The Human Multitude: How Many Is Enough?

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• The first part of this article appeared in the March issue. This part draws extensively on two earlier papers —the first sections on a contribution to a A.A.A.S. symposium (Dec. 29, 1969) entitled "Is there an Optimal Size of Population? Genetic and Evolutionary Considerations" (in press), and the later sections on B. Glass, 1967 (see references).

The question "Is there an optimal size of the human population?" poses to a geneticist the immediate need for definition of several terms. First, of course, one must ask: optimal for what? Second, precisely what are the definitions of "population" and "size of population"? Third, is one to be concerned chiefly with the welfare of man in the immediate present or in the distant future? Finally, if the optimal size of population is related to changing parameters of the environment, can we expect to preserve an environment sufficiently buffered against change that a prescription today will have any validity whatsoever for tomorrow?

Conditions of Human Adaptability

A biologist must examine these questions in the light of "mankind evolving," to use Theodosius Dobzhansky's apt phrase. The primary characteristic of *Homo sapiens,* in contradistinction to other mammalian species and in particular his closer primate relatives, is the high order of intelligence he possesses—a quality that enables him to adapt his environment increasingly to his own desires instead of awaiting the far slower genetic adaptation of himself to his changing environment. Man's own adaptability, including his power to learn from experience and, through science and technology, to enlarge his power to exploit and modify the environment, depends on the considerable diversity of the human gene pool. It seems to me that although a "brave new world" is conceivable—that is, one in which man is artificially constrained to become genetically homogeneous or is reshaped into a few genetic castes—it is neither likely to develop within a democratic society nor is as optimal as a continuance of extensive genetic diversity. For mankind, a continuance of his adaptability and maintenance of the diversity of his gene pool would seem to be optimal, at least for the remote future.

According to Sewall Wright (1960), the situation most favorable for progressive evolution is one that is provided by an oscillation between a relatively large population homogeneous in nature and a state of subdivision into many local, fairly isolated populations, at least some of which are of medium or small size. In that case the small isolates will come to differ from one another both in concealed genetic variability (genotypes) and in visible characteristics (phenotypes), and natural selection may discriminate between them. This view is generally accepted by population geneticists. Only in relatively small and isolated populations, because of inbreeding, do we find the genetic variability forced into expression and thus made subject to selection. On the other hand, if the total population of the species consists of only a few small isolates, there is too much danger that none of them can provide a phenotype permitting preservation in the struggle for existence. Here both chance and adverse selection will combine to magnify the likelihood of extinction.

In the one or two million years of existence of

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the human species, the total population was at first undoubtedly small, and it was also broken up into small, local breeding units that might be designated as bands, or extended families. Inbreeding was high; diversification among the isolates was probably great. The risk of extinction of the species was overwhelming until the total population of the species rose to 100,000 or so, when there would have been many bands. Later, as group methods of hunting developed and the usefulness of fire as a protective weapon was discovered, larger tribes succeeded the small bands. Ever since, we have moved steadily toward larger and larger Mendelian populations, with always a higher proportion of the variability in the gene pool concealed, and with less and less diversity of isolates and racial groupings. The human melting-pot came into being. The melting-pot has not yet eliminated all racial distinctions, but it is rapidly doing so. Genetic variability now chiefly differentiates individuals of the same breeding population, and a greater proportion of it is concealed in the recessive state. Populations have grown so vast that sheer distances, both geographic and social, have become primary factors in offsetting a purely random breeding pattern. Evolutionary change has thus slowed down, even without considering the diminution of the rigor of natural selection that has also taken place because of better standards of health and nutrition throughout the world. As the population structure of man has thus changed, his evolutionary prospects have altered.

Faster Change, Slower Selection

The present rate of change in the human condition is exceedingly great. No genetic change can occur fast enough to cope with it even under conditions of maximum mutation rates and rigorous selection. Mutation rates are in general low, although the great size of present human populations ensures that many mutations, of each and every gene, will occur in every generation. The new genes will also undergo extensive recombination, so that many different coadapted gene systems will exist. At the same time, our large populations ensure that most of the genetic variability will be concealed in the recessive state. Selection will consequently act mainly on the heterozygous effects of genes, which are commonly smaller in extent than the homozygous effects. Selection has been further slowed down by the advances in medicine and nutrition that now virtually guarantee that every child born alive, and some that previously could not have been born alive, will reach the reproductive years. The reduced rigor of selection is increasing the abundance of once-detrimental genes in our population, for these genes no longer lower their possessor's chance of reproduction. Dominant genes that are reduced from $s = 0.5$ (elimination of half the genes in each generation) to $s = 0.01$ will tend to increase 50 times in frequency. Recessives undergoing a similar moderation of selection will increase 10 times in frequency. Thus, in anomalous fashion, we have found a way to increase our genetic variability without requiring any alteration of the mutation rates—though these, too, may become greater through greater exposure in the modern world to ionizing radiations, chemical mutagens, and increased temperatures.

