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THE USE OF CHEMOSTERILANTS FOR VECTOR CONTROL

by

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1. INTRODUCTION

For about 20 years many arthropods of medical and veterinary importance have been kept under control by the intelligent use of residual insecticides, for the benefit of human health and welfare. But the mass spraying of insecticides, either for vector control or disease eradication programmes, as well as for agricultural and domestic uses, has selected insecticide-resistant populations of various vectors in many areas of the world. Year after year the number of resistant species and their distribution increases. Now 60 to 70 species of medical and veterinary importance, belonging to nine major families, are resistant to one or several chemical groups of residual insecticides, and their occurrence is a very serious complicating factor for the organization and development of many public health programmes (WHO, 1963; Coz et al., 1964; Pal, 1964; Shaw & Stones, 1964; Ungureanu, 1964). WHO has sponsored a co-ordinated research programme for the development and screening of new insecticides on a world-wide basis, the results of which are very promising, but it would be wiser not to rely entirely on one type of vector control and to investigate other vector control possibilities than insecticides.

Insecticides used for public health programmes are, as a rule, selective toxicants for insects, with a low mammalian toxicity. However, their use modifies more or less the environmental conditions, and the greater the treated area the greater the impact on the environment. Moreover, some of the most widely sprayed insecticides are chemically very stable and disappear only slowly from treated premises, soils, watercourses, and so on. Contamination risks of the environment belong to two major types: acute and immediate intoxications,

easy to detect and to prevent, and long-term accumulation of the most stable compounds; this last risk is less easily detected and nothing but time can clear the contaminated areas. Up to now this situation has not caused difficulties for human health, the sporadic damages being restricted to the most developed countries and being mainly induced in wildlife. However, such a situation underlines the necessity to combine all available methods of vector control to get the best of each of them in an integrated control programme, and to use residual insecticides only when and where they offer the best prospects of success, so as to avoid useless contamination of the environment. One of the newly-developed control procedures is based on the mass release of sterilized males.

2. THE THEORY OF VECTOR CONTROL BY MASS RELEASE OF STERILIZED MALES

In many vector species the female is inseminated only once for its whole life or, when inseminated several times, the first-received batch of spermatozoa is the major one, or the only one, employed for egg fertilization. There are, however, some exceptions (Roth, 1948; Goma, 1963).

If it is possible to release, in a stable population, as many sterile males as there are normal males, 50% of the virgin females will be inseminated by sterile males and either will not lay eggs or will lay sterile eggs, with the remote possibility of inducing parthenogenetic development. The next generation will be reduced to 50% of the initial generation and, if the number of released sterile males is constant, 33% only of the resultant females will produce a progeny, and so on along a decreasing exponential curve, until the disappearance of the species. Success will be achieved much more quickly if, from the beginning, the sterile males outnumber by several times the normal males (Knipling, 1955).

It would be more difficult to get the same results by release of sterile females as the males copulate many times during their first days or weeks of life and would be able anyway to inseminate normal females. The mixed release of both sterile males and females slows down the process, a proportion of the sterile males being diverted from the normal to the sterile females.

Sterile males, to be competitive with normal males, must have a normal expectation of life or at least must be sexually active in large numbers for as long as the normal males. They must also inseminate females with a normal amount of spermatozoa and accessory gland secretions, because the females with empty or partially empty spermathecae will agree to be inseminated a second time. Sterile males must be also potent inseminators. The difficulty to fulfil all these conditions is a second reason for releasing a number of sterile males several times higher than the estimated number of normal males, the ratio of sterile to normal males being at least 10:1. Finally, sterile males must be evenly scattered among wild populations. Difficulties increase with the natural density of the vector population, with species either with dormant eggs and/or with multiple inseminations, and with short flight-range species.

The first known method of male sterilization was based on gamma- or X-ray irradiation of larvae or pupae, which implies laboratory mass rearing of the vector to control. The first widescale scheme of vector control by mass release of sterilized males was carried out against a pest of veterinary importance, the screw-worm Cochliomyia hominivorax. The success of the screw-worm eradication programme, first in 1954 in Curaçao (Baumhover et al., 1955) and then in 180 000 km^2 of the south-eastern United States during 1958 and 1959 through the release of more than two billion sterile flies (Knipling, 1960), not only stimulated wide interest in insect control by male sterilization and in laboratory mass-rearing of pests of economic importance (Fay et al., 1963; Morlan et al., 1963), but also in control by sterilization with chemicals as well as by irradiation.

