CLINICAL REVIEW

Ethical and Practical Implications of the Human Genome Initiative for Family Medicine

S. Van McCrary, PhD, JD, MPH; Bill Allen, JD; Ray Moseley, PhD; Lee A. Crandall, PhD; Harry Ostrer, MD; R. Whit Curry, MD; Marvin A. Dewar, MD, JD; David Nye, PhD

Major advances in predictive genetic testing resulting from the Human Genome Initiative could change significantly the routine practice of family medicine. Family physicians should be aware that increased genetic information may affect patients' abilities to acquire and maintain insurance and employment and that interested parties will have incentives to seek this information. The social consequences of genetic information, as well as increased health promotion efforts, may raise problems of informed consent and confidentiality. In addition to their ethical implications, these developments will also affect the practice of family physicians in practical ways such as record keeping. We discuss cases that illustrate the potential impact of these emerging technologies on the practice of family medicine.

(Arch Fam Med. 1993;2:1158-1163)

During the next 15 years, scientists funded by the Human Genome Initiative (HGI) of the National Institutes of Health (Bethesda, Md) will attempt to map and determine the sequence of each of the estimated 100 000 genes in the human cell.[1] The information acquired as a result of this project will enable physicians to diagnose a greater number of diseases and predispositions to disease in asymptomatic persons than current technology permits.[2] This increased knowledge is likely to raise the visibility of preventive measures and health promotion as components of standard medical practice. It appears that the foreseeable genetic testing technologies will soon be inexpensive and available for an array of diseases with high incidence rates in the US population. Such developments could dramatically alter the routine practice of family physicians. Little has been written in the United States regarding genetic testing as it relates to family medicine.[3,4] This article addresses the following questions: What is the current state of genetic testing in family practice? What is the likely course of development of HGI-derived predictive testing? What are the implications of such expanded genetic screening for patients seeking insurance coverage and employment? What moral and practical issues must family physicians confront as a result of this emerging technology?

From the Human Genome Insurance Project, The Medical Humanities Program (Drs McCrary, Allen, Moseley, Crandall, and Dewar), Department of Community Health and Family Medicine (Dr Curry), University of Florida College of Medicine; Florida Insurance Research Center, Graduate School of Business Administration, University of Florida (Dr Nye), Gainesville; and Human Genetics Program, Department of Pediatrics, New York (NY) University Medical Center (Dr Ostrer).

THE HGI

The HGI was begun in October 1990 to describe and understand the composition of the human genome. Scientists estimate that by 2005, the HGI will have yielded massive amounts of information in the form of high-resolution genetic linkage and physical maps of all human chromosomes, as well as data on sequencing many of the 3 billion base pairs in human DNA.[2,5] The HGI funds teams of scientists nationwide at major medical and research institutions under the auspices of the National Center for Human Genome Research at the National Institutes of Health. In aggregate, the

project is one of the largest coordinated scientific endeavors in history. The projected result of the HGI will be an unprecedented amount of information about the genetic makeup of humans. This information will dramatically increase the understanding of many of the 3000 known inherited disorders, as well as conditions caused by gene-related physiological responses to environmental pathogens, mutagens, and toxins.[2]

CURRENT PRACTICE

At present, genetic testing is not a routine practice of family physicians. However, many physicians already use the most basic method of genetic analysis, namely, taking a case history and recording it into a family genogram. Family histories provide much useful information regarding an individual's potential susceptibility to diseases with genetic components (eg, coronary artery disease). Except for single-gene diseases such as Huntington's disease or hemophilia, however, the reliability of information from case histories is suggestive rather than predictive. In contrast, it is likely that tests produced from HGI-derived technology will offer much more precise prediction of health outcomes than genetic information derived from family histories and will be available for many more diseases than current screening technology allows.

