Bull. Org. mond. Santé / *Bull. Wld Hlth Org.* 1963, **29**, Suppl., pp. 89-97

Prospects for Vector Control through Genetic Manipulation of Populations *

GEORGE B. CRAIG Jr [1]

Since the development of insecticide-resistance and the consequent partial failure of the chemical approach to the control of disease vectors, interest in the biological approach has re-awakened. An aspect of the latter approach that is of great current interest is "autocidal control"—that is, the use of insects for their own destruction. This paper discusses the various ways in which genetic mechanisms can be used to bring about the destruction of harmful insects, with special reference to those of medical importance. The author considers that the prospects for the genetic control of vector species are good, but stresses that before genetic methods can be applied on a field scale certain requirements must be met. For example, genetic technology must be expanded, a firm background of genetic knowledge of vector species must be built up, a great deal more information about vector ecology, particularly population dynamics, must be acquired, and techniques for the mass production of vector insects under controlled conditions must be developed.

The disparity between our theoretical knowledge of genetic mechanisms in insects and our utilization of genetic knowledge in applied entomology is rather surprising. The disparity seems especially inappropriate in view of the spectacular accomplishments of modern genetics in agriculture and medicine, the parent fields of applied entomology. Certainly, many of our entomological problems of today are due to genetic phenomena. In vector control, changes in insecticide-resistance, host choice, habitat, and susceptibility to disease are usually due to changes in the genetic composition of a population. One wonders if these genetic problems might have genetic solutions.

The recent renewal of interest in biological control of insects is encouraging. Conventionally, one thinks of biological control as the use of parasites and predators. In a broader sense, however, biological control contrasts with chemical and physical control and constitutes all essentially biological approaches to the prevention of damage by insects. One of these approaches of great current interest is "autocidal control", the use of insects for their own destruction. Genetic technology can provide a variety of mechanisms which could be used in autocidal programmes.

Several recent papers have discussed some possible applications of genetics to insect control. Among these are works by Downes (1959), Knipling (1960), Sailer (1961), Jenkins (1962), von Borstel & Buzzati-Traverso (1962), and LaChance & Knipling (1962). The present paper attempts to summarize these possibilities and to list a few additional ways whereby genetic methods could be used to manipulate insect protoplasm for the welfare of man instead of the insect. While emphasis here is on vector species, examples from other kinds of insects are considered as appropriate.

Population replacement

Jenkins (1962) has suggested controlling pests by substitution of related but innocuous forms. Most control programmes result in insect habitats being vacated only temporarily. Following control, habitats are refilled, often with better adapted or more resistant forms. Why not fill these habitats with genetic varieties or species that are not noxious to man but have ecological requirements similar to the forms removed? Essentially, the idea is to immunize environments. Among characters which might be changed by replacement are host choice, nutritional

* The work of the author, reported in this paper, received support from the following sources: (1) Research Grant No. AI-02753-04, National Institutes of Health, Public Health Service, US Department of Health, Education, and Welfare; (2) Research contract No. DA-18-064-AMC-52 (A), US Army Biological Laboratories; (3) The Radiation Laboratory of the University of Notre Dame, US Atomic Energy Commission Contract No. AT (11-1)-38.

[1] Associate Professor, Mosquito Genetics Laboratory, Department of Biology, University of Notre Dame, Notre Dame, Ind., USA.

requirements, domesticity or other behavioural characters, insecticide susceptibility and the ability to transmit disease.

Substitution of one species for another may occur without the deliberate intention of man. Aitken & Trapido (1961) give an interesting example from the malaria eradication programme in Sardinia in the late 1940's. Control measures directed against the principal malaria vector, *Anopheles labranchiae*, led to replacement of that species by a non-vector, *Anopheles hispaniola*. Before the control project, *Anopheles hispaniola* was a rare species; afterwards it was common and remained so. Moreover, *Anopheles labranchiae* did not return. Aitken & Trapido suggest that a dynamic equilibrium exists between anopheline species and that when one species is brought to extremely low levels, another species may fill the vacated niche. Thus, malaria may be controlled by anophelism.

Similar changes could be made within species. In Alaska, *Aedes communis* is a serious pest of man; in the vicinity of Churchill, Manitoba, there is an autogenous variety which is abundant but does not feed on man. Larval habitats of the two forms seem similar. Jenkins (1962) suggests introduction of the non-biting variety into Alaska in the hope that it will compete successfully with the pest form. In view of the great difficulties encountered in the chemical control of arctic mosquitos, such an approach might be worth trying. In Africa, a similar situation exists for both *Aedes aegypti* and *Aedes simpsoni*. In certain areas, populations are abundant, as evidenced by larval collections, but are rarely taken as adults. Could these populations which do not feed on man be introduced into areas where these species are vectors of disease?

