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Letter to the Editor

Ethical Standards in Molecular Medicine: Will Anyone Care What Medical Geneticists Have to Say?

To the Editor:

With your permission, I am writing not to comment on a previous AJMG article, but to call the attention of clinical geneticists to developments in clinical medicine that may profoundly affect their genetic practices and the nature of the services provided to future patients seeking genetics services.

In October 1995, at a London conference, Dr. Patricia Jacobs of the Wessex Regional Genetics Laboratory, Salisbury, England, made the following observation [Dickson, 1995]:

> People assume that medical schools provide an excellent genetics education for the next generation of doctors. . . . Unfortunately, this is far from true; few medical schools incorporate genetics teaching throughout the curriculum. . . . As a result, we are going to have another generation of doctors who will be unable to cope with the so-called genetics revolution, and this also needs to be addressed urgently.

Evaluating U.S. primary care physicians in the early 1990s, Dr. Neil Holtzman of Johns Hopkins University and his colleagues found similar deficiencies and argued for greater emphasis on genetics at all levels of medical education and training to reduce the chance of physician error [Hofman et al., 1993]. Holtzman also found that nongeneticist physicians were more likely to be directive in counseling than geneticists [Geller et al., 1993; Holtzman, 1993]. Dr. Hiraku Takebe of the Faculty of Medicine of Kyoto University has observed the same inadequacy of genetics training in Japanese medical schools [Takebe, 1994].

Molecular medicine (or, as it is sometimes called, genetic medicine) incorporates the use of DNA-based technology for the diagnosis, prevention, and treatment of human diseases. It often utilizes postmendelian genetics (gene × gene × environmental cofactor(s)) in its application and theory. Molecular genetics, of course, plays a significant role in this new discipline, and as the Australian geneticist, Dr. David Danks, has written [Danks, 1993]:

> We are only just starting to see the fruits of this new discipline in the clinical practice of medicine, but it is clear that the benefits are going to be extensive in the coming years. Molecular genetics is here to stay as a major part of medicine and those who have not yet come to grips with this new science should do so because it will not go away.

Of course, it is rare to find a new technology whose use does not create any ethical or moral concerns, and molecular medicine is no exception in that regard. Many trees have been sacrificed to discuss ethical concerns about the control and confidentiality of genetic testing; the potential and actual discrimination by employers, insurers, and others against people with a family history of (or test results showing a predisposition for) genetic disease; fairer access to genetic services; the perceived dangers of "germline" vs. "somatic" gene therapy as well as gene therapy for trait enhancement—to mention but a few topics.

I wish to pose the question of what influence medical geneticists will have on the ethical discourse of molecular medicine. Put another way, given that genetics plays so crucial a role in molecular medicine and that the phrases "clinical genetics" and "medical genetics" are synonymous, wouldn't it be natural to assume that medical geneticists and genetic counselors or associates would be the resource to whom those in molecular medicine would turn for advice on ethical questions? Who else has had the clinical experience in dealing with genetic issues of great complexity?

Perhaps that will be the eventual outcome over the coming decades. Perhaps the College will be renamed the American College of Medical Genetics and Molecular Medicine. Without attempting to be rigorously scientific, however, we might ask what evidence exists to date of any such interest not only on the part of clinicians generally, but also on the part of the biotechnology companies who largely will supply these molecular tools.

Since its formation in 1948, the American Society of Human Genetics has seen itself as the voice of the United States human genetics community in articulating public policy positions with regard to ethical issues involving genetics. This role is now more complex, as the National Society of Genetic Counselors, the International Society of Nurses in Genetics, and the College have come into existence with equal interest in addressing these issues. For that reason, annual meetings are now being held to coordinate the agendas of the various social issues committees of these organiza-

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tions. Yet, I think we can agree that the ASHG has taken the lead in issuing the most visible public pronouncements to date, and for that reason, I will examine some of the Society's official pronouncements on issues relevant to molecular medicine for any signs of this possible interest in drawing from the experience and wisdom of medical genetics.

A 1994 Society statement deals with genetic testing for breast and ovarian cancer prediction. It urges that testing for *BRCA1* gene mutations, associated with early-onset breast and ovarian cancer, be offered initially on an investigational basis only by clinical geneticists and with careful counseling, and that testing be limited to "members of specific types of families with strong breast-ovarian cancer histories." Genetic counseling, the statement says, "should be provided by a health care professional who has a therapeutic relationship with the patient and/or family, to insure the availability of a permanent source of accurate information that is not limited by the duration of research funding."

What is the likelihood that such recommendations will be followed, particularly by for-profit laboratories and biotechnology companies? We do not yet know under what circumstances the company licensed by Myriad Genetics to develop a test kit, Hybritech Inc., plans to distribute such kits once they are commercially available and FDA-approved. We do, however, know that Oncor Inc., a biotechnology company in Maryland, was reported in late 1993 to have launched a genetic testing service, the Hereditary Cancer Consulting Service, that uses a software program to produce a family pedigree and blood samples to search for markers for gene mutations. This service will be made available to primary care physicians, and Oncor's chairman, Stephen Turner, said that "the company would provide genetic counseling by telephone if physicians request it. But other social and ethical questions surrounding genetic testing, such as confidentiality, will be left to the physician and patient to work out, much the way AIDS testing is now, Mr. Turner says" [Tanouye, 1993].

