tials. Equation A4 gives the spatial potentials unique to the tensor metric field and not present in the electromagnetic field.

It is the goal of experiments to determine the magnitudes of the dimensionless coefficients γ, β, α_1, α_2, α_3, ρ_1, ρ_2, which vary from one metric theory to another. Table 2 relates these PPN metric coefficients to the η_1 parameters used in the body of this article to scale the various experimental effects.

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$$M_G c^2 = \int T_{00} dv$$

But because of an accident of nature that any stable, free body has the properties

$$\int T_{xx} dV = \int T_{yy} dV = \int T_{zz} dV = 0$$

it is possible to have another definition of gravitational mass;

$$M_G c^2 = \int (T_{00} - T_{xx} - T_{yy} - T_{zz}) dV$$

The Lorentz-invariant combination $(T_{00} - T_{xx} - T_{yy} - T_{zz})$, called simply the scalar T, vanishes for pulses of light energy. Therefore, the latter choice of a definition of gravitational mass will generally alter the gravitational physics of light rays. Theories with scalar gravitational fields (*36*) are based, at least in part, on this definition of gravitational mass.
19. That the metric field determines the spatiotemporal intervals spanned by rulers and clocks is considered by many as a postulate of metric theories of gravity. It is not; it is a derived property of the theory, which can be shown explicitly by examining the equations of matter when coupled to the metric field in the universal manner and constructing the rulers and clocks of this matter.
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Genetic Control of Insect Populations

A wide variety of documented genetic methods should be considered for regulation of pest populations.

Roger H. Smith and R. C. von Borstel

Genetic control of population size has been applied most extensively to insect species, both in theory and in fact. There are two reasons for this—the long tradition of insect genetics, in which chromosome manipulation has become a refined science, and the long tradition of economic entomology, which developed from the need to control insects that carry diseases or compete with man for his food. In principle, though, the rules for genetic control can be applied to any eukaryotic species from rusts to rabbits that undergoes union of gametes during reproduction. Different problems are presented by prokaryotic organisms such as bacteria and viruses, by mitotic cell populations such as tumors, and by azygous species such as thelytokous mites, where females produce females from unfertilized eggs.

The conditions that lead to genetic collapse and extinction of a population were described by Wallace and Dobzhansky in 1959 (*1*). They considered the simplest cases—induced recessive lethal mutations and dominant lethal mutations—and formulated the dictum that only an overwhelming degree of dominant lethality could cause extinction. More insidious genetic mechanisms that could cause population collapse and obliteration have been suggested during the last decade. These include meiotic drive inseparably associated with genes for female sterility (*2*), conditional lethal mutations (*3*, *4*), and unstable genetic equilibrium caused by compound chromosomes (*5*, *6*) or translocations (*7*).

In this article we describe induced and genetically contrived mechanisms for producing dominant lethal mutations, and ways they can be used to eradicate or regulate populations of pests. We also discuss other genetic mechanisms that might be used alone or in concert to bring about collapse of populations.

One point that we make is that certain chromosomal anomalies can be used in several quite different ways to regulate population size. For example, chromosomal translocations can be used in four ways—as dominant lethal mutations, as induced dominant lethal mutations one generation removed, as inherited partial sterility, and as a way to fix deleterious genes by replacement of wild-type chromosomes. We consider each of these uses of translocations separately.

Radiation-Induced Dominant Lethality

Dominant lethal mutations are the most common of all types of mutations. In Muller's first paper on radiation-induced mutation he recognized that, after irradiation of males, events were induced in *Drosophila* sperm that resulted in dead embryos in the first generation (*8*). These he called dominant lethal mutations. Nevertheless, he was aware that the radiation might have inactivated the sperm and that the "dominant lethal mutations" might in fact have been sperm that had somehow been inactivated by x-rays and failed to fertilize the eggs. In *Drosophila*, fertilization of eggs is required for normal development, so these two possibilities could not be distinguished. By 1932, Stancati, working in Whiting's laboratory at the University of Pittsburgh, had shown that after the females of the parasitic wasp *Habrobracon* had mated with x-irradiated males, they laid inviable eggs (*9*). Since in *Habrobracon* an unfertilized egg always produces a normal haploid male (*10*), Stancati proved directly that radiation-induced dominant lethal mutations are a reality.

The exact genetic mechanisms underlying dominant lethality remained a puzzle for a number of years; analysis was undoubtedly slowed by the attitude of nonbelievers. After a lecture by P. W. Whiting on dominant lethality in oocytes, Morgan [see (*11*)] asked whether an egg would hatch if it were boiled. This was not a casual attitude, and as recently as the 1960's many investigators believed that cell damage from radiation was primarily from effects upon the cell cytoplasm. The controversy continues to this day in another guise; numerous radiobiologists believe that cell death from radiation may be not from chromosome breakage but from some other action of radiation on the nucleus of the cell.

When McClintock described the breakage-fusion-bridge cycle in maize (*12*), a genetic mechanism was perceived for the origin of the numerous chromosomal bridges and concurrent death of embryos that had been observed previously by cytologists (*13*) after irradiation of eggs from marine environments. McClintock's observation led to the concept that bridges could cause loss of chromosomes during mitosis, and that loss of chromosomes could cause death because of genic imbalance. Pontecorvo and Muller (*14*) devised experiments using excesses of certain chromosomes in sperm of *Drosophila*. After irradiation, if the extra chromosomes were lost because of a bridge, then a balanced and restored chromosome set would result. Such adults did emerge, but their frequency was too small to account for all the dominant lethal mutations induced.

Whiting (*15*) conducted a series of genetical and cytological studies of *Habrobracon*, in which she showed that a large proportion of eggs irradiated in the dose ranges at which most eggs fail to hatch carry chromosome bridges that appear in the second meiotic division and get into the pronucleus. Parker (*16*) proved genetically that bridges can be induced in *Drosophila* oocytes by the induction of compound chromosomes through irradiation of inversion heterozygotes. Thus chromosome bridges were believed to induce dominant lethality, but how this happened was not known. Muller (*17*) proposed a straightforward resolution of the paradox by stating simply that most dominant lethals result from the bridge formation itself and not through a loss of the chromosome or chromosomes involved.

The problem was compounded when Atwood *et al.* (*18*) discovered that at least three different types of dominant lethality are induced by x-rays in *Habrobracon*—one that occurs early in development, another that occurs late, and still another that occurs late but is delayed even further by the addition of an extra, unirradiated chromosome set. Parker (*16*) gave strong supportive arguments that dominant lethality can be caused by any of a number of chromosomal events, and von Borstel and Pardue (*19*) started a series of investigations on *Habrobracon* and *Drosophila* to determine whether such genetically contrived dominant lethal mutations would mimic any of the three types induced by radiation. It was found that the two types of dominant lethals that caused death late in development could be mimicked, respectively, by loss of chromosome parts from any one of several chromosome arms and by loss of one or more chromosomes. None of these losses, including loss of chromosomes containing the nucleolus organizer, would cause death early in the development in a way that would mimic the early deaths induced by radiation.

