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The Impact of Insecticide-Resistance on Control of Vectors and Vector-borne Diseases

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A questionnaire inquiring into the nature of schemes for the insecticidal control of disease vectors, the development of resistance in these vectors, and the effect of any such resistance on their control and on the extent of disease was sent to more than 100 health authorities throughout the world. The replies to the questionnaire are summarized in this paper.

Until recently, the use of insecticides in public health has been largely based on three organochlorine compounds—DDT, HCH and dieldrin. However, in some countries resistance to these has now severely affected control both of many insect species and of the diseases they transmit (e.g., malaria, yellow fever, filariasis, typhus, plague). Certain other public health problems (onchocerciasis, Chagas' disease, trypanosomiasis, leishmaniasis) have not so far been greatly affected by resistance, but it is difficult to be sure of the continued reliability of the organochlorines.

Research in the past 5 years, much of it sponsored by WHO, has shown the value of various organophosphorus and carbamate insecticides as replacements for the organochlorines, although resistance to them, too, can occur. Attention must therefore be focused on all facets of the use of these newer compounds and particular scrutiny made of possible instances of resistance to them.

In order to gather information on the extent of insecticide-resistance in the world and thereby to assess what might be its practical implications for the control of diseases transmitted by insect vectors, a questionnaire prepared by the World Health Organization was sent to more than 100 health authorities, governmental or otherwise, in various parts of the world.

This questionnaire was designed to elicit information on the following matters:

(*a*) the control schemes in a given country—what insecticides are used; and the scale of the control schemes (i.e., small, >10 km^2; medium, >100 km^2; large, 100 km^2–1000 km^2 or greater);

(*b*) the insecticide-resistance developed—to what group of insecticides; whether the resistance is suspected or confirmed; its effect on control (minor resistance entailing an increase in dosage or severe resistance threatening the success of the control scheme); what insecticides have had to be abandoned owing to resistance to them; and whether there is evidence of an increase in disease owing to resistance.

More than half of those receiving the questionnaire completed and returned it, the distribution of the inquiries and replies being tabulated below by WHO Region:

	Inquiries sent	*Replies received*
African Region	12	6
American Region	30	18
Eastern Mediterranean Region	14	10
European Region	28	18
South-East Asia Region	10	6
Western Pacific Region	15	12
	109	70

The following account summarizes the information contained in the replies received, amplified, where appropriate, by data from published accounts and from unpublished communications to WHO.

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EXTENT OF INSECTICIDE-RESISTANCE

ANOPHELINE MOSQUITOS (MALARIA)

African Region

For some years, *Anopheles gambiae* has been resistant to HCH and dieldrin over large areas of Africa. DDT may be a suitable alternative in forest regions but this insecticide has not interrupted malaria transmission in the savanna areas. *An. gambiae* is so irritated by DDT when it enters houses to bite that it leaves before receiving a lethal dose of insecticide. DDT-resistant strains have been discovered recently in Senegal and Upper Volta. Hence, there seems as yet to be no satisfactory economic alternative for effective suppression of transmission in savanna areas, with the result that the malaria eradication programmes in most countries in the African Region are facing a formidable obstacle.

An. funestus has developed HCH–dieldrin-resistance in several parts of West Africa, but this is of minor importance in view of the control difficulties due to resistance of the main vector.

In East Africa, dieldrin-resistance [1] has not developed to any extent in *An. gambiae* except in Madagascar, despite several fairly large control campaigns (e.g., the Taveta-Pare scheme in Tanzania). At the present time, however, there seems to be comparatively little systematic malaria control by residual insecticides.

American Region

North and Central America. In the USA, DDT-resistant *An. quadrimaculatus* have been known for some time and double resistance (to DDT and to dieldrin) can occur. This resistance occurred after the successful conclusion of the malaria eradication campaign. In Mexico, dieldrin–DDT-resistance in *An. pseudopunctipennis* is widespread; DDT-resistance in *An. albimanus* has developed in several areas. In the opinion of the Mexican Malaria Eradication Service, resistance is unquestionably responsible for continued malaria transmission in one eradication zone; but in the other zones where resistance occurs, it is only a secondary cause of refractory malaria.

Problems due to resistance of the vector *An. albimanus* extend to other countries in Central America. In British Honduras and in Costa Rica, dieldrin-resistance developed seriously and caused resumption of malaria transmission but in the former country at least the situation was controlled by DDT. In Nicaragua, double resistance to both DDT and dieldrin in the cotton-growing areas has vitiated the use of both insecticides. About 46% of the country's population live in this area (which constitutes only 13% of the malarious zone) and, if recourse was not had to other methods, they would now be wide open to the threat of malaria.

In Haiti, on the other hand, tests indicate normal susceptibility of *An. albimanus* to DDT.

South America. An. aquasalis was found resistant to dieldrin in north-eastern Venezuela, where it was contributing to a problem of refractory malaria. It is susceptible to DDT, but nevertheless malaria was eradicated only after additional measures. *An. albitarsis* is also dieldrin-resistant but DDT-susceptible in other parts of Venezuela. In 1965 a recrudescence of infection in an area where this mosquito was the vector was eliminated by DDT. Finally, *An. nuneztovari* is slightly resistant to dieldrin in a small area of western Venezuela. It is only slightly tolerant to DDT, but refractory malaria occurs nevertheless. *An. nuneztovari* is exophilic and exophagic, which accounts for continued malaria in its range in Venezuela.

The four main malaria vectors of Colombia are *An. nuneztovari*, *A. darlingi*, *An. albimanus* and *An. punctimacula*. Of these, *An. albimanus* is dieldrin-resistant but, like the other species, it is susceptible to DDT. A few survivors of *An. punctimacula* after exposure to 4%-DDT-impregnated papers suggest incipient resistance, but so far malaria eradication is proceeding successfully with DDT. In rice-growing areas, *An. albitarsis* has shown double resistance (DDT and dieldrin) but this has not prevented these areas moving into the consolidation phase of eradication.

An. aquasalis was reported in 1966 to be resistant to DDT in the Pará area of Brazil.

