in that order. Among the organophosphates, monocrotophos (azodrin), parathion, demeton (systox), dimethoate, azinphos methyl (gusathion), chlorpyrifos, malathion and phosfolan (cyolane), in that order, were applied in quantities greater than 50 tons of active ingredient. Over the years there has been a gradual reduction in organochlorines and a substantial increase in organophosphates and most recently synthetic pyrethroids (permethrin, deltamethrin, cypermethrin and fenvalerate) have made an appearance. Carbamates (almost entirely carbaryl) have formed a significant proportion which has fluctuated over the years (Table 1). What is remarkable is the extremely large quantities and variety of compounds (at least 9 organochlorines, 17 organophosphates, 2 carbamates and 4 pyrethroids) that have been distributed both from the ground and from the air. From

available figures the peak was more than 2 800 tons of active ingredients in 1969 in Chukurova. This compares with an annual peak of 650 tons of DDT used for the Attack Phase of the whole of the nationwide Malaria Eradication Programme.

The predominant anopheline mosquito species of the Chukurova Plain are Anopheles sacharovi, the malaria vector, and A. hyrcanus sensu lato. The former spends some of its time indoors though not all of its feeds are on man and not all of its intercurrent resting is in human dwellings. The latter is predominantly animal biting and is never found in human dwellings. Both, however, breed together in the irrigation channels and flooded areas derived from them in the crop-growing season. All these breeding places are directly subject to contamination from the insecticides used for crop-spraying.

In the actual anti-malaria operations involving the spraying of houses DDT was the first insecticide to be used, from 1953. In the Chukurova Plain area it was replaced by dieldrin from 1959 with annual applications until 1963 and then with focal sprayings in scattered villages until 1971. Malathion then became the insecticide of choice and has remained so.

DDT resistance was first detected in A. sacharovi in Chukurova in 1959 by de Zulueta and has since spread to other areas in that species and in A. hyrcanus, both of which are now resistant to dieldrin as well. Dieldrin resistance was slow to appear in A. sacharovi in Chukurova and was not found in significant proportion until malathion house-spraying began in 1971 and 1972. Ramsdale (1975) suggests that this unusual delay in the appearance of dieldrin resistance could have been due to a selection in the larval stage (and hence from agricultural usage) of DDT resistance combined with continuing irritability by quite old deposits of DDT, leading to a much reduced selection by house-spraying with dieldrin. Be that as it may, the fact is that the distribution of both organochlorine resistances bears

little relation to the use of these insecticides for anti-malaria purposes and thus by inference agricultural usage is suggested as the main cause (Figs 1 and 2, taken from Ramsdale, 1975). Certainly the widespread organochlorine resistance in the totally exophilic A. hyrcanus must have been due to agricultural practices. The persistence of organochlorine resistances in both species many years after these ceased to be used for house-spraying also suggests continuing selection through their use outdoors.

In spite of the massive use of both organophosphates and carbamates in Chukurova in the late 1960's and early 1970's resistance to them among the anopheline mosquitoes was not detected until the autumn of 1974. Then high resistance to fenitrothion was found, many A. sacharovi surviving 8 hours exposure to 1% impregnated papers (2 hours exposure being enough to kill susceptibles) with significant resistance also to fenthion and indications of resistance to propoxur and possibly also to synthetic pyrethroids, though this last awaits confirmation (Ramsdale et. al., 1980). Resistance to malathion was hardly evident in spite of the use of this insecticide both indoors and outdoors and has remained so to 1981 according to Clarke (personal communication). A number of other organophosphates and carbamates were also included in susceptibility tests carried out both in the field and in the laboratory. From these tests additional resistance in A. sacharovi was evident to chlorphoxim, phoxim, diazinon, chlorpyrifos, iodofenphos, dimethoate and mecabam among organophosphates and to carbaryl, dimetan, dimetilan and N-methyl carbamate among carbamates. A significant survival after exposures to pirimiphosmethyl might be attributable to the poor performance of this insecticide when in solution in dioctyl-phthallate. The resistance pattern in A. hyrcanus was similar though not identical. Among the organophosphates it seems more tolerant than A. sacharovi to chlorphoxim, iodofenphos and dimethoate and among the carbamates more susceptible to propoxur and carbaryl but more tolerant to dimetilan. It seemed to parallel A. sacharovi in its susceptibility to malathion.

The general similarity between the resistance spectra in the two species, both of which favour the same type of breeding place and the fact that one never rests in human dwellings while the other does, atleast for part of its life, all point to selection for resistance occurring in the breeding place through contamination from the outdoor use of insecticides for agricultural purposes rather than indoors for public health purposes.

Organochlorine resistance is widespread in another two anopheline species A. maculipennis sensu strictu and A. melanoon subalpinus in various parts of Turkey. Limited adult susceptibility tests with the former derived from the north of Turkey near to the Black Sea and maintained in the laboratory in London by the artificial mating technique indicated resistance to iodofenphos, fenitrothion, propoxur and carbaryl but again susceptibility to malathion. Both the species favour breeding grounds similar to those used by A. sacharovi and A. hyrcanus but in this case mainly where rice is grown rather than cotton. Rice like cotton is again subject to frequent spraying with a variety of insecticides. Little house-spraying has been carried out in areas where A. maculipennis and A. m. subalpinus occur and then only with organochlorines. It is of interest to note that another vector species A. superpictus which breeds in pools in river beds appears to have maintained its susceptibility to all the insecticides in spite of the fact that it rests in houses, some of which at least were included in the anti-malaria spraying campaign. These breeding places are usually some way away from crop-growing areas.

In conclusion it must be pointed out that while most of the resistance in the anopheline mosquitoes of Turkey can be directly attributed to the agricultural usage of insecticides, not all the resurgence of malaria can. To begin with, at least, agricultural spraying caused a reduction in mosquito densities and appeared to cover up deficiencies in anti-malaria activities. This led to complacency and reduced effort on behalf of the

public health authorities concerned. The search for the treatment of malaria cases declined in Chukurova where agricultural production and profit were the overriding concern of commercial organizations. As a result untreated cases became the source of the resurgence of the disease. By the time that the seriousness of this resurgence was recognised wide-spectrum resistance in the vector species was so well established that the number of insecticides of potential value for continuing house-spraying was limited in effect to malathion. Unfortunately this compound with its unpleasant odour has proved unacceptable to many of the householders in the area. Propoxur was considered as a possible alternative but indications of resistance to this compound ruled it out.

Table 1

Quantities (tons of active ingredient) of insecticides used for crop-spraying in Chukurova during the year 1968 to 1971 and 1978 and 1979

Year	Organochlorines	Organophosphates	Carbamates	Synthetic Pyrethroids
1968	2187	299	48	0
1969	2242	485	78	0
1970	459	568	77	0
1971	1092	754	101	0
1978	264	828	125	18
1979	132	454	56	35

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4-2 RESISTANCE INDUCTION IN VECTORS IN RELATION TO AGRICULTURAL
USE OF PESTICIDES IN SOUTH-EAST ASIA

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As a result of rapid population growth and development in countries of the third world there is an increasing demand for more food and better health. This situation has accelerated the development and wide use of chemical pesticides for pest and vector control.

The use of pesticides for agriculture and health purposes has been carried out simultaneously without much coordination and cooperation between the responsible governmental sectors. There is hardly any established and applied policy for the use of pesticides in the environment. However, in some cases as here in Sri Lanka, malathion the insecticide being used for malaria control has been banned from use in agriculture.

The impact of pesticides usage in the environment is greater on mosquitos, which breed in diverse surface waters in all types of situation, than other vectors. There is little doubt that the repeated application of various insecticides for pest control is bound to enhance selection of the resistant gene or genes to specific insecticides and also cross resistance to related ones in the mosquito populations. The problem is even greater with exophilic mosquitos which spend the greater part of their life outdoors. The exposure of generations of these populations to the agricultural insecticidal pressure results in the speedy selection for resistance to the insecticides used.

Present status of vector resistance in countries of South-East Asia

The speedy development of resistance to an increasing number of insecticides by an increasing number of vector species over wider geographical areas especially in rural situations has

impeded disease control programmes in many countries in the South-East Asia Region. The achievements of the malaria programmes during the late sixties and early seventies came to an end with major setbacks in some programmes and significant increase in the prevalence of the disease in the rest. Resistance to DDT, the conventional insecticide, and others has been reported in a number of malaria vectors and other anophelines from countries in South-East Asia (Table 1, Fig.1). Apart from malaria vectors, resistance has also been reported in vectors of other disease, e.g. dengue/DHF, filariasis, Japanese encephalitis, etc.

Cases of Vector resistance enhanced by the use of pesticides in Agriculture.

In India, Wattal et al¹ stated that in the sixties and seventies, when the application of pesticides became recognized as a vital input for increased productivity of foodgrains and other crops, the consumption of insecticides in agricultural practices rose at the rate of 15.8 per cent per annum. Unlike DDT, HCH and malathion and other organophosphates were used in agriculture much before their use started in public health. It is interesting to note that tolerance/resistance to HCH and or malathion has developed in populations of An. culicifacies in Andhra Pradesh, Haryana, Karnataka, Madhya Pradesh, Maharashtra and Punjab inspite of the fact that these insecticides either have not been used or been used only for a very short period by the malaria programme.

In Indonesia, An. aconitus, a typical rice field breeder, is the main malaria vector in Java and Bali. The first records on resistance to DDT and or dieldrin in populations of An. aconitus from different parts of Java were reported more than 20 years ago. Badawi² in 1961 reported the first development of resistance to

1. Wattal, B.L., Joshi, G.C. and Das, M. (1981). Role of Agricultural Insecticides in Precipitating Resistance, J.Com. Dis. 13 (1):71-74.

2. Badawi, S. (1961) Assignment report to WHO.

dieldrin in East Java, caused purely by the agricultural use of the insecticide. Similar results were also reported from areas in central Java where there was no history of dieldrin spraying in the malaria programme. Investigations on the use of insecticides in rice fields revealed that endrin was the most widely used insecticide against rice pests, followed by aldrin, dieldrin, DDT and HCH³. As a result of the wide use of these insecticides it may be concluded that the development of resistance to organochlorine insecticides in populations of An. aconitus has been greatly enhanced, especially in view of the mode of insecticide application through larviciding.

In Thailand, DDT residual house spraying has been in use for malaria eradication/control for more than 30 years. Early records of resistance to DDT were reported in two anopheline species, An. culicifacies and An. vagus. However, since 1975 there are indications from some areas in northern Thailand that other species including An. minimus, An. balabacensis, An. maculatus and An. philippinensis are becoming tolerant or probably resistant to the insecticide. Preliminary investigations on the use of insecticides in those areas have shown that DDT and a variety of other insecticides are applied more frequently and intensively for agricultural purposes, especially in cotton and tobacco cultivations. It has been speculated that the slow development of tolerance/resistance to DDT is probably due to the fact that these cultivations are, so far, limited in size and distribution⁴.

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3. Report on an assessment of malaria eradication programme, Indonesia (Java and Bali), 3 January - 23 February 1969 (SEA/MAL/71).
 4. Ismail, I.A.H. and Pinichpongse, S. (1980). Monitoring Susceptibility of Malaria Vectors and Suspected Vectors in Thailand. WHO/MAL/80.923, WHO/VBC/80.775.

Only if there is a greatly improved coordination and collaboration in the use of insecticides by the agricultural and health sectors will these adverse trends be arrested. The example in Sri Lanka of the restriction of malathion to public health is a most commendable step in the right direction, and if emulated more widely will be of great service to the cause of disease vector control throughout the region. The seriousness of the situation becomes evident when we realize that there are few, if any, new kind of insecticides down the road.

**TABLE 1 - Insecticide resistance in anopheline mosquitos
in countries of South East Asia Region.**

Country	Species	DDT	Dieldrin/HCH	Organophosphates
Bangladesh	<u>An. Annularis</u>	R	-	-
	<u>An. subpictus</u>	-	R	-
	<u>An. vagus</u>	R	-	-
Burma	<u>An. annularis*</u>	R	-	-
	<u>An. culicifacies*</u>	R	-	-
	<u>An. nigerrimus</u>	R	R	-
	<u>An. Balabacensis*</u>	V	-	-
India	<u>An. culicifacies*</u>	R	R	R
	<u>An. stephensi*</u>	R	R	R
	<u>An. fluviatilis*</u>	R	-	-
	<u>An. philippinensis*</u>	R	-	-
	<u>An. subpictus*</u>	R	R	-
	<u>An. tessellatus*</u>	R	R	-
	<u>An. annularis*</u>	R	R	-
	<u>An. nigerrimus</u>	R	R	-
	<u>An. vagus</u>	R	-	-
Indonesia	<u>An. aconitus*</u>	R	R	-
	<u>An. sundalcus*</u>	V	-	-
	<u>An. subpictus</u>	V	-	-
	<u>An. farauti*</u>	V	-	-
	<u>An. koliensis*</u>	V	-	-
	<u>An. barbirostris*</u>	R	R	-
	<u>An. nigerrimus</u>	R	-	-
	<u>An. peditaeniatus</u>	R	-	-
		<u>An. vagus</u>	-	R
Maldives	-	-	-	-
Nepal	<u>An. annularis*</u>	R	R	-
	<u>An. fluviatilis*</u>	V	V	-

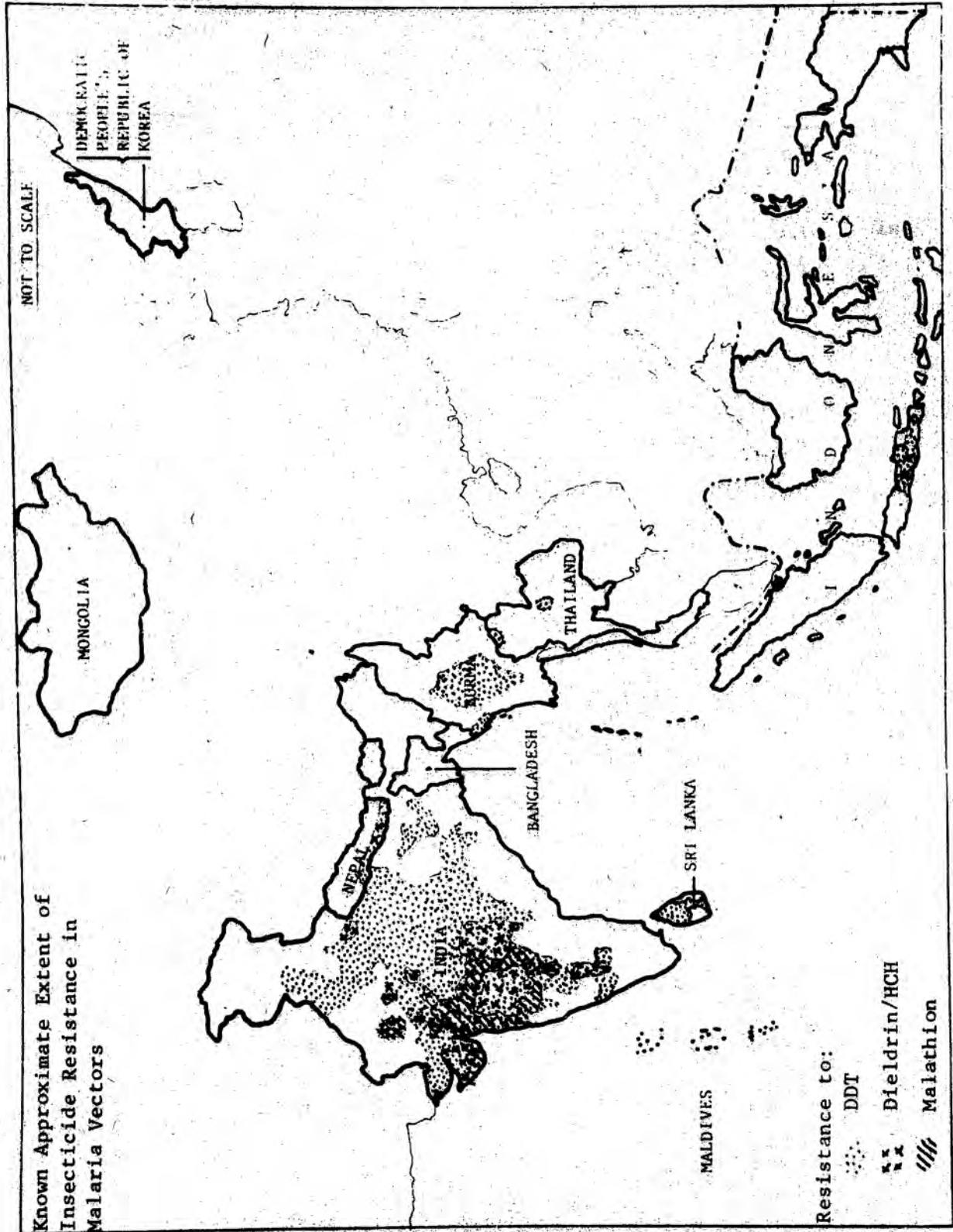
Country	Species	DDT	Dieldrin/HCH	Organophosphates
Nepal (contd.)	<u>An. culicifacies</u>	R	R	-
	<u>An. subpictus</u>	R	R	-
	<u>An. vagus</u>	R	R	-
Sri Lanka	<u>An. culicifacies</u> *	R	-	-
	<u>An. subpictus</u>	-	R	-
	<u>An. tessellatus</u>	R	-	-
	<u>An. nigerrimus</u>	R	-	-
Thailand	<u>An. minimus</u> *	V	-	-
	<u>An. balabacensis</u> *	V	-	-
	<u>An. maculatus</u> *	V	-	-
	<u>An. aconitus</u> *	V	-	-
	<u>An. culicifacies</u>	R	-	-
	<u>An. philippinensis</u>	V	-	-
	<u>An. annularis</u>	R	-	-
<u>An. vagus</u>	R	R	-	

* Proven malaria vectors

R = Resistant

V - Verification required.

Fig.1 WHO - South-East Asia Region



4-3 LIKELY CONTACT BETWEEN INSECTICIDES AND
ARTHROPODS OF MEDICAL IMPORTANCE

by G. Davidson

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The speed of build-up of insecticide resistance depends on the frequency of individuals in the population carrying resistance genes and on the selection pressure exerted on that population by the insecticide. The higher the selection pressure and the greater the mortality of susceptible individuals, the greater the chance of resistant individuals mating together to produce resistant offspring. Genetically speaking selection leads to a concentration of resistance genotypes, first of all in the heterozygous state followed by heterozygote-heterozygote mating which results in the appearance of homozygotes. The amount of pressure will not only depend on the insecticide and how and where it is distributed but also on the behaviour of the insect and the likelihood of it coming into contact with it.

Let us consider the insecticide first. It may actually repel at a distance before contact though what evidence exists does not indicate that this is of major significance. Repellency will reduce selection. It may irritate and cause the insect to leave treated surface before it would have left an untreated one. This probably occurs with many insecticides but none more so than DDT where irritability often leads to departure before the acquisition of a lethal dose. This is well known with mosquitoes and even the most efficient formulation of this insecticide never produces a complete kill of adults. The net result is a reduction in selection pressure the survival of susceptibles and a slowing down of the appearance of resistance. To compensate, so to speak, DDT resistant insects selected in the adult stage are not irritated as a rule. However, there is some evidence in mosquitoes that DDT resistance produced by larval selection can produce resistant adults which are still irritated by the insecticide.

Old deposits of DDT can continue to irritate even when partially covered with another insecticide. Thus the slow appearance of dieldrin resistance in Anopheles sacharovi in Turkey after house spraying with dieldrin succeeded the use of DDT, is attributed to the agricultural use of DDT contaminating the breeding places and selecting DDT resistant individuals which were still irritated by the old deposits of DDT. There is some evidence that permethrin among the new synthetic pyrethroids is significantly irritating to insects also.

The stability of the insecticidal compound obviously affects its persistence and hence the selection pressure. In this respect the organochlorines are much more stable than the organophosphates or carbamates. To the environmentalist biodegradability is a good thing. To the controller of insects the more persistent insecticides are more economically efficient usually. The selective effect of stable compounds can depend on the mode of application. Application as residual deposits to specific insect resting places, as in the spraying of houses against mosquitoes, will usually result in higher selection rates than their use in aerosols or ULV. The very frequent use of the latter or of non-residuals would be needed to compete with the efficiency of selective residual applications of persistent compounds. Many insecticides, including DDT and some pyrethroids, have a rapid knockdown effect which may occur before the acquisition of a lethal dose and may result in the insect falling onto an untreated surface and eventually recovering and escaping. This can only delay resistance selection.

Arthropods of medical importance can be broadly classified as :-

1. Ectoparasites, actually attaching themselves to man for some considerable period of time.
2. Domestic, spending part of their time at least living in man's dwelling.
3. Truly feral and only contacting man outdoors.

However, there are several instances of overlap between these situations.

There is a wide range of ectoparasites. These include the head lice and crab lice which are permanently attached to their host, the body lice which detach themselves periodically to rest in the clothes, and fleas, hard ticks and mites which detach themselves periodically to change hosts or to live a free life.

To control lice and scabies mites insecticides are applied to the body in the form of lotions and shampoos, or beneath the clothes as dusts. Resistance to the organochlorine insecticides is now quite commonplace in both head and body lice. The treatment of crops with insecticides would not normally be expected to exert much selection pressure on these organisms except in people working in the crop fields or involved in the insecticide application. Malathion resistance in body lice in Burundi is actually attributed to lousy coffee pickers contaminating themselves with the insecticide used to treat the bushes.

The fleas which attack man are brought into the domestic situation by rodents and pets. Those belonging to the latter spend their larval life in the floors of dwellings and may therefore be subject to insecticide selection from house spraying activities. Adult selection may arise from insecticidal treatment of the pets or of man himself. Those of rodents spend their immature existence in rodent burrows and both larvae and adults may be exposed to insecticides delivered into these burrows or to captured rodents which are later released to carry the insecticide back to the burrow. Organochlorine resistance is common in both rodent and cat and dog fleas while malathion resistance has been detected in the field-rat flea in central Java.

Hard ticks may be picked up outdoors and transferred to an indoor existence. They are primarily ectoparasites of domestic

animals and pets, particularly dogs. They include the vectors of Colorado tick fever, Rocky Mountain spotted fever and other diseases. Control is usually by treating the animals themselves with insecticide washes, sprays, dips or dusts or treating their haunts, e.g. pasture vegetation or animal sleeping areas. Invasion of houses may also necessitate spot applications to baseboards, floors, wall-cracks etc.

Agricultural usage of insecticides could presumably contribute to resistance selection in some cases. Resistances to both organochlorines and organophosphates are known in several species. The mite vectors of scrub typhus live primarily outdoors associated with patches of low-lying vegetation - grass or scrub- on the edges of forests or manmade by burning down forest for cultivation purposes. These are the so-called mite islands. The adult mite is free-living. It is the larva which attaches itself to man and remains attached for several days. Control on a large scale is seldom attempted but when it is directed against the mite islands usually by spraying with residual insecticides. It is not impossible that such breeding areas could be contaminated from drift of agricultural sprays used in neighbouring areas, though so far no insecticide resistance has been detected in scrub typhus mites.

Myiasis, the condition produced by the invasion of the body of animals by certain dipteran larvae such as the tumbu fly, Congo floor maggot, screw-worm, warble fly and botfly, is usually an occupational infection in people closely associated with domestic animals. The adult flies are free-living, outdoor species which will not normally come into very much contact with insecticides though animal treatment primarily directed against ticks may result in some insecticidal contact larvae. The chigger flea (Tunga penetrans) is unique among fleas in being parasitic as an adult female, but free-living as a male and as immatures. All the forms may have contact with insecticide deposits from house-spraying whether specifically directed to floor coverage or from fall-out from wall and roof spraying. No cases of insecticide resistance have ever been recorded in these species

but it is doubtful whether any specific susceptibility tests have ever been carried out.

