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Ethical, Legal, and Social Issues in Genetic Testing for Complex Genetic Diseases (with E. Zuiker)

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Lecture

ETHICAL, LEGAL, AND SOCIAL ISSUES IN GENETIC TESTING FOR COMPLEX GENETIC DISEASES

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I. INTRODUCTION

When Congress launched the Human Genome Project in 1990, concerns were raised about the ethical and legal implications of the endeavor. If the Project succeeded in identifying the genetic predictors of later disease, would currently healthy people be discriminated against by schools, insurers, or employers because they had a gene mutation signaling a higher chance of developing a genetic disease later in life?[1] How might the results of such a predictive genetic test change the way a person viewed himself or herself?[2] What would the duties of health professionals be in offering and conducting such tests?[3] And what type of intellectual property scheme might be necessary to assure the appropriate incorporation of the new genetic tests into social life?[4]

The first director of the Human Genome Project was James Watson, the Nobel Laureate who was a co-discoverer of the structure of DNA. He realized that the project constituted an unprecedented social experiment. On his own initiative, he decided to use 3-5% of the Human

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1 LORI B. ANDREWS, FUTURE PERFECT: CONFRONTING DECISIONS ABOUT GENETICS 130-50 (2001) [hereinafter ANDREWS, FUTURE].

2 *Id.* at 31-55.

3 Lori B. Andrews, *Torts and the Double Helix: Malpractice Liability for Failure to Warn of Genetic Risks*, 29 HOUS. L. REV. 149, 152 (1992) [hereinafter Andrews, *Torts*].

4 Lori B. Andrews, *The Gene Patent Dilemma: Balancing Commercial Incentives with Health Needs*, 2 HOUS. J. HEALTH L. & POL'Y 65 (2002) [hereinafter Andrews, *Patent*].

Genome Project's scientific budget to fund studies of the ethical, legal, and social implications of genetics.[5]

The resulting body of literature and debate has focused primarily on such implications as they relate to single gene disease.[6] The single gene disorders, such as Huntington's disease[7] and cystic fibrosis,[8] have provided an important paradigm for discussion of the complexity of the ethical, legal, and social issues of genetic testing. These issues include informed consent, counseling, medical confidentiality, discrimination, liability, and intellectual property rights.[9]

With the successful sequencing of the human genome in 2001,[10] however, the focus of genetics research has changed dramatically. Previously, research and clinical practice focused primarily on single gene disorders that were devastating but rare. In the United States, for example, Huntington's disease[11] and cystic fibrosis[12] each affect 10 per 100,000 people or about 30,000 people. But the diseases that have the greatest impact on our society's morbidity and mortality are not the rare, single gene diseases, but the much more challenging, complex, common diseases–diseases such as Alzheimer's, asthma, coronary heart disease, diabetes, and psychiatric illnesses. Consequently, major efforts are

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5 LORI B. ANDREWS, THE CLONE AGE: ADVENTURES IN THE NEW WORLD OF REPRODUCTIVE TECHNOLOGY 184 (2000).

6 A. Corisco & P. McGuffin, *Psychiatric Genetics: Recent Advances and Clinical Implications*, 10 EPIDMILOGOIA E PSICHIATRIA SOCIALE 253 (2001); *see also* Walter Neary, *Genetic Information and Patient Care*, U. WK., Feb. 28, 2002, *available at* http://depts.washington.edu/uweek/archives/2002.02.FEB_28/hs_a.html (last visited Jan. 16, 2003).

7 At any given time, about 25,000 Americans are suffering from Huntington's disease, but, at the same time, 150,000 others live knowing that they have a 50% chance of having inherited the gene and thus may develop the disease. *See* Peter Gorner, *Out of the Shadow a New Genetic Test Can Foretell Agonizing Death: Would You Take It?*, CHI. TRIB., Aug. 4, 1988, at C1.

8 Those who have one gene with a Cystic Fibrosis ("CF") mutation are unaffected carriers of the recessive disorder. If two carriers produce a child together, there is a 25% chance that the child will be affected with cystic fibrosis, a disorder of the exocrine glands that causes chronic obstructive lung disease. Office of Technology Assessment, HEALTHY CHILDREN: INVESTING IN THE FUTURE 263 (1988).

9 *See generally* ANDREWS, FUTURE, *supra* note 1.

10 Human International Genome Sequencing Consortium, *Initial Sequencing and Analysis of the Human Genome*, 409 NATURE 860 (2001); J. Craig Venter et al., *The Sequence of the Human Genome*, 291 SCI. 1304 (2001).

11 Hereditary Disease Foundation, *at* http://www.hdfoundation.org (last visited Jan. 16, 2003).

12 Cystic Fibrosis Foundation, About Cystic Fibrosis, What is CF, *at* http://www.cff.org.about_cf/what_is_cf.cfm?CFID=120046&CFTOKEN=2007255 (last visited Jan. 16, 2003).

under way to understand the genetic components of complex diseases with multiple potential influences.[13]

The focus of this Article is to explore whether the single gene disease paradigm has limitations when considering the much more challenging realm of multifactorial or common, complex diseases. The Article analyzes how complex genetic diseases differ from single gene diseases and how those differences may raise unique or additional ethical and policy considerations. Complex genetic diseases involve multiple genes or gene/environment interactions. Consequently, testing for them is less definitive than for single gene disorders, raising difficult issues for informed consent, counseling, and quality assurance. The intellectual property scheme that is presumed best for disorders involving a single gene may be inappropriate for disorders in which multiple genes (held by different patent holders) may each have a role.[14] Consequently, this Article concludes that, in many instances, research specifically focused on complex genetic disorders by psychologists, sociologists, anthropologists, and economists will be necessary to make viable policy choices.

II. RESEARCH IN COMPLEX GENETIC DISORDERS

The race is on, around the globe, to find specific factors that influence the occurrence of common, complex diseases. This endeavor is motivated by concerns about health and also by potential commercial gain due to the large number of people affected by such diseases. For example, sixty-two million Americans suffer from cardiovascular disease,[15] forty-four million from psychiatric illnesses,[16] sixteen million from diabetes,[17] nearly fifteen million from asthma,[18] and four million from Alzheimer's disease.[19]

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13 See for example, *infra* text accompanying notes 28-38 regarding the Icelandic studies.

14 For more information on gene patents and complex disorders, see Andrews, *Patent*, *supra* note 4, at 105-06.

15 American Heart Association, *2002 Heart and Stroke Statistical Update* 4 (citing National Health and Nutrition Examination Survey III, 1988-1994, Centers for Disease Control, National Center for Health Statistics, and the American Heart Association), *available at* http://www.americanheart.org/downloadable/heart/1014832809466101319099012 3HS_State_02.pdf (last visited Jan. 16, 2003).

16 NATIONAL INSTITUTE OF MENTAL HEALTH, THE NUMBERS COUNT: MENTAL DISORDERS IN AMERICA, NIH Publication No. 01-4584 (2001), *available at* http://www.nimh.nih.gov/publicat/numbers.cfm (last visited Jan. 16, 2003).

17 Jean Marx, *Unraveling the Causes of Diabetes*, 296 SCI. 686, 686 (2002).

In October 2002, the Center for Genetic Medicine at Northwestern University in Chicago announced plans for a large-scale gene bank. The center plans to recruit 100,000 participants over the next five years to learn more about common, complex genetic disorders.[20] The institution will begin its DNA database using 2000 blood samples from volunteers who are existing patients of the system who are at least eighteen years old and agree to allow ongoing access to their medical and billing records for as long as they are involved in the study.[21] After the blood is drawn, researchers will perform genetic tests on the samples, including whole genome scans, microsatellite analysis, SNP analysis, and DNA sequencing.[22] This information will be compared to each patient's medical records and answers to the questionnaire administered by genetic counselors.[23]

A similar effort is underway at the Marshfield Clinic in Wisconsin. The Marshfield Clinic operates forty-one health centers in the central/northern half of Wisconsin, serving some 400,000 patients from which it recruits participants for its Personalized Medicine Research Project.[24] The not-for-profit clinic has received $2.8 million in state and federal grants and pledged another $1 million itself for the first phase of this project.[25] The investigators plan to initially recruit 40,000

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18 NATIONAL INSTITUTES OF HEALTH: NATIONAL HEART, LUNG, AND BLOOD INSTITUTE, DATA FACT SHEET: *Asthma Statistics* (1999) [hereinafter *Asthma Statistics*], *available at* www.nhlbi.gov/health/prof/lung/asthmas/asthstat.pdf (last visited Jan. 16, 2003) .

19 Gerard Magill, *The Ethics Weave in Human Genomics, Embryonic Stem Cell Research, and Therapeutic Cloning: Promoting and Protecting Society's Interests*, 65 ALB. L. REV. 701, 707 (2002).

20 Peter Gorner, *DNA Donors Sought for NU Gene Bank; University to Use Data to Advance Medical Therapies*, CHI. TRIB., Nov. 3, 2002, at 1 [hereinafter Gorner, *DNA*]. The Mayo Clinic, Johns Hopkins University, and Duke University are reportedly in the process of starting a similar program to NUgene. Sarah Warning, *NU to Create 2nd U.S. Bank for Gene Code*, DAILY NORTHWESTERN ONLINE (Oct. 30, 2002), *at* http://www.dailynorthwestern.com/vnews/display.v/ART/2002/10/30/3dbf915cab03f (last visited Jan. 19, 2003); *see also* http://www.nugene.northwestern.edu (last visited Jan. 16, 2003).

21 Gorner, *DNA*, *supra* note 20.

22 Elizabeth Crown, *Northwestern Launches Gene Banking Project*, NORTHWESTERN UNIVERSITY NEWS RELEASE (Oct. 25, 2002), *available at* www.northwestern.edu/univ-relations/media_relations/releases/10_2002/nugene.html (last visited Jan. 19, 2003).

23 *Id.*

24 Peter Gorner, *Wisconsin Clinic to Form Huge Gene Bank; Researchers Seek Link to Disesases*, CHI. TRIB., Sept. 20, 2002, at 8; *see also* The Marshfield Clinic, A Legacy of Care, *at* http://www.marshfieldclinic.org/home/about (last visited Jan. 16, 2003).