By fortunate circumstance, however, a mutant occurred in *Habrobracon* which, when homozygous, caused the female to lay eggs that always died early in embryonic development and which in every respect resembled eggs that had died from dominant lethal mutations induced by radiation (*20*). Normally, the eggs are activated to develop not by fertilization but by being squeezed as they pass down the ovipositor. In the mutant, the egg emerged from the female without passing down the ovipositor, the nucleus maintained its central position, and after a time it underwent the production of Feulgen-negative nuclei, a characteristic of radiation-induced dominant lethality in *Habrobracon* (*21*). A concurrent experiment in *Drosophila*, in which tandem metacentric chromosomes were used (*22*), aided to clear up the puzzle from a qualitative standpoint. A certain proportion of recombinants from tandem metacentric chromosomes produce a chromosomal bridge at the second division. At the same frequency a group of embryos produced by females homozygous for tandem metacentric chromosomes died with a syndrome identical to that resulting from domi-

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nant lethal mutations induced by radiation. Therefore, it appears that the early deaths from radiation-induced dominant lethality are induced by chromosomal bridges, and the chromosomal bridges slow the process of mitosis sufficently for concurrent cytoplasmic differentiation and nuclear production to get out of phase. The results in *Habrobracon* are the Feulgen-negative nuclei, and the results in *Drosophilia* are the *metafasi i canestri* or basket metaphases, both causing death long before blastula formation (*23*).

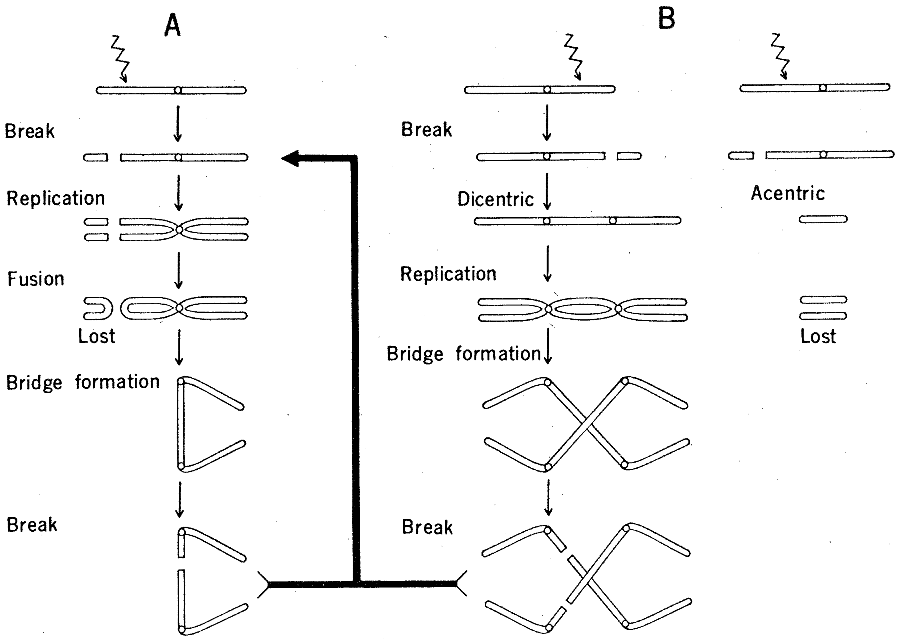

Fig. 1. Breakage-fusion-bridge cycle created by the breakage of a single chromosome (A) and the breakage of two nonhomologous chromosomes (B). [Redrawn from Curtis (*55*)]

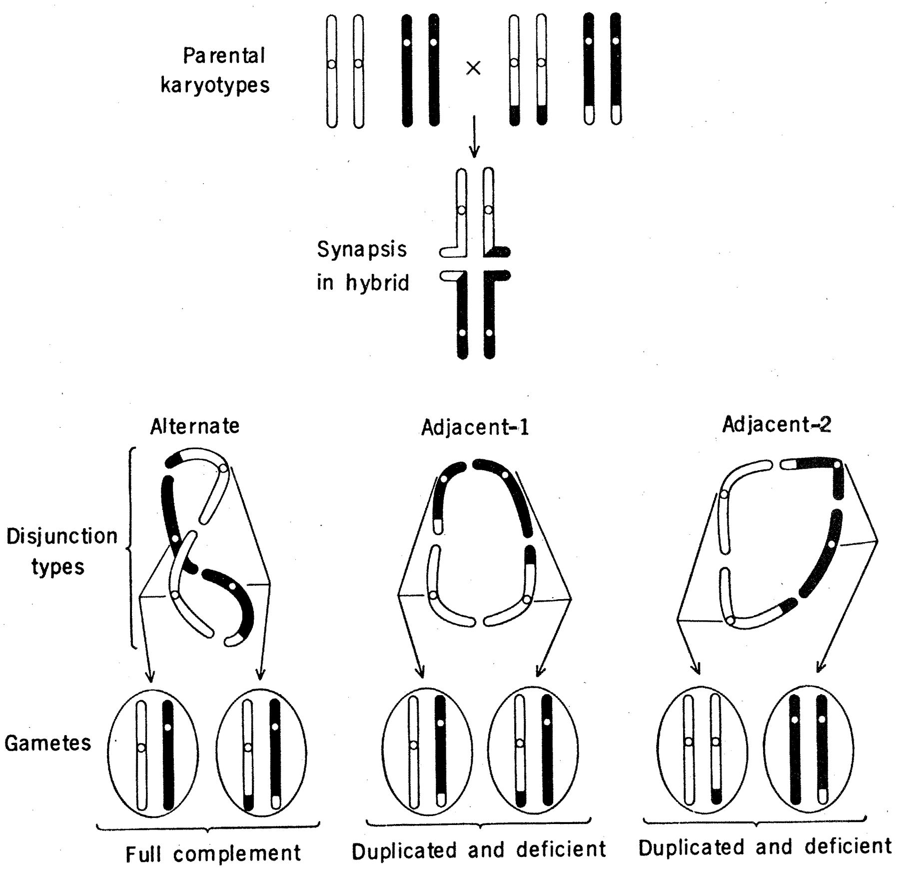

Fig. 2. The gamete types resulting from the three possible patterns of disjunction from a single reciprocal translocation heterozygote. For clarity, chromatids and crossing-over are not shown. The products of adjacent-1 and adjacent-2 disjunction are lethal as zygotes unless complementary gametes come together to form the zygote.

