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LEDERBERG: A MIND EXPLORING MAN

by David Perlman

An extraordinary scientist named Joshua Lederberg paused not long ago during a conversation that was ranging widely across a variety of topics from abortion laws to Martian life, from genetic molecules to germ warfare.

"I guess I've been interested in thought," Lederberg mused, "just about as long as I've been able to think."

It is unlikely that Lederberg began to cerebrate at the moment of his birth, but the beginning could not have occurred much later than that. For by 15 he was lecturing to public audiences on cells and their genes; by 21 he was deep in the genetic research that was to win him a Nobel prize a dozen years later. And by 22 he had confirmed his experiments, earned his Ph.D., and was on his way toward the loftiest posts in Academe. Today, at 44 (note: or 43; his birthdate was May 23, 1925), he is one of the most influential men in American science.

Consider a few of his responsibilities:

He is professor and executive head of the department of

genetics at Stanford University Medical School; he is a leading member of the Space Agency's biological team preparing experiments to search for life on the planet Mars; he is director of a major laboratory devoted to the application of molecular biological approaches to the problem of human mental retardation; he is deeply engrossed with a platoon of colleagues in endowing a computer with "artificial intelligence;" he is seeking ways to apply a therapeutic concept that few have yet heard of---"euphenics," a word he invented himself---to the treatment of human defects and the fulfillment of human potential; he is tackling, in his own laboratory, some of the most fundamental problems of biochemical genetics; and he is one of a dozen men in America responsible for reviewing and approving more than 5000 individual research grants a year, totaling $275 million, from the National Institute of Mental Health.

In addition to all these self-imposed assignments, any one of which might fill an ordinary man's day, Lederberg is also one of the few truly eminent scientists who is trying to narrow the three-way gap that now separates basic scientific research from its technological application, and from its comprehension by both public and politician.

Only by narrowing that dangerous gap, Lederberg feels, can rational social policies keep pace with the explosive potential of today's great strides in the biological sciences. He is, in fact, emerging as a new kind of public conscience

for science, and his impact is growing.

"I have discovered," Lederberg recently said, "that research is grounded far more deeply in human social activity than I had previously understood. Scientific advance is, by definition, a penetration from the frontier of existing knowledge. But the frontier bounds the insights available to the whole human species, not those of any single individual.

"There is a vast gap between scientific and political foresight about technological change. We scientists may argue about timing, but we know change is coming fast.

"I happen not to believe that scientific training confers any magical wisdom about human affairs, and I would be loath to relegate the management of a nation to its scientists any more than to any other restricted group. But the new era of biological science necessarily poses new opportunities and challenges, and the facts simply must be more widely understood."

This imperative has summoned even more activity and thought from Lederberg: Today, besides testifying before Congressional committees, advising the National Aeronautics and Space Administration, consulting for other government agencies and biologically-oriented industry, Lederberg has turned public commentator and writes a weekly column on science and public affairs that is circulated by the Washington Post to more than 250 American and foreign newspapers.

Concise, straightforward and at times almost cryptic in his speech, Lederberg in his book-lined office conveys an

impression of benign, bespectacled detachment, of the brisk but gentle scholar immersed in scholarship alone. His conversation is laced with mild irony and scholarly allusions---to Aschylus and Plato, Freud and Bertold Brecht, as well as the giants of his own scientific world like Herman Muller, Francis Crick, Peter Medawar and Arthur Kornberg.

Yet for all his air of detachment and the leisurely, reflective, humane quality of his talk, Lederberg never strays far from the urgent realities of today. His most fundamental scientific interests are still fundamental indeed, after 25 years of laboratory exploration into microbial genetics, DNA and the chemical nature of life. Yet he himself is quick to link each one of his interests to the "Promethean anxieties" of right now: disease, organ transplants, race, pollution, population, nutrition, war.

At the moment, for example, Lederberg is following closely the work of a group of colleagues---many of them his former graduate students---in exciting new genetics research, and is leading his own current graduate students along similar paths. Follow and lead are, perhaps, misnomers, for as Lederberg describes his laboratories: "We have a very, very loose structure around here; there is a kind of mutual inspiration that goes on, and it varies a great deal from one facet of research to another. I have a group of students whom I call my own, in the sense that they talk to me first before they talk to everybody else in the Department. But there's a lot

of independence too."

