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PRACTICAL IMPLICATIONS OF INSECTICIDE RESISTANCE

by

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1. INTRODUCTION

The definition of insecticide resistance, as formulated by the WHO Expert Committee on Insecticides at its seventh meeting, is the following: "Resistance to insecticides is the development of an ability in a strain of insects to tolerate doses of toxicants which could prove lethal to the majority of individuals in a normal population of the same species. The term 'behaviouristic resistance' describes the development of the ability to avoid a dose which could prove lethal."

The behaviouristic resistance supposes a change in behaviour of the insects due to selection following the use of insecticides. The importance of behaviouristic resistance is difficult to assess in the absence of universally accepted and available methods of measuring behaviour change. Besides, it now appears that at least one of the observations on behaviouristic changes was not caused by intraspecific selection, but by interspecific selection between sibling species of the *Anopheles gambiae* complex (Davidson, 1964b). One wonders how many of the other suspected cases of behaviour changes are in reality interspecific and not intraspecific as usually suggested. To avoid useless discussion on doubtful data the present paper is restricted to insecticide resistance.

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It is generally admitted that two types of insecticide resistance are possible: "physiological resistance" (= true resistance) and "vigour tolerance".

Vigour tolerance is a term suggested by Hoskins & Gordon (1956) to describe a generalized lowering of susceptibility to one or many types of poison, depending on non-specific mechanisms. The consensus of opinion seems to be that such non-specific mechanisms stem either from a high level of heterogeneity (heterosis vigour) or from the accumulation of several minor genes improving the natural defences of the insect against toxicants (increase of cuticle thickness, higher proportion of fat body, and so on). Nearly all published observations on vigour tolerance deal with strains developed by artificial selection by insecticides on laboratory colonies. In such cases the level of resistance is not very high and is soon lost when the selection pressure is removed. Some similar observations have been carried out on field populations in treated areas; there also the tolerance disappears with the removal of insecticide pressure (A. gambiae in the Ruzizi valley and in South-Western Ivory Coast). Vigour tolerance does not appear to be of serious practical importance (Busvine, 1963) except for some species which are already of a low natural susceptibility to insecticides and become almost immune if vigour tolerance appears.

Physiological resistance, which is specific to a particular type of poison, often gives a very high degree of protection, approaching complete immunity. The resistance mechanism responsible is inherited and it is comparatively easy to maintain resistant colonies for long periods without any constant selection by insecticides.

2. THE SELECTION OF PHYSIOLOGICALLY RESISTANT POPULATIONS

As far as we know, physiologically resistant populations appear by selection, under insecticide pressure. Natural populations generally contain a very low proportion of spontaneously resistant individuals; the big mass of susceptible specimens is killed by the insecticides, or gives rise to a less susceptible progeny, and gradually the proportion of resistant individuals increases, until the appearance of a resistant population.

The speed of selection varies according to several factors, namely:

- the intensity of the insecticide pressure,
- the natural frequency of resistant individuals, and the density of the vector,
- the genetic basis of resistance, dominant or recessive, monofactorial or polyfactorial, and the nature of characters linked with resistance,
- the amount of advantages conferred to the resistant individuals in treated and in untreated environments.

The speed of selection increases with insecticide pressure which, in turn, depends on the nature of the toxicant, of the application rate and methods, and of the surface of the treated areas. Large-scale larviciding operations with residual insecticides, to which immature stages cannot escape, exert a very strong insecticide pressure and are very favourable for selecting resistant populations. Such larviciding operations are very often a side-effect of crops protection by agricultural insecticides. The soil contamination stands for years after the last applications and ensures favourable environmental conditions for the long-term maintenance of resistant populations.

The speed of selection increases slightly with the natural frequency of resistant individuals, but this is not an important factor for the majority of insects with an abundant progeny and a very short life-cycle, at least in tropical countries. However, if the vector density is low-resistant, individuals have few chances to mate with each other, which delays the appearance of resistant homozygotes.