Quantitatively, the proof has been more laborious. First, it is self-evident that the proportions of different types of dominant lethal mutations depend on the dose of radiation administered; at higher doses those mutants that die early in development tend to swamp out those that would ordinarily die late in development. Therefore, we shall concern ourselves only with the proportion that die early in development (preblastula), those induced by chromosomal bridges.

Chromosomal bridges can arise in two ways: a chromosome can be broken, and when the end of the centromeric piece heals during replication it is continuous with the newly formed chromatid (*24*); or when two chromosomes are broken, the subsequent translocation and rehealing leaves one chromosome with two centromeres and one fragment with none (Fig. 1) (*25*). In each case centromeres separating during mitosis produce a chromosomal bridge extending from one anaphase set to the other. Nevertheless, the former condition should be induced according to the kinetics for one chromosome being broken (single target kinetics) (Fig. 1A) and the latter (Fig. 1B) should follow multitarget kinetics. If one assumes that chromosomal translocations among chromosome arms take place at random after irradiation, then at every dose of radiation the proportion of insects in the population with chromosomal arms having two centromeres (a dominant lethal translocation) is identical to the proportion with chromosomal arms having one centromere (a viable translocation). Therefore, if the proportion of individuals containing one or more viable translocations anywhere in the chromosome complement (Fig. 2) is subtracted from the frequency of the total number of early deaths (one-target plus multitarget), an exponential curve should remain (*26*).

So simple a statement, so arduous a task. In a study in which *Habrobracon* sperm were exposed to different doses of radiation (Fig. 3), subtraction of the proportion of viable translocations induced by radiation from the frequency of total preblastula deaths did indeed convert that part of the curve for early deaths into an exponential remainder. These results are consistent with the notion that the predominant portion of the early deaths from radiation are caused by dicentric chromosomal translocations at high doses and by breakage of chromosomes with fusion of chromatids at lower doses of radiation.

Contrived Dominant Lethality

Different ways of causing death of zygotes by genetic means have long been known. Boveri (*27*) showed at the beginning of this century that multiple fertilizations of an egg cause chromosomes to be unequally distributed in cells during early cleavage, because the multiple centrioles set up multiple spindle orientation sites and the chromosomes proceed to these sites at random. Boveri's study demonstrated that the well-being of the organism depends upon a full complement of chromosomes with corresponding total genic balance. Although most cases of genetically contrived dominant lethality in fact operate because they unbalance the genome, polyspermy is not a practical way to induce dominant lethality for population control.

The most usual examples of genetically contrived dominant lethality are the meiotic products of either a triploid or a translocation heterozygote. The former is the result of distorted chromosomal pairing during the meiotic process. Because pairing of homologous chromosomes is a two-by-two process (*28*), the chromosomes in triploids are not equally distributed to the two poles. Thus the gametes produced contain anywhere from the haploid to the diploid number of chromosomes, and inviable offspring result from the imbalance of chromosome number. Belling (*29*) demonstrated that offspring from translocation heterozygotes have deletions and duplications of chromosome arms produced by disparate separation of centromeres during meiosis. The pairing and separation behaviors of chromosomes during meiosis that result in such abnormal gametes are shown in Fig. 2. These mechanisms are now a part of the sapient lore of genetics (*30*).

Studies of the behavior of chromosomes heterozygous for translocations have had a marked impact on research into the genetic control of *Lepidoptera* during the past few years. These considerations stem largely from the work of Bauer (*31*) on the behavior of holocentric chromosomes during meiosis. Holocentric chromosomes have diffuse centromeres instead of localized centromeres on chromosomes, and organisms with centromeres of this type are notoriously resistant to the induction of dominant lethal mutations by radiation (*32*). With diffuse centromeres, dicentric and acentric chromosomes are not possible, so chromosome bridges do not occur in these organisms (*33*). During meiosis in their progeny, however, the chromosome pairing and segregation of holocentric chromosomes follow the rules for chromosomes with only one centromere, and deletion-duplication of chromosome arms ensues (Fig. 3) (*31, 34*).

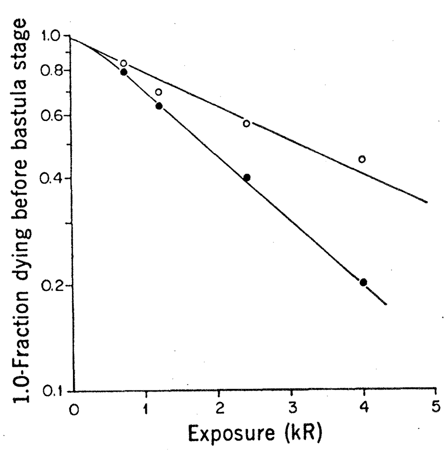

Fig. 3. Frequency of survival of eggs to the blastula stage after fertilization by irradiated sperm (●); frequency of survival after the subtraction of the F_1 offspring with heterozygous translocations (○). Exposure is expressed as kiloroentgens.

Other types of dominant lethality can be obtained genetically, but these, for the most part, require chromosome recombination to produce death. The type mentioned earlier, in which recombination during meiosis results in chromosomal bridges, is one. Other bizarre recombination products that result in death by genic imbalance have been cleverly engineered by Lindsley, Novitski, Sandler, and others [see (*35*)]. Since recombination is required to produce these imbalances, they would not be useful per se for population control.

Population Control by Induced Dominant Lethality

Induced dominant lethality, otherwise known as the sterile male technique, can be used to eradicate or regulate populations in two ways: individuals carrying dominant lethal mutations can be inserted into existing populations, or the entire population can be treated so that dominant lethal mutations are induced at an overwhelming frequency.

Knipling (*36, 37*) set forth the theoretical framework for the first successful attempt to eradicate an insect pest by genetic means in the field through the release of large numbers of insects carrying dominant lethal mutations. This was the effort mounted to eradicate the screwworm, *Cochliomyia hominovorax*. The first field study of consequence was carried out by Baumhover and his associates (*38*) on the island of Curaçao. In their classical exposition of applied team research in biology, these workers described the plans, the rigorous analysis of the island populations before the experiment, the enumerated and timed releases of the irradiated males, and the continual monitoring of the population (*38*). After four generations of release, no more viable eggs could be found; the island was pest-free. Knipling (*39*) has described the efforts that brought this experiment to fruition, as well as the subsequent releases of lethal males in Florida that rid that state of the screwworm. Ten billion irradiated adult *Cochliomyia* are now released yearly along the Mexico-Texas border, effectively controlling the natural screwworm populations on both sides. Plans have been formulated to drive the endemic population to the Isthmus of Panama, where continuous small releases could keep the North American continent free of the pest (*40*).

