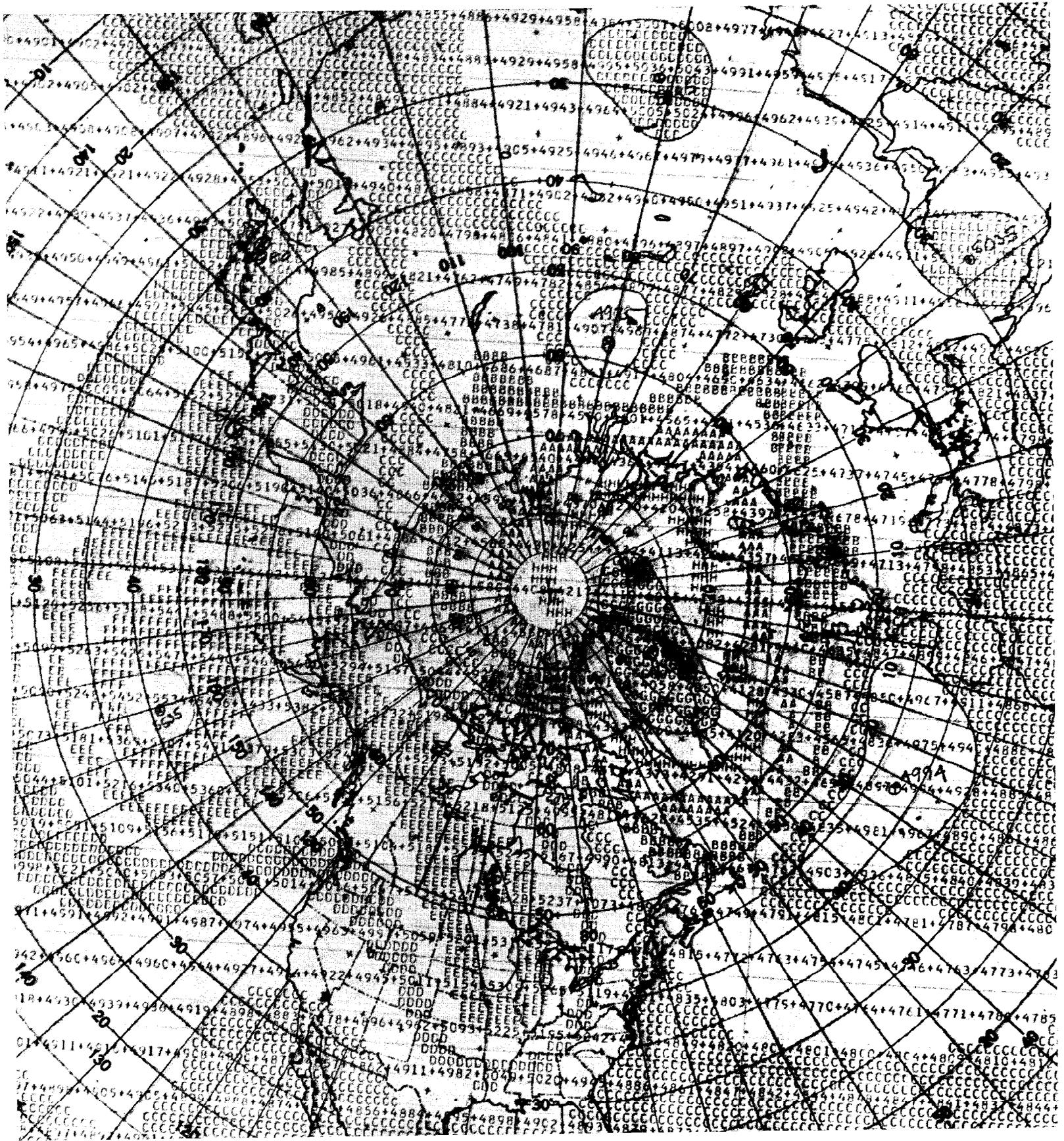


# T H I N K

see pp. 16-19

116  
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# **A Visit with Joshua Lederberg**

**by John E. Pfeiffer**

*We call on one of the world's foremost biologists, a leader in the field of biological engineering who at the age of 33 was awarded a Nobel Prize for his studies of heredity. He discusses spare-part medicine, the evolutionary crisis, mental retardation and modern man's need for a plan to shape his own destiny.*



THE PAST DECADE OR SO has seen an enormous increase in our understanding of living matter. Research on the master substance of heredity, deoxyribonucleic acid (DNA, for short), has brought fresh insights into the nature of immunity, protein synthesis, virus action, memory and other basic biological phenomena. The next step will be nothing less than a revolution in medicine, as doctors start applying the new knowledge. Coming advances promise to surpass, soon and by a wide margin, everything that has been achieved previously, from the days of Hippocrates to the present.

