The Implications of the Human Genome Project for Family Practice

Lori A. Whittaker, MD, PhD
Houston, Texas

The Human Genome Project is an international effort to map and sequence the human genome. The information it will generate has been referred to by some as the "new anatomy," and may play an important role in the future of medicine. However, as with any new technological advancement, the outcome of the Human Genome Project and the subsequent availability of new technology will raise a myriad of ethical, legal, and social concerns. The fear is that this technology will be applied in the clinical setting before the appropriate infrastructure is in place to deal with the issues it will raise. The family physician, far from being merely an interested observer in this process, will be responsible for the delivery of much of this technology as it becomes available. As an intermediary between the technology and the individual patient, the physician has a unique obligation to join in the thoughtful consideration and debate of these issues.

Key words. Research; ethics, medical; genetic screening; primary care; genetic intervention; genetic counseling.
J Fam Pract 1992; 35:294-301.

The Human Genome Project is a multibillion dollar, international effort to map and ultimately sequence the entire human genome. This project and the genetic technology that it will spawn have the potential to dramatically change the practice of medicine over the next decade. Gene mapping has been referred to as the "new anatomy"[1] and its impact likened to that of Vesalius' textbook of anatomy published in 1543, which formed the cornerstone for modern medicine.[2] With the information and technology gained from the Human Genome Project, it is anticipated that we will be able to identify by genetic screening most inherited disorders, produce genetic profiles of individuals to predict their risk for a variety of diseases such as heart disease and cancer, and reverse many genetic defects and treat diseases with gene therapy. While the implications of this technology are exciting, they also generate considerable ethical, legal, and social concerns regarding a person's right to privacy and autonomy and the possible misuse of the information obtained from genetic testing.[1–14]

To date, family physicians have watched this advancing technology largely from the sidelines. Most genetic testing and therapy has been within the realm of geneticists and specially trained genetics counselors. As the technology develops, however, its relevance to the primary care setting will expand. Genetic testing and diagnosis is moving from the research laboratory to the routine clinical laboratory and will have an impact on such areas as prenatal care, newborn and childhood screening programs, the determination of individual genetic risk profiles and preventive health care, and preemployment and insurance testing. As the number of available genetic tests grows, there will simply not be sufficient numbers of genetics specialists to meet the demand for information. The delivery and evaluation of these tests is likely to become the responsibility of primary care physicians as a routine part of medical practice.[4]

Of the primary care specialists, family practice physicians are in a unique position to be affected by these changes, since family medicine encompasses all stages of the human life cycle and thus may be influenced by the full range of genetic diagnostic possibilities. There is concern that physicians will be unprepared to meet the challenges this new technology will pose. Geller and Holtzman have suggested that several barriers exist that prevent primary care physicians from adopting genetic testing, including "lack of knowledge, inability to interpret problematic information, low tolerance for uncertainty, negative attitudes about their responsibility for genetic counseling and testing, lack of confidence in their clinical skills, and unfamiliarity with ethical issues raised by testing."[4] This paper is an attempt to break down

Submitted, revised, May 5, 1992.

From the Department of Family Medicine, Baylor College of Medicine, Houston, Texas. Requests for reprints should be addressed to Lori A. Whittaker, MD, PhD, Inuvik Medical Clinic, Inuvik, Northwest Territories, Canada X0E 0T0.

ISSN 0094-3509

some of those barriers and familiarize the family physician with the Human Genome Project and its applications, and to address some of the important ethical and legal issues that will arise as this new technology expands into the primary care setting.

The Human Genome Project: The Technology

There are 3 billion base pairs in the human genome, and an estimated 50,000 to 100,000 genes. By October 1990, when the official initiation of the Human Genome Project was announced, 1900 genes had already been mapped to specific chromosomes or chromosome regions and 600 genes, or approximately 1% of the total, had been cloned and sequenced.[2] It is estimated that the genome project will take 15 years and 3 billion dollars to complete. It will be necessary to develop new genetic technology as the project progresses if its goals are to be met within the anticipated time frame. The aim of the project is not to blindly sequence DNA strands, but rather to first produce a physical map of the genome, using restriction enzymes to generate chromosome fragments and known genetic markers to identify their location. Research groups in various countries will add new genes to the map as they are identified and sequenced. Eventually, all of the "gaps" in the genome will be filled in. The resulting genomic sequence will serve as an invaluable reference for future generations of scientists, geneticists, and clinicians.

