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OUTLOOK FOR FUTURE DEVELOPMENTS IN INSECT CONTROL PRACTICES AND METHODS

Riassunto. — Il problema della resistenza agli insetticidi prende un'importanza di maggiore portata dal fatto che le mosche domestiche, le zanzare, le pulci, i pidocchi del corpo, le cimici cominciano a diventare resistenti al DDT e le blatte al clordane. Vi sono però buone ragioni per sperare che si scopriranno insetticidi capaci di sterminare questi insetti per sempre. Le informazioni raccolte dall'autore sembrano dimostrare che le mosche domestiche solo lentamente diventano resistenti al fosforo organico, al piretro ed agli insetticidi contenti l'alletrina. I pidocchi del corpo divenuti estremamente resistenti al DDT dopo un numero di generazioni relativamente piccolo, acquistano lentamente una resistenza al lindano (isomero gamma del HCH) al piretro ed al cloro-metil-p-clorofenilsone.

Per arrivare ad una soluzione soddisfacente, il problema della resistenza richiederà la continuità e lo sviluppo delle ricerche con lo scopo di scoprire nuovi agenti chimici efficaci e, parallelamente, delle ricerche suscettibili di determinare quali sostanze possono essere utilizzate con ogni sicurezza. L'autore sottolinea la necessità di completare le misure di lotta chimica contro gli insetti con i metodi di bonifica e l'importanza della ricerca di nuovi metodi per distruggere gli insetti.

Résumé. — Le problème de la résistance aux insecticides prend une importance accrue du fait que les mouches domestiques, les moustiques, les poux de corps et les punaises commencent à devenir résistants au DDT et les cancrelats au chlordane. Il y a cependant de bonnes raisons d'espérer que l'on découvrira des insecticides capables d'exterminer ces insectes pour une durée indéfinie. Les renseignements recueillis par l'auteur semblent indiquer que les mouches domestiques ne deviennent que lentement résistantes au phosphore organique, au pyrèthre et aux insecticides contenant de l'allethrine. Les poux de corps qui sont devenus

extrêmement résistants au DDT après un nombre relativement restreint de générations, acquièrent lentement une résistance à la lindane (isomère gamma de HCH), au pyrèthre et au chlorométhyl-p-chlorophénylsulfone.

Pour être résolu de manière satisfaisante, le problème de la résistance exigera la continuation et le développement des investigations visant à découvrir de nouveaux agents chimiques efficaces et, parallèlement, des recherches tendant à déterminer les substances susceptibles d'être utilisées en toute sécurité. L'auteur souligne la nécessité de compléter les mesures consistant à employer des procédés chimiques pour lutter contre les insectes au moyen de méthodes d'assainissement, et l'importance qu'il y a à rechercher de nouvelles méthodes de lutte contre les insectes.

Summary. — The importance of the insecticide resistance problem is emphasized because of the occurrence of house flies, mosquitoes, body lice, and bed bugs highly resistant to DDT and cockroaches to chlordane. However, there is reason for optimism that insecticides can be found that will control these insects for an indefinite period of time. Available information suggests that house flies are slow to acquire resistance to organic phosphorus, pyrethrum, and allethrin insecticides. The body louse, which becomes highly resistant to DDT after a relatively few generations, is slow to develop resistance to lindane, pyrethrum, and chloromethyl p-chlorophenylsulfone.

Satisfactory answers to the resistance problem will require maintenance and expansion of research to find new chemicals that are effective and concurrent studies to determine which materials can be used safely. The need for instituting sanitation practices to supplement chemical control measures and the importance of investigating new methods for controlling insects are emphasized.