At this time, genetic testing generally occurs in family practice settings only in the following circumstances: (1) when there is obvious underlying disease; (2) when particular family histories are remarkable for rare mendelian conditions with grave implications for morbidity and mortality; (3) when developmental delay or abnormality in children raises suspicions of disease with unidentified origin; or (4) as part of limited screening among practitioners who engage in prenatal, obstetrical, and neonatal care. Even these applications of genetic tests are not uniform, however, owing to variation among clinicians and diversity in practice settings (eg, urban vs rural practice sites). Thus, systematic, widespread genetic screening is not yet the prevailing standard of care in family practice settings.

FUTURE GENETIC TESTING TECHNOLOGIES

Genetic factors play a substantial role in common diseases, such as cancer, cardiovascular disease, and neurodegenerative disorders, that affect 30%, 40%, and 20% of the US population, respectively.[6] In addition, genetic influence also plays a role in mendelian disorders, individually rare, which affect 1% of the population cumulatively.[6] At present, genetic testing technologies exist for cystic fibrosis and fragile X syndrome through carrier testing and prenatal diagnostic tools. The widely publicized screening for Huntington's disease uses familial tracing of genetic characteristics rather than actual DNA analysis. Other tests that are available at present include Duchenne type muscular dystrophy, hemophilia A, sickle cell disease, and various thalassemias. Tests that are due very soon include those for predisposition to various types of cancers, including colorectal, breast, melanoma, and some leukemias.[7] Germline mutation analysis will be the tracing technology for identifying some cancers. Testing expected in the longer term will likely identify genetic components of various multifactorial diseases, including heart disease, schizophrenia, and neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease.[7] Thus, the trend in the development of genetic testing technology is a movement from expensive tests for rare diseases to low-cost screening for diseases with high incidence, including the most frequent causes of death in the United States. As new testing technologies become cost-effective and readily available for use in family practice settings, the family physician will have a vast array of screening services for use in health promotion and preventive care.

Issues of predictive value become critically important when considering the expanding class of genetic testing technologies. For particular tests to become professionally accepted, it will be necessary to establish minimum acceptable levels of sensitivity and specificity. Specificity is critical because large numbers of false-positive test results could produce extreme mental suffering for healthy persons who are told that they may (or, in rare cases, will) develop serious genetic disorders. Similarly, sensitivity is crucial because false-negative test results should be avoided to identify as much potential disease as possible and to encourage health promotion efforts in persons with genetically based susceptibilities. The extreme emotional connotations of false-positive test results, combined with the potential adverse health effects of false-negative test results, make professional standardization of predictive value in genetic screening tools a moral imperative.

Issues of incomplete penetrance and variable expressivity must also be considered. Common diseases are multifactorial in cause, requiring numerous adverse genetic and environmental events to occur for frank disease to be expressed (penetrant).[6] The timing and severity of these events accounts for marked variability in age at onset and severity of manifested disease. Users of genetic tests must consider, first, that some persons who test positive for a genetic disease will never mani-

Tests that are due very soon include those for predisposition to . . . cancers, including colorectal, breast, melanoma, and some leukemias

fest symptoms and, second, that even if symptoms arise in particular individuals, their severity is subject to substantial variability. Thus, the predictive value of a positive genetic test may be limited for determining the age at onset, severity, or absolute likelihood of disease.[6] Penetrance and variable expressivity are critical in two contexts: first, clinicians should be aware that identified genetic characteristics do not definitely determine clinical outcomes in particular patients; second, family physicians who counsel patients must understand and be able to explain clearly to patients the implications of the potential for extreme variability of the same genetic trait among family members.

