As new tests are developed, it will be important to have discussions with families about the implications of genetic testing for cardiovascular disease. Families should be made aware of the benefits and limitations of testing before they proceed. There must be appropriate follow-up mechanisms for those who have positive test results to ensure that both they and their family members are managed appropriately. ■

NOTES

1. American Heart Association, *Heart Disease and Stroke Statistics—2005 Update,* American Heart Association, Dallas, 2005, p. 3.
2. American Heart Association, p. 24.
3. A. A. Wilde and C. R. Bezzina, "Genetics of Cardiac Arrhythmias," *Heart,* vol. 91, no. 10, October 2005, pp. 1,352-1,358.
4. B. J. Maron, J. G. Seidman, and C. E. Seidman, "Proposal for Contemporary Screening Strategies in Families With Hypertrophic Cardiomyopathy," *Journal of the American College of Cardiology,* vol. 44, no. 11, December 2004, pp. 2,125-2,132.
5. Maron, Seidman, and Seidman, p. 2,126.
6. American Heart Association, p. 10.
7. M. A. Nordlie, L. E. Wold, and R. A. Kloner, "Genetic Contributors toward Increased Risk for Ischemic Heart Disease," *Journal of Molecular and Cellular Cardiology,* vol. 39, no. 4, October, 2005, pp. 667-679.
8. Nordlie, Wold, and Kloner, p. 668.

CARDIOLOGY AND GENOMICS

AN ETHICAL VIEW

BY JAN C. HELLER, PhD; & MARIA WALLINGTON, MD

Dr. Heller is system director, theology and ethics, Providence Health & Services, Seattle; and Dr. Wallington, a pediatric cardiologist, is medical ethicist, Providence Health System Alaska, Anchorage, AK.

Jessie Hastings's article summarizes the increasing role that genetic research is playing in the diagnosis, treatment, and prevention of cardiovascular disease. In our own article, we discuss some of the ethical implications of this research, concentrating primarily on issues that patients and their families may confront. The wider, societal implications and the implications for access to health care are not discussed.

FRAMING THE PROBLEM

As the Human Genome Project (HGP) officially got under way in 1990, observers realized even then that the project was going to give rise to a wide array of ethical concerns. These concerns, it was thought, would arise primarily as a result of two predicted consequences of the project, namely, a rapidly growing "therapeutic gap" between the project's diagnostic findings and its therapeutic capabilities, on one hand, and, on the other, an "information overload" problem having to do with managing the enormous amounts of information generated by the project.

The "therapeutic gap" refers to that stage of the research and development process in which large numbers of diagnostic tests and screens would become available to detect and predict genetic diseases, while at the same time there would be few, if any, genetically based therapies available to treat those diseases. With some important qualifications that will be discussed below, it is safe to say that medical science is currently in this stage. We are discovering numerous genetic markers but have yet to develop any significant genetic therapies.*

The "information overload" problem refers to the sheer volume of information being generated by research efforts in genetics—by the HGP itself and then by ongoing research spun off by the project in public and private laboratories around the world—and to the rapidity with which this information is being moved from the research setting into the clinical setting. It is, in particular, the interaction of the therapeutic gap and the information overload problem that gives rise to most of the ethical implications around genetic testing and screening. Clinicians can at present and for the foreseeable future test for many, many more diseases than they can meaningfully treat.

Testing is not without merit, however, and cardiovascular disease may represent a possible exception to the generalization above, since many of its symptoms can be treated conventionally with surgery or drugs. Nevertheless, because of the multifactorial patterns of inheritance behind most cardiovascular diseases, it will probably be a

*Early observers hoped that this therapeutic gap would be short-lived, but it is likely to be with us for quite a while, for at least two reasons. First, genetic therapies per se have proven to be elusive. Second, the HGP's discovery that humans have far fewer genes than originally thought means that disease processes must be tracked to the interaction of genes and to gene projects, which is a far more complex undertaking than tracking single-gene defects.

long time before genetic treatments per se are developed that can cure or prevent them in a given individual. These background issues will thus give rise to a number of ethical concerns around genetic testing and treatment that will continue to have relevance for those who have or might develop cardiovascular disease.