The sterilization by irradiation requires costly installations, not very easily handled in field conditions. Moreover, many workers have stressed that irradiated males have a shorter expectation of life and are less competitive for mating than normal males (Sacca, 1961 - Musca domestica; Ramakrishnan et al., 1962 - Culex pipiens fatigans; Henneberry & McGovern, 1963 - Drosophila melanogaster; Stahler & Terzian, 1963 - Aedes aegypti . . .), the safety margin between the 100% sterilizing dose and the lethal one being often very narrow. Chemosterilants offer better prospects of development and practicability (Schmidt et al., 1964), and the screening of thousands of chemicals for sterilizing properties against insects was begun some years ago in laboratories of the Agricultural Research Service of the United States Department of Agriculture.

3. THE CHEMOSTERILANT COMPOUNDS

3.1 Chemical nature and properties

Chemosterilants are chemicals capable of causing sexual sterility; they prevent reproduction in insects or other organisms. Insect chemosterilants may act in one of the three following principal ways:

(a) they may cause insects to fail to produce ova or sperm;

(b) they may cause the death of sperm and ova after they have already been produced;

(c) they may injure severely the genetic material in the sperm and ova and, although the sperm and ova remain alive and the sperm retains full motility, the zygotes, if formed, do not complete development into mature progeny.

The two first ways are not very efficient for vector control as normal females can be induced to mate later on with fertile males if their spermathecae are empty. The third type of action presents the greatest interest at the present time and is that shown by the so-called "radiomimetic" compounds.

The selection of insect chemosterilants has been guided from the beginning by the relationship between compounds effective in cancer chemotherapy and mitotic agents (Smith et al., 1964; Fahmy & Fahmy, 1964; Chang, Tsao & Chiang, 1963). Other investigations have been carried out with compounds similar to normal insect metabolites which could replace these metabolites and stop cellular development. Then some guidelines have been established in selecting chemical and structural features characteristic for chemosterilants amongst all the candidate compounds investigated.

The chemosterilants can be classified into two main categories, the anti-metabolites and the alkylating agents, which are also radiomimetic. Some other agents, for the time without practical importance, cannot be easily classified (Mouchet & Rageau, 1963; Kenaga, 1965). The antimetabolites are mainly active against female insects and their action may be of a temporary nature. The alkylating agents are mutagenic and damage the genetic material of ova and sperm but generally do not inhibit live spermatozoa formation; their action is of a more permanent nature.

The most promising alkylating agents are the derivatives of aziridine, some of them having been used for several years in the textile industry and in cancer therapy. The commonly investigated aziridine derivatives for insect chemosterilization are now the following:

tepa = tris(1-aziridinyl)phosphine oxide

metepa = tris[1-(2-methylaziridinyl)]phosphine oxide

thiotepa = tris(1-aziridinyl)phosphine sulfide

apholate = 2,2,4,4,6,6-hexahydro-2,2,4,4,6,6-hexakis(1-aziridinyl)-1,3,5,2,4,6-triazatriphosphorine

The toxicological risks inherent in the mutagenic properties of alkylating agents restrict their study as insect sterilants to laboratory experiments and to very limited field trials under close supervision. However, recent research has shown that some compounds, hempa (= hexamethylphosphoramide) and hem (= HMM = hemel = hexamethylmelamine) structurally similar to tepa and to tretamine (= 2,4,6-tris(1-aziridinyl)-S-triazine) respectively, but lacking alkylating properties and being of low toxicity to mammals, still retain the property of sterilizing insects (Chang et al., 1964). We can hope that further investigations will lead to the discovery of insect chemosterilants more acceptable for practical usage than those hitherto available.

Used as dry deposits, tepa and metepa disappear rapidly by volatilization and they are also actively sorbed on porous surfaces (Dame & Schmidt, 1964). Thiotepa is probably slightly less volatile and has been active against female Aedes aegypti during 23 days after application at the dosage of 400 mg/m^2 on filter-paper (Bertram, 1964).

In solutions, alkylating agents are slowly decomposed in inactive compounds. Tepa and metepa are more stable in neutral or in slightly alkaline solutions than in acid solutions. Decomposition rates vary directly with temperature, but even at 25°C the half-life may attain 32 days for tepa and 72 days for metepa (Beroza & Borkovec, 1964. In Bertram, 1964). However, Dame Woodard & Ford (1964) stress that, in field conditions, tepa solutions lose their efficacy in three days.