This genetic variability, however, is of little advantage to us in producing any real adaptation. We now modify the environment around us by technological means and create for ourselves a novel and artificial world in which our defective genes, even though active, fail to impede us in reproduction. The man of tomorrow will clearly need many more pills and prosthetic devices. That need not worry us so long as the social cost is not too great and so long as we can maintain our artificial environment unimpaired. By natural standards we may become degenerate physical beings, but we will not wish to apply natural standards any longer.

What is the optimal size of population? Man has achieved his present status chiefly through intelligence and adaptability. That evolutionary process occurred in populations very much smaller, and much more broken up into breeding isolates, than we now see. Evidently the great size of our present populations is not needed for progressive evolution and the maintenance of diversity. Our new condition provides us with added genetic diversity, but at a considerable cost: the social repair of genetic defects. This excess of diversity seems neither necessary nor advisable.

There is, I believe, only one condition under which it may actually save our species. If in the end we blunder into a nuclear war and thereby eliminate nine-tenths of the human lives on our planet, the scattered survivors will find themselves once more in the population structure of early Pleistocene man. Those who survive the direct effects of heat and blast and radiation and who are later spared by the fallout may still perish in large numbers because of their inability to provide themselves with the special foods, drugs, and devices on which they depend for life itself. Among the others, in remote inbreeding isolates, there will very likely be sufficient genetic diversity to enable *Homo sapiens* to make a wiser fresh start.

Improving on Nature's Ways

It should be feasible, by the year 2000, to bank human reproductive cells of both sexes in frozen state, as we now do with the sperms of domestic animals, especially sheep and cattle. In this way the reproductive cells of selected individuals might be utilized even long after their deaths to produce in the laboratory embryos that might be implanted in the womb of a foster-mother, or might even, after sufficient development of technique, be grown in bottle cultures. The latter "brave new world" technique I do not expect to see realized by the turn of the century. On the other hand, I do expect that techniques will be developed for the cultivation in the laboratory of portions of human ovary and testis, permitting successful continuous production of mature ova or sperms. Recent successes in the production of mature ova from cultured mouse ovaries lead me to expect that only persistence by a sufficient number of skilled biologists is needed to attain successful cultivation of human reproductive organs, continuous production of eggs and sperms, and formation by fertilization in the laboratory of as many human embryos as may be wished.

I am frequently asked why anyone should wish to pursue this goal. "Aren't the age-old ways of making babies good enough?" Several reasons may be given why such exploration of new possibilities is desirable. Only by studying the development of the human embryo and fetus under continuous observation and under various conditions can medical scientists really learn what factors produce particular kinds of abnormalities and how these may be corrected or avoided. Moreover, the practice of "prenatal adoption"—that is, the implantation of a healthy selected embryo in a foster-mother's womb—appears to meet with fewer religious and legal objections than the present practice of artificial insemination of a woman, whether with or without the consent of her husband. The development of the implanted fetus within the mother and its normal delivery at full term will engender far stronger maternal and paternal feelings in the "parents" than adoption of a child already several years old. Moreover, most couples who are sterile may in this way have virtually all the experiences of parenthood.

There are other reasons why such practices might be adopted—if not in the United States, then possibly in other countries. Banking of reproductive cells taken from individuals around 20 years of age may serve to prevent the accumulation of detrimental mutations with advancing age. From the standpoint of eugenics, parents should have their children while they are young. From the standpoint of economics and population control, marriage is often long postponed, and children are produced by parents in their thirties and forties. Healthy children may of course be produced by parents even at an advanced age, but the odds are not so good. By banking reproductive cells under conditions where mutation is reduced to the lowest level, and using implantation of an embryo produced by artificial fertilization, older parents may have children as free of defect, on the average, as when they were young. Persons such as astronauts who venture into especially hazardous environments, where they are very likely to be exposed to sizable doses of high-energy radiations, might be similarly well-advised to bank their reproductive cells under safe conditions.