The literature contains many instances of strain variation within vector species with regard to the ability to transmit disease. While relatively few genetic analyses have been made, there are reports of single genes which can make vectors refractory to pathogens. In *Culex pipiens*, Huff (1931) showed that susceptibility to *Plasmodium cathemerium* is inherited as a simple Mendelian recessive factor. Macdonald (1962) has isolated a sex-linked recessive factor in *Aedes aegypti* which confers susceptibility to *Brugia malayi*. A preliminary report by Macdonald & Wharton (1963) indicates that susceptibility to other filariae (*Brugia pahangi*, two strains of *Wuchereria bancrofti*) may be controlled by the same locus. Another gene in *Aedes aegypti* controls susceptibility to *Plasmodium gallinaceum* (Craig, manuscript in preparation). Unlike the previous cases, the refractory condition here is recessive. Owing to technical difficulties, the genetics of susceptibility to the arboviruses of vertebrates has not been well studied. However, genetic factors controlling the transmission of plant viruses are known from aphids, coccids and leafhoppers (Carter, 1962).

Uses for genes controlling ability to transmit disease seem evident. Jones (1957) called for further work on the isolation of strains refractory to malaria. He suggested that such strains could be introduced into areas where vector strains have been reduced in number by standard control measures. Thus, disease vectors could be rendered harmless, even though the population size is not reduced.

Parenthetically, it must be added that vector species also contain many genes affecting susceptibility to insect pathogens. Some of the current efforts to control insects with micro-organisms may be expected to fail because of the development of disease-resistant varieties. One suspects that such varieties will develop even faster than insecticide-resistant ones.

Induced sterility

In recent years, there has been a great deal of interest in the sterile-male method of insect control. This method involves mass rearing and release of sterilized individuals to compete with field populations. Knipling (1959) has called attention to the so-called bonus effect which occurs when a substantial portion of a population is sterilized instead of being killed outright. Obviously, the sterilized individuals fail to reproduce. Additionally, they compete with the fertile members of their sex for gametes of the opposite sex. When this mating competition is successful, those gametes are rendered ineffective. Knipling gives calculations showing a theoretical comparison of treatment causing sterility as opposed to lethality from an insecticide. Following his assumption of 90% effectiveness for each treatment in each generation, the sterility treatment gives extinction in five generations while the killing method requires twenty generations to achieve the same effect.

The dramatic success of radiation-induced sterilization for eradication of the screw-worm fly from the south-eastern States of the USA (Bushland, 1960) has stimulated extensive research on physical agents for the sterilization of insects. Radiation has been used in experimental programmes for the control of mosquitos, tsetse flies, houseflies, codlin-moths,

fruit-flies and others. Chemicals that induce sterility are receiving increasing attention (Knipling, 1962). It must be noted that programmes using either radiation or chemosterilants are surely genetic in nature. These agents are mutagens and they act by induction of dominant lethal mutations in the gametes (von Borstel, 1960). Such mutations generally cause mortality in the zygote rather than inactivation of sperm or ova.

Since both radiation and the chemosterilants often reduce vigour and mating competitiveness in treated individuals, techniques using naturally occurring sterility mechanisms may be more promising. Many evolutionary mechanisms causing isolation through sterility barriers between strains or species are available. If the isolation is reproductive but not sexual, mating will occur but fertile offspring will not be produced. Mass release of one form into the area of another will therefore result in sterility in field populations. A further benefit may accrue if sterile F_1 hybrids are produced. Such individuals often show heterosis or hybrid vigour and may have an advantage in mating competition.

A few examples of sterility barriers which might be used are given in Table 1. Vanderplank (1947) suggested that control of *Glossina swynnertoni* might be accomplished by massive introduction of *G. morsitans* into its territory. These largely allopatric species cross readily in the laboratory and in nature. Mating seems to be at random. Yet the crosses yield only a few offspring, mostly sterile. An experiment was set up for field release when *G. swynnertoni* was reduced to a low level by other means. The early results were said to be favourable, but the final outcome has not been reported.