Arthur Kornberg, another Stanford Nobel laureate who first persuaded Lederberg to come West 11 years ago, led a group that electrified the world last year when they artificially duplicated the active, living core of a virus after purifying the crucial enzyme responsible for linking together the single strand of the synthetic virus's genetic material, its DNA.

Now Lederberg's laboratory is working in the vastly more complicated field of bacterial DNA, and one of his former students, Assistant Professor A. T. Ganesan, has independently developed a system for replicating the complex DNA molecule of a bacterium called Bacillus subtilis. Where Kornberg's test-tube DNA was a single-stranded molecule and contained some 5500 error-free links of DNA components known as nucleotides, Ganesan's self-replicating bacterial DNA is double-stranded, and contains somewhere between 50,000 and 100,000 nucleotides.

Closely linked to this work is the current research of Lederberg himself and his semi-autonomous graduate students. They are seeking to pin down the mysterious activity of biological catalysts called enzymes that govern the way long-stranded molecules of DNA repair themselves when they are torn apart by environmental assaults such as radiation. A common germ that resists radiation damage to its genetic core is called Micrococcus radiodurans, and one of Lederberg's students

has recently discovered a flock of hitherto unknown bacteria that also resist radiation and that live in the heavily-irradiated open soil near an unshielded gamma-ray source at Brookhaven National Laboratory on Long Island.

Just how these microbes keep repairing their sundered DNA is unknown. There must be an enzyme, or more than one, that stitches the long, coiled DNA molecules back together when they are severed; if Lederberg's group finds the enzyme system they will have a method for taking highly complex genes apart and putting them together again---more importantly, a system that may let them link up the genes of organisms of wholly differing species.

An exciting future could result:

"What you might call the long-range goal of this work," Lederberg says, "is to put together in one organism DNA that has originally been obtained from different sources. Strangely enough, we don't know how to do that yet. With all the tricks that we know how to play with DNA, we can't yet take DNA from a human source, for example, and get some segment of it into a bacterial chromosome to see how it functions in that background. But this is exactly what we'd like to learn how to do.

"There would be many interests, both basic and applied in being able to accomplish such a trick. The most obvious would be to produce enzymes characteristic of human origin within bacteria---to alter a bacterial gene so it codes for a human enzyme, and then produces it in quantity by normal

* N.B. 3/99
DNA splicing

bacterial fermentation.

"Suppose, for example, you could get a DNA segment that codes for human pituitary growth hormone, transplant it into a bacterium, and then fire up this bacterium to produce the growth hormone. You'd have a full-scale human growth hormone factory operating in your laboratory."

Obviously, the ability to transplant human segments of DNA into a culture of microbes that would reproduce it in quantity raises exciting prospects of made-to-order enzymes for all kinds of purposes: to alter patterns of human antibody reactions and thereby solve the most vexing problems of organ transplants, for example; to attack a host of diseases, from diabetes to cancer to aging, where the genetic material of cells lies at the basis of the defect; to synthesize missing amino acids essential to proper nutrition.

Human nutrition---and malnutrition---concern Lederberg deeply as world problems today, and the most significant scientific problem in nutrition is the fact that far too many millions of people in the world live on diets dangerously deficient in one or more of the 20 amino acids that are critical to the manufacture of all proteins.

The human organism can make only 9 or 10 of those amino acids itself; the rest must come from foods. "Amino acid deficiency," observes Lederberg, "is a genetic disease that we now treat by dietary replacement. An alternative solution would be a vaccine-like inoculation to take the place of the genes that normal men never had."

Malnutrition, holding within it the seeds of war and racial annihilation, is typical of the issues that Lederberg sees as ripe for scientific intervention. There are others.

Many scientists before Lederberg have prophesied a day when man's heredity can be altered at will; when "genetic engineering" will change the human species into a new strain more effectively adapted to this planet's environment. The late Herman Muller, whose Nobel prize came for his discoveries of artificial mutation by x-rays, advocated long term genetic change by selective breeding, or eugenics, and later seriously suggested sperm banks where the frozen seed of the world's great people could be stored and then used to upgrade the race.

