Genetic Testing: For Whose Benefit is it Provided?

by Michael L. Begleiter

Human genetics is the study of variation in man. Medical genetics concerns itself with the application of hereditary principles to the practice of medicine. While the basic principles of genetics have been known for 125 years, the application of these principles to medicine goes back but thirty years.

The era of medical genetics began in 1959 with the description of the chromosomal etiology of Down syndrome. The subsequent thirty years have seen an astounding accumulation of information concerning more than 4,000 genetic disorders. Most of this data has been gathered through the study of families and statistical analysis of how traits are transmitted from generation to generation.

Beginning in the early 1980s powerful new tools for studying genes were developed. Radioactive segments of DNA which are complementary to specific sequences of DNA can be used to determine if a patient has that gene (DNA sequence). These radioactive DNA sequences (DNA probes) can be used in two ways: (1) to directly detect the defect in a gene, or (2) to identify a unique segment of DNA which lies very near the gene in question. DNA probes are used to identify individuals who are carriers for specific genetic diseases and therefore at risk to produce affected children. The probes can be used in prenatal diagnosis to predict the genetic status of a fetus for a specific trait. DNA probes can also be used to diagnose disease states long before symptoms develop.

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Current recombinant DNA technology would, in appropriate families, permit the diagnosis of Huntington's disease (a degenerative disease of the nervous system with onset in the fourth or fifth decade of life) at any age. Predictive genetic screening opens the way to avoiding human suffering, but creates the potential for abuse in how our information will be used. It is with these concerns in mind that Neil Holtzman has written *Proceed with Caution: Predicting Genetic Risks in the Recombinant DNA Era* (The Johns Hopkins University Press, 1989).

Holtzman advises caution because the information gained through genetic testing can be misused. He cites three examples of abuses:

(1) Early in this century a eugenics movement arose in the United States. Positive eugenicists sought to encourage reproduction between individuals with desirable traits. Negative eugenicists discouraged the sick, mentally retarded and disabled from childbearing. Much of the research done in this movement was of poor quality. "Genetic disorders" such as "violent temper," "wandering trait," "criminality" and "feeblemindedness" were described. Eugenicists enjoyed popularity among some of the American public and a number of states passed laws permitting sterilization of individuals with a variety of traits (including criminality and feeblemindedness) for which there was no good evidence of inheritance. In addition, the eugenics movement produced "scientific" evidence that Americans of northern and central European origin were more productive citizens than individuals from southern Europe and Asia. This led to quotas which curtailed immigration from southern Europe and Asia.

(2) The commercialization of high technology testing has already created a situation where information is gathered without participation by individuals who are adequately trained to interpret and follow up on the findings. During the Carter presidency biotechnology companies approached the Food & Drug Administration about marketing an alpha fetoprotein test for the detection of neural tube defects (spina bifida and anencephaly) by testing blood from pregnant women. These requests were denied because the FDA felt there was a strong possibility for termination of normal fetuses because the lay and medical communities had a poor understanding of the sensitivity and

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specificity of the test, and professionals were poorly prepared to provide definitive counseling and testing. The Reagan administration felt that restricting the sale of test kits would infringe on the physician's ability to practice medicine. We now find ourselves in a position where we are using a screening test which will identify 5% of all pregnant women as needing further evaluation and 2% of the 5% (1/1,000) as actually carrying a fetus with a neural tube defect. The test will not detect 1 of every 5 or 6 affected fetuses. The commercial availability of a profitable test has created a situation in which offering the test to pregnant women has become a standard of care even though we lack the appropriate number of trained individuals to provide counseling and follow-up. In addition, the testing creates anxiety for a large number of women while identifying serious problems in only a few. And, some women are provided reassurance when in fact the baby has a neural tube defect.

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(3) Laboratory diagnostic tools frequently are developed years before mechanisms for managing patients are available. Technology currently exists at the DNA level to identify cystic fibrosis and Duchenne muscular dystrophy in the unborn. Both disorders are lethal, with death occurring in the second or third decade of life. To date, no management techniques (drugs, diet, etc.) have been shown to alter significantly the outcome of either condition. Also, Huntington's disease and Alzheimer's disease are diagnosable by DNA technology years before any symptoms would be demonstrated. Clearly, some families will choose to be tested in order to prepare themselves for untreatable diseases. Others will choose to avoid conception rather than risk producing a child with a life-limiting illness. Still others will choose to abort pregnancies with affected children as a way of avoiding tragedy. Most genetics workers have no difficulty providing this type of information for individuals to use as they see fit. But what about third party interests? Should health and life insurance companies be given access to this information? And if so, should they use it to deny coverage? If employers are advised of the results, should they be permitted to deny health care coverage or employment to individuals who might significantly increase the financial liability of the company-funded health insurance plan?

Dr. Holtzman has written an important book, but not one that is easily read. The first three chapters provide a clear and concise summary of the basic principles of human genetics and the application of these concepts to human diseases. Chapter four is an excellent overview of DNA testing techniques. The reward to the uninitiated for struggling through these chapters is a better understanding of the issues addressed in the rest of the book.