Because of the widespread belief that the sterile male technique could only be applied to species in which the females mated but once, there was for a time a general reluctance to use this method for pest control on other species. In 1959 Knipling (*36*) suggested that monogamous matings may not always be required, and von Borstel (*41*) described in detail why monogamous mating was not required for the method to be effective. In brief, the competition is not between normal males in the wild population and "sterile" males but between normal sperm and lethal sperm. Thus it does not matter how many times the female mates.

With this erroneous belief dispelled and with the effectiveness of the method so dramatically demonstrated by the successful eradication of the screwworm in Florida, research on dominant lethal induction with radiation and chemical mutagens in numerous other species moved ahead rapidly, and now investigations are being conducted on numerous pest species (*42*). Successful population elimination or regulation has been achieved, for example, with the melon fly on the island of Rota (*43*), the Mediterranean fruit fly on Capri (*44*), the Oriental fruit fly in the Marianas (*45*), and the mosquito, *Culex pipiens*, on Seahorse Key (*46*). Because of the difficulties encountered in rearing large populations of many of the pest species for irradiation, island populations are the easiest to control, whether they are on actual islands or in ecologically isolated landlocked areas. The size of the area has to be matched by the size of the effort, but it has been shown clearly that large land areas are conquerable.

A variety of mutagenic agents have been used to induce dominant lethal mutations. As has been observed for radiation, cells at various stages in both spermatogenesis and oogenesis show differential sensitivity to the many chemosterilants (*47*). Over 8000 separate chemicals have been screened for their effectiveness in inducing sterility in the housefly (*48*). Most of the effective chemicals are also mutagenic, however, and each mutagenic agent has its advantages and disadvantages. The principal reason for using x-radiation is that it induces a high frequency of chromosome breakage, and the radiation can be both uniform and accurate. The chemical mutagens (chemosterilants) are often potent alkylating agents with long half-lives. Their advantage is that occasionally one of them may induce a high frequency of dominant lethality without the concurrent weakening of the adult that often accompanies radiation-induced dominant lethality.

As would be expected, it also has been found that the optimum result sometimes can be obtained by using or combining different qualities of radiation and different types of chemicals (*49*). Indeed, Ducoff and his collaborators (*50*) have developed the important concept that fractionated doses of radiation permit maximal repair to midgut tissues and minimal repair of induced dominant lethality (*51*). Organisms that are long-lived as adults are often killed at doses of radiation lower than the doses required to induce a high incidence of dominant lethality. By careful determination of the time intervals between fractions of the dose administered, it is possible to work out an irradiation regime that does not weaken the males. Ducoff showed that this principle can be used to induce large numbers of dominant lethal mutations in the flour beetle, *Tribolium confusum*. These beetles thrive for a minimum of 5 weeks after the treatment, competing actively for the attentions of the females.

The disadvantage of chemosterilants is that those with long half-lives can be spread, either by carelessness or by the treated individuals themselves, to households, foodstuffs, and other species of plants and animals. This disadvantage might become an asset, however, if chemical mutagens were passed from treated to untreated individuals in the population, thus enhancing the overall lethal potency of the chemical mutagen to the population (*52*).

When populations are treated directly, a sizable effort is required. Wallace (*53*) found that populations of *Drosophila* in cages were eradicated slowly over several generations only when protracted radiation exposures of 10^4 roentgens per generation were delivered. Clearly, it would be impossible to control most species or populations in this way.

Occasionally the conditions are such that field induction of dominant lethals is both feasible and practicable. The most interesting case is the management of the cockchafer, *Melolontha vulgaris* F., by Horber (*54*). The cockchafer lives in behaviorally isolated colonies. During its life cycle it lives in the ground as a grub, and as an adult it flies to the highest skyline on the horizon, usually a tree-covered hill. Horber selected one field site as a reservoir, dug the cockchafers out of the ground, irradiated them, and then released them in another location where eradication of the population was wanted. The eliminations were usually complete, and reinfestation came about only slowly from a few accidental or hungry migrants.

Insects living in stored grain can also be eradicated by irradiation of whole populations. Each pest differs in its response, so pest-dependent doses of radiation can be delivered to insect-infested grain as it is moved from one storage area to another.

Population Control by Contrived Dominant Lethality

Two methods will be described here that could be used for inserting contrived dominant lethal mutations into a population. One of the problems with the release of irradiated males is that the supply of lethal sperm is usually limited to those cells irradiated as first spermatocytes or in later stages of spermatogenesis. It is necessary to kill all spermatogonial cells, otherwise the testes will be repopulated with normal cells. Therefore the radiation exposure is limited to a narrow range at which spermatozoa are not "inactivated," and males are not weakened but all spermatogonial cells are killed and a high proportion of dominant lethality is induced in the later stages of spermatogenesis (*32, 51*). When the sperm are inactivated and the spermatogonial cells are killed, the males are truly sterile (being without sperm), and, under this circumstance, competition is between males rather than sperm. Therefore, monogamy of a species is requisite for any substantial effect from these truly sterile males. In fact, the "dominant lethality" induced in some Lepidoptera may indeed be from "inactivated" sperm (*55*); but fortunately, many species of Lepidoptera are monogamous, and for these, sterility of any type will suffice.

These conditions, which are necessary for successful irradiation-eradication programs, can not always be fulfilled. In such cases contrived dominant lethality could be developed by a carefully planned breeding program. Two separate lines could be established, each homozygous for a number of different chromosomal translocations. Matings between the two lines would produce offspring heterozygous for all the translocations. If each line contained three different translocations, over 98 percent of the gametes would be lethal. Such a genetically contrived dominant lethal method would be a substantial improvement over the radiation-induced dominant lethal method, since the lethal gametes would be produced over the entire life-span of each animal. Furthermore, there is every reason to believe that the males would be vigorous and compete successfully with wild males.

This method could be used profitably in species such as the boll weevil, *Anthonomus grandes* Boleman, which is strikingly sensitive to radiation and therefore can be killed at exposures less than that needed to obtain a high frequency of dominant lethality in the sperm. With contrived dominant lethality, even if the parent lines are genetically weak, there is every reason to believe that the hybrid offspring would be vigorous and long-lived.

Another type of contrived dominant

lethality could be produced by releasing triploid males into a population. Lepidopteran species with large numbers of chromosomes, where females are the heterogametic sex, would be ideal candidates for genetic control by this type of procedure.

Population Control by Induced Inherited Sterility

Delayed dominant lethality occurs when organisms with holocentric chromosomes, such as Lepidoptera, are irradiated at doses that induce few dominant lethal mutations but many broken chromosomes, so that the obliterative effects on the population are delayed a generation. The effect is then drastic. With a multitude of heterozygous translocations present in each individual, there is little chance for any zygote to have a balanced chromosome set.