Probably more important are the genetic bases of resistance. A monofactorial character will be selected more quickly than a polyfactorial one. Besides, if the resistance character is recessive the hybrids will not possess any advantage on the susceptible, and the selection will be very slow; but if the resistance character is more or less dominant, the hybrids will survive to insecticide exposure in higher proportion than the susceptible, and the character will spread out very quickly in the whole population. Sometimes the character of resistance, even when monofactorial, seems to be linked to unfavourable characters which are usually transmitted with it and delay its spreading in treated areas (Busvine, 1964); the first phase of selection is then very slow and resistant populations can appear only after a long period of insecticide pressure; gradually new combinations of characters appear, the selection for resistance speeds up and later on the resistant populations are stable even after removal of the insecticide pressure.

The exact origin of resistant characters has been widely discussed, as it is very difficult to prove their existence before any use of the corresponding insecticides. However, it is well known that insecticide pressure exerted on laboratory colonies of insects, even during very long periods, generally failed to develop any resistance. On the contrary, some authors have succeeded in developing resistant populations from laboratory colonies containing the character for resistance, without any contact between the selected insects and the toxicant.

Bennett (1958) has worked on a heterogeneous stock of Drosophila melanogaster produced by combining 26 laboratory and wild strains. After establishment the colony was divided into sub-colonies, and the DDT susceptibility of each sub-colony was assessed. Only the more resistant and the more susceptible sub-colonies were used to raise F1 generations. The same process was repeated for 15 generations resulting in a resistant sub-strain 625 times less susceptible than the corresponding susceptible sub-strain. Since in such a selection the direct ancestors of the resistant sub-strain have no more been in contact with DDT than those of the susceptible sub-strain, the insecticide could not itself have been the direct cause of the resistant variants. That a resistant strain could be produced by this procedure shows that the pre-adaptation hypothesis is sufficient to explain the results.

However in laboratory conditions strains of resistant insects have been selected from apparently susceptible colonies by exposure of adults to sub-lethal doses of insecticides, without any noticeable mortality of the treated adults. But, as shown by Derbeneva-Ukhova (1962 and 1963) and by Beard (1964), the sub-lethal doses cause in females pathological ovogenesis irregularities. So the progeny of the susceptible females is far less numerous than the progeny of the resistant ones, and after some generations the laboratory population is almost only composed of resistant individuals, the selection being done indirectly through the differential reproduction rate of susceptible and resistant females exposed to sub-lethal doses of insecticide. In such conditions the selection can be complicated by the occurrence of resistance-linked unfavourable characters which are more liable to be maintained in laboratory colonies than in wild populations.

3. VARIOUS TYPES OF PHYSIOLOGICAL INSECTICIDE RESISTANCE

Each type of physiological resistance appears to be specific to a particular type of toxicant, typified usually not by one compound but by a group of related compounds.

The major types of physiological insecticide resistance correspond respectively to: DDT and related compounds; BHC, dieldrin and related compounds; pyrethrins; organophosphate compounds; and carbamate compounds. However, resistance to organophosphates can be limited to only malathion and malaoxon, or to dimethyl-organophosphates, or to diethyl-organophosphates. Each type corresponds to specific ways of detoxification of the corresponding insecticides and several types can coexist in the same species (Brown, 1964; Busvine, 1964; Georghiou, 1964).

Besides there is some relationship between organophosphate-resistance and carbamate-resistance, and both can induce, in some circumstances, DDT-resistance. Pyrethrin-resistance may also induce DDT-resistance.

In field conditions the situation is further complicated by the frequent selection of populations with multiple resistance but generally each resistance mechanism acts separately. However, Davidson (1964a) has recently stressed that the DDT-susceptibility of *Culex p. fatigans* adults varies according to their dieldrin-susceptibility, the DDT-susceptible DL-resistant adults being far more DDT-tolerant than the DDT/DL-susceptible ones; for the time such a phenomenon is unexplained.

4. THE GENERAL PREVALENCE OF INSECTICIDE RESISTANCE IN ARTHROPODS OF MEDICAL AND VETERINARY IMPORTANCE

Before the second World War resistance to insecticides was very uncommon. The first instance occurred as long ago as 1908, when the San José scale was found to be resistant to lime sulfur in Washington State, United States of America, but by 1946 only one arthropod of veterinary or medical importance was resistant (Brown, 1958). However, the development of modern synthetic insecticides and their large-scale use all over the world has favoured the selection of many resistant populations of arthropods.