Lederberg, however, sees "genetic engineering" in a different context. "The very concept of selective breeding as a method of engineering human improvement," he says, "has been discredited as a violation of elementary human right." So he has invented the term "euphenics" as opposed to eugenics---and he defines it as "the constructive engineering of human development." From conception on, as Lederberg sees the future, it should soon be possible to intervene euphenically all along the course of life to improve human intelligence, to turn aside disease, to forestall or correct enzymatic defects.

Already, Lederberg's laboratory is tooling up to implant bacterial DNA into the developing egg of a frog in order to alter the egg's development predictably. One day---perhaps

in five years, perhaps in 20, this may occur in human embryos too. The goal; in Lederberg's words: "the fulfilment of human capability."

With techniques already available for predicting many congenital and hereditary defects before birth by analyzing cells from a mother's amniotic fluid, Lederberg sees no reason why many of these defects cannot soon be corrected in the embryo by using harmless "carrier organisms" like viruses to bear artificially coded DNA molecules into the unborn child's body. "Embryology is very much in the situation of atomic physics in 1900," he says. "Having had an honorable and successful tradition, it is about to begin!"

Euphenics may indeed attain reality; but until it does Lederberg is equally concerned with insidious social policies---"dysphenic", he calls them---that damage human development while society refuses to move. Global malnutrition, leading to permanently stunted young minds and bodies, is certainly one such policy, whether adopted deliberately by evil governments warring on one another, or as the inadvertent result of ignorance and unwillingness of white Americans to end poverty in malnourished American ghettoes. Selective malnutrition, as Lederberg says, ironically, is a "euphenic experiment practiced on a large scale in the world today---it is a central process in the world political system."

Another social policy Lederberg condemns as negative "human engineering" is the current legal status of therapeutic

abortion in almost all States.

"Laws that flatly prohibit abortion on grounds of known fetal defects," he says bitterly, "attempt to enforce a kind of genetic engineering, albeit of a nihilistic sort, that insists on the culmination of every fetus, however misconceived. On the one hand we promote innumerable personal tragedies by insisting on the absolute inviolability of the life of even a quasi-human not yet in being; on the other hand we have invested the larger part of our national budget in war machinery whose only exercise would be to extinguish the lives of most of the human race."

An even more maddening paradox, in Lederberg's view, is today's increasing tempo of what he calls "species-suicidal research"---the quest for more and more powerful and pervasive biological weapons in the form of lethal viruses, food-destroying agents, and mind-bending chemicals. Using these weapons in war would be an ultimate horror, but Lederberg is equally appalled at the lack of social controls over the research process itself.

"One of the insanities of the chase after military security," he says, "is the world-wide competition in research and development in biological warfare. These activities are aimed at practicing the large-scale deployment of the most contagious enemies of man that he can discover or invent. Our personal security must then depend on the depth of the technical competence of the men responsible for the research. This

is impossible to judge from outside the secrecy barrier. However, it is almost certain that the technicians willing to work in this area are self-selected for peculiar nonchalance about it.

"For his own personal security every Congressman should seek his own assurance---less readily available to the common citizen---that the internal surveillance of experiments with contagious weapons is prudent enough to suit him and his family."

Although his columns and public discussions often concern themselves with parallels between biological "disharmony" in the human organism and similar disorganization within the body politic---"We deplore violence as a method of solving problems," he has observed, "but the bombers still peacefully illuminate Vietnam with American wisdom."---Lederberg can generate tremendous enthusiasm for science rationally applied.

One of his major current interests, for example, is the problem of "artificial intelligence," and how to develop it through sophisticated computer programs. He and a group of colleagues have already developed a powerfully "intelligent" computer-based program that can, by generating new hypotheses as it confronts new ~~problems~~ data, actually reason its way toward solutions to practical problems.