25 Sharon Schmickle, *Wisconsin Clinic Fills Key Role in Genetic Research*, STAR TRIB. (Minneapolis), Sept. 20, 2002, at 1B.

participants.[26] The goal of the project is to use genetic, medical, and environmental information to find genes responsible for common, complex diseases, such as asthma, diabetes, hypertension, and cancer, and to determine whether a patient's genes will predict a response to certain drugs, in order to improve drug efficacy but avoid adverse reactions.[27]

The U.S. efforts are based on the landmark Iceland project, instituted by deCODE Genetics, to use a large set of DNA samples to identify genetic factors implicated in complex diseases. deCODE is a United States corporation founded by Kári Stefánsson of Iceland.[28] deCODE has created a national database using the medical records of Icelandic citizens to assist in the deciphering of genetic associations of disease risk and onset.[29] deCODE provides an important example of the tenuous relationship between commercial interests and scientific research.[30]

After much public debate, deCODE was granted permission, through the democratic process, to use the medical information of all of Iceland's citizens. This database has come to pass, but not without dissent among some of the citizens.[31] Instead of obtaining informed consent, deCODE used an opt-out procedure, or, more accurately, a "consent by default method."[32] The opt-out method is in direct conflict with informed consent because it assumes that all citizens are aware of the research and fully informed of the situation and have actively made a decision to opt-out.[33] However, not all people will be properly informed, and children and incompetent adults cannot participate in this option.[34] This is a troubling precedent because the opt-out method puts the onus

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26 *Id.*

27 *See* Marshfield Medical Research Foundation, Frequently Asked Questions, *at* http://www.mfldclin.edu/pmrp/prmp_faq.asp (last visited Jan. 16, 2003) (answering the question, "Why is this research being done?").

28 deCODE Genetics, Management, *at* http://www.decode.com (last visited Jan. 16, 2003).

29 *Id.*

30 *Id.*

31 George J. Annas, *Rules for Research on Human Genetic Variation–Lessons Learned from Iceland*, 342 NEW ENG. J. MED. 1830 (2000) [hereinafter Annas, *Rules*].

32 *Id.* at 1830-31.

33 *Id.* at 1831.

34 *Id.*

of informed consent on the people, in this case the research subjects, rather than deCODE or the for-profit research company.[35]

The company takes its genealogy database to determine which of its more than 65,000[36] patients (representing a third of Iceland's adult population) are affected by a particular disease, then applies computerized genotyping and other datamining procedures to identify small genetic regions that are shared by patients who are related. The company then uses this information to isolate disease genes and further study their function and interaction.[37] The company's model is to use its genetic discoveries and to partner with other companies to develop new diagnostic tests, as well as new treatments.[38]

Using what the company calls its "population genetics approach," deCODE claims to have mapped more than twenty genes involved in common diseases and isolated seven of them, including cerebrovascular disease (stroke), myocardial infarction, peripheral arterial occlusive disease, schizophrenia, non-insulin-dependent diabetes, osteoarthritis, and osteoporosis.[39] In deCODE's quest to discover and then patent a

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[35] *Id.* Despite a public relations effort on the part of deCODE, it has been reported that more than 18,000 Icelanders, slightly over 10% of the population, have opted out of the research project. *Id.*

[36] Nicholas Wade, *A Genomic Treasure Hunt May Be Striking Gold*, N.Y. TIMES, June 18, 2002, at F1.

[37] deCODE examines each patient's DNA at 1000 sites, which costs an estimated fifty cents per analysis. *Id.* deCODE also recently published data that improved upon the most recent maps of the human genome, based on a study of 146 Icelandic families that took genetic information from 869 parents and their children, which resulted in 5136 polymorphic microsatellite markers. James L. Weber, *The Iceland Map*, 31 NATURE GENETICS 225 (2002); *see also* Augustine Kong et al., *A High-Resolution Recombination Map of the Human Genome*, 31 *Id.* 241 (2002). Weber characterizes deCODE's improvement as "about five times the resolution of previous maps" and notes that the best previous map was based on genotyping of approximately 8000 short tandem-repeat polymorphisms in eight, three generation families from France. Weber, *supra*. However, he points out that the Iceland map did not type the grandparents of the families studied, making it more difficult to assign alleles than the study based on French families. *Id.* deCODE also apparently plans to make this map freely available to the public.

[38] For a description of deCODE's partnerships, see deCODE Genetics, Partners, *at* http://www.decode.com (last visited Jan. 16, 2003). The list includes Affymetrix, Applied Biosystems, Genmab, Merck, Pharmacia, Roche, Roche Diagnostics, and Wyeth. De CODE Genetics, Partners, *at* http://www.decode.com (last visited Jan. 16, 2003).

[39] deCODE Genetics, The deCODE Population Approach, Disease Projects, *at* http://www.decode.com (last visited Jan. 16, 2003). The list of mapped genes on the website includes, among others, psoriasis, rheumatoid arthritis, asthma, hypertension, Alzheimer's disease, multiple sclerosis, Parkinson's disease, and obesity. *Id.* Of these, the company has either been issued or has filed a patent application for three genes involved in

gene associated with schizophrenia, for example, 260 affected individuals and 334 of their relatives were originally genotyped.[40]

Although deCODE claims to have found genes responsible for a given complex genetic disorder, such as schizophrenia, what the researchers really discovered is a link showing that, if someone has the Neuregulin 1 gene, for example, he or she is twice as likely than average to develop schizophrenia, rather than a more straightforward correlation that would be found in single gene disorders like Huntington's.[41]

The research on common, complex disorders undertaken using a vast body of DNA samples raises issues with respect to informed consent, confidentiality, and discrimination that are similar to that of research on single gene disorders.[42] But it also raises unique concerns because the complex disease studies affect a larger number of people, are less focused, require the compilation of a larger set of private data about each individual, and raise greater concerns about informed consent.[43] The common, complex disease studies are likely to lead to more "surprises" for participants and have greater risks.

The need to obtain informed consent for genetic research is widely recognized.[44] Participants in research involving a single gene disorder (such as Huntington's disease, cystic fibrosis, or breast cancer) generally know what gene is either being sought or analyzed. People with Huntington's disease and their relatives participate in studies of the Huntington's disease gene. Even presumably healthy individuals in the control group know what disease is being studied.

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complex genetic disorders. *See, e.g., Human Narcolepsy Gene*, U.S. Patent No. 6,410,712 (issued June 25, 2002) & U.S. Patent No. 6,319,710 (issued Nov. 20, 2001); *Human Osteoporosis Gene*, U.S. Patent App. No. 20,020,072,066 (June 13, 2002); *Human Schizophrenia Gene*, U.S. Patent App. No. 20,020,165,144 (Nov. 7, 2002).

40 *Human Schizophrenia Gene*, U.S. Patent App. No. 20,020,165,144 (Nov. 7, 2002).

41 Nicholas Wade, *Gene-Mappers Take New Aim at Disease*, N.Y. TIMES, Oct. 30, 2002, at A23; *see also* Hreinn Stefansson et al., *Neuregulin 1 and Susceptibility to Schizophrenia*, 71 AM. J. HUM. GENETICS 877 (2002). Another group of researchers at Virginia Commonwealth University in Richmond who studied mental patients in Ireland found another possible gene associated with schizophrenia on the 6th chromosome called dysbindin.

42 Henry T. Greely, *Breaking the Stalemate: A Prospective Regulatory Framework for Unforeseen Research of Human Tissue Samples and Health Information*, 34 WAKE FOREST L. REV. 737, 740-42 (1999); Monique K. Mansoura, *Medical Implications and the Genetic Revolution*, 1 J. HEALTH CARE L. & POL'Y 329, 344-45 (1998).

43 Greeley, *supra* note 42, at 740-42; Mansoura, *supra* note 42, at 344-45.

44 *See, e.g.*, American Society of Human Genetics, *ASHG Report: Statement on Informed Consent for Genetic Research*, 59 AM. J. HUM. GENETICS 471 (1996).

In contrast, participants in the large-scale DNA bank studies of common, complex diseases are not part of an effort related to a single disease. Their DNA might be analyzed to find genetic mutations for any number of complex diseases, behaviors, or receptiveness to pharmaceuticals. Indeed, a participant's DNA might be used for studies that the participant might not approve of–or studies that would ultimately disadvantage him or her, either individually or as a member of a group.[45] For that reason, some commentators have argued that it contravenes the basic principles of informed consent to ask a person to provide a blanket waiver for research on their DNA.[46] At the very least, thought needs to be given to the construction of consent forms so that people can determine whether to reject certain types of research on their DNA, such as behavioral research or research that will lead to commercialization such as gene patenting.[47]

Informing participants about the categories of research that could conceivably be undertaken on their DNA is especially important when, as in the Northwestern study, patients are given the opportunity to "opt-in," giving researchers permission to look up their code number to identify and notify them if any strong correlations to a disease are found.[48] A participant might be horrified to be notified that he or she has a genetic mutation linked to an untreatable disease. As with the

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[45] "Genotyping that is appropriate to pharmacogenomic research might not produce information regarding susceptibility to disease or early death, but it might reveal evidence of genetic variation that could lead to individuals being classified as 'difficult to treat,' 'less profitable to treat,' or 'more expensive to treat.'" Mark A. Rothstein & Phyllis Griffin Epps, *Ethical and Legal Implications of Pharmacogenomics*, 2 NATURE REVIEWS GENETICS 228, 229 (2001). The "more expensive to treat" individuals might be discriminated against by insurers. *Id.*

[46] George J. Annas, *Privacy Rules for DNA Databanks: Protecting Coded 'Future Diaries,'* 270 JAMA 2346, 2349 (1993). Annas suggests that there should be rules in place protecting individual privacy in medical research that utilizes DNA databanks. *Id.* Specifically, he offers that there should be "no waivers or boilerplate statements that permit other uses" of the DNA samples. *Id.*; *see also* Richard R. Sharp, *The Evolution of Predictive Genetic Testing: Deciphering Gene-Environment Interactions*, 41 JURIMETRICS J. 145, 162 (2001).

[47] Participants in genetics research who later learn that their disease gene has been patented without their consent sometimes have expressed dismay at the fact that gene patents allow the holder to charge an excessive fee for testing. Some participants have filed suit on grounds of breach of fiduciary duty, lack of informed consent, conversion, and fraudulent concealment when the potential for commercialization was not disclosed to them. Greenberg v. Miami Children's Hosp. Research Inst., Inc., 208 F. Supp. 2d 918 (N.D. Ill. 2002), transferred to the United States District Court for the Southern District of Florida, Case No. 02-22244-CIV-MORENO; *see also* LORI ANDREWS & DOROTHY NELKIN, BODY BAZAAR: THE MARKET FOR HUMAN TISSUE IN THE BIOTECHNOLOGY AGE 51-52 (2001).

[48] Crown, *supra* note 22.

informed consent to participate, the informed consent to contact needs to be nuanced to assure participants will be able to exercise a true choice about whether, or to what extent, they want to participate in the study.

Even when informed consent to research on a specific complex disorder is gained, information may be generated that is unexpected. Patients seeking testing for one specific complex disease–for example, coronary heart disease–may find in the process that they are at increased risk for another complex disease about which they were not inquiring. The presence of a variant of the apolipoprotein E (ApoE) allele is a marker for coronary heart disease, but the ApoE4 variant is also a marker for Alzheimer's disease.[49] Yet, a person might have consented to participate in research or a clinical test for coronary heart disease because of a belief that he could change his behavior in some way to minimize the risk. He might be devastated to learn that the test result also signals a new risk–that of Alzheimer's disease, which gives him information he may not have wanted. Alzheimer's is not treatable, and the person tested might be psychologically harmed. Each time he forgets something, he may worry that he is exhibiting the initial stages of Alzheimer's.