Sterility factors causing unilateral incompatibility between populations provide other possibilities for control. In *Culex pipiens*, Laven (1959) has isolated at least 15 different crossing types. There are no barriers to mating or insemination between the types, but in various crossing combinations, some of them are fertile in one direction and sterile in the reciprocal cross. The sterility is due to a cytoplasmic factor, transmitted through the egg, which kills incompatible sperm after entry into the egg and before karyogamy. A similar situation exists in the *Aedes scutellaris* complex (Smith-White & Woodhill, 1954) and most probably in other mosquitos. It would seem that control could be effected by mass rearing, segregation of the sexes in the pupal stage, and release of males into an area with an incompatible crossing type. The principle of control is that of the sterile-male method as used in programmes with radiation sterilization. However, the incapacitating effects of radiation are avoided.

TABLE 1

SOME STERILITY MECHANISMS POTENTIALLY USEFUL FOR INSECT CONTROL

Species	Mechanism	Reference
Glossina (Tsetse fly)	Hybrid between *G.morsitans* and *G.swynnertoni* is sterile, yet the two species mate readily.	Vanderplank (1947)
Porthetria dispar (Gypsy moth)	Cross between weak and strong sex races produces ♀ offspring that are intersex and sterile. Suggests control by release of strong sex ♂ ♂ into north-east North America (weak sex).	Downes (1959)
Drosophila sp.	Insemination reaction (in many species crosses, a hard, mucoid plug forms to block vagina of ♀).	Patterson & Stone (1952)
Culex pipiens complex	Cytoplasmic factor causes unidirectional sterility between populations.	Laven (1959)
Aedes scutellaris complex	As above.	Smith-White & Woodhill (1954)
Anopheles gambiae	♂ progeny of many strain crosses are sterile.	Davidson & Jackson (1962)
Drosophila melanogaster	Maternally inherited sterility of ♂. Affects all ♂ offspring; must be maintained by continued outcross to normal ♂ ♂.	Lefevre & Jonsson (1963)

Alternatively, appropriate genetic crosses under controlled conditions can be used in mass-production of sterile males for subsequent release. Davidson & Jackson (1962) found crossing types in *Anopheles gambiae*. Crosses between types in either direction result in an F_1 with fertile females and sterile males. Although the latter have atrophied testes, usually devoid of spermatozoa, their sexual activity remains undiminished. Unlike the situation in *Culex*, the isolating factor here is chromosomal, acting as a single, sex-limited factor which is operational only in the heterozygous condition. Davidson & Mason (1963) have conducted small-scale laboratory experiments on the influence of these sterile males on populations. They established cages

with ratios of 1 normal female to 1 normal male to 10 sterile males. Almost all of the eggs deposited in these cages were sterile.

Self-propagating deleterious genes

A more subtle, yet potentially more effective, control method is provided by the introduction of deleterious genes which may spread through field populations. Such factors need not necessarily be lethal or act immediately. Knipling (1960) gives theoretical calculations showing that a constant low-mortality level, superimposed on normal environmentally caused mortality, results in drastic reduction of a population. In a discussion of various ways that insects can be used for their own destruction, Knipling suggests the development and release of strains carrying deficient genetic characters such as inability to fly or diapause or with special nutritional requirements or temperature sensitivity. He proposes that control could be accomplished with this method, provided such factors (*a*) do not prevent rearing under controlled conditions, (*b*) do not interfere with mating ability, and (*c*) act at particular times, i.e., lethals expressed in immature progeny or in adults during hibernation. LaChance & Knipling (1962) present calculations that support the feasibility of using insects with inherited lethal factors to control their own populations. They use a hypothetical programme directed against the boll weevil, *Anthonomus grandis*. Following their assumptions, extinction of the species in a limited area could be accomplished in a few years through repeated release of males carrying two lethal genes.

Seasonal lethals and density-dependent factors are particularly promising. In the latter case, factors should be incorporated in a population when it is at a low ebb. Such factors would then be expected to operate when the population is expanded. Indeed, any attempt to introduce genes into a species should be timed to take advantage of the natural fluctuation in population cycles.