Zusammenfassung. — Das Problem der Resistenz gegen Insektiziden wird hervorgehoben aus der Tatsache dass Hausfliegen, Mücken, Läuse und Wanzen gegen DDT, und Blatten gegen Chlordane resistent zu werden anfangen. Es gibt doch gute Gründe, die uns hoffen lassen, dass einige Insektizide entdeckt werden, die fähig sind diese Insekten für unbestimmte Zeit zu vernichten. Die Angaben, die vom Verfasser gesammelt wurden, weisen scheinbar auf die langsame Resistenz der Hausfliegen gegen organischen Phosphor, Pyrethrus und gegen Insektiziden die Allethrine enthalten. Die Kleiderläuse die nach einer verhältnissmässig beschränkte Generationszahl DDT-resistent geworden sind,

erwerben allmählich die Resistenz gegen Lindane (HCH gamma-isomere), Pyrethrus und Chloro-methyl-p-chlorophenilsulphone.

Damit man dem Resistenzproblem eine befriedinge Lösung geben kann, muss man Forschungen verfolgen und entwickeln um neue wirksame chemische Agenten zu entdecken und gleichzeitig Untersuchungen die dazuführen empfängliche Stoffen zu bestimmen, die man mit voller Sicherheit anwenden kann.

Der Verfasser hebt die Nötigkeit hervor, durch einige Sanierungsmethoden die Vervollständigung der Bekämpfungsmassnahmen mit Anwendung der chemischen Verfahren. Er lenkt die Aufmerksamkeit auf die Wichtigkeit der Forschungen nach anderen neuen Methoden Insekten zu bekämpfen.

The development of resistance to insecticides by many of the important insect vectors of human diseases poses serious problems that should receive the consideration of scientists throughout the world. The organizers of this meeting are to be commended for the selection of this theme for discussion.

During the past decade we have relied almost completely on the use of chemicals to control disease vectors. The new highly active insecticides have provided the only generally practical approach to their control under many conditions. We have every reason, therefore, to be alarmed over the failure of DDT and other insecticides to control certain important species at the present time, and it is appropriate that we review the current status and attempt to formulate long-range plans to meet present and future problems.

In formulating such plans we should consider three major questions: (1) What are the prospects for developing new chemicals that will provide the high degree of control for resistant flies, mosquitoes, body lice, and other insects formerly obtained with DDT and other insecticides? (2) What are the prospects for maintaining satisfactory control with insecticides currently used against species that have not yet developed resistance? (3) What are the prospects for developing methods of control that will replace or supplement chemical methods when necessary or desirable?

We cannot provide complete answers to these questions at the present time. Research is under way by many institutions, but it is apparent that more information must be obtained before we can outline the best course to follow in developing future control practices for the more important arthropods of medical importance throughout the world. Progress is being made, however, and certain lines of investigation show sufficient promise to justify an optimistic outlook. The current status of control methods for certain arthropods of medical importance and prospects for future developments will be discussed briefly.

HOUSE FLIES

Insecticides

It is now well known that intensive use of DDT for 2 or 3 years to control the house fly (*Musca domestica* L.) invariably results in the development of strains that are highly resistant to this insecticide. Moreover, the insect becomes highly resistant to methoxychlor, lindane, chlordane, dieldrin, and other chlorinated hydrocarbon insecticides when they are employed as substitutes. Investigations in the laboratory by Decker and Bruce (1) demonstrated that DDT-resistant flies become highly resistant to most chlorinated hydrocarbon insecticides within a short time. Efforts to maintain high standards of fly control prompted Federal, State, and industrial institutions to advocate the use of any available substitute insecticide that offered promise of control. Consequently house flies resistant to most of the currently available chlorinated hydrocarbon insecticides are now prevalent in many areas in the United States and other parts of the world. The repeated failure of one chlorinated hydrocarbon insecticide after another suggests that this type of insecticide will not provide the weapon we need for controlling house flies in the future.

What are the prospects for developing types of insecticides to which flies do not develop high resistance? The fact that there is a considerable range in the dosages required to kill 1 and 100 percent of a given insect indicates that a given species subjected to intensive treatment with an insecticide can be expected to develop resistance that will approach the highest level initially present among individuals in the insect population. It seems reasonable to expect, however, that there will be great differences in the degree of resistance that flies can develop to various insecticides.

