The increasing resistance to insecticides is threatening the impressive gains in control of vectorborne diseases. The Communicable Disease Center is studying the biological mechanisms of resistance and means of detecting and counteracting this phenomenon, and is providing technical assistance for other Federal agencies and the States.

Insect Resistance to Insecticides

R. J. HAMMERSTROM

SOME of the major achievements in public health since 1944 have been realized through the use of newer insecticides, beginning with DDT. Important vectorborne diseases, such as malaria, typhus fever, yellow fever, and insectborne enteric infections, have been controlled effectively in certain parts of the world and virtually eradicated in others through the use of insecticides. In the United States, for example, malaria is considered to be near eradication; endemic typhus fever morbidity has fallen from a peak of 5,401 reported cases in 1944 to an alltime low of about 100 cases annually. These phenomenal achievements in this country and elsewhere are attributed for the most part to the use of DDT.

The development of resistance to insecticides by many important disease vectors, however, threatens the continuation and extension of worldwide progress in the control of vectorborne diseases. For this reason, insect resistance is internationally recognized by leading health authorities as the most important problem facing organized vectorborne disease control programs today.

Mr. Hammerstrom, formerly deputy chief of the Technology Branch, Communicable Disease Center, Public Health Service, Atlanta, Ga., is now the regional sanitary engineer, International Cooperation Administration, Department of International Health, Lima, Peru. *This paper, with minor changes, was presented at the meeting of the United States-Mexico Border Public Health Association, April 8, 1958, in Juarez, Chihuahua, Mexico.*

Worldwide Significance

Resistance of houseflies to DDT was first noted in Italy in 1946. In immediately following years, the phenomenon was reported from other countries, including the United States in 1948. Resistance of houseflies to DDT led in subsequent years to the use of related chlorinated hydrocarbon insecticides, such as methoxychlor, TDE, lindane, chlordane, heptachlor, and dieldrin, with the result that resistance to these compounds also developed. Today, housefly resistance to DDT and to other chlorinated hydrocarbons is evident in practically all countries of the world. In some areas, including the United States, houseflies are beginning to show resistance to the more recently developed organic phosphorus compounds.

Mosquitoes began to show resistance to DDT at about the same time as houseflies. The first observations of resistance were reported for *Culex pipiens*, also in Italy. Resistance to DDT and other chlorinated hydrocarbons soon became evident in a number of species of culicine and anopheline mosquitoes in many countries. As with houseflies, certain species of mosquitoes are now resistant to some organic phosphorus compounds.

Resistance to insecticides on the part of insects of public health importance is by no means restricted to houseflies and mosquitoes; certain cockroaches, fleas, lice, and bugs are also resistant. There are now 44 species of vectors and pestiferous insects that are resistant to one or more insecticides (*1*). The geographic areas involved and the number and type of insecticides to which insects have become resistant are increasing steadily.

There are 26 species of resistant insects that are vectors of diseases such as malaria, yellow fever, encephalitis, diarrhea and dysentery, typhus, filariasis, dengue, and Chagas' disease. Nine species of anopheline vectors of malaria in 7 countries, including *Anopheles quadrimaculatus* in the United States, have been found resistent to one or more of the insecticides generally used in residual spraying of homes for malaria control.

The continued effectiveness of insecticides against malaria vectors is important to our ability to cope quickly with localized outbreaks of reintroduced infection and consequent possible spread of the disease. In the fight against insectborne enteric diseases, resistance in houseflies has necessitated the development of newer and more effective insecticidal measures and greater dependence on elimination of fly breeding. The rising standard of living in the United States, particularly since World War II, has been accompanied by rapid expansion in organized mosquito control programs and other types of community insect control activities. In addition, household use of insecticides in the United States has increased tremendously during this period. It is estimated that from $75 to $100 million is expended annually in America for chemical control of insects of public health importance. Resistance to insecticides, therefore, is an important consideration in both the effectiveness and cost of control activities.