INFORMED CONSENT AND CONFIDENTIALITY IN GENETIC SCREENING: MORAL AND PRACTICAL ASPECTS

Informed consent and confidentiality are two key elements of relationships between patients and physicians. The way that physicians choose to treat information—both in its disclosure to patients and the guarding of it from those without a right to access—is one determining characteristic of whether physicians respect their patients as persons with moral claims. Ethicists and legal scholars have long recognized the three basic elements of informed consent as disclosure of appropriate information, competence, and voluntariness. Normally, disclosure requires that the physician (1) inform the patient of his or her medical status, including prognosis with and without medical intervention; (2) inform the patient of treatments that might improve the prognosis, including a description of the risks and benefits that a reasonable patient would want to know before consent; and (3) offer a professional opinion regarding any alternatives.[8] Competence requires that the patient be able to understand the information disclosed and be able to weigh the alternatives, considering all the circumstances in light of his or her preferences and values. Voluntariness requires that the patient's decision be made without undue influence or coercion, considering all the circumstances in which consent is sought and obtained or refused.

For purposes of the HGI, a critical element of informed consent is disclosure, since the emerging genetic technologies may provide large numbers of new genetic tests that patients might choose to undergo, with implications that will probably not be obvious to the average person. Increased volume of genetic testing in routine practice will also highlight the need for improved physician counseling skills. Thus, family physicians have a moral obligation to counsel their patients about the practical implications of the new technology in addition to appropriate medical issues. Most important, these new genetic tests have far-reaching implications for the future of patients' lives in ways that transcend their medical status.

INSURANCE IMPLICATIONS FOR PATIENTS

Physicians engaged in family practice must also be aware that the likely proliferation of genetic information about their patients has significant potential to harm patients' ability to obtain insurance, including health, life, and disability income coverage. The critical components of these issues are the use and the potential for negligent handling or abuse of medical records containing genetic test results.[6,7] However, even proper use of medical information may also have serious implications for insurance and employment.[6,7] Although insurers presently obtain genetic information from family histories, the predictive value of such information in most cases is not sufficiently high to serve as a basis for underwriting decisions. The new understandings generated by the HGI are likely to increase the amount and precision of predictive information. Since information of this type will, under present practice, be included in the medical record, insurers will seek access to data regarding genetic tests performed on particular patients applying for insurance.[6,7] Once obtained by insurers, such information could be used to deny coverage, charge higher rates, or establish exclusions from coverage for particular diseases.[6,7] Such genetic information will also be included in medical information databases, which share information and to which other insurers may obtain access.[6,7,9]

The insurance implications of genetic information will depend to a great extent on whether the disease identified is chronic or acute, the probable life expectancy of the patient, and the likely severity of symptoms. Insurer interest in genetic data will also depend on the type and value of the insurance policy the patient is seeking to buy. For example, a healthy person who has genetic tests showing a likelihood of developing a chronic and debilitating disease may be unable to purchase health and disability income insurance or might be offered these insurance policies only at unaffordable rates. However, such a person might still be able to purchase life insurance at an affordable premium. On the other hand, a currently healthy patient predicted to develop an acute and inevitably fatal disease early in life may be completely unable to purchase life insurance.

THE ESCALATING costs of employee health care benefits provide employers with incentives to avoid hiring employees whose risk of expensive claims will increase their costs or to devise ways to exclude or to limit coverage of such employees, at least for the condition(s) most likely to result in claims. Federal courts have ruled that the 65% of US employers who self-insure, instead of buying commercially insured health plans, are subject to no state regulatory restraints on limiting coverage for particular conditions. Several compa-

nies have limited coverage for claims related to human immunodeficiency virus or acquired immunodeficiency syndrome to unconscionably low caps, such as $5000 lifetime health benefits.[10] Thus, state insurance regulations cannot prevent similar cost-saving devices for many employees whose genetic test results indicate substantial risk of costly future health claims.