Inside insects, alkylating agents distribute themselves quite rapidly into all tissues, as shown by Dame & Schmidt (1964) with radio-labelled metepa and mosquitos. But the compounds are rapidly excreted and detoxified and retain their sterilizing form no more than six to eight hours after the end of the insect treatment (Plapp et al., 1962)

3.2 Biological action of chemosterilants in laboratory experiments

In laboratory experiments, chemosterilants have induced sterility in a great variety of organisms (Cressman, 1963 - acarina; Burden & Smittle, 1963 - cockroaches; Chang & Chiang, 1963 - moths), including mammals (Gaines & Kimbrough, 1964), and their efficacy and limitations have been assessed on some of the major insects of medical importance (Smith, 1964). Some compounds are much more toxic for some species than for others, and the order of efficacy of chemosterilants varies according to the species used and the application method employed in screening tests (Gouck et al., 1963a).

Chemosterilants can be applied to insects by various methods: dipping, dusting, topical application, tarsal contact with treated surfaces, or ingestion of treated baits (Dame, Woodard & Ford, 1964; Dame & Schmidt, 1964; Crystal, 1964). Physical properties varying with the compounds, standardized assessment techniques cannot be used for all candidate compounds; however, the majority of routine assessments are done by oral application (Gouck et al., 1963a; Chang, Tsao & Chiang, 1963).

3.2.1 Biological action on vectors

3.2.1.1 Males

The sterility induced by apholate treatment of Aedes aegypti larvae is caused by chromosomes damaging, with dilatations, linkages, splittings, and so on. Testes have a normal size, but produce less spermatozoa (Rai, 1964). Bertram (1963) has found active sperm in thiotepa-sterilized males of A. aegypti, mating and insemination being still possible; the sterility was complete in the days following the treatment, but later on some of the inseminated females gave eggs with a hatch rate of 13%. Similar results have been obtained in Drosophila sterilized by tretamine by Fahmy & Fahmy (1954). Such results are probably the consequence of the greater susceptibility to chemicals of post-meiotic stages (sperms, spermatids) than of earlier pre-meiotic stages in spermatogenesis. It is possible that longer exposures to, or increased concentrations of, the toxicants could kill the primary germinal tissue and eliminate all possibilities of recovery.

Chemosterilized males are not always as vigorous or able to copulate as the normal males (Dame & Schmidt, 1964; Crystal, 1964), and the amount of sperm is sometimes insufficient, leaving the females amenable to further copulation with normal males and subsequent formation of fertile eggs (Dame, Woodard & Ford, 1964).

However, for practical application, chemosterilized males are generally (but not always) competitive with normal males (Murvosh et al., 1964; Labrecque et al., 1962a), and the sterile spermatozoa accomplish a high rate of fertilization giving unfertile eggs, even when they are mixed with normal spermatozoa in the female spermatheca (Labrecque et al., 1962a). Nevertheless, in some species, like Culex p. fatigans, the safety margin between the sterilizing and the lethal concentrations is very narrow for the majority of the most promising chemosterilants (Mulla, 1964).

3.2.1.2 Females

If the vector control programme is based upon the release of laboratory-bred insects into wild populations, it is not worthwhile to release sterilized females, firstly because their impact on the spermatozoa availability of wild males will be almost nil, and secondly because such a procedure will increase the size of the biting section of the population. But, as we shall see later, chemosterilants offer wider prospects to vector control operations than irradiation procedures and, under some restrictions, will probably be used in the future directly against wild males and females.

Wild-caught female mosquitos, already inseminated, are sterilized by resting on tepa- or thiotepa-treated surfaces even when follicles of the treated females are as developed as stage V, as shown by Weidhaas (1962) with A. quadrimaculatus, and by Bertram (1963) with A. melas. Similar results have been observed in laboratory conditions with A. aegypti, A. togoi and C. pipiens (Bertram, 1964).