Because the research protocols for DNA are so different than for most other previous research to date, the consent process itself presents scientists with a challenging dilemma. Providing medical records to be used for research without individual consent is already a common practice,[50] yet medical records are distinctly different from DNA in that they reveal a person's past.[51] The contents of medical records are a known entity, and if confidentiality is protected, there is no harm in looking for whatever is medically relevant to the research protocol, in effect giving a blanket informed consent.[52] DNA, however, is an unknown entity, with the potential to reveal untold bits of information about individuals and their families. Further, DNA can be replicated

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49 AMERICAN HEART ASSOCIATION, UNEXPECTED CONSEQUENCES: WHEN ONE GENETIC MARKER IMPLICATES MORE THAN ONE DISEASE–CASE STUDY: NO 2 (1997), *available at* http://www.pbs.org/gene/images/pdf/drader.pdf (last visited Jan. 16, 2003); *see also* Gina Kolata, *If Tests Hint Alzheimer's, Should a Patient Be Told?*, N.Y. TIMES, Oct. 24, 1995, at 1A.

50 George J. Annas, *The Limits of State Laws to Protect Genetic Information*, 345 NEW ENG. J. MED. 385, 387 (2001) [hereinafter Annas, *Limits*].

51 Annas, *Rules*, *supra* note 31, at 1832.

52 *Id.*

indefinitely,[53] and because of the nature of the field of genomics research, scientists may design research protocols that were not known to the individual subject at the time they consented to the use of their DNA.

Because of the newness of genomics and the seemingly infinite realms of potential discovery and applicability to disease diagnosis and treatment, pharmacogenetics, and even reprogenetics, the research is rapidly evolving.[54] The research being conducted today is helping to answer the questions that scientists have today. Many people, including scientists, could not have predicted the pace of genetic discovery over the last ten years. Therefore, information that is being stored in large databases today and for which research subjects provide their consent is useful to scientists in regards to the questions they are asking today. However, some of the information and samples obtained may become even more useful to scientists in the future as the field of genomics continues to develop. If an individual consents to research today, and the scientists are not even aware of the possibilities for future research because so little is known today about complex disease, how can the research subject provide informed consent?[55]

All genetics research also raises concerns about confidentiality, privacy, and potential discrimination. A participant in a colon cancer gene study, for example, lost his health insurance as a result.[56] The nature of research on common, complex disorders makes the potential breach of confidentiality both more likely and more risky. In the usual research for a single gene disorder, participants are members of families at higher risk for the disorder. They already run the risk of discrimination based on family history, whether or not information leaks out about their own particular gene status. Moreover, limited personal information is collected about each individual. The researcher wants to know which participants in the study already show symptoms of the particular disease.

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53 *Id.*

54 Lee M. Silver, *How Reprogenetics Will Transform the American Family*, 27 HOFSTRA L. REV. 649, 650-51 (1999). Pharmacogenetics and reprogenetics are the processes by which the genetic technologies are combined with the field of pharmacology and reproductive technologies respectively. *Id.* at 651.

55 Tom Wilkie, *Genetics: Scientific Promise and Social Concern*, 11 CONSUMER POL'Y REV. 126, 130 (2001).

56 Lori Andrews, *Body Science*, 83 A.B.A. J. 44, 47 (April 1997).

In contrast, in the studies of common, complex disorders, the entire medical record and family genealogy is often linked to the sample. Genetic analysis might be undertaken for a disorder for which the individual is not even aware that he or she is at risk. Even though the DNA samples may be "anonymized,"[57] it may be difficult or even impossible to anonymize a medical record or a genealogy. The deCODE approach links patients who may not have known they were related.[58] Even though the information in the deCODE database is encrypted, it is possible for leaks to occur that could have devastating effects on individuals and their families, which could be exacerbated by the tiny size of the island nation, where everyone seems to know one another.[59] What if, for example, a man discovers that the person he always thought was his grandfather is not even related to him because his grandmother had an affair? Or could an Icelander lose her job because someone told her employer that she carries genes predisposing her to schizophrenia?

III. CLINICAL IMPLICATIONS

The first chromosomal and genetic tests that were offered clinically tended to be for disorders such as Down Syndrome or Huntington's disease, where the prediction made from the test is quite deterministic. An extra chromosome 21 in a fetus means the resulting child will have Down Syndrome, although the exact characteristics of the disease (such as the level of mental impairment) cannot be predicted in advance. With Huntington's disease testing, a mutation in the gene indicates that the person will almost invariably suffer from Huntington's disease, a debilitating, untreatable genetic disorder, even though the age of onset cannot specifically be predicted.

As additional gene mutations linked to diseases have been identified, the nature of prediction has changed. A mutation in a breast cancer gene, for example, does not predict future disease with the same level of certainly as, for example, the Huntington's disease test. For

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57 American Society of Human Genetics, *supra* note 44, at 471 (discussing the collection of anonymous samples as "anonymized"). In the deCODE studies and the Northwestern studies, the samples are "anoymized," but in the Northwestern study, participants can agree to be identified in order to be informed of research results that may have a "significant impact" on their healthcare. Rex Chisholm, Principal Investigator, *NUgene: Gene-Disease Associations and Treatment Outcomes,* Consent Form, p. 4, Northwestern University Center for Genetic Medicine, Sept. 18, 2002 (form on file with the Law Review).

58 Wade, *supra* note 36.

59 Laurie Garrett, *The Biological Revolution Raises Many Questions: Not Just About What Science Can Do, But What It Should Do,* NEWSDAY, Dec. 12, 1999, at A19.

women with the 185delAG mutation, the risk of developing breast cancer is approximately 50%.[60]

Genetic tests for common, complex disorders such as heart disease and asthma are likely to have even lower predictive values.[61] The test of a particular mutation for a complex genetic disease may shift the odds that an individual will develop a disease by only a few percentage points. This raises questions about what types of counseling will be appropriate, what types of actions people will take based on the test results, and what types of judgments social institutions will make about people based on genetic tests related to complex disorders. More importantly, it raises a question of how the ethical principles developed in the context of testing for rare genetic disorders may need to be re-assessed when more common, complex disorders are involved. Indeed, genetic research upon and testing for common, complex disorders raise fundamental questions of what should be considered a "genetic" disorder in the first place-and what the psychological, social, ethical, and legal implications are of labeling a common condition like heart disease as "genetic."

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[60] Bernadine Healy, *BRCA Genes-Bookmaking, Fortunetelling, and Medical Care*, 336 NEW ENG. J. MED. 1448, 1448 (1997).

[61] A large number of recent medical journal articles address the genetics of complex disorders. *See, e.g.*, B.E. Aouizerat et al., *Novel Genes for Familial Combined Hyperlipidemia*, 10 CURRENT OPINION LIPIDOLOGY 113 (1999); Eugene R. Bleecker et al., *Genetic Susceptibility to Asthma in a Changing Environment*, 206 CIBA FOUND. SYMP. 90 (1997); Larry Borish, *Genetics of Allergy and Asthma*, 82 ANNALS ALLERGY ASTHMA & IMMUNOLOGY 413 (1999); N. Craddock et al., *Increasing the Efficiency of Genomic Searches for Linkage in Complex Disorders by DNA Pooling of Affected Sib-Pairs*, 1 MOLECULAR PSYCHIATRY 59 (1996); Abhilash Desai & George Grossberg, *Risk Factors and Protective Factors for Alzheimer's Disease*, 7 CLINICAL GERIATRICS (1999), *available at* http://www.mmhc.com/cg/articles/CG9910/grossberg.html (last visited Mar. 3, 2003); Michael B. Gorin et al., *The Genetics of Age-Related Macular Degeneration*, 5 MOLECULAR VISION 29 (1999); John Hardy, *The Genetic Causes of Neurodegenerative Diseases*, 3 J. ALZHEIMER'S DISEASE 109 (2001); Peter Holmans & Nick Craddock, *Efficient Strategies for Genome Scanning Using Maximum-Likelihood Affected-Sib-Pair Analysis*, 60 AM. J. HUM. GENETICS 657 (1997); Karen Huss & Richard W. Huss, *Genetics of Asthma and Allergies*, 35 NURSING CLINICS N. AM. 695 (2000); Bobby P.C. Koeleman et al., *Familial Thrombophilia: A Complex Genetic Disorder*, 34 SEMINARS HEMATOLOGY 256 (1997); Esther E. Kors et al., *Genetics of Primary Headaches*, 12 CURRENT OPINION NEUROLOGY 249 (1999); F.R. Lashley, *Genetic Testing, Screening, and Counseling Issues in Cardiovascular Disease*, 13 J. CARDIOVASCULAR NURSING 110 (July 1999); Conxi Lázaro et al., *Missense Mutations in the Cystic Fibrosis Gene in Adult Patients with Asthma*, 14 HUMAN MUTATION 510 (1999); H. Los et al., *The Importance of Genetic Influences in Asthma*, 14 EUR. RESPIRATORY J. 1210 (1999); Cees Mulder et al., *Genetic and Biochemical Markers for Alzheimer's Disease: Recent Developments*, 37 ANNALS CLINICAL BIOCHEMISTRY 593, 594 (2000); Stefansson et al., *supra* note 41; Paul Van Eerdewegh et al., *Association of the ADAM33 Gene with Asthma and Bronchial Hyperresponsiveness*, 418 NATURE 426 (2002).

Single gene diseases are those diseases which are caused by a mutant allele of a single gene.[62] Single gene diseases are classified as either dominant or recessive, where alleles that are inherited from one or both parents respectively are responsible for the onset of the disease.[63] With some single gene diseases, such as Huntington's disease, a mutation in the relevant single gene is almost invariably expressed in the phenotype of that individual.

Complex diseases, however, are vastly different because the mutation for the disease may be present in a person's genotype-for example, the mutation in the gene that is linked to late-onset Alzheimer's disease-but that does not necessarily mean that it will be expressed in one's phenotype.[64] Polygenic disorders, or complex genetic disease, are the result of the combined action of alleles of more than one gene, often in combination with environmental or lifestyle factors.[65] Complex genetic disease are those disorders "[t]hat have a genetic predisposition due to more than one gene that may produce illness independently in different families, or acting together to cause illness in all susceptible individuals."[66] In short, complex genetic diseases "cannot be ascribed to mutations in a single gene or to a single environmental factor. Rather they arise from the combined action of many genes, environmental factors, and risk-conferring behaviors."[67] Determining how the various contributing factors interact and influence disease onset is one of the greatest challenges to biomedical researchers today.[68]

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62 Genome Glossary, Human Genome Project Information, United States Department of Energy, *at* http://www.ornl.gov/TechResources/Human_Genome/glossary/glossary_s.html (last visited Jan. 16, 2003); *see also* Paula Kiberstis & Leslie Roberts, *It's Not Just the Genes*, 296 SCI. 685, 685 (2002).

63 M.J. Khoury & W.D. Flanders, *On the Measurement of Susceptibility to Genetic Factors*, 6 GENETIC EPIDEMIOLOGY 699, 702 (1989); *see also* Jerry Elmer, *Human Genomics: Toward a New Paradigm for Equal-Protection Jurisprudence, Part I*, 50 R.I. B.J. 5, 26 (March/April 2002) [hereinafter Elmer, *Part I*].

