THE FATEFUL CODE

Genes and Human Destiny

Every day seems to bring fresh news of astonishing discoveries on the frontiers of genetic research. Genes "for" homosexuality, alcoholism, and dozens of diseases. A dazzling array of genetically engineered medicines and goods, from cancer-fighting drugs to coffee plants that yield caffeine-free beans. Now, with the launching of the $3-billion U.S. Human Genome Project, comes the prospect of unlocking the last secrets of the gene and, some critics assert, the dread possibility of discoveries that will allow scientists to create a super-race. Yet genetic research is surrounded by misunderstanding. Many supposed "breakthroughs" are only beginnings, and some have little more substance than cold fusion. Our authors explore the science behind the headlines, assessing the specter of eugenics and pondering the impact of genetic research on our understanding of human nature itself.

THE DOUBLE-EDGED HELIX

by Joel L. Swerdlow

Over the centuries, medical progress has eased human suffering and prolonged human lives without asking much in return. Vaccinations, antibiotics, and open-heart surgery, to name a few advances, have not generally posed significant moral problems. Today, however, the dawn of an era of gene-based medicine holds out tantalizing promises that carry with them a growing list of new and often disturbing choices for individuals, for physicians and researchers, and for society at large.

Some dilemmas are distant, including the possibility that growing mastery over genes will give us unprecedented power over our children's genetic makeup. Others are upon us already, namely the question of who has a right to possess genetic information about individuals' susceptibility to certain diseases. Some of the more urgent conundrums arise because science is still at an awkward "halfway" point: It offers significant new knowledge about genes but few ways to respond.

One of these halfway points is the discovery of the "genetic marker" for Huntington's disease, an inherited nerve disorder that appears at around age 40 and slowly kills the brain. No one knows why, and no treatment exists. The responsible gene is dominant. When one parent has Huntington's, each offspring has a 50-50 chance of developing it. Before the discovery of the marker, children of such parents could only wait to see if they would die. One of these is Nancy Wexler, a Columbia University psychologist whose mother died of Huntington's. Beginning in 1979, she recruited some 2,000 Venezuelan donors—all of them descendants of a single 19th-century woman who suffered from the disease—whose pedigree and blood samples made possible in 1983 the discovery of the genetic marker for Huntington's. If one of a person's parents had Huntington's and that person's DNA includes this marker, he or she likely will develop the disease.

Wexler was elated when her colleagues discovered the Huntington's marker. But nine years later, researchers are no nearer to developing anything that prevents, treats, or cures Huntington's. That creates terrible dilemmas for people at risk. Imagine a man whose father died of Huntington's. To find that he does not carry the marker liberates him. But if he finds that he does have the marker, he is compelled to count the days until horror and death hit. Faced with this choice, less than 15 percent of those at risk have decided to undergo genetic screening. Wexler herself will not reveal whether she has been screened.

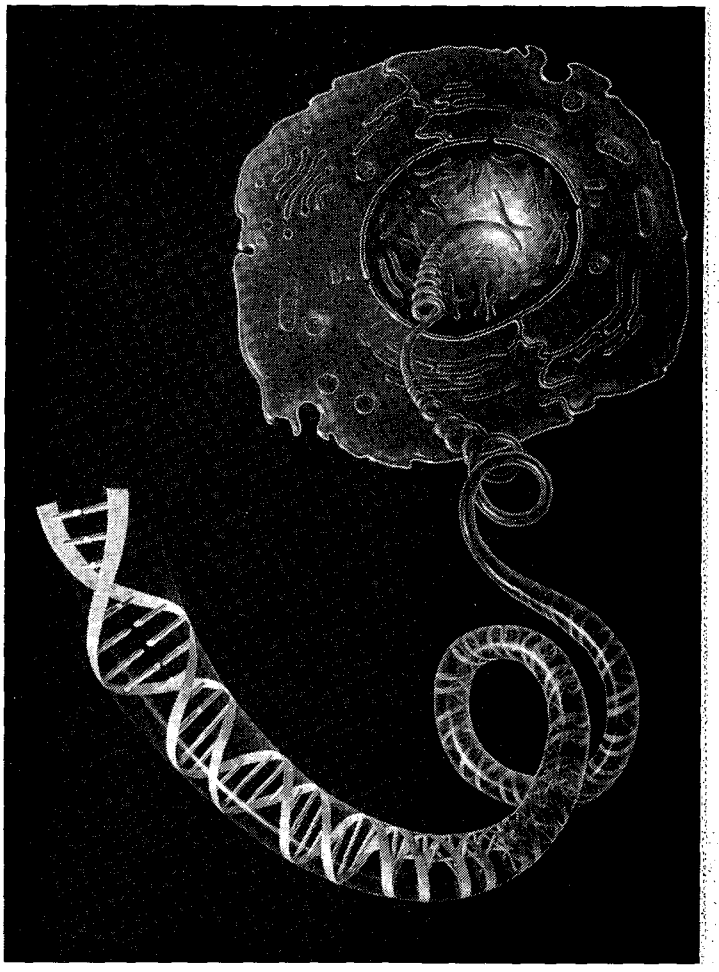
The genetic revolution that is gathering force today, says science journalist Harold Schmeck, can be understood as "scientists' growing ability to read and write in the language of the gene." Modern scientific un-

derstanding of genetics dates from 1866, when an Augustinian monk named Gregor Mendel, who had been experimenting with pea plants in Austria, published a paper laying out the basic laws of inheritance. Mendel made his discovery without knowing about genes or chromosomes, and it was only in 1900, after scientists had, among other things, observed chromosomes through a microscope, that his work was rediscovered.

Advances—such as the recognition by George W. Beadle and Edward L. Tatum in 1941 that the function of genes is to create enzymes and proteins—built steadily. The big breakthrough came in 1953, when James Watson and Francis Crick at Cambridge University deciphered the structure of deoxyribonucleic acid (DNA), the molecule that carries genetic information. Each cell has six to nine feet of DNA coiled on 23 pairs of chromosomes. The DNA, in the now familiar shape of a double helix, consists of two strands of nucleotides, which are made of sugar, phosphate, and one of four different bases. The strands are joined by either of two pairs of bases: adenine (A) and thymine (T), or cytosine (C) and guanine (G). That base-pair rule means that when cells (and thus strands of DNA) divide, each strand can make a copy of its former partner.

Every genetic instruction is encoded through the linear order of the four bases on a segment of DNA, much as computer information is stored in a binary code of 1's and 0's. In 1959, Crick and others found the intermediary that carries each instruction from the DNA to the ribosomes, where the instruction is translated into action through the creation of proteins. This messenger is a chemical cousin of DNA called ribonucleic acid, or RNA.

That, of course, is only the beginning of the mystery, for each chromosome has as many as 300 million base pairs. In order to understand the human genome (the total of all genetic information), scientists will have to decipher some three billion human base pairs. Listing them would fill 13 sets of the *Encyclopedia Britannica*. Most of the genes bearing specific instructions vary in length from about 100 to 30,000 base pairs, and even now scientists are not sure how many human genes there are. Estimates generally



A double helix of DNA, joined at intervals by base pairs, uncoils from the nucleus of a cell in this artist's conception.

range from 50,000 to 100,000. So far, researchers have "mapped" the location of nearly 2,000 genes (up from 579 in 1981) and have identified some 4,000 diseases caused by single-gene defects. Most of these diseases are relatively rare, such as Duchenne muscular dystrophy, retinoblastoma, neurofibromatosis, and one form of Alzheimer's. Most common diseases that have genetic roots probably will be traced to more than one gene.

During the 1960s and '70s, scientists realized that variations in DNA may be associated with diseases and that "markers," patterns of base pairs, appear on the same place of the same chromosome of virtually everyone. A number of technological advances—in microscopy and related areas—dramatically increased researchers' ability to isolate genes and tinker with various genetic components. Yet most of these experiments were performed on bacteria and other simple organisms. Turning their attention to more complex organisms in the late 1960s, scientists discovered that similar methods could still be used. In 1973, these techniques were given the name "recombinant DNA"—popularly known as gene splicing or, more ominously, genetic engineering.

Recombinant DNA involves snipping sections of the DNA molecule from a complex organism using restriction enzymes and transplanting the snips into host bacteria or yeast cells. (The use of yeast cells is actually a more recent innovation, giving rise to yet another of the acronyms so beloved by scientists, YACs, for yeast artificial chromosomes.) The host cells then multiply normally, creating many new "clones" of the transplanted DNA at the same time. These clones contain anywhere from a few hundred to one million base pairs.

Clones created by this method (and others) have a variety of uses. Applying other techniques, for example, scientists found that they could transplant and "turn on" some genes, getting them to produce vital biochemical substances such as human growth hormone and insulin. More significantly, perhaps, cloning meant that researchers could create large "libraries" of DNA fragments for further manipulation or study in the laboratory.

By the mid-1980s, these and other technological advances made the prospect of exploring the entire human genome seem feasible. One of the most important developments was the 1983 discovery by Wexler and her collaborators of the genetic marker for Huntington's disease. Finding such a genetic malfunction is a monumental enterprise, somewhat analogous to locating a broken pipe in a house somewhere on Earth (the cell). You narrow your search first to the United States (a particular chromosome) and then to Pennsylvania (chromosome fragment). Finally you focus on Philadelphia (gene) and begin walking block-by-block looking for signs of the leak. Eventually you get close enough to search each house (nucleotide base pairs). The "leak" is an incorrect nucleotide.