Factors distorting the sex ratio should be useful, especially where only one sex is noxious, as in the case of mosquitos. In *Drosophila*, there are many genes which result in progeny that are all or predominantly of one sex. For an example from *D. melanogaster*, the mutant *daughterless* of Bell (1954) is an autosomal recessive factor. When homozygous females are mated to any male, they produce normal sons but no daughters. In *Aedes aegypti*, Craig, Hickey & VandeHey (1960), have described an inherited factor which causes a predominance of males in certain strains. In single-pair crosses, this factor caused production of progeny of about 20% females. In more recent work by Hickey & Craig (1962), a new stock producing an average of 10-12% females has been isolated. Single crosses producing up to 130 males and no females from a single egg batch are not uncommon. The factor does not act by selective mortality. It operates only in males and is passed from male-producing fathers to their male offspring. The mechanism seems to be meiotic drive operating at or near the sex locus and causing selective production of male-determining gametes.

Infective factors can also distort sex ratios. In the *Drosophila willistoni* group, a spirochaete causes production of all-female progeny (Malogolowkin & Poulson, 1957; Poulson & Sakaguchi, 1961). This agent is passed through the egg cytoplasm from mother to offspring but infection can also occur by ingestion (Carvalho & da Cruz, 1962). Moreover, it acts in several related species (Malogolowkin, Carvalho & da Paz, 1962). One can well imagine the effect of spraying such an agent on field populations. It is evident that this would be a form of genetic control because various genotypes differ in their sensitivity to the spirochaete. Distortion of sex ratios must result from certain of the microsporidial infections described by Kellen (1962). In infections of *Culex tarsalis* with *Thelohania california*, male larvae die but females survive to pass the parasites on to their progeny by transovarian transmission. It would be interesting to conduct population cage experiments to determine the effect of male lethality and disproportionate sex ratio on the frequency of fertilization of females.

Methods for propagating genes in populations

In the past, the use of deleterious genes for control has seemed impracticable because of the difficulty in incorporating these factors into field populations. However, modern bio-engineering and genetic technology provide ways of surmounting this obstacle. By mass production and release, populations can be overwhelmed by a flood of unfavourable genes. Repeated release of genetic defectives should maintain a pressure which would depress the size of the reproducing population. The screw-worm programme has demonstrated the practicability of this measure.

However, less drastic measures are available. Certain genes or special combinations of genes can increase in frequency in a population in spite of

their deleterious effects. Among prospective mechanisms to increase gene frequency are heterosis and meiotic drive.

Some heterotic factors are carried in populations even though they are disadvantageous as homozygotes. In *Drosophila melanogaster*, there is a recessive lethal gene, *l*(2)55i, which increases the fecundity of heterozygous females so that they produce 30% more eggs than the wild type (Schnick, Mukai & Burdick, 1960). Mukai & Burdick (1959) started two population cages with 5% of individuals $l/\pm$ and two other cages with 100% $l/\pm$. After about 16 generations, all four cages reached the same equilibrium point, about 42% of individuals being $l/\pm$ in each cage.

A. B. Burdick (personal communication) of Purdue University designed a mechanism for the control of *Drosophila* using *l*(2)55i plus *daughterless*, a gene previously described. These two genes are closely linked on the second chromosome. Burdick combined the two in trans-phase in a single stock and released it near a bottling-plant in Wakayama, Japan, an area heavily infested with *Drosophila*. While the experiment could not be followed closely, it is significant to note that one year after the release, *D. melanogaster* was rare in the area but abundant elsewhere. In samples collected exactly 12 months after release, 35 of 75 flies carried the lethal chromosome. It is not unreasonable to suspect that this mechanism depressed the population in the area.

Perhaps the best hope for field propagation of deleterious genes is through the distortion of segregation ratios brought about by meiotic drive. In classical Mendelian genetics, one learns that gametes in a heterozygote are produced in a 1:1 ratio. In an increasing number of cases, there is evidence of preferential segregation favouring one kind of gamete at the expense of the other. Thus, a locus or a chromosome which exhibits meiotic drive has an advantage because it is present disproportionately often in the gametes contributing to each generation. Such a factor will tend to increase in a population. This provides a mechanism whereby a few individuals introduced into a population will have their chromosomes pass into the genetic make-up of the whole population. Meiotic drive is probably a widespread phenomenon. As indicated in Table 2, examples are known from plants, mammals and insects. Since much of current genetic theory is based on the assumption of 1:1 segregation, this area has stimulated a considerable amount of interest among geneticists.