Among the most permanent occupants of houses are some of the soft ticks (Argasidae), bed-bugs, cockroaches and triatomine bugs. *Ornithodoros moubata* the soft-tick vector of relapsing fever is one which hides itself in floor cracks in dwellings between nocturnal feeds. Its control is usually by the treatment of floors with an insecticide like HCH and no resistance has yet been found in it. Bed-bugs similarly rest in cracks and crevices in the daytime though these are more often in walls and furniture. Organochlorine resistance is common in both Cimex hemipterus and C. lectularius, while organophosphate resistance has been recorded in the latter species in Israel and the USSR. This resistance is undoubtedly attributable to house spraying and its common occurrence is a frequent cause of friction between public health authorities and householders who object to having their houses sprayed by something which does not eliminate all biting nuisances. Mostly domestic, but unlike the soft ticks and bed-bugs, capable of flight in the adult stage, are the cockroaches and the triatomine bugs, the vectors of Chagas' disease in South America. Organochlorine resistance is common in both Blatta orientalis and Blattella germanica. Organophosphate resistance has been found in the latter species in Canada and the USA and indications of carbamate and pyrethroid resistance also. Rhodaius prolixus is resistant to dieldrin in one part of Venezuela. These resistances in cockroaches and triatomines must come from the treatment of houses with insecticides.

Adult mosquitoes are frequently found resting in houses especially those that bite man and especially in the tropics. The extent of indoor resting varies with the species and among the vectors of malaria, filariasis and virus diseases it is this degree of endophily that may determine the success or failure of control of these diseases by the use of insecticides in houses. Anopheles funestus and A. minimus are examples of highly endophilic malaria vectors and there are many instances of control

to a point of local eradication of these species by house spraying. A. balabacensis on the other hand is one which only rests for a short time indoors and most attempts to control malaria transmitted by this species by house-spraying have failed. Most other vector species fall between these two extremes, but there seems to be no positive correlation between the degree of endophily and the frequency and extent of insecticide resistance. Resistance in A. funestus and A. minimus is confined to dieldrin for example, even though DDT has been frequently used in houses and over long periods against these species. A. arabiensis, A. stephensi and A. culicifacies on the other hand, though only partially endophilic, frequently show resistance to both DDT and dieldrin and now to malathion also. At the extreme are A. hyrcanus and A. pharoensis which seldom, if ever, enter houses and yet the former in Turkey is resistant to organochlorines, organophosphates and carbamates and the latter resistant to DDT and dieldrin throughout the Nile Delta in Egypt, where no organized house-spraying has ever taken place. There seems little doubt that resistance in these two species has arisen through the agricultural rather than the public health usage of insecticides. However, there is some doubt as to whether the selection of the resistance occurred through adult outside resting on insecticide contaminated ground or plants or through larval contact in breeding places. Probably both make some contribution.

In the case of mosquitoes, of course, there are other stages in the live history and other places where the insect can contact insecticides. The larval stages are aquatic and may be subjected to insecticidal contact (from which they cannot escape) from their deliberate use as larvicides or from the contamination of breeding places from their use in agricultural spraying. Larviciding for malaria control purposes, particularly in rural areas, is rarely practised on a large scale. Against nuisance mosquitoes and against those species of culicines which are the vectors of the viral encephalitides, larvicides may form the main method of control and where their use coincides

with agricultural insecticide usage, as it often does in the USA for example, it may be impossible to unequivocally attribute resistance to one usage rather than the other. One curious anomaly which has recently come to light is the fact that in some anopheline species, e.g. A. arabiensis from the Sudan and A. stephensi from Iraq and Iran, although the adult shows resistance to malathion the larva does not. This would seem to suggest that resistance arose through adult selection and therefore through house-spraying rather than through agricultural practices. The area in which malathion resistant A. arabiensis has been found is in the very extensive Gezira Irrigation Scheme south of Khartoum where cotton is the main crop and where large quantities of organochlorines, carbamates and pyrethroids have been distributed outdoors over a number of years. Resistance to both DDT and dieldrin in this important malaria vector and a major epidemic of the disease necessitated a change to malathion for house spraying in 1975. After only two spray rounds in this year and one in 1976 resistance was apparent in adults, specific to malathion. This was confirmed in the laboratory in London where single gene inheritance was established and the enzyme carboxylesterase incriminated as the degradation mechanism involved. With the absence of larval resistance it looked certain that the resistance arose through house-spraying. This has been confirmed by the fact that the proportion of resistant individuals is high, if not higher, in neighbouring sugar-growing areas, where agricultural insecticides are hardly used at all.

Outdoor resting by adult mosquitoes occurs to some extent in all species. What happens during the period spent between emergence from the pupa and host-seeking by the female is somewhat uncertain. We know that most females will not feed during the first 24 hours of life and we know that male mosquitoes are incapable of copulation during much the same period, during which their terminalia rotate through 180°. It is possible that both sexes spend this time resting in fairly open vegetation in

the immediate vicinity of the breeding places and could therefore be exposed to insecticide drift from crop spraying if these sites are near to crop fields. Whether males migrate far from breeding places seems unlikely and though some may be found in houses this is usually taken to be merely an indication of the proximity of breeding places. Outside resting by females after oviposition is again likely to be in the vicinity of the breeding place but such resting after feeding and before oviposition may be more deliberately chosen and seems likely to be in a situation less prone to insecticide contamination from outdoor usage, viz. in well-shaded earth banks, tree holes or buttresses, termite mounds, rock cavities etc. or else in dense vegetation, in both of which types of site the insect is likely to be well protected from excessive water loss in the heat of the day. However, there are exceptions to this and some species habitually rest in more open situations though these are usually under the overall cover of forest canopy. A. pharoensis is reputed to rest in cotton fields and hence selection for resistance could have occurred through adult exposure as well as larval. It seems unlikely that adult A. arabiensis could survive the much greater extremes of climatic conditions in the same situation in the Sudan, though this remains to be established.

As with the mosquitoes some species of sandflies (Phlebotomine) rest indoors while others, the majority, are entirely outdoor feeders and resters. The larval life is usually spent in the ground and almost always outdoors. The only case of insecticide resistance (to DDT) so far recorded is in Phlebotomus papatasi in Bihar, India and this is a predominantly endophilic species.

The biting midges (Ceratopogonidae) are predominantly feral by nature and breed in damp ground or marshy situations. Some enter houses to feed but do not rest there for long as a rule. Two species have been recorded as resistant to organochlorines but whether there is any connection between this and agricultural spraying is unclear.

The common housefly and associated synanthropic flies breed outdoors in situations created by man and his domestic animals. They often rest indoors but particularly in animal shelters. Insecticide resistance is more widespread and more complicated in Musca domestica than in any other insect species and undoubtedly stems mostly from specific attacks on its resting places and breeding habitats.

The truly feral species include the tsetse flies, blackflies and Tabanids. The first of these are characteristic of areas unlikely to be used for crop-growing but may be associated with animal grazing areas (wild or domestic). Both aerial insecticide spraying and the spraying of specific adult resting sites has been extensive in some parts of Africa but in spite of this no case of insecticide resistance has yet been found. The immature existence is spent inside the mother fly and below ground.

Blackfly larvae characteristically breed in rapidly flowing water and have been controlled by the addition of insecticide at the origin of streams and rivers. As a result, resistance to DDT has arisen in some species including onchocerciasis vectors. The current onchocerciasis control project in West Africa employs temephos as a larvicide and resistance to it in only a small part of the total area under treatment has led to a change local to chlorphoxim.

Agricultural spraying is unlikely to contribute to the selection of resistance in onchocerciasis vectors because those areas where the disease is most prevalent are precisely those avoided by man and it is only through the control of the blackfly that these areas will be opened up for agricultural development.

Chrysops, the Tabanid vector of Loa loa is an outside daytime feeder and the disease is an occupational one of plantation workers in West Africa. Little contact with insecticides is likely to occur at any stage in the life of this insect and no resistance is known in it.

Thus of all the arthropods of medical importance mosquitoes, which include the vectors of malaria, filariasis and various virus diseases, are the most likely to be affected by the use of insecticides for agricultural purposes. The effect of crop spraying seems more likely to be on the aquatic larval stages than on the adult and on those species occupying places near to the crop-growing areas and therefore most likely to be contaminated. If this happens to be the same insecticide used for attack on the adult by house-spraying (or belong to the same group on which resistance genes present in the insect population will act), this can only intensify resistance selection. Therefore it becomes imperative for both public health and agricultural authorities to come to an agreement over which insecticides each uses so that such intensive selection is avoided.

5-1 A SUMMARY OF REPORTS PRESENTED BY COUNTRY REPRESENTATIVES

5.0 Papers and reports concerning pesticide usage and resistance problems presented by the representatives of Bangladesh, Burma, China, India, Pakistan, the Philippines and Thailand; some delegations presented more than one paper and some oral presentations were made. There follows a precis of the major points made in these papers.

5.1 Bangladesh

The insecticides used for agricultural pest control are mainly the organo-phosphates Malathion, Fenitrothion, Diazinon, Dimecron; while Dieldrin and Heptachlor are used as soil insecticides. For public health control Malathion, Diazinon, Fenthion, Dichlorvos are used, and two chlorinated hydro-carbons, BHC and DDT, the last being manufactured and formulated locally.

In practice for insect control in the field of agriculture, Malathion, Diazinon, Fenitrothion and Carbaryl have been in use in Bangladesh for more than 20 years. But no study has yet been undertaken anywhere in the country to evaluate if resistance of insects towards these insecticides has been developed, but there have been general complaints from the users and the national press that Malathion and other common agricultural insecticides are no longer useful for control.

During the last two years there were severe infestations of rice hispa (*Di cladispa armigera*) in epidemic form in some parts of the country. This insect was not of importance prior to 1979 but it is now one of the major pests causing economic injury. There have been again complaints from the farmers and national press that pesticides which are available in the markets are not working effectively in controlling this insect.

Most of the major cities in Bangladesh are heavily infested by public health vectors (*Culex fatigans*, *Aedes aegypti*); while in 1975 adequate control was possible using Malathion and Fenitrothion, this is no longer the case, and the Government intends to begin a resistance survey.

5.2 Burma

The incidence of agricultural pests seems low in Burma compared with surrounding countries. Major pests of important crops are *Spodoptera mauritea*, *Dicladispa armigera*, *Tryporyza incertulas* and *Mythimna separata* on rice, *Sesamia* and *Chilo* on sugarcane, and *Spodoptera*, *Agrotis*, *Plutella* and *Epilachna* on vegetables. Cotton pests are the same as those found in India.

To control these the most widely used pesticides are malathion, DDT, Endrin, Sevin, Lindane and Aldrin, but trials are now being carried out with the synthetic pyrethroids.

The major public health problems and vectors are malaria (*Anopheles minimus*, *A. Annularis* and *A. culicifacies*), Dengue Haemorrhagic Fever (*Aedes aegypti*), Japanese Encephalitis (*Culex tritaeniorhynchus*, *Cx. vishnui* and *Cx. gelidus*), and Filariasis (*Culex fatigans*).

To control these vectors DDT is widely used, and Malathion and Fenthion are also used. No systematic studies on resistance have yet been made in Burma, but arrangements are being made for a survey of resistance in agricultural pests. Resistance exists in public health vectors; *A. annularis* and *A. culicifacies* are resistant to DDT, and *Aedes aegypti* may also be resistant to that compound, while *Culex*

fatigans is resistant both to some organo-chlorines and Fenthion.

The procurement and distribution of pesticides in Burma is a Government monopoly, but there is no legislation relating to their control, sale, or use in the country. Work is in progress to set up a central testing laboratory and to develop training courses in the safe use of pesticides.

.3 China

A survey of mosquito resistance to insecticides was started in the late 1950s. Since 1978 a co-operative group, including Shanghai Institute of Entomology, Academia Sinica, Provincial Institutes of Parasitic Disease Control and Centres of Sanitary and Epidemic Prevention, has been responsible for the surveillance of the mosquito resistance to insecticides.

The following is an outline of the status of mosquito resistance to insecticides.

a) *Culex pipiens fatigans* (*quinquefasciatus*) and *Cx. pipiens pallens*

Since 1949, large quantities of DDT and BHC were used in the mosquito control programmes. *Cx. pipiens fatigans* developed resistance to these insecticides rapidly, especially in the urban areas of South and East China.

Widespread resistance to organo-chlorines of these mosquitoes forced the use of organo-phosphate insecticides and since the 1960s Dipterex, DDVP, Malathion and others have been used as the substitutes in most districts. Ten years later resistance to Dipterex and Malathion was demonstrated in some districts.

b) *Anopheles sinensis*

This species is an important malaria vector in the plains of central china. It was demonstrated that this species has a significant behaviour resistance to DDT. The large scale use of insecticides in the rice fields for the controlling of agricultural pests also gives a resistance selection pressure to *A. sinensis*.

When the organo-phosphate insecticides were substituted for organo-chlorines, BHC resistance has decreased gradually, but the high tolerance to DDT is maintained.

Recently, this species has demonstrated more tolerance to Malathion and Sumithion.

c) *Anopheles minimus*

This is an important vector of malaria in mountainous and hilly regions of South China.

In 1979-81, the co-operative group made a survey of the tolerance of *A. minimus* to insecticides in some parts of China, and it was found that the DDT and BHC susceptibility of *A. minimus* had decreased. However, control with DDT and BHC house-spraying continues to be satisfactory, despite the low-level organo-chlorine resistance of *A. minimus*.

d) *Aedes albopictus*

This species in the urban and suburban area of South and East China has developed a high-level DDT resistance, and BHC resistance has been suspected, but it is sensitive to organo-phosphate insecticides.

e) *Culex tritaeniorhynchus*

This species has developed a low-level DDT and BHC resistance and a high level organo-phosphate resistance, as reported recently from Shanzi Province.

5.4 India

Development of resistance to pesticides by insect and other vectors of relevance to public health and agriculture has been of great concern to India ever since the national eradication of malaria (N.E.M.P) Programme was initiated in the early fifties. In the beginning interest was confined to mosquitoes which act as vectors for malaria and filaria. Later investigations have covered vectors of other diseases, non-target organisms, house fly, lice etc. The most significant recent finding of ominous consequence is the fact that the sandfly *Phlebotomus papatasi* has developed resistance to DDT in Bihar.

With the increasing use of chemical control of pests in the pre-harvest and post harvest phases of agricultural operations and food production, attention has also been directed to assess the emergence of resistance in the vectors concerned with plant diseases and in the insects responsible for spoilage of food during post harvest storage.

5.4.1 Insecticide Resistance in Mosquitoes and Other Arthropods

Three years after the institution of the malaria eradication programme low-levels of DDT resistance in *A. culicifacies* described earlier as tolerance were reported in 1959. Initially this resistance was not of serious consequence but by 1965-66 DDT and BHC spraying had failed to control the epidemics that broke out during the phase

of consolidation of the programme. Since then malaria transmission has remained unchecked and the number of cases has been steadily increasing. Malathion was introduced in 1966 and there was demonstrable decrease by a factor of three or four over a period of two to three years.

However, by 1980, *A. culiafacies* the major vector of malaria had become resistant to DDT, BHC and Malathion in areas holding a population of more than 250 millions. A significant finding has been the detection of Malathion resistance in areas where the compound is being used for the control of agricultural pests and not in public health programmes.

5.4.2 Insecticide Resistance in Agriculture

India took part in the global survey on pesticides susceptibility of stored grain pests conducted by FAO during 1972-73.

Both Malathion and Lindane have been reported to give high failure rates of control of pest infestation in stored grains. Using discriminating dose tests it would appear that the above failure is due to emergence of resistance of the pests to Malathion and Lindane. In specific failures with *Tribolium castaneum* and *Sitophilus oryzae* in the field, monitoring tests and laboratory assays have given definite indication of resistance.

The table given below summarises some information for certain public health vectors.

<u>Insecticide Resistance in Arthropods</u>				
	<u>DDT</u>	<u>Dieldrin/BHC</u>	<u>Malathion</u>	<u>Carbamates</u>
<i>A. culicifacies</i>	+	+	+	+
<i>A. stephensi</i>	+	+	-	-
<i>A. fluviatilis</i>	+	-	-	-
<i>A. annularis</i>	+	-	-	-
<i>A. philippinesis</i>	+	-	-	-
<i>A. albopictus</i>	+	-	-	-
<i>A. vittatus</i>	+	-	-	-
<i>Pediculus humanus</i>	+	-	-	-
<i>Xenopsylla chepis</i>	+	-	-	-
<i>Xenopsylla astia</i>	+	-	+	+
<i>Phleopotorus papatasi</i>	+	-	-	-

5.5 Pakistan

Malaria is the most serious vector borne disease in Pakistan, the vectors being *Anopheles stephensi* and *A. culicifacies*. These vectors were originally controlled with DDT manufactured locally between 1955 to about 1971 but a survey carried out by the Directorate of Malaria Control confirmed resistance to DDT at that time and Malathion was then used until about 1979, when Sumithion and synthetic pyrethroids were also brought into use. Some slight resistance to Malathion has appeared in some areas but it is still in widespread use.

In the sphere of agricultural pests, organo-chlorine resistance was detected in *Pyrrilla* spp on sugarcane in 1961. By 1973 the species was reported resistant to Dimecron, but although tests suggested this

was due to incorrect dosage and application, Fenitrothion and Diazinon were substituted.

In relation to reports on resistance of cotton pests to Dimecron, Thiodon and Endrin, investigations again suggested this was due to incorrect dosages and defective application. Emphasis has now been placed on the need for resistance surveys and adequate insecticide screening trials to guard against the further development of resistance.

5.6 Philippines

Several species of agricultural pests have become resistant to pesticides in the Philippines, the worst cases including the major pests of rice, the planthopper *Nilaparvata* spp and the leafhopper *Nephotettix*. DDT resistance was noted a long time ago and now resistance to organo-phosphates and carbamates is present.

The regulatory body in the Philippines, the Fertiliser and Pesticide Authority, is concerned to develop resistance surveys and also to investigate the environmental aspects of pesticide usage.

5.7 Thailand

The major diseases and associated vectors are malaria, with five major vectors *Anopheles minimus*, *A. balabacensis*, *A. maculatus*, *A. sondaicus*, *A. aconitus* and several minor ones. Japanese Encephalitis *Culex tritaeniorhynchus*, *Cx. gelidus*, *Cx. fuscocephala*, *Cx. vishnui*, * Dengue Haemorrhagic Fever *Aedes aegypti*, and Filariasis *Mansonia* spp and *Aedes niveus*.

Large scale vector control with DDT emulsifiable concentrate has been carried out since 1950, but resistance does not seem to have developed on a wide scale.

However, Temephos, Malathion and Fenitrothion have been used for vector control, notably against *Aedes aegypti* and a careful resistance country-wide survey of Thailand suggests that while resistance to Malathion is gradually increasing Temephos and Fenitrothion are not affected. One of the interesting conclusions from this work was that pesticides used in agriculture had no impact on urban mosquito resistance.

As regards agricultural pests, the most serious pests, which have developed rather wide spectrum resistance, are the American bollworm (*H. armigera*) the diamond back moth (*Plutella xylostella*) and the armyworm *Spodoptera exigua*. Resistance has appeared to organo-chlorines, organo-phosphates and carbamates and has been induced in the laboratory to synthetic pyrethroids.

Because of these problems, microbial pesticides such as *Bacillus thuringiensis* are now being used.

There are some resistance surveys of agricultural pests undertaken but not in a systematic manner, but because 60% of all pesticides applied in Thailand are used on cotton and vegetables further resistance problems can be expected.

6-0 PESTICIDE USAGE AND INDUCTION OF RESISTANCE
IN PESTS AND VECTORS

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Role of Agriculture

Agriculture has been the main occupation of the people of this island from ancient times. After we attained Independence the agricultural goals of this country have been:

- (a) to sustain a high level of productivity in the major export oriented crops of tea, rubber and coconut;
- (b) to achieve self sufficiency in food, and more recently
- (c) to diversify crop production.

The possibilities of increasing agricultural production still exist in our major export crops. However, the scope for the future lies in the cultivation of other crops for export and food. The characteristics of the environment such as topography, soils, temperature regimes and variations in precipitation determine the prevailing land-use, cropping patterns and development potentials in the country. Today Agriculture contributes 33 percent of the GNP earning 80 percent of the foreign exchange and employing 50 percent of the wage earners. Export oriented crops such as tea, rubber and coconut together with rice the staple food constitute the main agricultural production of the island.

The performances of the major and minor export crops is an important determinant of the country's import capacity, while the volume of rice production has an important bearing on the

total quantity of cereals imported. Despite an import bill of Rs. 6000 million on rice, flour, wheat, sugar, dairy products, etc., the trends in agriculture production appear optimistic (Table 1). In the last 3 years rice production varied only 3% from the targets set by the Ministry of Agricultural Development and Research. If the current year's implementation target of 112 million bushels of paddy is achieved self-sufficiency would have been achieved in the staple food of our 14½ million people (Agriculture Implementation program 1981 - 1982). Successive governments have supported the drive for self-sufficiency in food and diversification of export crops by implementing policy measures, such as the restoration of old irrigation reservoirs, the building of new ones, the developing of river valley schemes (Table ii), providing incentives to the cultivators in the form of attractive floor prices providing credit and subsidy schemes, the introduction of high yielding strains, and the use of improved cultivation practices (inclusive of fertilizer use and crop protection techniques).

Although biological research on non-chemical crop protection is receiving frontline attention in the major crops, tea, rubber, coconut and rice, yet control recommendations for several of the annual crops are mainly chemical in nature. Measures for pest control in the major and minor export crops are recommended by the respective commodity research Institutes. About two decades ago, the major user of pesticides was the tea industry. From Table III it is apparent that over 20% of their pesticide bill accounted for insect control. But today, as in the case of other permanent tree crops, the use of insecticides is minimal, as management of the crop and biological control are the main techniques adopted to keep pests down to sub-economic levels. Further, due to the small number of clients involved in the plantation sector, there is good rapport between planters and their servicing units, official advice being accepted almost in toto. The Departments of Agriculture and Minor Export Crops service the peasant

farmer with small land holdings 0.5 to 5 acres in extent.

Policy changes in the agricultural sector such as attractive open market prices for paddy and other crops have helped to increase substantially agricultural production. However, the lack of manpower to advise these innumerable "small farmers" on the improvement of crop management as an initial crop protection measure has stalemated the need based pesticide policy of the Department. Extension staff have observed that the small farmer is not sufficiently vigilant and he often uses chemicals when it is too late for economic returns. This is because of a lack of appreciation of the "need based" use of pesticides.

Policy on Pesticides:

In the developing countries the introduction and use of pesticides in agriculture remained unrestricted until recently. In Sri Lanka the need to exercise control over the supply, distribution and use of pesticides had been recognized for quite sometime (from the early sixties), and a draft "Act on Poisons Used in Agriculture" had been prepared and forwarded to the legal draftsman in 1964. However, it was only in the early 70's that Government took definite steps and sought through the FAO advice on the establishment of a national organisation for the official control of pesticides and assistance in reviving the Bill on Pesticide Legislation (FAO Report Bangkok 1972).

After much deliberation the Control of Pesticide Act No.33 was gazetted in 1980. Procedural and recruitment delays have postponed the implementation of this Act. In the history of pesticide marketing in Sri Lanka, it is evident that various measures were instituted to bring it under Government control. Agrochemicals were more or less freely imported into this country by 40-50 importers up to October 1962. In 1963, to conserve the dwindling Foreign Exchange reserves, the Controller of Imports and Exports limited the exchange for the import of agrochemicals to Rs.5.23 million. Vehement protests by the importers resulted in the appointment of a government committee to draw up a list of "Drugs, Chemicals and

proprietary preparations required for use in Agriculture". The committee recommended that a policy of strict import restrictions would negate the nations' efforts to boost local production. They also submitted a list of agrochemicals (Insecticides and Acaricides 26, Fungicides 19, Weedicides 17, Rodenticides 2, Fumigants 3, and Molluscides 1), to be supplied by 15 approved importers.