Wexler and her colleagues set out in search of the gene in 1979. Using restriction enzymes, which snip DNA strands at particular locations, James Gusella, Wexler's collaborator at Massachusetts General Hospital, chopped up the DNA from the blood samples she supplied. The fragments were separated by size, using a process called gel electrophoresis. Then the hunt began. The idea was to identify segments of DNA that were different in people with Huntington's. Gusella took advantage of the fact that the segments created by

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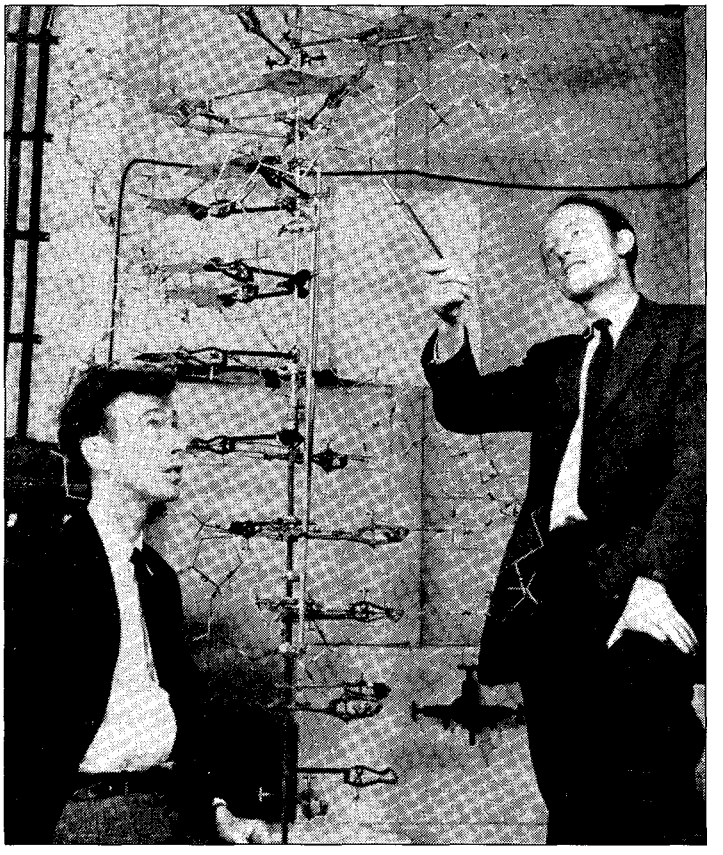
restriction enzymes vary from person to person, resulting in what are called restriction fragment length polymorphisms (RFLPs). He created radioactive RFLP "probes" and added them to the chopped up DNA. The probes then bonded to their complementary segments of DNA and lit up in a banded pattern. Performing this exercise on many samples, Gusella could then compare them to see if all those from people with Huntington's had a pattern of bands distinct from all those without the disease. Still, this was the equivalent of the proverbial search for a needle in a haystack. It could have required the development of thousands of different RFLPs and thousands of tedious tests before stumbling upon the proper segment. But Gusella got lucky. With one of his very first probes, he discovered the variation.

Because *all* of the DNA in each sample had been chopped up, he still did not know which chromosome the culprit snip appeared on. Further laboratory and computer work determined that it was on chromosome 4. The gene for Huntington's disease had been "mapped"—it was within a mere four million base pairs of one end of chromosome 4—but still not precisely located. Indeed, it is a measure of the difficulty of genetic research that, nine years later, researchers still have not found the Huntington's gene. They are, to return to the analogy of the search, still only in Pennsylvania. What Gusella, Wexler, and their colleagues had shown, however, was that RFLP mapping, once dismissed as a fantasy, was feasible.

This and a rapid succession of other developments gave rise to what may be described as a Manhattan Project mentality. The prospect of mapping and sequencing the entire human genome, long a vague dream of a few scientists, now seemed a real possibility. Several leaders of the scientific community, including Nobel laureate Renato Dulbecco, Harvard's Walter Gilbert, and Robert Sinsheimer, a scientist-turned-university administrator, called for a crash program. In Washington, the U.S. Department of Energy (DOE) seized upon the idea in 1986, but its leadership was almost immediately challenged by the National Institutes of Health (NIH). In 1987, Congress, encouraged in part by the prospect of building an insurmountable U.S. lead in the emerging biotechnology industry, gave the two competing agencies $29 million. But many issues were still unresolved.

Some biologists feared the encroachment of bureaucratized Big Science, previously restricted to particle physics and a few other fields. "Many of us oppose brute force sequencing of the human genome because we believe it is an inefficient use of scarce research dollars," one researcher wrote in a letter to *Science*. "[B]iomedical research dollars are generally more efficiently spent on investigator-initiated research. We believe that innovation from scientists in the field produces better science than do narrowly targeted, top-down big science projects."

Defenders of the approach replied that costs of piecemeal research are higher and that a human genome project would stimulate technological innovations that would spare even the independent-minded investigator a great deal of tedious and time-consuming labor in the laboratory and speed the pace of research. Since then, researchers have pointed out that the discovery of the gene that causes fragile X syndrome—the most frequent cause of inherited mental retardation—came roughly five years ahead of schedule because of the Human Genome Project. Some 5,000 babies are born every year in the United States with fragile X syndrome. Minimal health-care costs for each are $100,000. If science can



James Watson (left) and Francis Crick show off the 1953 model of a DNA molecule for which they were later awarded a Nobel Prize.

develop a treatment or cure—admittedly, a big "if"—this discovery alone could allow the Project to pay for itself.

But there was (and continues to be) much disagreement about the need to sequence all of the DNA, since 90–95 percent of it consists of "introns" that do not "code" for genes and may be useless litter left over from evolution. "[T]his vast genetic desert holds little promise of yielding many gems," says Robert A. Weinberg, of the Whitehead Institute for Biomedical Research. "As more and more genes are isolated and sequenced, the argument that this junk DNA will yield great surprises becomes less and less persuasive." Nobel Prize-winning biochemist Paul Berg, by contrast, says, "There is already clear evidence that specific sequences in introns and in intergenic [noncoding] regions constitute important regulatory signals.... Are we prepared to dismiss the likelihood of surprises...?"

At a deeper level, there has been a fundamental philosophical disagreement. James Watson argues that studying genes "will provide the ultimate answers to the chemical underpinnings of human existence." Opponents such as Harvard microbiologist Jon Beckwith believe that such views, magnified by the news media, "promote the conception that genetics is all-explanatory," "reinforce a distorted perception of the basis of the human condition," and devalue other biological work.

These larger differences will not likely disappear soon, but in 1988 a committee of the National Research Council that included several critics of Big Biology (such as David Botstein, one of the inventors of RFLP mapping) recommended a 15-year project carried out at 10 major research centers around the country and costing some $200 million annually. It was not the kind of crash Big Science effort some of these critics had feared, and funds were not merely to be shifted from other areas of biomedical research to pay for it.

At the behest of Congress, the two competing bureaucracies reached agreement in 1988. The NIH will focus on mapping, the Energy Department on sequencing. Watson, named to lead the NIH program, has

become the de facto head of what is loosely called the U.S. Human Genome Project. At a projected $3 billion over the next 15 years, the U.S. effort dwarfs those of Japan and Europe.

The project's first priority is to create rough maps of the human genome, while working to improve sequencing technology. Phase two, beginning after 10 years, is to determine the exact sequences of the three billion human nucleotides. Sequencing has become fairly routine, but it is tedious and expensive. ("Virtually any monkey can do it," Watson scoffed last fall when an NIH official announced plans to seek patents for sequences.) With today's technology, it would take several centuries to "read" the entire genome. But a proposed DNA computer chip might analyze sequence data 100 times faster than is now possible.

The challenge of the 21st century will be to interpret the cornucopia of raw information produced by the project and to determine how to make use of it. In a sense, the project will provide only the infrastructure for the research of the future. Genes will still need to be located, their functions understood. Knowing that a base sequence is GGATCC, for example, is not enough to reveal what function is served by the protein it encodes. Scientists will need to explore the complex *interplay* among genes that influence or produce human traits and diseases. And they will need to discover how one fetal cell's DNA is told to multiply into brain cells and another's into bone cells.

Even so, practical applications of genetic research already are permeating medicine. On September 14, 1990, for example, Dr. W. French Anderson and two colleagues at the National Institutes of Health in Bethesda, Maryland, made medical history by performing the first sanctioned "gene therapy" on a human being. A *New York Times Magazine* profile noted that Anderson needed political skills nearly as great as his medical ones to win approval from the bureaucracy and Congress. The patient was a four-year-old girl who suffered from adenosine deaminase (ADA) deficiency, an inborn inability to produce an enzyme essential to the immune system. Anderson and his colleagues inserted the gene for ADA into a retrovirus that had been stripped of most of its own genetic material. When mixed with a sample of the girl's own white blood cells, the retrovirus went about its normal business of penetrating the nucleus of each cell, carrying with it the ADA gene.* On that September day, the process reached its historic if undramatic culmination when the girl's "improved" white blood cells were returned to her by transfusion. Since then, she has continued to receive the controversial therapy, and other researchers have won permission to begin similar treatments for cancer, hemophilia, and cystic fibrosis.