The delayed effect from irradiation of Lepidoptera was first observed by Proverbs and Newton (*56*) on *Laspeyresia pomonella* and then again by Husseiny and Madsen (*57*) in *Paramyelois transitella* and by Cogburn *et al.* (*58*) in *Sitotroga cerealella*. The work of Bauer (*31*) led to the discovery of the chromosomal basis of this effect by Walker and Quintana (*59*) working with *Diatraea saccharalis* and by North and Holt (*60*) working with *Trichoplusia ni*. A review that includes theoretical considerations of insect control by induced inherited sterility has been written by Knipling (*61*).

An important aspect of inherited partial sterility as a control measure is that the effect on the population is markedly enhanced by addition of females as well as males. When dominant lethality alone is used for population eradication in a polyandrous species, the released males alone contribute to population decline. The enhanced zygotic destruction that results from adding insects of both sexes of Lepidoptera was noted in earlier experiments but the underlying chromosomal basis seems to have been understood clearly for the first time by Walker and Quintana (*59*).

Population Control by Contrived Inherited Partial Sterility

The potential use of translocations for the control of insect populations was pointed out by Serebrovsky (*62*) in 1940. His paper was lost to the Western World until Curtis rediscovered how translocations could be used. At a meeting in Vienna in 1968, Shumakov suggested to Curtis and Hill that Serebrovsky developed similar ideas nearly 30 years before (*7*). Serebrovsky and Curtis thus proposed independently that a translocation between chromosomes in a pest species could produce viable and fertile homozygotes and partially sterile heterozygotes. The strain homozygous for the translocation could then be bred in large numbers and released into the wild population. Matings between the translocated (TT) and wild (AA) strains would produce offspring heterozygous (AT) for the translocation, reducing the general fertility of the population.

The alternate disjunction (Fig. 2) would preserve the two translocated chromosomes in the population. During meiosis in subsequent generations, the heterozygote would again produce adjacent-1 and adjacent-2 segregations, which are lethal except under special conditions. Thus, the partial sterility would be inherited from generation to generation. Because the heterozygote (AT) is semisterile, it would be less fit than either of the homozygotes (AA, TT); and if AA and TT are equally fit, the more frequent chromosome type would replace the other in the population (*7, 62*). A temporary equilibrium could exist at a frequency of 50 percent, but once the relative frequencies changed by chance in one direction or the other, selection would start the replacement process.

Chromosome replacement would occur because the heterozygote, being less fit, would become a lethal sink for the increasingly rare chromosomes. If random mating is assumed, the individuals homozygous for the rare chromosomes would mate most often with individuals homozygous for the other chromosomes, creating the heterozygote and thus speeding their own elimination (*62, 63*). As the process of elimination continued, the heterozygotes would possess a relatively higher proportion of the rare chromosomes. Negative heterosis (*64*) would prevail, and the population finally would become homozygous for the more common chromosomal types.

To use translocations for the regulation of population size, the maximum effect would be achieved when the number of individuals of the homozygous translocation strain (TT) was equal to the number of the wild strain (the equal fitness of each homozygous type again being assumed). In order to keep the negative heterotic effect maximal (and general fertility minimal) in a natural population, the population would have to be monitored, and one set of chromosomes or the other would have to be added to drive the population back to the equilibrium point (*7, 62*).

A derivation of this method is now being investigated intensively for use against several different insect pests, including the housefly (*65*), the tsetse fly (*66*), and five different species of mosquitoes (*67*). It may be difficult to obtain vigorous strains homozygous for translocations. Only 30 percent of the strains of *Drosophila* that are homozygous for translocations are viable and fertile; the other 70 percent have severely reduced fitness. Fitness appears to be reduced severely in most insect pests with homozygous translocations, but viable and fertile translocation homozygotes are known in mice (*68*), *Habrobracon* (*69*), and in natural and laboratory populations of *Drosophila*. There is reason to believe that useful translocations would be found or induced in insect pests as well.

It is evident that the use of multiple chromosomal translocations could reduce the fitness of the heterozygotes even more than a single translocation would. In principle, fitness could be reduced to zero. The theory for the behavior of multiple translocations (homozygous and heterozygous) in a population is well developed (*62, 64, 70, 71*).

Recessive Conditionally Lethal Mutations

A conditionally lethal mutation permits an individual to survive in one environment but not in another. The organism can live and reproduce under "permissive" conditions but cannot survive under "restrictive" conditions. Knipling (*72*) recognized particular heritable characteristics in insects as a potential means for controlling insect populations. The inability to diapause (hibernate) and the ability to adapt to artificial media but not to wild conditions were suggested as characteristics that might be useful for reducing insect populations. Now the idea of conditional lethals for insect control has been developed still further (*3, 4, 73*).

Temperature-sensitive mutations are one kind of conditional mutation. Although temperature-sensitive mutations of many different types have been known for about 40 years, the molecular basis for the most widely occurring of these alterations has been elucidated only within the past two decades (*74*). Such mutations result in a single amino acid substitution in the protein encoded by the mutant gene. This protein fulfills the function of the wild-type or normal protein at permissive temperatures but malfunctions or is nonfunctional at restrictive temperatures. In almost all cases temperature-sensitive mutations are of the base-substitution type, because the addition-deletion (frameshift type) of mutation usually causes a gross change in protein structure, which renders the protein nonfunctional. Although Whiting (*75*) described an x-ray-induced temperature-sensitive mutation in *Habrobracon* as early as 1932, it is only in the past 5 years that temperature-sensitive lethal mutations have been used in higher eukaryotes for genetic studies (*76*). In *Drosophila*, temperature-sensitive lethal mutations are heritable as single units, show linkage to other genes, usually are recessive, and are produced most efficiently by mutagens that induce a high frequency of base-pair substitutions.

The time of gene action or, probably more accurately, the time when the gene product is necessary for survival, can be determined for each conditionally lethal mutation. Individuals homozygous for a particular conditional mutant gene are exposed to restrictive and permissive conditions. At various points in the life cycle individuals are moved from the restrictive to the permissive conditions, and vice versa. The shift from restrictive to permissive defines the time and stage of development at which the gene product needs to be present for the developing individual to survive. The shift from permissive to restrictive conditions defines the time at which the product is no longer necessary for survival. Patterns of gene action have been studied extensively in *Drosophila* (*76, 77*), and monophasic, polyphasic, and sexually dimorphic periods of gene action have been found. The lethal phase, or the stage of actual death, may occur during or several days after the time of gene action.