[1] Recently the WHO Anopheline Control and Research Unit at Kisumu, Kenya, has sent eggs of species A and B of the *An. gambiae* complex from Kenya to the London School of Hygiene and Tropical Medicine, where they have been found to be resistant to dieldrin.

In Bolivia, DDT continues to be satisfactory against *An. pseudopunctipennis* and *An. darlingi*, with no evidence of resistance.

Eastern Mediterranean Region

In the countries of the Near East the major vectors, *An. sacharovi* and *An. superpictus*, have continued to be susceptible to organochlorine insecticides for many years. However, in 1968 indications of DDT-resistance in *An. sacharovi* were found in the Ghab area of Syria and in certain districts of adjoining countries. The situation is certainly fluid and is being watched.

In Israel, no resistance of local anopheline mosquitos to DDT has been reported; and since 1960 *An. sacharovi* has disappeared completely from the country. However, dieldrin-resistance has been known since 1958 in *An. sergenti* in one district near the Dead Sea.

In the United Arab Republic, double resistance to DDT and to dieldrin has been confirmed for *An. pharoensis*, moderately affecting control by DDT and severely reducing the effectiveness of dieldrin. There is said to be no change in the malaria situation. In the countries around the Persian Gulf, there has been serious difficulty in malaria control owing to double resistance on the part of *An. stephensi.* This has been noted in the oil-bearing regions of Saudi Arabia, and in southern Iran, causing a recrudescence of malaria, which may need an alternative insecticide such as *o*-isopropoxyphenyl methylcarbamate (OMS-33). DDT was used successfully until resistance appeared in 1957, when dieldrin was introduced. At first this was much more effective but after about 2 years dieldrin-resistance appeared, spreading and becoming so serious that a recurrence of malaria resulted. DDT was reintroduced in 1963, and for 3 years was effective with no change in the resistance level of *An. stephensi.* In 1966 and 1967, however, DDT-resistance started to increase, especially in certain localities in the south, where it is preventing satisfactory control.

In West Pakistan, there are numerous localities where resistance has been confirmed in *An. culicifacies* and *An. stephensi.* This does not, however, appear to affect malaria control.

At the extreme east of the Region, in East Pakistan, tests of *An. philippinensis*, *An. minimus* and *An. sundaicus* all show normal sensitivity to DDT, which continues to be effective in the field in the malaria eradication programme.

European Region

Reports from Greece in 1951 were notable as these were the first accounts of DDT-resistance in anopheline mosquitos. Subsequently, dieldrin-resistance developed and became so serious that dieldrin was abandoned, though DDT continued to be used. Resistance of the vector did not nullify the malaria eradication campaign, although it added to the difficulties.

In Yugoslavia, some tolerance of *An. maculipennis*, *An. messeae* and especially *An. sacharovi* to DDT has been shown, but there appears to be no persistent transmission of malaria. Other Eastern European countries (Bulgaria, Romania) have eradicated malaria mainly by the use of DDT and report only a minor degree of DDT-resistance for the *maculipennis* group of mosquitos. In Romania there is evidence of HCH–dieldrin-resistance in these mosquitos, apparently owing to the agricultural use of aldrin. *An. sacharovi* is an important vector in Turkey, where it has developed double resistance to DDT and dieldrin in the Adana region. This has not prevented the area reaching the consolidation phase of malaria eradication. There is, indeed, an area of persistent malaria in south-east Turkey, but the vectors appear to be normally susceptible there.

In the western part of Europe (Portugal) there seem to be low levels of DDT-resistance, but not sufficient to prevent adequate control. In Morocco, no evidence of resistance has been found in *An. labranchiae*, the main vector species.

South-East Asia Region

Perhaps the most widespread vector in India is *An. culicifacies*, which has proved to be DDT-resistant in a number of places. In general this has not prevented the satisfactory progress of the malaria eradication programme. In 1966, however, transmission was found to be rising in part of Maharashtra State, and DDT was replaced by HCH, so far satisfactorily.

Of other Indian anophelines, *An. stephensi*, vector in urban districts, has shown double resistance (to DDT and HCH) and is controlled by petrol, oil or Paris Green.

In Nepal, several non-vector anophelines have become DDT-resistant.

In northern Thailand, *An. culicifacies* has recently been confirmed as DDT-resistant, but this is of minor importance, as it is not a vector in that country. The five other anophelines are *An. m. minimus*, *An. b. balabacensis*, *An. maculatus*, *An. sundaicus* and *An. aconitus*. All of them remain normally susceptible to insecticides.

Western Pacific Region

There is no evidence of resistance among malaria vectors in the following areas:

West Malaysia (*An. maculatus*, *An. sundaicus*, *An. umbrosus*, *An. b. balabacensis*),
Taiwan (China) (*An. m. minimus*, etc.),
Territory of Papua and New Guinea (*An. punctulatus*, *An. farauti*, *An. koliensis*, *An. subpictus*.
Sarawak (East Malaysia) (*An. leucosphyrus*, *An. b. balabacensis*).

In the Philippines, malaria eradication received a setback owing to dieldrin-resistance of *An. minimus flavirostris*, but DDT is now being used satisfactorily.

CULICINE MOSQUITOS

Aedes aegypti

In West Africa, *Ae. aegypti* is HCH–dieldrin-resistant in most big cities and DDT-resistant in restricted areas. Specific control programmes are not generally in operation; but in an emergency situation neither DDT nor HCH could be safely recommended.

In the American Region, an *Aedes aegypti* Eradication Campaign has been in progress for some years. By 1963, considerable progress had been achieved and eradication was claimed for 17 countries in the neotropics (Kerr et al., 1964). At that time, double resistance of *Ae. aegypti* was reported to have reversed the trend of eradication in the Caribbean Islands. Since that time there have been further reinvasions on the mainland (Brazil, El Salvador, Guatemala, Honduras) and further extension of double resistance (DDT and HCH–dieldrin) has been reported. In the USA an extensive search for suitable alternatives (especially for safe larvicides which can be applied to drinking-water) has been proceeding. Some promising new compounds have been found, but it must be realized that resistance to phosphorus compounds can also develop. One must conclude that resistance offers a serious threat to the possibility of successfully achieving and maintaining the desired eradication.