The greatest practical benefits from genetic research so far have come in the form of "biotech" drugs. They have spawned a $12 billion industry—dominated by American firms such as Amgen, Genzyme, and Immunex—that is expected to grow to $40–60 billion by the end of the decade. Many biotech drugs are substances normally produced in the human body that are synthesized in the laboratory by taking the relevant genes and inserting them into yeast or bacteria cells, then harvesting the natural substances they create. Tens of millions of patients now use these genetic products to combat afflictions such as diabetes, hepatitis, and anemia. The drugs include not only such familiar substances as

*Cell transplantation is a related procedure, cruder in that entire cells are used to correct for genetic defects. For example, researchers can obtain insulin-producing "islet" cells from dead donors and place them in the livers of patients unable to produce their own insulin.

insulin but epogen, which stimulates the production of red blood cells and thus allows kidney dialysis patients to avoid transfusions, and neupogen, which increases the production of white blood cells in cancer patients undergoing chemotherapy.

Finally, and most significantly, genetic research has made possible "predictive," presymptomatic medicine. In 1991, for example, researchers discovered a gene responsible for a rare colon cancer. Those with a family history of the disease can be tested for the gene; if they carry it, they can get regular colonoscopies and surgeons can act at the first sign of trouble. However, most predictive medicine lies in the future. A genetic early warning, for example, may some day allow physicians to intervene against juvenile onset diabetes, a disease that afflicts more than one million Americans. By the time it is diagnosed—usually after the appearance of symptoms such as fatigue—most of the victim's insulin-producing islet cells are dead and the patient must begin daily insulin injections.

As in the case of Huntington's disease, however, locating a gene (or marker) and finding a response are two different matters. Researchers discovered dozens of disease-causing genes in the 1970s and '80s without finding the means to prevent or cure the diseases. "We need," says University of California geneticist Paul Billings, "a new physiological revolution. We need new insights and approaches. Until this happens, work with genes can carry us only so far."

Knowledge from the frontiers of genetic research will increasingly pose difficult problems for policymakers and for society at large. Should certain forms of genetic screening be required? Should others be barred or restricted? Most states already require the screening of newborn babies for biochemical disorders such as phenylketonuria (PKU), a hereditary enzyme deficiency that causes mental retardation but which can be offset by a special diet. Indeed, because of other nongenetic medical advances, the list of required tests may soon extend later into childhood. Some state legislatures are considering laws that require the testing of all children at age one or two for lead poisoning. Such mandatory screening arouses little opposition, largely because it is easy, inexpensive, and effective.

But consider the case of cystic fibrosis, the most common inherited fatal disease of children and young people in the United States. Roughly five in 100 Caucasian Americans—about 12 million people—carry a responsible gene. Since it is recessive, such "carriers" are not affected. If two carriers conceive a child, however, it has a one-in-four chance of developing the disease. In the late 1980s, a test was developed to identify carriers. However, results can be ambiguous, in part because more than 100 known mutations of the gene cause cystic fibrosis. The *New York Times* reports, however, that screening for cystic fibrosis is "quietly creeping into clinical practice." The driving force is physicians' fear of malpractice or "wrongful life" lawsuits. To screen all possible carriers in the United States using current technology would cost billions of dollars every year and would provide limited benefits. To forego screening, however, may require more discipline and understanding than most couples can muster. Must the state set limits?

Some genetic discoveries create moral dilemmas. Each year, about 300,000 pregnant women in America seek fetal tests for certain inherited diseases. In some cases experimental treatment of the fetus through surgery or transfusion is possible if an "abnormality" is found. But usually the options are to continue the pregnancy without treatment or to abort the fetus. Many people choose abortions. Since a fetal test

for Tay-Sachs—a fatal neurodegenerative disease—became available in the early 1970s, the number of children born with Tay-Sachs has declined by 90 percent.

Screening, however, does not always encourage abortion. It can allow couples who have had one genetically abnormal child to feel free to conceive another, knowing that a fetal screening will reveal any problems. Yet fetal screening still makes many ethicists and physicians uncomfortable. In Russia, for example, the medical literature shows that a large number of abortions have occurred because screening has revealed that fetuses *might* have the gene for juvenile-onset diabetes. "I don't know if a 20 percent disposition to diabetes is a disease or an abnormality," says Arthur Caplan, director of the Center for Biomedical Ethics at the University of Minnesota. "I'm certainly not sure whether it morally justifies anyone aborting a fetus with that genetic profile. We haven't thought very much yet about how to draw that line between what is a disease and what isn't."

Moreover, many people seem willing to abuse prenatal choices. Demographers have concluded that 100 million Asian females are "missing" from the total population, most presumably aborted because their parents wanted sons. As researchers discover the genetic components of intelligence, will parents abort fetuses lacking Ivy League genes? Will they practice prenatal "heightism," aborting some male fetuses because they will not grow tall enough?

"At what point," asks biotechnology critic Jeremy Rifkin, "do we move from trying to cure horrible genetic diseases to trying to enhance genetic traits?" Despite some vocal dissent in professional journals, the scientific and medical communities have made work on human germ (sperm and egg) cells taboo, but this self-imposed limitation seems destined to end. Experiments with plant and animal germ cells offer enticing prospects—such as no-caffeine coffee beans and "natural" low-fat cow's milk—while doing no known harm. Advocates of germ-cell research point out that physicians already alter eggs or sperm when exposing cancer patients to some forms of radiation and drugs. And finally the ban on germ-cell research forces us to reexamine our notions of nature itself. Is it "natural" to get sick? Isn't medicine constantly fighting nature?

What if your physician said, "You have a family history of heart disease. I can offer a painless and safe injection that will correct this defect in your reproductive cells and guarantee that your children and every descendant thereafter will have a significantly reduced chance of heart disease." Your doctor would explain possible side effects. "It is not clear-cut," the experts would explain. "Gene defects, including those in recessive genes, may do unknown things or defend the body in undiscovered ways, just as the gene for sickle cell anemia offers protection against malaria." Yet it is nevertheless hard to imagine people saying no to such an offer.

While the dilemmas of genetic research give many reasons to pause and reflect, they do not justify slowing or stopping the research itself. In many cases, the best way to eliminate dilemmas—and protect human life—is to push back genetic frontiers. Admittedly, there are risks involved. The more we master genes, the more options—many of them morally questionable—we will have. But making choices, after all, is what being human is all about.

CONTROLLING THE GENETIC ARSENAL

by Daniel J. Kevles

In April 1991, an exposition opened in the hall atop Paris's great arch of La Defense under the title, *La Vie En Kit (Life in a Test Tube)—Éthique et Biologie*. Along with the displays about molecular genetics and human genome research were a catalogue and placard by psychoanalyst Monette Vaquin. The latter captured many of the anxieties aroused by this subject:

> Today, astounding paradox, the generation following Nazism is giving the world the tools of eugenics beyond the wildest Hitlerian dreams. It is as if the unthinkable of the generation of the fathers haunted the discoveries of the sons. Scientists of tomorrow will have a power that exceeds all the powers known to mankind: that of manipulating the genome. Who can say for sure that it will be used only for the avoidance of hereditary illnesses?

Vaquin's apprehensions, echoed frequently by scientists and social analysts, are a powerful reminder of the shadow of eugenics that looms over human genetic research. Ideas about eugenics can be traced back at least to Plato, but modern eugenics originated with Francis Galton (1822–1911), a younger first cousin of Charles Darwin and a brilliant scientist in his own right. In the late 19th century, Galton proposed that the human race might be improved, in the manner of plant and animal breeding, by eliminating so-called undesirables and multiplying so-called desirables. It was Galton who named this program of human improvement "eugenics," taking the word from a Greek root meaning "good in birth" or "noble in heredity." Through eugenics Galton intended to improve human stock by giving "the more suitable races or strains of blood a better chance of prevailing speedily over the less suitable."

Galton's ideas gained popular acceptance after the turn of the century, finding large followings in the United States, Britain, Germany, and many other countries. One of the organizations formed to promote Galton's ideas was the American Eugenics Society in 1923, which sponsored exhibits at state fairs and other activities. The backbone of the movement consisted of people from the white middle and upper-middle classes, especially professionals, scientists, and physicians. The movement brought together a variety of prominent figures from all points of the ideological compass, including a number of the progressive-minded, such as sexologist Havelock Ellis, anarchist Emma Goldman, and George Bernard Shaw. ("Being cowards, we defeat natural selection under cover of philanthropy," Shaw wrote, "being sluggards, we neglect artificial selection under cover of delicacy and morality.") Eugenicists declared themselves to be concerned with preventing social degeneration, which they perceived all around them in urban industrial society. They took crime, slums, and rampant disease to be symptoms of so-

Taking eugenics to the people: At an exhibit at the Kansas State Fair in the mid-1920s, the high rate of illiteracy among immigrants and blacks was attributed to inferior genes.

cial pathologies that they attributed primarily to biological causes—to "blood," to use the term for inheritable essence common at the turn of the century.

Eugenically minded biologists were intent on rooting out the causes of social degeneration. Their study of medical disorders such as diabetes and epilepsy was motivated not only by the intrinsic interest of these diseases but by concern over their social costs. A still more substantial part of the research program consisted of the analysis of traits alleged to make for social burdens—traits involving qualities of temperament and behavior that might lie at the bottom of alcoholism, prostitution, criminality, and poverty. These biologists were especially interested in mental deficiency—then commonly called "feeblemindedness"—which was thought to be at the root of many varieties of socially harmful behavior and which could be identified through recently invented intelligence tests.