Lederberg, Professor Edward A. Feigenbaum, and a team of engineers, chemists and mass spectroscopy specialists have tooled up their brainy computer at Stanford to identify the

structure of specific organic molecules given only their mass spectra and the various theories that link the structure of molecules to the spectra of the atoms that compose them. Since the theories are not fixed, the machine program must not only compute probabilities, but puzzle out new theories as it summons up new data. This is a giant practical step beyond the computer programs whose "intelligence" is limited to playing a passable game of chess.

"It's very, very difficult to match human intelligence in common-sense situations," Lederberg says of the artificial intelligence program he has dubbed DENDRAL because of the branching nature of its logical reasoning pathways. "Just remember the kind of subtlety that the human mind has---for drawing analogies of a very far-fetched kind, for transforming one problem into another one, for making shaky and tentative trials in one area and then giving up and trying something else while always remembering what had been tried before--- these are very, very hard things to put into a computer program.

"I'm quite convinced that there will never be a complete emulation of human behavior by machinery, and I'm not sure that anyone designing a machine will ever want to bother to do it. But we are still trying to learn how far we can go to free human minds for what they can really do best, because this is as much an exercise in psychology as it is in machine engineering. We can certainly think more efficiently if we have machines helping us out, because right now we can spend only

a very small part of our total intellectual effort at things that could in any sense be called inspired; and inspired thinking is what we can't reduce to a machine program."

The current artificial intelligence effort, Lederberg feels, has proved remarkably successful, and is already advancing toward more complicated reasoning tasks.

"If we can bootstrap this work four or five levels higher and get fast enough machines to go further," he says with a smile, "then we might have enough flexibility where an afternoon of conversation with a machine might result in instructing it to do something as useful as an afternoon's conversation with a bright student. But we're very, very far away from that at the moment."

Actually, the Artificial Intelligence Project has at least one extremely practical goal down the line: some day an intelligent mechanical descendant of the present DENDRAL program may, in fact, become a computerized researcher itself, independently selecting and then analyzing from among a choice of unmanned experimental tools on distant planets to examine life processes there.

In Lederberg's fecund mind it all links together: the examination of DNA as the basis of evolution on earth; the perfection of machine intelligence as a quantum jump in human reasoning potential, and the search for universal principles governing the universe's life.

For a decade now Lederberg has been extremely active in

the space program, and today he is one of the leaders in the search for extraterrestrial life. In 1960, at the first International Space Science Symposium in Nice, France, Lederberg coined another of his new words to give the search for life beyond the earth its official and now widely-used name: Exobiology.

Since then Lederberg's research group at Stanford has published more than 100 scientific papers dealing with the science of exobiology and has been awarded more than $1,500,000 by the Space Agency for theoretical research and the development of automated life-detection systems to be packaged aboard future spacecraft. The Instrumentation Research Laboratory at Stanford's genetics department, directed by Dr. Elliot Levinthal, has devised all manner of ingenious gadgets to sample planetary soils, culture their micro-organisms, and examine them for evidence of the metabolism and optical activity that could reveal life.

The lab has also proved of enormous benefit in medical research too, and under the inventive guidance of Professor Leonard Herzenberg many of its new instruments have already been adapted for examining physical and biochemical properties of cells and cell surfaces that may prove relevant to medical advances from organ transplants to cancer therapy to radiological diagnosis.

No one in the space program seriously expects the Apollo Astronauts to find signs of life on the moon when they land

there this summer, but in the minds of most astronomers and space scientists Mars is indeed a likely candidate for life in the solar system. Two Mariner space probes will be flying past Mars, photographing the planet, this July and August. In 1971 two more spacecraft are scheduled to orbit Mars for 90 days on a more detailed reconnaissance; and in 1973 an ambitious mission called Viking will send two unmanned vehicles to land on the Martian surface, sample its atmosphere directly, and deploy the first life-seeking instruments there.

Lederberg has already examined the earliest Mariner IV photographs, and he will be looking more closely still at this summer's pictures. For 1971 he is a member of the Space Agency's reconnaissance team that will screen the orbital photographic evidence minutely to select landing spots where life appears most plausible: the "wave of darkening"---a possible sign of vegetation---along the edge of seasonal ice caps, for example; or even more mysterious areas beneath "clouds" that could be hovering over warm, moist oases where sub-surface heat sources may be melting permafrost to provide enough essential moisture for precarious life.