A number of researchers realize that such things are definitely on the way. But few of them have considered the full implications as carefully as Joshua Lederberg, director of the Kennedy Laboratories for Molecular Medicine at Stanford University and one of the world's foremost biologists. The son of a rabbi, Lederberg entered Columbia University at 16 and became an assistant professor at the University of Wisconsin six years later. Since then, he has won practically every scientific honor worth winning, including a 1958 Nobel Prize for studies of heredity-transmitting mechanisms in bacteria.

Today, at the ripe young age of 39, Lederberg can hardly be considered an elder statesman. But as a member of various President's panels and special committees he has already helped shape national policy involving space exploration, research in mental retardation, the dissemination of scientific information and other problems. He is also very much concerned with the even broader problem of predicting and preparing for expected medical breakthroughs which, in the absence of adequate plans, could easily become mixed blessings.

I talked with Lederberg not long

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ago in his office at the Stanford Medical Center. He is small and soft-spoken, with an impressive non-nonsense quality in the tone of his voice and in the way he looks at you — clearly a man who is impatient with trivialities and does not intend to become more patient in the foreseeable future.

"About two years ago, I was invited to present a paper at a symposium on the future of man. As a geneticist I had to give special thought to the prospects of eugenics. For a long time now we have been hearing about the possibility of breeding superior people as we breed livestock, the idea being that superior men and women would have superior offspring and that the species could thereby improve itself by artificial selection. Another eventual possibility is directed mutation, the production of 'desirable' traits by deliberately modifying the chemical structure of our genes.

"Such developments may come, and they might even be wished for — provided, of course, that we can agree on the wide diversity of desirable traits and avoid thinking in terms of master races. But I do not think that they will come in a hurry. Eugenics affects human *populations*, which take many generations to change appreciably, and it seems to me that our greatest advances will involve individuals, at least as far as the near future is concerned. Instead of tinkering with the hereditary material and influencing the nature of future generations, we can work with existing people and help them make the most of what they already have, the physical constitutions they inherit from their parents."

Lederberg has coined a word for this form of biological engineering, "euphenics," which refers to the improvement of the individual and contrasts with the species-improving viewpoint implied in eugenics. Euphenics is closely related to the daily progress of medicine but is concerned with those aspects of "human modification," especially during development, that produce fundamental changes in the character of the organism. I wanted to know how

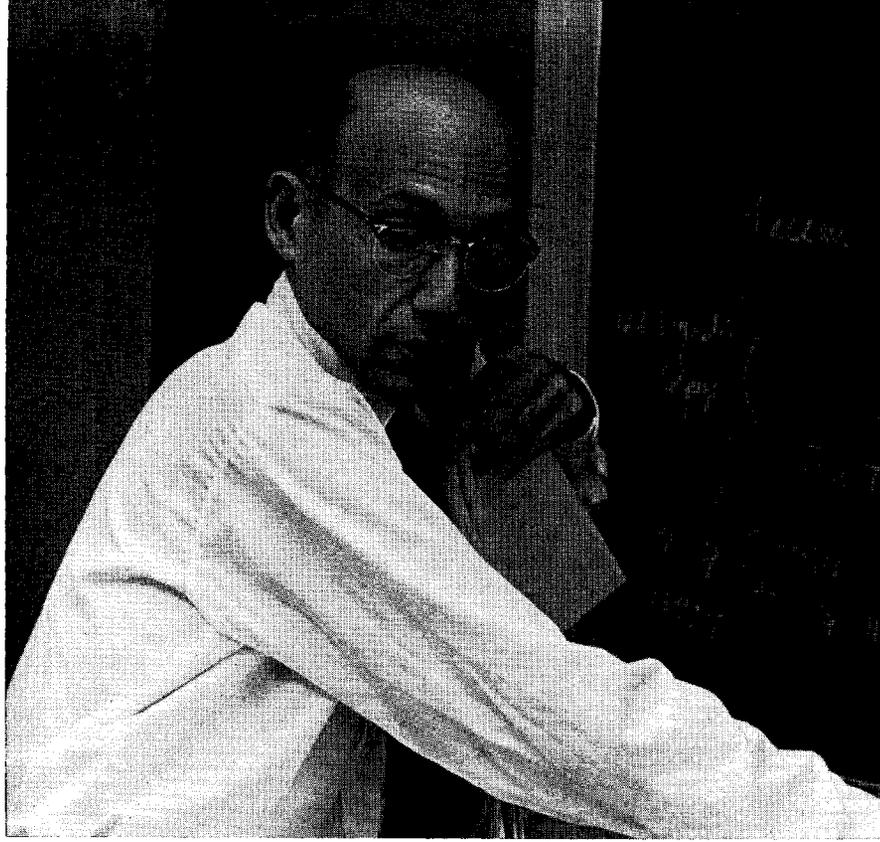
such changes would affect medical practice.