A variety of methods may be used to isolate genes. The first, and simplest, is to identify the protein product, determine a partial protein sequence, and work backwards to determine the gene sequence. This method has allowed the sequencing of those genes that encode blood group antigens, clotting factors, structural proteins, growth factors and their receptors, hormones, enzymes, and oncogenes. Alternatively, when the protein product is not known, the study of inherited genetic defects can yield valuable information. Family linkage studies may be carried out to identify known genetic markers that cosegregate with, and are therefore closely linked to, the gene of interest. Using restriction enzymes to generate DNA segments of varying lengths and using the markers as probes, specific restriction patterns may be identified in affected individuals that are not present in unaffected family members. These *restriction fragment length polymorphisms* (RFLPs), as they are called, can be used in genetic screening, and are useful in the eventual isolation of the gene. Examples of genes originally identified by RFLPs for which the sequence is now known include Marfan's syndrome, Duchenne muscular dystrophy, and cystic fibrosis. A partial list of diseases mapped by RFLPs is shown in Table 1. A description of more sophisticated means of gene isolation is not within the scope of this paper, but has been discussed elsewhere.[2,3]

Table 1. Some of the Diseases Mapped by Restriction Fragment Length Polymorphisms (RFLPs)

Acoustic neuroma, bilateral
Alport syndrome*
Amyotrophic lateral sclerosis
Aniridia
Ataxia telangectasia
Charcot-Marie-Tooth disease
Craniosyntosis
Cystic fibrosis*
Duchenne muscular dystrophy*
Familial polyposis coli*
Fragile X*
Friedreich ataxia
Hemochromatosis
Huntington's disease
Kallmann syndrome*
Long QT syndrome
Multiple endocrine neoplasia, types I and II
Myotonic dystrophy
Nail-patella syndrome
Neurofibromatosis*
Polycystic kidney disease
Retinoblastoma*
Retinitis pigmentosa*
von Hippel-Lindau syndrome*
Wilms' tumor*
Wilson's disease
Wiskott-Aldrich syndrome

**Indicates diseases in which the gene has been isolated.*

Potential Applications of Genetic Technology in Family Practice

Prenatal and Parental Screening

The developing genetic technology will have applications in a variety of settings in primary health care. The first of these is in the area of prenatal care and counseling, and involves both prenatal diagnosis of fetuses and determination of the genetic status of prospective parents.

Prenatal diagnosis, for the most part, requires amniocentesis or chorionic villus sampling to obtain fetal cells, both of which are invasive procedures with their own risk of morbidity and mortality. These procedures are now routinely done only in cases of increased risk for genetic abnormalities, such as advanced maternal age or family history of genetic disease. Even then, analysis is done for only specific genetic or chromosomal aberrations, as the current cost of screening for all detectable genetic aberrations is prohibitively high.

As technology improves, the cost of DNA analysis

tion. Screening automatically, making multiple analyses on individuals affordable. Some have suggested that, if the information that can be obtained cost-effectively is crucial enough, routine amniocentesis for genetic screening may become the norm for prenatal care. Given the potential for complications, however, this remains an unlikely possibility.

Alternatively, the advent of new genetic technologies may simplify prenatal diagnosis. The technique of polymerase chain reaction (PCR) allows minute amounts of DNA to be detected and amplified for subsequent analysis. A recent study has used flow cytometry to isolate fetal cells from maternal blood samples. Fetal DNA was then amplified using the PCR technique, and analyzed for Y chromosome status,[15] thereby circumventing the need for invasive procedures to obtain fetal cells. In other cases, the protein products of fetal genes may be detectable in maternal serum. One such example already available is the maternal serum α-fetoprotein test, now used routinely in screening for Down's syndrome and neural tube defects.

Routine screening of parents for carrier status is likewise not current practice. In the case of cystic fibrosis (CF), for example, there are over 60 mutations in the CF gene that lead to disease; the most common of these account for 49% of cases and 68% of carriers of the disease.[16] A routine screening test for this mutation in prospective parents would thus be at best only 68% sensitive (assuming 100% sensitivity of the test itself). On the other hand, testing for carriers in a family with a history of CF is nearly 100% sensitive, because family linkage studies in addition to mutational analysis can be performed. The National Institutes of Health (NIH), in a recent position statement, does not recommend routine screening of all individuals for CF carrier status, but does strongly recommend that testing be offered to all couples with a family history of CF.[17] As new genetic tests become available, it will become increasingly important for physicians to obtain detailed family histories of their patients. The medicolegal consequences of failing to offer the appropriate tests could be significant.