By 1965 the c.i.f. value of the country's annual agro-chemical requirement was Rs.8,550,000/- (Manickavasagar 1979). The import of agro-chemicals became more and more restrictive as export earnings of the country declined. The Formulary Committee on Agro-Chemicals was given the responsibility of deciding the pesticide requirement of both plantation and domestic agriculture. The foreign exchange was released on a 6 month basis and only chemicals in the Formulary could be imported. No other agro-chemical could be imported, unless at the insistence of the Government either for use in pest epidemics or as samples for experimental purposes.

A change in government policy in the latter part of the last decade and the liberalization of imports, made the control of pesticides difficult. Agro-chemicals whether in the Formulary or not were being imported by persons outside the approved list under Open General Licence. Subsequently, as an interim measure action was taken by the Ministry of Agricultural Development and Research and the Ministry of Trade and Shipping to restrict import of agro-chemicals that were gazetted. The few loop holes that still exist for import of non-recommended pesticides can only be blocked by the implementation of the Pesticide Control Act.

Pesticide use in Agriculture - Past and future

It is timely now to address our minds to the main object of our deliberations here. The problem of practical importance which is under discussion is the effect of pesticides used in

agriculture on the development of resistance in agricultural pests and vector species of human diseases.

As resistance in pests is conditioned by sustained selection over a long period of time on a large pest population possessing a high rate of reproduction, insecticides used widely in rice cultivation especially in areas such as Amparai, Kurunegala, Hambantota and Puttalam or where intensive cultivations of cash crops motivates the farmer to use several rounds of insecticides as in Jaffna, Vavunia, Mullativu, Puttalam, Matale, Nuwara Eliya and Welimada (the last two cultivation areas are over two thousand five hundred feet above sea level) could be expected to exert selection pressure on target species.

The use of chemicals in agriculture dates to the early post war era. DDT was used in 1946 and continued until the early sixties, when the chlorinated hydrocarbon insecticides were generally recommended for pest control. They were then replaced by organophosphates and carbamates, with the synthetic pyrethroids being recommended only for selected use on onion and cotton. The use of chlorinated hydrocarbons in agriculture is limited now to gamma BHC (as dusts and granules) Aldrin and Chlordane. In the rice environment, both organophosphate and Carbamates (as granules and sprays) are used on a need basis. Today, the common agrochemicals favoured, by the rice farmers are carbofuran (3% granules) BPMC (concentrate) Propoxur, (granules & emulsion concentrates) and emulsion concentrates of Parathion and Monocrotophos. In cash crop cultivation Monocrotophos, Parathion, Methamidophos, Fenthion Quinalphos and Dimethoate are used intensively, often in the form of cocktails.

The Agriculture Department's research efforts to develop varieties of rice, resistant to the two major pests are already bearing fruit. It is envisaged that with the use of these varieties and the intensive programs on plant protection and

farmer education, the pesticide usage in the rice environment will decrease. (Table IV).

Although research on cropping patterns and the Integrated approach to pest management in cash crops is receiving attention, the impact on the environment will not be felt in the immediate future. The implementation of Pesticide legislation would further reduce the misuse or overuse of insecticides on cash crops.

Resistance in Agricultural pests

Amongst the major pests of rice the following show field resistance to insecticides after prolonged use in the field. Paddy bug (gamma BHC) paddy plant hoppers (gamma BHC, endrin, diazinon, carbaryl) paddy field crab (endrin, telodrin). Pests of other crops that have resistant or tolerant populations are paddle legged bug (gamma BHC) aphids on vegetables and tobacco (to several contact and systemic organophosphates), cabbage caterpillars (DDT, endrin, parathion), brinjal shoot and fruit borer (carbaryl) onion caterpillars (parathion). The degree of resistance attained by these species has been confirmed by laboratory studies in the case of Leptocoryza varicornis (paddy bug) Paratelphusa spp (paddy field crabs), Plutella maculipennis cabbage worm Spodoptera exigua (onion caterpillar).

Reports from various countries in the tropical belt indicating that mosquito control was becoming progressively more difficult in areas of intensive agriculture, forced the Government of Sri Lanka in 1976 to retain two pesticides (in the first instance) specifically for vector control; these were the relatively low hazardous, cheap organophosphate chemicals (malathion and fenitrothion).

The phasing out of these two chemicals for use in agriculture was very abrupt:

	<u>Malathion</u>	<u>Fenitrothion</u>
	<u>50ec 5% dust</u>	<u>50ec 1000 g/litre</u>
1975	2,275 gals 5T	30,000 gals
1976	2,500 gals	7,000 gals
1977	nil	nil

(Formulary of Agrochemicals 1975, 76, 77).

At this time Malathion had been recommended for use mainly against pests of vegetables such as gourds, onions and cowpea which are picked at frequent intervals, while the broad spectrum, more efficacious, fenitrothion had extensive use against major crop pests especially of rice and several high value drops (Annexe I).

Of the two pesticides withdrawn from use in agriculture the possibility existed for Fenitrothion resistance to be built up by selection pressure in the non-target organism the adult mosquito population in agricultural areas or by the contamination of larval habitats. However the probability of developing malathion resistance was extremely low as the quantity imported for agricultural use was small compared to that now used in anti-malaria work. (Table V).

The objective of this workshop is to arrive at guidelines to delay the onset of resistance in pests and vector species. Looking at it from a parochial point of view, how high is the probability of agricultural pesticide usage having a direct bearing on malaria control in Sri Lanka? Currently, in the malarial areas the bulk of the insecticides are used for rice or chilli cultivation. The adoption of the new improved varieties of rice and of cultural practices have and will continue to influence the rice field fauna and flora. Changes in the economic status of various pests have already been recorded (Fernando 1967 Wickremasinghe 1978, 1979). The loss of certain

fish fauna from irrigated rice fields is evident in Amparai and Kurunegala districts (Elikawela 1980). The authors are not aware of side effects on mosquito fauna in the rice environment. The penetration of sunlight through the rice canopy has changed over the last two decades, making it a poor harborage for adult mosquitoes. Land preparations of ploughing and levelling before sowing of rice, reduces the occurrence of larval sites though suitable habitats are available in the drainage systems - "the lunu or kanu elas". However, these receive no direct insecticide treatments. The superimposition of the areas under rice cultivation on a map of malaria incidence (Figs I and II) reveals that high incidence is not necessarily associated with rice cultivation but, on the otherhand, malarial areas in the eastern foot hills and the western dry zone belt abut on forest reserves, national parks and wild life sanctuaries which would act as a gene pool. The presence of several rivers which show pooling during the dry spells and at the onset of the first rains of the North east monsoon add to the availability of mosquito larval habitats. The Antimalaria authorities are confident of the continued susceptibility of the vector Anopheles culicifacies to malathion even after several years of spray coverage with the insecticides. However, they voice a note of warning on the necessity for vigilance and quick remedial measures in the Maduru Oya and Girandurukotte areas (Admin. Report 1980). The authors hypothesize that insecticide selection pressure will not be exerted on the anopheline population in these settlement areas due to the maintenance of heterogeneity from the surrounding reservoirs.

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TABLE I

QUANTITY IMPORTED AND LOCAL PRODUCTION
OF SELECTED CROPS
(IN 1000 METRIC TONS)

	RICE		CHILLIES		ONIONS		POTATOES	
	Import	Prod.	Import	Prod.	Import	Prod.	Import	Prod.
1959/60	542	614 ⁺	17509	14376 ⁺	10331	37394 ⁺	56633	1088 ⁺
1969/70	537	1106 ⁺	13356	32197 ⁺	65862	38217 [✓]	186	32446
1979/80	189	1460	13383	25459 [✓]	18609	79115 [✓]	11071	52451 [✓]

✓ Source : Department of Agriculture

+ Source : Census & Statistics

Import of Rice - Food Commissioner

Import of onions |
potatoes | Customs Returns
chillies |

TABLE II

EXTENT OF RICE FIELDS UNDER IRRIGATION SCHEMES
(IN HECTARES)

YEAR	MAJOR IRRIGATION SCHEMES	MINOR IRRIGATION SCHEMES
1960	131,676	136,847
1967	162,602	156,630
1977	208,460	161,051
1980	238,633	167,423

Source : Department of Census and Statistics

TABLE III

AGROCHEMICAL REQUIREMENTS FOR 1965
(C.I.F. value in Rupees)

Agrochemicals	C R O P S				Total val.
	Tea	Rubber	Coconut	Paddy and other field crops	
Weedicides	1,000,000	200,000	75,000	350,000	1,625,000
Insecticides	1,200,000	8,000	90,000	600,000	1,895,000
Fungicides	2,800,000	1,750,000	10,000	30,000	4,590,000
Fumigants & others	200,000	17,000	-	20,000	237,000
Total	5,200,000	1,975,000	175,000	1,000,000	8,350,000
Distribution among crops	60.9%	23.6%	2.1%	12%	

Value of imported material required for local formulation

200,000
8,550,000
=====

Source : P.Manickavasagar 1979.

TABLE IV

AREA UNDER IMPROVED VARIETIES
OF RICE

NEW IMPROVED VARIETY	AREA UNDER CULTIVATION (hectares)			
	TOTAL	PERCENTAGE	MAHA 81/82	YALA 82
All age groups	789,400	100	506,020	283,380
Resistent Varieties	146,465	18.54	88,630	57,825
G.M. - Bg 400-1 Bg 276-5				
BPH - Bg 379-2	5,570	0.71	3,980	1,590

Source Agriculture Implementation
Progress 1981-82 (M/AD & R)

TABLE V

MALATHION IMPORTS

Year	50 ec.	<u>AGRICULTURE</u>	<u>ANTI MALARIA</u>
		5% DUST	WP CAMPAIGN
1975	2,275 gals	5 T	450 T
1976	2,500 gals	5 T	40 T

T = ton

ANNEXE I

INSECTICIDE RECOMMENDATIONS - 1975/76

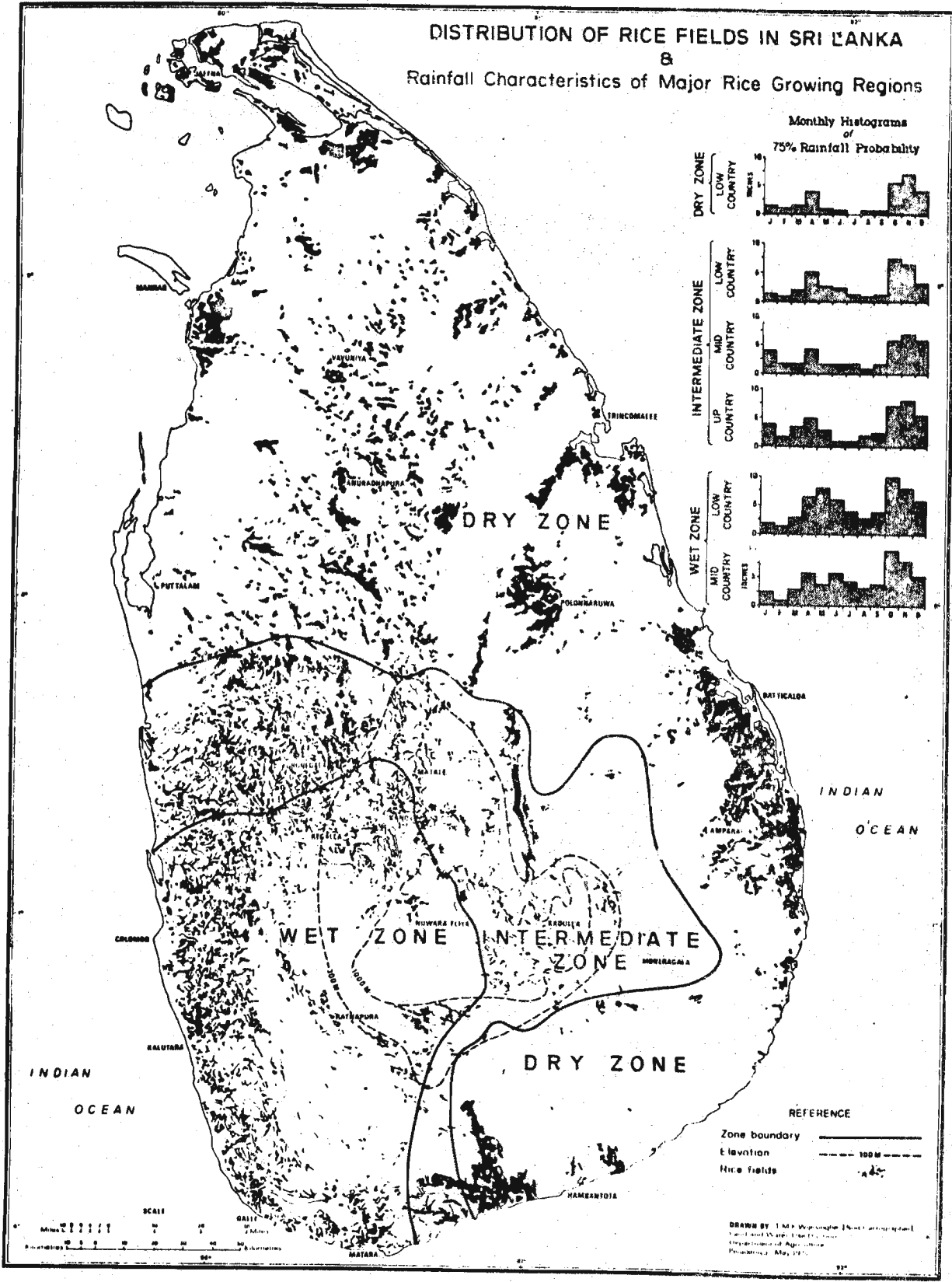
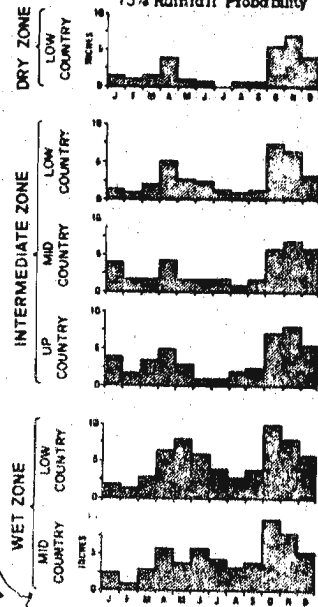
INSECT PEST	MALATHION	FENITROTHION
Paddy bug ^R (BHC)	1 ^a	2 ^a
Leaf folder	-	1
Other caterpillars	-	1
Paddy Field Crab	-	1
Plant Hoppers ^R (BHC)	1	2
Pentatomid bug	2	3
Paddy Stem Borer	-	4
Paddy Thrips	3 or	3
Paddy whorl Maggot	-	4
Fruit Fly Vegetable & Mango	1	-
Auloophora adults	1	1
Epilachna	1	3
Semi Looper	2	-
Leaf eating caterpillar	1	-
Bagrada bug	1	1
Brinjal Borer & webber	-	1
Lace Bag	3	3
Cowpea pod borer	2	2
Sweet Potato Tortoise beetle	2	2
Onion caterpillar	1	-
Citrus leaf roller & caterpillar	1	1
Mango leaf hopper	1	-
Pineapple mealy bug	1	2
Aphids vegetables	1	2
Tobacco stem borer	-	2
White Fly	-	2
Green bug and capsid	-	2

^a Numbers indicate priority of use.

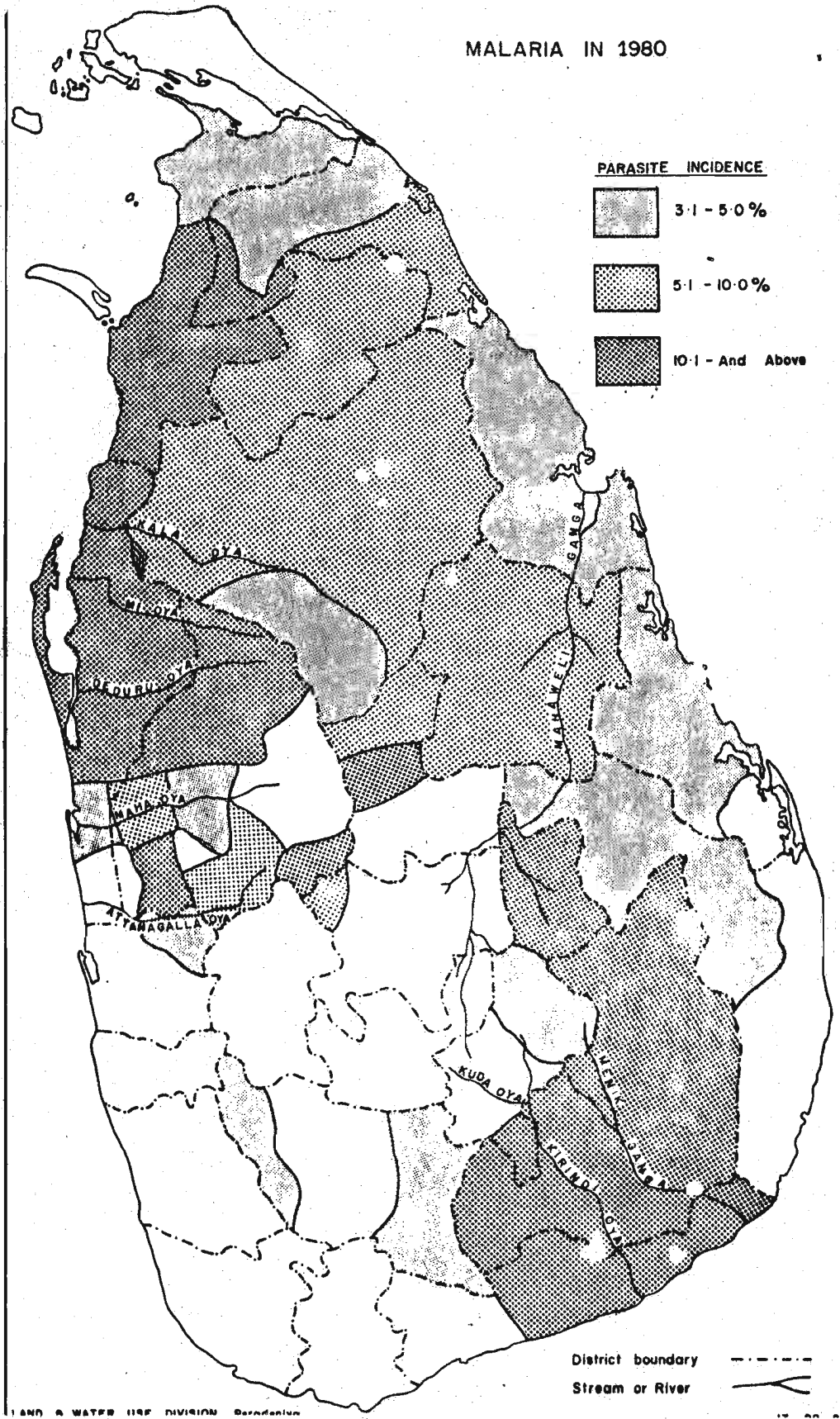
DISTRIBUTION OF RICE FIELDS IN SRI LANKA

B Rainfall Characteristics of Major Rice Growing Regions

Monthly Histograms of 75% Rainfall Probability



MALARIA IN 1980



6-1 PESTICIDE RESISTANCE AND MALARIA CONTROL IN SRI LANKA

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With the advent of DDT with its dramatic impact on deceases vectors the flobal concept of vector control was revolutionised. The concept of malaria eradication was an outcome of this. Sri Lanka was one of the countries which relied on DDT for malaria control as far back as 1946. With an initial experience of an highly effective control, the subsequent aim of eradication was almost achieved with only 17 recorded cases of malaria in the country in 1963. The subsequent failures in the control of malaria and the epidemics that followed in the later years was attributed mainly to the development of vector resistance to DDT. Table I summarises the data pertaining to the trends in DDT resistance in the malaria vector Anopheles culicifacies during the years 1961-1981.

The implication of the high levels of DDT resistance resulting in control failure was reflected by the continued increase in malaria incidence despite continued usage of this insecticide. This necessitated a change in vector control strategy-the replacement of DDT by more expensive malathion in late 1977.

At present malathion is sprayed as a residual insecticide on a total coverage basis for which the Government incurs an annual expenditure of approximately Rs.90 million. At the same time, fenitrothion has been reserved as the next alternative to malathion in the event of development of vector resistance towards the latter. As an early precautionary measure to avoid/delay/minimise early selection of A. culicifacies for resistance to these insecticides the Government of Sri Lanka banned the use of malathion for all purposes other than malaria control and curtailed the use of fenitrothion for all purposes.

In addition, a number of currently available alternative control measures involving the use of biological control agents and environmental management approaches are being investigated and put into practice in certain limited situations. All these methods being primarily based on larval control, even if effective, could have limited applicability in malaria control in countries like Sri Lanka, in view of the nature, extent and versatility of the breeding sites of A. culicifacies.

Therefore it is clearly apparent that inspite of the economic, technical (resistance) and environmental implications, insecticides will continue to remain the method of choice, specifically in large scale application in the control of disease vectors, particularly of malaria, in the foreseeable future (unless equally effective methodologies are developed).

Sri Lanka has already experienced the implication of DDT resistance in the malaria vector. There is also awareness of the increasing trends in resistance development in many vector species, including those of A. culicifacies from India, towards malathion, fenitrothion and other insecticides. Considering these aspects, the Government has recognised the need to prolong the operational life of the limited available insecticides for Public Health by delaying/avoiding/minimising development of resistance through their rational use.

The selective insecticide application being the most appropriate approach feasible for achieving this objective, the Government of Sri Lanka is to undertake selective malathion spray operations in the malaria control programme commencing March 1982, on the basis of stratification of malarial areas. In the absence of adequate, reliable epidemiological information, the initial attempt will be based on the transmission/vector breeding potential. In appropriate areas, the spray operations will be withdrawn or applied on a seasonal/perennial basis, instead of the current practice of insecticide application on:

a total coverage basis both in terms of time and space.

Apart from selective insecticide application, concepts of mixtures, rotations, optimum sequential usage of insecticides are considered as possibilities to be investigated, for the rational use of insecticides. To attempt these approaches in the long term planning of vector control strategies using insecticides, information is required on the identity of resistance mechanisms with broad cross resistance spectra, insecticides likely to select these, the presence and frequency of different resistance factors, geographical variations, importance of species characteristics etc. At present, with the exception of a limited anopheline species, most of such information is based on house-flies. Therefore related information if obtained from as many populations/species from different geographical areas/countries where resistance has already developed would be extremely useful.

Considering all these aspects, the studies related to insecticide resistance currently attempted in the malaria control programme in Sri Lanka is as follows:

- a. monitoring vector resistance to malathion in terms of its susceptibility status and behaviour in attempts to detect early appearance of resistance to malathion in the population (the programme is given in annexe 11),
- b. If and when malathion resistant individuals are detected, monitoring changing trends in resistance levels and studying the characteristics of the resistance(s) involved,
- c. Establishing operational implications of higher levels of resistance for consideration of alternative counter measures,
- d. monitoring susceptibility status towards other candidate insecticides available for public health i.e. fenitrothion, chlorphoxim, pirimiphos-methyl, propoxur, dieldrin, etc;

- e. monitoring changing trends in resistant levels to DDT to determine possible reversion to susceptibility;
- f. making an attempt to determine the nature of malathion/OP resistance mechanisms and relevant cross resistance spectra in populations of different anopheline species in Sri Lanka (in particular A. culicifacies) under varying conditions of selection pressure as guiding information to justify the banning or curtailment of malathion and fenitrothion in agriculture, in view of the nature of breeding and resting habits of A. culicifacies; and clarifying early (if feasible) the feasibility of using fenitrothion or other candidate insecticides for the control of malathion resistant populations of A. culicifacies if eventually encountered in the country.