Issues in Testing and Treatment

Even if we discount the problems of false positives and false negatives, genetic tests generally provide patients and providers with probabilistic results at best. Most genetic tests are not like chromosome deletions or additions, which provide a clear answer to the question of whether or not a person has a genetic disease. In some cases, if the test is positive, it will confirm a suspected clinical diagnosis; most often, however, the test will be used to tell the individual that he or she has a certain *risk* of developing a given disease.

Even if we discount the problems of false positives and false negatives, genetic tests generally provide probabilistic results at best.

The problem becomes one of interpretation. If the risk is very low, it may be possible to discount it. But tests that indicate low risks—or even produce negative results—cannot entirely rule out the possibility that the person tested will *eventually* develop the disease (because of the possibility of as yet unrecognized additional genetic abnormalities). If the disease in question is multifactorial (that is, resulting from a combination of genetic, environmental, and behavioral factors), as is the case with most cardiovascular diseases, it can be very hard to interpret the test's results. An adequate interpretation usually requires genetic counseling. And even when such counseling is available, it may leave patients with highly ambiguous choices or significant misunderstanding about possible interventions or lifestyle changes.

Also, different patients perceive risk differently, and, when advised to change their lifestyle to minimize the risk of developing a cardiovascular disease, they may understand those changes to entail very different implications. Consider a hypothetical example: A patient has a family history of myocardial infarctions but has had no prior genetic testing. Having been tested, she learns that she has a gene that suggests a 20 percent chance of developing hypertension and a gene that is associated 55 percent of the time with diabetes. Her other tests are normal, and none of her relatives has diabetes. She is advised to maintain a normal weight, exercise regularly, reduce the salt in her diet, and have her blood pressure and blood sugar tested periodically.

The patient will need to understand the importance of preventing diabetes, since it will certainly add to her risk of heart disease if it occurs. She will also need to understand that the genetic contributions, if any, to her family's heart problems have not been documented, so it may be that she is at risk for heart problems even though the other genetic tests she had were negative. If she believes that she is not really at risk for diabetes (because no one in her family has it) or that she is not at risk for heart disease (because the test was normal), she may not be inclined to follow the recommendations.

Individual genetic testing also has implications for the families of the individuals being tested. It is often very difficult for a family member to keep the results of his or her tests confidential and refrain from sharing them with other family members. Sometimes the symptoms of the disease in question cannot be hidden in any case, and sometimes the individual will want to share information in the hope of protecting or warning other family members. If that occurs, the other family members may learn information about themselves that is neither requested nor desired. Or they may experience social pressure from their families to be tested when, left to themselves, they would prefer not to know the test results. Further, should they agree to genetic testing, it may reveal unexpected information about family members that has long been secret or even unknown, such as paternity or adoptive status. These results can disrupt long-established family relationships in ways that can have permanently lasting effects.

Within families that are willing to be tested, there can also be questions about when to inform certain family members about the results of the test. Testing minors raises such questions, and the decisions families make in these cases may differ according to the age of the minor, the family's cultural or ethnic background, and, perhaps most importantly, whether the knowledge can be used to prevent or treat the disease in question. For example, long QT syndrome can result in sudden death. Unfortunately, however, an EKG of a person with the syndrome may not be abnormal, so the diagnosis can be missed. In a family with a history of long QT, a genetic test developed for the family's lesion would allow early detection and the initiation of preventive measures, even in an infant.

Finally, individuals and families are often concerned about third-party access to their test results. They may fear that insurance companies

or employers will use the information in ways that will adversely affect those being tested. For example, if a family with hypertrophic myocardiopathy had a marker that revealed, say, a 60 percent chance of developing the clinical manifestations of the disorder, a family member with the gene but no clinical findings might still have trouble being accepted for a job requiring hard physical labor, because of a misunderstanding about how slowly the disease develops. He might also not be allowed into the military, either because of concerns about long-term return on the training cost for that person or the expected later costs of treatment, should the disease occur.