The possibility of widespread use of noninvasive prenatal and preconception genetic testing raises several basic ethical issues. One of the major conflicts involves the concept of "procreative liberty."[18] Procreative liberty refers both to the individual right *to* procreate and the right *not to* procreate. The right to procreate may also be considered in terms of reproductive responsibility. Consider the example of a couple at risk for having a child with a particular genetic defect. With the availability of genetic tests, bringing an affected child into the world could be construed by some as reproductive irresponsibility. How seriously should couples and their physicians consider the suffering of the child or the cost to society when making reproductive decisions? It is conceivable that there will be persuasive pressure placed on the couple at risk from family, friends, and society in general to undergo preconception or prenatal screening. What role will the physician play in this process? Physicians certainly have an obligation to offer genetic testing to couples at risk, but some couples may opt not to be tested. In these cases, should the physician pressure the couple to comply with testing or should he try to *protect* couples from societal or legislative efforts to require genetic testing? If the couple does undergo prenatal testing, and decides to proceed with a pregnancy despite positive test results, who will bear the cost of raising an affected child?

Recently, a couple in California with a family history of cystic fibrosis desired prenatal screening to determine whether their unborn child would be affected. Their insurance company agreed to pay for the cost of the screening, but stipulated that if the fetus was affected, and the couple chose not to terminate the pregnancy, the insurance company would not provide health care coverage for the child.[19] The company backed down when the parents threatened to sue, but this case serves to illustrate the potential for conflict in this area.

The counter side to these arguments is the right *not* to procreate. The Supreme Court decision in *Roe v Wade* (1973)[20] guaranteed women the right to choose to terminate a pregnancy for any reason. However, individual states may adopt more restrictive legislation (upheld in the Supreme Court decision in *Webster v Reproductive Health Services*, 1990),[21] and antiabortion groups have continuously lobbied for the reversal of *Roe v Wade*. Indeed, the recent Supreme Court ruling in *Planned Parenthood of Southeastern Pennsylvania* has allowed some restriction of abortion rights in individual states. How would this affect a couple's reproductive choices in light of information they may gather from prenatal screening? Already there are strong arguments against pregnancy termination for perceived trivial reasons such as sex selection, although most people would support abortion for serious genetic defects.[18] But what constitutes a serious genetic defect? Will a predisposition to heart disease later in life or a risk of cancer if exposed to certain carcinogens be sufficient reasons to terminate a pregnancy? What about a disease such as cystic fibrosis? Persons with CF now live well into adulthood, lead productive lives, and occasionally have children of their own. Can it be said, then, that cystic fibrosis is a serious genetic defect? Where and how would one draw the line, and who would make such decisions? These questions have no easy answer, and the concept of procreative liberty will undoubtedly engender much serious and emotional debate in the years to come.

Neonatal and Early Childhood Testing

Mandatory neonatal screening is already in place for diseases such as PKU, sickle cell anemia, congenital hypothyroidism, galactosemia, and congenital adrenal hypoplasia* because early intervention for these diseases can have a profound effect on outcome. As testing for a variety of genetic disorders becomes possible and the development of individual genetic risk profiles becomes the norm for preventive medical care, it may seem that infancy is the best time to determine an individual's genetic makeup, at least for certain conditions for which early intervention could have an advantageous effect. It is even conceivable that the government could legislate mandatory testing of all infants, denying parents the right to refuse such testing. What effect could such intervention have on child-rearing practices? If, for example, a child is determined to have a predisposition for heart disease, it may seem prudent to institute an approved American Heart Association diet as soon as possible in order to instill beneficial lifelong eating habits. Could parents then be said to be negligent if they fail to force their child to strictly adhere to this diet?