According to the results obtained so far (Table 11) A. culicifacies in Sri Lanka has developed resistance towards only DDT and remains susceptible to dieldrin (BHC), fenitrothion, malathion, chlorphoxim, etc. (Table 111). Among other anopheline species prevalent in the same areas A. subpictus and A. hyrcanus (mostly nigerrimus) (Tables IV & V) have so far shown resistance to malathion, fenitrothion, chlorphoxim, DDT, dieldrin, etc. A. barbirostris has shown resistance to malathion, the other insecticides have not been tested.

Usage of DDT, the only residual insecticide used for malaria control until late 1977, is undoubtedly the major contributant in the selection for DDT resistance in this highly endophilic vector species. Although a variety of insecticides are known to be used in agriculture there is no direct evidence so far to suggest any possible selection of A. culicifacies by this means. In general, contamination by agricultural pesticides, and therefore selection in the usual breeding sites of the species is likely to be minimal. However, the increases in levels of DDT resistance encountered in the periods 1963-1968

(Table 1) when DDT usage was withdrawn for malaria control and the reports of the presence of organochlorine residues such as endrin, aldrin, etc. in the water resources which are the breeding sites of mosquitoes could suggest possibilities of selection to a certain extent by agricultural pesticide usage. The stability of the organochlorine insecticides should be noted in this context in comparison to the organophosphates.

Anopheles subpictus being endophilic (Table VI) and more versatile in its breeding habits (Table VII) is likely to be subjected to selection pressure by pesticides used for agriculture as well as for malaria control. A. hyrcanus and A. barbirostris, both highly exophilic, are not likely to be selected by malathion used for malaria control. The nature of breeding habits (Table VII) could however, favour selection by agricultural pesticides.

There is no strong direct evidence so far from the limited experience and information to suggest possible selection for resistance in the malaria vector from agricultural usage of pesticides in Sri Lanka. It seems unlikely that the extent of agricultural usage of pesticides could be comparable to that used on cotton plantations in Turkey or El Salvador. However at present it is difficult to foresee the implications following changing patterns of agricultural practices, water management, etc. following the completion of the new development projects.

ANNEXE I

INSECTICIDE SUSCEPTIBILITY/RESISTANCE
PROGRAMME CURRENTLY ATTEMPTED IN
MALARIA CONTROL PROGRAMME, SRI LANKA.

1. Early detection of malathion resistance in Anopheles culicifacies:

1.2 Programme to attempt improved coverage in space:

Health Area:	Total No. of villages in existence:	No. of villages/localities sprayed in '81:	No. of villages/localities examined in '81:	Approximate coverage (villagewise)
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Number of Villages/Localities examined per Health Area will be in proportion to the number of villages sprayed in the respective health areas. For example if Health Area 'A' has 100 villages sprayed and 'B' 1000 villages sprayed, more villages should be tested/examined in Health area 'B'.

1.2 Programme to attempt improved coverage in time:-
(Monitoring trends in malathion susceptibility tests).

Health Area:	Locality :	Dates of testing:

N O T E - A periodicity of 6 months per locality is planned.

ANNEXE II

For optimum utilisation of limited facilities such as trained manpower, finances etc., localities examined for early detection of malathion resistance are selected on the following order of priority:-

- (i) areas, with possible inadequate vector response to malathion/with high vector densities guided through reports of areas with -
- (a) high malaria incidence
 - (b) Plasmodium falciparum foci
 - (c) persistence transmission

The above information is to be obtained through the countrywide case detection operation.

- (ii) areas considered to have maximum selection pressure i.e. with maximum spray coverage.

This information is to be obtained from spray operational section.

- (iii) localities where resistance to DDT was detected earlier.

- (iv) any area visited for entomological investigations inclusion of those visited for trend observations.

- (v) localities which can be considered as having potential for high vector breeding/densities.

In monitoring changing trends in resistant levels to DDT (to determine possible reversion to susceptibility) a programme comparable to that in 1.2 is attempted.

TABLE I

DATA ON DDT SUSCEPTIBILITY TESTS FROM
1961 - 1981

Anopheles culicifacies

<u>Y E A R</u>	<u>Range of % Mortalities at 60 minute exposure to 4% DDT</u>
1961 - 1982	94 - 100
1966	97 - 100
1968	74 - 100
1969	32 - 75
1970	14 - 58
1971	12 - 51
1972	21 - 53
1973	25 - 58
1974	18 - 59
1975	13 - 69
1976	35 - 36
1977	13 - 49
1978	16 - 56
1979	12 - 47
1980	21 - 74
1981	12.5 - 100

TABLE III
 PERCENTAGE MORTALITIES OF WILD CAUGHT ANOPHELES CULICIFACIES IN ANGUN AREA,
 HAMBANTOTA HEALTH AREA TO VARIOUS INSECTICIDES FOR DIFFERENT EXPOSURE PERIODS

Insecticide & Concentration	Exposure time in minutes										
	2 1/2	5	7 1/2	10	12 1/2	15	20	30	45	60	75
Malathion	45.6 (195)	58.7 (327)	72.0 (376)	80.0 (100)	89.6 (97)	99.0 (304)	97.9 (147)	100.0 (264)	-	-	-
Fenitrothion	17.7 (362)	62.9 (388)	83.1 (344)	95.3 (149)	100.0 (50)	99.1 (344)	-	100.0 (175)	-	-	-
Chlorphoxim	79.9 (298)*	100 (50)	-	-	-	-	-	-	-	-	-
Fenthion	81.2 (501)	98.6 (293)	99.4 (197)	100 (20)	-	100 (206)	-	-	-	-	-
DDT	4.0%	-	5.0 (80)	-	8.1 (49)	-	-	-	11.5 (95)	35.7 (1265)	67.5** (219)
Dieltarin	12.0 (125)	28.3 (208)	85.2 (122)	92.0 (75)	83.0 (100)	100.0 (100)	100.0 (50)	100.0 (100)	100.0 (75)	-	-
Propoxur	19.7 (223)	67.7 (406)	87.8 (361)	98.9 (96)	-	100.0 (165)	-	100.0 (45)	-	-	-
Deltamethrin	80.0 (261)	98.0 (254)	96.0 (25)	100.0 (20)	-	100.0 (63)	-	100.0 (20)	-	-	-
Permethrin	0.0 (100)	5.0 (99)	10.5 (95)	-	-	16.8 (89)	-	54.0 (100)	77.0 (96)	100.0** (99)	-

* - 1 minute exposure ** - 120 minutes exposure () - sample size.

TABLE IV
 PERCENTAGE MORTALITIES OF LABORATORY BRED ANOPHELES SUBPICIFUS
 (F1 GENERATION) * FROM ANGUN ARA IN HAMBANTOTA HEALTH AREA
 TO DIFFERENT INSECTICIDES FOR VARYING EXPOSURE
 PERIODS

Insecticide & Concentration	Exposure time in minutes						
	5	7½	15	30	60	120	240
Malathion	1.8 (110)	6.1 (97)	22.2 (126)	23.0 (139)	41.0 (200)	79.6 (123)	100.0 (91)
5.0% Fenitrothion	0.8 (124)	2.6 (76)	19.3 (150)	27.7 (101)	56.3 (87)	83.9 (156)	100.0 (160)
1.0% Chlorphoxim	25.6 (109)	71.7 (99)	80.3 (122)	98.0 (105)	99.0 (102)	98.7 (80)	-
D.D.T.	-	-	4.8 (21)	-	0.0 (40)	-	-
4.0% Propoxur	66.5 (40)	74.6 (83)	96.1 (77)	96.9 (99)	100.0 (44)	-	-

() - sample size. * - less than one day old adult males and females tested.

TABLE V

PERCENTAGE MORTALITIES OF WILD CAUGHT ANOPHELES HYRCANUS GROUP
(MAINLY A. NIGERRIMUS) FROM COMMUNA IN KURUNEGALA HEALTH AREA
FO DIFFERENT INSECTICIDES FOR VARYING EXPOSURE PERIODS

Insecticide & Concentration	Exposure time in minutes									
	15-20	30	45-50	60	70	80	90-95	120		
Malathion 5.0%	-	20.0 (20)	85.0 (159)	91.0 (43)	96.0 (49)	96.0 (25)	100.0 (55)	-	-	-
Fenitrothion 1.0%	-	24.0 (25)	28.0 (159)	67.0 (49)	54.2 (48)	72.0 (25)	-	93.6 (63)	-	-
Fenithion 2.5%	-	52 (25)	65.8 (158)	76.5 (47)	91.6 (48)	90.0 (20)	100.0 (55)	-	-	-
Dieldrin 0.8%	-	-	-	4.0 (25)	-	-	8.0 (25)	12.5 (24)	-	-
Decamethrin 0.025%	-	34.7 (23)	56.3 (160)	67.3 (49)	80.4 (46)	83.3 (24)	-	95.5 (67)	-	-
Prpoxur 0.1%	-	95.0 (20)	81.6 (153)	88.6 (53)	90.5 (44)	95.8 (24)	-	98.4 (65)	-	-

() - sample size.

RESULTS OF PYRETHRUM SPRAY SHEET COLLECTION SHOWING NUMBERS OF
INDOOR RESTING ANOPHELINE MOSQUITOES

TABLE VI

Days after spraying	<u>A. culicifacies</u>	<u>A. subpictus</u>	<u>A. varuna</u>	<u>A. vagus</u>	<u>A. hyrcanus</u> group	<u>A. annularis</u>	<u>A. tessalatus</u>
1 - 30	82 (30)	1243 (284)	2 (1)	39 (7)	4 (0)	0 (0)	0 (0)
31 - 60	344 (151)	1973 (267)	13 (1)	27 (2)	3 (0)	6 (3)	0 (0)
61-90	364 (84)	2130 (326)	8 (0)	16 (1)	2 (1)	3 (0)	0 (0)
Beyond 90+ unsprayed	1250 (384)	6349 (1072)	28 (3)	154 (11)	40 (3)	01 (0)	2 (0)
TOTAL	2040 (649)	11695 (1949)	51 (5)	236 (21)	49 (4)	10 (3)	2 (0)

() - Males.

TABLE VII

RESULTS OF HABITATWISE LARVAL COLLECTION FOR ANOPHELES SPECIES - 1981

	Paddy fields	Irrigation Channels	River bed pools	River/Stream Margins	Rock Pools	Gem pits	Rain water undrains	Foot/hoots	Barrow Pits	Wells
<u>A.culicifacies</u>	0	137	343	61	11	13	9	2	31	0
<u>A.subpictus</u>	618	345	164	62	77	112	386	67	41	0
<u>A.vagus</u>	358	239	417	42	111	87	285	24	32	0
<u>A.varuna</u>	260	67	216	44	74	0	24	22	3	0
<u>A.barbirostris</u>	124	8	3	4	9	2	0	0	0	0
<u>A.annularis</u>	104	69	21	67	22	46	52	32	23	0
<u>A.pallidus</u>	21	14	25	25	0	0	10	0	0	0
<u>A.nigerrimus</u>	289	93	53	52	28	11	113	22	59	0
<u>A.aconitns</u>	30	0	0	0	23	0	0	0	0	0
<u>A.tessellatus</u>	11	17	100	9	2	0	0	0	0	0

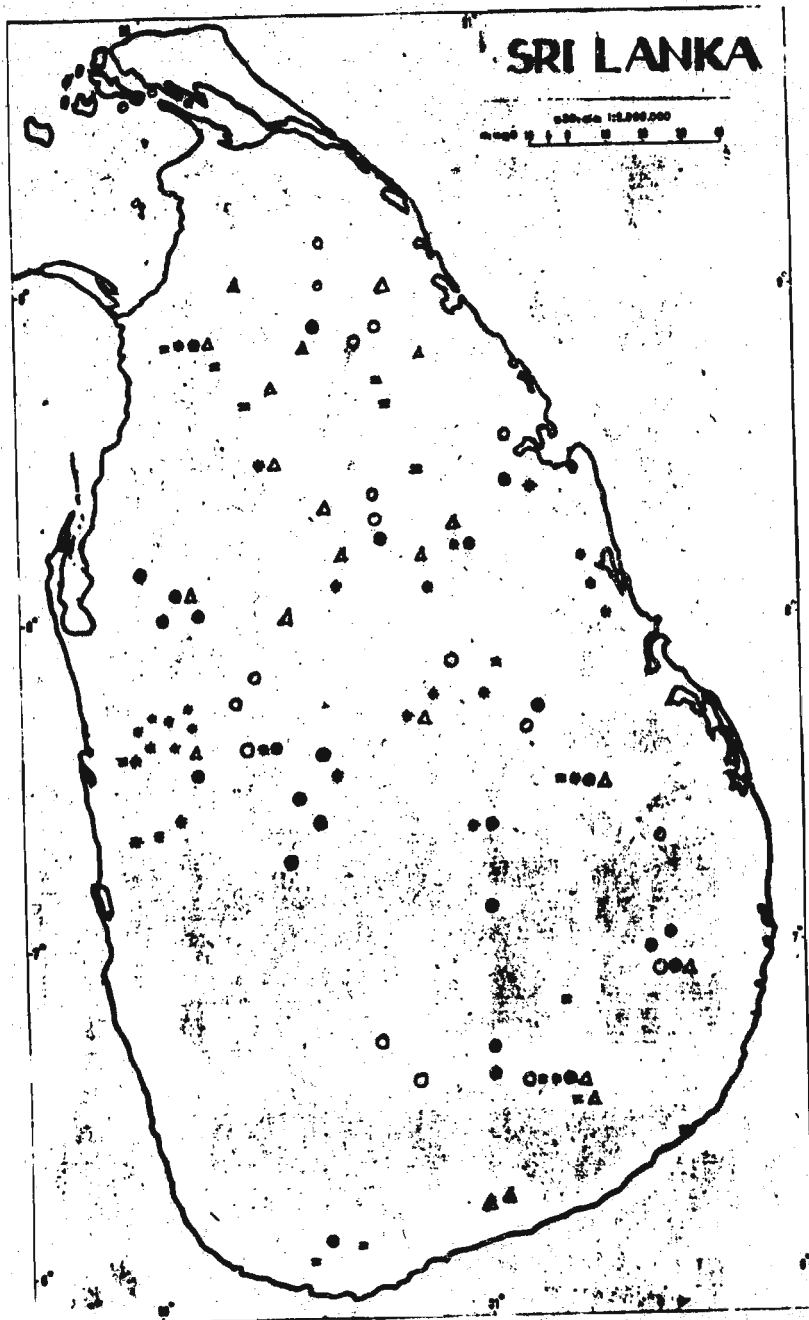
TABLE VIII

ANOPHELINE MOSQUITOES COLLECTED
RESTING OUTDOORS IN 1981

SPECIES	NUMBER	
<u>A.culicifacies</u>	18	(8)
<u>A.subpictus</u>	102	(29)
<u>A.vagus</u>	5	(0)
<u>A.varuna</u>	9	(0)
<u>A.tessellatus</u>	1	(0)
<u>A.nigerrimus</u>	3	(2)
<u>A.annularis</u>	3	(2)
<u>A.hyrceanus</u>	2	(0)

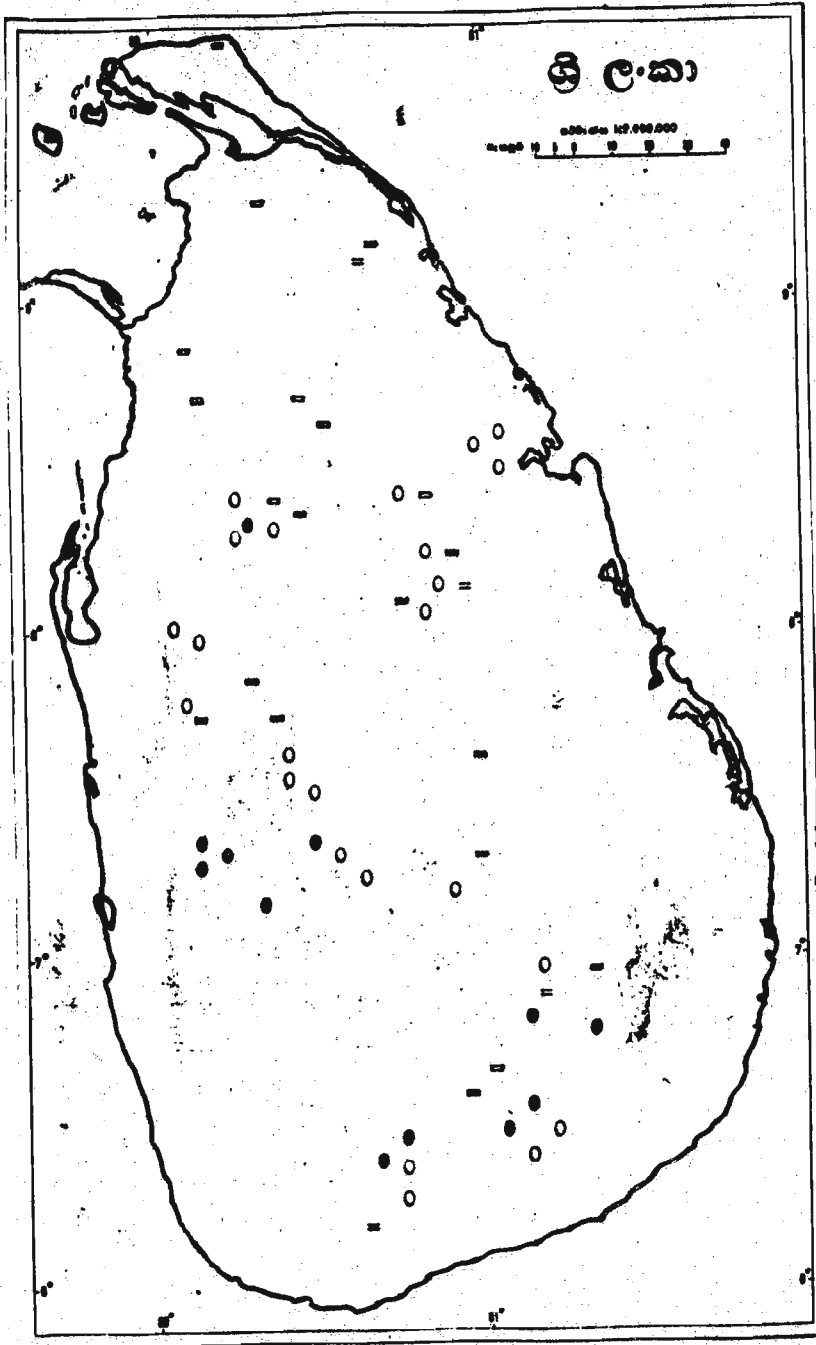
() - Males.

SURVEILLANCE FOR DETECTION OF MALATHION RESISTANCE IN
A. CULICIFACIES



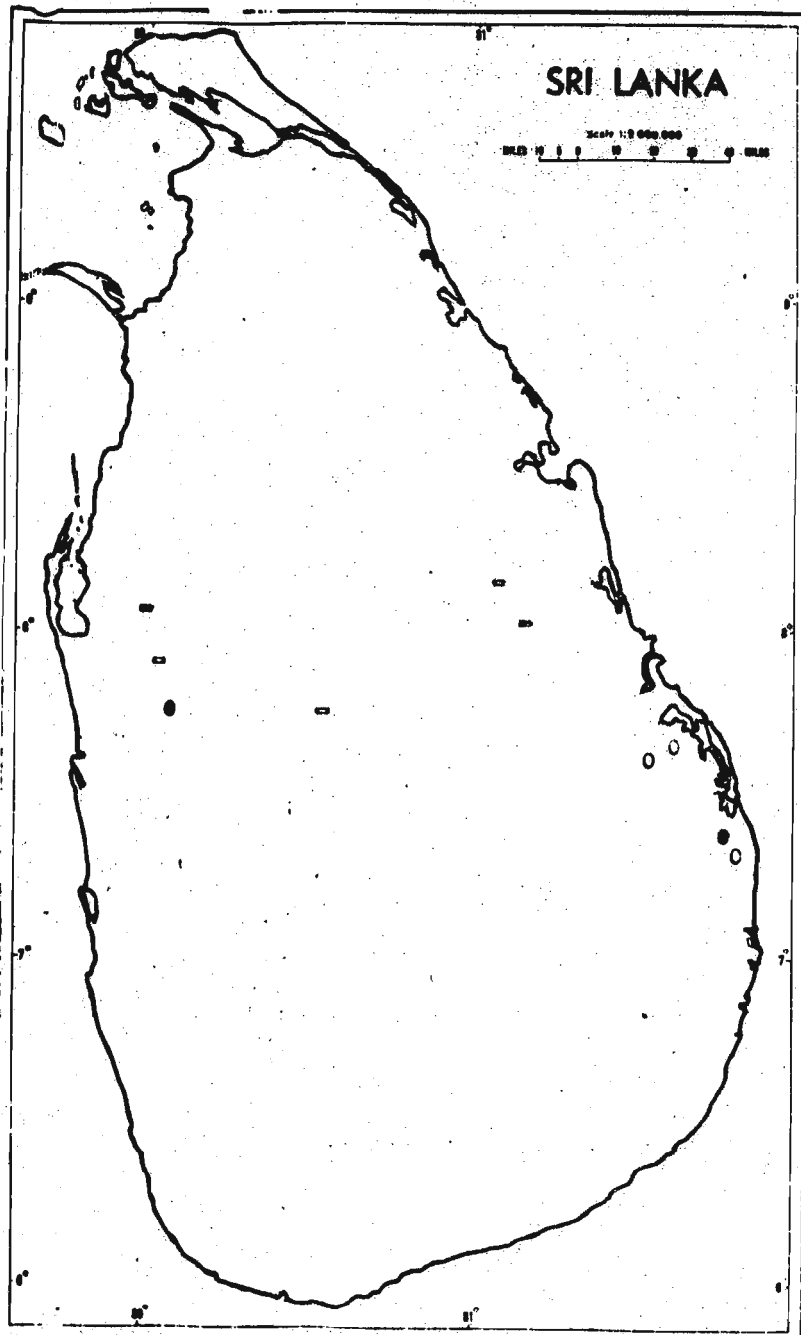
KEY : O - 1977
 = - 1978
 * - 1979
 ● - 1980
 ▲ - 1981

SURVEILLANCE FOR DETECTION OF MALATHION RESISTANCE
IN A. SUBPICIUS



	1980	1981
Resistance	●	○
Susceptible	○	●

SURVEILLANCE FOR DETECTION OF MALATHION RESISTANCE
IN A. BARBIROSTRIS



	<u>1980</u>	<u>1981</u>
Resistance	●	-
Susceptible	○	○

6-2 USE OF INSECTICIDES TO CONTROL THE VECTORS
IN MALARIA AND FILARIASIS - DESCRIPTION OF THE PROBLEM
IN SRI LANKA

by K.Subramaniam and
M.V.Samarasinghe

(Anti-Malaria Campaign, Sri Lanka)

The two major vector borne diseases in Sri Lanka that use insecticide to control the vector are Malaria and Filariasis.

DDT has been used against the vector A.culicifacies in malaria since 1946. Within 2 years the number of cases of malaria had dropped from 2.7 million to less than one million and 5 years later in 1953 only a hundred thousand cases were reported.

Similar dramatic results were achieved in all countries of the South East Asia Region. Then on the expert advice of the WHO the activities of the Anti-Malaria Campaign intensified and altered to achieve a new objective i.e. the complete eradication of malaria instead of control.