The pattern of gene action of a conditional mutation would be an important consideration if it were to be used for regulating population size (*4*). As one might expect, there is considerable variation between genes in the length of time of gene action and in the degree of penetrance. In *Habrobracon*, the

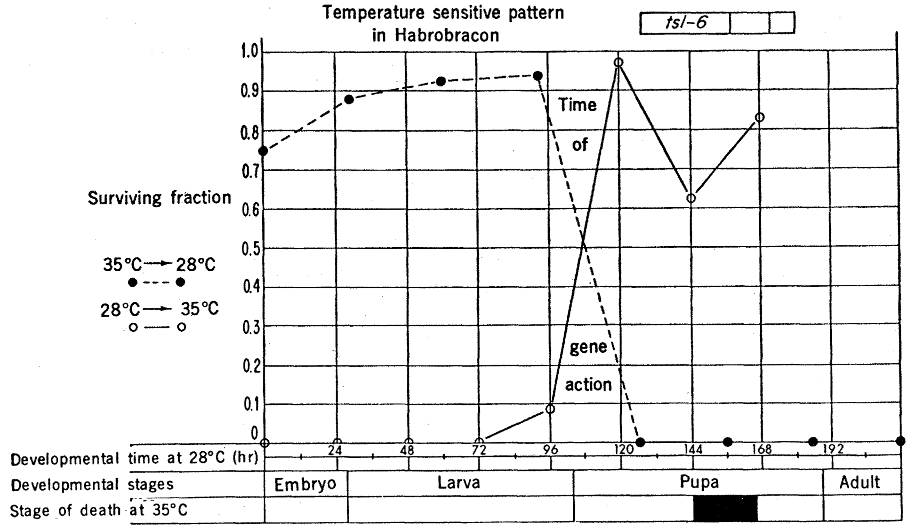

Fig. 4. The pattern of temperature sensitivity for a temperature-sensitive mutant (*tsl-6*) in *Habrobracon serinopae*. [After Smith (*4*)]

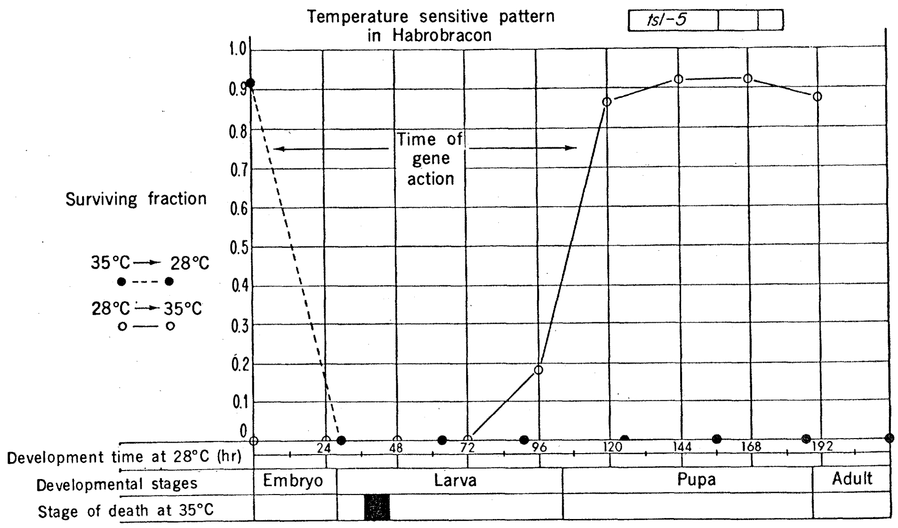

Fig. 5. The pattern of temperature sensitivity for a temperature-sensitive mutant (*tsl-5*) in *Habrobracon serinopae*. [After Smith (*4*)]

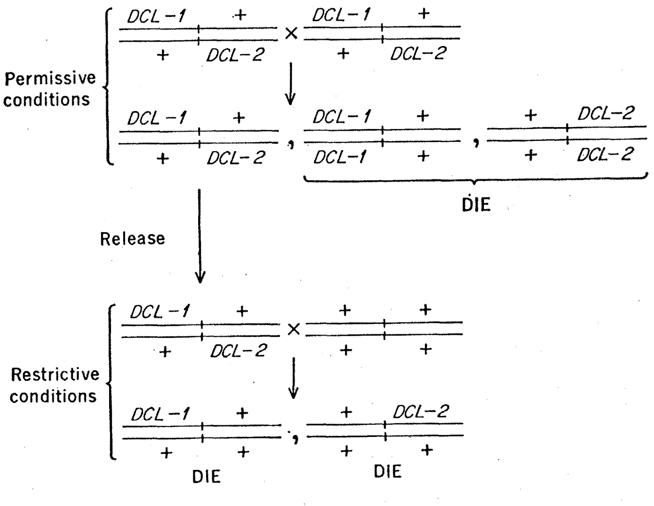

Fig. 6. The double heterozygote for complementing dominant conditional lethal mutations (*DCL-1*, *DCL-2*) is maintained in the laboratory under permissive conditions. Only the heterozygous combination survives, because each homozygous combination acts as a regular recessive lethal gene under permissive conditions, and no crossing-over occurs between the two genes (because of crossover suppression, for example).

temperature-sensitive lethal mutant *tsl-6* has a narrow period of gene action during the prepupal stage (Fig. 4). Death at the restrictive temperature of 35°C occurs only during the early to midpupal stage. Such a pattern of gene action would make this an ill-advised mutant to use for pest control. Many individuals might escape the restrictive conditions by chance. The mutant *tsl-5*, however, has a very broad temperature-sensitive period. All individuals die when they are exposed to the restrictive temperature at any time from egg to prepupa (Fig. 5). Therefore, daily fluctuations in the field would not be critical, and there should be less chance for any developing individuals to escape the restrictive condition.

There may not be a generalized or ideal pattern of gene action for the control of insect populations, nor any particular type of conditional lethal mutant that is best suited for all species. The best way to select mutants useful for control is to examine the life cycle, behavior, and feeding preferences of the species in question. Then a heritable characteristic can be chosen with the result that some normal stress in the environment such as temperature extremes, desiccation, wetness, or phototrophic or geotrophic conditions will become restrictive.

Dominant Conditionally Lethal Mutations

Temperature-sensitive dominant lethal mutations were discovered by Suzuki and his collaborators (*78*). Such mutations do not cause visible chromosomal rearrangements, as do nearly all of the other contrived or radiation-induced dominant lethal mutations; but they can be recognized genetically, since they cause death of the zygote in a heterozygous condition at the restrictive temperature. Thus, they are potentially useful for population control.

In *Drosophila*, many of the "dominant" lethal temperature-sensitive mutations turn out to be recessively lethal at the permissive temperature when homozygous (*77*). Unfortunately, such mutations would not be ideal for use in insect control. However, it might be possible to use closely linked dominant conditionally lethal genes that complement one another (*79*). If insects heterozygous for two dominant conditionally lethal mutations in the trans arrangement were released into a wild population, the effect should be the same as releasing insects homozygous for a single dominant lethal gene; all progeny from a cross between the released insects and the wild insects would die when exposed to restrictive conditions (Fig. 6). The crossover frequency between the genes would have to be zero to allow the stock to be mass-reared without loss of the lethal genes. This could be accomplished by using crossover suppressors (for example, chromosomal inversions). Ideally, the two mutants could be maintained in a balanced condition if one were contained within a crossover-suppressor region of the chromosome so that only the double heterozygote survived. Under permissive conditions, one or both homozygotes would act as though they had regular recessive lethal genes and the insects would die.