While Mars pictures so far show no evidence for liquid water on the planet's surface, Lederberg still ~~believes---and wants fervently to believe---that~~ moisture does indeed exist.

insists on keeping an open mind on whether

"In my mind," he says, "the Mariner pictures have been extrapolated beyond reason in terms of trying to make a model of complete aridity. We've all heard how there's no water

anywhere on Mars, how it's a dead planet covered with unweathered craters and all the other cliches. But there are a few places where craters seem to show wavy rills, evidence of some kind of fluid in past history there, and one of the Mariner pictures does show what may be a cloud and its shadow. If that cloud hangs above a crack in the crust, and the crack extends to moisture below, life could indeed be there."

The instruments for Viking have been neither chosen nor designed yet, but among the means for seeking life on the planet Lederberg and his co-investigators envisage several possibilities: one might be to inoculate a sample of Martian soil with radioactively labeled sugar, and then to look with a simple instrument for evidence of radioactive carbon dioxide emerging---a sign that some living organism is digesting the sugar. Another could be to plant radioactive DNA on the Martian surface and seek evidence of its degradation; for any living system whose reproduction is based on DNA must have a way of destroying the chemical too, Lederberg reasons.

Ever since the first programs for Lunar and planetary landers were detailed, Lederberg has been one of the leading scolds and prods within the space establishment on the question of earthly contamination of the solar system. If Mars---or even sub-surface Moon crevices---can support life, he and astronomers like Harvard's Carl Sagan argue, then it is absolutely vital that no terrestrial organisms be permitted to

contaminate the new-won territory. On Mars, for example, a single dose of microorganisms from earth---and many can survive under extreme conditions of heat, cold or radiation---might pollute the planet completely before terrestrial scientists could ever determine the characteristics of the original life there. The key facts---of Martian metabolism and evolution---would become unknowable forever. Lederberg has also helped shape policies to protect the earth against unexpected contamination by extraterrestrial organisms carried back aboard returning future spacecraft.

Fortunately, there now is tacit agreement between both American and Soviet space mission planners that all vehicles and instruments heading for the moon and planets must be thoroughly sterilized before they leave earth. Three years ago a space scientist smuggled an unauthorized and unsterilized American flag aboard the first Surveyor vehicle that soft-landed on the moon, and Lederberg was outraged. He branded the incident a "patriotic prank," and declared publicly: "The bootlegged flag is an actual violation of an important aspect for the protection of the moon and planets against avoidable contamination with earth organisms, a policy to which this country's honor has been attached." It seems unlikely that this summer's Apollo Astronauts will leave any ham sandwiches on the lunar surface when they come home.

Despite his activity in exobiology, Lederberg is not too happy about the 1973 Viking mission which, because of budget

limitations, will land only small scientific payloads of 40 pounds or so on the Martian surface. A few years ago, before the NASA planetary exploration program was cut back by Congress, Lederberg's lab and many others too were looking toward the Voyager program, which envisioned 1000-pound payloads to Mars, boosted by Saturn V rockets. Vietnam war priorities have ended that dream.

"Frankly, I have grave doubts about the adequacy of the current landing mission to do a real job," Lederberg now says. "It's rather a hasty proposition being put together with quite limited funding. I myself would have preferred to see another orbiter do a much more detailed and thorough high-resolution reconnaissance of the surface before we land there. But policy is made by many, many people, and we didn't prevail. So although I'm opposed to the heavy emphasis on a lander in the 1973 mission as a matter of strategy, I'm involved in it as a matter of tactics, ~~It still is really a~~ in responding to a very exciting challenge, to see whether life and evolution are occurring elsewhere in our solar system. If I had my druthers I would place other priorities ahead of intense exploration of space, but the opportunity is here---both as a scientific challenge and as a challenge to develop the utmost finesse in instrumentation. That finesse, in turn, has already had considerable feedback along other important avenues of medical-biological research, so the program is really very attractive.