These practices would of course be ineffective without employment of effective contraception. In spite of personal and religious objections, it seems clear that the use of present means, especially of steroid "pills" and intrauterine loops, will soon become worldwide. A promising recent advance, still being tested for safety and efficacy, appears to be that of inserting a dose of progesterone, enclosed in a capsule, under the skin of the female. Under these conditions, microdoses seep into the circulation and prevent conception even without modifying the usual female cycle. The capsule can be easily and painlessly put in place and may be removed at any time. Modern methods of contraception, it seems clear, will if adopted be the quickest and surest means of securing control over the population increase; and they seem infinitely superior to the widespread use of legal abortion, as in Japan today and more recently in some states of the U. S. We might even go so far as to predict that by the year 2000 many countries will have reached such a population density in relation to their food supply that no further increase can be tolerated. A marriage certificate might then bear two coupons entitling the couple to produce two children, no more. Restrictive tax measures, such as an income tax graduated more heavily as the number of children increases, or even temporary sterilization by court order, might be imposed by countries under desperation. Temporary sterilization of the female by implantation of a progesterone capsule would be effective enough.

Medical Aspects of Eugenics

We must now consider questions of eugenics, for complete and perfect control by individuals and by society over reproduction opens up certain eugenic possibilities like those of *Brave New World* (Huxley, 1932). First we must recognize that under our present application of ethics to medical practice, human society is already doing itself a considerable eugenic injury. When an infant or child with a genetic defect is kept alive by medical means and its defect is controlled or even eliminated, the child grows to adulthood. The most common sequel is marriage and parenthood. In the past, under a more cruel rule of nature, such persons never lived to reproduce, and their defective genes were thus eliminated from the population. The population thus maintained a balance between the defective genes being eliminated in each generation and the new ones being produced through mutation. (Not all mutations produce defective genes, but a considerable majority do so, for the simple reason that genes are the products of millions of years of selection of the best alternative means of guiding development in the normal environment and of working harmoniously together.) Medical practices thus tend to increase the frequency of defective genes in the population. To a certain extent, doctors are only making more work for themselves: since they have not removed the cause of the defect, which is the gene, but have only corrected symptoms, the defective gene when transmitted does the same harm once again.

Geneticists are looking forward to the day when they can practice genetic surgery or genetic manipulation; that is, really reach in and transform a defective gene and make it functional again. That will not be easy. The technique depends first of all on finding an effective but harmless human virus capable of transducing human genes from a donor of a sound gene to a recipient possessing a defective allele. The transduction would have to be done either in a very young embryo, before the cells have begun to multiply, or in the reproductive cells that actually produce a new individual. Before the technique is usable, then, we must perfect the means of culturing embryos and reproductive cells in the laboratory. Even so, it will probably always remain easier and simpler to discard defective reproductive cells and to select others from banked or cultured material that is free of known defect.

Now we come to the most difficult aspect of the crisis of values and goals. How can one select good strains of reproductive cells? If the same material is used to produce a great many embryos that are reared into babies, they will be too much alike—like members of the same caste in *Brave New World*. This difficulty might be avoided by never using a single line of reproductive cells more than a few times. There is another difficulty. Nearly all of us carry some defective genes; the average is probably around eight. We lack visible signs of defect because most defective genes are recessive; that is, they must be inherited in a double dose, coming from both father and mother, in order to produce an evident defect. As long as we have one working gene belonging to any particular pair of genes, enough of the protein it controls is produced to satisfy general needs. Close relatives, however, have a greatly heightened probability of carrying the same defective gene, because of possessing a common ancestor. It would therefore be necessary to have strict rules to prevent offspring being produced by persons who were derived from the same lines of banked or cultured reproductive cells, and careful records on the lineage of each person would have to be kept.

Detection of Harmful Genes

One new development seems certain to come within a few years, since rapid strides are already being taken to make it possible. Tests are being developed that enable the laboratory specialist to determine whether or not a particular person carries even a single dose of a particular defective gene. For example, take the case of the disorder phenylketonuria (PKU), which in an untreated affected baby produces a certain kind of idiocy. The disorder results because the enzyme that transforms one amino acid into another is lacking. If you put such a child, very young, on a special diet with only a very little of the amino acid, phenylalanine, which is the one that cannot be properly utilized, the child will develop a normal mentality, and after it passes a certain age it will not relapse if taken off the special diet. Yet of course this individual has a double dose of the defective recessive gene and in adulthood will transmit the gene to its own offspring; and if the marriage partner also carries the gene, PKU may result. Prediction therefore depends on identifying the parents as carriers. It has been found that these parents are themselves not quite normal in their ability to utilize phenylalanine. They possess enough enzyme for ordinary purposes, and their mentality is in no way affected, but if injected with a rather large dose of phenylalanine they take about twice as long to get rid of it as do normal persons who lack the gene.