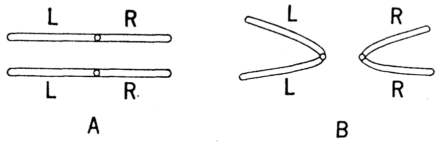

Fig. 7. A pair of homologous chromosomes, (A) the wild-type set and (B) the compound set (*L*, left arm; *R*, right arm).

An important consideration for dominant conditionally lethal mutations is the pattern of gene action. It should occur during the immature stages of development but not during the adult stage, similar to the pattern seen in Fig. 5. This would allow the adults that carry the dominant conditionally lethal mutations to be released and to interbreed with the natural population under the restrictive conditions. However, all progeny that result from these matings would die.

Meiotic drive is another possible method for the introduction of dominant conditionally lethal mutations into a population. In this case the problem of inviable or subvital homozygous individuals could be surmounted in a different way. Meiotic drive is "any alteration of the normal process of meiosis with the consequence that a heterozygote for two genetic alternatives produces an effective gametic pool with an excess of one type" (*80*). An individual would be heterozygous for the dominant conditionally lethal mutation, but all the gametes would possess this mutation because of its linkage to the meiotic drive chromosome (*79*). Such a mechanism could be tested in *Drosophila melanogaster*, where segregation distorter (*SD*) in conjugation with activator (*Ac*) and stabilizer (*St*) on the second chromosome can cause a segregation distortion of 99.9 percent (*81*). Multiple releases of individuals would be necessary for effective control, because individuals homozygous for either the conditional mutation or the segregation distorter gene would not be viable (*82*). This method of control would produce population kinetics similar to those of the sterile male method. The possibility of using dominant conditionally lethal mutations linked to segregation distorter genes should be investigated for other organisms. Meiotic drive has been reported for a wide variety of species (*83*) and therefore would probably be found in insect pests.

Conditionally Lethal Mutations: The Genetic "Time Bomb"

Hypothetically it should be possible to set a genetic "time bomb" in a population by introducing conditionally lethal mutations that would replace the wild-type alleles. We shall discuss four methods by which alleles might be replaced in populations. With the first two methods, many individuals must be released; with the other two methods, the release of many individuals would be desirable but theoretically unnecessary.

In the first method, individuals would be released that are homozygous for a translocation or a complex of translocations inseparably associated with a conditionally lethal gene. As was pointed out in the section on contrived inherited partial sterility, if enough individuals are released so that the translocation types predominate in the population, then the wild-type chromosomes will be eliminated from the population (*7, 62*). Curtis (*84*) was the first worker to suggest that deleterious genes could be introduced into populations this way. If the translocated chromosomes are associated with a conditionally lethal mutation, then when the restrictive conditions appear the population will collapse (*4, 70*). This method has the added desirable feature that the translocation heterozygotes produce a high frequency of dominant lethal mutations, so the population is depressed while allele replacement is taking place. If the translocation heterozygote is completely sterile and the homozygotes are equally fit, replacement could occur within five generations (*85*).

In the second method, individuals would be released that are homozygous for the type of translocation known as compound chromosomes. Whitten (*5*) suggested the use of compound chromosomes for the introduction of conditional mutations into pest populations. A compound chromosome possesses two homologous chromosome arms attached to the same centromere (Fig. 7). In order to be viable, an individual must also possess the other two arms of the same chromosome. In *Drosophila*, strains have been synthesized in which chromosomes 2 and 3 are compound chromosomes (*86*). Crosses between strains containing compound chromosomes and strains containing the normal complement produce zygotes that die because they carry duplicated and deficient genetic material. With the complete isolation of each type from the other by the complete lethality of the hybrid, negative heterosis can be used to fix an allele in a population without the necessity of linking the gene to any particular chromosome. Experiments with *Drosophila* have indicated that compound chromosomes can be used to fix alleles in populations within three to eight generations (*6*).

In the third, more hypothetical, method, meiotic drive would be used to exert a powerful force to make a population homozygous for a deleterious gene, even if only a few individuals with this gene were introduced into the population. It has been suggested that meiotic drive could be useful for insect control if the chromosome containing the factor responsible were associated with genes for female sterility in such a way that they could not be uncoupled (*2*). Conditionally lethal genes could serve instead of genes for female sterility. So far, however, every case of meiotic drive that has been investigated was a spontaneous mutation derived from a natural population. It is not likely that a case would be found in nature if it were not already in some sort of balanced condition (*87*). The kind of meiotic drive most useful for insect control would be one that had been induced or obtained from a completely isolated pest population that had not yet devised a selective procedure for countering, balancing, or eliminating the driven chromosome. Obviously, the gene for segregation distortion would have to be homozygous, and in viable and fertile individuals—criteria that may be difficult to fulfill (*88*).

Table 1. Trend of an insect population into which 9 million sterile males were released in each generation. [After Knipling (*99*)]

Generation	No. of insects in population	Ratio of sterile to fertile males	No. of progeny
Parent	1,000,000	9 : 1	500,000
F_1	500,000	18 : 1	131,580
F_2	131,580	68 : 1	9,535
F_3	9,535	942 : 1	50
F_4	50	180,000 : 1	0

The fourth method for introducing conditionally lethal mutants into a population would be to link them tightly to genes that would give the introduced population a selective advantage over the natural one. There are numerous possibilities, such as the use of mutants with higher egg production than the natural population, or with greater longevity, higher hatchability, or better patterns of mimicry to ward off natural predators. Again, for greatest effectiveness such mutants should probably be induced rather than sought in natural populations.

Kinetics of Population Collapse by the Sterile Male Principle

Knipling (*36, 37*) made the first study of the characteristics of population decline after the release of irradiated males. Because the economics of rearing, release, and monitoring were considered in this study, it well deserves attention. An example of one of Knipling's simplest models is presented in Table 1. Three primary assumptions are made in this model. (i) Every sperm from the released males contains at least one dominant lethal mutation. (ii) The released males are as competitive for females as are the wild males. (iii) There is a natural fivefold increase in population size each generation. When 9 million males are released in each generation, the ratio of sterile to fertile males increases in each generation. By the fifth release the ratio is 180,000 to 1, no progeny are expected to survive, and eradication is accomplished.

