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Genetic Testing and the Use of Information

Edited by Clarisa Long

This book presents the thinking of six distinguished scholars about key ethical and policy issues related to genetic testing, including genetic privacy, the regulation of genetic testing, and genetic discrimination.

Clarisa Long edited the volume and contributed the introduction. She worked on this project as an Abramson fellow at AEI, and she is now an associate professor of law at the University of Virginia and a research fellow at the Kennedy School of Government at Harvard University. The other contributors are Ellen Wright Clayton, an associate professor of both pediatrics and law at Vanderbilt University; David Korn, the senior vice president for biomedical and health sciences research at the Association of American Medical Colleges and the vice president, dean, and professor of pathology emeritus at the Stanford University School of Medicine; Philip R. Reilly, executive director of the Shriver Center for Mental Retardation; Karen Rothberg, the Marjorie Cook Professor of Law and the founding director of the law and health care program at the University of Maryland School of Law; and Michael S. Watson, the vice president for laboratory affairs and a director of the American College of Medical Genetics. The following summary is based on Long's introduction to the volume.

A few important trends indicate that we are in the early years of a technological revolution arising from our understanding of the genetic basis of life. Scientists' ability to manipulate and decode genes is advancing with extraordinary speed. The biotechnology industry is one of the United States' most innovative sectors. The Human Genome Project, a fifteen-year multinational effort to decipher all the genetic information contained in human DNA, is proceeding faster than anticipated.

Since its inception, genetic research has created high hopes for some and deep anxieties for others.

Recent developments in genetic research have only multiplied the number of vexing legal, economic, ethical, and social issues. A few of those issues are: Should individuals be allowed personal property rights to their DNA, cells, or tissues? How should the industry be regulated so as to maximize safety without stifling innovation? What are the appropriate uses of gene therapy and other genetic manipulations?

The information contained in our genes is being discovered at an ever-increasing pace. Perhaps the most worrisome developments created by the combination of genetic research and information technology involve questions of privacy and genetic discrimination: Who should have access to information derived from a genetic test? Should there be an obligation to tell a spouse or a child test results? Are there times when federal, state, or local governments may appropriately mandate individual genetic testing or community-wide genetic screening? Will employers be able to require the release of genetic records as a condition of employment? Will insurance companies be allowed to use genetic information to determine risk, thus limiting the pool of insured persons so as to contain costs for the group? How will we prevent adverse selection against insurance companies by individuals? At what point does a genetic condition qualify as a disability under the Americans with Disabilities Act?

The Human Genome Project

The foundation for understanding the unique genetic profile that each of us carries is being laid by the research conducted through the Human Genome Project. The Human Genome Project is an international effort, begun in October 1990 and slated for completion in 2003, to identify all the genes in human DNA and make them accessible

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for further analysis. The effort is coordinated by the National Institutes of Health's National Human Genome Research Institute (NHGRI) and the U.S. Department of Energy. The human genome, which is the entire sum of human DNA, is estimated to contain approximately three billion subunits, or nucleotides, that make up an estimated 50,000 to 100,000 genes.

One of the project's products will be a biological database that will serve as a resource for a generation or more of future research. The complete sequence of the human genome will help us understand our biochemistry, metabolic processes, neural development, aging, and a host of other factors that make us human. Large-scale automatic sequencing techniques will allow scientists quickly and easily to conduct mutation research and compare tiny variations in genetic sequences. The information generated can be used in biomedicine to understand the genetic basis of thousands of human diseases and eventually to diagnose diseases and develop optimal therapies.

No one can predict exactly what serendipitous discoveries lie ahead, beyond the detailed picture of human DNA. The Human Genome Project combines the exploratory nature of basic research with the cost-benefit considerations of applied research—an important thing in these days of concern over public spending on scientific research projects. In addition to its expected benefits, the genetic information generated by the project carries far-reaching ethical and social implications, such as the danger of misuse and potential threats to personal privacy.

Testing for Genetic Disorders

Each person inherits two copies of every gene, one from each parent. Those genes in turn can give rise directly to disorders, can create a predisposition to developing diseases, or can work with a constellation of other genes to influence one's general health.