Thus we can detect carriers of the defective gene in the population, and advise them not to marry, or at least not to have children. In the past decade the ability to detect the carriers of specific recessive harmful genes has been extended to about 60 conditions. It consequently seems very likely to me that considerably before the year 2000 we will have genetic clinics in which by a battery of tests each prospective couple can learn whether or not both of them are carriers of the same defective genes. Advice to avoid having children and to substitute prenatal adoption could then be given. On the other hand, since the risk of having a defective child because of a specific recessive gene is only one in four when both parents are carriers, some couples may wish to take the risk. Whether advice or compulsion is to be used by society in these cases would seem to rest with the severity of the condition. If the prospective defect is one that would leave a baby a hopeless imbecile or idiot throughout life and a ward on society, or cause it to be born without limbs, or make it otherwise gravely defective, avoidance of parenthood ought to be mandatory. If, on the other hand, the condition is one that the new surgery or other methods of treatment might correct, as in the case of phenylketonuria, the risk might be taken. In any case, a new type of medical man, the human geneticist, is going to take his place along with the other specialists in the near future.

Questions of Freedom and Constraint

In a population suffering severely from overcrowding and subject to rigorous limitations of births, eugenics might be related rather simply to the measures for population control. For example, if a couple that had used up its coupons for two babies wanted additional children, they might be required to meet certain genetic tests before receiving a special permit. Some additional children above two per couple would be needed in some families to maintain the population at a given level, since some women have no children or only one, for a variety of reasons. The simplest eugenic test, yet one that in the long run might be quite effective in improving the population, would be simply to examine the first two children in order to assure that neither one was physically or mentally below average. Beyond the application of so simple a test, eugenic selection runs into frightful dilemmas. Who really possesses a "good" genotype? How do you judge, when what is the optimum genotype in one set of circumstances may be inferior in another? If we knew how to define the goal of a "good race" objectively, we might breed for it as we do animals; but the warning seems clear. In selecting for certain characteristics in their animal breeds, the breeders seem always to have sacrificed other, very desirable traits. The human races are not animal breeds, but each has been tested out by selection in a natural environment. Probably each is somewhat superior in its own way.

The control of human behavior by artificial means will have become by the year 2000 a frightening possibility. Government—"Big Brother"—might use tranquilizers, or hallucinogens like LSD, to keep the population from becoming unruly or overindependent. More and more subtle forms of conditioning will lead people to react in predictable ways desired by government or by commercial interests, without people quite knowing how they are hoodwinked. The added possibilities of controlled reproduction I have already described make these psychological methods of control over learning and behavior even more drastic. Here is our "brave new world" in full, with bottled babies in different kinds of solutions that would condition their mental growth to suit a certain caste. One wonders, moreover, what might be the effect of the complete liberation of the sexual life from its relationship to reproduction upon society and upon the family in particular. Recently Robert Morison (1967) of Cornell University, has pointed out the grave threat to the continuance of the family as the basic social unit. Can we safely, after a million years of human and prehuman evolution during which the family has been the basis of all protection, education, and nurture, give it up? What will be the psychological consequences of a population with no personal ties either to the older generation or to the younger generation? Can we look forward to the brotherhood of mankind when there are no more parents, brothers, or children—only people?

I have asked many questions that cannot at present be answered. I have predicted a future in which many cherished values of our society and many ethical standards may be questioned or superseded. It is not sufficient to have a few scientists raise such issues. Only prolonged and profound attention by many of the wisest men of our time, men of philosophy and religion, students of society and of government, and representatives of the common interests of men throughout the world, together with school administrators and scientists, may achieve a wise and sober solution of the crisis evoked in our world by scientific discoveries and their applications.

When is there overpopulation? Obviously, the question cannot be answered in simple terms. There is one answer to be given if you are thinking in the purely quantitative terms of numbers of people per square mile. But what sort of land is it? And what is the standard of living of the population? Quite another answer must be given if you are concerned with the quality of the population in genetic and evolutionary terms, and not merely with the state of its affluence. I am personally ready to accept the thoughtful definition I recently received from John A. Moore in an unpublished manuscript:

> *Overpopulation* exists in a unit of society when that unit uses the earth's resources at a greater rate than they are restored by natural or artificial means.

In that case Americans live in the most overpopulated land in the world, for they use and destroy, waste and dissipate the irreplaceable resources of the world at a rate that is estimated to be 50 times as great per person as it is for an Indian or African. Our enormous technological power is eating away the earth's limited supplies of fossil fuels and scarce metals at a rate that will exhaust them in a century, more or less. We devote little effort to the development of a new technology that will enable us to recycle and reuse materials to a maximum extent.

We are now entering a new era in the dimensions of human power—a day when we can modify the quality of the human population genetically as well as through improvement of the environment, a day when the course of human evolution will be placed in human hands. If we cannot solve even the relatively simple problems of controlling the quantity of human life on this so tiny planet, can we reasonably expect to manifest a greater wisdom in remodeling human nature and enlarging human capacities? We may foretell what man can be, but what *should* man be?

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