"Making prophecies is a risky business," Lederberg remarked cautiously, "especially in science, where practical applications depend to such a large extent on the unpredictable course of basic research. But some developments are already well under way. For example, it is only a matter of time before we learn to replace diseased organs with healthy ones. Current attempts to replace kidneys represent a beginning which hints at far more successful procedures in the future. Also, we should learn to reduce the failure of blood vessels, and to improve brain function."

**Evolutionary Crisis**

"Before discussing specific cases, however, it should be emphasized that we are totally unprepared to accept the consequences of our success. We simply cannot continue to ignore anticipated and inevitable changes in man's biological constitution. The population explosion is one example of what can happen without planning and, as of now, there is no striking evidence that we have learned our lesson. We have policies for foreign aid, civil defense, television programming, advertising campaigns, and so on. But as far as the most important thing of all is concerned, what man himself is going to be, we have no policy.

"Furthermore, the pressure is increasing. Scientific knowledge has been doubling every 10 or 15 years and the rate is still increasing exponentially. Perhaps even more important, our culture has learned the benefits of supporting research on an unprecedented scale. Thus our potential leverage encourages a new confidence that any scientific or technological problem can be solved — merely provided it can be formulated in precise terms. In biology and medicine this realization, euphenics, is an evolutionary leap of the same dimensions as the original divergence of man from the primates, and the discovery of agriculture, language and politics. Pre-



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dictions of the ultimate significance of biological advance are not new; what should be stressed now is 'there is less time than you may think.'

What are some current examples of intensive research in such areas? Lederberg cited studies involving tissues and organ transplants, studies which show that immunity may not always be a beneficial thing. Most grafts fail to take because the body mistakes them for dangerous invaders. It fights back by producing the same sort of proteins which help neutralize the harmful effects of germs and viruses.

"Currently this fighting back is the major obstacle to spare-part medicine. But the solution suggests itself. If we could prevent the formation of specific proteins which cause the rejection of specific grafts, if we could inhibit immune mechanisms with selective drugs, the way would be clear for the large-scale use of substitute tissues. Considerable progress has indeed been made in the use of such drugs, and we should soon reach the point of confident reliance on them."

Lederberg indicated that hearts,

lungs and livers may be obtained from human cadavers and eventually from genetically pure, inbred strains of chimpanzees or cattle. A contrasting approach is the use of artificial organs made out of plastics and other materials. (Already, special transistorized devices built into the chest wall can take over one of the heart's functions, that of pacemaker, and produce regular rhythms in defective hearts that cannot beat regularly on their own.)

"Because of difficult technical problems involved in overcoming immune reactions," Lederberg explained, "the use of artificial organs might well become practical before the use of natural organs. Unfortunately, however, this line of attack is receiving only a fraction of the support it deserves, especially in relation to the benefits of bypassing serious problems of allocating natural organs."

He went on to point out that even more serious problems lie ahead. As soon as medical investigators learn how to provide patients with substitute organs, natural or artificial, we may expect real trouble.

"We cannot sit back and leave everything up to the customary practices of the marketplace, as if spare parts for sick people were household appliances or television sets. Demand is certain to outrun supply for several years or more, and you can imagine the macabre nature of a black market under such circumstances. We should establish rules for allocating organs in a humane and systematic fashion and thereby avoid the obvious abuses that might occur. At the very least, transplants should be formally registered to help an orderly evolution of legal and surgical procedures.

"You can see that euphenics is neither abstruse nor remote. As long as organ shortages prevailed we would be faced with, and forced to make terrible decisions on a broad social basis. Imagine a national roster of 30,000 patients, all of whom would die within a year unless they could be furnished with new organs. Suppose further that the entire supply for that period amounted to just 1,000 of the spare parts. How would you select among the patients? Would you choose a brilliant surgeon in his early 50's over a young student of uncertain future, or vice versa? A school-teacher over a housewife? A wealthy elderly widow who might donate money for a new laboratory or hospital wing over a young electrician?"

