RESISTANCE IN INSECTS

R. A. HARRISON
Lincoln College, Christchurch

Summary

A review of the problem of resistance is given and the following aspects of resistance are discussed: The incidence of resistant species in New Zealand and the world; the known mechanisms of resistance to modern synthetic insecticides; the known pattern of cross-resistance within and between the major chemical groups; the genetics of resistance; the development of resistance within a population; and methods of overcoming resistance.

Some conclusions are made on the application of this knowledge to the situation of resistance in New Zealand pest species and on the best pattern of use of the insecticide groups available.

INTRODUCTION

THE HISTORY of the incidence of insect and arthropod species becoming resistant to insecticides is well documented in several reviews (Brown, 1961; Oppenoorth, 1965). The story starts in 1908 when San José scales were proved to have become resistant to lime sulphur in some parts of U.S.A., and it carries through to 1965 when over 160 species of arthropod pests are known to have developed resistant strains. Fewer than 10% of these are resistant to insecticides in use before the advent of DDT (cyanide, lead arsenate, lime sulphur, etc.), about 40% are resistant to DDT or related chemicals, about 60% to the BHC-cyclodiene group, and 20% to the organophosphorus chemicals. Many, of course, are resistant to more than one group of insecticides. Most resistance occurs in the Diptera, where about 50% of resistant species occur, about 20% occur in the Hemiptera, 12% in acarina and smaller numbers in Lepidoptera, Coleoptera, Thysanoptera, Siphonaptera, Orthoptera and Anopleura.

In New Zealand, the record of resistance is one which concerns agricultural pests rather than insects of medical importance and the following species are either known to be resistant or are suspected but not yet proven to be so:

Musca domestica, Lucilia sericata, Chironomus zealandicus, Panonychus ulmi, Tetranychus telarius, Cydia pomonella, Epiphyas postvittana, Costelytra zealandica and *Wiseana* spp.

There are some cases of resistance occurring in a population by individuals of that population developing the ability of avoiding a lethal dose. But the commonest resistance is physiological and is the case where individuals survive a dose that normally would be lethal.

MECHANISMS OF RESISTANCE

The important concept to realize at the outset is that resistance is a population phenomenon and not an individual phenomenon. Populations change in their level of resistance to insecticides but

individuals do not do so during their own life-time. So the obvious must be stated — a resistant population consists of individuals which are resistant and a susceptible population of susceptible individuals.

What makes one individual susceptible and another individual resistant? All sorts of ideas have been looked at to answer this question. In the case of DDT-resistant insects, investigations were made of the rate of penetration through the cuticle, the speed of development, level of oxidation enzymes and lipoid content, but in all these cases the differences in these characters in resistant individuals to those found in susceptible insects proved to be associated with the geographical origin of the strain rather than its DDT resistance.

However, there was shown to be one consistent feature with DDT resistance. Resistant flies can detoxify DDT by breaking it down to HCl and a non-toxic metabolite (DDE). This conversion is accomplished by an enzyme called DDT-dehydrochlorinase (DDT-ase) and susceptible individuals do not have this feature.

Thus, in resistant insects DDT is made impotent by being progressively and instantly destroyed as it penetrates the insect cuticle. There also is a high concentration of the enzyme in the nervous tissue itself which acts as a final defence.

DDT-ase has been found in most DDT-resistant strains of insects and it appears that this mechanism is the usual one but not necessarily the only one for DDT resistance. The enzyme is also present in normally DDT-tolerant species. It is interesting to contemplate on the fact that DDT-ase has not developed since the advent of DDT. Thus DDT-resistant insects or potentially resistant insects were present in Julius Caesar's time!

It will be seen later that the presence of DDT-ase is under genetic control. Investigations show that in most cases penetrance of the mutant gene for resistance is usually very low indeed but that occasionally it may be appreciably high. Thus, in unsprayed populations of *Anopheles gambiae* in West Africa, it was found that from 0.04% to 12.0% of individuals were heterozygous for the dieldrin-resistant gene.

The mechanisms for resistance to BHC and the cyclodienes is not yet completely understood. Some dehydrochlorination is involved but certainly DDT-ase has got nothing to do with those processes.

With organophosphorus insecticides, resistance appears to be due to an increased detoxification of materials which are inhibitors of cholinesterase. These materials may be the insecticide — *e.g.*, malathion — or the oxidation product — *e.g.*, malaoxon. There is high inhibition of other enzymes — *e.g.*, aliesterase — and also definite evidence that in some species cholinesterase can be altered actually at its site of action.

