The Significance of House Fly Resistance to Insecticides in Fly Control Operations

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The chronicle of house fly (*Musca domestica* Linn.) resistance to or tolerance for insecticides has passed the point of recounting as an interesting phenomenon and now is depressing to read. Since first documented by Wiesmann (1) and Sacca (2) in 1947, reports of this resistance have increased alarmingly. Many of these reports serve both as obituaries for one insecticide and as birth announcements for another. The reader's depression is increased by sequent publications, sometimes after an incredibly short interval, that the recently announced youngster had enjoyed excellent health for a time but had suddenly passed into limbo with doubtful expectancy of resurrection. DDT was the first of the miracle insecticides and enjoyed the longest useful life. A wishful hope may lie in the fact that although DDT was losing ground rapidly from 1947 to 1950, it again holds some promise when coupled with other compounds (3) to prevent detoxification of the DDT within the house fly. Thus far, under field conditions, no other species of non-biting muscoid fly has presented a problem of resistance to insecticides comparable to that of the house fly.

DISTRIBUTION OF RESISTANT HOUSE FLIES

Unfortunately, resistance in house flies has occurred where the benefits of DDT are most needed. This is hardly surprising, however, because in general the need for fly control reflects both a large volume of house fly breeding and proportionate usage of DDT. Furthermore, such problem areas generally develop coincident with agricultural crops requiring extensive usage of insecticides, as pointed out by Quarterman (4). Therefore, these same areas are sites of extensive trials of new insecticides and, at least thus far, of further failure to achieve lasting effectiveness. In brief, the geographical distribution of insecticide resistance in house flies is dependent upon only two factors, good breeding potentials for the flies and intensive usage of the insecticide. DDT probably has been more widely and intensively used in the United States than any other insecticide. As a result, wherever house flies are a problem in this country, their naturally occurring populations are resistant in some degree to DDT. The only house fly populations that remain as susceptible as they were prior to the general use of DDT are those maintained in laboratory colonies out of contact with all insecticides. Most of these colonies have been maintained free of insecticides since before resistance became widespread. A few laboratories, however, have succeeded in selecting for susceptibility by applying the tedious selection procedure of collecting eggs from individual female house flies, subsequently subjecting these females to minimal doses of insecticide, and saving only the progeny of those easily killed. Even with this technique, difficulty has been encountered in attaining the degree of susceptibility originally present.

THE NATURE OF INSECTICIDE RESISTANCE

In 1947, the resistant house fly populations encountered were recognized as being a result of the selective action of DDT but the method of selection was not obvious. It was first attributed to race or species selection, assuming either that the original species had been composed of two or more hitherto unrecognized forms or that resistant mutations occurred frequently and were isolated by the killing of the normal susceptible strain. Careful comparisons were made of morphological differences between resistant and susceptible strains, particularly with regard to the pulvilli and tarsal structures where primary contact with residual surfaces took place. Thickness of cuticle, pigmentation, size, and vigor also were compared. No consistent or significant differences of any kind were found until the work of Sternburg, Kearns, and Bruce (5), and Perry

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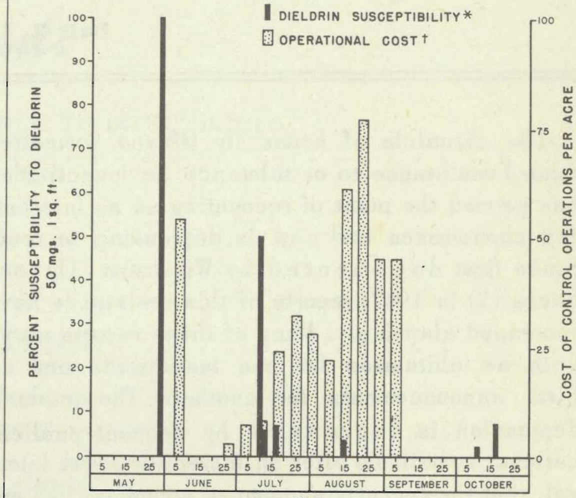
and Hoskins (6) showed that the resistant flies possessed the ability to detoxify DDT to relatively nontoxic metabolites. Further work of Babers and Pratt (7), Sacktor (8), and others showed that resistant flies were characterized by higher cholinesterase and cytochrome oxidase activity than were susceptible flies. However, flies resistant to DDT are not necessarily resistant to other groups of insecticides, suggesting that differences in enzymatic systems are involved in imparting the ability to detoxify the various groups of insecticides. It is possible, even probable, that the nature of resistance to any given insecticide in one area may not be exactly comparable to that causing resistance in another area. Moreover, house fly colonies developed for resistance to dieldrin and chlordan only are nearly as susceptible to DDT as are the nonresistant flies, further emphasizing the fact that simultaneous resistance to several insecticides found at any one time is due to combinations of systems existing in these flies through previous selections.