CDC Investigations of Resistance

The Communicable Disease Center of the Public Health Service initiated laboratory and field investigations of insect resistance when the problem was first recognized. These continuing studies, conducted by the Technical Development Laboratories in Savannah, Ga., may be grouped as (*a*) fundamental investigations of the biological mechanism involved; (*b*) detection, measurement, and evaluation of the importance of insect resistance; and (*c*) development of remedial measures. Throughout the period of these studies, technical assistance has been given to other Federal agencies and the States.

Resistance may be defined as the ability of an insect population to withstand a toxicant to a greater degree than a normal population and to transmit this characteristic from one generation to another (*2*). Three types of biological mechanisms of insect resistance are generally recognized: (*a*) physiological mechanisms which enable insects to withstand or detoxify insecticides within their bodies, (*b*) morphological mechanisms which prevent a toxicant from entering the body, and (*c*) behavioristic mechanisms which permit changes in the insect's behavior patterns so as to avoid exposure to lethal dosages of insecticides. Studies conducted by the Communicable Disease Center have been concerned primarily with physiological and behavioristic mechanisms.

Physiological Resistance

In the CDC laboratory investigations of the physiological mechanism of resistance, strains of various insect species, principally houseflies and mosquitoes, are selected for resistance by exposure through a number of generations to a particular insecticide. Information on the mechanism of resistance then is obtained through studies of the absorption and metabolic fate of insecticides in both resistant and susceptible strains of the insect species.

Research is continuing on the physiological mechanism of resistance of houseflies to DDT and other chlorinated hydrocarbons and to certain organic phosphorus compounds. Results of these investigations have supported the finding that the cause of resistance to DDT is the conversion of DDT to DDE, a degradation product less toxic or harmless to the insect. This conversion process is effected through the action of an enzyme, DDT-dehydrochlorinase (*3*).

Physiological resistance in insects other than houseflies also has been investigated. For example, the enzyme system involved in the degradation of DDT by DDT-resistant body lice has received some attention. The products of the metabolized DDT, however, have not yet been identified (*4*).

Colonization of a dieldrin-resistant strain of *A. quadrimaculatus* is underway in the laboratory, and the mechanisms of resistance to this insecticide will be studied when the resistant laboratory colony has been established.

Consideration of the subject of physiological resistance would not be complete without some mention of genetics in relation to the acquisition of resistance. It is generally recognized that more understanding of genetics is essential to explain how a population of susceptible insects can become resistant through exposure to insecticides. Limited genetic studies by CDC have included observations on the paterns of acquisition and loss of resistance in resistant houseflies. It is apparent that more than one pattern of resistance may arise from selection of a given strain and also that the pattern of resistance loss in partially reverted strains may not parallel the pattern of resistance acquisition.

Behavioristic Resistance

While changes in insect behavior patterns are recognized as a mechanism of resistance to insecticides, there have been relatively few confirmed cases of behavioristic resistance (*5*). The lack of a greater number of such cases is generally attributed to the paucity of studies and observations of insect behavior prior to the use of insecticides for control of the selected species involved.

Several examples of behavioristic resistance have been found in our work. As a result of reduced flight in the presence of DDT-synergist space-spray applications, resistant flies contact less spray than susceptible flies. Studies of the resting habits of flies in rural and urban areas have suggested that following exposure to residual DDT applications these insects changed their nocturnal resting places from indoors to outdoors during the warmer periods of the year (*6, 7*).

In 1956, both behavioristic and physiological resistance to malathion was demonstrated in a strain of houseflies in the Savannah, Ga., area (*8*). This was the initial reported occurrence of resistance to malathion by houseflies in the United States. Following 12 weeks of effective control at a dairy with a malathion bait preparation (2 percent malathion at a dosage of 4 ounces of bait per 1,000 square feet of floor area), fly populations began to increase in spite of more frequent treatment and changes in types of bait formulations. Observations revealed that the flies were no longer attracted to the malathion baits, but actually appeared to be repelled by them. The majority of the flies approached the bait in flight but failed to alight on it: a true behavioristic response. Both the behavioristic and physiological types of resistance in this strain of houseflies were confirmed in subsequent laboratory and field studies (*9*).