Ae. aegypti is scarcely relevant to Europe but it seems to have been eradicated from Greece by the malaria programme. Hardly any mention is made of this species in replies from the Eastern Mediterranean Region.

In the South-East Asia and Western Pacific Regions, the continued absence of yellow fever induced a certain complacency about *Ae. aegypti* in past decades. This has been sharply disturbed by the spread of haemorrhagic fever due to types of dengue and chikungunya viruses transmitted by that mosquito. From the first outbreak in the Philippines in 1964, this has spread to Thailand, Malaysia, Viet-Nam, Cambodia, India and Burma. Since dengue-type viruses are poorly antigenic there are difficulties in immunization and the only practical large-scale means of controlling the diseases they cause is to control the vector. Small-scale pilot control projects have been carried out in Bangkok and Singapore, with some success; but widespread resistance to DDT is likely to curtail general use of this convenient insecticide.

Culex pipiens fatigans

In the American Region there is no record of co-ordinated campaigns against *C. p. fatigans*; and such insecticides as are used are usually intended to counter the nuisance due to this mosquito. Once again, resistance to chlorinated insecticides is widespread. Recourse to organophosphorus compounds has induced incipient resistance to these in some places.

In the Eastern Mediterranean Region, species of the *C. pipiens* complex have shown double resistance to DDT and dieldrin in the United Arab Republic. This is said to have had a moderate effect on field control by DDT and to have severely limited the value of dieldrin, but no increase of disease (filariasis) has been observed.

Over many parts of the South-East Asia Region, resistance has precluded the satisfactory control of *C. p. fatigans* by insecticides. In India, the National Filaria Control Programme was started in 1955. Almost at once (1956) DDT was rejected as being ineffective as an adulticide. In 1957, HCH was tried and in 1958–59 dieldrin, but resistance soon rendered them both ineffective. Since 1960 antilarval oiling has been widely used, with small trials of new insecticides. The WHO Filariasis Research Unit in Rangoon, Burma, has achieved a high degree of control of *C. p. atigans* larvae by the use of fenthion emulsifiable concentrate.

In the Western Pacific Region, a similar situation exists: resistance has for some time rendered chlorinated insecticides useless, so that control has reverted to such measures as oiling (Malaysia, Hong Kong, and parts of Australia).

The situation in the African Region appears to be similar to that described above for the other regions.

Mansonia spp.

A report from Malaysia states that mosquitos of this genus were normally susceptible to DDT and dieldrin. This is perhaps not surprising in view of the small-scale use of insecticides for control of this vector.

SANDFLIES (*PHLEBOTOMUS*)

There seem to be no confirmed instances of resistance recorded for sandflies, against which DDT is still generally very effective. As a result of DDT house-spraying in Europe, cutaneous leishmaniasis has virtually disappeared from Italy (Corradetti et al., 1966), Romania and Greece. Sandflies disappeared at the time of the spray compaigns, but reappeared subsequently.

In the Eastern Mediterranean Region cutaneous leishmaniasis vanished as a secondary result of antimalarial house-spraying. However, the rural or sylvatic form of *Phlebotomus* has persisted and oriental sore remains an epidemiological feature in certain areas. The sylvatic form of *Phlebotomus* resting in rodent burrows has not been affected by DDT-spraying. In Iran, following the eradication of malaria from the central region of the country, house-spraying was stopped and the *Phlebotomus* have returned with resumed transmission of oriental sore. The likelihood of a similar course of events in West Pakistan has been pointed out by Nasir (1964). During the course of the malaria eradication programme, sandflies have been controlled incidentally, since a single DDT treatment prevents their appearance in a room for a year. Nevertheless, sandflies can be found in untreated (newly built) houses in a village, so that it is fairly certain that they will return when house-spraying ceases with completion of malaria eradication.

No other information on effects of current insecticide campaigns on *Phlebotomus* is available. It is doubtful whether such campaigns would be directed specifically against *Phlebotomus* to prevent sandfly fever or dermal leishmaniasis alone, although the presence of kala-azar might change the situation.

BLACKFLIES (*SIMULIUM*)

There are a few scattered reports of resistance in blackfly larvae. *Simulium aokii* has been shown to be resistant to DDT and to HCH in an area near Tokyo, Japan (Suzuki et al., 1963). *S. venustum* has developed DDT-resistance locally in Canada (A. W. A. Brown—present questionnaire). Quite recently there has been suspicion of DDT-resistance in *S. damnosum* in southern Ghana.

These cases must be set against the following background of insecticide use.

In the area near Tokyo, Japan, where resistance has been reported in *Simulium*, DDT and lindane have been in use since 1954.

Moderately extensive use of insecticides against nuisance blackflies is made in Quebec Province, Canada. Control of *Simulium* in New York State is being undertaken by Dr H. A. Jamnback. Comparatively little is being done in the Central American onchocerciasis areas owing to the very difficult terrain. The Mexican Onchocerciasis Service is using DDT for the control of an onchocerciasis focus in Chiapas.

In East Africa, 4 foci of *S. neavei* were eradicated from Kenya. Applications of DDT to the Victoria Nile (Uganda) against *S. damnosum* are made every 3 or 4 years. Similar treatments have been carried out on the Murchison Falls in Uganda as well as some larvicidal use of DDT against *S. neavei* in Budongo Forest, western Uganda. In West Africa there are 3 application areas in Mali, Ivory Coast and Upper Volta. At least one zone (Sikasso, Mali) has been regularly treated with DDT since 1962. Some trials have been done in Ghana and others in Nigeria (Abuja scheme and Kanji Dam). McMahon (1967) has reviewed the control of *Simulium* vectors of onchocerciasis in the African region.

In most of these campaigns there is a tendency for possibly emergent resistant strains to be diluted by invading susceptible flies from untreated areas.

TSETSE FLIES (*GLOSSINA*)

So far there are no records of insecticide-resistance in tsetse flies. The use of insecticides in *Glossina* control schemes is considerable and is growing rapidly. Some examples of the extent of the coverage may be cited as an indication of the cale on which the chlorinated hydrocarbons have been applied; they do not, however, present the total picture. It is also well to bear in mind that the area occupied by *Glossina* is far greater than the area treated.