According to Lederberg, comparable decisions are already being made on a small scale. Doctors at the University of Washington Medical School in Seattle, for example, have developed an artificial kidney center, which supports a machine designed to remove toxic waste products from the bloodstreams of persons suffering from advanced kidney diseases. Patients are kept alive by visiting the medical center once or twice a week to have their blood cleaned by passing it through the "mechanical kidney." These people are lucky. They were chosen by a special jury; for every one of them two to three other patients had to be rejected. It costs about \$10,000 a year to treat a patient, and at present there is not enough money

to treat all those who need help.

"All this is merely a faint hint of things to come," Lederberg continued, "a kind of rehearsal of problems which may become widespread. Sooner or later, and probably sooner, we must be prepared to weigh many lives in the balance — and who will do the judging? Research advances are being made at a breathtaking rate. Organ transplantation will be perfected as a reliable procedure certainly within five to ten years — but where is the system for preserving and allocating precious organs?"

Lederberg is extremely effective in communicating his deep feeling for the urgency of things, the feeling of an investigator who knows science from the inside and knows how fast things are happening.

"One result of spare-part medicine, and concomitant developments in biochemical medicine, of course, will be an appreciable extension of the human life span. With limitations of heart failure removed, many people could already expect to live 90 to 100 years. As we deal with the other organs, which become the limiting factors when we reinforce the more vulnerable organs, we could anticipate an indefinite extension of the life span."

### **New Hearts, Old Bodies**

I asked what good it would be to have a new heart if the rest of the body aged as it does now—wouldn't we simply be extending the period of human uselessness by a few decades?

"That's just the point," Lederberg replied. "We must scan all problems beforehand and consider their interrelated consequences and establish research priorities in some balance where they touch on such vital applications. If we remain indifferent to such things and try to muddle through somehow, our world could well become a nightmare world. Technically, we have the ability to solve practically all our present-day problems, but we hardly know how to apply this power.

"For example, the next 20 years will see enormous advances in our

techniques for mitigating the effects of aging. My point is not the specifics of the solutions, but some possible directions might help make the discussions more tangible. Many aging effects seem to be due to a kind of accumulated scarring. Little accidents are occurring all the time. Blood vessels become blocked, fragments of nerve and muscle die, and not all the debris leaves the body. The increasing load of clogging tissue takes its toll in the long run. To counteract such tendencies we may find custom-built enzymes, compounds designed to dissolve specific types of scar tissue without affecting normal tissues. We might reduce scarring in the first place by introducing into the bloodstream special substances to prevent the formation of tiny clots in the blood vessels, a major cause of trouble.

"Treatment of this general sort can be expected as we learn more about chemical changes that accompany the aging process, notably changes in the hereditary material and the proteins whose syntheses it controls. Some of the most important applications will involve the functioning of the brain. This organ seems to be particularly vulnerable to blood-vessel accidents and clot formation, and anything we do to reduce such troubles will help it operate effectively longer. Euphenics might go even further and deliberately improve the brain's circulatory system by modifying the course of its embryological development before birth."

Lederberg has a special interest in the workings of the brain. The laboratories he directs were built with funds provided by the Joseph P. Kennedy Jr. Memorial Foundation and are dedicated to a broad attack on biological problems which, among other applications, are fundamental to mental retardation—a condition afflicting more than five million adults and children in the United States. This research could have far-reaching implications for all peoples.

"Studies of mental retardation need not apply to afflicted persons only. The more we learn about the basic causes of this condition, the

better we shall understand the chemical workings of normal brain tissues — and the greater the chances of artificially enhancing intelligence, perhaps with the aid of appropriate drugs during development. After all, in a very basic sense, we are all mentally retarded in comparison with what we could be if we realized the full potentialities of our brains."

Lederberg had reached a natural turning point in his discussion.

### **A Potential Tragedy**

"There is nothing sacred about any one of these suggestions as to possible future advances in applied biology," he emphasized quietly. "They are significant only as examples to illustrate the type of problems that will arise, and the fact that we cannot afford further delays in facing up to such problems. We cannot continue to immerse ourselves in the past, as if research were still moving at the relatively sluggish pace of a generation ago.

"But above all please do *not* give the impression that I have a program, or that anyone else has a program. Indeed, the whole point is precisely that no program exists. This is the danger, the potential tragedy, of the situation we find ourselves in today. To arrive at a platform of carefully considered recommendations, we must establish a community of opinion. Scientists should be working along these lines, of course, but the problem is far too big to be left to scientists alone.

"The problem here involves the lack of communications between the sciences and the humanities. People who distrust or are hostile to science, and our educational system still continues to produce them in quantity, often find a strange delight in turning away from problems whose solutions call for some scientific knowledge—that is, from practically all the major problems of our times. The universities can take the initiative in defining a broader humanism, and providing an atmosphere for provocative and productive discussions. And we desperately need such discussions." ●