In 1957, Schoof and Kilpatrick observed a similar pattern of behavioristic resistance in the Anderson strain of houseflies collected at a chicken ranch near Savannah, Ga. (*10*). Laboratory tests indicated that a colonized strain of this housefly was highly resistant to malathion and less susceptible to parathion and Diazinon than a standard laboratory strain.

The ecology and biology of both resistant and normal populations of vectors are important aspects of CDC's research on resistance. Studies are conducted of breeding requirements, biting and resting habits, and changes in life cycles or biotic potentials of resistant and susceptible strains. Such information is important in detecting and understanding behavioristic resistance and for developing and applying effective control measures.

Detecting and Measuring Resistance

One of the most important problems confronting those responsible for carrying out vector control programs is the early detection and measurement of resistance to insecticide in an insect species. Evidence of resistance is observed through reduced insect mortalities following the use of insecticidal formulations and application techniques which previously provided effective control. Many factors other than resistance can influence the degree of control, and too frequently the failure to obtain control has been attributed to resistance when other factors were responsible.

A method and a kit have been recently developed for wide-scale use in detecting the presence and extent of resistance in adult mosquitoes in malaria and other control programs. Such a method, if standardized, would also provide a valuable means of measuring in the field the susceptibility levels of various species of mosquitoes. The testing apparatus is a modification of equipment developed earlier by Fay and associates (*11*). In general, the test procedure entails exposing adult mosquitoes to commercially prepared paper surfaces treated with formulations of DDT or dieldrin in Risella oil. Papers selected for use in the test kits provide surfaces of 0.25 to 4 percent DDT or 0.05 to 1.6 percent dieldrin to be used at specific exposure periods. Mortality is determined following a 24-hour holding period (*12*). The test procedure and kits are being evaluated in the field in the United States and in other countries.

The Technical Development Laboratories make every effort to keep up to date on the occurrence of insect resistance, especially in the United States. Instances of resistance that arise in the course of CDC's studies are investigated thoroughly. The finding of malathion resistance in a strain of houseflies in the vicinity of Savannah, Ga., in 1956 has already been described. In Bolivar County, Miss., in 1955, *A. quadrimaculatus* was found to be highly resistant to dieldrin. Followup laboratory studies indicated that this strain also was highly resistant to BHC and chlordane (*13*). This finding represented the first detection of resistance in *A. quadrimaculatus* to chlorinated hydrocarbon insecticides in the United States.

Information on reported or suspected insect resistance is received from State health departments, mosquito abatement districts, agricultural agencies, research institutions, and other sources in this country. These reports are studied carefully with such followup inquiries as may be necessary to ascertain whether or not the resistance actually has been confirmed on the basis of experimental data. In some instances, the Technical Development Laboratories have confirmed specimens submitted from the field. For example, laboratory studies recently have been conducted on a colonized strain of housefly against which both malathion and Diazinon became ineffective at a dairy in Phoenix, Ariz. (*10*). This strain had been successfully controlled with malathion from 1954 to July 1956, at which time Diazinon was substituted for malathion because of inadequate control. Effective control again was achieved until June 1957. Topical applications of malathion, Diazinon, and parathion at CDC's laboratories indicated the strain to be resistant to all three compounds.

Technical Assistance

In addition to laboratory confirmation of suspected resistance in field operations, technical assistance is available from CDC's State Aids Section to State and local health departments and other organizations concerned in determining or confirming the presence of resistance in an insect species. In the past few years, a number of such requests from States have been met. Currently used and other available insecticides have been evaluated in field operations, and changes in control measures have been recommended.