Particular genetic labels might have lasting effects on parent-child bonding, peer relationships, school performance and expectations, and in adolescence, on career choices and life plans. All new parents are understandably hopeful that their child will be physically "perfect," meaning that he or she has no identifiable abnormality. With the advent of genetic testing and the information it will generate, the concept of the perfect child may be changed forever. It is expected that a "perfect" genetic profile will be exceedingly rare. Family physicians and pediatricians will be called on to explain and interpret the results of a multitude of tests to anxious parents, and the manner in which this information is presented may permanently affect the parents' view of their child. The importance of the primary care physician as genetic counsellor in this regard cannot be overemphasized.

Individual Genetic Profiles

As described above, one of the potential offshoots of the Human Genome Project is the development of "genetic profiles" of individuals. These profiles would identify predispositions to a variety of diseases known to have a strong genetic component, such as heart disease, stroke, cancer, diabetes, hypertension, alcoholism, and schizophrenia. Examples of such predisposing genes that have already been identified include the p53 tumor suppressor gene associated with the Li-Fraumeni cancer syndrome and a variety of sporadic cancers including breast and lung carcinomas, osteosarcomas, brain tumors, and leukemias[22]; the APC gene associated with familial polyposis[23]; and the extensive metabolic phenotype of the cytochrome p450 enzyme CYP2D6 associated with an increased risk of lung cancer, especially in the face of exposure to asbestos or polyaromatic hydrocarbons.[24]

The identification of such predispositions could have far-reaching consequences for affected individuals. Some would argue against such knowledge, saying it could only have an anxiety-provoking and deleterious affect on the lives of those with unfavorable genetic profiles. There has been much controversy over the identification of individuals with Huntington's disease, a progressive neurological disorder with onset in late adulthood, for which presymptomatic genetic testing is available. As there is no treatment for Huntington's disease, the usefulness of detecting affected individuals early in life is questionable. Such knowledge would understandably be associated with some degree of hopelessness and despair, and undoubtedly would affect many premorbid life stages, such as peer and family relations, marriage, education, career choices, and so forth. Indeed, the only clear advantage of early detection, and this is the main argument in its favor, would be in making reproductive choices.

Another example of early detection is von Hippel-Lindau disease, a hereditary syndrome characterized by tumors and cysts in multiple organ systems. Recent identification of tightly linked genetic markers for this syndrome now permits accurate early diagnosis.[25] Unlike Huntington's disease, however, early intervention can alter the course of the disease, and thus provides strong argument for the importance of presymptomatic detection. Likewise, early identification of cystic fibrosis has implications for aggressive early interventions and treatment. These latter examples are perhaps more in line with the development of genetic profiles for predisposition of disease.

Theoretically, premorbid intervention in the form of modification of risk factors would be advantageous in individuals predisposed to certain diseases. Individuals predisposed to heart disease, for example, could attempt to lower other risk factors by following low cholesterol diets, exercising, not smoking, practicing stress-reduction techniques, and aggressively managing hypertension and diabetes. Although these are recommendations most physicians currently make to all their patients, we are well aware of the problems of compliance. Perhaps knowledge of having a genetic risk for a particular disease would increase a patient's compliance in areas of preventive health care.

**These are the neonatal screening tests currently required by law in the state of Texas. Each state varies with respect to the tests they require.*

Gene Therapy

One of the most exciting and controversial aspects of the new genetic technology is gene therapy.[26–32] It is unlikely that family physicians will be directly involved in this highly technical field, but they should be aware of gene therapy as a treatment option for a variety of conditions and disease states. Somatic gene therapy involves the replacement of an absent or defective gene with a normal gene by targeting specific somatic cells. Clinical trials are already underway to replace the adenosine deaminase (ADA) gene in children with ADA deficiency and the resulting severe combined immunodeficiency syndrome.[26] In another study, tumor-infiltrating lymphocytes genetically engineered to contain a neomycin resistance marker were safely infused into melanoma patients and successfully targeted to tumor sites.[31] Plans are underway to use this technique to introduce tumor-necrosis factor, interferon alpha, or interleukin-2 into the tumor-infiltrating lymphocytes to improve their antitumor activity.[31,32] It is hoped that gene therapy will provide a revolutionary new approach to diseases such as inborn errors of metabolism, specific genetic defects, cancer, and AIDS.