In Kenya, *G. fuscipes* was exterminated in 1955–58 from 480 km of river by dieldrin. By the end of 1959 about 1600 km of river and lake margin had been cleared of fly. In Zambia, a substantial reduction (99.5%) of *G. morsitans* was achieved in 1961 in an isolated area of 300 km^2 by dieldrin spraying. In Southern Rhodesia, insecticidal control has been widely used since 1961, and over 3100 km^2 were treated in 1966 alone. In Nigeria, *Glossina* had been exterminated from some 26 000 km^2 in the 5 years up to 1966; total projects in Northern Nigeria cover more than 31 000 km^2. In Tanzania, 9 campaigns covering 520 km^2 were carried out in 1966. Over 1550 km^2 in Uganda were sprayed with dieldrin in 1963–64 for eradication of *G. morsitans*. Aerial spraying against the same species was carried out in Rwanda in 1961–62. Control operations have also been conducted against *G. tachinoides* by dieldrin spraying in Mali.

HOUSEFLIES (*MUSCA DOMESTICA*)

A high proportion of those who replied to the questionnaire mentioned resistance in houseflies and several of those who omitted to do so were professionally concerned with malaria eradication programmes and consequently less interested in houseflies. An analysis of the replies seems to indicate a relation between intensive use of insecticides against flies and the development of resistance:

Region	*No. of replies indicating resistance*		
	Not mentioned	*To DDT–dieldrin*	*To DDT–dieldrin and organophosphates*
Africa	5	1	0
America			
North	2	1	4
Central and South	7	4	0
Eastern Mediterranean	4	2	2
Europe			
Western	2	3	3
Eastern	1	9	0
South-East Asia	4	1	1
Western Pacific	6	3	3

Most of the replies which recorded housefly resistance stated that no increase in fly-borne disease had been noticed. There were, however, statements—from Hungary, India and Canada—that control failure had increased disease.

This is clearly a difficult matter to establish, since fly-borne diseases can also be transmitted in other ways. Indeed, it was only by special comparisons of sprayed and unsprayed areas that the value of DDT for reducing enteric disease was established (in Italy and in the southern USA) in the early years before resistance became widespread. Accordingly, there is little doubt that the failures in fly control following resistance in many countries must allow fly-borne disease to reach levels common before the discovery of the new insecticides.

LICE (*PEDICULUS*)

Pediculus humanus humanus

Replies to the questionnaire were not particularly informative as to the impact of body-louse resistance on control. From South Africa it was suggested that increases in typhus in eastern Cape Province during recent years might be due to the failure of DDT and HCH dust. These two insecticides have been replaced by carbaryl; so far, successfully. From the Eastern Mediterranean Region, resistance in lice was recorded from the United Arab Republic and Dhahran, Saudi Arabia. In the latter instance, resistance tests followed a small typhus outbreak which was arrested by intensive dusting (DDT and later a DDT–HCH mixture). From the European Region 7 replies mentioned lice and 3 recorded resistance (Hungary, Yugoslavia and Romania), 2 of them recording control difficulties. From the Western Pacific Region replies from Japan and Hong Kong mentioned DDT-resistance leading to the replacement of that insecticide by pyrethrum or HCH.

The over-all picture of body-louse resistance is well defined by the survey of Wright & Pal (1965). On the basis of genetic experiments, Busvine (1967) confirmed the choice of 5% DDT dust as a discriminating dose and on this basis the extent of resistance in different countries in the Wright & Pal survey is as shown in the following tabulation, where " No resistance " expresses 0 survival with 5% DDT, " Incipient resistance " expresses 1%V-% survival, " Distinct resistance " expresses 6%–20% survival, and " Well established resistance " expresses >20% survival:

Country/Area	*No. of tests showing:* *No resistance*	*Incipient resistance*	*Distinct resistance*	*Well established resistance*
African Region				
Madagascar	3	0	0	0
Mozambique	2	0	0	0
South Africa	2	0	0	1
West Africa	2	0	0	0
American Region				
Chile	1	0	2	2
Mexico	0	1	0	0
Eastern Mediterranean Region				
Gaza Strip (UNRWA)	0	1	0	4
Jordan and Syria	0	1	0	1
Pakistan	9	0	0	0
Sudan	0	0	0	1
United Arab Republic	0	0	1	15
European Region				
France	1	1	0	1
Yugoslavia	7	0	0	0
South-East Asia Region				
Afghanistan	0	0	4	8
India	6	3	1	0
Western Pacific Region				
Hong Kong	0	1	0	0

There is little doubt that the degree of resistance is a reflection of extensive use of DDT dust, much used, for example, in anti-louse campaigns in the UAR, the Gaza Strip (UNRWA) and Afghanistan. There has been quite extensive use of DDT dust for lice in Eastern European countries, and while results were negative there in Wright & Pal's survey, there were positive results in the questionnaire under discussion.

In the past, DDT dusting has been able to arrest epidemics of louse-borne disease; whether it will continue to do so is a matter for anxiety. Recent outbreaks of typhus (e.g., in Burundi and Sudan) are putting this to the test.

Pediculus humanus capitis

Although closely related to the body-louse systematically, the head-louse represents a totally different problem in public health. Its continued presence, albeit in a small proportion of children, in the developed countries, is especially notable in view of the effective control agents available. DDT and HCH are most widely used and this was recorded in questionnaire answers from Germany, Greece, the United Kingdom and the USA (plant products are used in Poland). No records of resistance have been established, but there is *prima facie* evidence of HCH-resistance in one centre in England.

FLEAS (*XENOPSYLLA*)

Scattered reports of resistance in plague fleas occurred in the answers to the questionnaire. In Israel, *Xenopsylla cheopis*, which is a local vector of murine typhus, has become resistant to DDT. Other reports of resistance to chlorinated insecticides came from India, Taiwan and Puerto Rico. Extensive resistance to DDT and—at rather lower levels—to HCH have been known in India for some time (Krishnaswami et al., 1963). A a result there have been control failures in South India, where a number of plague cases occurred a few years ago.

