GENETIC ORIGINS OF INSECTICIDE RESISTANCE

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INTRODUCTION

Resistance to insecticides has been demonstrated in most important pest insect species, and this widespread occurrence is thought to provide proof of Darwinian evolutionary theory. That is, exposure to insecticides has acted as a powerful selecting force, which concentrates the various preexisting genetic factors that confer resistance.

The next step in the process, a careful evaluation of the nature of these genetic factors, remains to be taken. We shall try in this report to provide some insight into the problem and, hopefully, identify some of the approaches that can be taken to elucidate more fully the nature of resistance.

Given the widespread occurrence of insecticide resistance, it is discouraging to have to report that we know very little about the basis for it in genetic terms. Our understanding of resistance biochemistry is in somewhat better shape, but it, too, suffers from a lack of comprehension of the genetic factors actually involved.

Entomologists have gained considerable knowledge of the biochemical mechanisms involved in metabolic resistance to insecticides. First, we know the detoxifying enzymes conferring metabolic resistance are remarkably nonspecific; that is, they have very broad ranges of activity. Secondly, we know these enzymes are inducible. In susceptible insects, detoxifying enzymes are present at relatively low levels, but the level can be increased, often by several fold,
if the insects are exposed to appropriate inducers of enzyme activity. In resistant insects, amounts of detoxifying enzymes are often much greater. These, too, are frequently inducible but often to a lesser degree, at least on a percent basis, than in susceptible insects. Surprisingly, it is unclear if the higher levels of activity of resistant insects are due to better detoxifying enzymes (higher specific activity), to more enzyme (increased enzyme synthesis), or to a combination of both.

Thus, we do not know if resistance to insecticides is due to changes in structural genes, i.e., those genes actually specifying the nature of the enzymes, or to changes in regulatory genes or regulatory loci associated with the structural genes, i.e., changes that control the rates of synthesis of the enzymes. It will be the hypothesis of this paper that at least as far as metabolic resistance to insecticides is concerned, both types of change occur and resistance is due to the interaction of the two types of gene effects.

Fortunately, enough is known concerning the effects of the different types of genetic changes that, by means of appropriate genetic and biochemical assays, it is now possible to gain a good idea of the nature of the changes that may be involved in resistance.

If changes occur in a structural gene resulting in a detoxifying enzyme with higher specific activity, one would expect the enzyme to be as inducible as the enzyme in susceptible strains. Also, in a cross with susceptible flies, enzyme activity in the $F_1$ should be intermediate and show no change in inducibility. Note, however, that experience suggests that changes in structural genes are usually associated with a loss, not an increase, in enzyme activity. The best example of this in insecticide resistance is the mutant aliesterase of certain organophosphate-resistant house fly strains. Here, activity towards substrates such as methyl butyrate shows a significant decline (Van Asperen and Oppenoorth, 1959). The theory is that the mutant enzyme has lost activity towards normal substrates and has gained in its ability to metabolize certain toxic organophosphates (Oppenoorth, 1965).

Other possibilities for resistance involve changes that are regulatory in nature. These changes may occur with a separate regulatory gene or at a regulatory site associated with the structural gene. They may be transcriptional, posttranscriptional or translational in nature. Whatever their precise nature, they should lead to synthesis of increased amounts of detoxifying enzymes with no changes in specific activity levels. Unlike structural genes, the inheritance of regulatory gene effects is frequently either dominant or recessive, rather than intermediate in the $F_1$, and many differ in control and induced flies. However, for unknown reasons this model of inheritance that is derived from analogy with studies