In the hope of explaining these pathologies biologically, eugenic researchers such as psychologist Henry H. Goddard resorted to Mendel's laws of heredity, which had been rediscovered in 1900. They fastened on the idea that biological characteristics were determined by single elements—only later identified as genes. They generally assumed that not only could certain physical characteristics (e.g., eye color) or diseases be explained in a Mendelian fashion but also characteristics of mind and behavior. Charles B. Davenport (1866–1944), head of the biological laboratory at Cold Spring Harbor on Long Island, New York—which in 1918 became the Carnegie Institution of Washington's Department of Genetics—was one of the nation's more prominent scientists. He searched for Mendelian patterns of inheritance in many supposed be-

havioral categories, including "nomadism," "shiftlessness," and "thalassophilia"—the love of the sea that he discerned in naval officers. (He concluded that thalassophilia must be a sex-linked recessive trait because, like color blindness, it was almost always expressed in males.)

While some eugenic investigations into human heredity proved to have merit, most of them were recognized in the end to be worthless. Combining Mendelian theory with incautious speculation, scientists favored relatively simple single-gene Mendelian explanations, neglecting the fact that many traits are influenced by more than one gene. They also paid far too little attention to cultural, economic, and other environmental influences on behavior and mental abilities. And like Davenport's behavioral categories, many of the traits that figured in eugenic research were vague or ludicrous, filled with class and race prejudice. In northern Europe and the United States, eugenicists specified standards of fitness and social value that were predominantly white, middle class, and Protestant—and identified with "Aryans." They reasoned that poverty was the result not of inadequate educational and economic opportunity but of the meager moral and educational capacities of the poor, rooted in their biology. When eugenicists celebrated Aryans, they demonstrated nothing more than their own racial and ethnic biases. Davenport, for example, found the Poles "independent and self-reliant though clannish," the Italians tending to "crimes of personal violence," and the Hebrews "intermediate between the slovenly Serbians and the Greeks and the tidy Swedes, Germans, and Bohemians" and given to "thieving" though rarely to "personal violence." He expected that the "great influx of blood from Southeastern Europe" would rapidly make the American population "darker in pigmentation, smaller in stature, more mercurial... more given to crimes of larceny, kidnapping, assault, murder, rape, and sex-immorality."

Eugenicists like Davenport urged interference in human propagation in order to increase the frequency of "good" genes in the population and to decrease that of "bad" ones. The interference was to take two forms: One was "positive" eugenics, which meant manipulating the human heredity or breeding to produce superior people. The other was "negative" eugenics, the elimination of biologically inferior human beings from the population by discouraging such people from reproducing or by restricting immigration.

In practice, little was done for positive eugenics, although arguments in favor of increasing the number of offspring born of "desirable" types did figure in the advent of family allowance policies in Britain and Germany during the 1930s. It was also an implicit theme of the American Eugenics Society's Fitter Family contests in the "human stock" sections at state fairs during the 1920s. At the 1924 Kansas Free Fair, winning families in three categories—small, average, and large—were awarded a Governor's Fitter Family Trophy, presented by Governor Jonathan Davis. "Grade A Individuals" were awarded a medal that portrayed two diaphanously garbed parents, their arms outstretched toward their (presumably) eugenically meritorious infant.

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Judging from the photographs that survive, it is hard to know what made these families and individuals stand out as especially fit, but some evidence is supplied by the fact that all entrants had to take an IQ test—and the Wassermann test for syphilis.

Much more was done in the name of negative eugenics, notably by means of eugenic sterilization laws. By the late 1920s, some two dozen American states had enacted such laws, which, in general, permitted state prisons and other institutions to perform vasectomies or tubal ligations on inmates who were epileptic, insane, or "feebleminded," especially if they had been incarcerated for sexual offenses. The laws were declared constitutional in the 1927 U.S. Supreme Court decision, *Buck* v. *Bell.* Justice Oliver Wendell Holmes, Jr., delivered the opinion that "three generations of imbeciles are enough." The leading state in this endeavor was California, which by 1933 had subjected more people to eugenic sterilization than had all other states of the union combined. By 1941, nearly 36,000 Americans had been sterilized under various state eugenics programs.

The most powerful union of eugenic research and public policy occurred in Nazi Germany. Much of the research in Germany before and even during the Nazi period was similar to that in the United States and Britain, but during the Hitler years Nazi bureaucrats provided eugenic research institutions with handsome support, and their programs were expanded to complement the goals of Nazi biological policy. Ongoing investigations into the inheritance of disease, intelligence, and behavior were plumbed for knowledge that could guide the government's sterilization policy. Eugen Fischer's Kaiser Wilhelm Institute for Anthropology, Human Heredity, and Eugenics, which included among its staff the prominent geneticist Otmar von Verschuer, trained SS doctors in the intricacies of racial hygiene and analyzed data and specimens obtained in the concentration camps. Some of the material—for example, the internal organs of dead children and the skeletons of two murdered Jews—came from Josef Mengele, who had been a graduate student of Verschuer's and was his assistant at the Institute. In 1942, Verschuer succeeded Fischer as head of the Institute (and would serve postwar Germany as professor of human genetics at the University of Muenster). In Germany, where sterilization measures were partly inspired by the California law, the eugenics movement prompted the sterilization of several hundred thousand people. Ultimately, as we know, it helped lead to the death camps.

Since the beginning of the DNA era, many scientists and laymen alike have wondered whether our growing body of genetic knowledge will be exploited for a new program of positive eugenics, for attempts to engineer new Einsteins, Mozarts, or Kareem Abdul-Jabbars. (Curiously, brilliantly talented women such as Marie Curie or Nadia Boulanger or Martina Navratilova are rarely if ever mentioned in the pantheon of superpeople.) Today, hardly a conference is held on human genome research without somebody expressing the fear that the state will seek to foster or enhance desirable human qualities or characteristics. Such apprehensions are not entirely unfounded. In 1984, for example, Singapore's Prime Minister Lee Kuan Yew scolded his country's educated women, supposedly possessed of above-average intelligence, for their relatively low birth rate. The elite's reluctance to reproduce, he said, was diminishing the quality of the country's gene pool. Embracing a crude positive eugenics, Singapore's paternalistic government—which also recently banned chewing gum as a national nuisance—has since offered preferential

school enrollment for offspring of such women and a variety of other incentives to increase their fecundity. Their less-educated sisters have been offered similar incentives to have themselves sterilized after the birth of a first or second child.

Engineering a super-race in the laboratory, however, is quite a different matter from extending carrots and sticks to parents, and there are many reasons to doubt that advances in genetic knowledge will lead to any serious engineering efforts. While the U.S. Human Genome Project and its counterparts overseas will undoubtedly accelerate the identification of genes for certain physical and medical traits, it is unlikely to reveal with any speed how genes contribute to the formation of the abilities, behavior, or personal qualities that the world admires. It is quite likely that the genetic contribution (if there is any) to, say, a good sense of humor derives in very complicated ways from more than one gene. And of course most such complex traits are probably influenced by much more than inheritance. Equally important, the designing of entire or substantial parts of human genomes is impossible with current technology and will not likely become much easier in the near future. The only kind of human genetic engineering scientists have attempted thus far is a primitive form of gene therapy to overcome a relatively simple, if deadly, immune disorder, adenosine deaminase deficiency. It will be quite a long time before scientists possess the knowledge and technology that would enable them to attempt significantly more sophisticated forms of designer human genetics.

The prospect of a revival of negative eugenics has stirred far more concern, voiced by people like the late Nobel laureate biologist Salvador Luria and rights-for-the-disabled advocate Barbara Faye Waxman. Since it will in principle be easy to identify individuals with genes for "undesirable" physical or supposedly antisocial traits, the state may intervene to discourage such people from passing them on. Indeed, in 1988, China's Gan-su Province adopted a eugenic law that would—so the authorities said—improve "population quality" by banning the marriage of mentally retarded people unless they first submitted to sterilization. Since then, such laws have been adopted in other provinces and have won the endorsement of Prime Minister Li Peng. As the official newspaper *Peasants Daily* explained, "Idiots give birth to idiots."