TABLE 2

SOME CASES OF MEIOTIC DRIVE IN DIVERSE ORGANISMS

Organism	Modified element	Reference
Drosophila obscura	Sex ratio	Gershenson (1928)
D. pseudoobscura, D. affinis, D. azteca, D. athabasca	Sex ratio	Sturtevant & Dobzhansky (1936)
Corn	Knob chromosome	Rhoades (1942)
House mouse	Tail-less alleles, recessive lethal	Dunn (1957)
Tobacco plant	Pollen killer gene	Cameron & Moav (1957)
D. melanogaster	*SD* gene near centromere, right arm, chromosome 2	Sandler, Hiraizumi & Sandler (1959)
D. paramelanica	Sex ratio	Stalker (1961)
Housefly (?)	Sex ratio	Sullivan (1961)
Aedes aegypti	Sex ratio	Craig, Hickey & VandeHey (1960)

Sandler & Novitski (1957) suggest that meiotic drive may act as a powerful evolutionary force. According to theoretical expectation, this force can increase the frequency of a factor and spread it through a population, even though the factor is deleterious and results in reduced fitness for the whole population. Hiraizumi, Sandler & Crow (1960) have tested this concept in populations of *Drosophila melanogaster*, using a locus designated as Segregation-distorter (*SD*) on chromosome 2. Males (but not females) of the genotype $SD/\pm$ transmit the *SD* chromosome in great excess. Individuals homozygous for the *SD* locus show a larval viability of only 68% of that of a standard laboratory stock. Yet some natural populations contained *SD* in high frequency. Moreover, population cage experiments showed marked increases in the frequency of *SD* following introduction, in spite of the fact that it reduces fitness. Thus, the theory is confirmed.

Species can develop protective mechanisms against the deleterious effects of meiotic drive. For the *SD* locus, segregation distortion occurs only when the *SD* allele is in synapse with its wild-type counterpart on the homologous chromosome (Sandler, Hiraizumi & Sandler, 1959). An inversion in the homologous chromosome renders it insensitive to the *SD* effect. In some of the population cage experiments, insensitive chromosomes accumulated and part of the detrimental effect of meiotic drive

was counteracted. Other examples of protective mechanisms are given by Stalker (1961) and Sandler & Novitski (1957). The latter authors emphasize that time is required to develop these "resistance" mechanisms. If distorters come by chance into a sensitive genotype, they could and may have caused species extinction before resistance could develop.

It appears that von Borstel & Buzzati-Traverso (1962) were the first to suggest the application of meiotic drive to insect control. They propose the synthesis and release of a meiotic drive chromosome containing a gene for female sterility. As this chromosome sweeps through a population, the homozygous females would be useless for further propagation but the males would still be produced in disproportionate numbers. Eventually, every female would become sterile. A similar mechanism could be used to spread seasonal lethals or other unfavourable characters.

Control of the yellow fever mosquito, *Aedes aegypti*, might be accomplished through the meiotic drive mechanism which distorts sex ratios. The male-producing factor in this species has already been described (Craig, Hickey & VandeHey, 1960). This factor can be carried in insensitive strains without showing its effect, expression occurring only on outcross. Therefore, mass production of male-producing males for release in field populations is entirely feasible. Craig & Hickey (manuscript in preparation) have introduced such males into cage populations of a sensitive strain and reared subsequent generations. The sex ratio was distinctly modified for at least ten generations after the initial release. There was gradual loss of sensitivity to the factor. However, the number of females produced, and hence the number of potential disease vectors, was reduced by more than 50% during the ten generations. While much further work with population cages is required, preliminary results have been promising.

Areas requiring further research

A number of areas of knowledge must be developed before genetic control of vectors can become a reality. A genetic technology must be developed for vector species. Studies of genes, chromosomes, linkage, mutants, physiological and especially behavioural genetics are required. Considerable progress is being made for the housefly, the screw-worm fly and the three major genera of mosquitos: *Anopheles*, *Culex* and *Aedes*. Much less has been done with other vectors.

It seems probable that "insect genetics" must develop into a discipline comparable to, say, insect physiology. Support for genetic work on pest species must come from entomologists, not geneticists. The latter are primarily concerned with other problems, such as gene action, evolutionary mechanisms or ways to improve species. The impetus must come from applied sources. Of course, comparative studies of genetic mechanisms in pest species will contribute much information of value to basic genetic theory.