In spite of the standardization of susceptibility-testing methods by WHO, all field and laboratory workers did not use the same assessment techniques and it was not always clear whether or not they were dealing with resistant populations. So the number of resistant species varies slightly from one author to another, according to the criterion used and according to the group of insects included under the label "of medical and veterinary importance".

The number of insecticide-resistant arthropod species has increased from 1 in 1945 to at least 18 in 1955 and 60 in 1965. If we include some semi-domestic pest diptera and some mosquito species for which we do not have the full set of data, the progression of insecticide resistance is 1 species in 1945, 37 in 1955 and 75 now. Almost all major groups are involved: house-flies, blowflies, mosquitos, fleas, lice, bed-bugs, ticks, stable-flies, biting midges (WHO, 1963) and since two years *Simuliidae* (Suzuki et al., 1963).

The first steps in the discovery of vector resistance to insecticides can be very easily illustrated by the following events:

1946: DDT-resistance of *Musca domestica* in Denmark and Sweden.
1947: DDT-resistance of *Culex pipiens* in Italy.
1947: DDT-resistance of *Cimex lectularius* in Hawai.
1948: Dieldrin-resistance of *Boophilus decoloratus* in South Africa.
1949: DDT-resistance of *Pulex irritans* in Peru.
1951: DDT-resistance of *Anopheles sacharovi* in Greece.
1951: DDT-resistance of *Pediculus humanus* in Korea.
1963: DDT-resistance of *Simulium aokii* in Japan.

In the beginning, almost all resistant populations were DDT-resistant because this insecticide was the most commonly used in vector control operations, and the resistant populations were restricted to small areas. Now the most common resistance is the BHC-dieldrin-resistance and the resistant populations are much more widespread. The present status of resistance of each of the major groups of vectors and pests of medical and veterinary importance is discussed below.

4.1 Synanthropic flies

4.1.1 House-flies

House-flies have been submitted to very strong insecticide pressures by many wide-scale house-fly control programmes and much more by millions of domestic applications of insecticides against household pests. So it is not surprising that house-fly resistance has been encountered almost everywhere and towards almost all insecticide groups.

DDT-resistance developed first in 1946 and is present now all over the world, the most recent records coming from Eastern Europe, the USSR, China, Japan and India (Kovchasov, 1963; Suzuki, 1963; Lupasco et al., 1963; Tsukamoto, 1964; Derbeneva-Ukhova, 1963). Resistance to BHC and dieldrin, which appeared in 1948, is also becoming ubiquitous. In areas of developing resistance, DDT or BHC can sometimes still effectively control house-flies at higher dosages than usual, but with dieldrin the control fails.

Organophosphate-resistance (to parathion and diazinon) developed in 1955, and malathion-resistance (which is slightly different from the general O.P.-resistance) appeared in 1956. They are now present in Western and Northern Europe, in the United States of America and in Japan. Carbamate-resistance, which is not a single entity (Hoskins & Nagasawa, 1961; Georghiou, 1964), occurs often in the same areas. Pyrethrin-resistance, first developed in Sweden, is present now in several areas of Western Europe and the United States of America.

In laboratory conditions, insecticide-resistance can be very stable in house-flies (Mallis & Miller, 1964), but in field populations it is not always so stable as only peridomestic populations of house-flies are affected by the control operations; after the withdrawal of the insecticide, resistant individuals are slowly diluted into the wild house-fly populations unaffected by the treatments (Yasutomi, 1961; Peffly & Shawarby, 1956; Ozburn & Morrisson, 1963; Keiding, 1963). However, due to the residual effect of most of the chlorinated insecticides, the selection pressure can stand for months, and even years, after the last application. The situation is less serious with organophosphates and carbamates, which are not so stable, especially if they have been used in baits or on treated cords. As organophosphates and carbamates compounds seem to select for DDT-resistance, and sometimes for dieldrin-resistance, as well as for homologous resistance, chlorinated insecticides become less and less efficient for house-fly control (Keiding, 1963; Winteringham & Hewlett, 1964). The situation is not the same in all countries because DDT- and carbamate-resistance do not have the same genetical basis everywhere (Milani, 1963; Tsukamoto & Suzuki, 1964; Rahman & Khan, 1964; Georghiou, 1964).