While additional knowledge on the mechanism of resistance is being gained through research, the necessity of combating the present problem requires continuing studies for the discovery and development of new and improved insecticides and methods for their use. CDC is conducting laboratory and field tests to evaluate the insecticidal activity of experimental and available commercial compounds against both susceptible and resistant strains of arthropods. Both recognized arthropod vectors of disease and those species generally regarded as pestiferous are used in such tests. Principal attention is given to insects indigenous to the United States, but resistant strains from other countries are also tested. Such tests not only determine the most effective commercial compounds but also are used in the development of new and improved insecticidal materials.

For the control of houseflies, DDT and other chlorinated hydrocarbons are being evaluated as larvicides and also as adulticides in the form of residual deposits and space sprays. Organic phosphorus compounds are being studied as larvicides and as adulticides in the form of residual treatment and poisoned bait. One of the more significant developments in recent years has been the discovery of DDVP, which is being used widely in poisoned baits (*14*). Another valuable contribution has been the development of impregnated cords using organic phosphorus compounds, such as parathion and Diazinon, as residual insecticides for housefly control (*15*, *16*). In the development of new and improved insecticidal formulations, attention is given to the combination of insecticides and to the use of synergists, additives, and attractants.

Similar research is being done on the use of various chlorinated hydrocarbon and organic phosphorus insecticides and methods of application for mosquito control. Here again, the objective is to develop improved formulations and techniques necessitated, in part, by resistance. In recent years, attention has been directed to preflood and postflood treatment of irrigated areas for control of ricefield and other irrigation mosquitoes, residual larviciding against a variety of anopheline and culicine species, and fogging and barrier strip spraying for control of salt-marsh mosquitoes. In addition to laboratory and field investigations of improved insecticides and application techniques for the control of flies and mosquitoes, more limited studies of a similar nature are made on the control of cockroaches, fleas, and other insects.

The results of these investigations have been summarized as recommendations in CDC's annual report of public health pesticides, which for the past several years has been published in the March issue of *Pest Control*. This report, which also includes current data from the literature and unpublished data from other research organizations, is a valuable source of up-to-date information on the control of both resistant and susceptible insects of public health importance.

The growing problem of resistance has necessitated reemphasizing time-honored and proved methods of prevention and control of insect breeding through sanitation and other environmental measures. No insect has developed or ever will develop resistance to the elimination of its breeding area. Consequently, more attention is and will continue to be devoted to improved sanitation practices for prevention of housefly breeding and to drainage, filling, diking, and improved water management practices as a permanent means of eliminating mosquito breeding. The Communicable Disease Center supports this philosophy and is directing much of its research and technical assistance activities to that end. Research is being conducted at Savannah, Ga., and at Chandler, Ariz., on composting as an effective means of refuse disposal. In many areas of the western United States, CDC's Encephalitis Section is investigating improved methods of water management as a basic approach to the prevention and control of mosquitoes associated with irrigation and other water resource developments. In the cooperative community vector control demonstration projects in which CDC is participating, emphasis is placed on permanent sanitation improvements, such as better refuse storage, collection, and disposal, elimination of privies, and improved sanitation of animal pens, as a means of effective vector control. Insecticides are used on these projects only as a supplemental measure and then with due regard to insect resistance.

While I have discussed primarily the CDC research and technical assistance activities in connection with insect resistance, I realize that the question naturally arises, What can a member of a State or local health department do? First of all, he can stimulate broader recognition among health authorities of the growing importance of this problem. He can become more familiar with and support research activity, not only in this country but on a global basis, to overcome or combat insect resistance. All can be alert to the reported or observed instances of resistance in local areas and make this information known to those who are interested, and that includes the Communicable Disease Center. For those who are engaged in operational programs, particularly the control of mosquitoes, available field tests should be employed to detect early resistance to effect both economy and adequacy of control. Finally, improved sanitation and other environmental measures can be applied.