The accomplishments of the agricultural geneticists in building organisms adapted to the purposes of man are indeed impressive. In entomology, we must apply the techniques of the plant and animal breeders in building better parasites and predators. Sailer (1961) calls attention to the vast possibilities through breeding strains of beneficial insects having superior tolerance to adverse climatic factors, higher fecundity or improved host-finding ability. Sailer indicates that agents for biological control can be obtained in two ways: (*a*) by the exploration, introduction and colonization of new forms and (*b*) by the development of improved varieties through breeding programmes. The first method has been used for 75 years, the second has yet to be tried. It seems remarkable that so little progress has been made in the genetic improvement of insects. A major exception to this statement is provided by the outstanding and highly productive research by the Japanese on the genetics of the silkworm, *Bombyx mori*. The silk industry routinely applies genetic knowledge to breeding and to improvement of the quality of silk (Tanaka, 1953).

For effective genetic control, much more information on insect ecology is required, especially in the area of population dynamics. Such items as minimum population size for survival, natural population density and nature of population cycles are essential. LaChance & Knipling (1962) indicate that the final eradication of the screw-worm fly from Florida occurred because the population had been reduced below the critical density required for survival. When a population becomes small, density-dependent factors such as source of a mate become vital. More information is also needed concerning behaviour, reproductive physiology and mating activity. It is surprising, for example, how little is known about the biology of male mosquitos.

The development of technology for mass production of insects under controlled conditions must be continued. Bio-engineering can provide economical

assembly-line techniques for the factory production of insects. The record of the Florida screw-worm factory in producing 3 800 000 000 flies in 22 months is impressive (Smith, 1960). At top production, 15 430 000 were produced in one day. In field tests of the sterile-male method for the control of *Aedes aegypti*, Morlan, McCray & Kilpatrick (1962) report that 10 620 000 males were produced during 43 weeks. In similar experiments with *Anopheles quadrimaculatus*, Weidhaas, Schmidt & Seabrook (1962) produced 433 600 males in 14 months. In sterilization tests with *Culex fatigans*, Krishnamurthy, Ray & Joshi [1] released 24 000 males in six weeks. Of course, the factory production of silkworms has been going on for a very long time. There is little doubt that economic methods of mass-rearing could be developed for many species of insects, provided sufficient research effort was expended in this direction.

A number of arguments against genetic control may be proposed. It is sometimes said that species will evolve or develop mechanisms to avoid these measures. Of course this is true, but it is equally true for other types of control. A reluctance to introduce new genes into field populations is often expressed. For species as highly plastic as *Aedes aegypti*, this hardly seems a problem. Craig, Vande-Hey & Hickey (1961) have shown that this species contains a rich gene pool with a high level of heterozygosity. The work of Milani indicates similar variability in *Musca domestica*. Thus, many of the genes which might be introduced are already present in populations. The problem is one of managing this variability. Moreover, field trials in limited areas and on island populations should indicate any unexpected repercussions from the introduction of new forms.

In summary, the prospects for the genetic control of insects are good but much research remains to be done. The search for ideas and applications in this area has just begun. Marked development of this concept may be expected in the next few years.

[1] Krishnamurthy, B. S., Ray, S. N. & Joshi, G. C. (1963) *A note on preliminary field studies of the use of irradiated males for reduction of* C. fatigans *Wied. populations* (unpublished document WHO/Vector Control/14).

RÉSUMÉ

L'entomologie appliquée ne tire pas le parti que l'on pourrait souhaiter des études de génétique théoriques faites sur les insectes. La plupart des problèmes actuels de lutte relèvent en effet de phénomènes génétiques (résistance, modifications de l'habitat, de la quête de l'hôte ou des lieux de ponte).

Il est toutefois de bon augure qu'un regain d'intérêt se dessine en faveur des méthodes de lutte biologique. Il faut y voir la conséquence du développement de la résistance aux insecticides et de l'échec partiel des produits toxiques ou des techniques biocides qui, en dernière analyse, ont exercé une influence favorable en conduisant à chercher des procédés de lutte plus perfectionnés. A titre d'exemple, on peut mentionner une expérience récente en Floride où la stérilisation obtenue par rayonnement a permis d'éliminer totalement la lucilie bouchère. La lutte génétique revêt deux aspects l'un « positif », l'autre « négatif ».