CROSS-RESISTANCE

Incomplete as current understanding of the resistant mechanisms is, the knowledge that there are different mechanisms for different groups of chemicals helps to formulate and explain a simple rule. This is that insects which develop resistance to one insecticide are resistant at the same time to other insecticides in that group but not to insecticides in other groups. However, it does not explain the very important exceptions to that rule. These exceptions are (1) that, generally, organophosphate-resistant insects simultaneously acquire a very strong resistance to the DDT group and also the carbamates, and (2) that selection for carbamate resistance results initially in little resistance to the carbamate but considerable organophosphate resistance and high DDT resistance.

GENETICS OF RESISTANCE

Most of the recent advances in knowledge of resistance have come from genetical and biochemical studies. Genetical research is being used analytically to separate out the different mechanisms which may occur simultaneously in a single strain. This helps in the discovery of causes of resistance by establishing relationships of resistance with physiological or biochemical characters.

Genetical studies on D.D.-resistant insects have shown that there are at least four separate genes for resistance. The well established mechanism described above, involving DDT-ase, is dependent on one of these genes but the biochemical role of the other three is not yet known. More research will show whether these three are responsible for DDT-ase production or not.

DEVELOPMENT OF RESISTANCE IN POPULATIONS

Insect populations put under any type of selection pressure, whether environmental or insecticidal, will develop greater tolerance to these factors. This has been conveniently called vigour tolerance and its mode of inheritance indicates a polygenic origin. This tolerance in terms of increase in resistance to insecticides is usually only a very small factor — perhaps 2 or 3 times. This is in great contrast to the truly insecticidal-resistant populations which may be 50, 100 or in some cases over 1,000 times as resistant as normal susceptible populations.

In is considered that the processes involved in selecting populations to the level of vigour tolerance involves multiple genes and the accumulation and concentration of these genes allows the specific resistant gene or genes to express themselves. Vigour tolerance and initial selection and accumulation of the satellite genes may be 50, 100 or in some cases over 1,000 times as resistant as resistance asserts itself and rapid selection for high resistance results.

COMBATING RESISTANCE

Much thought has gone into the problem of overcoming resistance but none of the methods tried has really been able to come to grips with the situation and achieve permanent success.

The most obvious counter to DDT resistance was to synergize DDT with a DDT-ase inhibitor. Several such materials were found — *e.g.*, DMC — and they achieved initial success. But in due course resistance to the DDT-synergist mixture developed.

A search was made for materials which might be non-resistant inducing. Pyrethrins almost fit this category and the organophosphates were thought and hoped to be of this type. It does appear, however, that if a chemical can select in a population then resistance will develop.

Negatively correlated insecticides have shown some promise but have not yet developed up to be as useful as their initial work promised. These materials are more toxic to insecticide-resistant individuals than normal ones and thus would enable selection to take place in reverse.

A thorough investigation of the possibility of alternating the use of insecticides of various groups or of combining them and so delaying the onset of resistance has been made. Neither of these approaches has been worth continuing with, because resistance develops to all groups used in approximately the same time as it develops to any one of them.

The only method of assuring continued control of pests by chemicals has been to discard the insecticide to which resistance has developed and to use one from a different chemical group. This seems to be the only policy worth following at the moment and the information available on resistance points out that it is best to use one group to its limit then change to another and use it to its limit, and so on, keeping the organophosphates well back in the order of use because of cross-resistance. The limitation to this principle is obvious and the day can be anticipated when many pest insects have become resistant to all known groups of insecticides. Nor is there much hope of previously used insecticides being used successfully again after a period of non-use. Reversion to susceptibility when pressure is released does frequently occur, but under fresh insecticidal pressure the reverted populations quickly achieve a high level of resistance again.

PROSPECTS FOR THE FUTURE

In New Zealand the knowledge already gained from the many studies on resistance can be applied. Thus, New Zealand could now be entering a critical period when resistance could become far more widespread than it is at present. Enough generations of annual cycle insects have been treated repeatedly for a degree of tolerance to have developed. Grass-grub and *Wiseana,* for instance, may be on the verge of a major spread of resistance beyond the relatively small resistant populations known to occur already. A search for suitable alternative insecticides for pasture pests is warranted, but the best policy would be to persist with DDT until it fails and thus ensure the maximum use of the chemicals known at present.

On a world scale, the prospects for the future are directly related to the basic research that is in progress. The biggest problem at present is to determine detoxification mechanisms. The genetical study of resistance is aimed at doing just this. The advances in enzymology and protein chemistry should yield an understanding of these mechanisms before long. And with complete understanding will come the possibility of conquering the problem.

REFERENCES

Brown, A. W. A., 1961: *Bull. Entom. Soc. Am.*, *7*: 6–19.
Oppenoorth, F. J., 1965: *Ann. Rev. Entom.*, *10*: 185–206.