Much more controversial is the concept of germ line gene therapy, which involves the introduction of foreign DNA into germ cells, thus perpetuating a genetic change for future generations. French Anderson, whose group is responsible for the ADA trials, has said that germ line gene therapy "has a greater impact on society as a whole than treatment confined to a single individual. The gene pool is a joint possession of all society. . . . [T]he decision to initiate germ line gene therapy demands assent from more than the individual involved."[27] To date, the NIH Recombinant DNA Advisory Committee has not permitted any clinical trials of germ line therapy, and considerable ethical debate will likely ensue before such trials are allowed.

Further Implications and Issues for the Family Physician

Legal and Malpractice Issues

In our current litigious climate, no aspect of the practice of medicine is free of liability, and this includes the applications of developing genetic technology.

One of the most contentious areas is that of prenatal diagnosis. The concepts of *wrongful birth* and *wrongful life* have been invoked in the courts to deal with this issue. *Wrongful birth* is an action taken on behalf of parents claiming that negligence on the part of a physician or other party led to the wrongful birth of a genetically defective child, the contention being that if the parents had known of their genetic risk, they would have chosen abortion or contraception to prevent the birth of that child. There are several examples of cases in which a wrongful birth claim has been upheld. In *Becker v Schwartz* (1978),[33] the plaintiff was awarded economic (but not emotional) damages when a physician failed to warn a 37-year-old mother of a Down's syndrome baby of the genetic risks of her pregnancy and to offer amniocentesis. *Karlsons v Guerinot* (1977),[34] which also involved the birth of a child with Down's syndrome, was one of the few cases in which recovery of damages for emotional suffering by the parents was awarded. In two other cases, the physician was found negligent in having failed to take an adequate family history and identify the risk of genetic disease. In both *Goldberg v Ruskin* (1984)[35] and *Howard v Lecher* (1977),[36] the physician failed to identify and warn prospective parents of their risk of having a child afflicted with Tay-Sachs disease. Liability may also be based on the physician's failure to diagnose, or identify as genetic, a disease in a previous child and thus offer appropriate counseling for subsequent pregnancies, as in *Park v Chessin* (1977; polycystic kidney disease),[37] *Schroeder v Perkel* (1981; cystic fibrosis),[38] or *Turpin v Sortini* (1982; hereditary deafness).[39]

The second concept to be brought before the courts is that of *wrongful life*. This is a cause of action brought on behalf of the defective *child*, claiming that his birth has caused him undue pain and suffering, and that he would have been better off not having been born. In general, courts have denied such claims, citing the "sanctity of life and the difficulty of comparing life in an impaired state—even a severely impaired state—to no life at all."[40] To date, only two wrongful life claims have been upheld. The first of these was *Park v Chessin* (1977; also argued on a wrongful birth claim)[37] in which infant Lara Park recovered damages for her "conscious pain and suffering" for having been born with polycystic kidney disease. Her parents had had a previous child who died of the condition several hours after birth. An autopsy had been performed on that child, and the parents informed that the chances of having a second child born with the disease were "practically nil." They had relied on this information when they conceived Lara, who died at the age of 2 years.[40] The second case was *Curlender v Bioscience Laboratories* (1982),[41] in which the defendant was not a physician, but a medical testing laboratory that offered inaccurate information to a couple with a family history of Tay-Sachs disease, stating that they were not at risk for having an affected child. When their child was born with the disease, a suit was filed on his behalf against the medical testing laboratory in which he recov-

ered damages for pain and suffering endured during his lifetime. Today, only four states, California, Washington, New Jersey, and Colorado, recognize the wrongful life action.[40]

This discussion has focused on the liability inherent in prenatal testing and counseling, but no application of genetic technology is immune from litigation. For example, a physician could be held liable for failing to diagnose or improperly interpreting a particular genetic risk of disease and offer appropriate preventive measures to the patient; or for failing to offer gene therapy as a therapeutic option to a patient who might benefit from it. As with any other area of medicine, physicians are obliged to keep abreast of current medical practice. The prevailing legal opinion on this subject is summarized in the following article published by the *Yale Law Journal:*

> Because knowledge of human genetics is expanding rapidly, doctors should not be exonerated when they have failed to be reasonably current in this area. It has long been recognized that physicians are bound to stay abreast of major medical developments. . . . In evaluating the adequacy of physicians' detection of genetic risk, courts should go beyond the limits of this traditional requirement by strictly compelling doctors to be aware at least of techniques widely known within the medical community.[42]

Confidentiality and Access to Information

The potential misuse of the information gathered from genetic screening is another area of great concern. Determining who should have access to that information is a difficult question. Some argue that even patients should not have full access to their own test results, since the implications of certain results may not be clear and could only result in anxiety or false conclusions on the part of the patient. This concept of withholding information from the patient, however, exemplifies the practice of beneficence, which is no longer considered acceptable in most medical circles. The argument does emphasize, though, the importance of proper interpretation, counseling, and discussion on the part of the physician administering genetic tests and communicating the results to the patient.