Par lutte génétique positive, il faut entendre l'introduction dans des habitats préalablement débarrassés de leurs occupants par une campagne d'éradication, de variétés ou d'espèces génétiques qui ne sont pas nocives pour l'homme, tout en ayant approximativement les mêmes besoins écologiques que les insectes éliminés. L'environnement serait alors protégé contre l'éventualité d'un repeuplement par des espèces plus robustes et plus résistantes. Au nombre des caractères susceptibles d'être ainsi modifiés, on peut citer: le choix de l'hôte, les besoins nutritionnels, le cycle des repas de sang, le comportement ou la présence à l'intérieur des habitations, la sensibilité aux insecticides et la capacité de transmettre des affections. Ce dernier point est particulièrement prometteur en ce qui concerne les moustiques: les gènes dont dépend la réceptivité à certains parasites bien définis — entre autres de nombreuses espèces de *Plasmodium*, de *Brugia*, de *Wuchereria*, voire de virus — ayant pu être isolés, il a paru logique d'envisager de lutter contre le paludisme en procédant à l'élevage de moustiques réfractaires qui seraient ensuite disséminés dans l'environnement.

La lutte génétique négative recourt à des facteurs susceptibles de réduire quantitativement, et à plus ou moins longue échéance, une espèce donnée, tels que la stérilisation par agents chimiques ou rayonnement. Ces agents semblent faire apparaître dans les gamètes des mutations létales dominantes. Certains gènes létaux, liés au sexe, pourraient être utilisés dans un but analogue. Mieux encore, on pourrait avoir recours à des gènes nuisibles qui se diffuseraient parmi les populations et se perpétueraient naturellement. De tels gènes ont été découverts chez *Drosophila*, et plus récemment chez *Aedes aegypti*. Cette méthode de lutte par dissémination de mutants létaux a été étudiée sur l'anthonome du cotonnier et, si les évaluations sont exactes, cette espèce pourrait être éliminée d'une zone donnée et limitée en l'espace de quelques années.

Les processus d'isolement qui aboutissent à la stérilité entre certaines races ou espèces intéressent également la lutte génétique négative.

Les facteurs génétiques qui dévient la sex ratio représentent aussi une possibilité de lutte négative. Bien étudiée chez *Drosophila*, ils ont été récemment mis en évidence chez *Musca domestica* et *Aedes aegypti*. Dans cette dernière espèce, un facteur héréditaire détermine la prédominance des mâles; une fois le gamète constitué, il n'entraîne pas de mortalité. Ce facteur se transmet à la descendance mâle, et semble agir au niveau du locus qui détermine le sexe ou à son voisinage. Latent dans une souche donnée, il peut ne se manifester qu'à l'occasion d'une hybridation. Introduit dans une souche réceptive, le facteur exerce ses effets sur les générations successives. La sélection finit par diminuer la sensibilité de la souche réceptrice, en sorte que la production de lignées mâles est moins marquée. Les facteurs qui influent sur la méiose offrent de grandes possibilités de lutte contre les insectes.

Il est nécessaire de satisfaire à certaines conditions avant d'appliquer sur une vaste échelle la génétique à la lutte contre les vecteurs. Il convient en effet d'en développer la technique et de lui donner pour base une connaissance bien établie de la génétique de l'espèce vectrice. A cette fin, il y a lieu de procéder à l'étude des gènes, des chromosomes, des mutants, du linkage et de la génétique de la physiologie — surtout en ce qui concerne le comportement. Dans la plupart des cas, on ne dispose actuellement d'aucune information, et seules quelques espèces d'importance médicale commencent à être connues de ce point de vue.

La biologie appliquée est en mesure de proposer des techniques de production massive d'insectes, à peu de frais. Ainsi, l'entreprise de Floride qui a produit 3,75 milliards de lucilies bouchères en l'espace de 22 mois a établi un précédent impressionnant. On vient de procéder de même avec *Anopheles quadrimaculatus* et *Aedes aegypti*.

Il ressort de tous ces travaux que la lutte génétique contre les vecteurs offre des perspectives favorables. Elle est encore à ses débuts, mais les années qui viennent seront marquées par son développement. Dans un avenir assez proche, elle pourrait déjà être appliquée à un petit nombre d'espèces.