64 Hardy, *supra* note 61, at 109. Late onset Alzheimer's disease is to be distinguished from autosomal dominant Alzheimer's, or early onset Alzheimer's disease, which has three known genes associated with the disease, and the presence of at least one of the three is sufficient for definitive diagnosis. *Id.* at 109-13.

65 Genome Glossary, Human Genome Project Information, United States Department of Energy, *at* http://www.ornl.gov/TechResources/Human_Genome/glossary/glossary_p.html (last visited Jan. 16, 2003).

66 Sarah H. Shaw et al., *A Genome-Wide Search for Schizophrenia Susceptibility Genes*, 81 AM. J. MED. GENETICS 364, 364 (1998).

67 Kiberstis & Roberts, *supra* note 62.

68 *Id.*

Genetic tests for both single gene disorders and complex genetic disorders are defined according to their penetrance. Penetrance is the measure used to determine the relationship between genotype, a person's set of genes,[69] and phenotype,[70] the physical characteristics of the individual.[71] When a genetic disorder is completely penetrant, 100% of the individuals with the genetic mutation will develop the disease.[72] Few diseases are completely penetrant, but instead have a range of penetrance; many factors determine the disease penetrance, including environmental influences, the gene's protein product, and the influence of other genes.[73] Therefore, the test results that attempt to convey penetrance are difficult to interpret for less penetrant, single gene disease and even more challenging with complex disease given the known multiplicity of other factors involved in disease development.

Despite the limitations, genetic tests are widely used, and, to date, some 900 genetic tests are available within the clinical setting, 450 of which physicians can routinely order.[74] The categories of tests include those that are predictive of disease,[75] prognostic,[76] probabilistic,[77] and prophylactic.[78] Predictive and prognostic tests involve highly penetrant alleles but differ in regards to the treatment options. For example, a test for phenylketonuria (PKU), a single gene disorder, is a highly penetrant, predictive test, and therapy is available to alter the manifestation of the

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69 JOANNE L. HUSTEAD ET AL., CALIFORNIA HEALTH CARE FOUNDATION, GENETICS AND PRIVACY: A PATCHWORK OF PROTECTIONS, IHEALTH REPORTS 8 (April 2002), *available at* http://www.chcf.org/documents/ihealth/GeneticsAndPrivacy.pdf (last visited Jan. 16, 2003).

70 A phenotype is the detectable characteristics associated with a particular genotype (an individual's genetic makeup underlying a specific trait or constellation of traits). DAVID SUZUKI & PETER KNUDTSON, GENETHICS: THE CLASH BETWEEN THE NEW GENETICS AND HUMAN VALUES 355, 358 (rev. ed. 1990).

71 HUSTEAD ET AL., *supra* note 69, at 8, 30.

72 Fiona Miller et al., Ontario Ministry of Health and Long Term Care, PREDICTIVE GENETIC TESTS AND HEALTH CARE COSTS: FINAL REPORT PREPARED FOR THE ONTARIO MINISTRY OF HEALTH AND LONG TERM CARE ii (Jan. 10, 2002), *available at* http://www.gov.on.ca/health/english/pub/ministry/geneticsrep02/chepa_rep.pdf (last visited Jan. 16, 2003).

73 HUSTEAD ET AL., *supra* note 69, at 30.

74 Howard Bell, *Gene Generation: Is Genetic Testing the Ultimate Diagnostic Tool, or a Hazy Crystal Ball at Best?*, PHYSICIAN'S WKLY., Feb. 25, 2002, http://www.physweekly.com/article.asp?issueid=9&articleid=16 (last visited Jan. 16, 2003).

75 Eric T. Juengst, *The Ethics of Prediction: Genetic Risk and the Physician-Patient Relationship*, 1 GENOME SCI. & TECH. 21 (1995).

76 *Id.*

77 *Id.*

78 *Id.*

genetic mutation.[79] The genetic test for Huntington's disease, also a single gene disorder, is prognostic, and there are no available therapeutic measures to alter the unavoidable health outcomes associated with the disease.[80] Probabilistic and prophylactic tests involve less penetrant alleles and reveal a statistically increased risk of disease; they also differ in respect to treatment options.[81] Even with highly penetrant single gene diseases, however, unknowns remain after diagnosis, such as when and to what degree the disease will manifest in the individual.[82]

The degree of penetrance is significantly less for many complex genetic disorders. Therefore, unlike genetic testing for some single gene diseases, genetic testing for complex genetic disease can only provide a probability, or a statistically informed estimate, of one person's chance for developing the disease. The genetic tests currently available for complex genetic diseases offer only the limited knowledge that the presence of a particular gene mutation is a predisposing factor for the development of the disease in question, but the results cannot be presented with as much certainty as they are with some single gene diseases.[83] Scientists simply do not know with certainty what causes the complex, common diseases because, as their name implies, multifactorial diseases are the result of an intricate web of causality between environment and genetic factors.[84] Such is the case of the presence of the ApoE4 allele, which is associated with an increased risk of Alzheimer's disease.[85] The genetic test available today for ApoE4 cannot provide an estimation of absolute risk because that risk varies by age, gender, exposure to toxins, and previous head injury.[86] The genetic test for complex disease is not a diagnostic tool, but rather an imprecise measurement of increased risk when compared to the general population.[87] As a result of this uncertainty, the informed consent issues which arise in the arena of genetic testing for multifactorial disease differ

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79 *Id.*

80 *Id.*

81 Sharp, *supra* note 46, at 160.

82 Dawna M. Gilchrist, *Medical Genetics: 3. An Approach to the Adult with a Genetic Disorder*, 167 CMAJ 1021, 1023 (2002), *available at* http://www.cmaj.ca/cgi/content/abstract/167/9/1021 (last visited May 21, 2003).

83 Elmer, *Part I*, *supra* note 63, at 26.

84 *Id.*; *see also* Kiberstis & Roberts, *supra* note 62.

85 Jeffrey Kahn, *Ethical Issues in Genetic Testing for Alzheimer's Disease*, 52 GERIATRICS S30, S30 (1997).

86 *Id.*

87 Elmer, *Part I*, *supra* note 63, at 26.

in their complexity and depth from those confronted in the arena of single gene disease.

Informed consent has been an important tenet of medicine for nearly half a century.[88] In the realm of genetic testing for single gene diseases, informed consent has been-and continues to be-of paramount importance. From the very early days of amniocentesis for chromosomal anomalies and single gene recessive disorders, liability has been found for failing to adequately inform patients about the existence of genetic testing and the results of genetic tests.[89] Today, the major medical organizations of geneticists have detailed requirements for informed consent in the contexts of research, diagnosis, and treatment.[90] In order to fully understand the implications of genetic testing, informed consent must involve full knowledge of the alternatives to and the risks, benefits, and effectiveness of testing.[91]

Testing for rare genetic disorders has been governed by a paradigm of extensive informed consent. In general, prenatal karyotyping, Huntington's disease testing, and breast cancer testing have been undertaken only after the patient has been counseled about the nature, risks, and benefits of the test, including nonmedical risks such as the potential for insurance discrimination. In contrast, nongenetic testing for common disorders-such as a chemistry profile undertaken on a blood sample-are routinely undertaken on patients' blood samples to assess risks of heart disease, kidney function problems, and liver function problems without advance counseling or specific consent. Now that DNA tests are available to provide predictive information about heart disease and other common disorders, will such tests follow the "genetic" disease model of enhanced consent, or will they follow the "nongenetic"

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88 *See, e.g.*, Salgo v. Leland Stanford Jr. Univ. Bd. of Trs., 317 P.2d 170 (Cal. Ct. App. 1957). For information about informed consent and genetics generally, see LORI B. ANDREWS, MEDICAL GENETICS: A LEGAL FRONTIER 105-34 (1987).

89 Andrews, *Torts*, *supra* note 3, at 164.

90 *See, e.g.*, CODE OF PROFESSIONAL ETHICS OF THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS (American College of Obstetricians and Gynecologists), *available at* http://www.acog.com/from_home/acoginfo.cfm (last visited Jan. 17, 2003); American Society of Human Genetics, *supra* note 44; American Society of Human Genetics, *DNA Banking and DNA Analysis: Points to Consider*, *at* http://www.faseb.org/genetics/ashg/pubs/policy/pol-02.htm (last visited Jane. 16, 2003); American College of Medical Genetics, *ACMG Statement: Statement on Storage and Use of Genetic Materials*, 57 AM. J. HUM. GENETICS 1499 (1995), *at* http://www.faseb.org/genetics/acmg/pol-17.htm (last visited Jan. 16, 2003).

91 American Society of Human Genetics, *supra* note 44.

model where specific consent is not sought but, instead, after the fact, the physician discloses to the patient any deviations from the norm? This question takes on increasing importance in an era where multiplex genetic testing is possible.[92] Already, physicians have said that they will not have time to inform people in advance of the nature of each of the diseases being tested for and the implications of the results of each of the tests.[93] Rather, they have indicated that they will test for a panoply of diseases and inform the person of the mutations they have. But some people may not want information about certain diseases-such as untreatable late-onset diseases.[94] There is considerable evidence that genetic information can cause anxiety to the individual tested[95] and to the individual's partner.[96] Adequately providing this information is consequently more challenging with respect to genetic testing for complex diseases.

One challenge to informed consent in the realm of complex genetic diseases is the issue of multiple diagnoses. Is the clinician ethically obliged to inform the patient, who underwent ApoE testing in the

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92 INSTITUTE OF MEDICINE, ASSESSING GENETIC RISKS: IMPLICATIONS FOR HEALTH AND SOCIAL POLICY 177-78 (Lori B. Andrews et al. eds., 1994) (discussing mutiplex testing).

93 *See Multiplex Genetic Testing*, 28 HASTINGS CENTER REP. 15 (July/August 1998).

94 Fewer than 15% of at-risk individuals decide to undergo genetic testing for Huntington's disease, for example. Maurice Bloch et al., *Predictive Testing for Huntington Disease: II. Demographic Characteristics, Life-Style Patterns, Attitudes, and Psychosocial Assessments of the First Fifty-One Test Candidates*, 32 AM. J. MED. GENETICS 217, 222 (1989); David Craufurd et al., *Uptake of Presymptomatic Predictive Testing for Huntington's Disease*, 2 LANCET 603, 604 (1989).