Similarly, the Genetics and IVF Institute of Fairfax, Virginia, in early 1996 advertised on the Internet and in major U.S. newspapers that it is offering screening for a mutation in the breast cancer gene, *BRCA1*, despite guidelines that urge that such testing "should be used only in the research setting until the true risk of the mutation is determined and appropriate counselling and intervention guidelines established" [McCarthy, 1996].

It has been estimated that over the next decade, the use of gene probes in molecular diagnostics will grow "from its current market of about $78 million to a market of $600 million in 2000 and $2 billion in 2004, implying 35% compounded annual growth" [Gene probes. . . , 1994]. In a commercial market of that size, is it likely that for-profit laboratories and companies will restrict access to testing by requiring the services of clinical geneticists and genetic counselors who can sit face-to-face with the patient?

Similarly, the Society issued two statements on cystic fibrosis carrier screening, first in 1990 [ASHG Statement on CF Screening, 1990] and then again in 1992 [Statement of the ASHG on CF Carrier Screening, 1992]. Both statements recommended against population screening for CF until the rate of CF carrier detection improves, and that such screening, as done when indicated by a positive family history, should be strictly voluntary. This makes good sense, of course, given the hundreds of mutations found in the *CF* gene on chromosome 7.

Nevertheless, Prof. Norman Fost has pointed out in lectures that for years the states of Colorado and Wyoming have been conducting CF population screening on newborns (measuring blood immunoreactive trypsinogen [IRT] levels). The Wisconsin program now uses a 2-tiered method (IRT and mutation analysis) which does pick up some carriers. Prof. Fost's point in mentioning such legally mandated population screening is that 8 years into a controlled study of such screening and therapy being done in Wisconsin, no benefits have been found when compared to unscreened controls. My more modest reason for mentioning these efforts is that they ignore the Society's recommendation that such screening not be done, and if done, on a voluntary basis.

Similarly, the Society's statement in 1987 on maternal serum α-fetoprotein screening programs [ASHG Ad Hoc Committee, 1987] urged that "MSAFP screening should be voluntary. The provider should indicate its availability, educate the patient about its potential, and allow the patient to make decisions concerning participation in screening and in consequent steps in the management of the pregnancy."

These recommendations did not keep the state of California (and perhaps other states and Canadian provinces) from coming as close to mandating MSAFP screening as they could without actually doing so by requiring written refusals by women not wishing such screening. Requiring written refusals is not the same as making the screening voluntary, but when a state has an interest in having such screening performed, these policy objectives may override the recommendations of others, much in the same way as commercial companies may find it less expensive and more efficient to offer genetic testing without requiring or using genetic counselors or clinical geneticists in the role of primary providers.

Permit me to insert a caveat at this point, however. Such random observations may underestimate the influence of the Society's recommendations because they don't confirm those instances in which companies, governments, clinics, or providers have been positively influenced by the Society's recommendations and have altered their behavior accordingly. Thus, I don't want to undervalue the possible influence that such statements may have had, nor do I think the issuance of such statements should end.

It is interesting to speculate (and it is only speculation and not wishful thinking) about the possible influence of clinical geneticists on the future of molecular medicine. To the degree that physicians in primary care practices in medicine, pediatrics, and obstetrics begin to use diagnostic probes and gene transfer therapies in

their routine practice over the next five decades, what is the likelihood that these clinicians will turn to the recently recognized medical specialty of medical genetics for advice on handling ethical issues that are quite similar to concerns with which clinical geneticists have struggled for many years?

This potential for either influence or professional isolation suggests a possible joint role for the American Society of Human Genetics and the American College of Medical Genetics (and its affiliated genetics organizations, the National Society of Genetics Counselors and the International Society of Nurses in Genetics) in planning a role for clinical geneticists in the evolution of molecular medicine and molecular genetics. Educational programs, publications, and the training of genetics fellows and counselors or associates should (in my view) anticipate this paradigm shift in the practice of medicine.

A coordinated effort by these organizations might be undertaken to influence the development of ethical standards in molecular medicine in at least two specific directions: (1) examining existing codes of ethics in medical genetics and genetic counseling (such as those of the Canadian College of Medical Geneticists [Roy et al., 1989] and the National Society of Genetics Counselors, Inc. [National Society of Genetics Counselors, Inc., 1991]) to see if applicable ethical standards in molecular medicine might be fashioned; and (2) seeking to develop liaison relationships with and to sensitize the ethics committees of major U.S. primary care societies and national medical organizations on these issues (e.g., the American Academy of Family Physicians, the American Academy of Pediatrics, the American College of Obstetricians and Gynecologists, the American College of Physicians, and the American Medical Association).

With the diminishing role in managed care for specialists of all kinds, it may be seen as undesirable to have medical geneticists of the future relegated only to classic mendelian genetic diseases that no one else wants to see. Clearly, there is no evidence of a certainty that medical geneticists and their associates will dictate or even heavily influence the field of molecular medicine if the field is left to evolve naturally.

Writing in the nineteenth century, Dr. Oliver Wendell Holmes, in his essay, "Currents and Counter-Currents in Medical Science," observed that "[t]he truth is, that medicine, professedly founded on observation, is as sensitive to outside influences, political, religious, philosophical, imaginative, as is the barometer to the changes of atmospheric density" [Holmes, 1861]. Were he alive today, he might add financial and institutional influences to that list.

The science of molecular medicine is quite powerful and elegant, and will become even more so as new techniques emerge in the future, but may easily overlook the potential contributions to the solution of ethical concerns that medical geneticists can offer based on their own professional experience. The ball, as they say, clearly lies in our court, and some might go so far as to say that the game is ours to lose.

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