The results were spectacular in 1961 barely 5 years after launching the eradication programme there were only a few more than 100 cases of malaria. During 1962, there were only 32 and in 1963 only 17 cases.

Equally exhilarating results were reported from neighbouring countries. Then something went wrong: In Sri Lanka the case load went up from 17 cases in 1963 to 150 in 1964, 308 in 1965, nearly 500 in 1966, almost 4,000 in 1968 and more than $\frac{1}{2}$ million in 1969. This pattern of increase was also seen in other countries in the region at the same time e.g. India, Indonesia and Philippines.

For it was soon discovered that the malaria mosquito in each of these countries had become resistant to DDT; In Sri Lanka this was first recorded in 1968. Subsequent studies in the later years on the practical implications of increased resistance levels which proved control failures with DDT necessitated the use of malathion - brought in as the only chemical in 1977.

Malaria control expenses have increased significantly since then. With DDT the cost was only US \$ 0.5 per house. With malathion the cost is 1.5 dollars per house and the price of malathion is escalating with the energy prices.

If the mosquito A.culicifacies was to develop resistance to malathion the cost of spraying per house is as shown below, provided the resistance pattern allows the use of these candidate insecticides.

1. Fenitrothion US \$ 2
2. Propoxur US \$ 10
3. Acetellic

It has cost us approximately Rs.90 million to import malathion for the 1982 programme. This is roughly 7% of the Health Budget and 0.24% of the National Budget. Could we afford to continue purchase of insecticides at this price?

A.culicifacies has already developed resistance to malathion in certain areas in India. In addition there is the increased cost of newer insecticides and better protective measures provided to workmen which are necessary and have to be considered.

A rapid rise in the usage of pesticides in Public Health has also given rise to additional health problems,

About 14,000 individuals are poisoned by pesticides in the U.S. annually. 6,000 seriously enough to require hospitalisation. Of the 14,000 poisoning about 200 fatalities occur annually. (1)

In addition to the direct effects are the indirect public health problems associated with pesticides used on crops. For example the extensive use of insecticides on cotton in the coastal plains of Central America has resulted (A. albimanus the vector of malaria) in the evolution of a mosquito population that is highly resistant to a wide range of insecticides.

It is estimated that house spraying with DDT in Central America cost only \$ 1-2 per house. After the mosquito developed resistance to DDT, propoxur was substituted and the cost of house spraying increased to about \$ 11 per house. If Landrin were to be used this would cost \$ 22 per house.

The most important factor responsible for this phenomenon of resistance in Central America is serial spraying. Thus most of the coastal plains habitats including the mosquitoes' aquatic habitats have been contaminated with cotton insecticide. The mosquito population has become highly tolerant to a wide variety of insecticides, resulting from such intense exposure to them. (2) Prof. Georghiou will elaborate on these points in his paper. Fortunately serial spraying is not in vogue in Sri Lanka and if I do remember right it was used once in the East Coast for the Brown hopper pest of paddy at a time when DDT was used for malaria control. During the last 3 decades the use of chemical methods for control of insect vectors of disease, considered a great advancement, must be, besides that in agriculture.

In the field of malaria before such chemical control programmes started, malaria was endemic in 148 countries and

by the end of 1974 it had been officially eradicated in 37 of these countries.

As is well known, however, the high hopes of total eradication have failed and the position while somewhat stationary in some areas, is regressing in other areas. The continued success of control of vectors of Public Health importance has been impeded by the growing problem of vector resistance to pesticides.

In addition to resistance, as might be expected with any new technology, health and environmental problems have also been recognised. These have been the problems of human and animal pesticide poisoning and the problem of human and environmental pesticide residues associated with the more persistent pesticides. All three i.e. resistance, poisoning and persistence are of mutual concern to **Medical and Agricultural** sciences and the common problems emerging from these issues are reasons why integration of the disciplines of Agriculture and Health is a vitally necessary union not only for the ultimate production of good food supply and good health, but also for the resolution of other problems that have arisen and are likely to arise in the future.

How can the economic benefits which accrue from the use of chemical control in Public Health be reconciled with the increased incidence of human poisoning and the human and environmental problems?

This is where the agro-medical approach comes in, for the problem of human poisoning is of equal concern to agriculture and health. The same is true with regard to the problem of persistence, for an excessive pesticide residue in food will prohibit the sale of food and the occurrence of human pesticide residue or the occurrence of delayed neurotoxicity is an eventuality of special concern in medicine. Likewise, where resistance develops not only is it a problem for the farmer but

it is one of increasing concern to Public Health workers and is one factor contributory to the resurgence of malaria.

In all three areas of pesticide management which are of special public health concern - human poisoning, body persistence of pesticides and vector resistance (with malaria resurgence) integrated pest control strategies offer the greatest prospect for resolution.

The setting up of an agro-medical organization frame work at national, regional and local levels could significantly reduce such episodes. In the areas of persistence and resistance too, medicine and chemistry have much to offer. (3)

In conclusion it is neither the common problem nor the threat of an enforcement organization which would divert the organizational responsibilities of pesticide management to an independently new organizational unit which should integrate the partnership of agriculture and health, but it is the inherent skills, knowledge and potential which both disciplines possess, which will be of ultimate benefit to man and his continued need to find enough food and better health.

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7-0 PRINCIPAL MECHANISMS OF RESISTANCE TO INSECTICIDES

by **George P. Georghiou**
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The principal mechanisms of resistance that have been identified to date include:

Enhanced metabolism of the toxicant by means of

- dehydrochlorinase
- mixed-function oxidases
- hydrolases, esterases and glutathion-dependent transferases

Reduced sensitivity of the target site

- nerve insensitivity
- acetylcholinesterase insensitivity

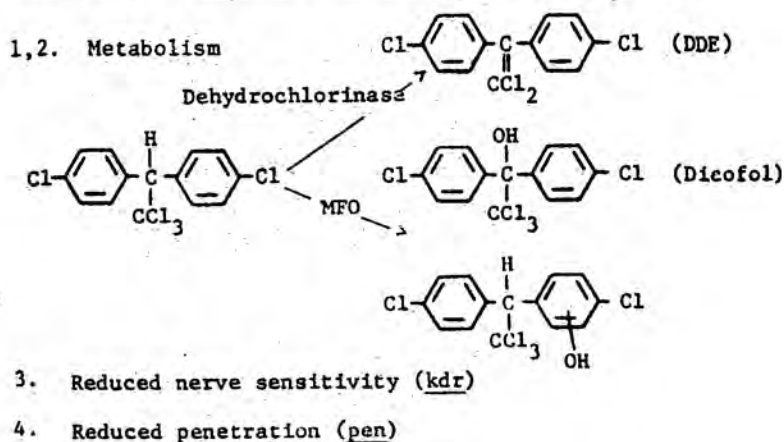
Reduced penetration to active site

These are discussed briefly below with emphasis on the areas in which interest is currently concentrated. For details the reader is referred to pertinent reviews (Brown 1976; Dauterman 1982; Hawa 1982; Wilkinson 1982; Hodgson and Kulkarni 1982).

Dehydrochlorinase

It was demonstrated early that the principal mechanism of resistance to DDT in house flies is via detoxication of the insecticide to its non-insecticidal metabolite DDE (Perry and Hoskins 1950; Sternburg and Kearns 1950). The enzyme responsible for this reaction, DDT-dehydrochlorinase, has been isolated from resistant house flies by high speed centrifugation and examination of the supernatant. It was shown to catalyze the degradation of p,p-DDT to p,p-DDE and the degradation of p,p-DDD to the corresponding ethylene TDEE (Fig. 1).

Fig. 1. Genetically identified mechanisms of DDT resistance



DDT-dehydrochlorinase is inhibited by chlorfenethol (DMC), thus the latter has been used to detect the presence of the dehydrochlorinase mechanism in DDT-resistant strains. Selection pressure by DDT in combination with DMC has led to higher resistance which is characterized by higher levels of DDT-dehydrochlorinase (Moorfield and Kearns 1955). It was suggested that the enzyme is present in different allelic forms, each with different levels of activity and substrate specificity (Oppenoorth 1965). DDT-dehydrochlorinase also has been found to be a principal mechanism of resistance in the small number of plant-feeding species that have been examined, including *Heliothis virescens* (Vinson and Brazzel 1966) and *Pectinophora gossypiella* (Bull and Adkisson 1956).

In addition to metabolism by dehydrochlorination, DDT was also found to be metabolized oxidatively in house flies by a mechanism that could be blocked by the microsomal oxidase (MFO) inhibitors sesamex and piperonyl butoxide (Sawicki and Farnham 1967; Oppenoorth and Houx 1968). MFO detoxication and two other mechanisms of resistance to DDT, namely reduced-nerve sensitivity and slower cuticular penetration, are discussed in the appropriate sections below.

Mixed-function oxidases (MFO's)

MFO's are associated with the microsomal fraction of cells and are derived from the smooth endoplasmic reticulum. Most of our early knowledge of MFO's came from research in mammalian systems, but MFO's have now been demonstrated in many other living organisms including insects, plants, fungi, and bacteria and at very low levels in fish.

MFO's are relatively nonspecific and catalyze the following overall reaction:



where S is the insecticide and NADPH is the electron donor for the reaction.

Studies on insect MFO's have established the operation of a unique electron transport system involving multiple forms of cytochrome P-450. These cytochromes can be induced to a higher level of activity by other insecticides in the environment, or by "inert" solvents commonly used in insecticide formulations (Brattsten and Wilkinson 1977), thus

enhancing the protection they afford the insect.

The discovery of the role of MFO in insecticide resistance comes from studies correlating the levels of enzyme with insect resistance and susceptibility. MFO's are known to:

- metabolize broad classes of chemicals including carbamates, organophosphates, pyrethroids and organochlorines
- are located in strategic tissue such as midgut/fatbody
- are synchronized to a time of need (MFO activity is highest during the larval feeding stage and lowest at adult stage).

Unlike esterases that occur in random individuals within a population, oxidases are present in every individual (even if in insufficient quantities to contribute to resistance) and offer a reservoir for potential resistance development through selection at a higher level of activity.

Although there is abundant evidence of the important role of MFO's in resistance to insecticides in flies, Lepidoptera and many other insects, their role in resistance of mosquitoes appears to be of lower importance. MFO's are detected *in vivo* through the use of the synergist piperonyl butoxide (p.b.), an inhibitor of MFO activity. In *Culex quinquefasciatus* (Ranasinghe and Georghiou 1979) and in *Cx. tarsalis* (Apperson and Georghiou 1975), only limited synergisms of organophosphates could be observed by use of p.b. However, a 30x resistance to propoxur in larvae of *Cx. quinquefasciatus* was shown by Shrivastava et al. (1971) to be due mainly on detoxication by MFO. This system was also involved in the metabolism of other carbamates including carbaryl, aldicarb and carbofuran. A low degree of synergism of carbamates by p.b. was also observed in a field population of *Anopheles albimanus* (Ariaratnam and Georghiou 1971).

Hydrolases, esterases and glutathion-dependent transferases

Phosphotriester hydrolases and glutathione S-transferases are mechanisms responsible for organophosphate resistance in certain species and strains of insects and appear to be strong factors of resistance in mosquitoes. The importance of triester hydrolases and glutathione

S-transferases is dependent upon the structure of the insecticide, its concentration and possibly the stage of insect development.

The hydrolysis of organophosphorus insecticides is mediated by a number of enzymes that are responsible for the cleavage of the phosphorus ester or the anhydride bond, and the overall effect is the detoxification of the parent compound.

Glutathione S-transferases (GSH) exist in different forms and their exact number and specificities remain to be established. Their biological role appears to be two-fold: conjugation of harmful electrophiles with the endogenous nucleophile glutathione provides protection for biological macromolecules such as nucleic acids and proteins from the potential toxic consequences of a covalent reaction, and additionally, it provides an effective means of excretion of the electrophile through the formation of an anionic, water-soluble product.

The involvement of GSH in the metabolism of organophosphorus insecticides was first observed in the metabolism of methyl parathion, which was dealkylated by a soluble enzyme that exhibited a preference for methyl groups. The high levels of GSH that have been reported in several resistant strains of insects, especially house flies, appear to be associated with high levels of GSH activity.

In the course of purifying GSH from the house fly, it was noted that non-specific esterase activity towards α -naphthyl acetate typically paralleled GSH activity and it is possible that the high non-specific esterase activity often found to be associated with organophosphate resistance is in reality due to high GSH activity (Dauterman 1980). This question requires further investigation. There is little doubt, however, that non-specific esterase activity that is manifested electrophoretically through the hydrolysis of α -naphthyl acetate is closely associated with organophosphorus resistance. These genetic associations have been established in several OP-resistant species of agriculturally important insects such as the aphid *Myzus persicae* (Beranek and Oppenoorth 1977), the leafhopper *Nephotettix cincticeps*, the planthopper *Laodelphax striatellus* in Japan (Ozaki et al. 1966; Ozaki 1969; Kasai and Ogita 1965), the spider mite *Tetranychus kanzawai* in Japan (Kuwahara et al. 1981), and in several species of mosquitoes, including

Cx. quinquefasciatus and *Cx. tarsalis* in California (Georghiou and Pasteur 1978), *Cx. pipiens* in southern France (Pasteur 1977), *Cx. fatigans* in East Africa (Curtis and Pasteur 1980), *Cx. pallens*, *Cx. fatigans*, *Cx. tritaeniorrhynchus* and *Aedes aegypti* in Japan (Yasutomi 1982). Organophosphate resistance that is based on esterases is suppressed by the synergist DEF[®], and this test may be applied in detecting the presence of this type of mechanism.

TABLE 1

Effect of synergists PB (oxidase inhibitor) and DEF (esterase inhibitor) on Resistance to Organophosphates in *Culex quinquefasciatus*^{1/}

	Resistance Factor		
	Insecticide	+PB	+DEF
chlorpyrifos	52.2	47.0	0.5
methyl parathion	24.0	25.0	1.3
methyl paraoxon	16.0	12.9	1.2

^{1/}Hanford field strain.
(Ransinghe and Georghiou 1979)

Much research is required on this major source of organophosphate resistance. It is known, for example, that malathion carboxylesterase is specific for malathion. But subsequent selection pressure by other organophosphates extends the spectrum of cross resistance to these as well, while genetic tests continue to provide evidence for essentially monofactorial inheritance (Georghiou and Pasteur 1980). It would be highly desirable to determine the genetic bases (gene amplification, duplication, regulation, etc.) that may provide the loci upon which additional OP-degrading esterases are selected, thereby expanding the multiresistance of the strain. A further question of practical concern, as well as of fundamental interest, arises from observations that homozygous resistance to an organophosphate may exhibit different levels of expression. We have recently isolated three strains of temephos-resistant *Cx. quinquefasciatus* exhibiting different degrees of resistance to this insecticide (Pasteur et al. 1980). The possibility that this phenomenon might be due to tandem replication of a resistant locus that thus yields ever larger amounts of a detoxifying esterase (Pasteur et al. 1982) may have important implications in any plan to render

resistance "functionally recessive" through the use of higher doses. Just how common this phenomenon of duplication of structural genetic material might be in mosquitoes remains to be determined. The same hypothesis of gene duplication was suggested by Devonshire and Sawicki (1979) to explain the variations of organophosphate resistance and of the highly active esterase associated with it in a series of strains of the aphid *Myzus persicae* (Table 2). Likewise, Schimke et al. (1978) have emphasized the possibility of the large scale occurrence of such phenomena in cases of drug resistance in cultured murine cells in which increased detoxication has been observed.

TABLE 2

Concentration of paraoxon-hydrolyzing esterase, E4,
in seven variants of *Myzus persicae*^{a/}

Clone	pmol E4 per mg aphid	Multiples of S
Susceptible	0.37	1.00
Resistant		
24ON	0.85	2.29
M51G	1.78	4.81
French R	4.80	12.97
T1V	6.70	18.11
Pir R	11.80	31.89
G6	24.70	66.75

^{a/} From Devonshire and Sawicki 1979.

Reduced sensitivity of nervous system

This mechanism of resistance which affects DDT and pyrethroids has been studied mainly in house flies and mosquitoes, but it also exists in other species as well. Interest in the mechanism has been greatly increased by concern over the viability of pyrethroids as lasting tools for insect control. To date, at least 22 species of pests have manifested some resistance to pyrethroids under field conditions (Table 3) and in some of these, especially house flies and mosquitoes, this resistance has been traced to the DDT-resistance factor *kdr*.

TABLE 3

CASES OF RESISTANCE TO PYRETHRINS/PYRETHROIDS IN ARTHROPODA^{1/}

Order	Species	Country or State
Lepidoptera	<i>Ephestia cautella</i>	Florida; Georgia
	<i>Heliothis virescens</i>	Arizona; California
	<i>Plodia interpunctella</i>	Georgia
	<i>Plutella mylostella</i>	Malaysia; Taiwan; Thailand
	<i>Scrobipalpula obsoluta</i>	Peru
	<i>Spodoptera exigua</i>	El Salvador; Guatemala; Nicaragua
	<i>S. frugiperda</i>	Louisiana
Diptera	<i>S. littoralis</i>	Egypt
	<i>Aedes aegypti</i>	Guyana; Thailand
	<i>Anopheles arabiensis</i>	Sudan
	<i>An. sacharovi</i>	Turkey
	<i>An. stephensi</i>	Pakistan
	<i>Musca domestica</i>	Denmark; Finland; Germany (F.R.); Ontario; Sweden; Switzerland; U.K.
Coleoptera	<i>Megascelia halterata</i>	U.K.
	<i>Leptinotarsa decemlineata</i>	New York
	<i>Sitophilus granarius</i>	U.K.
Homoptera	<i>Tribolium castaneum</i>	Georgia; Queensland
	<i>Myzus persicae</i>	Bt. Colombia; Japan; N.S. Wales; Queensland; U.K.; Victoria
	<i>Psylla pyricola</i>	Oregon
Orthoptera	<i>Trialeurodes vaporariorum</i>	U.K.
	<i>Blattella germanica</i>	Alabama; Canada; Colorado; Kentucky; Texas; USSR
Acarina	<i>Tetranychus urticae</i>	U.K.

^{1/}Details in Georghiou, 1981.

Based on crustacean models, Narahashi (1982) suggested that the mode of action of pyrethroids and DDT on nerve cells was the alteration of sodium channels. When nerve excitation occurs there is an influx of sodium ions into the nerve and an efflux of potassium ions, which is under the control of a sodium pump. DDT and pyrethroids affect the sodium channels within the nerve membrane, causing extremely slow opening and closing of the channels. This leads to an increase in the depolarizing after-potentials, which in turn induces repetitive after-discharges. Such repetitive activity in the nerve fibers causes disturbances in synaptic transmission and produces hyperactivity in the insect. Less than 1% of the channels need to be affected to cause toxicity. In the case of low nerve sensitivity there are few channels modified and fewer binding sites for toxicants.

A great deal remains to be known about the potential consequences of the nerve insensitivity mechanism in insect control by pyrethroids. The available evidence indicates that a single genetic factor is involved

(gene *kdr*) (Farnham 1973) which can also be expressed at a higher level of activity (super-*kdr*) by some unknown means, possibly allelism. The gene is largely recessive, imparting only a small degree of protection in heterozygotes, thus its selection may be expected to be slow, especially in populations in which other loci (MFO's, esterases) could provide greater protection. The relatively high activity of pyrethroids that is evident against field populations despite the presence of DDT resistance might thus be attributed to a relatively low frequency of *kdr* (as compared to dehydrochlorinase and MFO's) in these populations. There is concern, however, that the improved stability of new pyrethroids (permethrin, decamethrin, cypermethrin) against enzymatic attack diminishes the potential role of oxidase systems in resistance and thus might lead to more efficient selection of *kdr*. Resistance by *kdr* in the homozygous state may provide protection that is beyond the reach of practical dosages of these new pyrethroids.

Reduced sensitivity of acetylcholinesterase

Resistance to cholinesterase inhibitors (organophosphates, carbamates) due to reduced sensitivity of acetylcholinesterase (AChE) is analogous to resistance due to reduced sensitivity of the nervous system (see above). In either case, this type of resistance appears to arise following the application of extremely high and sustained selection pressure. By "overpowering" the usual metabolic defense mechanisms, such selection enables the far more "efficient" mechanism of insensitivity to predominate (Georghiou and Taylor 1976).

At least eight species of insects and acarina have been found to have developed resistance due to reduced sensitivity of AChE (Table 4). Only one species of mosquito, *Anopheles albimanus*, from Central America is involved (Georghiou et al. 1974).

In vitro studies (Ayad and Georghiou 1975) revealed major differences in the rate of inhibition of AChE by paraoxon and propoxur in two resistant and two susceptible strains of *An. albimanus*. The AChE of the resistant strains was on the average about 500x less sensitive to paraoxon and 15,500x less sensitive to propoxur than that of the susceptible strains (Table 5). Similarly, the K_m value was about 3.3x "poorer" in

TABLE 4
Cases of Resistance to Insecticides Related to Reduced
Sensitivity of AChE (After Hama 1980, with additions)

Species	Resistance	Places	References
<i>Tetranychus urticae</i>	organophosphates (parathion, diazinon)	West Germany	Smitsaert, 1964
	(parathion)	New Zealand	Ballantyne and Harrison, 1967
<i>Tetranychus pacificus</i>	parathion	USA (California) ^a	Zon and Helle, 1966
<i>Tetranychus telarius</i>	malathion	Israel	Zahavi et al., 1970
<i>Boophilus microplus</i>	organophosphates and carbamates (coumaphos, diazinon, carbaryl)	Australia	Lee and Bathan, 1966; Roulston et al. 1968
<i>Nephotettix cincticeps</i>	carbamates and organo- phosphates (propoxur, carbaryl, malathion)	Japan	Hama and Iwata, 1971, 1978; Iwata and Hama 1972
<i>Musca domestica</i>	organophosphates and carbamates (tetrachlor- vinphos, dichlorvos, propoxur)	USA (New York) ^a	Tripathi and O'Brien, 1973; Tripathi, 1976
	(dimethoate)	Denmark	Devonshire, 1975
<i>Anopheles albimanus</i>	organophosphates and carbamates (parathion, propoxur)	El Salvador ^a	Ayad and Georghiou, 1975
<i>Spodoptera littoralis</i>	organophosphates (monocrotophos, para- oxon, dichlorvos)	Egypt	Dittrich et al., 1979

^aPopulations selected with an insecticide further in laboratory.

TABLE 5

Sensitivity of acetylcholinesterase of S and R strains of *Anopheles albimanus* to inhibition by various insecticides.

Strains	Paraoxon	Propoxur	Fenoxon
	<i>K_i values</i>		
Susceptible (S)	7.8x10 ⁵	2.95x10 ⁵	4.6x10 ³
Parental (P)	1.1x10 ⁶	4.8 x10 ⁵	
Parathion-R (OP-R)	2.1x10 ³	0.19x10 ²	1.5x10 ³
Propoxur-R (Carb.-R)	1.7x10 ³	0.38x10 ²	
	<i>Sensitivity ratio</i>		
S/OP-R	371	15.5x10 ³	3.1
S/Carb.-R	459	7.8x10 ³	
P/OP-R	524	25.3x10 ³	
P/Carb.-R	647	12.6x10 ³	

one resistant strain (OP-R) than in the two susceptible strains, and V_{max} values were about 2x higher in the two susceptible than in the two resistant strains. These results showed that the AChE of the resistant strains is different from that found in the susceptible. In agreement with the bioassay data, the *in vitro* tests showed that AChE insensitivity does not extend to fenoxon. Studies with synergists revealed that MFO and esterase enzymes play a relatively small role in resistance to OP insecticides in the strain. Piperonyl butoxide in combination with methyl parathion and parathion caused a higher degree of antagonism against the resistant than the susceptible strain. However, *in vitro* studies showed only a small difference between the epoxidase activity of the resistant and susceptible larvae. The esterase inhibitor DEF[®] only slightly increased susceptibility in the resistant strain.

