Government Is Most Dangerous of Genetic Engineers

By Joshua Lederberg

A Nobel Prize winner, Lederberg is professor of genetics at the Stanford University School of Medicine. The following is adapted from his testimony before the House Appropriations subcommittee headed by Rep. Daniel Flood (D-Pa.).

FOUR BILLION YEARS of biological evolution are represented in the DNA of every cell of every living organism. In every sperm and egg, one 300-billionth of a germ stores an encyclopedia of genetic information, the blueprints that guide the development of the fertilized egg into a fish, a sequoia, a raccoon, a chimpanzee or a human being.

The DNA of a human cell is not a man, any more than a written constitution is a living democracy or than the architectural plans for a dwelling are a happy home. An ideal plan can be wrecked by clumsy implementation or by unpredictable accidents.

Many imperfections in engineering designs may give no trouble; an oversized auto piston may still work most of the time. Yet when we have a catastrophic failure, like the explosion of the oxygen tank of Apollo 13, we may discover that the fault was a weakness of design.

This view depends, however, on what we expect the engineer to allow for and how much we will invest to cover every contingency. Many run-of-the-mill breakdowns in automobiles could be called design failures; they are also faults in a market mechanism that makes it difficult for a consumer to buy reliability from the auto dealer.

Correctives of Culture

BLUEPRINTS ARE, then, important, but it would be a mistake to enshrine them as "all-important," if by that we meant that nothing else mattered. Much has been said about the prospect that new scientific knowledge will open the door to revision of our genetic blueprints, an idea that needs much analysis.

In my own view, the most important thrust of new research will concern everything else that matters. In the long run, the DNA information will then have a less compelling role in our personal destiny. As already happens, civilization will provide an ever-widening range of correctives to release human nature from the bounds of our biological origins.

This impact of culture, the progressive component of history, is, after all, what distinguishes man from every other living species.

The most glaring fault in the human design is surely war, or rather our failure as a species to institutionalize a global framework for peace. Some popular writers have invoked man's instincts for aggression as the root cause of war, but we know of too many communities that have evolved a harmony of life to justify that fatalism.

Of course, biological human nature includes some of the requisites of war, and military conflict has been too important in history to be disregarded as a factor in evolution. Nevertheless, I must call this a political problem because the possible solutions are political.

We can fantasize biological answers —for example, the evolution of adamant instincts in either of two directions that would make war impossible: utter submissiveness in a caste system, or aggressive self-assertion in an anarchical one. But even if we knew how to implement such changes in human nature, I would prefer learning how to live together as the route to survival.

Besides the general aspects of human nature, our evolutionary heritage also leaves us liable to a heavy burden of accumulated mishaps and errors in the genetic information. We each carry a load of about four serious faults in our DNA. We are saved from fourfold incapacitation by covering most of these faults with a normal gene from one of our two parents.

When obvious genetic disease does appear, it will often be the result of a defect having been shuffled into the sperm and the egg simultaneously. This also means that genetic disease is almost always transmitted by parents who are not themselves afflicted by it. For this reason, it is almost totally futile to try to block the spread of genetic diseases to future generations by sterilizing those who are affected in this one.

Many advocates of human improvement by controlled breeding point to our successes with crop plants and animals. They overlook the vital role of inbreeding as a way of exposing the latent defects of different genetic stocks. Even if we were to pass over the deeply engrained taboos against incest, inbreeding in man would have frightful consequences for the health of the immediate issue. And if we confined human reproduction to those individuals who were absolutely free from genetic taint, we would solve all of our problems, for such individuals probably do not exist on earth.

The Real Dimension

THE BURDEN of genetic disease is, nevertheless, much more serious than is generally realized. Only a few per cent of the population suffer from a serious disease of physical or mental development of the kind usually associated with faulty genes, but many common diseases have an important genetic component, some individuals being inherently more susceptible than others. If we prorate the genetic factor in disorders like diabetes, atherosclerosis and schizophrenia, we estimate that at least 25 per cent, and perhaps half, of our total health care burden has a genetic basis.

I will summarize the main technical approaches that we can foresee over the next decade to help ameliorate these problems. The most forthright attack on genetic disease has been developed in the last few years, the technique of prenatal diagnosis.

When an early fetus is confirmed to be stricken with the genetic mishap of serious, irremediable disease, it can be aborted. From the standpoint of a mother facing the dreadful prospect of bearing a malformed baby, this is a much more positive step than it may appear to a detached onlooker. She can have an abortion and try again to have the healthy baby which she has some odds of producing.