In spite of some cross-resistance between carbamate and O.P. compounds, these insecticides offer some promise even now, as a great variety of toxicants are available. WARF-antiresistant DDT compounds and deutero-DDT, which seem efficient against DDT-resistant A. aegypti, offer few hopes for controlling DDT-resistant house-flies (Spiller, 1963; Pillai & Brown, 1963; Fine, 1964); malathion-synergists are probably more promising (Plapp et al., 1963).

The best way to control house-flies is probably the combination of source reduction with the successive use of several unrelated insecticides, using each of them only for a short period before the reappearance of homogeneous resistant populations (Keiding, 1963).

4.1.2 Blowflies and other synanthropic flies

The situation is not so serious with blowflies because resistance is much more restricted to some compounds and to some areas.

Sheep blowflies (Phaenicia cuprina and Ph. sericata) have developed BHC/dieldrin-resistance in South Africa, Australia and New Zealand, but can be controlled by other conventional insecticides and, if necessary, could probably be controlled as well by systemic compounds (Bushland et al., 1963), like ronnel and Co-ral.

The African blowfly (Chrysomyia putoria) has developed resistance to DDT, BHC/dieldrin and to various O.P. compounds in the Leopoldville area where it has been submitted to very strong insecticide pressure during several years; populations resistant to DDT and BHC/dieldrin only have been recorded from Madagascar; in Leopoldville, where the situation was most serious, a good control has been obtained in replacing insecticides by environmental sanitation, including water-sealed latrines.

More recently, one sarcophagide fly, Sarcophaga peregrina, has developed a high dieldrin-resistance after exposure of only a few generations to the toxicant, in Nagasaki, Japan (Matsuo, 1963). This fly is susceptible to DDT and to O.P. compounds.

4.1.3 Stable-flies

DDT-resistant Stomoxys calcitrans has been reported in 1948 in Sweden, but without comparative studies of susceptible populations (Kjellander, 1949). More recent investigations have been carried out in Norway (Sömme, 1958) on natural farm populations as well as on laboratory colonies of St. calcitrans and strongly suggest that the stable-fly could be resistant to DDT and tolerant to BHC. More investigations are needed.

4.2 Anopheline mosquitos

The development of insecticide resistance in anophelines and its practical implications for the world-wide malaria eradication programme have been summarized and reviewed recently by Hamon & Garrett-Jones (1963), Davidson (1964), Coz et al. (1964), Ungureanu (1964) and by several WHO contributors (WHO, 1965). Almost all major vectors are involved and the situation is as follows.

Only two types of resistance are encountered in anophelines, DDT and BHC/dieldrin resistances. DDT resistance is of a low amplitude, does not preclude always the use of DDT, and is very slow to appear if house-spraying only is involved. BHC/dieldrin resistance has a very great amplitude, precludes any use of dieldrin, while BHC efficacy is reduced to some weeks only; this type of resistance is very rapidly selected by house-spraying alone.

In field conditions the selection of resistant anopheline populations has been speeded up by direct and indirect larviciding, either during vector control activities or much more commonly through agricultural pest control. The most important selection seems to have been due to cotton, coffee and rice spraying and dusting. In such conditions, DDT-resistant populations can be selected very rapidly because the whole anopheline population is submitted to a strong insecticide pressure, which occurs rarely with DDT house-spraying. With agricultural treatments, resistance has also appeared in Egypt and in West Africa.

In the field, DDT-resistance is not always very stable, and the proportion of resistant individuals decreases slowly after the removal of DDT sprays if no agricultural treatment is involved, but the dieldrin resistance is usually very stable for long periods and seems, at least in West Africa, to expand slowly in untreated areas (Hamon et al., 1958 and recent personal observations; Service, 1964; Service & Davidson, 1964). The situation can be different under laboratory conditions

(Keppler et al., 1964). In any case, the reintroduction of the insecticide having selected for resistance in the past is very soon followed by the reappearance of highly resistant populations.

In nearly every case the zone of resistance forms only a small part of the area of distribution of the species. Very often DDT-resistant and dieldrin-resistant populations of the same species do not overlap and one of these powerful insecticides can be used. As far as resistance alone is involved, its operational importance for malaria eradication is restricted to some zones where the vector presents double DDT/dieldrin resistance and where malaria is not eradicated as yet, like Persian Gulf coastal areas (A. stephensi), Central America (A. albimanus), Egyptian delta (A. pharoensis), Indonesia (A. sundaicus and A. aconitus). However, in many more areas insecticide resistance, either to DDT or to dieldrin, is a complicating factor augmenting very seriously other technical difficulties, such as mosquito behaviour, environmental conditions, nomadic habits of inhabitants, and so on.