Both field and laboratory tests have demonstrated that populations of house flies resistant to one insecticide may quickly become resistant to other insecticides applied. Under field conditions where breeding potentials are high, appreciable numbers of house flies resistant to a previously unused insecticide may be found after only two or three generations (3 to 4 weeks) of selection by the new insecticide. This has occurred even without the use of the same insecticide for larvicidal purposes, a practice which has been demonstrated to intensify selection for highly resistant house flies (9, 10). Under such conditions, satisfactory control can scarcely be maintained with insecticides previously used. Thus, resistance developed to one insecticide is also found to operate against chemically related insecticides in varying degrees; and genetic selection for resistance to one type apparently predisposes a house fly population to rapid selection for resistance to other nonrelated chemicals. Even the nonresidual insecticides, such as mixtures of pyrethrins and piperonyl butoxide, are not exempt from this accelerated selective action. Probably the high cost of the nonresidual types has limited their use to the extent that fewer failures due to resistance have been reported. Another factor of importance in limiting development of resistance in the field has been the fact that the nonresidual space

FIGURE 1
DECREASED INSECTICIDE SUSCEPTIBILITY MEANS INCREASED OPERATIONAL COST
WHIGHAM, GA.



*Susceptibility Tests Consisted of Standard 15-Minute Exposures of Field-Collected House Flies to Treated Glass Surfaces.

†Control Operations Involved the use of Dieldrin, DDT, and DDT-DMC Sprays as Needed for Fly Control.

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sprays manifest a discontinuous selective action as compared to the continuous selection exercised by the residual types.

Much study in many laboratories has been devoted to the length of time, or number of generations, that insecticide resistance will remain in house fly populations in the absence of the insecticide. The results of these studies have varied, but in most instances the resistance has remained at a high level for laboratory periods equivalent to 2 or more years in the field. Such tests are, of course, not representative of field conditions where we cannot immediately and completely remove the residual insecticides that have been applied and which continue to exercise selective activity. Under field conditions we once assumed that the gradual decrease in residual effectiveness of the insecticide would be augmented, in returning the house fly populations to their susceptible normalcy, with the invasion of the sprayed area by normal flies from nonsprayed areas. It currently appears either that these normal susceptible flies succumb to the insecticide before they can interbreed with resistant flies or that no such normal flies now exist. In any event, experiments designed on this premise have been fruitless.

Work is in progress in several laboratories to determine the enzymatic systems or other physiological functions which, when present in the resistant house fly, can detoxify the chemical used and render it relatively harmless. When these systems are determined it will increase the possibility for finding and using supplemental compounds to inhibit this detoxification process. Some success has been shown against DDT-resistant flies by adding to regular dosage rates of DDT an appreciable amount of the compound 1, 1-bis-(*p*-chlorophenyl)-ethanol (3). This compound, known more widely as p, p'-dichorodiphenyl methyl carbinol or DMC, caused remarkable increases in resistant fly mortality when added to DDT in quantities of 10 to 100 percent of the DDT. Preliminary reports of similar synergistic compounds are appearing but in field trials the synergized DDT, particularly in residual form, is rarely as effective against resistant flies as DDT alone is against susceptible flies. Part of this failure appears to lie in the shorter residual life of the DMC. Laboratory tests show relatively low mortalities among DDT-resistant flies at substandard dosages of the DDT-DMC mixture.