Investigations by March and Metcalf (8) have shown that the house fly is slow to develop resistance to parathion. After continued exposure to this insecticide through 60 generations, the level of resistance was only about 7 times that of the normal strain. Decker and Bruce (1) found that after 40 generations of exposure to para-oxon (diethyl p-nitrophenyl phosphate) a strain of flies was only 10 to 20 times as resistant as the original susceptible strain. Dr. Decker (1) indicated that there

(1) Personal communication.

was no marked change in the level of resistance after continued exposure for 20 additional generations. L. S. Chadwick and associates of the Army Chemical Center, Edgewood, Maryland (1), have found that house flies are slow to develop resistance to Diisopropyl fluorophosphonate (DFP).

On the basis of these studies there is reason for optimism that among the organic phosphorus insecticides some may be found that will maintain fly control after continued use for many years. Unfortunately, some of the insecticides are highly toxic to higher animals. There is no basis for concluding, however, that all of them are too hazardous to use for this purpose. Malathion (0,0-dimethyl dithiophosphate of diethyl mercaptosuccinate), manufactured by the American Cyanamid Company, is a fairly effective insecticide for fly control. It is less toxic orally to mammals than most of the chlorinated hydrocarbon insecticides. Diazinon (0,0-diethyl 0-(2-isopropyl-4methyl-6pyrimidyl thiophosphate), developed by the Geigy Company in Switzerland, is highly effective against house flies (Hansens, [5]). Its mammalian toxicity to some animals appears to be considerably lower than that of parathion, one of the more toxic phosphorus insecticides now in extensive use for controlling agricultural pests. Other phosphorus insecticides are known that are highly active against insects but have moderate to low mammalian toxicity.

Exposure of flies to pyrethrum and allethrin likewise does not cause house flies to develop highly resistant strains within a short time. L. S. Chadwick and associates (1) reported that flies exposed to pyrethrum through many generations do not develop a high resistance. Decker and Bruce (1) found a level of resistance about 10 to 20 times normal after 30 generations of exposure to a combination of pyrethrum and piperonyl butoxide. During the same number of generations of exposure the chlorinated hydrocarbons can be expected to increase resistance several hundred or even several thousand times. F. H. Babers, of the Bureau of Entomology and Plant Quarantine, Beltsville, Maryland (1) found no increase in house fly resistance to allethrin after 20 generations of exposure to sprays.

Pyrethrum and allethrin are now widely used in space sprays or aerosols inside of buildings. They have limitations for general use in fly control, especially as residual treatments. However, in view of the low resistance, the development of more effective and more economical insecticides of this type offers great promise of controlling flies.

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(1) Personal communications.

ATTRACTANTS.

Fly traps containing attractants to lure the flies have been used for many years, but the value of trapping with baits under a wide range of circumstances has not been well demonstrated. GAHAN *et al.* ([4]) showed that a high degree of fly control was obtained on dairy farms near Orlando, Florida, when about 10 poison-bait stations were operated on each farm. At each station was placed a pan containing 2 kilograms of bait composed of 50 percent of molasses, 2 percent of sodium arsenate, and 48 percent of water.

To make a satisfactory bait, it is necessary to employ a poison that is not hazardous to animals and man. Since sodium arsenate is considered hazardous, other materials are under study at the Orlando laboratory of the Bureau of Entomology and Plant Quarantine. Preliminary unpublished results indicate that malathion is a promising substitute for the arsenicals.

Because of the extensive migration of flies, it is likely that attractants will prove most satisfactory when employed in a community-wide program. Sanitation practices to eliminate competing attractive substances may also be necessary. However, I am of the opinion that the use of attractants in permanent bait stations may offer an effective and economical way to control flies in some situations. especially if the right materials can be found. Further research seems warranted to find materials more effective than molasses, the attractant used in the United States.

Another method of using baits is to sprinkle them on the floors of animal buildings. A water solution containing 3 percent of syrup or molasses and 0.05 percent of the insecticide TEPP is being used in this way with good results by dairy farmers in southern States where it is not possible to obtain control with any of the available residual insecticides. This method and the results obtained have been discussed by GAHAN *et al.* ([4]) and FARRAR and BRANNON ([3]).