"Above all, our mission to Mars will examine a most fundamental condition---the process we call evolution---why

p. (19A) Re - role on NIMH Council.

~~Finished~~

Even more important, ~~in his view,~~ ~~it~~ is the effort to achieve a balanced perspective, a better rapport ~~among those~~ among scientific expertise, ~~laboratory scientists and those whose vital contribution is~~ the insightful observation of human behavior and intense compassion for the miseries of mental illness.

Even more important, in his view, is ~~the role~~ building a balanced perspective, to harmonize the rigor of research, ~~scientific~~ ~~expertise~~, the insightful observation of human nature, and intense compassion for human miseries ~~of mental illness~~. All of these points of view must influence policy decisions on the wisest allocation of social investment for the management of the incredible costs of mental illness.

we're here and how it happened to come about. I'm concerned basically about man's place in nature, and you can focus on the word man, or on place, or on nature, and that pretty well covers the gamut."

With his focus on the word human, Lederberg long ago undertook to serve on the late President John F. Kennedy's Scientific Panel on Mental Retardation, and he is today the director of the Lieutenant Joseph P. Kennedy, Jr. Laboratories for Molecular Medicine at Stanford, where scientists are seeking basic understanding of human developmental biology, neurobiology, and ~~attacking~~ a broad range of problems in mental retardation.

Similarly, Lederberg serves on the Advisory Council of the National Institute of Mental Health, where he and a dozen scientists, psychiatrists and laymen annually review select some $250,000,000 worth of research grant applications for final award. Lederberg sees his role on the Council as "trying to inject a stronger biological point of view into the research and training programs concerned with mental illness." This can involve selection of projects that vary from studies of chromosomal "super-males" and aggression, to the biochemical basis of schizophrenia, to the exploration of new drugs and their effects on the mind. (19A)

From this vantage point Lederberg has vigorously entered recent controversies over the nature of human intelligence, its genetic aspects and the relationship, if any, between race and IQ. Not long ago William B. Shockley, Stanford Nobel laureate

in physics, questioned the adequacy of research into race and intelligence and suggested there has been, among American Negroes, a decline in "genetic potential for intelligence" compared to American whites since World War I. To this kind of talk Lederberg---seldom a polemicist---replied in a public letter signed by ~~virtually~~ his entire Genetics Department. The group termed Shockley's arguments a "pseudo-scientific justification for class and race prejudice," called his statistical questions "prejudgments" and charged that they fell "between mischief and malice." The controversy still simmers on the Stanford campus.

In his own thinking Lederberg argues that "what part of an individual's success can be fairly attributed to his genes as against his education remains a practically unanswerable question." While heredity certainly accounts for the major share of an individual's characteristics, Lederberg says, each person's performance is deeply affected by his culture as well: his language, his social organization, and his skills at coping with the world he faces.

"So we must concentrate today," Lederberg says, "on individual performance, not group labels." And in an introspective mood, he has written about racial discrimination:

"I know little about black suffering, less about its attendant humiliation and personal degradation. Like most whites, I am sorry. I believe it is wrong. I do not personally discriminate, as far as I am aware. Am I culpable?

"Being <u>willing</u> (ital) to look aside makes me have to answer 'yes.' But this is no remarkable human failing. Being <u>able</u> (ital) to is the real sin; not a personal one, but an institutional one. The responsibility for institutional racism is too heavy for any one individual to bear. There are no easy ways to change it. But the first step is honest awareness. As long as we tolerate white dominion, let us admit we are white racists, whatever the color of our skin, the profession of our tolerance, or the Gemütlichkeit of our commiseration."

Throughout his writing, his thinking and his contacts with the three worlds of public, politicians and scientists these days, Lederberg is growing more and more concerned with the difficulty of reconciling scientific advances and the ways which society will choose to control those advances.

By forbidding therapeutic abortions, for example, Lederberg charges that State governments perpetuate "barbarous laws" denying mothers an elementary right. While he is profoundly concerned about the impact of uncontrolled population growth, he is completely opposed to a growing school of population biologists and demographers who see a need for compulsory family limitation around the world.