The Americans With Disabilities Act (ADA) offers some protection against employment discrimination based on disabilities, but its limited scope, exceptions, and enforcement difficulties leave job applicants and employees vulnerable to discrimination despite the law.[7] Although it restricts the ways employers are supposed to use medical test results, the ADA does not prevent employers from implementing such tests, including genetic tests, at the time of hiring or as part of voluntary wellness programs. In addition, the ADA does not prevent employers from obtaining genetic information or test results through the claims-filing process. The use of such information for making insurance coverage, exclusions, or pricing decisions is explicitly allowed by the ADA.[7] Moreover, as long as employers can provide a plausible business reason for their decisions, it is very difficult to prove that their decision was based on disability.[7] Thus, it appears to be relatively easy for employers to avoid the enforcement provisions of the ADA.

The ethical, legal, and social implications of the potential effects of genetic information on insurance consumers and providers are yet to be determined, but it is probable that the impact will be significant and that changes in insurance practice and regulation will ensue. The issues are exceedingly complex and are likely not amenable to a simple solution. Clearly, some of the problems for health insurance generated by expanding genetic technologies, ie, access to health care, would likely be ameliorated by adoption of federal legislation providing universal coverage with mandatory community rating. Community rating would establish uniform rates for geographic communities based on the aggregate risk experience and extending coverage without regard to individual variation from aggregate risk. Given the current US system of health care, however, the problems raised by widespread genetic testing persist.

ISSUES TO CONSIDER

Insurance

We argue that the possible adverse effects of unfavorable genetic test results on patients' and their families' insurance consequences are risks about which every reasonable person would want to be informed before giving consent for testing. A case example follows.

A 42-year-old man, whose wife and adolescent children are covered under his employer-sponsored health insurance plan, presents for a routine physical examination. The patient informs the physician that he is considering a job with a different firm in town whose health benefit plan is self-insurance. The medical chart notes that there is a family history of colon cancer, making the patient a reasonable candidate for a new test that detects genetic susceptibility to colon cancer.

Before deciding whether to undergo the genetic test for predisposition to colon cancer, the patient should consider not only the medical benefits the test result could afford him, such as preventive measures or earlier detection and treatment, but also the risk that his potential new employer may exclude him for coverage of colon cancer by classifying his predisposition as a preexisting condition.

In view of the way some companies have evaded coverage of acquired immunodeficiency syndrome claims, it is not inconceivable that an employer who learns of the patient's genetic test result may look for other plausible ruses to release him or to discourage him from continuing employment to avoid the risk of high claims he represents. In light of the potentially serious insurance consequences of the patient's genetic test results, he should be informed of these possibilities before deciding whether to undergo the test or when to schedule the test so as to minimize the risk that it will affect insurance coverage for him or his family. Although his physician may believe that compelling medical reasons exist for him to have the test, the possibility cannot be ignored that the test will threaten his access to precisely the medical care for which the test may indicate a need. With such high stakes, the patient must make this difficult choice fully informed of its potential consequences.

Emotional Impact and the Need for Counseling

External factors affecting a moral analysis of disclosure also include the potential psychological effects of disclosure on patients' lives. Even if less than certain, predictions of one's possible long-term future health status may be especially threatening information that requires particular sensitivity on the part of the disclosing health professional. Some patients may not want to know such information, and others who initially think that they desire such knowledge may change their minds after careful consideration of the consequences. Thus, a threshold issue in disclosure is a predisclosure discussion of ways that genetic information may affect patients' lives psychologically and socially, as well as economically. Such discussions are a routine component of genetic counseling as currently practiced. Some family physicians may not have the requisite skills or access to genetic counselors to assist their patients in dealing with all crucial aspects of the decision to undergo genetic testing.

Case 1

A newly married couple—a 24-year-old man and his 22-year-old wife—come to the family practice clinic to discuss their plans to have children. There is an extensive family history of cystic fibrosis. The physician suggests that the patients have genetic tests for cystic fibrosis. The husband agrees but the wife adamantly refuses, saying "I just don't want to know." The physician's and husband's attempts at persuasion are ineffective. The wife reasons that the emotional consequences of such knowledge would be too burdensome on her marriage and her potential children's future.