Owing to the small amount of TEPP in the bait, its use is not particularly hazardous, after it is applied. However, the TEPP concentrates used to prepare the solutions are extremely dangerous to handle. This is a serious objection to the use of this method of fly control. Preliminary unpublished results obtained at the Orlando laboratory indicate, however, that less hazardous materials, including malathion and a dialkyl phosphate (Bayer No. - 13/59), and Diazinon can be substituted for TEPP without decreasing the effectiveness of the method.

Sanitation.

It is now generally agreed that clean-up measures to prevent the accumulation of fly-breeding material are essential in effective fly-control programs. Such measures should be emphasized as a basic practice to be instituted by all property owners. However, in the absence of a community-wide sanitation program, a serious fly problem may exist even though there is no breeding on the premises. An example of such a problem was encountered on a dairy farm in Florida. Within a week after a new dairy installation had been put into operation flies became very troublesome even though no fly emergence occurred on the farm. This example emphasizes the need for community-wide sanitation programs.

Biological Control.

Flies are known to be attacked by fungi and certain arthropod parasites. Spectacular results in the control of certain agricultural and forest-insect pests have been obtained in recent years through the dissemination of pathogens. The possibility of finding and culturing highly effective disease organisms for dissemination should be explored as a means for controlling flies.

Body lice.

The appearance of DDT-resistant body lice (*Pediculus humanus humanus L.*) in Korea, Japan, Egypt, and other countries has further emphasized the seriousness of the resistance problem in connection with the control of arthropod-borne diseases. As with house flies, body lice acquire an extremely high resistance to DDT. A high percentage of a Korean strain established at the Orlando laboratory survived exposures for 24 hours to dusts containing 10 percent of DDT. Lice of normal susceptibility generally succumb after 24 hours' exposure to 0.1 percent of DDT.

What are the possibilities for developing insecticides to which the body louse does not become resistant? G. W. Eddy and associates of the Orlando laboratory are attempting to answer this question. The results thus far are encouraging and lend hope that good louse insecticides may be found that do not cause the development of resistance as rapidly as does DDT.

Body lice from a laboratory strain that had never been exposed to

DDT or any other chlorinated hydrocarbon insecticide were used in these studies. A portion of this colony was selected for continuous exposure on cloth impregnated with an acetone solution containing 0.001 percent of DDT. The resistance of these lice in comparison with those from the regular colony was determined for subsequent generations. By the 12th generation the lice were about 1000 times as resistant as the regular strain.

A portion of the regular colony was exposed to lindane-impregnated cloth for 20 generations. The resistance at the end of that time was only about twice that of the regular strain. When a branch of the regular colony was exposed to chloromethyl p-chlorophenylsulfone (lauseto neu), the resistance was increased only about twofold after 21 generations. After exposure to pyrethrum for 15 generations, the strain was about two and a half times as resistant as the regular strain. After 15 generations' exposure to cloth treated with pyrethrum plus the synergist sulfoxide (n-octyl sulfoxide of isosafrole), resistance was no more than twofold.

These laboratory investigations substantiate actual use experience in the development of louse strains highly resistant to DDT. That such high resistance has not developed to other louse insecticides in the laboratory is encouraging. It is recognized that there may be considerable variation in the degree of resistance that different strains will acquire in the same period. For the present, however, it seems that lindane, synergized pyrethrum, and chloromethyl p-chlorophenylsulfone may be used effectively for body louse control for a much longer time than was obtained with DDT.

The long-range and ideal solution to louse control should be based on a program of sanitation. The body louse is not a health problem among peoples having the means and the will to maintain personal sanitation. The accomplishment of louse control by personal hygiene is dependent on basic living standards and social customs. It is recognized that these may be difficult to improve in a short time. Nevertheless the control of lice and louse-borne disease is an important point to stress in efforts to attain these objectives.

At the present time, especially during emergencies, the use of insecticides in powders or clothing impregnations offers the most feasible way to deal with the louse and louse-borne typhus problem. Therefore, every effort should be made to have effective louse insecticides available. Investigations should be undertaken with lice from various parts of the world to determine whether the insect is capable of developing resistance to insecticides now available.