DDT-and dieldrin-resistant anophelines can be controlled by O.P. compounds spraying, but these toxicants, up to now, must be used at short intervals, which is often very difficult to do in tropical countries and increases the costs of the programmes. In some conditions the only O.P. compound assessed, malathion, has not given satisfactory results, e.g. against A. pharoensis in Egypt (Shawarby et al., 1965). However, many other promising O.P. and carbamate compounds are under field assessment and will be available for mass spraying, which could improve the picture very soon (Bar-Zeev & Bracha, 1965; Coz et al., 1965).

4.3 Culicine mosquitos

The development of resistance in culicine mosquitos has followed about the same course as in anophelines and has been partly a side-result of malaria control and eradication programmes. Specifically anti-culicine programmes have been carried out against Aedes aegypti in the Americas and in some areas elsewhere, and against members of the Culex pipiens complex in almost all urban areas. Large insecticide operations have been carried out also against pest mosquitos in touristic or irrigated or arctic areas in developed countries. Recent general and regional surveys of the present situation have been presented by several WHO contributors (WHO, 1963; Pal, 1964; Gratz, 1964; Anonymous, 1965), and by many national specialists (Lewallen, 1960;

Yasutomi, 1961; Hamon & Mouchet, 1961 and 1965; Pigatti & Melo, 1961; Barr, 1962; Brown et al., 1963; Suzuki, 1963; Yu et al., 1963; Georghiou, 1964; Liu et al., 1964; Wu et al., 1964).

4.3.1 Aedes aegypti and related species

Aedes aegypti is normally fairly susceptible to DDT and dieldrin and house-spraying with these insecticides has virtually eliminated the species from a number of areas. An Aedes aegypti eradication campaign was started in the Americas in 1947 and success has been achieved in Mexico, all of Central America and all of South America except the Caribbean area, where A. aegypti has developed a high resistance to DDT and in some places also to dieldrin, and a low and indiscriminate resistance to O.P. compounds (Brown, 1964). Several territories from which A. aegypti has been eradicated have been reinfested by a resistant strain, e.g. French Guiana (Floch, 1964). A programme for the eradication of A. aegypti has also been started in the United States of America and the recent outbreaks of haemorrhagic fever in South-East Asia will probably induce the organization of A. aegypti and A. albopictus control programmes in several countries of South-East Asia.

Aedes aegypti resistance to DDT and dieldrin is now recorded from the majority of Caribbean Islands, the three Guianas, Colombia, Venezuela, as well as from South Viet-Nam. Populations resistant to DDT alone are much more widespread and occur in many countries of South-East and Far-East Asia, as well as in the United States of America. Strains with a high tolerance, or a low level of resistance, to malathion and other O.P. compounds, have been obtained from Puerto Rico and French Guiana, the resistance being mainly, if not only, noticeable in larvae (Flynn et al., 1964).

In Southern Viet-Nam, Aedes albopictus, which is almost as domestic as A. aegypti, and is also a very good experimental vector of several arboviruses, seems to be DDT and dieldrin-resistant.

In Fiji the local vector of Wuchereria bancrofti, Aedes pseudoscutellaris, has developed, on laboratory selection, a high resistance to DDT, showing that the resistance character is already present in wild populations.

In A. aegypti the level of resistance to DDT and dieldrin precludes their use as larvicides as well as imagocides and in some of the Caribbean Islands as well as in French Guiana the eradication programme is at a standstill, in spite of severe outbreaks of dengue in Jamaica. The situation is probably worse in South-East Asia, where

A. aegypti has never been considered in the past as a dangerous mosquito and was only controlled around and in the near vicinity of airports as required under the International Sanitary Regulations. However, in most areas O.P. insecticides can be used to give an effective control and, theoretically, deutero-DDT constitutes a substitute for DDT, being as efficient on DDT-resistant strains as DDT is against susceptible ones (Pillai et al., 1963b and 1963c). WHO has sponsored a research programme devoted to A. aegypti and related species control, with the aim of finding out insecticides and formulations which could be used in domestic environments without toxic hazards if introduced in drinking-water (Pal, 1964; Gratz, 1964).