Significant differences in the properties of AChE of resistant and susceptible strains have been reported in other species as well, viz. housefly (Tripathi and O'Brien 1973), mites (Ballantine and Harrison 1967; Swissaert 1964) and ticks (Roulston et al. 1968). That different AChE isozymes exist had been shown in both insects (Gomez 1966; Knowles and Arukal 1969) and mammals (Main 1969). On the basis of the present knowledge, it appears that under intensive pressure, AChE isozymes that are considerably less sensitive to inhibition by organophosphates or carbamates are selected preferentially.

If resistance is indeed due to a change in the relative frequency of sensitive and insensitive AChE isozymes, it might be profitable to re-examine compounds that were rejected earlier, since they may in fact be sufficiently active against the insensitive isozymes. Such a procedure was explored recently by Yamamoto et al. (1980) with the green rice leafhopper, *Nephotettix cincticeps*, in Japan. These workers found that populations of this species that are resistant to various *N*-methylcarbamates due to altered AChE are sensitive to *N*-propyl analogs. The latter are ineffective against the susceptible strain, but a 1:1 mixture of *N*-methyl and *N*-propyl carbamates was found to be synergistic and is being recommended for field use. This is an example of negatively correlated cross resistance with a known biochemical basis. It must be pointed out that *N*-propylcarbamates would not necessarily be effective on other resistant species since the altered AChE of these may be different. *N*-propylcarbamate analogs were found ineffective against resistant strains of *An. albimanus*.

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7-1 SELECTION DYNAMICS OF POPULATIONS - PRESSURES DUE TO
AGRICULTURAL PEST AND VECTOR CONTROL

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Introduction

The basic formula of population dynamics -

$$\Delta n = b + i - d - e$$

where Δn = change in number

b = replacement by reproduction

i = inflow by immigration

d = outflow by death

e = outflow by emigration

- can also be taken as representing the situation as regards the dynamics of change in proportion of alleles in a population gene pool. Here, however, we must add another factor, namely -

m = mutation

- which can act in either direction, but normally at a very low frequency .

The expression now therefore becomes -

$$\Delta n = b + i - d - e + m$$

In the normal situation, where inflow tends to be balanced by outflow, and where the mutation rate is small, the proportion of a particular allele in the gene pool is affected mainly by its initial proportion and the selection pressure on this, i.e. d in the above expression.

Point at which selection acts

In diploid organisms, the fusion of haploid gametes initiates each new generation which then proceeds :-

(LARVA)
ZYGOTE \longrightarrow ADULT \longrightarrow GAMETE FORMATION \longrightarrow MATING \longrightarrow NEW ZYGOTE

Selection may act therefore on the following stages :-

- a) ZYGOTE $\xrightarrow{\text{(LARVA)}}$ ADULT (By differential survival)
- b) GAMETE FORMATION (By differential production or differential survival)
- c) MATING (By non-random mating)

The processes of interest in the present context are :-

Zygotic selection and
Gametic selection

We will return to this subject later.

Concept of genetic equilibrium

Differential selection obviously upsets the genetic equilibrium of a population. How is the equilibrium expressed?

If a gene A affecting a particular character exists in the form of two alleles A_1 and A_2 , and the proportion (or frequency) of these alleles are p and q respectively (i.e. $p + q = 1$), then the proportions of the three genotypes A_1A_1 , A_1A_2 and A_2A_2 are given by p^2 , $2pq$ and q^2 respectively.

		<u>♂ gametes</u>	
		p	q
<u>♀ gametes</u>	p	p^2	pq
	q	pq	q^2

Where allele frequencies p and q do not change, the genotype frequencies obviously do not change, and the population is in genetic equilibrium with regard to this particular gene. This is the HARDY - WEINBERG equilibrium, and the concept that populations do not change genetically unless there is some factor causing them to change has been called the Hardy-

Weinberg Law. This deceptively simple idea can be taken as the cornerstone of population genetics.

It may be said that the essence of evolution is the changing of gene frequencies in populations, and the importance of the Hardy-Weinberg Law is that it defines a base-line situation in which there is no evolution or upon which evolutionary processes act. Evolution may be viewed as deviation from the base-line, and the factors which may cause such deviations are those responsible for evolution. The Hardy-Weinberg equilibrium for different allele frequencies is illustrated in Fig. 1.

An alternative and useful method for expressing the Hardy-Weinberg relationship is shown in Fig. 2. Here all possible values for genotype frequencies can be represented as points on the triangle. This De Finetti triangle is particularly useful since the progress of gene and genotype frequencies under selection can be plotted on it (Fig. 3).

Factors affecting Hardy-Weinberg equilibrium

Possible factors influencing the basic Hardy-Weinberg equilibrium may be listed as follows :-

- a) Non-random mating
- b) Mutation
- c) Differential migration
- d) Genetic drift (sampling error)
- e) Selection

Of these we are concerned mainly with the last one, although in the context of control design, for example in the concept of refugia, migration may be extremely important in maintaining some sort of allele balance. Here however we will confine ourselves to a consideration of the dynamics of the selection process.

The concept of evolutionary "fitness" or "selective value" w of an organism is based primarily on reproductive success, and the same concept is applicable to the genetic components of this "fitness", i.e. individual alleles. The term "differential" is

used to indicate that there is a difference in the way selection affects two or more categories of an organism. Selective differential are expressed in terms of factors (co-efficients or values) which define the relative change in frequency of, for example, two forms over a given time. If the difference can be represented in an equation by a factor measuring the relative success of the two categories, then this factor is the selective value or relative fitness of one category compared to the other. A selective coefficient (s) on the other hand is a quantity such that $1 - s = w$.

In this way, selective differences are expressed as the disadvantage of the less fit compared with the more fit type. i.e. where $s = 1$ this indicates complete lethality.

Zygotic selection

By way of illustration, if we take a population in Hardy-Weinberg equilibrium which is diallelic for the alleles A_1 and A_2 of which the frequencies are $p = 0.6$ and $q = 0.4$ respectively, where A_2 is completely recessive and where selection pressure is applied so that all recessive homozygotes are eliminated before maturity, then :-

Genotypes	A_1A_1	A_1A_2	A_2A_2
Genotype frequency				
before selection	0.36	0.48	0.16
Fitness, w	1	1	0
Genotype frequency				
after selection	0.43	0.57	0

The new allele frequencies are $p = (0.43 + \frac{0.57}{2}) = 0.715$

$$q = \frac{0.57}{2} = 0.285$$

(i.e. $\Delta q = 0.285 - 0.4 = -0.115$)

Genotype frequencies				
in next generation	0.51	0.41	0.08

Some different types of zygotic selection which may operate can be listed as follows :- (Adapted from Cook, 1971)

	A_1A_1	A_1A_2	A_2A_2
fitness		
a) Complete recessivity, selection against A_2A_2	1	1	1 - s
b) Complete dominance, selection against A_2 -	1	1 - s	1 - s
c) Heterozygote *			
intermediate	1	1 - $\frac{1}{2}s$	1 - s
@			
d) Heterosis	1 - s_1	1	1 - s_2

* This situation has particularly important consequences for selection, since the heterozygote may succumb to high field dosages but survive lower dosages, i.e. the allele dominance can be manipulated according to the dosage level.

@ This is a case where selection actually maintains and equilibrium.

Gametic selection

The situations shown above are ones where combination of gametes takes place at random to form zygotes in frequencies determined by the genotypic frequencies of the parental population, and where these zygote frequencies are subsequently changed by selection to form the parental population of the next generation, i.e. there is a zygotic selection. But it is also possible that the gametic frequencies may differ from those expected on the basis of random assortment of parental gametes because of gametic selection.

Gametic selection may occur independently or combined with zygotic selection. For example :-

Genotypes	A_1A_1	A_1A_2	A_2A_2
Relative frequencies in parent population	p_0^2	$2p_0q_0$	q_0^2
Relative frequency of gametes	p_0		q_0
Frequencies after gametic selection ($p + q = 1$) ...	$x_1p_0 (= p)$		$x_2q_0 (= q)$
New parental population after zygotic selection..	w_1p^2	$2w_2pq$	w_3q^2
New gametic frequencies..	$(w_1p^2 + w_2pq)$		$(w_3q^2 + w_2pq)$

As regards selection by insecticides, obviously the constitution of the gene pool and the dosage level would be the main factors operating here. In some situations, for example in houseflies, partially lethal doses have been shown to increase oviposition in the following few generations (Gratz, 1966), while at sublethal levels Lineva (1955) describes serious disturbance of oogenesis and Derbeneva-Uhova et al. (1966) also dealing with completely sublethal levels state "in our opinion it is difficult to explain the occurrence of resistance solely on the basis of selection of individuals which bear resistance factors". Beard (1965) demonstrated that DDT ingested by adult flies was passed on to the eggs and larval off spring.

Zaghloul and Brown (1968) and Brown and Pal (1971) mention the possibility of gametic selection in mosquitoes, and in general there is no reason to suppose that haploid organisms may not express phenotypic differences such as resistance. It is in the realm of "sublethal" doses that gametic selection may be most important, and if so, background residues of public health and agricultural pesticide applications may play a large part in

selection at this level. Gametic selection may act on both spermatozoa and ova, the former either in the male parent or in the spermatheca of the female. In this regard it is interesting to note that in Culex pipiens larval exposure introduced twice as much DDT into the adult ovaries as adult exposure did (Sharma and Sanchez, 1964).

This subject raises the question as to over what range of dosage levels gametic selection may operate, if at all. This is likely to be at much lower levels than zygotic selection, but little work seems to have been done on this.

Public health and agricultural pesticide applications

This brings us on to a consideration of possible differences in selective effect of pesticides as used in public health or agricultural applications.

a) Public health

In public health, for example in malaria programmes, most pesticide use has been in the form of residual deposits applied to the internal surfaces of human dwellings with the aim of killing or reducing the life expectancy of that section of the anopheline population coming in contact with man. The internal surfaces of cattlesheds also are often treated with the aim reducing the vectorial capacity of the anopheline population still further. This standard operational approach of most malaria control programmes therefore exerts selection pressure mainly on adult females, since the males (being purely nectar feeders) have no need to enter structures in search of a bloodmeal. As we have seen above, the components of this selection, although usually considered to be mainly zygotic, may also have a gametic element.

In some public health programmes larviciding is also employed, especially in urban or peri-urban areas, and here the selection pressure can act on all aquatic stages of mosquito development - egg, 4 larval instars and pupa. Again, although this selection

is regarded as mainly zygotic, as noted above there may be a gametic element due to carry-over of toxic material into the adult reproductive system and affecting both sexes.

An important point to note here with regard to use of larvicides in public health programmes is that where adulticides are also being used it is recognised practice that a different insecticide (preferably belonging to a different group) should be employed as a larvicide so as to minimise selection pressure as much as possible.

The occasional fogging or ULV treatments employed, usually in epidemic situations, being generally of short residual duration and limited in area, may not exert a significant amount of pressure on the population as a whole.

In general, through larviciding would be expected to exert stronger pressure than thorough adulticiding of domestic structures, simply because the adults, being mobile, can have other resting sites or show avoidance reactions, whereas larvae can not.

b) Agriculture

In agricultural applications on the other hand, the pesticide dispersions, often by air, do not affect the internal surfaces of human dwellings and cattlesheds but typically do affect the vegetation surrounding villages and often, unavoidably, the mosquito larval sites as well, either directly or by run-off in the drainage of treated fields. This is therefore a complementary situation to that in public health usage.

This means, in brief, that all sexes and stages of a given mosquito population may find themselves under selection pressure simultaneously from the same insecticide, since both males and females are exposed through resting on treated vegetation and aquatic stages are exposed in drainage channels.

Where the dosages of agricultural pesticides are sufficiently high, this situation may indeed depress mosquito densities and

longevity and so cause a reduction in vectorial capacity of the local population. Such reductions in density have been noted previously in cotton-growing areas of El Salvador and Turkey for example. However once deposits start to decay and dosage levels fall, a point is reached at which heterozygotes, either arising by local mutation or by immigration, will start to survive and thereafter resistance can be expected to build up rapidly due to the blanket type of pesticide coverage.

c) Summary

The situation may be summarised as follows :

- (a) Both public health and agricultural pesticide use results in zygotic, and possibly also gametic, selection.
- (b) Mainly female adults are affected by public health adulticiding whereas both sexes are exposed to agricultural applications by resting on treated crops.
- (c) Public health adulticiding is confined in geographical extent, whereas agricultural treatments typically cover larger geographical areas.
- (d) Public health larviciding is typically planned and restricted to urban or peri-urban situations, whereas agricultural "larviciding" is inadvertent and can be widespread.
- (e) Public health larviciding typically employs a different insecticide from that used for adulticiding, whereas agricultural "larviciding" implies that larvae are exposed to the same insecticides as are being used on the crops (and therefore the same as those to which adult mosquitoes are being exposed).
- (f) The more widespread background effect of agricultural usage, and the consequently greater opportunity for dilution and attrition of residues means increased chance of heterozygote survival and consequent development of resistance.

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FIG. 1. Graphical expression of the Hardy-Weinberg Law, i.e. for a panmictic population not subject to selection, migration or high mutation rate. The proportions of genotypes produced by a diallelic locus can be expressed as p^2 , $2pq$ and q^2 where p and q are the respective allele frequencies

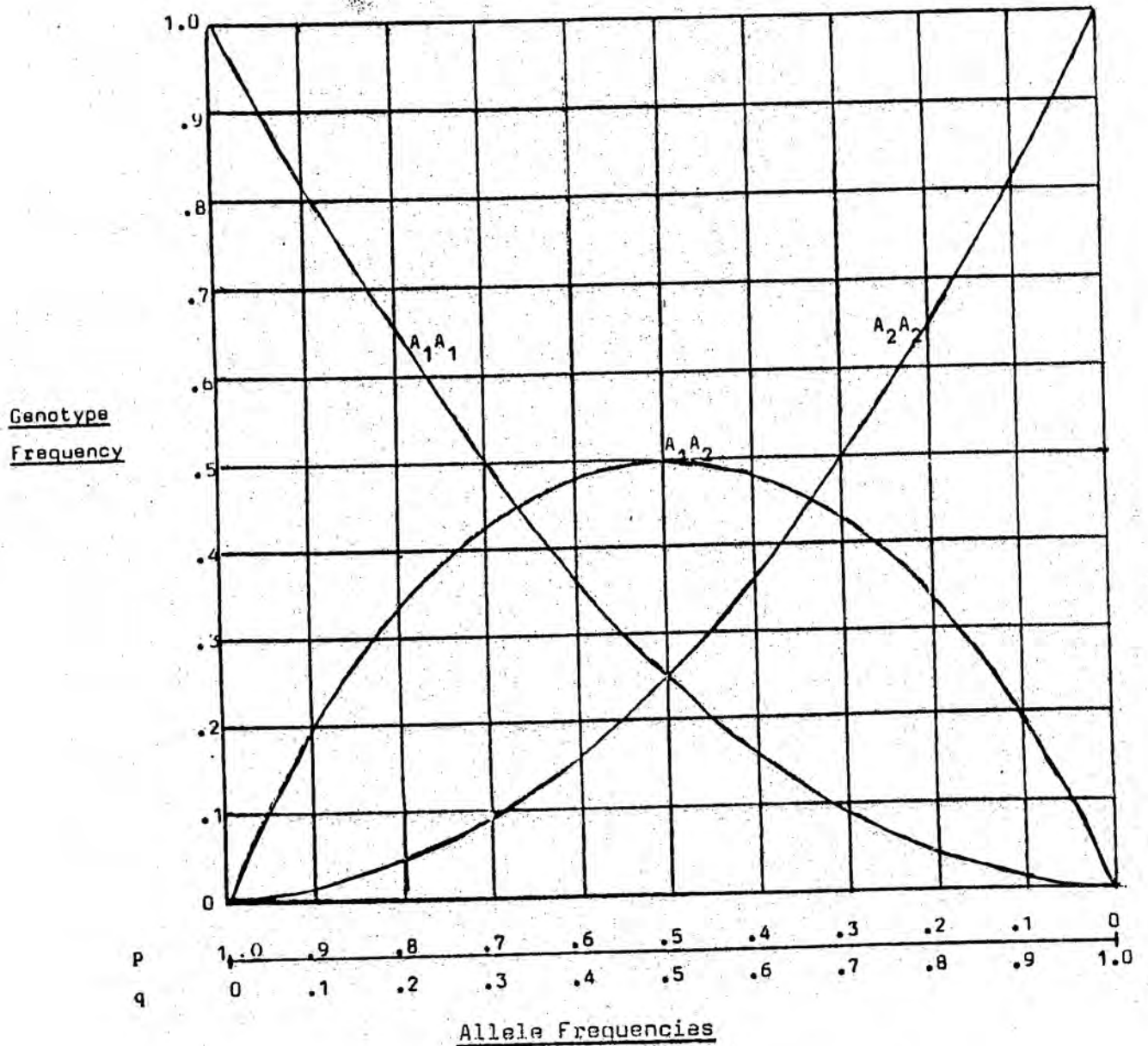


FIG. 2. The Hardy-Weinberg Law expressed on the de Finetti triangle. Here the lines of Fig. 1 can be shown as a single line. Any population, whose genotypic proportions do not fall on this line is not in Hardy-Weinberg equilibrium, and the further the proportions lie from the line the greater the disturbance to which the population is being subjected.

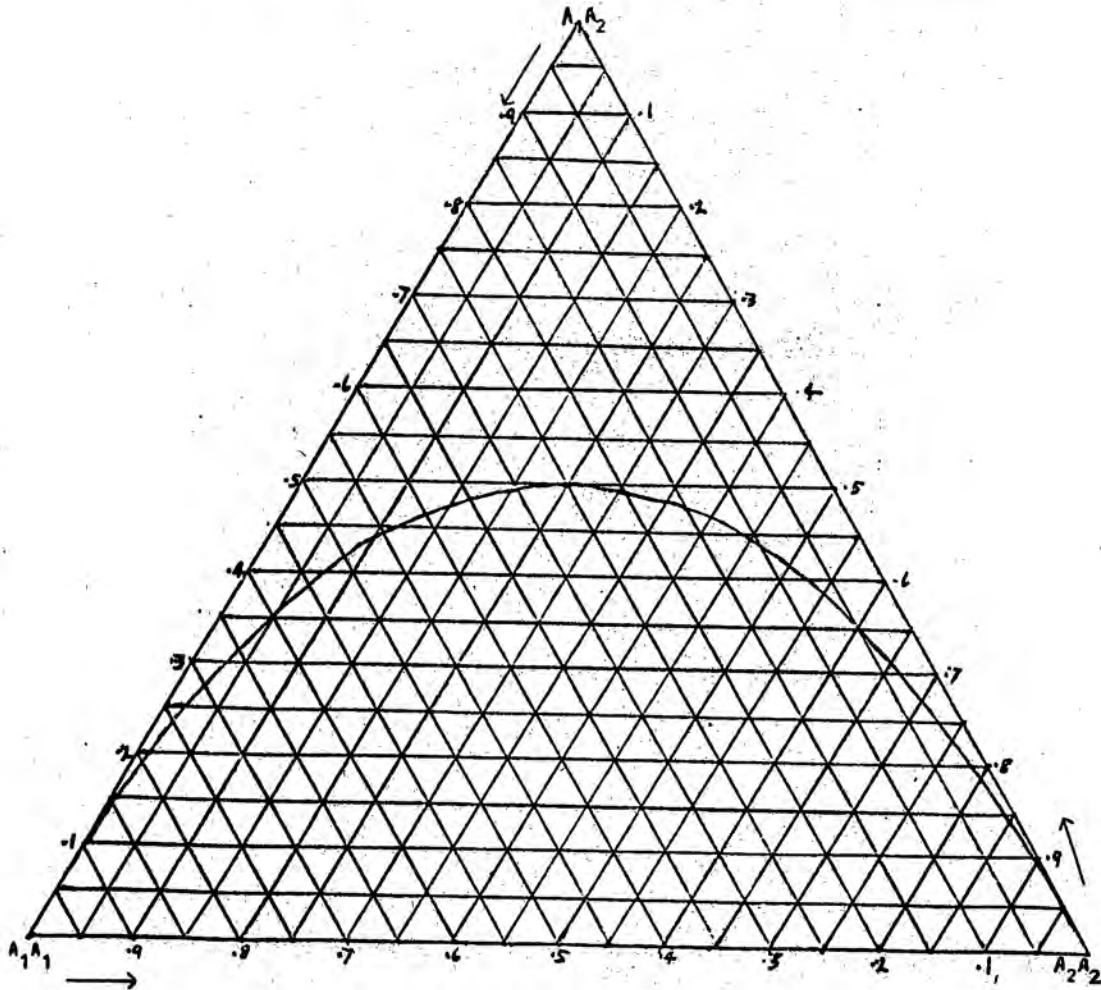
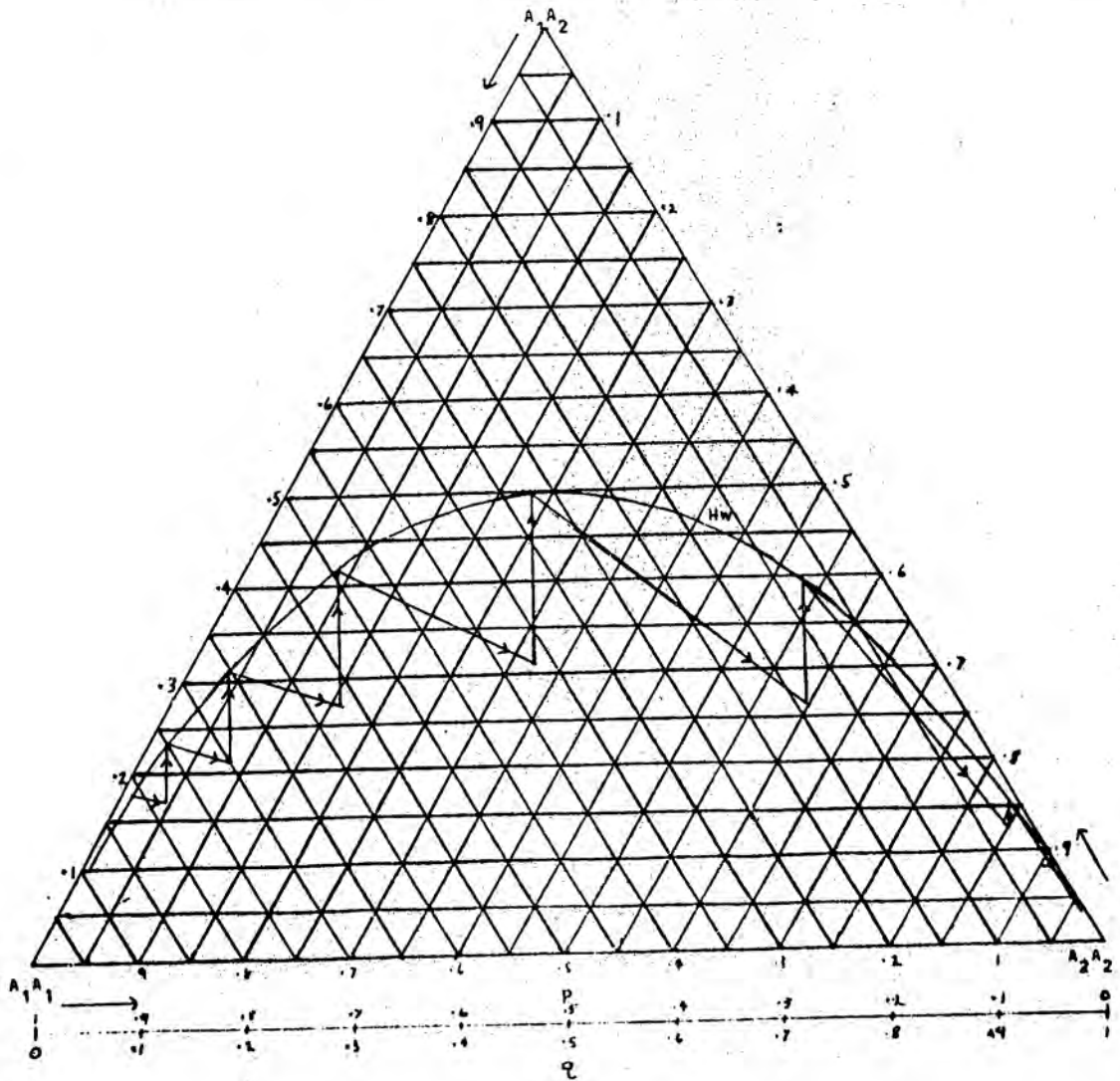


FIG. 3. Progressive change in allele frequency and genotype constitution for a population under a high selection pressure ($s = .8$). The starting allele frequency is taken as $p = .9$, $q = .1$. Since no selection is operating on the gametes, each generation starts off in Hardy-Weinberg equilibrium.