Severe plague outbreaks have occurred in Viet-Nam in the past few years and the high resistance of the local fleas to chlorinated insecticides has forced the US Army to employ diazinon dust (Cavanaugh et al., 1968). Some anxiety is expressed in Thailand, where susceptibility tests show that local *X. cheopis* are DDT- and dieldrin-resistant. A sizable plague epidemic occurred in 1968 in Indonesia (Central Java); the resistance status of the fleas is not known, but they appear to have been amenable to control.

REDUVIID BUGS (*RHODNIUS, TRIATOMA, PANSTRONGYLUS*)

Reduviid bugs, as vectors of Chagas' disease, are of public health importance in the southern and central American region right up to Mexico, where they present a domestic problem. A report from Brazil mentions suspected resistance to HCH–dieldrin, without specifying the species involved.

Chagas' disease is especially prevalent in Venezuela and Brazil, rivalling malaria in importance. Spray campaigns against the vectors are the most effective countermeasure in the prevailing circumstances (as there are no prophylactic drugs). About one million houses are sprayed annually in Venezuela, and perhaps five times as many in Brazil, with dieldrin or HCH. Extension of resistance would be a serious check to these campaigns.

ACARINA

Scarcely any mention of ticks or mites was made in the answer to the questionnaire. Information on this subject, however, was presented at the WHO Seminar on the Ecology, Biology and Control of Ticks and Mites of Public Health Importance,[1] from which most of the information below has been taken.

Ticks

Acaricides can be used against ticks in two ways: by spraying or dusting their habitat, and by treating infested animals. The latter method is more suitable for curbing tick-borne diseases of livestock and perhaps it has been done more extensively and persistently. Indeed, the only well established instances of resistance in ticks seem to have been provoked by this type of treatment (*Boophilus decoloratus*, *B. microplus*, *Rhipicephalus sanguineus*, *Amblyomma americanum*, *Dermacentor variabilis*).

Area treatments for tick control have been the subject of many field trials in the USA. On the other hand, it is difficult to ascertain how frequently or extensively such measures have been maintained.

In Eastern Europe area-spraying with DDT has been practised in recent years against *Ixodes persulcatus*, e.g., in the USSR and Czechoslovakia. So far, no instance of resistance has been recorded.

Against soft ticks, the only relevant information concerns intermittent use of HCH dust against *Ornithodoros moubata* in African dwellings and similar measures against *O. tholozani* and *O. coniceps* in the Middle East. In neither case has its use been very persistent and there are doubts whether acaricides represent the best measures against *Ornithodoros* ticks. (*Ornithodoros* is naturally tolerant of DDT; no definite HCH-resistance has been recorded.)

Mites

Probably the only mite worth discussing in the context of human disease transmission is *Trombicula* spp. (including *Leptotrombidium*). The area control of these mites is fully discussed by Traub & Wisseman (1968). They point out that scrub typhus is still an important disease today, despite the fact that it can be effectively prevented and readily treated, because prevention is not always adopted and difficulties in diagnosis sometimes delay or prevent proper medication. The eradication of the disease is, of course, not feasible in view of the vast areas in which it is endemic. But very dramatic and well sustained reduction (up to 2 years) over substantial areas can be achieved by spraying with dieldrin, HCH or aldrin. Obvious targets should be such places as resorts, camps, golf courses, mines, estates and roadsides in suburban areas. It is not clear how much protection of this kind is now done; but the unique value of dieldrin should be noted. DDT is much less satisfactory and the organophosphorus compounds have a limited persistent effect.

[1] Unpublished document WHO/VBC/68.57. A limited number of copies of this document is available to persons officially or professionnally interested on request to Distribution and Sales, World Health Organization, 1211 Geneva, Switzerland.

BEDBUGS (*CIMEX*)

There were numerous records of resistance in bedbugs, from all regions, in the answers to the questionnaire. The usual report was of double resistance to DDT and to HCH–dieldrin; and this was equally true of *Cimex lectularius* and *C. hemipterus*. Exceptional observations were as follows.

Resistance does not seem to have been recorded in northern Europe, where DDT has been used successfully for some 20 years (Germany, United Kingdom). A report from Berlin alleges that resistant bugs are being introduced from southern Europe.

Organophosphorus resistance has so far been confirmed only in Israel, and suspected in Greece.

COCKROACHES (*BLATTELLA GERMANICA*)

Since the German cockroach is naturally rather immune to DDT it has been commonly treated with dieldrin, which has been very effective, especially when applied in the form of a persistant lacquer. Unfortunately, an HCH–dieldrin type of resistance is now widespread and mention of this occurred in answers to the questionnaire from Czechoslovakia, Germany, Poland, the United Kingdom, Hong Kong, Japan, Canada and British Honduras. Carbamates and organophosphorus compounds are being tried as alternatives, the choice being somewhat limited by the toxicity hazard, since kitchens are often involved. Malathion-resistance has been reported from one or two places, especially in the USA.

NUISANCE MOSQUITOS

Culex pipiens pipiens or *C. p. molestus* was named as a nuisance mosquito in many answers to the questionnaire from warm temperate regions. Resistance was reported from Portugal, Greece, Bulgaria, Turkey, Israel and Japan. (*C. p. fatigans* was mentioned as a nuisance mosquito from more tropical areas; but this has been dealt with earlier, considering it as a vector species.)

Anopheles pulcherrimus and *An. coustani* were mentioned as nuisance mosquitos in Dhahran, where they have become dieldrin-resistant. Other anophelines which have become noticeably resistant are *An. aconitus* and *An. subpictus* in India but these are not disease vectors in that country.

It is in the North American continent that the most active use of insecticides has been made against nuisance mosquitos, with consequent development of resistant strains. Fairly recent accounts of the situation have been given by Sutherland (1966), Lewallen & Peters (1966) and Gahan et al. (1966). These may be summarized as follows.