Conclusion

Insect resistance to insecticides should concern all public health workers and especially those engaged in the control of vectorborne diseases. Resistance is increasing more rapidly than research can develop ways and means of preventing or combating it. In the United States, Federal agencies, universities, and private research laboratories are conducting research on insect resistance. The Communicable Disease Center will continue its research and technical assistance activities following leads from current studies as well as any new approaches that may be indicated, and it will continue to work closely with State and local public health officials and other personnel engaged in insect control activities.

With these resources and with increased support through greater recognition and appreciation of the insect resistance problem, ways will be found to protect and advance the progress that has been achieved in the control of insects of public health importance.

REFERENCES

(*1*) Simmons, S. W., and Grant, J. S.: Current status of insecticide resistance. *In* Proceedings, 3d Conference of Industrial Council for Tropical Health, April 16–18, 1957. Cambridge, Mass., Harvard School of Public Health.

(*2*) Hess, A. D.: The significance of insecticide resistance in vector control programs. Am. J. Trop. Med. & Hyg. 1: 371–388, May 1953.

(*3*) Perry, A. S., Fay, R. W., and Buckner, A. J.: Dehydrochlorination as a measure of DDT-resistance in house flies. J. Econ. Entom. 46: 972–976, December 1953.

(*4*) Perry, A. S., and Buckner, A. J.: Biochemical investigations on DDT-resistance in the human body louse, *Pediculus humanus humanus*. Am. J. Trop. Med. & Hyg. 7: 620–626, November–December 1958.

(*5*) Quarterman, K. D., and Schoof, H. F.: The status of insecticide resistance in arthropods of public health importance in 1956. Am. J. Trop. Med. & Hyg. 7: 74–83, January 1958.

(*6*) Kilpatrick, J. W., and Quarterman, K. D.: Field studies on the resting habits of flies in relation to chemical control. Part II. In rural areas. Am. J. Trop. Med. & Hyg. 1: 1026–1031, November 1952.

(*7*) Maier, P. P., Baker, W. C., Bogue, M. D., Kilpatrick, J. W., and Quarterman, K. D.: Field studies on the resting habits of flies in relation to chemical control. Part I. In urban areas. Am. J. Trop. Med. & Hyg. 1: 1020–1025, November, 1952.

(*8*) Kilpatrick, J. W., and Schoof, H. F.: A field strain of malathion-resistant house flies. J. Econ. Entom. 51: 18–19, February 1958.

(*9*) Fay, R. W., Kilpatrick, J. W., and Morris, G. C., III.: Malathion-resistance studies on the housefly. J. Econ. Entom. 51: 452–453, August 1958.

(*10*) Schoof, H. F., and Kilpatrick, J. W.: Housefly resistance to organophosphorus compounds in Arizona and Georgia. J. Econ. Entom. 51: 546, August 1958.

(*11*) Fay, R. W., Kilpatrick, J. W., Crowell, R. L., and Quarterman, K. D.: A method for field detection of adult-mosquito resistance to DDT residues. Bull. World Health Organ. 9: 345–351 (1953).

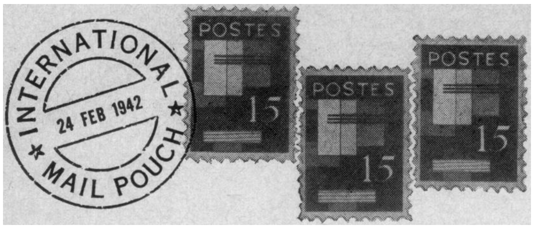
(*12*) Mathis, W., Schoof, H. F., and Fay, R. W.: A technique for measuring susceptibility levels in adult mosquitoes. Mosquito News. In press.