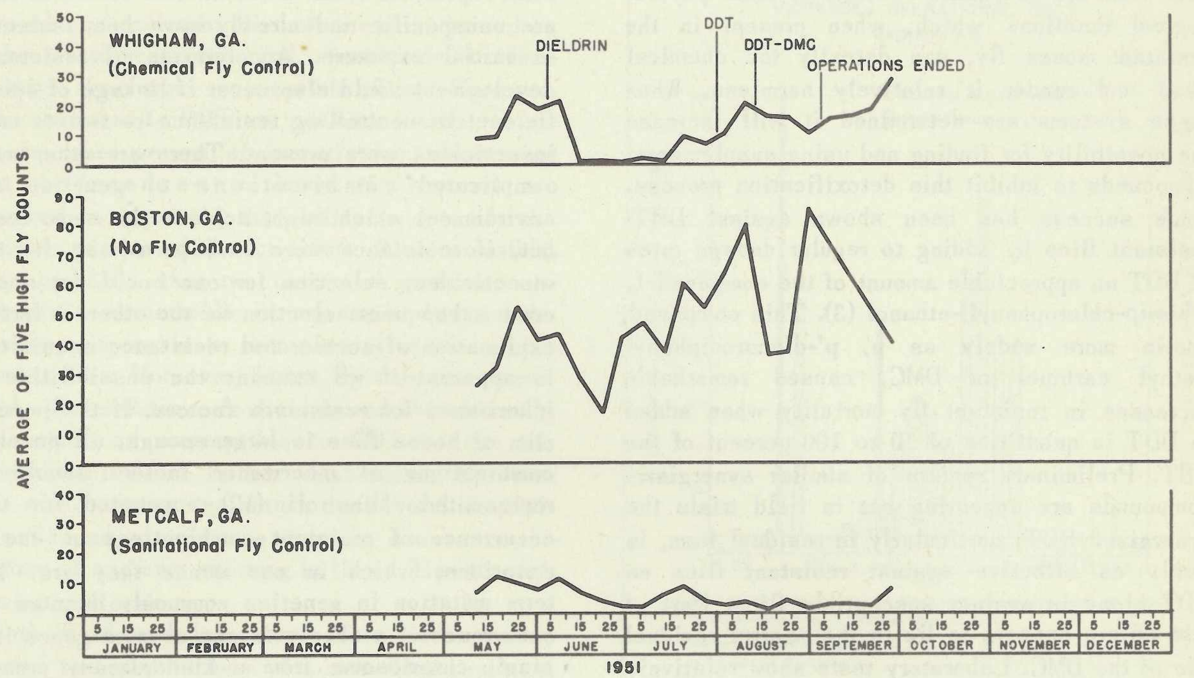
A second basic investigation of considerable importance is determination of the inheritance patterns of these physiological systems. In spite of an article by a British worker (11) declaring that the DDT-resistance in the experimental flies used (of Italian origin) was controlled by a single pair of allelomorphs, workers in this country are generally agreed that DDT-resistance is due to complex multiple factors. There is little reason to believe that house fly resistance to other insecticides is less complex. If it is possible to find both the physiological function and the pattern or patterns of inheritance for the resistance of the house fly to each insecticide, then there is hope that insecticides may be used in planned alternation to minimize interaction of specific selection methods. It is at least of equal likelihood that even the knowledge sought for will be of little practical use when discovered.

Recent work in many areas has demonstrated that house fly populations may attain a high degree of resistance at greatly accelerated rates as compared to rates observed in the early years of the residual insecticides. This accelerated acquisition is associated invariably with the prior existence of resistance in some degree to a previously used insecticide, usually DDT or chlordan. Resistant populations may develop more rapidly if some of the factors for resistance are nonspecific and already have been selected in initial exposure. Acceleration of resistance development could also occur if linkage of specific factors controlling resistance to two or more insecticides were present. There are other more complicated combinations of genetics and environment which might achieve the same result but, if resistance were independent for two insecticides, selection for one could not accelerate subsequent selection for the other. A further explanation of accelerated resistance acquisition is apparent if we examine the possibilities of inheritance for resistance factors. If the population of house flies is large enough, all possible combinations of inheritance factors should be represented. Missiroli (12) accounted for this occurrence of resistant combinations as due to mutations, which in one sense they are. The term mutation in genetics commonly denotes the occurrence of a change in one or more genes in a single chromosome from a kind already present to a new kind. It is the penchant of some people to attribute any unexplained evidence of a new kind of gene to mutation rather than to an ignorance of what has really occurred. A simple recessive gene present in a large and freely interbreeding population in a frequency of 1:1000 will produce only one offspring per million exhibiting the phenotypic expression of this gene. Actual conditions are but rarely this simple, and the presence of a gene in a population may be very difficult to detect in the absence of any selective agent that operates against the more frequently occurring, normal, and often dominant factors. The efficient residual insecticides serve as that selecting agent and, by the simple expedient of killing most of the susceptible flies, very rapidly increase the frequency of genes for resistance. The selection pressure of the insecticides may thus allow the phenotypic expression of existence of a gene or set of genes possibly present for countless preceding generations.