"I don't know that there are any purely technical answers to this problem yet," he says, "but here again I'd like to see us come closer to exhausting what we can do by way of general education and enlightenment so we can respect individual choice

without trying to impose politically inoperable systems to control population."

Even on fluoridation, where Lederberg, like virtually all scientists, is convinced of its tremendous social value, he holds political reservations.

"The mere fact that there are some people who are opposed to it [he says, "seems"] to me enough to suggest that we take stock of the situation and ask, can we, without violating the overriding interests of the majority, accommodate even the apparently irrational concerns of the few in order to maintain the spirit of individual choice? In vaccination programs, of course, the failure of an individual to vaccinate himself is not just an issue of private consequence, but can also influence the spread of disease to others, so there is a social interest there that can't easily accommodate to private choice.

"But I'm very deeply concerned about maintaining the integrity of individual choice in an increasingly complicated world, and it becomes even more complicated when there are options that have to do with biological modifications."

Lederberg summed up these concerns last year in testimony before a Senate Subcommittee on Government Research:

"Many forms of compulsion are available to the state in its dealings with individuals," he said. "The perfection of biological engineering will add only a few minor subtleties to the existing repertoire of a totalitarian government. The only assurance we have for the preservation of individual

dignity comes from a political system that minimizes the role of the state in private life. Indeed the very guise of 'protecting' individuals from the impact of new technology may cloak the most pernicious intrusions of the state into individual freedom."

People who know Lederberg well are not surprised at his constant concern over the dilemmas posed by technological advance and society's need to direct those advances within a framework of freedom. A technological world is a complex world, and yet its complexities must be dealt with by ordinary citizens. Lederberg has always confronted complexity, and pondered its ambiguous consequences.

"As a scientific culture we have no way to evade the future," Lederberg has written. "And this tells us the ultimate responsibility of the scientist: to educate. He should first educate himself to be sensitized to the subtler implications of the work he himself best understands. His foresight then focuses on the most urgent areas for social education.

"It is obvious that the most important innovations in the science of the near future will be in human biology. We already have some glimmerings of this in our newly-won understanding of the molecular chemistry of DNA and its role in genetics; but we are also beginning to see a little light on the way the brain functions.

"However, I do not associate the enormous importance of this kind of science with awful forebodings about its abuse.

I cannot point to novel legislation that should be passed in anticipation of the biological revolution. But it is obvious that human biology needs to be given much more emphasis in higher education if the next generation is to have the intellectual base to deal with its most crucial problems."

Certainly Lederberg began preparing his own intellectual base early in life. His childhood in New York was an intellectual one; his father was an immigrant Rabbi who had brought to the United States from Palestine an abiding interest in ancient Hebrew literature. His mother was a teacher of Hebrew. From both parents Joshua was exposed to the life of the mind as a very young boy. Later Lederberg went to Stuyvesant High, and then to Columbia; he finished each four-year course in three years, combining science with extensive, thoughtful reading in political philosophy. While he was still a high school student he gave public lectures in cytogenetics at the New York World's Fair, and as an undergraduate at Columbia he performed significant research on mutations in Neurospora, a red mold that grows on bread. He won his A.B. at 19.

Lederberg was a sophomore in medical school at Columbia's College of Physicians and Surgeons when Dr. Edward L. Tatum at Yale invited him to spend the summer doing research in Tatum's genetics laboratory. After three months young Lederberg wrote back to his Dean at P. & S. to ask for a leave of absence.

In his letter he disclosed he had found "compelling evidence, not yet conclusive, for the existence of a primitive

sexuality in bacteria."

And lest the Dean fail to understand the implications of the research, Lederberg added: "The importance of this concept in considerations related to epidemiology, chemotherapy and the study of gene action and growth in general is such that I could hardly allow myself to interrupt its development and pursuit." Lederberg got the leave of absence and never returned to medical school; instead, a year later, he won his doctorate at Yale.