In this case, the 22-year-old wife is initially certain that she does not want to know about her genetic profile. This should not rule out genetic counseling in which she is presented with information regarding the relative benefits and burdens of testing. However, she apparently remains adamant and has expressed rational reasons for refusing testing that may be in accord with her values. Under such circumstances, it is doubtful whether the requisite moral standard of voluntariness for informed consent could be met. Many patients will not be as certain as she. In such cases, physicians should be prepared to offer counseling that presents information regarding genetic testing in as neutral a manner as possible in keeping with health promotion goals. Any attempts by the physician to persuade a patient to decide differently must avoid coercion and should focus on efforts to ascertain whether the patient's values are truly being furthered by the decision or whether he or she is reacting precipitously under the stress of circumstances. An appropriate method of pursuing such goals seems to be to provide general screening programs in family practice settings (when such screening becomes the standard of care) that offer an option for patients who simply "don't want to know" to refuse testing after appropriate discussion. Such an approach would preserve health promotion goals without compromising the moral interests of patients with conscientious objections to acquiring genetic information.

Case 2

A 36-year-old married woman presents for an initial visit at a family practice clinic requesting a recently developed genetic test for colon cancer that has been widely publicized in the media. She states that she has "never been to a doctor before," that she has a family history of cancer, and that she must know what are her "chances of dying from cancer." She offers a brief family history, refuses pretest genetic counseling and a complete physical examination, and says to the physician, "I want to know as soon as possible, so just call me on the phone when the results are in."

This case is a very likely scenario if genetic tests continue to attract more media attention. Increased publicity of developments in genetic testing may produce large numbers of persons seeking tests in first-time medical encounters who are unaware of the potential consequences to themselves and their families, and of the limited predictive value of genetic testing. This case is an excellent example of ways that the general public may misunderstand issues about genetic testing and highlights the need for physicians to augment their knowledge and skills regarding this sensitive area of patient care. Moreover, informing patients of the results of genetic testing should never be done by telephone because immediate counseling for emotional support and explanation will be required if results are positive. In this case, the physician must explain to the woman, in terms understandable by laypersons, that variable expressivity and penetrance mean that he or she cannot tell her with certainty when, or even whether, she will develop cancer even if her test is positive. This case also highlights the necessity of personal pretest genetic counseling in all cases. At present, we find no record of specific resources available to assist family physicians in augmenting their counseling skills for genetic screening. We recommend that such programs be instituted by organizations conducting continuing medical education.

Handling Genetic Information in Family Practice

Confidentiality between physician and patient prohibits disclosure of medical information, including genetic information, to those not authorized by the patient or by law. The sensitive nature of genetic information may require clinicians to adopt a higher standard of protection for such information than that provided by the standard medical chart. Thus, family physicians should use extreme caution when disclosing genetic information about their patients. An appropriate level of protection for such information may require special educational programs, as well as stringent record keeping and disclosure policies and practices by family physicians and their staffs. A case example follows.

A 28-year-old woman and her 32-year-old sister are patients of the same physician. Their mother died at age 38 years of breast cancer. Their physician recommended that both sisters undergo a recently developed genetic test for breast cancer. The younger sister's test was positive, and she requested that neither the test nor the result be disclosed, not even to her family. On learning the results of the younger sister's test, the physician again urged the older sibling to have the genetic test done, but she declined. Although the physician did not disclose to the older sibling her sister's positive test results, he did note in her chart that this recommendation was based on her mother's breast cancer and her sister's positive test. The test has not been performed.

Now, the older sister has applied for a life insurance policy and the physician's office has received a request for her chart from a mutual life insurance company. A signed consent form is included. It is routine practice in the office to respond by sending a complete copy of the patient's chart.