In discussing genetic testing in health care, the author touches on a number of difficult issues. He reviews the concepts of validity and reliability of testing systems. Does the test actually identify the disorder it is supposed to find? How often is it incorrect? How well do families understand results conveyed in probabilistic terms?

Should health and life insurance companies be given access to genetic information? Will the insurance industry view genetic screening as a way to avoid costs?

Most follow-up studies of families seen for genetic counseling suggest that understanding is limited to subjective interpretation such as high or low risk. Given the shortage of individuals trained in human genetics, the likelihood seems small of improving the degree of understanding while expanding the testing being performed.

Ultimately, the decision to use genetic testing will be hampered by the lack of understanding by most physicians and health care professionals. Companies marketing these tests will nevertheless target physicians and consumers and thereby speed the adoption of testing. We may find ourselves in a situation where health insurance companies will view genetic screening as a means of cost avoidance. Recently, a couple in another state had prenatal diagnosis for cystic fibrosis. The child was affected and their decision was to continue the pregnancy. The health insurance carrier notified them that the child, if born, would not be covered under the parents' health policy. Ultimately, after much discussion, the insurance company backed down. This frightening story demonstrates the potential

strength of the insurance industry to control our health care and our genetic destiny. Although this situation was resolved in a reasonable fashion, the reality of our situation is that the number of health care dollars available is limited. The Oregon state Medicaid system has taken the first steps in legislating this type of behavior. They have constructed a prioritized list of health problems and will provide care only for a limited number of these difficulties. The inequity of such a system is astounding. Only low-income families who require Medicaid assistance will be limited. Families with commercial health insurance will still be covered for the listed conditions. The application of these financial restraints on the utilization of genetic testing could create a most distressing situation.

From an ethical perspective, perhaps the most significant challenge is to guarantee autonomy. Each person must have the right to choose whether or not to participate in predictive testing.

The clinical genetics service is often viewed as providing society with a means for decreasing the load of genetic diseases. However, not only are these services unable to significantly lower the incidence of genetic disease, but numerous plant and animal models have demonstrated the need for genetic diversity, even when that diversity produces undesirable effects. The whole model of evolution requires a preexisting diversity when environmental stresses make one genetic type more favorable than another. The best example in humans is sickle cell disease. The child affected with this disorder is significantly debilitated and rarely survives to reproduce. Yet the normal carrier is immune to malaria. If one looks at a world map with markings for areas of high incidence of sickle cell disease it will overlap a similar map which identifies areas with high incidence of malaria. The carriers of sickle cell trait are immune to malaria and therefore survive to reproduce. The children with sickle cell disease succumb to their genetic problem prior to reproductive age. Those individuals free of the gene have reduced survival and reproduction because of their susceptibility to malaria. Nature has created a situation in which being at risk to produce a child with a life threatening genetic problem creates survival advantages over not facing that risk.

There are solutions to the problems presented. Dr. Holtzman proposes an expansion of genetics training for physicians and other health care workers. At the present time, genetics education in American and Canadian medical schools is woefully inadequate. A 1988 survey of 140 medical schools, conducted by the American Society of Human Genetics, considered 47% of schools to have nonexistent or poor human genetics teaching. Only 21% of schools were providing good or excellent human genetics education. Even in this era of increasing knowledge about genetic diseases, most physicians apparently enter medical practice without an adequate understanding of the role of genetics in the cause and pathogenesis of human disease. This problem could be quickly solved by providing adequate instruction in genetics. Dr. Holtzman also strongly suggests that the public needs to become educated about issues of genetic screening and testing. (It is interesting to note that the July 1990 issue of *Consumers' Report* featured a cover story on genetic screening.)

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Activities aimed at achieving this goal have been stated. The last decade has seen an expansion of genetics instruction beginning at the elementary school level and continuing through high school. At least one federally funded project is training teachers in human genetics. The plan is for each of these individuals to serve as lead teachers in their school districts to help their colleagues develop the knowledge necessary to teach about this rapidly changing area.

Perhaps the most crucial issue from an ethical perspective is to guarantee autonomy. Each person must have the right to choose whether or not to participate in predictive testing. Genetic testing presents some unique problems not encountered in other areas of medicine. Frequently, in order for one person to be tested, samples and information must be obtained from other family members. Without the cooperation of those who may not wish to be tested, help cannot be offered. Sometimes the reluctance to participate is based on the fact that testing will reveal their genetic status. If providing information to the original consultant does not also define the hesitant family members, then often they will comply. But what about identical twins? By definition, any information we learn about one twin is the same for the second

twin. In such situations both twins must agree or the testing cannot be provided.

The testing systems in use must be improved, and validity and reliability guaranteed. In order to insure personal freedom, strict control of genetic testing by insurers and employers is a must. Finally, society must find a way to guarantee the confidentiality of any laboratory test performed. If we can find a way to meet these recommendations, then DNA testing will be a safe, accurate and reasonable service to offer families.♦

A Word of Thanks

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