The question of third-party access to information is somewhat more complex. One area of concern is that of health insurance screening. Already there is a precedent for insurance companies to deny coverage to persons who test positive for HIV. Attempts at keeping this information confidential have met with only marginal success. It may be expected that a similar experience will be had with genetic information. It is likely that genetic testing and screening will require the use of computer-based information systems for analysis, processing, and storage of the data generated. Once the information has been logged into such systems, confidentiality may not be feasible. Indeed, insurance companies may well argue that if they are denied access to genetic information, then those individuals with unfavorable profiles might buy more insurance on the basis of that information, placing an increased burden on the insurer.[19] The concept of prior knowledge of disease may then be brought to bear. If, on the other hand, insurance companies did have access to the information, how might this affect the health care system? Might insurers offer differential rates based on genetic profiles? Would someone with a truly unfavorable profile be denied health care coverage altogether?

It is likely that if testing becomes universal, most people would be found to have some "good" genes and some "bad" genes, and that these would cancel each other out and offer no clear medical advantage or disadvantage. Initially, however, certain predispositions might be given priority. It is possible that governmental intervention will be required to determine how genetic information will be used by the health insurance industry. Some have suggested that these concerns may actually be an impetus to a national health care plan, stating that "the injustice of private health care schemes will be accentuated once additional genetic information becomes available."[43]

Another area of concern is that of discrimination in the workplace. Genetic screening by employers could seriously limit an employee's right to privacy and autonomy. Jeremy Rifkin voiced these concerns at a meeting of the NIH Recombinant DNA Advisory Committee 2 years ago, when he stated that "the major civil liberties questions of the coming decades are going to be the right of genetic privacy . . . versus mandatory screening . . . in order to have people be congenial to the environments the corporations or institutions want to place them in."[44] He cited as examples of past discrimination Dupont's screening of black employees for sickle cell anemia, and chemical companies in the 1970s requiring sterilization of female employees as a prerequisite to employment in certain high-risk areas. Following public outcry and congressional investigations in the early 1980s, such practices are rare today. A 1987–1988 survey of 245 corporate executives revealed that only three companies admitted to using any form of genetic screening (the type and purpose of the screening was not specified).[45]

Recent legislation has provided a legal basis for the prohibition of genetic testing in the workplace. The Americans with Disabilities Act prohibits employers with 25 or more employees (and in 1994, 15 or more employees) from discriminating on the basis of disability. It also forbids the use of medical tests to detect disabilities

in employees, unless the testing relates to the ability to perform a specific job-related function.[5]

Nonetheless, as an increasing number of genetic tests become available, employers will more than likely develop justifications for their use, ostensibly to enhance worker or public safety, but at the same time trying to limit their own liability and health care costs. For example, certain genes have been identified that may result in increased susceptibility to cancer following environmental exposure to specific carcinogens.[24] It may seem prudent for those individuals who are at increased risk to avoid exposure to the carcinogens if possible. Such medically prudent behavior may limit their access to a given job, however, and must be weighed in the context of that individual's personal circumstances (such as financial resources, number of dependents, education and training, job desirability, and the availability of alternative jobs) as compared with the actual degree of risk.

The concepts of worker autonomy and the right to make informed personal decisions were key factors in the US Supreme Court's landmark decision in *United Auto Workers v Johnson Controls, Inc* (1991), in which the company's policy of excluding fertile women from areas of lead exposure was declared unconstitutional.[46]

Family physicians are frequently responsible for the administration of preemployment physical examinations and medical tests, and therefore have an obligation to be actively involved in the determination of what constitutes fair and ethical employee screening. The Council on Ethical and Judicial Affairs of the American Medical Association has recently issued guidelines designed to help physicians deal with this complex issue. Their opinion reads in part:

> It would generally be inappropriate to exclude workers with genetic risks of disease from the workplace because of their risk. Genetic tests alone do not have sufficient predictive value to be relied upon as a basis for excluding workers. Consequently, use of the tests would result in unfair discrimination against individuals who have abnormal test results.[5]

Only in very limited circumstances, such as when occupational disease might develop so rapidly that monitoring of exposure to a given toxin would not be possible, and the cost of lowering the level of the toxin in the workplace would be prohibitively high, would the AMA condone genetic screening of employees.