1. In the North-East American States, the main nuisance mosquitos are *Aedes sollicitans*, *Ae. stimulans* and *Culex pipiens fatigans* (= *C. quinquefasciatus*). Generally speaking, DDT is still used as a control measure, applied commonly by air, and without developing resistance except locally where heavy and frequent spraying occurs. Most resistance tests show no increase in tolerance of the *Aedes* species, although *C. p. fatigans* is now reaching resistant levels.

2. In California, the main nuisance mosquito is *Ae. nigromaculis*, followed by *Culex tarsalis*. Both species developed resistance to the chlorinated insecticides by about 1955. Control failures led to use of a series of organophosphorus insecticides, beginning with parathion or malathion and continuing with methyl parathion and then fenthion. Newer materials, such as Abate and Dursban, are being resorted to, with varying degrees of success.

3. In Florida, the main nuisance species is *Ae. taeniorhynchus* followed by *Ae. sollicitans*. As in California, resistance to chlorinated insecticides developed by 1955, when malathion was introduced. This was effective for several years, partly because of rather careful use. By 1964, however, control failures with *Ae. taeniorhynchus* developed which were traced to resistance. At present fenthion, naled and Dursban are maintaining control.

IMPACT OF INSECTICIDE-RESISTANCE ON DISEASE CONTROL

It will be convenient to consider the various insect vectors in two groups; one in which resistance has had a major impact (see the map) and the other in which resistance has, so far, not been very important.

RESISTANCE AS A MAJOR PROBLEM

Malaria (anopheline mosquitos)

Resistance of the principal malaria vectors has occurred in many places in malaria eradication programmes. The effect ranges from an inconvenience to an apparently insuperable obstacle. Thus, in temperate regions, such as Europe, where malaria does not reach hyperendemic levels, resistance has not prevented the achievement of eradication. Dieldrin-resistance was generally more intense and it was usually DDT which completed the campaigns, dieldrin being abandoned.

In warmer climates, where malaria is more fully established, there are even now areas where resistance challenges the outcome of the campaigns (e.g., the area around the Persian Gulf, Mexico and several countries in Central America). Again, dieldrin-resistance usually leads to this insecticide being abandoned while a simultaneous DDT-resistance (which is less intense) renders the final stages excessively difficult.

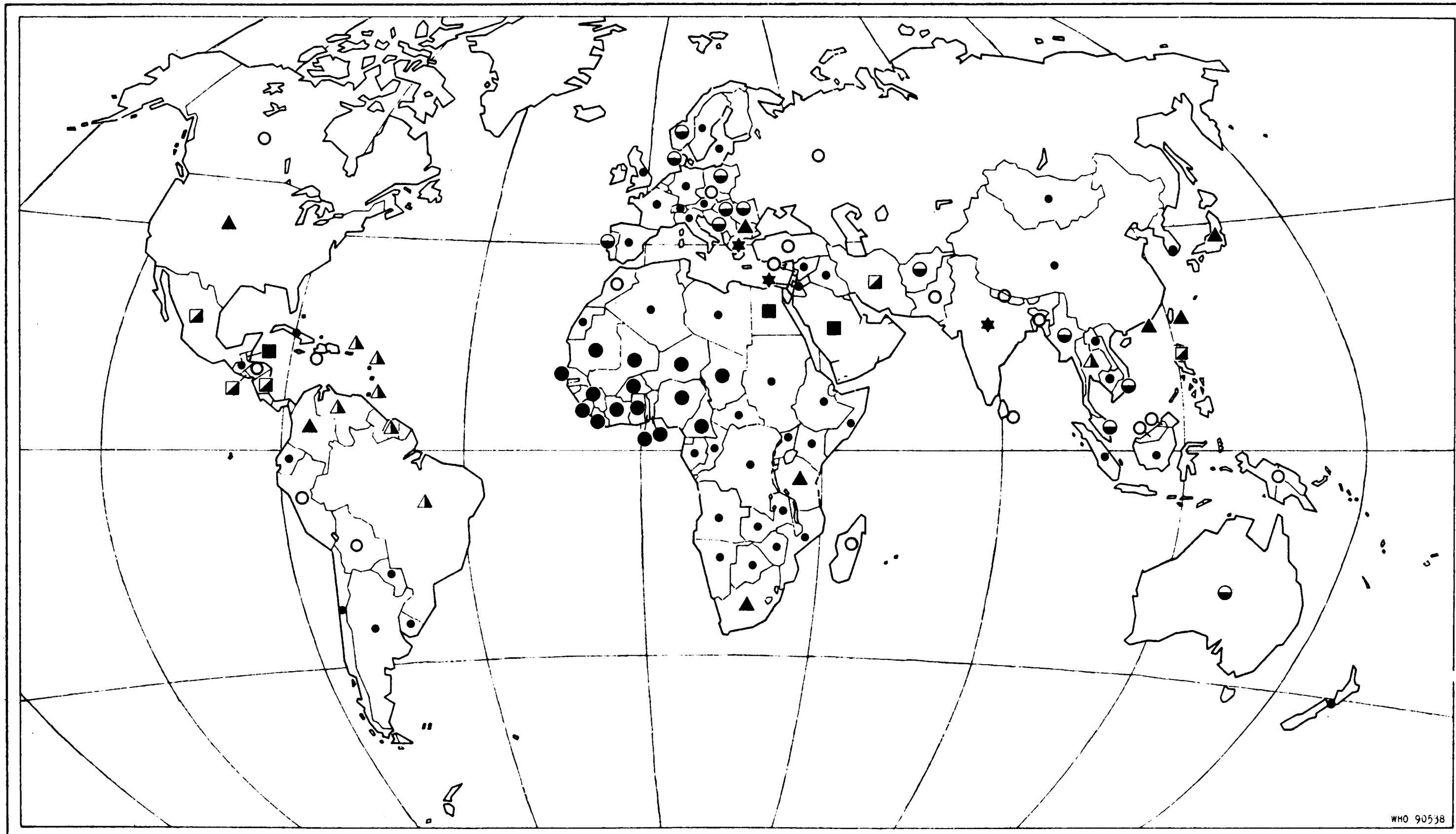
Finally, on the African continent, the difficulties of control and eradication are very considerable and could only be attacked with a highly effective insecticide such as HCH or OMS-33. The widespread dieldrin-resistance in West Africa renders HCH useless there.