In treated females the ovarian development is soon anarchic, each follicle having its own rate of development. The amount of laid eggs is often nearly normal during the first oviposition, but decreases sharply in the following ovipositions due to somatic deterioration of ovarioles, and there is no hatching. At least in mosquitos damages to the spermatozoa in the spermathecae of treated females seem to be the main reason for sterility of the first batch of eggs laid after exposure; in comparative experiments with low dosages of chemosterilants the percentage of infertile eggs is far higher if females are inseminated before exposure than if they mate after exposure (Bertram, 1963). Oogenesis can also be inhibited from the beginning if females are exposed to chemosterilants soon

after their emergence, but such a susceptibility of the follicular epithelium is restricted to the first hours of life; later on the effects of chemosterilants on ovogenesis are only conspicuous on a long term basis (Bertram, 1963; Crystal, 1963; Weidhaas, 1962; Dame & Ford, 1964; Crystal & Lachance, 1963).

3.2.1.3 Larvae

Insects can also be sterilized as adults following their treatment as larvae or pupae by alkylating agents, but the mortality is generally increased at moulting and emergence periods. Tepa and thiotepa seem to be more promising than apholate for such usage. The treatment of natural breeding places cannot be considered, as the compounds are mutagenic, and should be applied at short intervals, but larval treatment could be a method of choice for mass sterilization of reared mosquitos (Dame, Woodard & Ford, 1964).

3.2.2 Biological action on transmitted parasites

Chemosterilants can act in two ways on transmitted parasites during the sterilization of infested vectors. They can either kill the parasites, or cause mutations of the parasites into new strains of different pathogenicity. If females are treated before becoming infested the action of chemosterilants is nil, as the compounds disappear from treated insects in the hours following their absorption. Up to now, investigations have been carried out only on malaria and filarial parasites.

3.2.2.1 Malaria parasites

Several investigations have been carried out, all based on A. aegypti and Plasmodium gallinaceum.

Altman (1963) reported substantial but variable reduction of malariometric indices (by about 85%) by exposing the vector for 90 to 540 min to 100 mg/m^2 of tepa on glass immediately before and after the infective meal and also, on one occasion, when sporozoites had reached the glands.

Using different strains of the same mosquito and Plasmodium and thiotepa, Bertram, Srivastava & Msangi (1964) have got on the whole similar results, but with an average reduction in malaria transmission of 25% only. The deposit used was 400 mg thiotepa per square metre. Contacts of the mosquitos with the treated surface for one or two hours were almost inefficient, but better results were obtained with three hours of contact. The action of the chemosterilant seemed particularly important when the mosquitos were exposed some hours only after the infectant blood meal (when gametocytes become gametes), but less efficient later on. In the most favourable conditions, only 9% of the chickens were infected by the treated mosquitos, with 100% infections in the controls. However, a second period of important susceptibility of malaria parasites occurred 48 hours after the infectant blood meal, during the meiosis in early oocysts (30% of chickens infected). When the transmission to chickens occurs, the transmitted Plasmodium is normal and can be further transmitted by A. aegypti without modification of its pathogenicity; when occurring, the reduction of transmission is not only caused by the interruption or decrease of oocysts and sporozoites production, but also the loss of effectiveness of the sporozoites, probably through genetic damages (Bertram, 1964b).

The vector in both these experiments has been more easily sterilized than the parasite.

3.2.2.2 Filarial parasites

The only experiment dealing with the action of chemosterilants on filarial parasites has been carried out by Bertram (1964a), with Brugia patei and Aedes togoi exposed for one to three hours to 400 mg thiotepa per square metre deposits on glass.

Contact of one hour does not change the speed of development of filarial worms in the mosquito, but two hours' and more than three hours' exposure slows down the development of the parasite, which apparently never reaches the infective stage and dies in the thoracic muscles. It must be noted that the chemosterilant dose received by female mosquitos during such experiments is far higher than the required one for sterilization, and is sufficient to kill 95% of the males in the 24 hours following exposure.

3.2.3 Biological action on mammals

The toxic hazards of chemosterilants have recently been investigated and summarized by Barnes (1964), Gaines & Kimbrough (1964) and Hayes (1964).

The present conclusions are of a very temporary nature, as new compounds are discovered every year, some of them not belonging to the previously investigated chemical groups. Moreover, minor chemical substitutions can transform a compound of low mammalian toxicity into another one far more toxic. The two main categories into which are classified the chemosterilants do not correspond to specific physiological action but to large chemical or biological groups, alkylating agents and antimetabolites. So no extrapolation of the toxicological investigations already carried out will be permissible in dealing with new compounds (Barnes, 1964; Hayes, 1964).