A few genetic diseases are inherited through dominant genes. A dominant gene is one that is "expressed" or determines a specific trait or condition. Only one copy of a dominant gene is necessary for it to be expressed. Huntington's disease, which is a rare but progressive and fatal neurological disorder, is an example of a dominant-gene disorder. Thus, a person possessing even a single copy of the gene for Huntington's disease will almost surely develop the disease. Each child of a parent possessing a dominant gene has a 50 percent chance of inheriting the copy of that gene.

In the case of Huntington's disease, a genetic test has been developed to diagnose presymptomatic individuals,

although no treatment has yet been developed. Extensive pre- and post-test counseling to help patients deal with the emotional and psychological issues surrounding Huntington's disease accompanies the test. Before the genetic test was developed, most (approximately 80 percent) of the people at risk for developing Huntington's disease stated that they would want to be tested when a test became available. Experience has shown, however, that in the absence of treatment, the actual percentage of people opting to take the test is much smaller.

Most of the genetic diseases we know about today are recessive disorders. A recessive condition requires two copies of a gene to be expressed. Cystic fibrosis is an example of a recessive disorder. Thus, a person who develops cystic fibrosis has two abnormal copies of the gene, one inherited from each parent. A person who has only one abnormal copy of a gene for a recessive condition is called a "carrier." While carriers will not develop the condition themselves, they have a 50 percent chance of passing on the gene to any one of their children. Children of parents who are both carriers have a 25 percent chance of inheriting both copies of the abnormal gene and developing the condition, and a 50 percent chance of being a carrier.

By far the vast majority of diseases fall into a third category, the multigenic conditions, which are influenced by multiple genes working in conjunction with environmental factors. Technologies are being developed to test for the existence of thousands of genes simultaneously, in the hopes that someday we will be able to understand how these genes interact with each other.

The genetic material for a test can be obtained from any tissue, including blood. Doctors can use genetic tests for several purposes: (1) carrier testing, or discovering whether a person is a carrier for certain genetic diseases, which involves identifying unaffected individuals carrying one copy of a gene for a disease that requires two copies for the disease to be expressed; (2) susceptibility testing, or learning whether a person has a predisposition to develop a particular disease; (3) prenatal diagnostic testing, which helps expectant parents know whether their unborn child will have a genetic disease or disorder; (4) presymptomatic testing either for predicting the occurrence of disorders such as Huntington's disease or for estimating the risk of developing a disorder such as Alzheimer's disease; (5) confirming the diagnosis of certain disorders that are initially diagnosed through other means; and (6) forensic or identity testing. The cost of a single test can reach thousands of dollars, depending on the size of the genes and the number of mutations tested.

In addition to conditions traceable to a single gene, such as Huntington's disease (caused by one copy of a single dominant gene) and cystic fibrosis (caused by two copies of a single recessive gene), genes have been implicated in predisposition to heart disease, Alzheimer's disease, diabetes, breast cancer, multiple sclerosis, the ability to mount an immune response to parasites, and other conditions ranging from the innocuous to the lethal. Such tests have so far been available mostly to families at high risk for genetic conditions or to participants in research studies. A predisposition to a disease does not mean the person will get the disease; it only means the person will have a certain increased risk of developing the disease. One must also take account of environmental factors that can lower or increase the risk. Counselors are trained in helping individuals understand the nuances of a genetic predisposition to a disease.

Hundreds of thousands of people are at risk for genetic diseases for which tests have been developed. Most of those tests are available only to research laboratories and are offered only to family members of individuals who have been diagnosed with a particular condition. The information provided by the tests is a mixed blessing, depending on whether they are carried out properly and on how the information is used. Testing will soon be possible not just for dozens of genes that have been directly linked to serious disease and for single genes that merely predispose their carriers to certain conditions, but also for disorders that are multigenic, or due to the interaction of multiple genes.