MOSQUITOES

A number of species of culicine mosquitoes have become resistant to DDT. The status of resistance of mosquitoes to insecticides has been summarized by HESS (6) and KNIPLING (7). The mosquito-control organizations in Florida and California are encountering difficulty in obtaining satisfactory control of certain species of *Aedes* and *Culex* with DDT and some of the chlorinated hydrocarbon insecticides that have been employed as substitutes.

The pattern of resistance of certain culicine mosquitoes has followed closely that developed by flies. There is less information, however, on the rapidity and magnitude of resistance that different mosquito species develop, primarily because of the difficulty of maintaining laboratory colonies of some species. A. W. LINDQUIST and associates of the Corvallis, Oregon, laboratory of the Bureau of Entomology and Plant Quarantine, have been exposing larvae of *Culex quinquefasciatus* Say to DDT and to EPN (O-ethyl O-p-nitrophenyl benzenethiophosphonate) for generations in efforts to determine the amount of resistance that will be acquired by this species. Thus far the level of resistance has been rather low, the dosages giving 50 and 90 percent mortality, being only about 2.5 and 2,9 times normal for DDT and 2.0 and 2.2 for EPN.

The manner of using insecticides may be an important factor in determining the rapidity and degree that resistance will develop. It may be significant that the resistance problem has been most serious where the insecticides have been used as larvicides or against adults on such an extensive scale that all or a high percentage of the breeding places in an area were treated, thus exposing both larvae and adults to the insecticide.

The resistance problem against *Anopheles* mosquitoes apparently is not serious at the present time. To my knowledge no malaria-control programs have failed because of acquired resistance of these vectors to DDT.

We have little assurance, however, that resistance to DDT, BHC, dieldrin, or other insecticides now used for their control will not be a serious problem in the future. The studies by TRAPIDO (9) indicate that *Anopheles albimanus* Wied has developed a change in behavior following several years' use of DDT residual treatments of villages in Panama. DERRYBERRY and GARTREL (2), of the Tennessee Valley Authority, have reported that the larvae of *Anopheles quadrimaculatus* Say are more difficult to control with DDT now than when large-scale antilarval measures were first instituted in about 1945.

Insecticides, particularly residual sprays, have been of such great value in the control of mosquito-borne disease, especially in rural areas, that every effort should be made to develop insecticides and methods for their use that will assure satisfactory control for an indefinite period of time. To attain this objective we should intensify research to find alternate materials. Promising insecticides should be tested against important species under controlled conditions, as is being done for flies and body lice, to determine their ability to become resistant to them. Studies should be conducted in connection with malaria-control programs under way in various parts of the world to obtain precise information on the trends toward development of strains resistant to the insecticide in use.

Further research should be conducted to develop methods of control that will supplement or replace the use of insecticides. Search for biological agents for mosquito control seems warranted. Highly virulent virus, bacterial, or protozoan organisms might be found, cultured, and disseminated for controlling mosquitoes in the same way that organisms have been disseminated for controlling certain agricultural and forest pests.

Permanent methods of control should be instituted wherever feasible so that less dependence on insecticides will be necessary. Drainage, filling, impoundments, flushing streams, water-level management in impounded areas, and destruction of aquatic vegetation are measures that are known to accomplish control under certain conditions.

Other insects

Strains of other arthropods of medical importance are known or suspected to be resistant to the chlorinated hydrocarbon insecticides. Data recently obtained show that bed bugs (*Cimex lectularius L.*) highly resistant to DDT occur in the Far East and the United States. The presence of DDT-resistant bed bugs has been indicated for several years from observations made by personnel of the Department of the Navy. Recently, however, the Orlando laboratory in cooperation with the Navy and the National Pest Control Association definitely proved that this insect is now highly resistant to DDT in some areas. Lindane and synergized pyrethrum appear to be effective in controlling bed bugs but no information is available as to the rapidity that resistance may develop to these insecticides.