95 Hilary Bekker et al., *The Impact of Population Based Screening for Carriers of Cystic Fibrosis*, 31 J. MED. GENETICS 364, 365 (1994); Barton Childs et al., *Tay-Sachs Screening: Social and Psychological Impact*, 28 AM. J. HUM. GENETICS 550, 550 (1976); Robert T. Croyle et al., *Psychological Responses to BRCA1 Mutation Testing: Preliminary Findings*, 16 HEALTH PSYCHOL. 63, 69 (1997); A.C. DudokdeWit et al., *BRCA1 in the Family: A Case Description of the Psychological Implications*, 71 AM. J. MED. GENETICS 63, 64 (1997); Marlene Huggins et al., *Predictive Testing for Huntington Disease in Canada: Adverse Effects and Unexpected Results in Those Receiving a Decreased Risk*, 42 AM. J. MED. GENETICS 508, 508 (1992); Theresa M. Marteau, *Psychological Implications of Genetic Screening*, 28 BIRTH DEFECTS: ORIGINAL ARTICLE SERIES 185, 185 (1992) (stating that, although Tay-Sachs carriers viewed their current health status no differently than non-carriers, carriers' perception of future health and risk of illness was significantly more negative than non-carriers); Eila K. Watson et al., *Psychological and Social Consequences of Community Carrier Screening Programme for Cystic Fibrosis*, 340 LANCET 217, 218 (1992); Susan Zeesman et al., *A Private View of Heterozygotes: Eight-Year Follow-Up Study on Carriers of the Tay-Sachs Gene Detected by High School Screening in Montreal*, 18 AM. J. MED. GENETICS 769, 772 (1984).

96 Huggins et al., *supra* note 95, at 514; Aad Tibben et al., *Presymptomatic DNA Testing for Huntington Disease: Identifying the Need for Psychological Intervention*, 48 AM. J. MED. GENETICS 137, 141 (1993).

coronary context, that the same genetic pattern reveals a predisposition to Alzheimer's disease? The patient did not consent to the test for that purpose.

Genetic testing for common, complex disorders leads to challenges in counseling as well. These tests will present probabilistic information that may only slightly change the odds that an individual will manifest the particular disease. Yet, both physicians and patients have difficulty dealing with probabilistic information.[97]

Moreover, labeling a disorder "genetic" may create stigma and guilt for the individual who may be concerned with passing the gene on to his or her children.[98] Some women report feeling ashamed or freakish when they learn through prenatal testing that their fetus has a genetic disorder.[99] Other parents blame themselves for the disorder.[100] Being given a "genetic" diagnosis of heart disease or asthma may have a different impact than a nongenetic one because of the potential transmission of the genetic mutation to children.

The discovery of one's genotype through genetic testing has profound implications for individual self-esteem and self-perception.[101] Much research has been conducted about the psychological impacts of tests for single gene diseases.[102] The genetic information that is generated through the use of genetic technologies has an impact on people's emotional well-being and self-concept.[103] Individuals' carrier

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97 Francis Giardiello et al., *The Use and Interpretation of Commercial* APC *Gene Testing for Familial Adenomatous Polyposis*, 336 NEW ENG. J. MED. 823, 826 (1997); *see also* ANDREWS, FUTURE, *supra* note 1, at 109.

98 Dorothy C. Wertz, *How Parents of Affected Children View Selective Abortion*, *in* ISSUES IN REPRODUCTIVE TECHNOLOGY I: AN ANTHOLOGY 161, 176 (Helen Bequaert Holmes ed., 1992); Elena A. Gates, *The Impact of Prenatal Genetic Testing on Quality of Life in Women*, 8 FETAL DIAGNOSTIC THERAPY 236, 240 (Supp. I 1993); Rose Green, *Letter to a Genetic Counselor*, 1 J. GENETIC COUNSELING 55, 58 (1992).

99 Green, *supra* note 98, at 58.

100 Timothy S. Rooney, *Family Learns to Cope with Child's Fragile X Syndrome*, CHI. DAILY HERALD, Oct. 1, 1997, at 6.

101 Michele A. Carter, *Ethical Aspects of Genetic Testing*, 3 BIOLOGICAL RES. FOR NURSING 24, 26 (2001).

102 *Id.*

103 *See, e.g.*, M. Lipkin et al., *Genetic Counseling of Asymptomatic Carriers in a Primary Care Setting: The Effectiveness of Screening and Counseling for Beta-Thalassemia Trait*, 105 ANNALS OF INTERNAL MED. 115 (1986). There are also philosophical writings about how genetic technologies might change self-concept. *See, e.g.*, Dan W. Brock, *The Human Genome Project and Human Identity*, 29 HOUS. L. REV. 7, 20 (1992).

status for a recessive disorder will have no effect on their health, and, although they may understand that fact, carriers as a whole have more negative feelings about their future health than a member of the general population.[104] In an eight-year follow-up of individuals who had been screened for Tay-Sachs carrier status in high school, 46% recalled that they were upset at the time of their result.[105] Nineteen percent remained worried eight years later.[106]

Presymptomatic genetic testing for late-onset disorders can be even more problematic since the results may signal future health risks for an individual. In a preliminary study of BRCA1 testing for a predisposition for breast cancer, a substantial number of women with the mutation experienced psychological distress.[107] Learning that one has a BRCA1 or 2 mutation can create a schism between a woman and her body. After DNA testing revealed she had a BRCA1 mutation, one woman said: "It felt as if there was a time bomb ticking away inside me."[108]

Genetic information also affects relationships with spouses and potential spouses. Men are more likely than women to say they would alter marriage plans if they learned that their fiancé was the carrier of a recessive genetic disorder. Eight years after having participated in Tay-Sachs testing, 95% of female carriers responded that they would not alter marriage plans upon discovering their partner or intended partner was also a carrier.[109] In contrast, only 69% of male carriers responded definitively that they would not alter marriage plans if their intended spouse was also a carrier.[110] Another study of Tay-Sachs testing found 25% of carriers and 6% of carriers' spouses felt that knowing their own or their spouse's carrier status would have affected their marriage decision.[111]

Short of breaking up, couples' relationships might be strained in other ways due to genetic knowledge. People who learned they were likely to suffer from Huntington's disease experienced a significant

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104 Marteau, *supra* note 95, at 185.

105 Zeesman et al., *supra* note 95, at 772.

106 *Id.*

107 Croyle et al., *supra* note 95.

108 Jo Revill, *Why I Had a Mastectomy Before Cancer Was Diagnosed*, EVENING STANDARD (London), Dec. 1, 1993, at 12.

109 Zeesman et al., *supra* note 95, at 773.

110 *Id.*

111 Childs et al., *supra* note 95, at 552.

decline in their satisfaction with their primary relationship during the two-year follow-up period after receiving test results.[112] Follow-up of twenty-one couples who had gone through Huntington's disease testing found that six had divorced, with three specifically attributing their divorces to the testing.[113]

Nor does knowing one's risk prior to onset necessarily make an individual more able to cope with the disease once it manifests itself. A study found that carriers who coped with the initial results of Huntington's disease testing became depressed, suicidal, or showed disturbed functioning once they manifested symptoms.[114]

The psychological risks of genetic tests could be magnified in the arena of common, complex diseases. Knowing the presence of one "defective" gene can lead a person into severe depression, but the knowledge of several "defective" genes without a clear sense of their meaning and implication for future disease has the potential for devastating results. Genetic knowledge, despite its nuances and inaccuracies, can alter people's ideas of self-efficacy, esteem, personal locus of control, and even risk-taking behaviors.[115]

But the opposite may also be equally true–knowledge of the risk of complex genetic disorders might be less psychologically troubling to the individual than knowledge of a single gene recessive disorder. The information may be less definitive, indicating, say, a 20% increased risk over the general population rather than an 80% risk. Moreover, unlike rare recessive disorders, such as Canavan disease, where genetic testing (or the birth of a child with the disease) may reveal the existence of a mutation that a person had no idea that he or she carried, genetic testing for complex disorders probably will focus on known family diseases about which the person already feels at risk (such as heart disease). In addition, there may be something less frightening to a person about learning that she carries the mutation for a common disease, widely

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[112] Tobin Copley et al., *Significant Changes in Social Relations After Predictive Testing (PT) for Huntington Disease*, 55 AM. J. HUM. GENETICS A291 (#1707) (1994); Kimberly A. Quaid & Melissa K. Wesson, *The Effects of Predictive Testing for Huntington Disease on Intimate Relationships*, 55 AM. J. HUM. GENETICS A294 (#1728) (1994).

[113] ANDREWS, FUTURE, *supra* note 1, at 54 (citing L.B. Jakobsen et al., *Psychological Consequences of Presymptomatic Genetic Testing*, 119 TIDSSKR NOR LAEGENFOREN 1913 (1999)).

[114] Tibben et al., *supra* note 96, at 143.

[115] Carter, *supra* note 101, at 26.

discussed in the population, than a rare recessive disease with a tongue-twisting name that she has never heard of before.

According to Maren Scheuner, of the University of California, Los Angeles, School of Medicine and director of GenRISK at the Cedars-Sinai Medical Center, "Genetic information can help improve disease management by clarifying diagnosis, improving the prognosis, and helping to identify individualized treatments."[116] This is a common sentiment among those with a financial incentive in the genetics field, but despite the optimism of many geneticists, the preliminary results are sketchy at best.[117]

In the future, genetic tests for predisposition to heart disease, for example, may be used in conjunction with efforts to influence people to change their diet or exercise more. Questions will arise as to whether such personalized public health interventions are appropriate or even whether they are effective.

Health care professionals have already begun to integrate testing for single gene disorders into programs to attempt to change people's behavior, such as to encourage people to stop smoking.[118] The rationale was that people who knew they had a genetic predisposition to lung cancer would be more likely to quit smoking than would a smoker with no evidence of a personalized risk.

Despite the hypothesis that smokers who knew they had a higher risk for cancer based on genetic test results would be more inclined to quit smoking, the early data from smoking research shows no greater likelihood that smokers who were informed of their genetic cancer risk would quit smoking.[119] Preliminary research reveals that the genetic information provides no great motivation, but also does not undermine a person's desire to quit for those who are not genetically susceptible to smoking-related cancers.[120] Moreover, the genetically informed people

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116 M. J. Friedrich, *Genetic Screening to Offset Adult Disease*, 284 JAMA 2308, 2308 (2000).

117 Neil A. Holtzman, *Putting the Search in Perspective*, 31 INT'L J. HEALTH SERVS. 445 (2001).

118 Caryn Lerman et al., *Incorporating Biomarkers of Exposure and Genetic Susceptibility into Smoking Cessation Treatment: Effects on Smoking-Related Cognitions, Emotions, and Behavior Change*, 16 HEALTH PSYCHOL. 87, 96 (1997).

119 Amy Austell, *Understanding Genetic Cancer Risk Might Not Help Smokers Kick the Habit*, DUKE NEWS, July 5, 2002, http://www.dukemednews.duke.edu/news/article.php?id=5657 (last visited Jan. 27, 2003).

120 *Id.*

were more depressed and fearful. The researchers concluded that the use of genetic testing might backfire: "Distress could lead some smokers to deny or to underestimate their smoking problem, which would increase resistance to behavioral change. Distress could also promote smoking to achieve the mood-enhancing effects of nicotine."[121] Given the interplay between genetic factors, environmental influences, and risk-taking behaviors in the development of complex diseases, the belief that the knowledge of one's genetic information will lead to a more informed lifestyle and be an important catalyst for preventive medicine may be unrealistic.