It is only reasonable to assume that progressive selection occasioned by a succession of different insecticides will continue to eliminate the physiological systems that function only in the absence of these insecticides. As implied above, such theoretical selection is feasible only in populations of great size and in which

FIGURE 2

COMPARATIVE RESULTS OF CHEMICAL AND SANITATIONAL FLY CONTROL *



* Note Temporary Period of Dieldrin Effectiveness in Whigham, Ga.

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all, or nearly all, of the possible genetic combinations are represented. If such occurs, there is scarcely a more likely organism than the house fly in which it might be demonstrated. The house fly not only possesses a tremendous biotic potential, but coupled with its reproductive ability it has an unsurpassed adaptability to a wide variety of breeding media and environmental conditions. The fact that it far exceeds other species of flies in this latter respect probably accounts for its currently unique position with regard to the failure of chemical insecticides in fly control. Less versatile species will be slower in selecting for insecticide resistance. Furthermore, lest initial successes create undue optimism, we must consider that similar selections will probably occur to eventually overcome any advantage we may temporarily gain through the use of synergists which block the detoxification processes. We have through our "superinsecticides," selected a "superfly" which will remain with us indefinitely.

THE FUTURE OF FLY CONTROL PROGRAMS

In spite of the fact that we can expect no single chemical insecticide to long remain effective against such an adaptable organism as the house fly, and that rotations, combinations, and synergists may well share the same fate, we still have the same opportunity for fly control that we had before DDT. We weren't so discouraged then and we should not be now. Then as now we had a means of fly control that worked, the application of prophylactic sanitation. The promise of immediate and sometimes undeserved insect control by means of DDT and more recently developed insecticides, was more attractive. In one respect, the great strides of the past 30 years in developing insecticides may have delayed the general application of prophylactic sanitation to prevent fly breeding. Insecticides promised easier fly control than did cleaning up. Our experience in this country since 1945, and particularly since 1948, has probed both extremes in fly annoyance. We have enjoyed almost complete freedom from flies and we have endured the frustration and indignation that has accompanied the failures with chemical control. Although large sums of money have been expended without lasting effect, we have profited immeasurably. The house fly stands indicted, and under centain conditions has been convicted, as a disease vector of shigellosis and possibly of other enteric infections (13, 14), as long has been suspected from laboratory studies. In addition, we have had the opportunity to evaluate the other benefits of fly control.

During this same period of time in which we have suffered disillusionment by chemical control of flies we have continued studies in improving sanitation on many fronts. These studies must be intensified. The concomitant benefits of improved sanitation are sure to be reflected in the reduction of certain other infections as well, regardless of their mode of spread. In every study of the methods and effects of improved sanitation, it has been found that results are measurable even from small efforts. Virtual freedom from fly annoyance and vector-borne disease is a real possibility within our reach. Municipal problems are nearer solution than are the rural and agricultural problems, but both types are regulated by the principle of eliminating fly breeding. An effort equal to that expended during the past 6 years can demonstrate the effectiveness as well as the economic feasibility of fly control by sanitation.

Meanwhile we should recognize the chemical control of house flies in its true perspective as an adjunct and not a substitute for sanitation (13). The insecticides which we have, as well as the new ones being developed, are valuable tools as stopgaps and emergency measures and should be used as such. Decker and Bruce (15), in a recently published article pointedly entitled, "Where Are We Going With Fly Resistance?", have set forth three good basic rules for the use of insecticides. They recommend firstly, that mixtures of adulticides be avoided in order to prolong the value of each type; secondly, that if larvicides are used they should not be closely related chemically to the adulticide in order to prevent unnecessary acceleration of resistance to the adulticide; and lastly, that the larvicidal effect of adulticides contaminating breeding material should be avoided for the same reason. To these we should add a fourth borrowed from the doctor's prescription: Use only as needed.

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