Although a prudent concern for liability warrants the physician's inclusion of his *recommendation* that the older sister have the genetic test for predisposition to breast cancer, his inclusion of her sister's *test result* is inappropriate, since the older sister may obtain her chart and see the note about her sister's positive test result. Moreover, the younger sister's positive test result will be inappropriately disclosed to the insurance company when the record is released, which may adversely affect the older sister's coverage. The implications for other family members of a patient's genetic test results require health care providers to devote great care and attention to the documentation and disclosure of genetic information. This problem raises the specter of circumstances that pit one family member's genetic information and interests against the interests of another family member—a dilemma that runs counter to the traditional model of family practice as providing care for the family unit. Current insurance practices thus present a challenge for the continuation of family medicine as a holistic practice. Family practitioners should engage in informed debate about this issue and respond accordingly.

CONCLUSION

During the next decade, many new genetic tests for common disorders will be incorporated into the routine practice of family physicians. As this occurs, the standard of care will rise accordingly. In such circumstances, physicians engaged in family practice may acquire an obligation to inform patients routinely about genetic risks and the availability of genetic tests. Increased use of genetic tests could oblige physicians to monitor laboratory procedures for accuracy and selection of particular tests. Since family practitioners emphasize preventive efforts and health promotion, the professional standard may change rapidly. Thus, family physicians may find themselves on the cutting edge, medically and morally, with respect to developments in the application of genetic information. The professional role of the family practitioner as an advocate of health screening tools may have to be redefined in response to the problems of potentially restricted access to health insurance and employment and the negative implications for the mental health of patients who do not desire genetic information about themselves. When genetic test results could potentially leave patients without insurance or employment, universal genetic screening in family practice settings must be accompanied by a rigorous informed consent process that explains the potential implications of the uses of test results. Even universal screening should have a "conscience clause," allowing those who are unwilling to learn their genetic profile to decline testing. In the absence of such practices, the costs of unauthorized or negligent disclosure of genetic information could be high for patients and physicians.

In summary, it is clear that the HGI presents dramatic new challenges for health professionals and policy makers. Practitioners of family medicine will soon have large numbers of new preventive tools that may improve the health of patients and raise the usual standard of care. Accompanying this expanding genetic technology, however, will be increased problems of confidentiality of records and informed consent for testing. Family physicians should be prepared to address these ethical issues within their own practices and should take the lead in developing new practical solutions to these emerging dilemmas.

Accepted for publication September 8, 1993.

This work was supported by grant HG00402 from the US Public Health Service, National Institutes of Health, Bethesda, Md.

Reprints not available.

REFERENCES

1. Council on Ethical and Judicial Affairs, American Medical Association. Use of genetic testing by employers. *JAMA.* 1991;266:1827-1830.
2. Juengst ET. The Human Genome Project and bioethics. *Kennedy Inst Ethics J.* 1991;1:71-74.
3. Rogers JC, Rohrbaugh M. The SAGE-PAGE trial: do family genograms make a difference? *J Am Board Fam Pract.* 1991;4:319-326.
4. Whittaker LA. The implications of the Human Genome Project for family practice. *J Fam Pract.* 1992;35:294-301.
5. Gilbert W. DNA sequencing, today and tomorrow. *Hosp Pract.* 1991;26:129-138.
6. Moseley R, McCrary SV, Allen WL, et al. *The Ethical, Legal, and Social Implications of the Human Genome Initiative for Health Insurance: Policy Analysis and Recommendations.* Gainesville, Fla: The Human Genome Insurance Project; 1993.
7. Ostrer H, Allen WL, Crandall LA, et al. Insurance and genetic testing: where are we now? *Am J Hum Genet.* 1993;52:565-577.
8. Jonsen AR, Siegler M, Winslade WJ. *Clinical Ethics.* 2nd ed. New York, NY: Macmillan Publishing Co Inc; 1986:61-65.
9. Kratka J. *For Their Eyes Only: The Insurance Industry and Consumer Privacy.* Boston: Massachusetts Public Interest Research Group; 1990.
10. *McGann v H & H Music,* 946 F2d 401 (5th Cir 1991), *cert denied,* 61 USLW 3352 (1992).