4.3.2 Culex pipiens complex

Members of the Culex pipiens complex are pest mosquitos almost all over the world, and are good Wuchereria filariasis vectors in most of the urban areas of tropical countries. The larvae of the C. pipiens complex are normally very susceptible to insecticides, but adults have always been naturally DDT-tolerant.

DDT-resistance appears in the C. pipiens complex as early as 1947 in Italy and was followed in 1950 by the development of dieldrin-resistance in the same country. Since then, DDT and dieldrin resistance have been observed in the C. pipiens complex almost everywhere. Malathion and diazinon resistance were recorded twice in that group, in Southern Cameroon and in Sierra Leone, but the resistance disappeared rapidly after the withdrawal of O.P. spraying. Dieldrin and DDT resistance are more stable and the frequency of resistant individuals decreases only slowly after the removal of the insecticide pressure (Yu et al., 1963; Wu & Djou, 1964; Liu et al., 1964) and both DDT and dieldrin cannot be used any more, either against adults or very often against larvae. Carbamate-resistance has been observed in laboratory-selected strains (Georghiou, 1964).

A special screening of toxicants which could be used safely as larvicides for the C. pipiens complex in urban areas is being carried out by the WHO Filariasis Research Unit of Rangoon, with very promising results, and it will be possible very soon to control larval stages of this mosquito. But the control of adult mosquitos of the C. pipiens complex raises the same difficulties as the control of anophelines with double resistance.

4.3.3 Pest mosquitos

The salt-marsh mosquitos Aedes sollicitans and Aedes taeniorhynchus have developed DDT-resistance in 1947 in South-Eastern United States of America, then dieldrin-resistance in 1951, but can be controlled by O.P. compounds.

Both Aedes melanimon (previously known as A. dorsalis) and Aedes nigromaculis from irrigated areas became DDT- and dieldrin-resistant in 1949-51 in California, United States of America, followed by parathion-resistance in 1958-1962 and the resistance in the second species was also present for malathion and other O.P. compounds (Brown et al., 1963). The resistance of A. nigromaculis to O.P. compounds is not very stable and decreases with the number of insecticidal treatments and with a rotation of the O.P. toxicants used (Lewallen, 1960).

Culex tarsalis has been found to be DDT- and dieldrin-resistant in 1951 in California and has developed a specific and high malathion-resistance in 1956. The malathion-resistant populations are susceptible to other O.P. compounds and the first discovered malathion-resistant populations, in the Fresno County, were found to have entirely reverted to malathion-susceptibility by 1960 after four years of control by other organophosphates.

Half a dozen of other culicine mosquitos have developed resistance to chlorinated insecticides but do not raise specific control problems up to now (WHO, 1963; Pal, 1964).

4.4 Bed-bugs

Only two species of man-biting bed-bugs are widespread; both have developed DDT- and dieldrin-resistance - Cimex lectularius, 1947 and 1954, and Cimex hemipterus 1952 and 1956. Bed-bug populations resistant to malathion and fenthion have been observed in Israel (Barkai, 1963), and C. hemipterus can develop a pyrethrin-resistance in laboratory conditions (Fine, 1963; Busvine, 1958).

DDT-resistant populations of Cimex lectularius, first observed in areas in Hawaii and in the United States of America, now exist in tropical America, in Europe, in the Mediterranean region, in India, in the Western Pacific and in some areas of Africa. Dieldrin-resistance in the same species has been observed first in the Mediterranean zone, then in Africa and in Southern and Eastern Asia. In the tropical bed-bug Cimex hemipterus, DDT- and dieldrin-resistance have developed in tropical Asia and in Africa (Busvine, 1958).

Bed-bug resistance to chlorinated insecticides is probably more widespread, but is sometimes unrecorded in the absence of proper surveys. In most part of their range, bed-bugs are O.P.-susceptible and can be easily controlled by malathion.