On the whole, alkylating agents are far less carcinogenic than expected by the workers using them as tools in cancer research. Human beings in cancer therapy have supported 0.6 mg thiotepa/kg (in three successive doses of 0.2 mg/kg) and thiotepa can be tolerated with as high a dose as 10-40 mg a week, with some variation in individual susceptibility. Tetramine has been used up to doses of 15-25 mg initially and 2.5-5 mg weekly, but some patients can only support one tenth of these amounts without bone-marrow depression.

On rats, which are probably less sensitive than humans to at least some of the actions of alkylating agents, five daily doses of 0.4 mg/kg of thiotepa rendered males sterile for five weeks, and tetramine given as 25 doses of 0.05 mg/kg over a period of 30 days gave the same results; such rats remained fully active and mobile, sexually active, and their spermatozoa has been observed to penetrate the ovum of the female, but without resulting progeny. These effects of thiotepa and tetramine on fertility are completely reversible (Jackson, Fox & Craig, 1959; Boch & Jackson, 1957). Susceptibility of rats is very variable, and so are the damages to the spermatogenesis which are comprised between slight damage to the sperm and complete destruction of the seminiferous epithelium, thiotepa and tetramine, although non-persistent in the tissues, having some cumulative action (Jackson, Fox & Craig, 1961).

During experiments with rats, Gaines & Kimbrough (1964) have observed that metepa and apholate in one administration in the diet are about as toxic as DDT, and that tepa is about as toxic as dieldrin; tepa and metepa are also toxic if introduced by dermal application. In such conditions, the CL 50, in mg/kg, is 136 for metepa and 37 for tepa. When rats received daily small doses of metepa in their diet (5 mg/kg/day), the general condition of the animals was good, but a cumulative action of the chemosterilant caused atrophy of testis in 77 days (in 55 days when the daily dose was 10 mg/kg) and in 197 days with 2.5 mg/kg. Low doses of 1.25 mg/kg/day were apparently not harmful. The damage to testis was to some extent reversible, but this aspect has not yet been adequately studied. When the male sterility is not complete, some reduction in the number of babies occurs, but their further development seems perfectly normal, without any effect of parent treatment on their potentialities and survival.

The chemosterilants which are now under investigation have not shown any sign of carcinogenic activity. They exert on mammals about the same effects as on insects, and at low dosages have a highly specific and localized action on the developing sperm of mammals. It is only at far higher dosages that these compounds depress the bone-marrow activity (Barnes, 1964; Hayes, 1964).

Hempa has a sterilizing action at concentrations 50 times higher than tepa, but its CL 50 for rats is as high as 2600 to 6400 mg/kg, against only 37 mg/kg for tepa. Besides, hempa has no mutagenic or carcinogenic properties.

Tepa, metepa, thiotepa and apholate are more toxic than the commonly used insecticides. They are quickly metabolized and excreted without apparent accumulation in the organism; however, they seem to exert a cumulative effect when routinely absorbed, and may sterilize human beings at dosages which are not harmful if only behaviour and survival are taken into account. So it seems unthinkable to use the compounds now available for indoor house-spraying or for extensive treatment of breeding places (Barnes, 1964; Hayes, 1964).

3.2.4 Possibilities of resistance to chemosterilants

Hazard et al. (1964) have investigated the possibility of selecting a strain of A. aegypti resistant to apholate sterilization by larval exposure. In standardized rearing and treatment conditions the percentage of sterility decreased from 96% to 46%

in four generations with 5 ppm apholate in breeding water, and from 100% to 72% in six generations with 15 ppm apholate. So Aedes aegypti seems able to develop some resistance to apholate, with a decrease of efficacy of four to five times of that compound.

3.3 Possible use of chemosterilants for insect control

As available now, the chemosterilant compounds can either replace sterilization by gamma radiation, on laboratory-bred vectors for subsequent release, or be used to sterilize wild populations.

Sterilization by chemicals would be simpler and cheaper than by gamma radiation, and the facilities required would be more readily movable. Moreover, the males treated with chemosterilants are far more competitive than the irradiated ones (Weidhaas & Schmidt, 1963), but the general limitations of the methods would be the same as with sterility induced by irradiation.