Converting what previously seemed to be an externally mediated event (a complex disease) into one that appears to be caused internally (by someone's genes) may convert the situation into one where additional counseling and resources are necessary. Yet, "geneticizing" all of medicine creates resource demands that are untenable. There are not enough health care providers to apply the single gene model of counseling used with respect to Huntington's disease or even breast cancer to a series of complex disorders that not only affect greater numbers of people, but require vastly more complex messages. Complex genetic disorders have a greater band of uncertainty. Several genes and several environmental factors may be involved, and perhaps information about some of these will be available and others will not yet be understood. Think about the complicated series of alternative interactions that are possible, all of which might have to be disclosed. Add to that mix the fact that both physicians and patients have difficulty dealing with probabilistic information.[122] Entirely new means of providing information about complex genetic disorders may need to be developed, just as we needed to develop new computer capabilities to deal with vast quantities of genetic information before we could sequence the human genome.

The risk of misunderstanding and misuse of genetic information may be increased as genetic tests are marketed directly to consumers. Much like the pharmaceutical industry, biotech is already taking its message about genetic tests directly to the consumer, altering the dynamics of the doctor/patient relationship. Some individuals visit their doctor and request specific genetic tests based on a direct-to-consumer marketing approach rather than sound medical advice. Direct

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121 Lerman et al., *supra* note 118, at 96.

122 ANDREWS, FUTURE, *supra* note 1, at 109; Giardiello et al., *supra* note 97.

marketing may represent the benefits of the test without full disclosure of the risks.[123] Recent estimates project that the potential market for clinical genetic tests could grow to between $3 and $4 billion over the next few years.[124]

In September 2002, Myriad Genetics initiated a direct-to-consumer advertising campaign for breast and ovarian cancer genetic testing.[125] Recent trends in prophylactic mastectomy for women who test positive for the genetic mutation, but who are asymptomatic for disease, illustrate the power and potential misuse of genetic information. Dr. Susan Love is a staunch critic of the procedure, and she warns that our society will look back on the practice as a "barbaric response" for treating women.[126] Genetics are powerful, and the information that the genetic tests provide, with or without appropriate genetic counseling, will inevitably alter the way many people view themselves and view the world.[127] One study published in *The Journal of Clinical Oncology* found that, of women who underwent mastectomies, 27% in Minnesota and 15% in Massachusetts had never been told of other breast-conserving surgical options.[128] In order to ensure proper treatment, women must be fully informed of their options, the risks of surgery, and the meaning of the genetic tests.

The direct-to-consumer marketing approach could lead to an increase in medical costs and a misuse of the tests because people will demand genetic tests for all sorts of complex diseases, and doctors may provide them indiscriminately, without a thorough analysis of patients' risk based on lifestyle and family history. The challenge of complex disease is that so little is known to date. The current tests will only be useful to a small percentage of the population whose family history suggests a direct genetic link to a specific disease, for example, breast

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123 James Meek, *Public 'Misled by Genetest Hype,'* THE GUARDIAN, Mar. 12, 2002, at 9.

124 Scott Hensley, *Applera to Catalog Genetic Variations*, WALL ST. J., July 24, 2001, at B6.

125 *Myriad Launches Direct-to-Consumer Advertising Campaign for Breast Cancer Test*, WOMEN'S HEALTH WKLY., Oct. 24, 2002, at 14. The campaign is targeting Atlanta and Denver utilizing radio, print media, and television to inform women with a family history of cancer of the recent advances in prevention and early disease detection. *Id.*

126 Sally Jacobs, *Facing Down the Fear Genetic Test Showing High Risk of Cancer Spurs Some Women to Opt for Breast Removal Rather Than Live in Dread of the Disease*, BOSTON GLOBE, June 6, 2001, at D1.

127 *See generally id.*

128 Hilary Macht Felgran, *Mastectomies, Sometimes Unneeded, Prevail*, N.Y. TIMES, Jan. 23, 2001, at F1.

cancer.[129] If the tests are given to the general population without appropriate genetic counseling and information, the consequences of mainstreaming genetic testing could be catastrophic and include rising health care costs, increased anxiety, and discrimination. The information can be valuable, but the potential for misapplication is great. Genetic testing for breast cancer is useful, but with more than 200 mutations in the two BRCA genes,[130] deciphering the meaning of the test and determining exact levels of penetrance and disease risk is difficult. Prophylactic mastectomy should be used, if at all, for carefully screened groups of women who will most benefit from such an invasive therapy.[131] This example illustrates the possibilities that arise with the distribution of numerous genetic tests for complex diseases that may unduly influence people's lifestyle decisions before appropriate counseling by trained genetic counselors can be provided.

IV. LIABILITY AND GENETIC TESTING FOR COMMON, COMPLEX DISORDERS

When people seek genetic testing, genetic counseling, or other genetic information, health care providers have an obligation to provide the information in a high quality way.[132] When patients might benefit from genetic services, physicians have a legal obligation to offer them.[133] Medical malpractice cases have held health care providers liable for not informing patients they were in a high-risk group with respect to certain genetic risks[134] and for not performing genetic tests accurately.[135]

The rationale for finding physicians liable is that such liability deters low quality genetic services. However, the vast majority of these cases deal with single gene disorders such as Tay-Sachs disease[136] or chromosomal abnormalities such as Down Syndrome.[137] The courts in the cases involving malpractice liability in the genetic testing area have assumed that the test not offered or undertaken incorrectly was highly

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129 Theresa Agovino, *Advertising Genetic Tests*, MILWAUKEE J. SENTINEL, June 15, 2002, at 3D.

130 Healy, *supra* note 60, at 1448.

131 *Id.* at 1448-49.

132 *See generally* Andrews, *Torts*, *supra* note 3 (analyzing legal cases on the issue).

133 *See, e.g.*, Becker v. Schwartz, 386 N.E.2d 807 (N.Y. 1978); James G. v. Caserta, 332 S.E.2d 872 (W. Va. 1985).

134 Philips v. United States, 566 F. Supp. 1 (D.S.C. 1981); *James G.*, 332 S.E.2d 872.

135 Curlender v. Bio-Science Labs., 165 Cal. Rptr. 477 (Cal. Ct. App. 1980); Nelson v. Krusen, 678 S.W.2d 918 (Tex. 1984).

136 *Curlender*, 165 Cal. Rptr. 477.

137 *Becker*, 386 N.E.2d 807.

predictive. The harm in the case was in not providing the patient with highly predictive genetic information. In one case, for example, a court refused to hold a physician liable for failing to offer a genetic test when the test would have predicted only 20% of the instances of the disorder.[138] The court held, "A mere 20 percent chance does not establish a 'reasonably probable causal connection' between defendants' negligent failure to provide the [genetic] test and plaintiffs' injuries. A less than 50-50 possibility that defendants' omission caused the harm does not meet the requisite reasonable medical probability test of proximate cause."[139] Yet, when dealing with common, complex disorders, a particular genetic test may not predict more than 20% of the cases. If courts continue to apply such precedents in the arena of common, complex disorders, they will refuse to find liability for failure to offer a test for a complex, genetic test or for failure to perform it correctly (because the test's predictive value would have been low in any case). Such an approach is short sighted, however. People may find it useful to find out, for example, that they are at a 40% increased risk of coronary artery disease, and their healthcare providers deserve to be protected by being allowed to recover malpractice damages from doctors who negligently undertake such testing. The legal approach laid out in the single gene context may not provide sufficient incentives for quality assurance in the realm of complex genetic diseases.

V. INSURANCE AND GENETIC TESTING

Another concern raised by genetic testing for complex diseases is whether, if the testing becomes a routine part of primary care, it will be covered by healthcare and whether it will be used to determine insurance rates. One argument against creating a legal scheme that limits insurers' ability to use genetic information is that, by doing so, insurers do not have access to valuable information with which to determine individual rates. Some argue that insurance companies already use actuarial data to estimate risk and charge smokers, elderly people, or individuals with a significant family history higher premiums based on epidemiological data.[140] Attorney Jerry Elmer argues that, if private insurance is to remain a for-profit, competitive industry, the

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138 Simmons v. W. Covina Med. Clinic, 260 Cal. Rptr. 772 (Cal. Ct. App. 1989).

139 *Id.* at 776 (citations omitted).

140 Elmer, *Part I, supra* note 63, at 27-28.

information gained from genetic tests must be permissible; the alternative would be to provide a socialized insurance system.[141]

While science is universal, the social and ethical significance of DNA may differ according to differing social and economic circumstances. Genetics and insurance is a classic example. Genetic information has a different significance in the United Kingdom compared to the United States because the United Kingdom delivers healthcare through the National Health Service, "whereas the United States does so through the marketplace, backed by a private insurance system. The science is the same, but it acquires a different social meaning in a different context."[142]

The genomics revolution could be the impetus for socialized medicine. The converse of this is that private industry will simply discriminate against people whose genetic constitution indicates an increased risk for disease. And because the tests for complex disease are so imprecise and offer little insight into the defining elements of environment as it relates to disease development, the concerns of many people are great.[143] John Fletcher, an ethicist and Director of the Center for Biomedical Ethics in the School of Medicine at the University of Virginia, hypothesizes that people's fear of genetic discrimination may have much more to do with the fear and uncertainty of their health insurance status in terms of access to and amount of coverage than with any documented discrimination by insurers.[144] This is a plausible hypothesis, given that more than a third of Americans–nearly 90 million people are without insurance or covered by Medicaid–lack access to adequate preventive and primary care.[145]

VI. COMMERCIALIZATION AND GENETIC TESTING

Complex genetic diseases are much more common than any of the single gene diseases.[146] The desire of people to know their genetic risks for common diseases is presumed to be great. Therefore, the potential

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141 Jerry Elmer, *Human Genomics: Toward a New Paradigm for Equal-Protection Jurisprudence, Part II*, 50 R.I. B.J. 11, 15 (May/June 2002).

142 Wilkie, *supra* note 55, at 126.

143 John C. Fletcher, *The Long View: How Genetic Discoveries Will Aid Healthcare Reform*, 7 J. WOMEN'S HEALTH 817, 819 (1998).

144 *Id.* at 821.

145 *Id.* at 818.

146 *See* Kiberstis & Roberts, *supra* note 62.

market for genetic testing for complex diseases has the potential to far exceed that of single gene diseases.

The cost of the actual genetic test may be greater if there is a need to test for multiple genes, and the numbers of people interested will significantly exceed those undergoing single gene testing.[147] In the case of colon cancer, several techniques exist to test two specific genes, HNPCC and FAP, mutations in which indicate a high risk for disease onset.[148] The tests for HNPCC range in price from $250–$3,000,[149] and for FAP the range is $235–$1,000.[150] For two of the breast cancer genes, BRCA1 and BRCA2, the gene sequencing test is $1,290 for each gene.[151] The cost of the tests depends on the type of information one is seeking. The less expensive tests often detect a subset of mutations or screen for parts of a gene, whereas the gene sequencing tests can identify whole genes and detect mutations that have not been previously identified in a family.[152] But even the examples of colon and breast cancer are manageable with two genes each. What happens when more than 100 genes need to be analyzed to determine risk? For example, recent research has identified 149 genes that are involved in the development of asthma,[153] though the latest findings show a significant relationship between the new gene dubbed the "asthma gene," ADAM33, and asthma.[154]

In the intellectual property realm, the patent laws have assumed that the best way to stimulate the development of diagnostic and treatment technologies has been to give a single owner rights to a particular gene. Myriad Genetics, for example, has patents on the BRCA1 breast cancer gene.[155] But while that might conceivably work for a single gene

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147 People without a family history of disease are often less likely to undergo genetic testing.