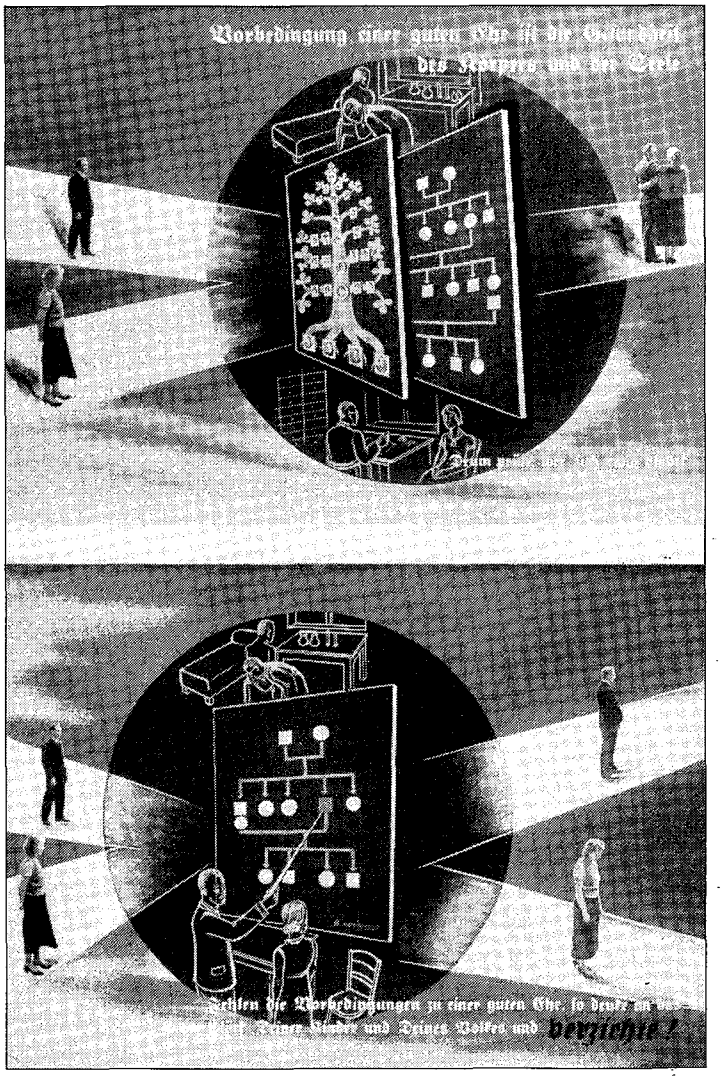
Closer to home, the European Commission, the executive arm of the 12-nation European Community, seemed to be motivated by an interest in negative eugenics in its July 1988 proposal for a European human genome project. Billed as a health measure, the proposal was called "Predictive Medicine: Human Genome Analysis." Its rationale rested on a simple syllogism—that many diseases result from interactions of genes and environment; that it would be impossible to remove all the environmental culprits from society; and therefore that individuals could be better defended against disease by identifying their genetic predispositions to fall ill. Predictive medicine, said a summary, "seeks to protect individuals from the kinds of illnesses to which they are genetically most vulnerable and, where appropriate, to prevent the transmission of the genetic susceptibilities to the next generation." The Commission, which apparently had in mind susceptibilities to such illnesses as diabetes, cancer, stroke, and coronary disease, believed that the proposal would make Europe more competitive—indirectly, by helping to slow the rate of increase in health expenditures, and directly, by strengthening its scientific and technological base.

Such economic considerations may

well prove to be a powerful incentive to a new negative eugenics in the future. They clearly played a role in the emergence of the early eugenics movement. At the 1926 Sesquicentennial Exposition in Philadelphia, the American Eugenics Society's exhibit included a board that, in the manner of the population counters of a later day, revealed with flashing lights that every 15 seconds $100 of taxpayers' money went for the care of persons with bad heredity, that every 48 seconds a mentally deficient person was born in the United States, and that only every seven-and-a-half minutes did the United States enjoy the birth of "a high-grade person . . . who will have ability to do creative work and be fit for leadership." Such cost-consciousness may have been behind the fact that, in California and several other states, the rate at which eugenic sterilizations were performed increased significantly during the 1930s, when state budgets for the mentally handicapped were squeezed.

In our own day, the more that health care in the United States becomes a public responsibility, payable through the tax system, and the more expensive this care becomes, the greater the possibility that taxpayers will rebel against paying for the care of those whom genetics inclines or dooms to severe disease or disability. Public officials may feel pressure to encourage or even to compel people not to bring genetically marked children into the world—not for the sake of the gene pool but in the interest of keeping public-health costs down.

All this said, however, there are many reasons to doubt the rise of socially controlled reproduction, let alone a revival of a broad-based negative eugenics. Eugenics profits from authoritarianism—indeed, al-



A Nazi publicity poster (circa 1941) encouraged hereditary screening prior to marriage. Ironically, many German racial hygienists privately considered Hitler an "inferior" un-Nordic East Slav.

most requires it. The institutions of political democracy may not have been robust enough to resist altogether the violations of civil liberties wrought by the early eugenics movement, but they did contest them effectively in many places. The British government refused to pass sterilization laws. So did many American states, and where they were enacted they were often unenforced. It is farfetched to expect a Nazi-like eugenics program to develop in the contemporary United States so long as the democratic process and the Bill of Rights survive. If such a program ever does threaten to take shape, the country will have a good deal more to worry about politically than just eugenics.

Awareness of the barbarities and cruelties of state-sponsored eugenics in the past has tended to set most geneticists and the public at large against such programs. During the 1950s, for example, genetic counselors, fearful of the eugenic taint, made it their standard practice to offer their clients information but no advice. Most geneticists today know better than their early-20th-century predecessors that ideas concerning what is "good for the gene pool" are highly problematic. Then, too, the handicapped and victims of inherited diseases, as well as minority groups, are much more organized and politically powerful than they were in the early 20th century. They may not have enough power to counter all quasi-eugenic threats to themselves, but they are politically positioned, with allies in the media, the medical profession, and elsewhere, including the Roman Catholic Church, a staunch opponent of the eugenics movement, to block or at least to hinder eugenics proposals that might affect them.

The European Commission's proposal mobilized just such an anti-eugenics coalition. Guided by Benedikt Härlin, a West German Green, the European Parliament's Committee on Energy, Research and Technology quickly raised a red flag against the Commission's approach to genome research. Its report reminded the Community that in the past eugenic ideas had led to "horrific consequences" and warned of the "eugenic tendencies and goals" implicit in the intention of protecting people from contracting and transmitting genetic diseases. Using human genetic information for such purposes would almost always involve decisions—fundamentally eugenic ones—about what are "normal and abnormal, acceptable and unacceptable, viable and nonviable forms of the genetic make-up of individual human beings before and after birth." The Härlin report also warned that the new biological and reproductive technologies could ultimately make for a "modern test tube eugenics," a eugenics all the more insidious because it could disguise more easily than its cruder ancestors "an even more radical and totalitarian form of 'biopolitics.'"

Härlin was not a Luddite, opposed to a genome program in principle. "You can't keep Germany out of the future," he later said about his own country's involvement in genome research. He was searching for a way to make a genome program palatable. Approved by the Committee in January 1989, the Härlin report urged 38 amendments to the Commission's proposal, including the deletion of the phrase "predictive medicine" from the text. In the European Parliament, the Härlin report won support not only from the Greens but from conservatives on both sides of the English Channel, including German Catholics. As a result, Filip Maria Pandolfi, the new European commissioner for research and development, froze Community research subsidies in April 1989. "When you have British conservatives agreeing with German Greens," he explained, "you know it's a matter of concern."

In mid-November, the European Com-

mission issued a revised proposal. It called for a three-year program of human genome analysis as such, without regard to predictive medicine, and committed the European Community in a variety of ways—most notably, by prohibiting human germ cell research and genetic intervention with human embryos—to avoid eugenic practices, prevent ethical missteps, and protect individual rights and privacy. It also promised to keep the Parliament and the public fully informed via annual reports on the moral and legal basis of human genome research. Formally approved the following June, the EC's human genome program will cost 15 million ECU (about $17 million) over three years, with some one million ECU devoted to ethical studies. (The much larger U.S. Human Genome Project also devotes a share of its budget to such studies; it conducts only basic research and its activities are closely regulated by various review boards and by Congress.)

As this experience suggests, the eugenic past is prologue to the human genetic future in only a strictly temporal sense—that is, it came before. Of course, the imagined prospects and possibilities of human genetic engineering remain tantalizing, even if they are still the stuff of science fiction, and they will continue to provoke both fearful condemnation and enthusiastic speculation. However, the near-term ethical challenges of human genome research lie neither in engineering human genetic improvement nor in some state-mandated program of eugenics. They lie in the grit of what the project will produce in abundance: genetic information. They center on the control, diffusion, and use of that information in a market economy, and they are deeply troubling.

The advance of human genetics and biotechnology has created the capacity for a kind of "homemade eugenics," to use the term of analyst Robert Wright—"individual families deciding what kinds of kids they want to have." At the moment, the kinds they can choose (if they are willing to abort the fetus) are those without certain disabilities or diseases, such as Downs' Syndrome or Tay-Sachs. Most parents would probably prefer a healthy baby. In the future, even without the development of the means to alter the genome, genetic analysis of embryos may give parents the opportunity to select the "best" of their fertilized embryos, selecting children who are likely to be more intelligent or more athletic or better looking—whatever those terms may mean.

Would people exploit such possibilities? Quite possibly, given the interest that some parents have shown in choosing the sex of their child or that others have pursued in the administration of growth hormone to offspring who they think will grow up too short. A 1989 editorial in *Trends in Biotechnology* recognized a major source of the pressure: "'Human improvement' is a fact of life, not because of the state eugenics committee, but because of consumer demand. How can we expect to deal responsibly with human genetic information in such a culture?"

Even this challenge, however, is distant, since the means of identifying the relevant genes are likely to remain beyond our grasp for a long time to come. More urgent are the questions of social decency posed by the torrent of new human genetic information (and misinformation). There is, for example, the distinct possibility that employers may use genetic screening and seek to deny jobs to applicants with a susceptibility—or an alleged susceptibility—to disorders such as manic depression or illnesses arising from special susceptibility to certain chemicals or other workplace hazards. Around 1970, for example, a single questionable case raised the fear that people with sickle-cell trait—that is, who pos-

sess only one of the two recessive genes needed to develop a full-blown case of the disease—might suffer the sickling of their red blood cells in the reduced oxygen environment of high altitudes. For a time, the U.S. Air Force Academy barred people with the trait from its entering classes, and several major commercial air carriers restricted them to ground jobs. Some people with the trait were charged higher premiums by insurance companies.

As more information becomes available in the future, life and medical insurance companies may well wish to know the genomic signatures of their clients, their risk profile for disease and death. Even national health systems may choose to ration the provision of care on the basis of genetic propensity to disease, especially to families at risk for bearing diseased children.

