Development of Resistance in Insects to Insecticides

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Several of the previous topics have in one way or other pointed out limitations which are imposed on the use of newer insecticides. What once seemed a simple and nearly ideal situation has yearly acquired new legal, toxicological and biological restrictions. Perhaps the biological implication, expressed in the occurrence of resistance, is the most disconcerting. It is also the most challenging, because it presents a need for research in areas of toxicology, physiology, ecology, and genetics not previously pursued or appreciated by entomologists.

There have been several good reviews published on the development of resistance (1, 2, 10, 15). The most recent one by R. L. Metcalf of California (14) is exceptionally good and should be read by any one interested in the many ramifications of this subject. Our hope in preparing this paper is simply to point up the present position of insect resistance, and to present for your consideration some of the still unsolved problems relating to it.

Considering the suddenness with which the problem of insect resistance has so recently developed, there is a surprising number of proven instances of resistance (at least 25) and about as many others suspected. Table 1 summarizes the present situation. Regretfully entomologists originally displayed only token interest and some doubt about the early observations of Melander in 1914 (13) on San Jose scale resistance to lime-sulfur sprays, and those of Quayle (17) concerning California red scale resistance to hydrogen cyanide. These instances and the subsequent codling moth "resistance" to lead arsenate were of course isolated occurrences, and lack of greater research interest at that time in the genetical-physiological field involved is perhaps understandable. It remained for the wonder chemical DDT and its supposedly most easily subdued adversary, the housefly, to awaken us to the problem and stimulate the research which is now under way. The list of resistant species is growing. Four reports were made last year, including that of an apple leafhopper, *Erythronura lawsoniana* Baker, by our section chairman D. W. Hamilton (11). Fortunately the total is still well below 1% of our economically important pests, but even so this minority is causing a reevaluation of our long range plans for the chemical control of insects.

There is still scattered doubt in the minds of some as to the origin of group resistance as we know it today. The current interest in mutations brought about by exposure to an unusual agent is of course a natural consideration. However, there seems to be no reason, in fact no precedent, for believing that an organism would develop a mutant protecting it from the very chemical causative agent itself. If DDT, for example, were to act as a mutagenic agent, it would be more apt one time to cause some morphological change like curly hairs and another time twisted wings. As Dobzhansky (9) has pointed out, the origin of

variation is a problem entirely separate from that of the action of selection. It is a matter then of distinguishing between cause and resulting development of a selected strain. The generally accepted belief today is that exposure to insecticides results in a natural selection of already occurring individuals possessing some form of protective device. As will be mentioned later, this device is essentially physiological. The classic indication of natural selection is that of the housefly which simultaneously displayed DDT-resistance in various areas of the world, and under diverse conditions ranging from remote farms to food preparation rooms in city hotels where the flies breed the year around. A strong evidence that naturally resistant insects can occur sometimes even as a large percentage of a strain may possibly be found in the case of DDT-resistant Korean body lice. This is based on the still problematical contention that lice in the area had not been previously exposed to DDT.

The fact that there are degrees of resistance, both to single insecticides and to groups of insecticides, has led to considerable speculation as to initial cause of differences, rates of development, and subsequent inheritance. Busvine (6) relates the rate of development to: frequency of occurrence of resistant genes in a population, intensity of selection, and number of generations per year. Apparently the geographical distribution of genes relating to resistance can vary greatly even in small areas. Geneticists and entomologists alike have been caught short on their knowledge of insect inheritance (except for Drosophila which unfortunately does not display the "usual" manifestations of resistance to DDT). The problem has been further complicated by a lack of uniformity in measuring and reporting results. Much good work is now underway, however, and several indications are apparent from it. Knockdown response to DDT in the case of the housefly has been shown to be quite independent of the degree of resistance to lethal doses of a toxicant. Harrison (12) has shown that the resistance to knockdown is controlled by a simple Mendelian inheritance involving a single pair of allelomorphs; the susceptible strain is dominant. The problem of the inheritance of resistance to death is another situation. Various researchers (3, 16) have noted evidence that female parentage has more influence than the male, but this effect does not appear to be a case of sex-linkage. Bruce (5) still holds that there are factors, other than a single gene for dominance, which control the levels of resistance within individuals of a population. This point may lend possible explanation to the female influence. There is increasing evidence that housefly resistance, with its various manifestations, is governed by a number of genes. At best it can be said the problem is one of complex polygenic inheritance; this must be especially true in some instances of multiple resistance. The genetics of resistance is an area far from completely understood.

In our consideration of the future use of insecticides, we are especially interested in the possibility of reversion back to normal when the selective agent is removed from a population. The answer here is not really known. In the case of the California red scale, there has been

no evidence of reversions after the discontinuance of fumigation. A similar situation is present in the case of tartar emetic-resistant citrus thrips and the arsenic-resistant blue tick. In the laboratory, most strains of houseflies have tended to regain susceptibility. The degree of reversion however has varied greatly. One Illinois resistant strain seems fixed unless it is outbred with susceptible flies (8). Some multi-resistant strains have shown a resusceptibility to one insecticide, but not to another. Although Crow (7) has stated that reversion in any resistant strain is certain to occur eventually since genes for insecticide resistance must be detrimental, this seems rather difficult to support since the recent selecting agents have never before been present. There is actually some indication that increased species vigor accompanies resistance.