Conclusions

With the advent of the Human Genome Project, the next decade will see a revolution in genetic technology. Much of this technology, far from being restricted to the realm of research laboratories or clinical geneticists, will have direct application to a variety of primary health care settings. Family physicians, along with pediatricians, internists, and obstetricians will be involved in the development and administration of prenatal diagnostics and reproductive counseling programs, neonatal and childhood testing, and preventive medicine protocols based on individual genetic risks.

As with any new technology, the advances made by genetic research will generate difficult moral and ethical issues. Such fundamental rights as procreative liberty and reproductive freedom, confidentiality and access to information, insurability, employability, and individual autonomy may be brought into question. Potential areas of contention include the controversial and emotional issues of a woman's right to continue or terminate a pregnancy based on genetic information; a parent's right to refuse testing for his or her child; the emotional and social impact of genetic labels; an insurance company's right to deny coverage to certain individuals based on their genetic profile; or an employer's right to prohibit employment of those with a specific genetic trait or predisposition.

From a medicolegal perspective, it will be imperative for all physicians to be informed of the technology as it unfolds. The prevailing legal opinion is that lack of knowledge of genetic technology will be no defense for a physician's failure to offer the appropriate genetic test, counseling, or intervention. Inherent in this is the requirement for a critical appraisal and understanding of the applications and limitations of the tests themselves. As with any diagnostic modality, we must understand its therapeutic relevance and implications. Full interpretation will be possible only with applied clinical experience.

Public policies with regard to the use of genetic technology remain to be determined. It is important that physicians, who are in a unique position as intermediaries between the technology and the patient, add their voice to those of scientists, ethicists, legislators, and the lay public in setting these policies.

Acknowledgments

The author acknowledges the contributions of Adel Youakim, PhD, Warren Holleman, PhD, and Alan Blum, MD, for their support and encouragement of this work, their critical appraisal of the manuscript, and, with Larry McCullogh, PhD, for their thoughtful and insightful discussions on this subject. I also wish to thank the organizers and speakers of the conference, "Legal and Ethical Issues Raised by the Human Genome Project," given by The Health Law and Policy Institute of the University of Houston, March 7–9, 1991, whose informative presentations provided the impetus for this work.