HW = Hardy-Weinberg line



7-2 THE PREVENTION OF RESISTANCE TO AGRICULTURAL PESTS

by L. Brader

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The 2nd session of the FAO Panel of Experts on Pest Resistance to Pesticides and Crop Loss Assessment, held in Rome from 28 August to 1 September 1978, paid particular attention to strategies to avoid pesticide resistance. With respect to agricultural pests, it did this on the basis of the following working papers:

- G.P. Georghion. The management and suppression of insecticide resistance
- G.P. Georghion. Strategies in the use of pesticides to delay or avoid development of resistance
- J.W. Gilpatrick. Strategies in the use of pesticides to delay or avoid development of resistance in fungi
- J. Keiding. Strategies in the use of pesticides to delay or avoid development of resistance, and
- J. Dekker. Resistance mechanisms and countermeasures.

As a result, the report of this 2nd session contained two specific paragraphs on this matter, one on strategies for preventing or delaying resistance to fungicides and another on strategies for delaying or avoiding resistance in arthropods (FAO, 1979). Reproduced below is the section on resistance in arthropods.

It is generally recognised fact that resistance arises rapidly in some species and slowly or not at all in others. Also within some species, some populations have developed resistance faster under a given set of circumstances and other populations more slowly or not at all under a different set of circumstances.

An important requirement for developing strategies for avoiding or delaying the development of resistance is the elucidation of the factors which influence the evolution of these phenomena. These factors have recently (1977) been classified as follows by Georghion and Taylor:

- A. Genetic: (1) frequency of R alleles; (2) number of R alleles; (3) dominance of R alleles; (4) penetrance, expressivity, interactions of R alleles; (5) past selection of other chemicals; (6) extent of integration of R genome with fitness factors.

- B. Biological
 - a. Biotic potential: (1) Generation Turn-over; (2) offspring per generation; (3) monogamy/polygamy; parthenogenesis.

 - b. Behavioural: (1) isolation; mobility; migration; (2) monophagy/ polyphagy; (3) fortuitous survival; refugia.

- C. Operational
 - a. The chemical: (1) chemical nature of pesticide; (2) relationship to earlier used chemicals; (3) persistence of residues; (4) formulation.

 - b. The application: (1) application threshold; (2) selection threshold; (3) life stage(s) selected; (4) mode of application; (5) space- limited selection; (6) alternating selection.

Although these factors relate specifically to arthropod populations the principles involved generally apply to other types of organisms as well.

Factors in the genetic and biological categories are inherent qualities of the species and, therefore, are beyond management. However, knowledge of how these contribute to selection pressure is important, for it serves to assess the propensity for resistance in a population.

In contrast, factors in the operational category are man-made and, therefore, they are manageable. They can be modified to the extent dictated by the propensity for resistance as determined from the assessment of the genetic and biological factors mentioned above.

The panel has noted with interest the recent preparation of computer models to assess the possible course of development of resistance in population under various conditions. Further development of models which include resistance hazard-rate of development, and cost, as part of past management is recommended. Such models may be useful tools in devising strategies to retard evolution and affects of resistance. Long-term population data on the resistance responses of arthropods may serve as useful validation for resistance models.

Studies of the population dynamics and the genetics of development of resistance in field populations of agricultural pests are badly needed in order to make possible the construction of predictive models and should receive strong support from research organisations concerned with pest control.

Past experience and recent studies on resistance modelling show that reduction of selection pressure in its broadest sense is a key factor in reduction of development of resistance. In this connection, recent work has indicated the importance of parts of pest populations that have not been exposed to selective dosages, either in "refugia" within the treated population or by immigration from untreated populations (or by spacing treatments) in time. Practical ways should be developed, if possible, of using the "refugia" principle.

It appears from available studies that resistance may be delayed longer or possibly avoided, if the following conditions are fulfilled.

- (1) the pesticide has short residual life;
- (2) the pesticide is not related to a chemical used earlier with respect to mode of action or metabolism;

- (3) the formulation does not provide prolonged release of the chemical in the environment;
- (4) applications are made only when the population reaches relatively high levels of density;
- (5) the selection threshold is relatively low;
- (6) selection is directed mainly against adults;
- (7) the application is localized rather than area-wide;
- (8) certain generations (or periods, when generations overlap) are left untreated.

It must be clearly recognized that the type of pest and population concerned may have unique characteristics which determine the extent to which each of the above parameters influences the evolution of resistance. Likewise, it is evident that the possibility of meeting some or all of the above conditions is strongly dependent on the economics of crop production.

As indicated above, the choice of pesticides is an important factor in a strategy to reduce the effect of resistance. As far as possible the choice should be based on an evaluation of the resistance potential of the local pest to the available insecticides, taking previous use of insecticides, cross-resistance patterns and knowledge of existing resistance types into account. This requires that resistance types (mechanisms and genetics) be characterized, diagnosed and monitored (as has been done for example in the cattle tick in Australia, houseflies in Denmark, rice pests in Japan and recently in aphids in England). Such studies are useful for selecting effective substitute chemicals and avoiding compounds to which resistance will develop quickly. It is also of great importance to have information on the effect of sequential insecticide pressure in order to be able to recommend the best sequence of using insecticides with the aim of delaying or avoiding the evolution of multiple resistance. An important element of such work is to retain strains representing various steps and types of resistance development for further study and for testing of new insecticides.

Studies have shown that high resistance to a chemical is often due to the interaction of two or more resistance factors (e.g. detoxifications, reduced permeability and reduced sensitivity of the site of action) each of which only confers a moderate resistance.

Studies of multi-resistance in relation to sequential use of pesticides should be intensified and coordinated (e.g. by arrangement of meetings or workshops for research workers). The value of using mixtures or alternations of insecticides is still questionable. In general, it is desirable to avoid mixtures unless their use is based on careful investigations of their ability to reduce development of resistance. The Panel noted that such investigations are now in progress. In sequential use of insecticides the following general advice may be given: if feasible use first insecticides for which resistance depends primarily on a single specific resistance factor. Avoid, or use last, insecticides for which resistance depends on the interaction of several resistance factors (giving broad cross-resistance) or which, in other ways, act as effective selectors for resistance to other insecticides.

This is as far as the report of the 2nd session of the FAO Panel of Experts goes on this matter. During its third session held in Kyoto on 6 August 1980, the Panel did not report any new findings on this matter and it can be concluded that the above strategies are still considered valid. In fact, the Panel did report some new activities under this heading for resistance to fungicides (FAO, 1981).

The changing role of insecticides in crop protection was reviewed in detail by Metcalf in 1980 (Metcalf, 1980). The author subscribes largely to the above mentioned strategies and emphasizes that the basic components to decrease insecticide resistance in control programmes are reduced selection pressures, i.e. reduced use of pesticides and insecticide management or, in other words, choosing the optimum sequence of insecticides. He notes that the combination of the various enumerated principles

to reduce selection pressure is essentially a blueprint for integrated pest management.

This brings us automatically to the application at the field level of the various strategies to avoid or reduce insecticide resistance, and for this it might be useful to briefly comment on the practical possibilities to fulfil the above-mentioned conditions to delay or avoid pesticide resistance.

Pesticides with a short residual life should have preference. However, a conflict may arise here with the need for the most economic and effective pest control. In practice, providing the price is equal, the farmer would generally prefer to apply the insecticide with the longest residual life. Moreover, the apparent advantage of a rather short residual life may be lost should the need arise for an increased number of applications.

It is recommended that an insecticide be selected which is not related to a chemical used earlier with respect to the mode of action or metabolism. This condition can only be followed if an adequate choice of pesticides is available. Generally speaking in developing countries in particular, the economics of pest control make the choice of different insecticides rather limited.

The formulation should preferably not provide prolonged release of the chemical into the environment. The same comments can be made here as for the question of the residual life, in practice this will be difficult to realize.

Applications should only be made when the pest population reaches relatively high levels of density. Indeed, this should be the basic principle for pesticide use in general as it would result in a reduction of the use to a strict minimum. In addition to reducing the development of pesticide resistance, it has the advantage of being more economical and giving better technical results. The application of this criterion, which is the

key concept of integrated pest control, requires that the farmers have a good understanding of pest problems in their crops and that they have been taught, or are assisted to sample pests regularly. Progress has been made in this respect, but it is still the major shortcoming to the improvement of the effectiveness of current plant protection practices.

Resistance may be delayed if the selection threshold is relatively low, i.e. the portion of the population surviving a pesticide treatment is small. This depends in the first place on the frequency of resistance genes in the pest population and this is a given fact which cannot be changed deliberately. However, the effect of a rather large number of surviving species can be considerably reduced through immigration of untreated specimens from neighbouring areas. Thus, the overall result can be improved by the practice of localized treatments.

Selection should be mainly directed against adults. Adult insects can move freely and thus mixtures with untreated specimens can occur more easily. On the other hand, it seems that the occurrence of resistance to ovicides is virtually non-existent. Thus, it might be expected that treatments directed against the egg stage could be an excellent means to reduce pesticide resistance development.

Pesticide application should be localized rather than area wide. This is a practice that could probably be adopted successfully in most developing countries, particularly in crops that do not require a heavy schedule of insecticide applications. Otherwise the need for effective pest control will probably require regular and widespread, mostly aerial applications, and economic considerations will preclude the adoption of a system of localized spraying. The advantage of localized spraying is the same as mentioned above, i.e. a dilution of the surviving resistant specimens with untreated immigrants.

It is also suggested that certain generations be left untreated. The possibility to do this will of course depend on the

occurrence of periods during which the population is rather low. In fact it is the same principle as the one in which it is recommended to spray only when the population reaches relatively high levels of density.

In summary it may be concluded that under a given set of conditions, such as the genetic build-up of the pest population and socio-economic criteria, the build up of pesticide resistance depends primarily on the intensity of pesticide use. The guiding principle, therefore, should be that pesticides should be used as little as is really necessary for effective and economical pest control. It has already been mentioned that applications should only be made when pest populations reach a certain density, but in addition more effort should be made to reduce population build-up and this can be achieved through such measures as cultural practices, introduction of pest resistant crop varieties, safeguarding naturally-occurring parasites and predators, etc. In short, the application of integrated pest control would provide the best answer. Recently more and more efforts are being made in this direction, and it is therefore to be expected that the problems of pesticide resistance might be reduced in the coming years.

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8-0 RESISTANCE IN THE EIGHTIES :
AN INDUSTRY PERSPECTIVE

by W.N. Harnish

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For the past several years there has been a gradual withdrawal or retrenchment of several agro-chemical manufacturers. One reason is very basic to our economic structure, profit. Companies are in business to make money and may prefer investments that offer high return rates and carry low risks. Increasing costs of product development can seriously affect profit margins and thus persuade an organization to concentrate its investments in alternate areas.

During the last several years, the cost of developing new insecticides has increased dramatically. There are several factors which have contributed to the escalation of the price of a new compound. One is that pesticide development requires a diversity of technical expertise. The imagination of the synthesist chemist is needed to produce novel toxic molecules, the biologist to discover and evaluate the new compounds and both, working as a team, to select the most effective of closely related molecules for further work. During the next phase of a product's development, toxicologists, formulation specialists, patent lawyers, chemical engineers and marketing experts are needed to further evaluate a new compound's potential. It is not difficult to realize that these aggregate costs are high and are generally incurred within the first year. In addition, numerous expensive and time consuming tests must be conducted to meet government regulations.

Time is another important cost-related factor. If a new compound is accepted and performs as expected, the company may have only 5 - 7 years to recover its investment, produce a profit and finance the development of its next product. This is because it requires about 7 - 8 years work before the first sales occur and 2 - 3 more years to reach the point where development costs are met. That,

under the present US patenting system, leaves only 5 - 6 years of patent protection for the compound.

In addition to soaring development costs, the complexity of new chemistry has also made it more difficult to discover and develop new insecticides. As shown in Table 1, in 1956 only 1800 new compounds were screened to find one new product. By 1964, the number of new compounds had doubled and in 1970 it required 8000 newly synthesized compounds to discover one new product. At the present time, it is estimated that over 20,000 new molecules must be designed before a molecule of sufficient activity and other positive characteristics is found which can be produced as a commercial insecticide. Of course, part of the reason for the increased number of compounds which must be screened to find a new product, is that the new product must be superior to those already on the market. Another reason for fewer new products, is that insect resistance has eliminated several areas of chemistry which traditionally supplied new compounds. Regretably, the combination of all these factors has resulted in a significant decline in the number of new insecticides introduced in recent years as shown in Table 1.

Insect resistance has been reported in every major insecticide class. Georghiou (1981) summarized the status of resistance to the major insecticide classes from 1970 to 1980 (Table 3). As might be expected, greater percentage increases in resistance have occurred in this decade toward the newer classes of chemicals. Carbamate resistance has increased seventeen-fold, pyrethroid about seven-fold, and organophosphate only four-fold. Further, the increase in reports of resistance is a result of wider insecticide usage coupled with better detection.

It is critical that the insecticides presently in our arsenal be maintained as long as possible, because of this decline in new product introductions and the present tendency to search only for products that protect major crops, such as corn, cotton and rice. At this time when the only real short-term answer to the world-

wide food shortage is to prevent agricultural and food losses, it is imperative that universities, governments and industry cooperate to maintain current compounds and encourage the introduction of new insecticides. It is very evident that reinforcements will be slow in coming.

It is clear that misuse of our present chemicals can rapidly cause them to become ineffective pest control agents. Fortunately, there are strategies available which can effectively prolong the useful lifetime of our present insecticides. Georgiou (1980) reviewed a number of countermeasures to deal with resistance (Table 3). A number of these measures such as alternating insecticides and the application of chemicals in mixtures or in rotation have been used successfully. As our knowledge of the biochemistry and genetic of resistance increases, the potential for success will improve.

We can educate the grower and encourage the adoption of practices that will delay resistance. Universities should assume a strong role in understanding the mechanisms of resistance. Government needs to amend current regulations to create a more favourable regulatory environment. Industry should take the lead to encourage proper insecticide management to discover compounds with new modes of action.

Resistance to an insecticide by an insect does not usually involve any visible change in the behavior or morphology of the pests: it is generally caused by subtle changes in biochemistry. Therefore, the susceptibility of the wild-type population must be determined. Optimally the baseline range of susceptibility will be determined before a new insecticide is introduced. This is not always possible because insecticides are often introduced into new areas without thought of resistance development. In this case, baseline values for susceptible populations from other localities have to be used.

When a new compound is introduced, it is extremely important to monitor and measure changes in susceptibility of pest population being controlled. Monitoring studies are valuable in determining the presence of resistance and in understanding changes in the

insect population under various control regimes.

The only method available to measure resistance is by comparing the dosage response relationship of populations under selection pressure with one which has not been subjected to insecticide pressure. This must be done in the laboratory.

A good monitoring program can be rather extensive and expensive, depending on the insect species involved, the geographic range of the pest, the biology of the insect, the number of generations per year and the ease with which the species can be handled and tested in the laboratory. The expense of a program, however, is slight when compared to the cost of a crop loss or of developing a new insecticide. In any event, the most critical portion of a monitoring program is the test method. The test method used must be standardized so that the results obtained by different workers are comparable, e.g., FAO and WHO have published standard methods for many insect species. Readily obtainable standard materials must be employed to minimize as many variables as possible which might effect test results. In most cases, (exception-mites and aphids) topical test methods are used because the exact dose applied per insect is known. The insect life stage which can be most easily handled should be tested but it is preferable to test the stage which is being treated in the field. Many times, even though an insect is numerous enough to cause extensive damage, it is difficult to collect sufficient numbers of a given instar to permit testing. In these cases, the species must be reared for one or two generations in the laboratory. This can become quite labor intensive if the insect is difficult to rear or several sites are being sampled. Once baselines and dosage-mortality lines have been determined for the areas being sampled, populations can be tested by treating samples with a discriminating dose (in most cases the rate which produces 99.9% mortality in the susceptible population). The number of sites sampled for a particular insect depends on the size of a geographic area in question, the insecticide history of

different localities within the area and the compounds being used throughout the area. Experience has shown that resistance usually develops in small areas and spreads outward from these "hot spots". After an insecticide has been used for a number of years, the susceptibility of the insect population over a large area can vary considerable because of cultural practices, immigration of susceptible individuals, etc. Therefore, each area must be sampled to determine the level of susceptibility in those areas.

To summarize - to establish a monitoring program, several things are needed - a standard test method, baseline data, a knowledge of the biology of the insect in question, the insecticide history and use patterns throughout the range of the area of interest, and enough samples of the population to be able to estimate the susceptibility level of the population in each area.

In conclusion, insect resistance is one of the most serious problems facing mankind. The number of resistant insect species as well as the area affected continues to expand, whereas the number of new compounds being discovered is not keeping pace. It is imperative to keep our present pesticides effective through judicious use. Today we discussed a number of new approaches for coping with resistance. In a world with ever-expanding food requirements, dealing with resistance will require intensive research effort. We are confident it can be done.

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TABLE I

NUMBER OF COMPOUNDS SCREENED TO
YIELD A COMMERCIAL PRODUCT

<u>YEAR</u>	<u>NO. COMPOUNDS</u>
1956	1800
1964	3600
1969	5000
1972	10000
1980	20000

TABLE 2
NUMBER OF MAJOR INSECTICIDES
SINCE 1940

<u>DECADE</u>	<u>MAJOR COMPOUNDS</u>	<u>CLASS</u>
1940	9	CHLORINATED HYDROCARBON
1950	18	PHOSPHATE/CARBAMATE
1960	19	CARBAMATE/PHOSPHATE
1970	4	PYRETHROID
1980	?	?

TABLE 3

COMPARISON OF RECORDS OF RESISTANCE TO PESTICIDES IN ARTHROPODA

	1970	1980	FOLD INCREASE '70-'80
SPECIES WITH REPORTED RESISTANCE	224	428	1.91
CASES OF RESISTANCE BY PESTICIDE GROUP			
DDT	98	229	2.3
CYCLODIENE	140	269	1.9
ORGANOPHOSPHATE	54	200	3.7
CARBAMATE	3	51	17.0
PYRETHROID	3	22	7.3
FUMIGANT	3	17	5.7
OTHER	12	41	3.4
TOTAL FOR ALL PESTICIDE GROUPS	313	829	2.6

FROM: GEORGHIOU 1981 FAO IN PRESS

TABLE 4

POTENTIAL RESISTANCE MANAGEMENT STRATEGIES

- . ALTERNATING CHEMICALS
- . COMBINING CHEMICALS
- . CHEMICAL ANALOGS
- . SHORT RESIDUAL FORMULATIONS
- . APPLICATION THRESHOLD
- . RESISTANT PREDATORS
- . SYNERGISM

ADAPTED FROM: GEORGHIOU 1980
RESIDUE REVIEWS 76:131-145

8-1 INDUSTRY'S DIRECTION IN RESISTANCE MANAGEMENT

by John R. Leeper

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The dynamics of an undisturbed ecosystem are frequently overlooked because the natural checks and balances within it normally regulate and prevent violent population fluctuations. In agriculture, and most dramatically by establishing monocultures, man has drastically disrupted the ecosystem with the intent of producing a single crop as inexpensively and easily as possible. Man has found that, in so doing, his crop can be attacked and destroyed by insect pests. This represents a violent reaction to man's action and has, in turn, required the development of numerous techniques to combat these pests. Chemical insecticides were developed for that purpose and have served man well. However, in response to their use, insect pests have developed resistance to the insecticides. A similar scenario of action and reaction can be given for public health and the development of resistance in arthropod vector populations.

The first recognized case of insect resistance to insecticides was that of the San Jose scale, Quadraspidiotus perniciosus (Comstock), to lime-sulfur in Washington state (USA) apple orchards in 1908. The next was the development of resistance in the housefly, Musca domestica L., to DDT in northern Sweden in 1946 (Brown, 1958). This first case of resistance to a synthetic insecticide was quickly followed by additional cases. By 1976, there were 364 documented species resistant to insecticides (Georghiou and Taylor, 1977). To date, there are over 428 resistant insect species, with examples resistant to every synthetic insecticide class (Georghiou, 1982).

An underlying concern is that resistance is inevitable yet unpredictable. Based on historical perspective, we can assume that insects will develop resistance to any new class of insecticide discovered. We cannot, however, determine before the fact the mode or mechanism of resistance, or when or where it will occur.

Cost of Resistance

An additional concern is the cost of resistance, both the tangible and intangible. The manufacturer has the potential to suffer the greatest financial loss. Let me use the life of a hypothetical pesticide to demonstrate the potential losses due to resistance (Figure 1). For this hypothetical case we must assume that the selling price of the product is US \$ 3.33 per pound; the annual sales volume is 10 million pounds; net profit after tax is 14% of sales; fixed capital or cost of manufacturing facilities is US \$ 20 million; and working capital is 50% of sales. Once a commercial product, the pesticide must be marketed for a period before incurred costs are recovered. Once the breakeven point, F, has been reached, the pesticide has paid for itself. It becomes profitable and begins paying for the research and development of future pesticides. The development of resistance early in the life of an insecticide could lengthen the time before the breakeven point is reached, or prevent it from becoming profitable. Resistance to a profitable insecticide can severely reduce the cash flow and operating capital required for the research and development of future products. Banning an insecticide in agriculture in order to preserve it for public health may delay or prevent it from becoming profitable. As a result the manufacturer may decide to terminate production. In reality, it takes longer and costs more to develop an insecticide than is shown in the above hypothetical case. It is estimated that in the 1980's it will take 8 to 10 years, at a cost of US \$ 35 million, to develop an insecticide. An additional US \$ 40 to 100 million is required to build a manufacturing plant (Hill, 1982).

The potential cost of resistance to the individual may not be as great financially as to the corporation but is socially significant. A producer's inability to protect crops can threaten his livelihood. But, most costly is the intangible loss of human potential through suffering and death from disease, malnutrition and starvation.

It is important that a coordinated programme for resistance management be developed. Resistance is a complex problem for which a coordinated programme offers the greatest potential returns. That is why we, representatives of government, academia and industry are attending this meeting.

Industry's Research Thrust

Industry does not usually disclose research programs in order to protect proprietary information. However, a company with an interest in insecticides is probably conducting resistance research.

Monitoring important species for susceptibility/resistance in key market areas is the most obvious industrial effort. Monitoring initially provides baseline data and answers the immediate question of efficacy by documenting the degree of susceptibility/resistance. The cost of monitoring and industry's responsibility to work with local governments and independent researchers will be addressed by Dr. Harnish.