Bed-bug-resistance in itself is not a major public health problem, but it interferes very often with main vector control programmes. When the insecticides used against vectors are no longer efficient against bed-bugs, the inhabitants of treated premises complain about insecticide and do not co-operate any more with the spraymen; sometimes they refuse to have their houses sprayed if bugs cannot be killed. It could be possible to kill the bugs by adding O.P. compounds to conventional insecticides, but this adds to the cost of the programme. Better basic health education can help to avoid such misunderstandings, but will never give a smoother development of the disease control activities than a good bed-bug control.

4.5 Lice

During the end of the Second World War and thereafter until 1951, DDT was used with full success to control the body-lice Pediculus humanus.

DDT-resistance in body-lice was observed simultaneously in Korea and Japan in 1951 and then in the Middle East in 1952. Since then, DDT-resistance has been recorded in many areas of the world but, even now, is not present everywhere. Subsequently body-lice have developed resistance to BHC and dieldrin in Europe, Africa and Asia, and to pyrethrin mainly in Japan (Wright & Brown, 1957). These resistances raise big concern, as body-lice are the vector of endemic typhus caused by Rickettsia prowazeki.

The resistance is moderately stable and is only conspicuous in regularly-treated populations (Yasutomi, 1961; Shawarby et al., 1962). Wright & Pal (1965) have recently compiled the results of a second survey of insecticide resistance in lice carried out in 22 countries from 1958-1963.

Laboratory and large-scale experiments have been carried out to assess the efficacy of substitute O.P. and carbamate insecticides on DDT/dieldrin-resistant populations of body-lice. Shawarby et al. (1962) have shown in Egypt that 1%-malathion powder, which is innocuous for human beings, is fully efficient for at least one to three weeks when dusted on infested carriers. In an area of South Africa, 2.5% carbaryl powder has been used with very good results to stop a typhus epidemic, this last formulation having the big advantage of being almost odourless (de Veld, 1963).

So, for the present time, body-lice-resistance is no longer a serious problem.

4.6 Ticks

Insecticide-resistance developed in ticks following tick-control operations for cattle protection by dipping or area sprays.

Boophilus decoloratus has been arsenic-resistant since 1938 in South Africa. It developed BHC/dieldrin-resistance in 1948 and DDT-resistance in 1956 in the same country, and also appeared to be pyrethrin-tolerant (Whitnall et al., 1952; Whitehead, 1956; Fine, 1963). Boophilus microplus has developed arsenic-resistance in the past and became BHC/dieldrin-resistant since 1950 in Australia, Brazil and Madagascar (Uilenberg, 1963), and DDT-resistant since 1954 in Australia and Brazil. BHC/dieldrin-resistance has spread very rapidly in B. decoloratus and B. microplus populations and decreases only slowly when the insecticide pressure is removed (Whitnall et al., 1952; Stone, 1962; Roulston, 1964).

Dermacentor variabilis, which is a potential vector of Rocky Mountain spotted fever, has shown resistance in Massachusetts, United States of America, to both groups of chlorinated insecticides applied as area sprays since 1959.

The other insecticide-resistant tick species which are only resistant to the BHC/dieldrin group of toxicants are Amblyomma americanum in the United States of America since 1954, Rhipicephalus evertsi in South Africa since 1960 (Whitehead & Baker, 1961), and Rh. sanguineus in Central America and in the United States of America since 1954 (Hansens, 1956).

Several organo-phosphorus insecticides can be safely applied to cattle for tick control by dipping. Diazinon has been used in South Africa and in Australia (Morel, 1963), and sevin has given promising results in Madagascar (Uilenberg, 1963), as well as malathion in the United States of America (Hansens, 1956). Extension of insecticide-resistance in ticks to O.P. compounds could be serious because the resistant species include some major vectors of cattle diseases.

4.7 Fleas

DDT-resistance has evidently developed in Pulex irritans about 15 years ago in Greece and in the Near East, but direct susceptibility tests were not performed. Dieldrin-resistance has been confirmed by laboratory tests in P. irritans in Tanganyika following dieldrin house-spraying operations, and DDT-resistance has been strongly suspected in Senegal as P. irritans reappears as a pest in sprayed villages (Hamon & Mouchet, 1961).