148 Amanda Ewart Toland, *Costs of Genetic Testing*, http://diabetes.rezulin.com/cache/108863/ (last visited Mar. 20, 2003).

149 *Id.*

150 *Id.*

151 *Id.*

152 *Id.*

153 *Asthma: Genomic Study Breathes New Life into Research*, GENOMICS & GENETICS WKLY., June 28, 2002, at 8 [hereinafter *Asthma*].

154 Paul Van Eerdewegh et al., *Association of the ADAM33 Gene with Asthma and Bronchial Hyperresponsiveness*, 418 NATURE 426, 429 (2002).

155 *See 17q-Linked Breast and Ovarian Cancer Susceptibility Gene*, U.S. Patent No. 6,162,897 (issued Dec. 19, 2000); *Carboxy-terminal BRCA1 Interacting Protein*, U.S. Patent No. 6,030,832 (issued Feb. 29, 2000); *170-Linked Breast and Ovarian Cancer Susceptibility Gene*, U.S. Patent No. 5,753,441 (issued May 19, 1998); *17q-Linked Breast and Ovarian Cancer Susceptibility Gene*,

disorder, it may not work for a complex genetic disorder. When a disorder is caused by the interaction of several genes, giving individual patents on each gene may actually thwart the development of tests and cures since the individual patent holders may not cooperate adequately. Michigan law professors Michael A. Heller and Rebecca S. Eisenberg have shown how multiple patents relating to the same disease can deter innovation in biomedical research.[156] They stated, "A proliferation of intellectual property rights upstream may be stifling life-saving innovations further downstream in the course of research and product development."[157]

Heller and Eisenberg likened the situation in genetics to that of postsocialist economics.[158] The expectation in Eastern Europe was that private stores would be loaded with goods once a free market was introduced, but the stores remained bare-while street vendors flourished.[159] The reason: no individual could set up shop without collecting full ownership rights from workers' collectives, privatization agencies, and local, regional, or federal governments.[160] Similarly, with genetics, wrote Heller and Eisenberg, "privatization can go astray when too many owners hold rights in previous discoveries that constitute obstacles to future research."[161]

This is a sufficiently serious concern that the U.S. Patent and Trademark Office is beginning to explore the possibility of patent pools to deal with it. Attorneys and others at the U.S. Patent and Trademark Office published a paper noting that, "[i]f proprietary information is not freely available or licensed in an affordable manner, researchers will be precluded from using these protected nucleic acids to develop new therapeutics and diagnostics."[162]

U.S. Patent No. 5,710,001 (issued Jan. 20, 1998); *Linked Breast and Ovarian Cancer Susceptibility Gene*, U.S. Patent No. 5,709,999 (issued Jan. 20, 1998); *Linked Breast and Ovarian Cancer Susceptibility Gene*, U.S. Patent No. 5,693,473 (issued Dec. 2, 1997).

156 Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698, 698 (1998).

157 *Id.*

158 *Id.*

159 *Id.*

160 *Id.*

161 *Id.*

162 JEANNE CLARK ET AL., UNITED STATES PATENT AND TRADEMARK OFFICE, Patent Pools: A Solution to the Problem of Access in Biotechnology Patents? 3 (Dec. 5, 2000), http://www.uspto.gov/web/offices/pac/dapp/opla/patentpool.pdf (last visited Jan. 17, 2003).

A potential solution would be something similar to the American Society of Composers, Authors and Publishers ("ASCAP"), which handles the licensing of music under the copyright laws.[163] A patent pool could extend nonexclusive licenses to any interested parties potentially for set fees. That way, a researcher who wanted to develop a treatment for heart disease would not be prevented from doing so by the holder of a gene related to heart disease. Nor would the researcher have to negotiate with each holder of each related gene for the disease or a researcher for the treatment, thus saving transaction costs and preventing future litigation.

VII. "GENETICIZATION" OF DISEASE

The "geneticization" of disease is the assumption that most diseases have a major genetic basis which overrides all other factors, including environmental ones.[164] If our society begins to focus exclusively on genetics to explain the health disparities between groups, then this geneticization of disease may become severely limiting to society.[165] For example, if asthma is found to be simply a result of a genetic mutation, why bother to clean up our polluted cities or control automobile emissions? Or if diabetes is solely genetic, why should individuals be concerned with healthy diets and exercise routines?[166] We are only beginning to understand the complex relationship between the environment and genetics, and yet the single gene predictive testing paradigm lends itself to the geneticization of disease because people place so much weight on the predictability of genetics, ignoring, or at least blurring, the lines between genetic influences and those of the environment. The presence of the mutation in a single gene, for example

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A patent pool is defined as an "agreement between two or more patent owners to license one or more of their patents to one another or third parties." *Id.* at 4. By implementing patent pools, one can more easily access patented genomic inventions, which would promote research and development while promoting competition. *See id.* at 8-11.

163 *See* AMERICAN SOCIETY OF COMPOSERS, AUTHORS AND PUBLISHERS, COMMON MUSIC LICENSING TERMS, *at* http://www.ascap.com/licensing/termsdefined.html (last visited Mar. 18, 2003); *see also* Michael J. Meuer, *Copyright Law and Price Discrimination*, 23 CARDOZO L. REV. 55, 111 & n.231 (2001) (explaining that the "blanket license itself could be a tactic used to achieve price discrimination").

164 Sharp, *supra* note 46, at 162.

165 *Id.*

166 *Cf. id.* (hypothesizing the shift in focus from a hazardous workplace to the genetically vulnerable worker).

the Huntington's gene, can be predictive of disease,[167] but it is perhaps an erroneous assumption that genes are more predictive for common, complex disease than lifestyle, environment, and personal choice. The research from twin and migrant studies indicates that most of the important cancers in Western populations are the result of environmental factors and not genetic ones.[168] But the fact remains that scientists simply do not know precisely how most complex diseases develop. The vast majority of complex diseases are the result of an intricate and perplexing interplay between one's environment and genetic makeup. By focusing exclusively on the power of genes to predict disease, we may be missing many of the larger problems that plague our society and lead many to ill health.

Genetic testing for common, complex disease puts a spotlight on these issues because of the vast numbers affected by disease. Most people are not concerned about their risk for Huntington's disease unless they have a family history of the disease. So, most people are not seeking testing for such a rare condition; only 500 Americans are tested annually for Huntington's disease.[169] Diabetes and heart disease, on the other hand, are all too common, affecting younger and younger generations. Type 2 diabetes affects fifteen million Americans, and the annual costs of the disease are estimated to be $98 billion.[170] Those figures are staggering. Globally, the picture is even bleaker; the World Health Organization estimates that by 2025, the incidence of diabetes will more than double, affecting nearly 300 million people.[171] Asthma plagues 100 million people worldwide, and 5000 people in the United States die each year from asthma-related illnesses.[172] The annual domestic costs for the disease are $11.3 billion.[173]

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167 Janet K. Williams & Debra L. Schutte, *Genetic Testing and Mental Health: The Model of Huntington Disease*, 5 ONLINE J. ISSUES NURSING (Sept. 30, 2000), http://www.nursingworld.org/ojin/topic13/tpc13_4.htm (last visited Jan. 17, 2003).

168 Walter C. Willett, *Balancing Life-Style and Genomics Research for Disease Prevention*, 296 SCI. 695, 695-96 (2002).

169 Peter Gorner, *Unlocking Secrets, Closing Doors*, CHI. TRIB., Jan. 14, 2001, at 1 [hereinafter Gorner, *Unlocking Secrets*].

170 Peter Gorner, *Scientists Link Gene to Adult Diabetes; U. of C. Team's Work Opens Door to Study of Complex Diseases*, CHI. TRIB., Sept. 27, 2000, at 1 [hereinafter Gorner, *Scientists*].

171 Sarah Sexton, *Deceptive Promises of Cures for Disease*, 15 WORLD WATCH 18 (2002).

172 *Asthma*, *supra* note 153.

173 *Asthma Statistics*, *supra* note 18, at 1 (noting the estimated costs in 1998 totaled $11.3 billion).

Not only are the cases of diabetes on the rise, but what is even more disconcerting is the fact that Type 2 diabetes disproportionately affects certain groups. The American Diabetes Association estimates that 13% of African Americans and 10.2% of Hispanics have diabetes, compared to 6.5% of whites.[174] The incidence of Type 2 diabetes is highest among the Pima Indians of Arizona; 50% of adults have the disease.[175] If the general public accepts genes as the sole cause of disease, before scientific research has sorted through the myriad possibilities and the interplay between environmental influences and genetics, what becomes of the larger societal problems that we know contribute to disease? In the case of diabetes or heart disease, we know that an unhealthy lifestyle–specifically, a high fat diet and lack of exercise–significantly increases one's risk for the onset of disease.[176] For every ethnic or racial group, the risk of developing Type 2 diabetes increases with obesity.[177] The importance of environment is highlighted by studies that have looked at cardiovascular disease and major cancers and have shown immigrant populations that have adopted the disease rates for their new home, as they have moved from low to high-risk environments.[178] What becomes of personal and societal responsibility for health if we move to a geneticization of healthcare, wherein genes are viewed as predicting everything?

Further, not only are some groups disproportionately affected by disease, but mortality rate variance is disturbing. For example, among African Americans, the death rate for heart disease is 40% higher when compared to whites, and, for all cancers, it is 30% higher.[179] African Americans are also at higher risk of mortality from asthma, 3.8 per 100,000 versus 1.3 when compared to whites.[180] Hispanics are twice as likely to die from diabetes than non-Hispanic whites.[181] And the infant mortality rates among African Americans, American Indians, and Alaska Natives are nearly double those of whites.[182] Even if genetic testing

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174 Marx, *supra* note 17, at 686.

175 *Id.*

176 Nearly all of the members of the Pima Indian tribe afflicted by Type 2 diabetes (50% of the tribe) are overweight. Gorner, *Scientists, supra* note 170.

177 Marx, *supra* note 17, at 686.

178 Willett, *supra* note 168, at 695-96.

179 Sandra Soo-Jin et al., *The Meanings of "Race" in the New Genomics: Implications for Health Disparities Research*, 1 YALE J. HEALTH POL'Y L. & ETHICS 33, 41 (2001).

180 *Asthma Statistics, supra* note 18, at 3.