Once resistance is detected, additional research into its mode and mechanism, gene dominance, degree of reversion, change in strain vigor, etc., should be initiated. Biochemical/physiological and population genetics research may begin to determine the above points and provide answers to the following resistance management questions. What is the best combination or alternation of insecticides? Is there a benefit to alternating insecticides? Is there a role for synergists? Plapp (1981) and Dittrich (1981) have called attention to these research areas. There is a need for cooperation and exchange in this area among government, academia and industry (Hill, 1979).

The screening of candidate materials on resistant strains can provide valuable information. Early detection of activity on resistant strains by insect control candidates can strengthen the case for a material's further development. Conversely, a material's failure to control resistant strains can quickly stop the costly process of research and development.

Resistance Management in the Field

Resistance management should be recognized as a primary component within locally developed Integrated Pest Management programs. They are finely tuned to local crop, pest beneficial

arthropods, pesticide and environmental conditions. This expertise offers the greatest possibilities for efficacy and satisfaction by the insecticide user and manufacturer. Monitoring and action thresholds developed in IPM programs allow beneficial species to be utilized in controlling sub-economic insect pest levels. Insecticides can then be better timed and directed to help prevent the development of resistance.

The use of combinations or alternations of insecticides with different modes of action and mechanisms of resistance have been suggested as means of delaying, preventing or ameliorating resistance. I do not want to become involved in the argument of which method is best, and under what conditions. They both offer potential benefits within resistance management programs. In contrast, it is difficult to consider using a single insecticide until there is control failure, and then switch to another, as a part of a management philosophy.

A relatively recent and innovative approach to controlling resistant insects has been to direct chemical controls at the egg and adult stages (Dittrich 1976, 1981; Young, Harrell and Mane 1979; Campbell, Counselman, Ray and Terry 1979; Pitts and Pieters 1980) rather than the traditional, damaging, larval stage. The uses of chlordimeform and methomyl to control Heliothis spp. on cotton are the best known examples of this concept in practice. And, there appears to be no cross resistance between life stages for either material.

Summary

Industry has long recognized the problem of resistance and has been addressing it through monitoring, screening of candidate insecticides and attempting to develop innovative control strategies. Industry also recognizes the importance of locally developed IPM programs in resistance management. There is an abundance of industrial resistance research that has not been published. In the case of non-proprietary information, industry should consider publishing that which would contribute to resistance management state of the art.

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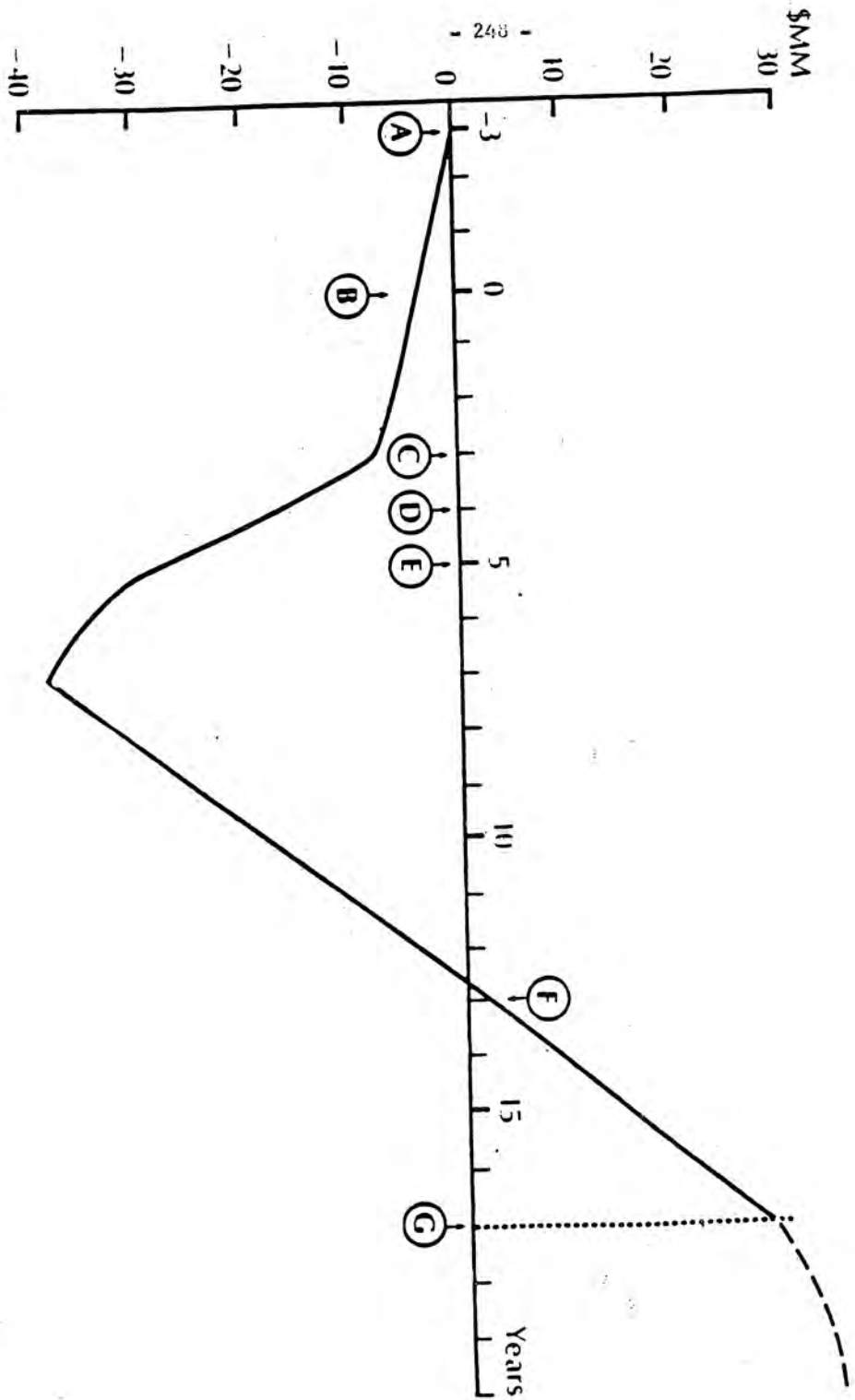


FIGURE 1. Life of Hypothetical Pesticide. A: Initial Synthesis and Screening (Year -3). B: U.S. Patent Issued (Year 0). C: First Label Registered (Year 3). D: Commercial Plant Construction (Years 4-6). E: Commercial Sales Begin (Year 5). F: Breakeven Point (Year 13). G: Patent Expires (Year 17).
 (Extracted from Saegbarth, K. A., Biochemicals Department, E. I. du Pont de Nemours, Inc., 1981, unpublished.)

APPENDIX 1International Advisory Committee

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3. Dr. N.G. Gratz - (Director, Vector Biology & Control Division, WHO)
4. Dr. L. Brader - (Chief, Plant Protection Service, FAO)

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5. Mr. Y. Elikawela - (Entomologist, Central Agricultural Research Institute, Sri Lanka)
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APPENDIX 2

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APPENDIX 3

PROGRAMME FOR THE INTERNATIONAL WORKSHOP ON RESISTANCE
TO INSECTICIDES USED IN PUBLIC HEALTH AND AGRICULTURE

INAUGURAL SESSION

22nd February (Monday)

- 8.30 a.m. Registration of Participants
- 9.00 a.m. Opening remarks - Dr. R.P. Jayewardene
Secretary General/NSC
- 9.05 a.m. Address of Welcome - Hon. E.L. Senanayake
Minister of Agricultural
Development and Research
- 9.20 a.m. Inaugural Address - Hon. Gamini Jayasuriya
Minister of Health
- 9.30 a.m. Background to and Objectives
of Workshop - Dr. P.T. Haskell
(Centre for Overseas Pest
Research, England)

10.00 a.m. TEA BREAK

SECTION 1 SETTING THE SCENE

Chairman : Dr. P.F. Haskell

- 10.45 a.m. Election of Rapporteurs
- 11.00 a.m. Surveillance of Pest
Resistance to Insecticides
in Agriculture - Prof. G.P. Georghiou
(Div. of Toxicology
Univ. of California)
- 11.30 a.m. Resistance Problems in Public
Health Vector Control on a
Global Basis - Dr. N.G. Gratz
(Vector Biology & Control
Division, WHO)
- 12.00 noon Discussion
- 1.15 p.m. LUNCH

24th February (Wednesday)

SECTION 2 (Contd.)

- 10.30 a.m. Experience of Sri Lanka
Pesticide Usage and Induction of Resistance in Pests and Vectors - Dr. N. Wickremasinghe & Mr. Y. Elikawela (Central Agricultural Research Institute, Sri Lanka)
- 11.00 a.m. Pesticide Resistance and Malarial Control in Sri Lanka - Dr. P.R.J. Herath (Anti Malaria Campaign Sri Lanka)
- 11.30 a.m. Use of Insecticides to Control Vectors in Malaria and Filariasis - Dr. K. Subramaniam & Dr. M.V. Samarasinghe (Anti-Malaria Campaign Sri Lanka)
- 12.00 noon Discussion
- 12.45 p.m. Principal Mechanisms of Resistance to Insecticides - Prof. G.P. Georghiou (Div. of Toxicology, Univ. of California)
- 1.05 p.m. Selection Dynamics of Populations - Dr. D. Muir (WHC)
- 1.25 p.m. Discussion
- 1.45 p.m. LUNCH

SECTION 3 THE PREVENTION OF RESISTANCE

- Chairman : Prof. G.P. Georghiou
- 2.45 p.m. General Strategy of Prevention
- 2.45 - 3.05 (a) Agricultural Pest - Dr. L. Brader (Plant Protection Service, FAO)

SECTION 3 (Contd.)

- 3.05 - 3.25 (b) Vectors - Dr. N.G. Gratz
(Vector Biology & Control
Div., WHO)
- 3.25 p.m. Discussion of the Interaction
between agricultural pests &
Vector Control
- 3.45 p.m. TEA BREAK
- 4.00 p.m. Resistance in the eighties
An Industry Perspective - Dr. W.N. Harnish
(International Group of
National Associations of
Manufacturers of Agro-
Chemical Products)
- 4.20 p.m. Industry's Direction in
Resistance Management - Dr. J..R. Leeper
(International Group of
National Associations of
Manufacturers of Agro-
Chemical Products)
- 4.45 p.m. General Discussion

25th February (Thursday)

Chairman : Dr. P.T. Maskell

- 9.00 a.m. Discussion of recommendations
- (a) Alternatives to Pesticides
1. Environmental Management
 2. Biological Control
 3. Semio - Chemical
- (b) Practical Possibilities of
optimal sequential use of
insecticides including the
regulatory and compliance
approach
- (c) Further Research

25th February (Contd.)

- 1.00 p.m. LUNCH
- 2.30 p.m. Plenary session - Drafting of
recommendations in groups
(a), (b) & (c)
- 5.00 p.m. Close
- 7.00 p.m. Reception to delegates at the
SLAAS Auditorium

26th February (Friday)

SECTION 4 CONCLUSIONS AND RECOMMENDATIONS

- Chairman : Dr. P.T. Haskell
- 10.00 a.m. Discussion of draft report and
recommendations
- 1.00 p.m. LUNCH
- 2.30 p.m. Presentation and adoption of
conclusions and recommendations
- 4.30 p.m. Official closure
- to
- 5.00 p.m.

APPENDIX 4

LIST OF DOCUMENTS ON PEST RESISTANCE TO INSECTICIDES

PREPARED BY FAO

- FAO 1965 Report of the First Session of the FAO Working Party of Experts on Resistance of Pests to Pesticides. FAO Meeting Rep. PL/1965/18. 106 p.
- FAO 1966 Report of the Second Session of the FAO Working Party of Experts on Resistance of Pests to Pesticides. FAO Meeting Rep. PL/1966/M/13. 8 p.
- FAO 1967 Report of the Third Session of the FAO Working Party of Experts on Resistance of Pests to Pesticides. FAO Meeting Rep. PL/1967/M/8. 20 p.
- FAO 1968 Report of the Fourth Session of the FAO Working Party of Experts on Resistance of Pests to Pesticides. FAO Meeting Rep. PL/1968/M/10. 45 p.
- FAO 1969 Report of the Fifth Session of the FAO Working Party of Experts on Resistance of Pests to Pesticides. FAO Meeting Rep. PL/1969/M/7. 5 p.
- FAO 1969 Report of the FAO Symposium on Resistance of Agricultural Pests to Pesticides. FAO Meeting Rep. AGP/1970/Symp/1. 22 p.
- FAO 1970 Report of the Sixth Session of the FAO Working Party of Experts on Resistance of Pests to Pesticides. FAO Meeting Rep. AGP: 1970/M/9. 10 p.
- FAO 1971 Report of the Seventh Session of the FAO Working Party of Experts on Resistance of Pests to Pesticides. FAO Meeting Rep. AGP: 1971/M/7. 19 p.
- FAO/WHO 1972 Report of a Joint FAO/WHO Meeting on Insect Viruses. The Use of Viruses for the Control of Insect Pests and Disease Vectors. FAO Agricultural Studies No. 91. World Health Organization Technical Report Series No. 531. 48 p.

- FAO 1973 Report of the Ninth Session of the FAO Working Party of Experts on Pest Resistance to Pesticides. FAO Meeting Rep. AGP: 1973/M/10. 17 p.
- FAO 1974 Report of the Tenth Session of the FAO Working Party of Experts on Pest Resistance to Pesticides. FAO Meeting Rep. AGP: 1974/M/9. 28 p.
- FAO 1976 Report of the FAO Global Survey of Pesticide Susceptibility of Stored Grain Pests. FAO Plant Production and Protection Series No. 5. 297 p.
- FAO 1976 Report of the First Session of the FAO Panel of Experts on Pest Resistance to Pesticides and Crop Loss Assessment. FAO Meeting Rep. AGP: 1976/M/10. 42 p.
- FAO 1979 Report of the Second Session of the FAO Panel of Experts on Pest Resistance to Pesticides and Crop Loss Assissment. FAO Meeting Rep. AGP: 1979/M/2. 41 p.
- FAO 1981 Report of the Third Session of the FAO Panel of Experts on Pest Resistance to Pesticides and Crop Loss Assessment. FAO Meeting Rep. AGP:1981/M/2. 35 p.
- FAO 1970 Pest Resistance to Pesticides in Agriculture - Importance, recognition and countermeasures. AGP: CP/26. 32 p.
- FAO 1971 Model Extension Leaflet on Pest Resistance to Pesticides. AGP: CP/42. 10 p.
- FAO 1980 Model Extension Leaflet on Resistance of Plant Pathogens to Pesticides. AGP: CP/111. 8 p.
- FAO 1981 The Occurrence of Resistance to Pesticides in Arthropods. An Index of Cases reported through 1980. 172 p.

Recommended Methods for the Detection and Measurement
of Resistance of Agricultural Pests to Pesticides

- FAO 1969 1. General Principles. FAO Plant Protection Bulletin. 17(4), 1969.
- FAO 1969 2. Tentative Method for Adults of Root Maggot Flies (Hylemya spp.) and Adults of the Carrot Rust Fly (Psila rosae). FAO Plant Protection Bulletin. 17(4), 1969.
- FAO 1969 3. Tentative Method for Larvae of the Rice Stem Borer (Chilo suppressalis Walker). 17(6), 1969.
- FAO 1970 4. Tentative Method for Adults of the Peach-Potato Aphid (Myzus persicae). FAO Plant Protection Bulletin. 18(1), 1970.
- FAO 1970 5. Tentative Method for Adults of the Green Rice Leafhopper. (Nephotettix cincticeps Uhler). FAO Plant Protection Bulletin. 18(3), 1970.
- FAO 1970 6. Tentative Method for Adults of the Red Flour Beetle, Tribolium castaneum (Herbst). FAO Plant Protection Bulletin. 18(5), 1970.
- FAO 1971 7. Tentative Method for Larvae of Cattle Ticks, Boophilus spp. FAO Plant Protection Bulletin. 19(1), 1971.
- FAO 1971 8. Tentative Method for Larvae of the Egyptian Cotton Leafworm (Spodoptera littoralis Boisd.). FAO Plant Protection Bulletin. 19 (2), 1971
- FAO 1971 9. Tentative Method for Nymphs of Cocoa Mirids (Distantiella theobromae Dist. and Sahlbergella singularis Hagl.). FAO Plant Protection Bulletin. 19(3), 1971.
- FAO 1974 10. Tentative Methods for Spider Mites and Their Eggs. Tetranychus spp. and Panonychus ulmi (Koch). FAO Plant Protection Bulletin. 22(5/6), 1974
- FAO 1974 11. Tentative Method for Adults of the Codling Moth, Laspeyresia pomonella (L) FAO Plant Protection Bulletin. 22(5/6), 1974.
- FAO 1974 12. Tentative Method for Adults of the Colorado Potato Beetle, Leptinotarsa decemlineata (Say). FAO Plant Protection Bulletin. 22(5/6), 1974.

- FAO 13. Tentative Method for Adult Locusts, Schistocerca gregaria Forsk.,
1974 Locust. migratoria migratorioides R. and F. and Nomadacris
septemfasciata Serv. FAO Plant Protection Bulletin. 22(5/6), 1974
- FAO 14. Tentative Method for Larvae and Adults of Sheep Blowflies, Lucilia sp.
1974 FAO Plant Protection Bulletin. 22(5/6), 1974.
- FAO 15. Tentative Method for Adults of some Major Beetle Pests of Stored
1974 Cereals with Malathion or Lindane. FAO Plant Protection Bulletin.
22(5/6), 1974.
- FAO 16. Tentative Method for Adults of some Major Pest Species of Stored Cereals,
1975 with Methyl Bromide and Phosphine. FAO Plant Protection Bulletin.
23(1), 1975.
- FAO 17. Method for Adult Aphids. FAO Plant Protection Bulletin. 27(2), 1979
1979
- FAO 18. Method for Lygus Plant Bugs. FAO Plant Protection Bulletin. 27(2),
1979 1979.
- FAO 19. Tentative Method for Mite Pests of Stored Products (e.g., Acarus
1979 siro L.) FAO Plant Protection Bulletin. 27(2), 1979.
- FAO 20. Method for Tephridid Fruit Flies. FAO Plant Protection Bulletin.
1979 27(2), 1979.
- FAO 21. Method for the Diamond-Back Moth (Plutella xylostella L.). FAO
1979 Plant Protection Bulletin. 27(2), 1979.
- FAO 22. Method for Lepidopterous Larval Pests of Stored Products and
1979 Tentative Method for detecting resistance in Adults of Stored-Product
Lepidopterous Pests. FAO Plant Protection Bulletin. 27(2), 1979.
- FAO 23. Method for Whiteflies (e.g. Trialeurodes vaporariorum Westw.) and
1979 Tentative Method for detecting resistance in Adult Whiteflies. FAO
Plant Protection Bulletin 27(2), 1979.
- FAO 24. Recommended Methods for Measurement of Pest Resistance to
1980 Pesticides. FAO Plant Production and Protection Paper No. 21. 132 p.

APPENDIX 5

LIST OF IMPORTANT PUBLICATIONS ON RESISTANCE

PUBLISHED AND ISSUED BY WHO OVER THE LAST 10 YEARS

- 'Insecticide Resistance in Arthropods', Brown, A.W.A. and Pal, R.,
Monograph Ser., No. 38, 1971;
- 'Insecticide Resistance and Vector Control', TRS No. 443, 1970;
- 'Resistance of Vectors and Reservoirs of Disease to Pesticides',
TRS 585, 1976;
- 'Resistance of Vectors of Disease to Pesticides', TRS 655, 1980;

WHO/VBC Documents

- 'Instructions for determining the susceptibility or resistance
of rodents to anticoagulant rodenticides', 82.843;
- 'Chemical methods for the control of vectors and pests of public
health importance', Ed. by A. Smith, 82.841;
- 'Instructions for determining the susceptibility or resistance of
fleas to insecticides', 81.815;
- 'Instructions for determining the susceptibility or resistance of
adult ticks to insecticides', 81.814;
- 'Instructions for determining the susceptibility or resistance of
houseflies, tsetse, stableflies, blowflies, etc. to insecticides',
81.813;
- 'Instructions for determining the susceptibility or resistance of
mosquito larvae to insect development inhibitors', 81.812;
- 'Instructions for determining the susceptibility or resistance of
blackfly larvae to insecticides', 81.811;
- 'Instructions for determining the susceptibility or resistance of
adult blackflies, sandflies and biting midges to insecticides',
81.810;
- 'Instructions for determining the susceptibility or resistance of
adult bed-bugs to insecticides', 81.809;
- 'Instructions for determining the susceptibility or resistance of
body lice and head lice to insecticides', 81.808;

- 'Instructions for determining the susceptibility or resistance of mosquito larvae to insecticides', 81.807;
- 'Instructions for determining the susceptibility or resistance of adult mosquitos to organochlorine, organophosphate and carbamate insecticides - diagnostic test', 81.806;
- 'Instructions for determining the susceptibility or resistance of adult mosquitos to organochlorine, organophosphate and carbamate insecticides. Establishment of base-line', 81.805
- 'Note preliminaire sur une resistance au temephos dans le complexe Simulium damnosum (S. sanctipauli et S. soubrense) en Cote d'Ivoire...', P. Guillet et al, 80.784;
- 'Organophosphate resistance in vector populations of the Culex pipines complex', Curtis, C.F. and Pasteur, N., 80.782
- '(WHO/MAL/80.923) Monitoring susceptibility of malaria vectors to pesticides in Thailand, Ismail, I.A.H. and Phinichpongse, S. 80.775;
- 'Susceptibility to DDT, malathion, fenitrothion and dieldrin of three flea species in the Boyolali plague endemic area, Central Java, Indonesia', Lim Boo Liat et al, 80.773;
- 'Insecticide susceptibility of vectors of Chagas' disease in Venezuela', Nelson, M.J. and Colmenares, P., 79.736;
- 'Preliminary observations on the susceptibility of Phlebotomus argentipes and P. papatasi to DDT in two districts of North Bihar (India)', Kaul S.M. et al, 79.715;
- (WHO/MAL/78.896) 'Estimating selection pressures on insecticide resistance genes (preliminary note)', Wood R.J. and Cook, L.M., 78.683;
- 'Sensibilite et resistance des insectes aux insecticides en Afrique tropicale', Brengues, J. et Coosemans, M., 77.680;
- 'Doses diagnostiques de la resistance d'Aedes aegypti aux insecticides organophosphores', Coosemans, M et al, 77.679;

'DDT resistance of Simulium damnosum in West Africa', Guillet, P., Mouchet, J. and Grebaut, S., 77.678;

(WHO/MAL/77.885) 'Genetic aspects of developing insecticide resistance of malaria vectors'. 'Part II . Gene flow and control pattern', Muir, D.A., 77.659;

'Insecticide susceptibility and resistance in mosquito vectors in West Java, Self, L.A. et al, 76.638;

'Vector resistance to insecticides: a review of its operational significance in malaria eradication and control programmes,' WHO/MAL/883, 76.634;

'Resistance of disease vectors to pesticides' (Also in French), 76.609;

'Instructions for determining the susceptibility or resistance of reduviid bugs to organochlorine insecticides', 75.587;

'Tentative instructions for determining the susceptibility or resistance of cockroaches to insecticides', 75.593;

'Tentative test procedure for detecting resistance to dichlorvos and other persistent fumigants,' 75.594;

'Genetic aspects of developing insecticide resistance of malaria vectors. Part 1, selection pressure', Muir, D.A., 75.571;

'Insecticide susceptibility of Rhodnius prolixus and Triatoma maculata in Venezuela', Nocerino, F., 75.565.