Prevention-Related Issues

In discussions of genetic diseases, the notion of disease *prevention* must always be qualified. One use of the term refers to preventing an identified individual from developing symptoms of a genetically related disease for which the individual is predisposed or is expected to develop if untreated. In this sense, the notion of prevention slides easily into notions of testing and treatment. Thus, for example, if the genes for encoding the protein components of the cardiac sarcomeres, which are affected in hypertrophic cardiomyopathy, are identified and the discovery results in a medical treatment to supply the needed components to an affected individual, those components could either prevent the disease from developing or treat it once the disease did develop.

The second way prevention is used in the context of genetic diseases refers to preventing individuals from being born with a genetic makeup that leads to a given disease. Until medical science develops genetic-based treatments that allow individuals to have their disease genes corrected, or have the products of their disease genes suppressed, this second type of prevention will be the most effective way of keeping certain diseases from developing. Unfortunately, this is a difficult lesson to learn for the parents who have just given birth to their first affected child—which is the way most parents learn that they may be carrying certain disease genes themselves. Parents who want to prevent the disease from occurring in a future child have a limited number of options available to them, most of which are morally problematic for many parents and perhaps doubly so for conscientious Catholics.[1]

Such parents can choose to prevent future conceptions by using a variety of family planning approaches, most of which are not approved by the Catholic Church. If they do not choose this option, and want to have additional children of their own, they have other options. They can play a sort of genetic roulette and simply hope that the next child will not be affected. Doing so may be an ethically defensible choice, depending on the odds that the parents will pass their disease genes on to their next child; the odds that the symptoms of the disease will appear; and on the expected seriousness of the disease in question, should their future child be affected. Also, if an affected child is born and if the disease in question is a multifactorial type, it may be possible to monitor the child's development and environment in such a way that the disease's adverse effects are minimized.

For those families not strictly following Catholic moral teachings, other options will exist. One is to pursue conception, perform an in utero diagnosis for the genetic condition in question, and consider abortion if the unborn child is affected. In vitro fertilization and preimplantation genetic diagnosis, with the selective transfer of the unaffected embryos, is yet another option. Finally, parents can seek a genetic contribution from outside the relationship as a way of preventing the birth of an affected child.

New Technology, Old Issues

These ethical implications—only some of which we have discussed here—highlight something that ethicists working in genetics have recognized for some time: There are few, if any, novel ethical issues raised by the scientific discoveries and technological developments in genetics, even though these developments continue to occur at a dizzying pace. Of course, the fact that the ethical implications of this research have been anticipated by ethicists will not necessarily make them easier for individual patients and providers to face, but it does mean that we as a society should have a better sense of how to respond to them today than we could have done, say, 15 years ago, when they began to be studied in earnest under the HGP's Ethical, Legal, and Social Implications program.*

*The U.S. Department of Energy and the National Institutes of Health dedicated from 3 percent to 5 percent of the HGP budget to the study of associated ethical, legal, and social issues. For more information, go to www.ornl.gov/sci/techresources/Human_Genome/elsi/elsi.shtml.

NOTE

1. For a more comprehensive discussion of Catholic teachings on genetic testing than we have space to provide here, see an excellent article by Carol A. Tauer, PhD: "Obstetrics and Pediatrics: An Ethical View," *Health Progress*, July-August 2005, pp. 13-18.

BIBLIOGRAPHY

Heller, Jan Christian, *Human Genome Research and the Challenge of Contingent Future Persons: Toward an Impersonal Theocentric Approach to Value*, Creighton University Press, Omaha, 1996.

White, Mary T., "The Many Faces of Genetic Testing," in David H. Smith and Cynthia B. Cohen, eds., *A Christian Response to the New Genetics: Relgious, Ethical, and Social Issues*, Rowman & Littlefield, New York City, 2003, pp. 27-52.