Cockroaches, important pests and potential disease carriers, have developed high resistance to chlordane in some areas in the United States. The occurrence of chlordane-resistant roaches was observed by pest-control operators a year or more before a resistant colony was established and tested. Chlordane is remarkably effective against normal strains of roaches and appeared to be a satisfactory solution to the cockroach problem. The occurrence of resistance to it among these insects is therefore viewed with considerable alarm.

As yet there is no definite proof that fleas have become resistant to DDT. However, the reported failure of DDT to control the cat fleas (*Ctenocephalides felic*, Bouche) and dog fleas (*C. canis*, Curt.) in certain areas in the United States during the last few years strongly suggests that DDT-resistant fleas do occur.

Discussion

The occurrence of insecticide-resistant flies, lice, mosquitoes, bed bugs, cockroaches, and possibly fleas after a few years' use of specific chlorinated hydrocarbon insecticides emphasizes the necessity for a careful appraisal of the situation. Long-range plans should be formulated in order that we can maintain the advances that have been made in controlling vectors of human diseases.

We cannot minimize the significance of the resistance problem. However, I believe that chemicals still offer the most generally practical method for controlling arthropods affecting man. Available information suggests that there is a marked difference in the capacity of a given insect to develop resistance to different insecticides. This optimism is shared by others. In this connection I am taking the liberty of quoting from a letter received from R. L. Metcalf of the Riverside Agricultural Experiment Station, University of California:

« We feel that particularly significant developments are the promise which have been shown in the field by the organic phosphorus materials which appear to be most effective for fly control. The very small degree to which fly resistance has developed in exposure of larvae and adults to parathion in over eighty generations and the failure of *Phormia regina* (Meig.) to develop resistance to lindane in over twenty-four generations of exposure, are highly indicative of a promising future for residual control of many insect species. Dr. Ralph B. March of our staff has been carrying on an experiment for the past several years in rearing codling moths on DDT-treated apples and has yet to find any appreciable amount of resistance.

« I am sure you will realize by this time that I personally feel quite optimistic regarding the overall future of chemical control. It appears to us that most insect species will probably not develop a serious degree of resistance and that, for those which do, more enlightened methods of treatment plus the ever increasing progress in new insecticides will enable us to keep ahead. Certainly, no one has proposed the abandonment of antibiotics and antimalarials because of the ever present resistant strains of micro-organism ».

We know that insecticides provide highly effective and practical means of dealing with almost all of the major vectors of human diseases. Every effort should therefore be made to develop satisfactory insecticides or combinations of insecticides that will assure effective control for an indefinite period of time.

Research to obtain more information about the normal insects, the mode of action of insecticides and synergists, and the nature of the resistance mechanism should be expanded. This may guide chemists in the preparation of more suitable materials.

There should be a continuous program of research to develop new types of insecticides and combinations of insecticides. This phase of the research should not terminate when an effective insect-control agent is found. An elaborate program should be instituted to determine in advance whether various insects in different parts of the world are capable of developing resistance to such agents. Only those materials to which the insects do not rapidly develop high resistance should be considered for practical use. Closely associated with this phase of research there should be investigations to determine the manner of using insecticides to avoid or delay the development of resistance.

Another vitally important phase of research on the development of chemical control agents for insects affecting man, which has been neglected, must be expanded and coordinated. I have reference to the toxicity of insecticides to man. Insecticides for controlling most insects affecting man must be employed in a manner that requires application to individuals or in homes and other establishments where opportunities for exposure are unavoidable. Therefore, for rapid and efficient progress in the development of new insecticides it is essential that biological and toxicological research be conducted concurrently.

In our efforts to assure effective means of controlling insects we must not ignore consideration of methods that may replace or supplement the use of chemicals. The importance of instituting sanitary practices as an aid to the control of insects such as flies, mosquitoes, and lice is obvious. New approaches, such as the possible utilization of biological control agents, should be investigated.

The World Health Organization should assume leadership in publicizing the world-wide significance of the resistance problem. It should through appropriate channels encourage substantial expansion of research by all nations in an effort to develop measures that will assure the maintenance of high standards of vector control throughout the world.

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