The big advance with the chemosterilants is their possibility of application to wild populations. If sterilizing chemicals could be safely applied to natural populations, control or even eradication would be realized by induced sterility without the necessity of rearing and releasing large numbers of insects. If wild males as well as wild females could be treated, the decrease of natural populations would be very sharp, a large proportion of the normal males inseminating sterile females and many normal females being mated by sterile males (Knipling, 1962). Up to now, the administration of chemosterilants in the adult food or on resting places seems to be the only practical method for field use and is dependent on the adjunction of powerful and selective attractants (Liu, 1962; Hocking, 1963; Lhoste, 1962; Steiner et al., 1961; Brown, West & Lockley, 1961), which could counteract the repellent effect of some of the chemosterilants (Sacca et al., 1965) and attract a high proportion of the natural populations.

Other developments in the use of chemosterilants await the assessment or discovery of new compounds without toxic hazards for mammals.

4. FIELD EXPERIMENTS WITH CHEMOSTERILANTS

Field experiments with chemosterilants have been restricted to a few small tests to explore possible methods of application and evaluation, mainly with house-flies, but some of the results of the field experiments carried out with gamma-irradiation sterilized males also gave useful information on the practical problems to be solved.

4.1 Anopheles quadrimaculatus

A. quadrimaculatus males from the laboratory colony of Orlando have been sterilized either by irradiation or by exposure to chemosterilants (contact with tepa or oral administration of apholate). The sterilized males were sexually potent and gave a high rate of fertilization of wild females in laboratory conditions, but they were unable to perform the same duties when released amongst the natural population of A. quadrimaculatus. When the experiment was duplicated using as sterile males the treated progeny of wild-caught females, the released males succeeded in inducing sterility in wild females. So it is probable that the initial failure was not due to chemosterilant-induced decrease in sexual competitiveness but to changes of behaviour during colonization and to basic inability of years-long colonized mosquitos to mate in field conditions with wild females of the same species (Dame et al., 1964).

4.2 Musca domestica

The results of only three field experiments carried out in Florida, each based on a different chemosterilant in cornmeal bait (with sugar, dried milk and dried egg added), have so far been published.

Labrecque et al. (1962) have assessed the efficacy of baits with 0.5% tepa on garbage dumps in one of the Florida Keys with once-a-week application for nine successive weeks. The island was relatively isolated and another dump, situated at about 50 km from the treated one, was used as a control. The house-fly and secondary screw-worm (Cochliomyia macellaria F.) densities were estimated in the most infested areas by the grid method. The sterility of females was investigated weekly on representative samples of the house-fly population. House-fly populations were reduced from 47 per grid to 0 within four weeks, and the proportion of egg masses (from females collected on the dump) containing at least one viable egg was reduced from 100% to 10% within four weeks; the per cent. hatch among all eggs laid was reduced to 1% within five weeks. After treatments were discontinued, the per cent.

viability rapidly returned to normal. During the entire period of the experiment, viability of eggs from females from the control dump ranged from 65% to 99%. It was not possible in this experiment to assess what proportion of the females was sterilized by feeding on the bait and what proportion by mating with sterile males. Blowfly counts in the treated area were also reduced markedly towards the end of the test, but all captured females oviposited freely on fresh meat and all the egg masses were viable; previous experiments have shown that blowflies are difficult to control with dry granular insecticidal bait.

Labrecque et al. (1963) have carried out an experiment with 0.5% metepa baits in a poultry farm near Orlando, in a non-isolated situation. Baits were distributed once a week during nine weeks and then once every two weeks. The density of house-flies was drastically reduced. The hatching rate of egg masses laid by the rare collected flies was less than 10%.

The third experiment was done by Gouck et al. (1963) with 0.75% apholate baits on garbage dumps of one island. Baits were distributed once a week during the first seven weeks and then five times a week during the last five weeks. The house-fly density decreased by 3 to 13 times during the first seven weeks, and by about 43 times during the last five weeks. The hatching rate of egg masses was decreased 2.6 times and 5 times respectively. Male fertility was not seriously affected by the weekly application of the baits, but decreased to 22% of the normal when baits were distributed five times a week.

4.3 Observations made during some of the field tests carried out with radiation-sterilized males

Four field experiments, three dealing with mosquitos and one with blowflies, based on release of radiation-sterilized males are very interesting.

Krishnamurthy et al. (1963) have worked with Culex p. fatigans in India. The results were not satisfactory, partly because the number of released males was not sufficient and partly because the human population did not agree to the release of any mosquito, even male and sterile.