References

1. McKusick VA. Mapping and sequencing the human genome. N Engl J Med 1989; 320:910–5.
2. McKusick VA. Current trends in mapping human genes. FASEB J 1991; 5:55–60.
3. Green ED, Waterson RH. The Human Genome Project: prospects and implications for clinical medicine. JAMA 1991; 266:1966–75.
4. Geller G, Holtzman NA. Implications of the Human Genome Initiative for the primary care physician. Bioethics 1991; 5:318–25.
5. McMurray RJ, Clarke OW, Barasso JA, et al. Use of genetic testing by employers. JAMA 1991; 266:1827–30.
6. Watson JD, Cook-Deegan RM. The Human Genome Project and international health. JAMA. 1991; 263:3322–4.
7. Dawson K, Singer P. The Human Genome Project: for better or for worse? Med J Aust 1990; 152:484–6.
8. Sillence D. The Human Genome Project. Med J Aust 1990; 152:486–8.
9. Danks DM. Some thoughts on the Human Genome Project. Med J Aust 1990; 152:488–9.
10. Sinsheimer RL. Whither the Genome Project? Hastings Cent Rep 1990; 20(4):5.
11. Miller J. Mapping and beyond. Hastings Cent Rep 1990; 20(6): 3–4.
12. Touchette N. Letting the genome out of the bottle. J Natl Inst Health Res 1990; 2:17–20.
13. Bankowski Z. Genetics, medicine and ethics. World Health 1988; Dec:3–5.
14. Capron A. Which ills to bear? Reevaluating the threat of modern genetics. Emory Law J 1990; 39:665–96.
15. Price JO, Elias S, Wachtel SS. Prenatal diagnosis with fetal cells isolated from maternal blood by multiparameter flow cytometry. Am J Obstet Gynecol 1991; 165:1731–7.
16. Light MJ, Harwood IR. Cystic fibrosis. Hosp Med 1991; 27:37–50.
17. Beaudet AL, Kazazian HH Jr, Bowman JE, et al. Statement from the National Institutes of Health workshop on population screening for the cystic fibrosis gene. N Engl J Med 1990; 323:70–1.
18. Robertson J. Procreative liberty and human genetics. Emory Law J 1990; 39:697–719.
19. Brownlee S, Silberner J. The assurance of genes: Bioethics—is disease prediction a boon or a nightmare? US News and World Report, July 23, 1990.
20. *Roe v Wade,* 410 US 113 (1973).
21. *Webster v Reproductive Health Services,* 109 SCt 3040 (1989).
22. Malkin D, Frederick PL, Strong LC, et al. Germ line p53 mutations in a familial syndrome of breast cancer, sarcomas, and other neoplasms. Science 1990; 250:1233–8.
23. Groden J, Thliveris A, Samowitz W, et al. Identification and characterization of the familial adenomatous polyposis coli gene. Cell 1991; 66:589–600.
24. Shields PG, Harris CC. Molecular epidemiology and the genetics of environmental cancer. JAMA 1991; 266:681–7.
25. Seizinger BR, Smith DI, Filling-Katz MR, et al. Genetic flanking markers refine diagnostic criteria and provide insights into the genetics of Von Hippel Lindau disease. Proc Natl Acad Sci 1991; 88:2864–8.
26. Verma I. Gene therapy. Sci Am 1990; Nov:68–84.
27. Walters L. The ethics of human gene therapy. Nature 1986; 320:225–7.
28. Anderson WF. Human gene therapy: scientific and ethical considerations. Recomb DNA Tech Bull 1985; 8(2):55–62.
29. Cournoyer D, Scarpa M, Jones SN, et al. Gene therapy: a new approach to the treatment of genetic disorders. Clin Pharmacol Ther 1990; 47:1–11.
30. Freidman T. Progress toward human gene therapy. Science 1989; 244:1275–80.
31. Rosenberg SA, Aebusold P, Cornetta K, et al. Gene transfer into humans—immunotherapy of patients with advanced melanoma, using tumor-infiltrating lymphocytes modified by retroviral gene transduction. N Engl J Med 1990; 323:570–8.
32. Cournoyer D, Caskey T. Gene transfer into humans—a first step. N Engl J Med 1990; 323:601–2.
33. *Becker v Schwartz,* 46 NY2d 401, 413 NYS2d 895, 386 NE2d 807 (1978).
34. *Karlsons v Guerinot,* 57 App Div 2d 23, 394 NYS2d 933 (1977).
35. *Goldberg v Ruskin,* 128 Ill App 3d 1029, 471 NE2d 530 (1984).
36. *Howard v Lecher,* 42 NY2d 109, 366 NE2d 64, 397 NYS2d 363 (1977).
37. *Park v Chessin,* 60 App Div 2d 80, 400 NYS2d 110 (1977).
38. *Schroeder v Perkel,* 87 NJ 53, 432 A2d 834 (1981).
39. *Turpin v Sortini,* Cal App 3d 220, 643 P2d 954, 182 Cal Rptr 337 (1982).
40. Fleischer LD. Wrongful births. Am J Dis Child 1987; 141: 1260–5.
41. *Curlender v Bioscience Laboratories,* 106 Cal App 3d 811, 165 Cal Rptr 477 (1980).
42. Anonymous. Mother and father know best: defining the liability of physicians for inadequate genetic counseling. Yale Law J 1978; 87:1488–1518.
43. Macer D. Whose genome project? Bioethics 1991; 5:183–211.
44. Department of Health and Human Services National Institutes of Health Recombinant DNA Advisory Committee: Minutes of meeting Jan 30, 1989. DNA Tech Bull 1989; 12:69–105.
45. Rothstein MA. Medical screening and the employee health cost crisis. Washington, DC: Bureau of National Affairs, 1989:70–1.
46. Rothstein MA. Johnson Controls, workplace risks and the limits of autonomy. University of Houston Health Law and Policy Institute. Health Law News 1991; V(1):2.

See editorial comment on page 256.