Ctenocephalides felis and Ct. canis have probably developed DDT-resistance in the very early days of DDT application in Southern and Northern America. Ct. felis has been investigated and proved DDT-resistant in the Southern United States of America, as early as 1952, and could not be controlled either by DDT or by chlordane (of BHC/dieldrin group) in 1956 in Florida. DDT-resistant Ct. felis is now a very troublesome problem in the United States (Brown, 1960). Ct. felis has been also strongly suspected to be DDT-resistant in Southern Cameroon after some years of spraying for malaria eradication (Hamon & Mouchet, 1961). Resistance in dog and cat fleas to DDT and BHC/dieldrin has forced the substitution of organo-phosphorus compounds in the Southern United States of America and these toxicants have been fully effective.

The first proven record of DDT-resistance in the primary plague vector Xenopsylla cheopis came from Western India in 1959, and similar populations were observed in the following years in Northern and Southern India (Krishnamurthy & Joshi, 1962). Soon X. cheopis and the other plague vector Xenopsylla astia developed simultaneous DDT- and dieldrin-resistance in some parts of Madras and Mysore States, India (Mohan, 1962; Choudhuri, 1963). In India the insecticide pressure selecting for resistance in fleas was initiated by the malaria eradication programme sprayings. The malaria eradication programme had largely put plague under control during past years, but the appearance of DDT/dieldrin-resistance could have serious developments in favouring new plague epidemics. Resistant fleas can be controlled by O.P. insecticide, such as malathion, which should be used in specific anti-flea campaigns, whereas in the past the chlorinated insecticides employed for malaria eradication were sufficient to control fleas and to prevent plague epidemics.

4.8 Ceratopogonide midges

Two species of midges, which do not carry any disease but constitute pests in some lowland areas, have developed insecticide resistance in America, Leptoconops kerteszii to DDT in California in 1961, and Culicoides furens to BHC/dieldrin in Florida and Panama since 1958, following specific pest control programmes.

When resistant to chlorinated insecticides, brackish marshes midges can probably be effectively controlled by application of fenthion pellets which have been very effective for controlling other midges (Patterson & Von Windeguth, 1964), but permanent control can be better established by impounding and filling salt marshes (Rogers, 1962).

4.9 Blackflies

There is only one record of an insecticide-resistant blackfly. Simulium aokii developed moderate DDT-resistance, as well as some BHC-tolerance, after six years of control by DDT and BHC larviciding near Tokyo, Japan (Suzuki et al., 1963). This species does not have any medical importance.

5. DISCUSSION AND CONCLUSIONS

Insecticides have probably induced vector control agencies to abandon many old methods of pest control by general sanitation and environmental manipulations. It must be remembered that even with powerful and safe insecticides source-reduction is always the best way to reach a state of permanent vector control. Source-reduction can also prevent, or delay for a considerable time, the appearance of insecticide-resistant populations. So it could be worthwhile to associate, whenever possible, environmental sanitation procedures and insecticide applications as a first measure to decrease the practical implications of insecticide resistance.

Insecticide-resistance has developed in many species of arthropods of medical and veterinary importance, and is present sometimes in the whole area of distribution of the species involved, but usually resistant populations occur only in restricted areas. Multiple resistance is widespread, but resistance to only one or two groups of insecticides is much more frequent.

WHO and national programmes for the development of new insecticides and better formulations have resulted in the discovery of new efficient insecticides. Investigations aiming to discover anti-resistant and synergist chemicals have been less successful but have supplied compounds which could be used in emergency situations. Associations of non-related insecticides can help to delay the appearance of purely resistant populations.

A better knowledge of dynamics of resistant populations in field conditions, and of cross-resistance phenomenon between chemically unrelated insecticides, could further help to employ more efficiently available compounds for controlling multi-resistant vectors.

The combination of insecticides or chemosterilants with selective and powerful attractants, and the development of biological and genetical methods of vector control offer other interesting opportunities to counteract insecticide-resistance. But a considerable amount of work is necessary before any of these methods are available for operational use.

The situation is serious but not hopeless. However, it must be stressed that in the first years of vector control with residual insecticides one or two compounds and less than 10 formulations were sufficient to control almost any vector. Now dozens of insecticides and hundreds of formulations have to be used, increasing the costs and the management difficulties of all vector control operations. As many developing countries lack funds and do not have extensive chemical industries, insecticide-resistance slows down human health and welfare improvements where they are most needed.

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