The evidence Lederberg had found did turn out to be conclusive. Contrary to all previous observation, that bacteria reproduced by splitting, Lederberg showed that some species actually mated in a form of sexual union that passed combinations of genes, and hence new characteristics, along to their bacterial offspring. The process was called genetic recombination, and it was this discovery---vital to the future understanding of biochemical genetics---that won Lederberg the Nobel award in 1958, along with his one-time mentor, Tatum, and Dr. George W. Beadle of the University of Chicago.

By the time his award was announced Lederberg was committed to leave the University of Wisconsin for Stanford, where his friend Arthur Kornberg had lured him with the promise of exciting new opportunities for research, for laboratory facilities, and for building a pioneering genetics department.

In his 11 years at Wisconsin Lederberg and a colleague, Dr. Norton D. Zinder, (now Professor at Rockefeller University) had added still more knowledge to the subject of microbial genetics. They had discovered, for

example, a phenomenon they called "transduction," by which certain bacterial viruses are apparently able to carry fragments of genetic information from one cell to another---fragments that were later to be identified as pieces of the DNA molecule, and that have since become the basis of Lederberg's prophetic thinking about the possibilities of "euphenic" therapy, as well as dire warnings from the less-informed about "genetic tampering" or "controlling heredity."

Recently Lederberg recalled that he was genuinely reluctant to accept the Nobel prize when it came in 1958 because, as he said, "the Nobel awards had always seemed to me to distort one of the most important features of the scientific enterprise---that every advance is based on the cooperative effort and criticism of a very large number of people whose part in crucial discoveries would be impossible to allocate fairly." He added: "Furthermore, I could easily point to dozens of scientific advances of equal or greater significance, whether judged by their humanistic value or their intellectual elegance."

However, Lederberg finally decided that turning down the award would only stir up a lot of notoriety and might well offend the conscientious Nobel judges. "These reservations," he reflected later, "were rather rabbinical, and a quiet acceptance was the simple answer." He took the proffered prize.

Today Lederberg lives simply in a modest residential section of Palo Alto near the Stanford Campus, enjoying music, enjoying walks through the unspoiled coastal hills above the

campus, and writing, writing, writing for a hobby. His wife Marguerite is a physician at Stanford, preparing to specialize in podiatrics. They were married last year, which also brings Lederberg to the arduous pleasures and responsibilities of the role of parent to David, Marguerite's four-year old son by her first marriage. Before their divorce in 1967, Lederberg had been married to Dr. Esther Marilyn Lederberg, herself an outstanding geneticist, who had collaborated in much of her husband's work after their marriage in 1946.

Although Lederberg in public is no spellbinder, no political activist, his reputation among colleagues is formidable indeed.

Dr. Richard S. Young of the National Aeronautics and Space Administration, for example, calls him "unique---a universal genius---a great biologist, mathematician, physicist and philosopher." Young heads NASA's exobiology programs and he says of Lederberg: "The guy really started things off for all of us in this area. His impact on laboratories all over the country---not just his own---is profound."

In Lederberg's own domain at the modern Stanford Medical Center, fronted by plashing fountains and honeycombed with labs surrounding flowered, tranquil inner courtyards, the same impression prevails.

Elliot Levinthal, a physicist who left a directorship at booming Varian Associates to found his own electronics firm, sold his company a few years ago and returned to Stanford to

work with Lederberg rather than continue pursuing an independent industrial career that had already earned him a comfortable fortune. Today, as director of the genetics department's Instrumentation Research Laboratory, Levinthal acknowledges the extraordinary influence Lederberg brings to it.

"There can't be a meeting here," Levinthal says, "without Josh raising the most important and provocative issues. You can hardly imagine the fantastic speed with which he can grasp the essentials of a discipline that's wholly new to him, and how quickly he can begin to ask the most disconcerting questions---questions that keep us all alert, that make us all strain to find answers, or that force us back to reexamine fundamental problems."

If Lederberg is aware of this role among his colleagues, his direct, yet engaging and at times diffident manner scarcely reveals it. He turns instead to reflective talk:

"I don't see," he says, "how we will ever evolve our highest capabilities if we don't allow full play for our intelligence and our capacity for innovation and experiment. We ought to be looking everywhere, all the time, as best we can, for new ways to deal with our problems. That demands intelligence; and intelligence is the unique possession man has."

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