Should individual genomic information be protected as strictly private? Many critics say so. However, a great deal more thought needs to be given to the rights of individuals to withhold and the rights of insurers to demand such information. Insurance, and insurance premiums, depend on assessments of risk. If a client has a high genetic medical risk that is not reflected in her premiums, then she would receive a high payout at low cost to herself but at high cost to the company. The problem would be compounded if she is aware of the risk—while the company is not—and she purchases a large amount of insurance. In either case, the company would have to pass its increased costs along to other policyholders, which is to say that high-risk policyholders would be in effect taxing others to pay for their coverage. Insisting on a right to privacy in genetic information could well lead—at least under the largely private system of insurance that now prevails in the United States—to inequitable consequences.

The eugenic past has much to teach us about how to avoid repeating its mistakes—not to mention its sins. But what bedeviled our forebears will not necessarily vex us, and certainly not in the same ways. In human genetics as in so many other areas of life, the flow of history compels us to think and act anew. It is important not to be swept away by exaggerated fears that genetic research will lead to a program to engineer superbabies or the callous elimination of the unfit.

America's state and federal legislatures, those most practical of governmental bodies, have already begun to focus on the genuine social, ethical, and policy issues that the Human Genome Project raises, particularly those concerning the use of private human genetic information. "One of the most serious and most immediate concerns," noted Representative Bob Wise (D.-W. Va.) at a House subcommittee hearing last fall, "is that genetic information may be used to create a new genetic underclass." At about the same time, the California state legislature passed a bill banning employers, health service agencies, and disability insurers from withholding jobs or protection simply because a person is a carrier of a single gene associated with disability. Vetoed by Governor Pete Wilson, it is nevertheless a harbinger of the type of public-policy initiative that the genome project will—and should—call forth. If we do not use our knowledge wisely, it will be a failure not of science but of democracy.

Are We the Sum of Our Genes?

by Howard L. Kaye

Applause and a collective sigh of relief greeted the announcement in 1990 that a portion of the U.S. Human Genome Project's budget would be set aside each year for studies of the social and ethical implications of genetic research. Mindful of past experience with the atom and other revolutionary research put to uses that were not fully anticipated, scientists and administrators now seemed prepared to grapple with the possible uses and abuses of their work while it was underway.

Yet amid this celebration, the project's more profound implications are being overlooked. Many of the prominent scientists involved believe that the logical consequence of unlocking the gene's secrets will transcend science, requiring nothing less than a fundamental change in our understanding of human nature. With the mapping and sequencing of the human genome, they believe, will ultimately come knowledge of the genes associated with the whole range of human behavioral, mental, and moral traits. As these putative "genes for" such things as schizophrenia, alcoholism, homosexuality, manic-depression, intelligence, and criminality are "discovered" and publicized, the cumulative effect will be a transformation of how we understand ourselves: from moral beings, whose character and conduct is largely shaped by culture, social environment, and individual choice, to essentially biological beings, whose "fate," according to project head James Watson, "is in our genes."

This claim of Watson and other scientists is the latest episode in the controversial "return to biology" that began with the ethology of the 1960s and the sociobiology of the '70s and '80s. But whereas behavioral biologists during the past three decades, like the late-19th-century Social Darwinists before them, simply speculated about the possible hereditary bases and adaptive value of human traits and conduct, the geneticists of today believe they are poised to discover such genes and the biochemical pathways by which they shape our lives. To them, the Human Genome Project marks the culmination of more than a century of debate over the "implications" of modern biology that began with Darwin's *Origin of Species* (1859) and Francis Galton's *Hereditary Genius* (1869)—a debate lucidly chronicled in Carl Degler's recent *In Search of Human Nature.*

Yet from the days of T. H. Huxley and Bishop Wilberforce to those of E. O. Wilson, Stephen J. Gould, and James D. Watson, there is a discouraging repetitiveness to the debate, despite the illusion of scientific and moral progress. In the opinion of some (including Darwin himself), biology sanctions traditional moralities and social ideals and provides the necessary tools for their realization. According to others, biology, for better or worse, utterly shatters

such notions. For example, James Rachels asserts in a recent work subtitled *The Moral Implications of Darwinism* (1990) that "Darwinism undermines traditional morality," "religious belief," and "the idea of human dignity," while other writers tell us that its "logical consequences" include eugenics, racism, and totalitarianism.

As for public policy, some declare as self-evident truth that modern biology sanctifies a conservative agenda and social inequalities, while others, such as molecular geneticist Christopher Wills of the University of California, San Diego, claim biology with equal conviction for social activism and liberal reform. Some see in the dogmas of molecular biology and Darwinism the ultimate ground of objective truth, toward which the humanities and social sciences must bow, while others insist on their essential irrelevance to such concerns.

Whatever particular forms it has taken, the debate has always centered on the "implications" and "logical consequences" of the biological sciences for our understanding of human nature and culture. Today, however, faced by the prospect of an increased capacity and desire to intervene in the human genome, I believe that we must change the terms of the debate and give up this misguided quest. To think in terms of "implications" and "logical consequences" is to suggest that certain facts or propositions about human social behavior are so inseparably entwined with certain facts or propositions about biology that if the biological statement is true, the social statement follows necessarily.

"Implication" suggests a connection that is objective and logical. Yet is this really the case, or do we not thereby grant too much to science—ultimately the ability to tell us objectively who we are by nature—and too little to ourselves? Does any natural scientific proposition logically entail some significant human conclusion, or is this connection derived from other sources? Does relativity in physics, for example, "imply" moral relativity, as was argued earlier in this century? Does Darwinian theory "imply" the falseness of the biblical account of creation, as many have claimed for over a century? Does the proposition that an organism is "only DNA's way of making more DNA" imply that we and our culture are also "survival machines" built by natural selection to preserve and replicate our "immortal genes"? And finally, does the discovery of genetic correlates to the full range of human capacities and conduct truly imply the knowledge that "fate is in our genes"?

The "logical consequences" discerned by the combatants in this debate are more properly understood as *interpretations*, more philosophical, sociological, and psychological in nature than objectively scientific. The theory of relativity in physics may have been seen by some individuals as lending "scientific" support to moral relativity, but the idea of moral relativity long predated 20th-century physics. For all the furor and spiritual anguish that we wrongly believe was experienced by the pious because of Darwin's theory of evolution through natural selection, many readers of Genesis, including many biologists (such as Francis Collins, codiscoverer of the gene for cystic fibrosis), perceive no incompatibility in the respective accounts and thus

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feel no need to redefine human nature or purpose. This is so because the perception of such "implications" depends not simply on knowledge of natural phenomena and scientific theory but on a host of background assumptions, philosophical orientations, and cultural commitments.

Pious Jews or Christians may read the account of creation in Genesis symbolically or as a charming but primitive myth, which, despite its outdated cosmology, contains important truths about life's ultimate origins and about our own problematic nature. For them, a God who creates by natural selection may be just as believable as one who creates through word and division. Yet to those already alienated from, and hostile toward, such religious visions—as well as their foes, those religious fundamentalists threatened by a "godless" modernity—the implications of Darwinism for biblical religion are obvious.

The recognition that natural selection acting on the genome can affect behavioral characteristics has stimulated much valuable research. Nevertheless, to argue that the findings reveal "the essence of humanity," as Christopher Wills does, or the "objective criteria" by which human conduct must ultimately be judged, as political theorist Roger Masters does, and the proper means for making ourselves, in Watson's words, "a little better," is an interpretation of nature and of man that is more metaphysical than scientific.

Unfortunately, it is not always clear to either scientists or to their lay audience when such claims are being made. A scientist or naive popularizer like the Pulitzer Prize–winning science reporter Natalie Angier, who tells us that "adultery" and "infidelity" are far more prevalent in the animal kingdom than had been previously thought and serve to increase the "adulterer's" reproductive fitness, appears to be describing only the facts of life. Yet what else is being conveyed by the use of human moral terms like "debauchery," "adultery," and "philandering" to describe nonhuman animals? Does this not imply that these

Plus ça change .... *From Charles Darwin to James Watson, the argument that biology is destiny has hardly changed at all.*

nonhuman and all-too-human sexual activities are essentially the same in their meanings, motivations, purposes, and consequences? Would it not also appear to be a logical consequence that human adultery is "natural" and our moral condemnation of it unrealistic and even unnatural?

From Pliny the Elder to Saint Francis of Sales, the elephant was held forth as a model of ideal conjugal conduct. Saint Francis wrote:

> It never changes females and is tenderly loving with the one it has chosen, mating only every three years, and then only for five days, and so secretly that it is never seen in the act; but it can be seen again on the sixth day, when the first thing it does is go straight to the river and bathe its whole body, being unwilling to return to the herd before it is purified.

Does the apparent faultiness of this ethology (so far only the California mouse has proven to be truly monogamous) mean that the ideal of mutual faithfulness and self-mastery is discredited or less desirable and noble? Would better ethology provide us with a better ideal? I think not. The ideal of fidelity was never put forth *because of* the behavior of elephants but because of the behavior of people. To understand human adultery and proper conjugal conduct, we have far more to learn from literature, religion, philosophy, and our own self-reflection than biology can ever provide.

Or when laypersons read in Wills's *Exons, Introns, and Talking Genes: The Science Behind the Human Genome Project* (1991) that the discovery of "genes for" intellectual abilities and personality traits is as "inevitable as the eventual discovery of genes for manic-depression or schizophrenia," how many will recognize the *a priori* beliefs that lie concealed behind the white coat of science? How many readers will fail to interpret such future "discoveries" as suggesting possible genetic *influences* on the development of certain traits and capacities in *some* of the individuals manifesting them and instead see the "implication" of genetic determinism?