Culicine mosquitos

Aedes aegypti. A campaign to eradicate the urban vector of yellow fever from the Americas was initiated about 15 years ago. At first, there was good progress and a number of countries claimed to be free of the vector. Later, trouble due to DDT-resistance and double resistance was encountered in the Caribbean Islands. In recent years there has been reinvasion of several mainland countries. Double, and even treble, resistance is appearing in such countries and there is a serious chance that this will jeopardize the whole undertaking.

Culex pipiens fatigans. This species is refractory to insecticides and has developed resistance to the

COUNTRIES IN WHICH SEVERE EFFECTS ON VECTOR CONTROL OWING TO RESISTANCE HAVE BEEN REPORTED



- ◪ Resistance in anopheline mosquitos
- ◭ Resistance in culicine mosquitos
- ◒ Resistance in other vectors
- ● Resistance in anophelines and culicines
- ■ Resistance in anopheline mosquitos and other vectors
- ▲ Resistance in culicine mosquitos and other vectors
- ✱ Resistance in all groups
- ○ No practical effect on control
- • No information received

chlorinated hydrocarbons in most places. However, it can be effectively controlled by the use of organophosphorus insecticides. Nevertheless, the fact that the chlorinated hydrocarbons can no longer be used represents a very serious loss and it is forcing consideration of control according to novel biological principles, which are far from being established as generally practicable.

Nuisance mosquitos. Coastal-breeding culicines in South-East Asia and the USA and flood-water culicines in California provided some of the first examples of resistance in mosquitos. Control is being achieved by substituting HCH for DDT and then using various organophosphorus insecticides to tackle different types of cross-resistance. When all the alternatives will be used up is a matter of conjecture.

Typhus and relapsing fever (Pediculus humanus)

A world summary of louse resistance in 1965 showed that it is prevalent in many places. Usually this develops as a result of intermittent delousing campaigns conducted by various health authorities. So far, resistance has not interfered with typhus control (although this is suspected in South Africa). Should an outbreak occur in a DDT-resistant area, it should be possible to employ an alternative insecticide.

Plague (Xenopsylla cheopis)

The most important weapons against plague are insecticides to kill the fleas and modern rodenticides to reduce the number of rats. Such measures have been generally successful, so that, for example, plague has disappeared from most of India, with small pockets remaining in Madras and Mysore. Urban epidemics are now exceedingly rare, but there is now some trouble in rural parts of Viet-Nam, and control is handicapped by resistance of the vectors. In India, too, it is said that the use of insecticides in the malarial campaign has induced resistance in fleas. This may hamper the elimination of remaining foci. Recent outbreaks of plague have been reported in Arusha, Tanzania.

Fly-borne diseases (Musca domestica, *etc.*)

Two kinds of disease are associated with flies: (1) enteric diseases (dysenteries) spread by *Musca domestica* (in Africa probably by *Chrysomya putoria*), and (2) ophthalmic diseases, the most serious being trachoma, spread by *Musca domestica* and *M. sorbens*. In both cases, there are other means of transmission of the disease, so that the part played by flies is less easy to assess than in infections which are exclusively insect-borne. Nevertheless, the association with flies is firmly established, since, in the early days before resistance was widespread, the use of DDT house-spraying was shown to reduce enteric infections. Resistance of houseflies is now so widespread and has extended to so many types of insecticides, that it is not possible to rely on chemical control in any region where conditions promote extensive breeding.

Bedbug infestations (Cimex lectularius, C. hemipterus)

Bedbug resistance (in both *Cimex lectularius* and *C. hemipterus*) is now exceedingly common in warm and tropical countries. The impact of resistance goes far beyond the loss of a simple method of eradicating a nuisance. By causing suspicion and antagonism in householders when spraying fails to kill bedbugs and houseflies, the success of antimalarial campaigns can be jeopardized.

Cockroach infestations (Blattella germanica)

The German cockroach must be given separate consideration from insects which are merely nuisances, in view of its possible implication in disease transmission. Sinca *Blattella germanica* is not very susceptible to DDT and since dieldrin-resistance is widespread, increasing reliance will have to be placed on organophosphorus and carbamate insecticides.

PUBLIC HEALTH PROBLEMS NOT GREATLY AFFECTED BY RESISTANCE

Onchocerciasis (Simulium *spp.*)

The use of DDT as a larvicide against the vector seemed a promising strategy, since applications to rivers can be effective for miles downstream. Treatments must be repeated over large infested areas (of perhaps different countries) until all adults die off, otherwise there will be reinfection. Nevertheless, eradication has been achieved and further success would have seemed to depend only on finance and logistics. Quite recently, however, resistance has been confirmed in Japan and Canada. Vigorous extension of control is likely to accentuate this trouble, but organophosphorus insecticides are a possible alternative.

Chagas' disease (reduviid bugs)

Reduviid bugs are naturally tolerant of DDT so that either dieldrin or HCH must be used. Both have been successful, but reports of resistance have recently come from Venezuela and Brazil. Substitute insecticides are therefore urgently required.

Trypanosomiasis (Glossina *spp.*)

Control of this vector has been largely dependent on making ecological changes in the habitat; and although this is expensive and slow, it is generally permanent. Changes through clearing are permanent only if followed up by settlement and development of the area. It is the expense of maintaining clearings that has resulted in the reduction of this method of control in many areas. Insecticides are coming more and more into use as technical developments lower their cost. So far there is no resistance, but the areas treated, though apparently large, represent only a small fraction of those occupied by tsetse flies.

Tick- and mite-borne diseases (Ixodidae, Argasidae, Trombiculidae)

Ticks and mites can be attacked while on the ground waiting for a host or by treatment once they have attached. The latter method commonly follows veterinary problems such as cattle ticks, and this has led to resistance in several species. Area treatment has been recommended for various hard ticks of medical importance and for the scrub typhus mite, while limited treatment of dwellings, caves, etc. has been used against soft ticks. So far, no resistance has been provoked by these measures.