Much of the recent debate over genetic testing has centered on commercialized tests for adult-onset diseases like Alzheimer's and some forms of cancer, like breast and ovarian cancer. Such tests only indicate a probability for developing the disorder and are targeted to healthy, presymptomatic people who are identified as being at high risk on the basis of family medical history. A positive result, being merely probabilistic, can be difficult to interpret. Many people who carry a mutation predisposing them to a condition never develop it. For any individual, it is difficult to determine the probability of developing a disease. Scientists believe that many diseases and predispositions are multigenic or are influenced by environmental factors. So the tests give rise to a plethora of questions, such as whether a particular genetic test is reliable and clinically valid; whether testing should be performed when no treatment is available; and whether parents should have the right to have their minor children tested for adult-onset diseases.

Genetic technologies and the information they generate are placing a new emphasis on the role of bioethics in medical and social decisionmaking. Government policymakers, lawyers, and other decisionmakers are turning their attention to genetics. Ethicists are debating whether genetic information is the exclusive property of patients or is instead properly the concern of insurers, employers, and society. Patenting genetic products, protecting personal genetic information, preventing genetic discrimination, and developing genetic laboratory safeguards are all issues that are drawing legal and legislative attention. The need for wider public understanding of the ethical, legal, and social issues surrounding genetic testing is particularly acute because many of the consequences will be fully felt only a decade or more in the future, long after the legal procedures and doctrines for dealing with genetic testing and the use of information have been established.

Much more fundamental scientific research will be necessary to put the results of genetic studies to use in the diagnosis and treatment of disease. In some cases, not enough is known about the meaning of genetic information or how it is being interpreted and used. Transmitting genetic information from physicians to patients and vice versa will require special caution and special counseling because genetic information affects people in ways not yet fully understood. Genetic information will rarely provide specific directions. It may predict events that will occur years in the future or not at all. It may predict the future of other family members. It has the potential to challenge and stigmatize both individuals and families.

Privacy, Regulation, and Discrimination

Perhaps the most urgent of social issues arising from genetic research are the questions of privacy and fair use of genetic information. As David Korn notes in chapter 2 of this volume, "Since every individual is a direct beneficiary of the historic medical knowledge base, the ethical principle of distributive justice would suggest that everyone should be obligated to contribute to that base." In chapter 3, Karen Rothenberg responds that we need to consider what she calls the "three Cs"—context, control, and community—when discussing a model that requires balancing concern for private rights with public benefit and research.

Chapter 4 deals with the regulation of genetic testing. The information produced by genetic research is changing the practice of biomedical research, the clinical diagnosis

of diseases, and public perceptions about genetic information and medical technology. Despite that, most health care professionals are not sufficiently knowledgeable about genetics, genetic technologies, and the ethical, legal, and social implications of having and using genetic information. Michael S. Watson argues that "medical genetics must be integrated into the broader health care delivery system rather than separated from it by genetics-specific regulations."

Chapters 5 and 6 present essays on genetic discrimination. Some scientists and physicians acknowledge that personal knowledge of genetic information can sometimes benefit an individual by allowing for early, more accurate, and effective treatment. But they fear that the uncertainties surrounding the interpretation of genetic tests, personal anxiety, and social stigmatization could outweigh the benefits of testing, and they claim that genetic testing carries with it a significant threat of discrimination by potential employers and insurers.

Philip R. Reilly disagrees. He believes that "little evidence exists to support the widespread fear that people who undergo genetic tests to determine whether they are at increased risk for developing a serious disorder face a significant risk of genetic discrimination." He admits that state laws have provided little actual protection

against genetic discrimination, but he argues that federal laws have "sharply reduced the risk of genetic discrimination in regard to access to health care and employment."

Ellen Wright Clayton disagrees with Reilly's conclusions that the risk of genetic discrimination is low. She points to other reasons why documented cases of genetic discrimination are few—the empirical studies to date on discrimination may have been flawed and our understanding of genetic tests is in its infancy—and remains skeptical of the actual effect federal legislation will have, in the long run, in preventing genetic discrimination.

These chapters collectively seek to address some of the major issues confronting a society on the brink of a new genetic information age. To what degree is biology destiny? To what extent are human talents and institutions the products of our anatomical, neurological, hormonal, or genetic constitution? We have much to learn about the complex interactions within an organism and between an organism and the environment that influences its development. In the meantime, we must decide the legal and ethical role we will accord genetic information as genetic research presents us with increasingly pressing and inescapable questions.

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