(*13*) Mathis, W., Schoof, H. F., Quarterman, K. D., and Fay, R. W.: Insecticide resistance of *A. quadrimaculatus* in Bolivar County, Miss. Pub. Health Rep. 71: 876–878, September 1956.

(*14*) Kilpatrick, J. W., and Schoof, H. F.: DDVP as a toxicant in poison baits for housefly control. J. Econ. Entom. 48: 623–624, October 1955.

(*15*) Fay, R. W., and Lindquist, D. A.: Laboratory studies on factors influencing the efficiency of insecticide impregnated cords for housefly control. J. Econ. Entom. 47: 975–980, December 1954.

(*16*) Kilpatrick, J. W., and Schoof, H. F.: The use of insecticide treated cords for housefly control. Pub. Health Rep. 71: 144–150, February 1956.



Women's Will

During the big dry season of 1957 in La Prosperité-Bersaba, a community of 260 persons in Surinam, the usual sources of water, rain barrels and Coropina Creek, dwindled. The soil formed a hard crust. Cassava, ananas (pineapples), bacove (eating bananas), napie (a sweet potatolike root), and gember (ginger) grew poorly. There were few crops to take to market along the railroad track, a 15-minute walk from the village, or in the town of Republiek, 30 minutes away.

Mothers of La Prosperité-Bersaba, shepherding their children to Republiek's consultatiebureau, heard how other villages were working together to get wells. The women decided to do something about their own community's plight and asked for a well.

Their request surprised the Surinaams Amerikaans Bureau Technische Samenwerking, because their village had previously been unenthusiastic about the bureau's well demonstration program. Now everyone wanted to talk to the health education assistant, the public health nursing trainees, and the sanitary inspector. They even stayed home from their kostground (fields) to be sure they would not miss seeing these people.

At a community meeting, they selected 3 men and 2 women to visit with the sanitary inspector to see what other villages had done. They also chose one of their most dependable citizens to supervise the voluntary crew that would work on their village well.

When the train brought the materials, everyone went to work, rolling the big concrete sections of pipe over the path to the well site, and bringing sand, gravel, and cement in wheelbarrows, baskets, and pails. Digging in the parched, sun-hardened earth was exhausting, but the well grew deep enough to insure a supply of water even in the long dry season. Several nights the work went on by lantern light.

Two weeks from the day the materials were unloaded, the well was finished. On November 1, 1957, La Prosperité-Bersaba proudly dedicated its new well.

—HILDRUS A. POINDEXTER, *chief public health officer, U. S. Operations Mission, Surinam.*

Potent Water

The well in Sunchon, Cholla Namdo Province, Korea, built with materials supplied through our sanitation program, has acquired an unexpected reputation. While I was inspecting the well soon after it was completed, a woman thanked me so effusively I wondered what had brought about such profound gratitude. I learned she had had seven daughters in succession, but after drinking water from the new well had given birth to her first son, to the delight of her family and the entire community.

—WALDO E. SMITH, *sanitation adviser, U. S. Operations Mission, Korea.*

Urban Improvement

A local sanitary inspector stimulated the cleanup of one of the older sections of Santa Cruz, Bolivia. He found 200 of the 280 homes lacked a potable water supply, and the 1,745 residents had only 11 latrines, all substandard. Garbage was thrown into the streets for animals to devour or the rains to wash away.

The sanitary inspector organized a health and sanitation committee among the residents. The committee surveyed the area and, with help from the local health center, started community meetings with discussions, films, and talks.

Enthusiasm and community pride led to the construction of a public well and 221 latrines. Streets were cleaned and graded, and nearly all the families began burning or burying their garbage. The residents themselves did all the work and provided the materials, except for a handpump and its accessories.

At the public dedication of the well, citizens from nearby sections of the city were so impressed that they asked the health center to help them make similar improvements in their own neighborhoods.

—HARALD S. FREDERIKSEN, M.D., *chief, Health and Sanitation Division, U. S. Operations Mission, Bolivia.*