Leishmaniasis (Phlebotomus *spp.*)

Comparatively little attack by insecticides has been directed against sandfly vector of the various forms of leishmaniasis. In several countries, however, DDT spraying against malaria vectors has had the effect of incidentally controlling *Phlebotomus* and stopping transmission of oriental sore and sandfly fever. No evidence of resistance has been adduced.

Headlouse infections (Pediculus humanus capitis)

Treatment with DDT or, preferably, gamma-HCH continues to give good results in most places. A recent report of suspected HCH-resistance in the United Kingdom is, however, disquieting.

CONCLUSIONS

To sum up, the problems arising out of resistance to the organochlorine insecticides have been apparent for some time and it has been evident that alternatives are required. Research in the past 5 years (much of it sponsored by WHO) has shown the value of various organophosphorus and carbamate insecticides. Almost certainly these will adequately meet the emerging requirements for most of the vectors mentioned. However:

1. Strategic policy, in the selection of the most suitable compound for use in different public health problems, is much more complex. Whereas DDT, HCH and dieldrin were generally effective for multiple uses, many new compounds are notably specific in application, and this involves both advantages and limitations.

2. It is known that resistance to organophosphates and carbamates can occur, and has occurred, in some species of public health importance. It is worth noting that:

(*a*) although the levels of resistance observed with organophosphates and carbamates are not generally of the very high order found with organochlorine compounds, yet they are often sufficient to preclude their effective use in the field;

(*b*) very little is understood about the liability of individual new compounds to provoke resistance;

(*c*) information on cross-resistance spectra is accumulating, but it is largely empirical. As a result, events in the field where these new insecticides have been tried are variable and largely inexplicable.

In view of the still growing problem of resistance, it is difficult to be sure of the continued reliability of the organochlorine insecticides. Therefore, control of insects of public health importance will increasingly depend on use of the organophosphates and carbamates. This being so, attention must be focussed on all facets of their use and of possible instances of resistance to them.

RÉSUMÉ

CONSÉQUENCES DE LA RÉSISTANCE AUX INSECTICIDES POUR LA LUTTE CONTRE LES VECTEURS ET LES MALADIES QU'ILS TRANSMETTENT

Un questionnaire élaboré par l'Organisation mondiale de la Santé a été envoyé à une centaine de services d'hygiène du monde entier afin de recueillir des précisions sur les méthodes d'utilisation des insecticides contre les vecteurs et sur les aspects et les répercussions des phénomènes de résistance. Le présent article résume les réponses obtenues et énonce un certain nombre de conclusions.

Jusque tout récemment, on a mené la lutte chimique contre les vecteurs en recourant surtout à trois composés à base d'hydrocarbures chlorés, le DDT, la dieldrine et l'HCH, qui se sont révélés remarquablement efficaces. Les deux premiers ont été employés sur une très large échelle au cours des programmes d'éradication du paludisme. L'apparition d'une résistance à l'un ou à l'ensemble de ces insecticides suscite de sérieuses difficultés lors des activités d'éradication du paludisme dans certaines régions (Mexique, Amérique centrale, golfe Persique); c'est également l'un des facteurs qui ont empêché la mise en œuvre de certains programmes d'éradication, notamment en Afrique.

La résistance au DDT est très répandue chez *Aedes aegypti* dans les Caraïbes. Elle a évolué vers la double résistance (DDT-dieldrine) et se propage maintenant sur le continent américain où elle compromet sérieusement les campagnes visant à l'éradication de ce vecteur. *Culex pipiens* spp. et *Culex p. fatigans* font preuve en de nombreux endroits d'une résistance au DDT et à la dieldrine et ces insecticides ne peuvent être utilisés pour combattre la filariose de Bancroft. La résistance au DDT est fréquente chez le pou du corps et chez la puce vectrice de la peste, cette dernière étant en outre, en beaucoup d'endroits, résistante aussi à l'HCH et à la dieldrine. On ne peut plus compter sur l'action des insecticides rémanents à base d'hydrocarbures chlorés pour lutter contre la mouche domestique. L'infestation par la punaise de lit ne peut être combattue dans les pays tropicaux et la blatte (*Blattella germanica*) devient difficile à éliminer dans les régions tempérées. Jusqu'à présent, on ne signale que peu ou pas de cas de résistance chez les mouches tsé-tsé, les simulies, les phébotomes, les triatomidés, les tiques et les acariens vecteurs de maladies humaines. Il n'y a cependant pas lieu de manifester un optimisme excessif, car une résistance confirmée est apparue récemment en plusieurs endroits chez les simulies, et la résistance est suspectée également chez les triatomidés.

Les problèmes que pose la résistance aux insecticides à base d'hydrocarbures chlorés sont connus depuis un certain temps et on s'est rendu compte de la nécessité de rechercher des produits de remplacement. Au cours des cinq dernières années, les études, souvent patronnées par l'OMS, ont mis en lumière l'intérêt de divers composés organophosphorés et des carbamates. Il est presque certain que ces produits permettront de faire face à la situation en ce qui concerne la plupart des vecteurs en cause. Cependant les modalités de la sélection des composés les plus aptes à résoudre les problèmes particuliers de santé publique sont complexes. Alors que le DDT, l'HCH et la dieldrine pouvaient généralement être utilisés dans toute une série de circonstances, ces nouveaux composés sont remarquablement spécifiques, ce qui comporte certains avantages, mais a aussi pour effet de limiter leur emploi. On sait en outre que la résistance aux organophosphorés et aux carbamates risque d'apparaître — et est en fait déjà apparue — chez certaines espèces de vecteurs. Bien que dans ce cas le degré de résistance soit généralement faible par rapport à celui qui se manifeste vis-à-vis des insecticides à base d'hydrocarbures chlorés, il peut cependant avoir pour résultat de rendre impossible toute utilisation pratique. On ne dispose que de données très fragmentaires sur l'aptitude de chacun des nouveaux composés à susciter la résistance et les observations que l'on réunit actuellement sur les modalités et l'amplitude des phénomènes de résistance croisée sont en grande partie empiriques. Il importe donc d'étudier attentivement tous les aspects de l'emploi des organosphosphorés et des carbamates et de dépister tous les cas éventuels de résistance à ce type d'insecticides.

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