Morlan et al. (1962) have released sterile males of A. aegypti in two areas of Pensacola neighbourhood, Florida, of about 1 square kilometre. They used two nearby untreated areas as control. The expected ratio of sterile to normal males (released as pupae) was 47:1 to 170 000:1 in the first area and 27:1 to 148:1 in the second area. Estimation of natural populations of A. aegypti was based on actual counts of larvae every second week; except for samples collected for identification, larvae were counted and returned to their original breeding places. Field-collected eggs, obtained by lining formerly infested receptacles with paper towels, were counted and submerged in a 24-hour-old mixture of 0.1 g brewer's yeast and 0.1 g ground dog chow in one litre of water; each hatching test was completed in the week following egg collection; larvae were identified and counted. In area 1 the releases were reduced, but failed to eradicate natural populations of A. aegypti; in area 2 the release of sterile males failed to reduce the natural population. The rate of egg hatching, on the average, was only 60% of the normal in the first area, but was 112% of the normal in the second area. Amongst the reasons for failure are the greater age of sterile males, released only once a week and competitive only some days with the normal wild males emerging every day, and the possible limited dispersion of the sterile males from the limited distribution of irradiated pupae.

Weidhaas et al. (1962) have released 1500 sterile males of A. quadrimaculatus per week and per square kilometre during 11 months in 10 different situations on islands of 5 km^2 in the Lakes Okeechobee and Panasoffkee, Florida. Another area was used as a control. To determine if these sterile males caused any reduction of, or sterility in, natural populations, the number of adult A. quadrimaculatus in resting stations, and the viability of eggs from females collected from these resting stations, were followed in the release and check areas. The releases did not conclusively induce any sterility in wild females, but it is possible that the natural population of one island was in the seasonal decline. Failure was attributed to the lack of basic knowledge of the biology and behaviour of A. quadrimaculatus (which is, en passant, one of the best-known American mosquitos), and in the difference in basic behaviour of colonized and wild mosquitos of the same species.

Donnelly (1964) has attempted to control the blowfly Lucilia sericata on one small island off the eastern coast of the United Kingdom. The treated area was about 2.5 km^2, with an estimated population of 2000 wild males of the blowfly. The releases were carried out for four to five months a year during two years, and the sterile males were overwhelming the wild ones. The failure of the experiment is partly attributed to density-dependent factors re-establishing the normal densities when the natural population was decreasing, and to a possible focal distribution of natural populations, the sterile males being less numerous than normal ones in such foci.

5. DISCUSSION AND CONCLUSIONS

Chemosterilants constitute a new class of vector control agents which offer promising possibilities for the future, but should be much more studied than they are.

According to the available published knowledge, the best-known compounds are not safe for field-scale use, except in special conditions. They are not chemically very stable, which in some aspects has the advantage of avoiding residual contamination of the environment, but decreases the possibilities of large-scale use of these compounds. The safety margin between the sterilizing dosage and the lethal one is not always very wide, although much more than with irradiation procedures. Sterile males are not always competitive with the normal males, and sometimes the sterility in both sexes may be of a temporary nature. New compounds will perhaps offer better prospects, but they are still to be discovered and we must not forget that one of our most potent residual insecticides was one of the first discovered ones; it could be the same for chemosterilants.

If chemosterilants are to be used as substitutes for irradiation to treat laboratory-bred vectors for further release in natural populations, a good deal must be learned on ecology, behaviour, dispersal, population dynamics, densities and genetics of natural populations of all vectors concerned (Birch, 1963; Knipling, 1963), and the methodology of mass colonization of competitive strains must be elaborated for the majority of pests and vectors.

If chemosterilants are to be used in an original approach to induce direct sterility in wild populations, they must probably be associated with powerful baits or attractants, and at the present time very few pests except house-flies can be controlled by efficient treated baits. Much more has to be learned about attractants if we want to exploit the full possibilities of chemosterilants (Hocking, 1963). However, in some circumstances, treated traps with periodic release could offer an efficient way to deal with species difficult to colonize but occurring in nature at low densities, like tsetse flies.

Chemosterilants, like other chemicals, are metabolized into inactive compounds inside insects, and we can expect the field development of chemosterilant-resistant populations of vectors, as we observed for insecticides. There is already one laboratory observation on apholate resistance in A. aegypti.

Vector control activities will probably be slowly modified by the development of chemosterilants, but these agents will rather supply additional possibilities of control than replace the already available methods and compounds. Their intelligent use requires the collection of basic information on the vector populations and will help to develop integrated control procedures.

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