181 Soo-Jin et al., *supra* note 179, at 41.

182 *Id.*

becomes readily available for diabetes and heart disease, can genes explain the disparities among mortality rates? Perhaps the marginalized groups in society, the racial and ethnic minorities, have different mutations in their genetic makeup, which results in higher mortality rates. Or perhaps the environmental factors as a result of their societal marginalization are what contribute to the higher mortality rates. As genetic testing for diseases such as diabetes and coronary heart disease become available, maybe we will have the tools to sort through these issues. By conducting longitudinal studies among these groups, controlling for income and education, we can try to illuminate the cause of the differing mortality rates and to determine if, indeed, a different genetic mutation is the explanatory variable.

Are individuals suddenly developing diabetes or asthma mutations within their genes, or do lifestyle and environmental factors play a larger role than genetic researchers purport?[183] Or, is the increased incidence simply a reporting issue? Several interesting epidemiological studies have revealed that, even without knowledge of the specific genetic factors involved in some complex diseases, individuals can reduce their attributable risk from nongenetic or environmental factors by as much as 90%.[184] For diabetes and coronary heart disease, the nongenetic factors contribute to 90% and 80% of disease onset respectively.[185] These studies affirm that environmental factors have played a significant role in the rising incidence rates. Yet despite the evidence, the availability of genetic tests may give people the impression that environment is insignificant and that instead genetics are the main predictors of disease. In the case of diabetes and heart disease, if genetic tests are marketed to predict disease and provide results without accounting for lifestyle or environment, how are clinicians supposed to counsel their obese patients who, because of lifestyle choices, place themselves at severe risk for disease onset?

There is also evidence that an overemphasis on genetics can impede the development of appropriate therapies. For example, when research on gene therapy became the rage, virtually every institute at the National Institutes of Health undertook research on such therapies, sometimes

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183 Sexton, *supra* note 171, at 19-20.

184 Willett, *supra* note 168, at 695.

185 *Id.* at 696.

overlooking easier-to-develop and less expensive nongenetic treatment alternatives.[186]

Another concern is that the development of genetic tests–for example, deCODE's work with the genetic mutation thought to be the cause of schizophrenia–will be useful to only a small percentage of people.[187] Because our ancestors and our environment heavily influence our genetic makeup, the identification of the genetic mutation for schizophrenia in Iceland (an extremely homogenous nation) can lead to a genetic test that is highly predictive for Icelandic people. That mutation, however, may not be the causative factor for schizophrenia among more diverse populations of the world.[188] What are the implications of marketing a genetic test developed based on DNA samples from a small, homogenous group of Nordic people?

Without full disclosure of the research and development conducted by deCODE, combined with direct marketing to consumers, the potential misuse of genetic testing for complex disease is overwhelming. The general public may not fully appreciate the complexity of genetic diagnosis and the nuances of diagnostic versus probabilistic results. This, coupled with the profit incentive on the part of private industry, has the potential to do great harm. The diversity of the human population is staggering, and genetic testing for complex diseases cannot be oversimplified.

The fact that certain ethnic groups have already been identified as having a higher risk for specific diseases illustrates the complexity of causality between environment and genes. For example, the Ashkenazi Jewish community has a much higher incidence of the 185delAG mutation in the BRCA1 gene, one of the genes associated with breast cancer.[189] The incidence of the mutation is 1 in 1666 in the general population but is 1 in 107 among Ashkenazi Jewish women of Eastern

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186 *See* Stuart H. Orkin & Arno G. Motulsky, *Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy* (Dec. 7, 1995), http://www.nih.gov/news/panelrep.html (last visited Jan. 17, 2003). For example, Dr. Joseph Goldstein commented that "some of the diseases now targeted by gene therapy researchers might be treated sooner, by other strategies, if investigators pursued more traditional studies . . . ." *Id.*

187 *See* Wade, *supra* note 36.

188 *Id.*

189 Kelly-Anne Phillips et al., *Frequency of p53 Mutations in Breast Carcinomas from Ashkenazi Jewish Carriers of BRCA1 Mutations*, 91 J. NAT'L CANCER INST. 469, 471-72 (1999).

European origin.[190] Scientists have hypothesized a "founder's effect."[191] Another interesting finding is a 3452delA on exon 11 in the BRCA1 gene among one extended family in Mongolia.[192] Or, as previously discussed, the overwhelming prevalence of diabetes among the Pima Indian tribe.[193] The Human Genome Project has been touted as a great equalizer, offering scientific proof that race is truly a social construct and not a genetic reality.[194] Yet, the genetic research being conducted continues to reveal great differences among groups within society. What are the implications for these groups as genetic testing for complex disease becomes readily available? Richard Sharp, Director of the Program in Environmental Health Policy and Ethics at the National Institute of Environmental Health Sciences, notes that the "'geneticization' of disease could foster the belief that social problems are primarily the result of genetic causes. The reduction of social problems to biological problems changes social priorities."[195]

This genetic focus could significantly influence public health strategies and shift funding initiatives from preventive strategies to genetic ones.[196] In fact, the Centers for Disease Control ("CDC") have created the Genomics and Disease Prevention unit, which focuses on the interplay of genetics and public health.[197] Since 2001, three respected universities have been awarded $300,000 each per year for a period of three years to create "Centers for Genomics and Public Health."[198] In addition to these dollars, in May of 1999, the CDC launched an extramural research funding project dedicated to genetics and epidemiological research.[199]

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190 Soo-Jin et al., *supra* note 179, at 34.

191 *Id.*

192 *See, e.g.*, L. Elit et al., *A Unique BRCA1 Mutation Identified in Mongolia*, 11 INT'L J. GYNECOLOGICAL CANCER 241 (2001).

193 *See supra* text accompanying note 175.

194 For a discussion on race as a social construct, see Alan H. Goodman, *Why Genes Don't Count (for Racial Differences in Health)*, 90 AM. J. PUB. HEALTH 1699, 1699 (2000).

195 Sharp, *supra* note 46, at 162 (footnote omitted).

196 *Id.*

197 Center for Disease Control, Genomics and Disease Prevention, *Centers for Disease Control and Prevention (CDC) Awards Funds for Genetics Programs, at* http://www.cdc.gov/genomics/activities/fund2001.htm. (last visited Jan. 17, 2003).

198 *Id.*

199 The studies include one entitled *Gene-Environment Interactions in Cardiovascular Disease*, directed by Molly Bray from the University of Texas at Houston. That study is using stored DNA from the multi-center Atherosclerosis Risk in Communities study to assess gene-environment interactions and cardiovascular disease. Another is a study

Further, the priorities of society are changing as "the elision of economic factors such as poverty, employment, and unequal access to resources that are manifested in differences in nutrition, housing and access to health care are subsumed by genetics discourse that reifies notions of physiological difference."[200] Despite the evidence that genetics alone are not the cause of many complex diseases,[201] society may begin to put all its faith in genetics research to cure disease and halt the important discussions regarding environmental and social factors, which also lead to ill health. Dorothy Wertz, a senior Scientist in the Division of Social Science, Ethics and Law at the Eunice Kennedy Shriver Center for Mental Retardation in Waltham, Massachusetts, has written extensively on various bioethics topics and makes the important point that society must focus on some of the major goals of the Human Genome Project–disease diagnosis, prevention, and therapy[202]–while at the same time not losing sight of the other factors that lead to ill health.[203] Issues such as poverty, malnutrition, illiteracy, war, and oppression of women, along with genetics, contribute significantly to poor health.[204]

Moreover, in the realm of common, complex diseases, more pressure may be put on the individual to change his or her lifestyle or behavior than in the realm of single gene disorders. With single gene disorders, neither physicians nor courts have forced treatment interventions on competent adults who have a mutation related to a single gene disorder. In large measure, this is because gene therapies have not generally been proven to be successful, so no one has been required to use them. In contrast, consider what might happen if an individual is identified who has a genetic mutation that indicates an increased chance of disease if the person is exposed to a particular environmental stimulus. Pressure

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entitled *Diabetes Elimination in Washington: Stratified Population Screen*, directed by William Hagopian from the Pacific Northwest Research Institute in Seattle, Washington. The study asks parents of four-year-olds to test their stored samples from newborn screening (dried blood spots) and test for juvenile diabetes. Those with 20% highest risk will be asked to participate in a follow-up study to measure autoantibodies. Genomics and Disease Prevention, *Prevention Research Using Genetic Information to Prevent Disease and Improve Health*, http://www.cdc.gov/genomics/about/99res_proj.htm (last visited Mar. 18, 2003).

200 Soo-Jin et al., *supra* note 179.

201 Kiberstis & Roberts, *supra* note 62.

202 Francis S. Collins & Ari Patrinos, *New Goals for the Human Genome Project: 1998-2003*, 282 SCI. 682 (1998).

203 Dorothy Wertz, *Did Eugenics Ever Die?* 3 NATURE REVIEWS GENETICS 408, 408 (2002); *see* http://www.umassmed.edu/faculty/show.cfm?name=wertz (last visited Mar. 6, 2003) (containing a biography of Dorothy Wertz).

204 Wertz, *supra* note 203.

might be put on the individual (by doctors, employers, or insurers) to radically change behavior or lifestyle in order to try to eliminate a small statistical chance of triggering the disease. Already, some healthcare providers recommend that parents of children with a genetic propensity to skin cancer move to a city with a rainy climate like Seattle.[205] Since there are many more potential factors that influence whether or not a person manifests a common, complex disorder, the chance for paternalistic interventions in the person's life are greater than for similar actions based on single gene mutations.

The genetic factors of disease cannot be considered in a vacuum. The single gene disease paradigm has been incredibly important for researchers as they attempt to understand the nuances of complex disease–for example, "the Huntington's test has come to symbolize both the promise and perils of genetic testing."[206] But this paradigm is limiting when considering complex diseases. The goals of the Human Genome Project are laudable. With complex diseases such as diabetes reaching epidemic proportions, the potential to introduce effective therapy offers much promise. But, at the same time, society must be diligent to prevent abuses. The sequencing of the human genome is a thrilling accomplishment, but with it comes tremendous responsibility. The challenge to ethicists, legal scholars, and policymakers is to guard against the potential abuses and misuses of genetic information while at the same time supporting continued research and development in the genomics field.

VIII. CONCLUSION

The complex diseases that play a significant role in the health and welfare of much of the population, and therefore have significant public health implications, raise exponentially greater ethical, legal, and social concerns than single gene diseases. Many of the ethical issues, such as informed consent, confidentiality, autonomy, access, and commercialization, do not differ categorically from those raised by the single gene diseases. But with respect to some issues, the solutions proposed for ethical or legal dilemmas in the single gene realm will be inappropriate for complex genetic disorders. Further, the sheer

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[205] Frederick Hecht & Barbara Kaiser McCaw, *Chromosome Instability Syndromes, in* 3 JOHN J. MULVIHILL ET AL., PROGRESS IN CANCER RESEARCH AND THERAPY: GENETICS OF HUMAN CANCER 105, 114 (1977).

[206] Gorner, *Unlocking Secrets, supra* note 169.

magnitude of the common, complex diseases-affecting hundreds of millions of Americans-creates a unique arena for ethicists, legal scholars, and policymakers to protect the rights of the individual while at the same time assuring the appropriate use of genetic technologies.