This procedure is now available for only a few diseases, but the principle could be developed for many more. I am not suggesting that abortion is an ideal solution but I believe that even those with strong religious convictions will temper their condemnation in the face of the human realities of this particular problem. Also, research on prenatal diagnosis can lead to new forms of prenatal therapy which may allow more satisfactory choices than abortion.

The most important advances are likely to concern the unfolding of the blueprints rather than direct changes in them. We have only vague ideas of how genetic defects contribute to diseases like diabetes or Huntington's chorea. We need more profound biochemical studies of every stage of development of such individuals before they actually come down with the disease itself, for by then there may be many secondary consequences to obscure the primary point of weakness and breakdown. It may also be necessary to develop preventive therapy for such diseases starting at a very early age.

Similar studies will also make it easier to identify prospective parents who are carriers of genetic disease to help them know whether they have more than the average risk of certain defects in the family they are planning.

Genetic Vaccines

FURTHER IN THE future are genetic vaccines. These would be viruses especially developed to carry correct genetic information to the body cells of patients with certain specific defects. This process is very similar to the present use of vaccines for the prevention of polio or smallpox. Here, already, we use specially developed viruses to modify body cell functions for the production of immunity.

This approach would make the most effective use of recent discoveries in molecular biology, like the chemical synthesis of a small gene by Prof. Gobind Khorana of the University of Wisconsin.

Virogenic therapy is not intended to modify the DNA of germ cells, but to add additional DNA to some body cells adversely affected by the natural endowment. The effects should not, therefore, be passed on to future generations, any more than those of a polio or smallpox inoculation. However, we badly need more research in this general area to understand more precisely the role of natural virus infections in causing genetic changes, about which we do have some alarming hints.

These kinds of laboratory studies, finally, are indispensable for scrutinizing our environment for new chemicals that will aggravate our burden of genetic deterioration. Many common chemicals will react with and alter DNA, but we have too little information to make precise estimates of their effects.

Radiation exposure is an inevitable side-effect of our atomic energy programs, as well as of medical X-rays and of our natural environment. The Atomic Energy Commission's standards of permissible exposure (about 30 times larger than the level we experience now from atomic energy activities) would increase the natural rate of mutation about 10 per cent. Over a period of generations the health cost of these additional mutations would be about $10 billion a year.

This estimate, and its probable uncertainty by a factor of 10 either way, needs to be factored into the economics of energy production and, more immediately, into the cost-effectiveness of the genetic research needed to plan on a basis of scientific certainty. Most of the atomic-energy related costs might even be canceled if we made sufficient efforts now to develop the countermeasures.

Caution Essential

THE WHOLE idea of responding to the challenge of genetic disease has excited some alarm among those who fear statist control of the genes or other forms of tinkering. That we must proceed with great caution is obvious, especially if we become enraptured by plans for utopian improvement beyond the repair of obvious misery.

The human organism is the most intricate of all mechanisms, refined, despite its imperfections, through costly natural selection, and it would be easy to program some would-be improvements at the price of some subtly connected catastrophes. However, we cannot ignore the experimental games that nature is continually playing with us; we suffer about one significant new mutation in every five to 10 germ cells. If, generally speaking, we do not know nearly enough to program superhuman beings, we do have unmistakable griefs about the burdens that prevent living out a normal life in reasonable health.

The greatest peril is, of course, that governments will take over individual decisions on reproductive matters. Not everyone agrees, but the main pressures that would lead to state involvement in reproduction do not come from genetic research but from some proponents of other community goals like population control. Even a concern for social welfare may be treacherous if pushed to passionate absurdities.

For example, doctors are often urged to concern themselves with the total environment of the poor; to root out all of the sources of disease; to re-engineer society, not merely treat the superficial outbreaks. By the same argument, they might also be pressed to re-engineer the genes of their patients, a task which is probably about as difficult. We should answer that both challenges need the care and attention of the whole community, to look for answers that preserve basic democratic rights.

The Hard Cases

WE WILL be stressed by a few hard cases. If the community pays all the bills, should it still stand aside if Mrs. Somebody decides to keep bearing children despite the certain knowledge that they will be deformed? I think yes; this is a small price to pay to protect the principle of private decision, and something less than coercion will usually influence such people to act in their own and the community's best interests.

Most people's fears about genetic engineering are probably more mythological than political, based on unfamiliarity with the role of genes and other factors in development, and on the sense that the DNA amounts to the inner personality. What do you think of a scalpel? It can cut out a tumor or repair a heart. It can also turn a stallion into a gelding. Genetic engineering will need much the same kind of legal control that surgery needs and has.