REFERENCES

Aitken, T. H. & Trapido, H. (1961) In: *Symposium on the ecological effects of biological and chemical control of undesirable plants and animals*, Leiden, Brill, p. 106

Bell, A. E. (1954) *Genetics*, **39**, 958

Borstel, R. C. von (1960) *Science*, **131**, 878

Borstel, R. C. von & Buzzati-Traverso, A. A. (1962) In: *Symposium on radioisotopes and radiation in entomology*, Vienna, International Atomic Energy Agency, p. 273

Bushland, R. C. (1960) *Advanc. vet. Sci.*, **6**, 1

Cameron, D. R. & Moav, R. (1957) *Genetics*, **42**, 326

Carter, W. (1962) *Insects in relation to plant disease*, New York, Wiley, p. 547

Carvalho, G. G. & Cruz, M. P. da (1962) *Science*, **138**, 51

Craig, G. B., jr, Hickey, W. A. & VandeHey, R. C. (1960) *Science*, **132**, 1887

Craig, G. B., jr, VandeHey, R. C. & Hickey, W. A. (1961) *Bull. Wld Hlth Org.*, **24**, 527

Davidson, G. & Jackson, C. E. (1962) *Bull. Wld Hlth Org.*, **27**, 303

Davidson, G. & Mason, G. F. (1963) *Ann. Rev. Ent.*, **8**, 177

Downes, J. A. (1959) *Canad. Ent.*, **91**, 661

Dunn, L. C. (1957) *Proc. nat. Acad. Sci. (Wash.)*, **43**, 158

Gershenson, S. (1928) *Genetics*, **13**, 488

Hickey, W. A. & Craig, G. B., jr (1962) *Bull. ent. Soc. Amer.*, **8**, 163

Hiraizumi, Y., Sandler, L. & Crow, J. F. (1960) *Evolution*, **14**, 433

Huff, C. G. (1931) *J. prev. Med.*, **5**, 249

Jenkins, D. W. (1962) In: *Symposium on radioisotopes in tropical medicine*, Vienna, International Atomic Energy Agency, p. 235

Jones, S. A. (1957) *Trans. roy. Soc. trop. Med. Hyg.*, **51**, 469

Kellen, W. R. (1962) *Mosquito News*, **22**, 87

Knipling, E. F. (1959) *Science*, **130**, 902

Knipling, E. F. (1960) *J. econ. Ent.*, **53**, 415

Knipling, E. F. (1962) *J. econ. Ent.*, **55**, 782

LaChance, L. E. & Knipling, E. F. (1962) *Ann. ent. Soc. Amer.*, **55**, 515

Laven, H. (1959) *Cold Spr. Harb. Symp. quant. Biol.*, **24**, 166

Lefevre, G. & Jonsson, U. (1963) *Drosoph. Inform. Serv.*, **37**, 98

Macdonald, W. W. (1962) *Ann. trop. Med. Parasit.*, **56**, 373

Macdonald, W. W. & Wharton, R. H. (1963) *Trans. roy. Soc. trop. Med. Hyg.*, **57**, 4

Malogolowkin, C., Carvalho, G. G. & Paz, M. C. da (1960) *Genetics*, **45**, 153

Malogolowkin, C. & Poulson, D. F. (1957) *Science*, **126**, 32

Morlan, H. B., McCray, E. M., jr & Kilpatrick, J. W. (1962) *Mosquito News*, **22**, 295

Mukai, T. & Burdick, A. B. (1959) *Genetics*, **44**, 211

Patterson, J. T. & Stone, W. S. (1952) *Evolution in the genus* Drosophila, New York, Macmillan, p. 359

Poulson, D. F. & Sakaguchi, B. (1961) *Science*, **133**, 1489

Rhoades, M. M. (1942) *Genetics*, **27**, 395

Sailer, R. I. (1961) In: *Symposium on Germplasm Resources*, p. 295 (*Publ. Amer. Ass. Advanc. Sci.*, No. 66)
Sandler, L., Hiraizumi, Y. & Sandler, I. (1959) *Genetics*, **44**, 233
Sandler, L. & Novitski, E. (1957) *Amer. Naturalist*, **91**, 105
Schnick, S. M., Mukai, T. & Burdick, A. B. (1960) *Genetics*, **45**, 315
Smith, C. L. (1960) *J. econ. Ent.*, **53**, 1110
Smith-White, S. & Woodhill, A. R. (1954) *Proc. Linn. Soc. N.S.W.*, **79**, 163
Stalker, H. D. (1961) *Genetics*, **46**, 177
Sturtevant, A. H. & Dobzhansky, T. (1936) *Genetics*, **21**, 473
Sullivan, R. L. (1961) *Proc. N.C. Branch ent. Soc. Amer.*, **16**, 20
Tanaka, Y. (1953) *Advanc. Genet.*, **5**, 239
Vanderplank, F. L. (1947) *Trans. roy. ent. Soc. Lond.*, **98**, 1
Weidhaas, D. E., Schmidt, C. H. & Seabrook, E. L. (1962) *Mosquito News*, **22**, 283