Other investigators have now developed more detailed mathematical models to describe the kinetics of population change after the release of insects bearing dominant lethal mutations in their sperm. The model presented by Berryman (*89*) and Bogyo and his colleagues (*90*) is a general equation with several components. The number of adult insects in the generation following a release of sterile males is expressed as

$$N_{g+1} = N_g F_p E S P_f$$

where N_g equals the number of adult insects in the initial generation, F_p equals the proportion of females in the population, E the average number of eggs per female, S the frequency of normal survival from egg to adult, and P_f the probability that a female will mate with a fertile (wild or "natural") male. The value of P_f decides the success of a release of sterile males when the remaining variables are determined. When $P_f \rightarrow 0$, then almost all females have mated with males that possess sperm with dominant lethal mutations, and $N_{g+1} \rightarrow 0$. P_f can be broken down into various components so that competition between wild and released males and competition between sperm from wild and released males can be considered in the equation.

This general equation has been used in computer programs to simulate release of sterile males in populations under different given conditions. It was found that the probability of survival from egg to adult (S) is probably the most crucial parameter affecting the outcome of a release (*64, 71, 90*). This factor can be affected by several different variables (food, weather, disease, for example) and can change from generation to generation. Also, it may be one of the most difficult to estimate for insect populations.

Kojima (*91*) also developed a stochastic model to predict the outcome of the sterile male method. In his first approach and, unfortunately, his only published paper on insect control, he elected to consider the case where individuals were truly sterile. All aspects of polygamy and monogamy were evaluated. One of the unique features of his model is the inclusion of a parameter for genetic improvement of pest populations from natural selection when control measures are used. It seems clear that release of billions of insects with genetically lethal chromosomes would set up a powerful selective force for a population that did not interbreed with the released insects. It is speciation at its best. Indeed, one can predict that screwworms will be found near the Mexico-Texas border that will have nothing to do with the screwworms that are reared, irradiated, and released.

These models should prove useful for predicting the outcome of future releases and should help in the design of release strategies. As their authors freely admit, the models are oversimplifications because it is difficult to determine the relative effects of the many parameters. They stress the importance of obtaining reliable estimates of the parameters in order to make realistic predictions. The models are not substitutes for biological data, but they bring to light the areas that need more research.

Special Problems, Special Considerations

We have examined some of the possibilities for controlling population size by genetic means. Other methods show considerable promise. For example, Walker and his collaborators (*92*) have discovered that both inbred and outbred lines of laboratory populations of *Diatraea* become extinct when a high incidence of inherited partial sterility is induced. This suggests that if enough detrimental mutations are induced or are already present in the chromosome set, then genetic collapse can possibly proceed in small populations from a variety of pressures. Each of these detrimental elements should be isolated and defined genetically. Further, there are enough male-determining factors in the housefly, *Musca domestica*, to permit the development of strains which, when introduced into natural populations, might cause only male offspring to be produced (*93*). The potentials of this insidious genetic device have hardly begun to be tapped. Another genetic method that has been used successfully in the field to eliminate mosquito populations involves a cytoplasmically inherited factor that prevents sperm nuclei from fusing with egg nuclei (*94*). If large numbers of males whose sperm are so affected are released into areas where the females containing the incompatible cytoplasm reside, then dead embryos result. A similar method would be the release of males from one species of insect into a population of another closely related species where matings are frequent but the hybrids are sterile (*95*).

It must be remembered that there are three major forces in evolution—spontaneous mutation, recombination, and natural selection. Some conditionally lethal mutations are unpredictable (or "temperamental") in their behavior. When moved from one genetic background into another they can disappear (*96*). Likewise, meiotic drive can be powerful in one population but be annulled in another, because compensating factors may demolish the effect (*87*).

On the other hand, evolutionary procedures might be used to advantage. For example, Foster and Gallun (*97*) have demonstrated that genetic control of the Hessian fly is possible by releasing flies with dominant avirulent genes into experimental populations which normally infect wheat. The different races of flies possess genes for virulence and avirulence and the different varieties of wheat possess corresponding genes for susceptibility and resistance. Also, selection systems can now be devised so that varieties of insects can be induced and selected that will not eat their natural food but only a synthetic diet. A second selection could be made so that the insect would eat only a pest plant instead of synthetic food. Conceivably, if an investigator is really imaginative, a species might be turned into a beneficial insect and made to replace the pest population. If the strategy were not planned cleverly, however, the result might be two independent, noninterbreeding pests—the old one and the new one synthesized in the laboratory.

Another example that can be cited, just to illustrate what we are up against, is the evolution of a harmless insect into a pest in Canada in 1906. The sawfly, *Cenhus cinctus*, is a native insect that confined itself to native grasses. But because of a very high population pressure in 1906 and 1907, when practically every stem of the native grass was infected, the sawfly took to the wheat fields. Now it prefers cultivated wheat and rye to the native grasses (*98*). This suggests that speciation itself can be initiated through conditional mutations.

Of course, the nature of evolution is such that it can often counteract the efforts of the geneticist, and complete eradication of a population may not be possible or desirable in many circumstances. Nevertheless, it is now possible to use genetic methods to regulate and control many populations of insect pests.

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100. Oak Ridge National Laboratory is operated by Union Carbide Corporation for the U.S. Atomic Energy Commission. This article is dedicated to Dr. Ken-ichi Kojima in memory of his contribution to the study of genetic control of insect populations (*91*).

Evaluation of Infant Intelligence

Infant intelligence scores—true or false?

Michael Lewis and Harry McGurk

The late Sir Cyril Burt once remarked of intelligence, "Of all our mental qualities, it is the most far-reaching; fortunately it can be measured with accuracy and ease" (*1*, p. 28). Although much progress has been made in the field of psychometrics since Burt's statement, his early confidence has hardly been justified with respect to the measurement of intelligence during the early stages of human development. In common with many others, Burt espoused the view that intelligence is a finite potential with which the individual is endowed at conception; the manifestations of this intelligence increase at a stable rate during the growth process, but intelligence is subject neither to qualitative change nor to environmental influence. "It is inherited, or at least innate, not due to teaching or training; it is intellectual, not emotional or moral, and remains uninfluenced by industry or zeal" (*1*, p. 29).

It is a sine qua non of this view that measures of intelligence have high predictive validity from one age to another. Such validity is singularly lacking in every scale used to assess intelligence during early infancy. For example, Bayley (*2*), employing an early version of her infant development scales, reported correlations between scores at 1, 2, and 3 months and scores at 18 to 36 months which ranged between −.04 and .09. Recently, Bayley (*3*, p. 1174) has concluded, "The findings of these early studies of mental growth of infants have been repeated sufficiently often so that it is now well established that test scores earned in the first year or two have relatively little predictive validity." Stott and Ball (*4*) and Thomas (*5*), after extensive