Irrespective of whether or not reversion is probable, we have to face the reality that insecticides prone to cause resistant strains must be abandoned, greatly restricted in use, or methods must be found to overcome the specific resistance which they produce.

The prospect of new chemical types of insecticides in the near future is not encouraging. The last twelve years have been characterized by extensive investigations that have produced numerous good insecticides within a few groups. We cannot expect the same successful pace to continue especially since it is new chemical groups which are most needed.

Fortunately there seems to be sufficient latitude in cross tolerance, at least in the case of resistant houseflies, to allow continued chemical control. Metcalf (14) has provided a table showing a logical grouping of chemical forms:

I. DDT and its relatives
II. Lindane, chlordane, aldrin, dieldrin, toxaphene
III. Nitroparaffins
IV. Organic phosphates
V. Pyrethroids
VI. Organic thiocyanates

Generally speaking, resistant adaptations fall within groups, although exceptions of varying degrees of intensity certainly do exist. Of these, the chlorinated hydrocarbons have been the principal selecting agents for insect resistance. Resistance to the organic phosphates (among insects, not mites) has been slow in development and low in intensity. The pyrethrins have long been in use and remain essentially the same in their effect on insects. From the grouping of organic insecticides above we must choose our insecticides. Entomologists in this state and others have long advocated programs against resistant flies consisting of using insecticides from one group for one control period, and switching to a chemical of another group during a successive period. Combining insecticides from different groups has generally been frowned upon for fear of establishing extreme multiple resistance. Metcalf, however, suggests that a corollary may exist between the successful use of mixtures of antibiotics and the application of combinations of insecticides properly chosen from the classification list given above. Except for the possible omission of combinations from groups I and II, this proposal may have

real merit, especially if resistance to different chemicals is proven to be physiologically and genetically independent and uncorrelated.

These observations point up a need for independent research at various institutions in different parts of the country. Resistance, irrespective of the insect, is quite a singular phenomenon, with strains of insects demonstrating different intensities of a particular resistance and various types of multiple resistance. Only by alert realization of individual problems, and therefore individual needs within states, can we expect to handle the resistance problem in stride. What may be the solution in Missouri, for example, may not be applicable to Indiana. What is disturbing is the fact that resistance cuts across several areas of concern in economic entomology, namely fruit production, vegetable growing, public health, and household pests. Such a situation further justifies specific investigational work.

This suggestion does not imply that a detailed toxicological program need be set up everywhere. In the midwest, for example, outstanding work is being done by Kearns' group at Illinois, where Sternburg (18) recently reported the discovery of DDT-dehydrochlorinase as a primary protective device in DDT resistant flies. Further research is being pursued in a search for other causes of metabolism, site of action, and synergists. With respect to the latter, several materials are known which apparently retard the normal detoxification mechanism of DDT. None of the synergists to date have practical use in the field, but research may yet reveal one, or at least in the study, find insecticidal properties not subject to detoxification. The implication made above with respect to state institutions and federal stations, however, is that all of them need to pursue a "watch dog policy" on resistance. Every actual and suspected case of resistance which arises—if it is of any economic importance—should be laboratory tested to learn the scope of the particular resistance, and to determine then the best chemical or other controls to employ.

Besides an appreciation of the complexity of the resistance problem, we would like to leave the thought that resistance is more challenging than insurmountable. A program that brings together the findings of the field men with the basic research of physiologist, toxicologist, and geneticist is the directive force towards resolving this problem.

TABLE 1[1] SUMMARY OF INSECT RESISTANCE

Insect	*Insecticide*	*Year Reported*
San Jose Scale	Lime sulfur	1913
California red scale	Hydrogen cyanide	1916
Black scale	Hydrogen cyanide	1916
Citricola scale	Hydrogen cyanide	1925
Grape leafhoppers		
Erythroneura elegantula	DDT	1953
E. variabilis	DDT	1954

1. Modified from Metcalf, R. L. 1955 (14).

TABLE 1. (Continued)

Insect	*Insecticide*	*Year Reported*
Apple leafhopper		
E. lawsoniana	DDT	1954
Walnut aphid	Parathion	1954
Bed Bug	DDT	1948
Citrus thrips	Tartar emetic	1942
Human body louse	DDT	1952
German cockroach	Chlordane	1953
	Lindane	
	DDT	
Codling moth	Lead arsenate	1928
	DDT	1954
Imported cabbage worm	DDT	1952
	DDD	
	MDDT	
Diamond back moth	DDT	1953
House fly	DDT	1947
	Chlordane	1951
	BHC	1949
	Dieldrin	1949
Pest mosquitoes		
Culex pipiens	DDT	1948
Culex tarsalis	Chlordane	1949
Aedes nigromaculis	DDT	1949
	Aldrin, dieldrin	
	Heptachlor	
Malaria mosquito	DDT	1952
Salt marsh mosquitoes		
Aedes sollicitans	DDT, DDD	1950
Aedes taeniorhynchus	DDT, DDD	1950
Filter fly (4)		
Psychoda alternata	DDT	1950
Blue tick	Sodium arsenite	1940
	BHC	1948
Cattle tick	BHC	1953
	DDT	
	Chlordane	
	Dieldrin	
	Toxaphene	
	Arsenic trioxide	
European red mite	Parathion	1952
Two-spotted spider mite	Parathion	1950
	Sodium selanite	

Highly suspected to DDT: Colorado potato beetle, lygus bugs, potato flea beetle, potato aphid, green peach aphid, and dog fleas.

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