In confronting such allegedly scientific accounts, we need to ask not what human propositions may be objectively drawn from a given body of biological fact but three other questions: What leads us to perceive, construct, and proclaim such interpretations as objective truths? How adequate are they as interpretations of nature and ourselves, based on *all* of the knowledge available to us? What might be their social and moral impact?

Enthusiasm over the explosion of knowledge about the genome is not the only, nor perhaps the most compelling, motive at work in the perception of implications. Beneath the surface of today's scientific optimism is a profound sense of cultural crisis and moral uncertainty. Thanks in part to challenges posed by science, communally binding and individually compelling religious faiths and moral ideals have long been eroding. For centuries our philosophers and social scientists have sought to unmask our cultures, our politics, and our very selves, presenting them as illusory structures shaped by forces beyond conscious control. In such a cultural climate, the specter of nihilism, cultural relativity, and individual disorientation seems a constant threat. Confused about who we are and how we should live, suspicious of all answers, we can agree on nothing beyond the primacy of individual desires or group demands in both private and public affairs.

For those who do not celebrate such a condition, the seeming certainties achieved by the natural sciences have been powerfully attractive. Ever since Thomas Hobbes, who in horror at the anarchy of the English Civil War turned to geometry for guidance,

the search for a secular morality has dominated social thought, driving us from science to science—mathematics, physics, biology, psychology, sociology—in hope of discovering a stable moral ground or law-generating method. Cut loose from religious traditions and systems of meaning, adrift in a sea of relativity, and buffeted by chance, expediency, and impulse, we continue to find both the "certainties" of scientific "fact" and its power to satisfy human desires alluring.

As our latest attempt at dropping some moral anchor, biology may prove as ambiguous and unsuccessful as previous scientific moralities—and perhaps even more harmful. Our current infatuation with biology, unlike that of a century ago, is occurring at a time when the humanities and social sciences have declared moral bankruptcy, thus depriving us of a vital part of the collective memory we need to regulate and resist our increased capacity for genetic manipulation. This sort of amnesia is painfully apparent, for example, in Wills's discussion of genetic influences on criminal behavior. Pointing to the common social backgrounds of police and criminals, Wills asks rhetorically, "Why should one group be law-abiding and the other not, if criminal behavior is engendered entirely by the environment?" For Wills, environmental and genetic determinism are apparently the only choices. What the former cannot explain must be attributed to the latter. Wedding a crude sociological determinism to an equally crude biology, Wills, like all for whom "nature and nurture" or "heredity and environment" are the only legitimate categories for understanding human life, utterly ignores the irreducible element of individual will, choice, and responsibility.

How are we to resist such irresponsible assertions—and the actions potentially sanctioned by them—if our scientists and opinion makers have forgotten what it means to be a moral and cultural being endowed, in Max Weber's words, "with the capacity and the will to take a deliberate attitude towards the world and to lend it significance"?

Fortunately, most nonacademics have not forgotten. Years ago, while literary and scientific intellectuals were extolling sociobiology's ethic of survival and "the morality of the gene," I overheard a doorman (married and the father of three) complain to a co-worker, "I'm not really living, just surviving." This is a sentiment I suspect we have all heard or experienced, but what was this man really saying? In distinguishing between *human* life and *biological* life was he not expressing the presence of a "self" or "soul" within him that aspired to a higher life, a more meaningful and fulfilling life than the life of biological survival and reproduction he was leading? Unlike our biologists, structural social scientists, and poststructural humanists, he recognized that we are meaning-craving and meaning-creating animals who aspire, however perversely, to the good. To understand such a nature, which desires "the good's being one's own always" and which experiences the pain of shame, resentment, and guilt at our inadequacy, Plato's *Symposium* remains a better guide than E. O. Wilson's *Sociobiology*. It is not that Plato's biology is better than Wilson's but that the question of human nature is not simply a biological one, no matter how many genetic correlates of character are discovered. Our capacity for culture—understood not in the trivial biological sense as all nongenetic means that enable organisms to adapt to their environments, but in its properly human sense as that system of ideals, practices, and prohibitions that comes into being both to protect us from

nature and from ourselves and "for the sake of living well"—may certainly be the product of natural selection. Our capacities for reason, symbolic expression, and imagination; our aspirations for esteem and respect; and our qualities of curiosity and self-consciousness all may have evolutionary origins and may have contributed to our species' biological success. But they have long since taken on applications and ends that transcend the narrowly biological and may at times contradict it. Indeed this need to dream of, reflect on, and feel shame before goods and ideals detached from and even contrary to both our "innate behavioral repertoire" and our ultimate biological ends is both our greatness and our curse. Nevertheless, it is precisely this capacity that is under attack, now on three fronts, as the natural sciences, social sciences, and humanities close in on their quarry: the self or soul.

It is this attempt to redefine fundamentally how we conceive of ourselves as human beings, and thus how we conceive of a good and proper life, that makes contemporary biological naturalism so culturally radical in its potential consequences. Yet however inadequate and even harmful this perspective may be, however unfounded its claim to the status of "scientific implications" for its moral prescriptions, it has indeed begun to alter our self-conception. This is not because scientific knowledge has social *implications* but because it has had and will continue to have social *impact*.

During the 1960s, the writings of ethologists like Konrad Lorenz and Robert Ardrey and evolutionary theorists like Theodosius Dobzhansky, G. G. Simpson, and C. H. Waddington stimulated a return to biologically grounded reflections on human nature and culture. In the 1970s and '80s, the even more reductionist writings of E. O. Wilson and other sociobiologists and of molecular biologists such as Jacques Monod and Francis Crick reached a surprisingly large audience. If the colleague of mine who told me he decided to have a second child, seven years after his first, because he was worried about investing his genes in a single offspring is any indication, these messages have indeed been heard.

In the years to come, I expect this redefinition of ourselves as essentially biological beings to continue and to have even greater influence on individual actions and public policy. But whereas this once was the work of scientists addressing the public directly in works that were explicitly philosophical and manifestly seeking to convert, its continued development will, I fear, be far more indirect and insidious. The Human Genome Project will play a crucial role, but not simply through its discoveries in the laboratory. Instead, I expect that the cumulative effect of the ways such knowledge is likely to be interpreted for and by the broader public will push us, like sleepwalkers, toward the biologizing of our lives in both thought and practice.

When a scientist such as Harvard's E. O. Wilson candidly acknowledges that the particular vision of human nature and culture he is advocating is drawn from the "mythology" of scientific materialism, the thoughtful reader is in a position to recognize Wilson's work for what it is—metaphysical speculation and natural theology—and evaluate it accordingly. Yet when the public reads in the newspaper of "genes for" various human attributes and behaviors and of the means for altering the human "blueprint" in seemingly desirable ways, few are able to recognize the moral and philosophical commitments that lie behind such statements. Yet such commitments are powerfully present, however unconscious or concealed behind "descriptive" language. When George

Cahill of the Howard Hughes Medical Institute asserts that the Human Genome Project is "going to tell us everything. Evolution, disease, everything will be based on what's in that magnificent tape called DNA," the "everything" he means is everything worth knowing about life. When Maynard Olson of Washington University states that "genetics is the core science of biology and increasingly it's going to be the way that people think about life," he is not offering just a prediction but a moral prescription: Genetics is how we *ought* to think about life. When Robert Sinsheimer, the prominent scientist who helped launch the drive for a genome project in 1985, tells us that it will provide "the complete set of instructions for making a human being," he certainly ignores everything else that goes into the making of a human being. More ominous, however, is his emphasis on "making," for this is the same Robert Sinsheimer who in 1973 advocated the conscious direction of human evolution toward a "higher state" through eugenics as the only unifying goal left that could save us from our cultural despair.

Heading the Human Genome Project is, of course, James Watson, codiscoverer of the structure of the DNA molecule. For Watson, the genome project is quite simply the culmination of his reductionist quest for understanding all of life including "ourselves at the molecular level." With this understanding we can and should increasingly control our fate. After all, why not? "A lot of people say they're worried about changing our genetic instructions," Watson acknowledges, "but those [instructions] are just a product of evolution designed to adapt us for certain conditions that may not exist today . . . [So] why not make ourselves a little better suited for survival? . . . . That's what I think we'll do. We'll make ourselves a little better."

The point here is not to raise the specter of mad scientists, hell-bent on eugenics, in charge of a multibillion-dollar government research project with important medical and political potential. Nor is it to suggest that a majority of researchers participating in the project share this metaphysical and social agenda. It is instead to argue that such pronouncements may have an important impact on public perception, public understanding, and ultimately public response to emerging biological knowledge and technologies. So pervasive is this highly reductive and deterministic view of life that it passes for self-evident and unproblematic scientific fact among those science writers and journalists who seek to keep the public informed about developments in biology. Newspapers and other media constantly refer to the genome as "the blueprint for a human being," "the formula for life" that "dictates . . . how an individual confronts the world" and that contains "the very essence" of our lives. They trumpet the discovery of "genes for" cancer, schizophrenia, manic-depression, and other maladies. In the *Philadelphia Inquirer* last fall, it was put quite simply: "Everything about us . . . is determined by genes."

Even those critical of some developments in modern biology find it difficult to escape from its reductive language. Robert Wright of the *New Republic*, in a highly caustic piece on Watson and the genome project, nevertheless adheres to what Watson's colleague Francis Crick dubbed the "Central Dogma" of molecular biology: that DNA makes RNA, RNA makes protein, and "proteins (to oversimplify just a bit) are us." The "implications" of such a dogma appear clear. DNA, as shaped by natural selection and chance, essentially determines who we are and how we live, yet like any "blueprint" can be altered to fit new needs.

That human beings, and perhaps other

organisms as well, are more than their DNA "blueprints" or the sum of their proteins; that DNA, however "magnificent" a tape it may be, does not constitute the "essence" of human life, nor tell us "what we are," in Watson's words, let alone who we are; that it is both incorrect and irresponsible to speak of having discovered "genes for alcoholism" or genes that "cause" schizophrenia, are ideas that have become so strange that they are virtually unthinkable. Yet because they have become unspoken and unthinkable, many will want to take actions and advocate policies on the basis of what passes for scientific fact.

When the news media announced the discovery of a "gene for alcoholism" in 1990, I recall mentioning to a colleague in chemistry that such language was dangerously misleading. After all, the research of Drs. Ernest Noble and Kenneth Blum had only suggested a possible genetic component contributing indirectly to the alcoholism of *some* individuals. To speak of a "gene for alcoholism" both exaggerates the degree of genetic influence and seems to attribute all forms and cases of alcoholism to the same biological cause. The study, moreover, has yet to be replicated by others and involved research on only 70 brains. Much to my surprise, the chemist strongly disagreed: "Now wait a minute! This may be a very important piece of knowledge," he said, "for it might mean that the best way of treating the problem of alcoholism is through its biological causes."

He was hardly alone in making the jump to possible biological interventions. Noble and Blum plan to develop a blood test within five years that would detect the presence of the relevant dopamine receptor gene so that screening and treatment by drugs can begin. Forgetting for a moment that the gene identified seems to be correlated with something vaguely defined as "pleasure-seeking activity" in general and not simply some cases of alcoholism, and ignoring temporarily the potentially devastating, stigmatizing effects of such screening, there is still a shocking lack of awareness that the question of the "best way" to treat a problem such as alcoholism is not purely a question of efficiency, speed, or cost. It is a moral and political question as well, or at least it is if we recognize that we are dealing both with a problem that has important social, cultural, and psychological causes and with a being who possesses a potentially free and responsible soul that ought to be respected. It may even be possible that the "best way" morally to treat such a person may not be the most cost-effective way.

In the years to come cases like this will only proliferate. Regular "scientific breakthroughs" will torment and excite us, yielding genetic "determinants" for dozens of traits and attributes, both desirable and undesirable. Powerful economic and political interests, coupled with the understandable desire of individual human beings to maximize the well-being of themselves and their children, will continue to tempt us to pursue courses of biological intervention that will dehumanize us all, unwittingly, in the name of scientific progress, individual freedom, and compassion. Yet the road to such dehumanization in action begins with our prior dehumanization in thought—our forgetting the kind of beings we are and our construction of a new self-definition seemingly sanctioned by the biological sciences which, in their ignorance and ambition, encourage us to forget.

THE FATEFUL CODE

The remarkable advances in genetics during the last 50 years have prompted an outpouring of books and articles about the science. Along with journalists, many of the more prominent researchers have weighed in with books for the general reader. This has proved to be a mixed blessing. While throwing considerable light on a complicated science, the array of books can be bewildering. While a number of these may *seem* to be about genetics—including François Jacob's **The Logic of Life** (Pantheon, 1973)—they in fact focus on such matters as human behavior and man's ultimate place in the universe. Many writers skirt the fringes of genetics, discussing the ethics, or implications, or mechanics of their science. Yet few provide a simple history of who, what, when, and how.

Two exceptions are Gunther Stent's **Coming of the Golden Age** (Natural History, 1969) and Horace Freeland Judson's **Eighth Day of Creation** (Simon & Schuster, 1979). Though somewhat dated, both contain a wealth of history. Stent, a molecular biologist at the University of California, Berkeley, offers an excellent thumbnail retrospective, sketching the now-familiar tale of the rise of modern molecular biology from its roots in Gregor Mendel's 19th century pea-plant experiments to Francis Crick and James Watson's 1953 discovery of DNA's structure. (Readers are forewarned that Stent indulges in a rather New Age meditation on the connection between genetic research and the evolution of human intellect.)

Judson, a professor of humanities and science at Stanford University, explains the late 20th-century breakthrough in biology and genetics as a "synthesis of particular lines from five distinct disciplines": x-ray crystallography, physical chemistry, genetics, microbiology, and biochemistry. What sets genetics apart from sciences such as physics or astronomy—each of which had its Newton or Copernicus—is that it evolved not through "great set-piece battles but by multiple small-scale encounters—guerrilla actions—across the landscape." Genetics had no "ruling set of ideas" such as the Ptolomeic system of the universe to overcome.

One event that was truly revolutionary—Crick and Watson's discovery of DNA's structure—is treated in Watson's highly personal account, **The Double Helix** (Norton, 1980). Reading this book, one is struck not so much by the magnitude of Watson and Crick's discovery as by the obsessive and, at times, graceless way they went about achieving it. Locked in a furious race with Nobel Prize–winning chemist Linus Pauling, Watson and Crick repaired to a local pub to drink a "toast to the Pauling failure" when the American published an early but incorrect description of DNA's structure. Recent editions of Watson's book, edited by Gunther Stent, provide further tantalizing glimpses of politics and etiquette inside the laboratory. Stent appends disapproving reviews of the original book, rebuttals, and recriminations, one coming from Crick himself, who calls it "a rather vivid fragment of [Watson's] autobiography, written for a lay audience."

The impression that the expanded book leaves of Watson—now the most visible leader of the U.S. Human Genome Project—is less than flattering. Robert L. Sinsheimer, one of the project's early promoters, talks about Watson and Crick's reliance upon "cadged data... overheard in seminars, pried out in conversations, even provided by Max Perutz from a privileged report." Sinsheimer suggests that others were close to reaching the same conclusions and that the scientists' "ingenuity and clutching ambition bought a year or two in time—and fame."

A common thread running through many recent books is the realization that modern geneticists—like the scientists who unlocked the secret of the atom—are delving into a realm of knowledge that man may lack the ethics to control. This concern echoes through several books that take the Human Genome Project as a point of departure. Among these are **Genome** (Simon & Schuster, 1990) by journalists Jerry E. Bishop and Michael Waldholz, **The Human Blueprint** (St. Martin's, 1991) by chemist Robert Shapiro, and science writer Lois Wingerson's **Mapping Our Genes** (Dut-

ton, 1990). Devoting less attention to past discoveries than to what *might* be discovered, all of these authors frame the various sides of the ethical debate. Shapiro takes the most hopeful view, trusting in our wisdom to reap what is best in genetic research while limiting abuses. By contrast, Jeremy Rifkin, author of **Algeny** (Viking, 1983) and **Declaration of a Heretic** (Routledge, 1985), warns that "with the emergence of genetic engineering, society entertains the prospect of a new and more deadly form of segregation . . . based on genotype."

The dismaying history of eugenics receives full treatment in historian Paul Weindling's **Health, Race and German Politics Between National Unification and Nazism, 1879–1945** (Cambridge, 1989) and in Robert Proctor's **Racial Hygiene** (Harvard, 1988). As Proctor points out, the legacy of the abuses of science under the Nazis is not just that Nazi racial policy was allowed to triumph but that "this struggle was played out, at least in part, in the spheres of science and medicine," forever tainting genetic research, at least in the public mind, with a sinister aspect.

One potentially sinister outgrowth of genetic research is the ability to screen individuals for genetic defects. **Ethics and Human Genetics** (Springer-Verlag, 1989), edited by D. C. Wertz and J. C. Fletcher, provides an international survey of such practices as the screening of unborn fetuses for fragile X syndrome and the testing of adults for susceptibility to depression. The authors' findings suggest that the geneticists seem more concerned about the burden of increased demand for such tests than about the possible moral dilemmas they may present individuals. Those wishing to ponder such choices may consult **Dangerous Diagnostics** (Basic, 1989), by Dorothy Nelkin and Laurence Tancredi; **Backdoor to Eugenics** (Routledge, 1990), by Troy Duster; **Proceed with Caution: Predicting Genetic Risks in the Recombinant DNA Era** (Johns Hopkins, 1989), by Neil A. Holtzman, M.D.; the Office of Technology Assessment's **Genetic Monitoring and Screening in the Workplace** (U.S. Government Printing, 1990); or, in a more visionary vein, Aldous Huxley's dystopian **Brave New World** (1932).

But as Daniel J. Kevles and Leroy Hood remind us in the introduction to their forthcoming collection of essays, **The Code of Codes: Scientific and Social Issues in the Human Genome Project** (Harvard, 1992), "science-fiction fantasies about the genetic future distract attention from the genuine problems posed by advances in the study of heredity"—particularly those that relate to insurers, employers, and the government. Assembling an impressive cast of commentators, including Nobel Prize winners Walter Gilbert and James Watson, the book explores the history, methods, and implications of the Human Genome Project. Readers may sample such exotica as Horace Judson's poetic musings on gel electrophoresis—"molecules of DNA behave in the electrical field like strands of aquatic weed strung out and floating down a flowing stream." Or they may learn how researchers compare the DNA of bacteria and fruit flies to human DNA to find the key to what makes us human, a quest that Gilbert likens to the "grail of human genetics." Part of that knowledge, says Gilbert, is "to realize that genetic information does *not* dictate everything about us." Science can only go so far. Society will still have to decide "how much of our makeup is dictated by the environment, how much . . . by our genetics, and how much . . . by our own will and determination."