Primary Care Clinicians and the Dilemmas of Genetic Testing

If even a fraction of the claims made about the impending impact of genetics on clinical practice came true, the clinical genetics services would be overwhelmed. We must not miss the opportunity to prepare primary care for the new genetics.
– Jon Emery and Susan Hayflick [1]

The Human Genome Project, Scientific Reality and Public Expectations.

There is little doubt that the sequencing of the human genome, announced on June 26th, 2000 by Francis Collins of the NIH and Craig Ventner, of Celera Genomics, represented one of the most significant achievements in the history of science. The formal announcement, which included both President Clinton and Prime Minister Tony Blair, crystallized the fact that after a half century of research, genetic knowledge had reached a critical mass and was now expected to transform our understanding of our biological selves.

Although the scientific achievement is unquestionable, the nature and degree of its impact on the current and future practice of medicine, is not clear. Some experts have predicted a rapid and profound revolution in medicine.[2] Others, even some geneticists, doubt that genetics will fundamentally change the nature of medical practice.[3]

While medical experts debate the impact of genetics on medicine, the public perception is that a significant change in medicine has already begun. *The Los Angeles Time*s, for example, called the recent advances in genetics, "official recognition that a new era in medicine had begun."[4] Healthcare providers are thus faced not only with the actual developments in genetic medicine, but also with powerful perceptions that the public has about the promises of genetic medicine.

The Role of the Primary Care Provider in Genetic Medicine

As primary care clinicians are becoming more conversant with the recent advances in genetics, the key issues that many are raising include: How will genetics impact my daily practice? What kinds of questions will patients be asking about genetic medicine? What is the appropriate role of the primary care clinician in the overall delivery of genetic services? What kind of education do I need to effectively fulfill this role?

In a household survey of patients conducted by the American Medical Association, over 80% of those surveyed were confident that their primary care clinicians could

assess the risks of their developing a genetic disorder and could appropriately recommend genetic testing when indicated. About 74% were also confident that their primary care clinicians could correctly interpret the results of a genetic test.[5] Thus, the general public has a high level of confidence in their primary care clinicians and an equally high set of expectations when it comes to genetic medicine.

Two areas of genetic medicine are currently most relevant to primary care and are thus most likely to impact daily practice. They are:

1) Prediction of risk for adult onset disorders with a known genetic component, (familial breast and colorectal cancers, Huntington's Disease and others) based on family history and/or genetic testing.[6]

2) Assessment of reproductive risk by testing for common autosomal recessive conditions such as hemoglobinopathies, cystic fibrosis, and muscular dystrophy.[7]

For the near future, these issues will probably define the focus of genetic medicine in primary care. However, over the next several years, as genetic medicine becomes more pervasive, primary care clinicians are likely to become involved with:

- Testing for the genetic components of common disorders that have multi-factorial etiologies such as ischemic heart disease, asthma, or diabetes, and
- Identifying normal genetic variations that predict drug response and side effect profiles.[8]

With respect to these areas of genetic medicine, primary care practitioners will probably have specific roles within a collaborative healthcare team that includes genetic counselors, clinical geneticists, and others. With rare exception, the primary care clinician will have the closest relationship with the patient and is therefore most likely to know the patient's medical history, family medical history, and attitudes towards healthcare.[9] In light of this, Jon Emery and Susan Hayflick have suggested that in the future, primary care clinicians might take on the following:[10]

- Identifying individuals who may benefit from genetic services.
- Recognizing physical and historical features of genetic disorders.
- Providing basic genetic information, and counseling to facilitate informed decision-making and informed consent for genetic testing and other genetic services.
- Recognizing the special psychosocial needs of a family in which a genetic disorder or susceptibility has been identified.

• Knowing the full range of genetic specialists available in one's area and when referral and collaboration are indicated.

• Collaborating with genetics specialists in managing patients with complex and rare genetic disorders.

These activities encompass what we might call the science and the art of genetic medicine.

The Science and the Art of Genetic Medicine

Grappling with the science of genetic medicine, while quite challenging, is not a unique problem. In all areas of medical research, knowledge is being produced at a daunting rate and keeping up with the advances, in the traditional sense of learning all the new material, has simply become impossible. However, utilizing this new knowledge in the best interests of patients is not only possible but it is a primary challenge in health care, as it transitions to an information-based model. To accomplish this, clinicians are increasingly using a few related strategies. There has been a shift from a focus on remembering information to a focus on judiciously applying information in the service of shared decision-making. This involves:

• Easy access to the relevant medical literature, (often electronic) and critical application of this knowledge to the case at hand.

• Formal and informal consultation with, and referral to medical specialists and other health care professionals who have specialized knowledge. In genetic medicine of course, this requires familiarity with the functions of genetic counselors, medical geneticists, and other specialists who may have genetic expertise regarding particular disorders.

• A greater reliance on the team approach to health care delivery including the involvement of the patient as an informed team member. This involves knowledge of consumer- oriented information sources that can help patients become active participants in their own care.

There is an enormous amount of genetic information available electronically as well as in print. The Resource section of this guide (page 37) lists a number of helpful articles, books and websites that can assist clinicians with the science of genetic medicine. It also includes sites for patient education.

Resources for practicing the art of genetic medicine on the other hand, are less readily available, and are the focus of this educational video and viewer's guide. The art of delivering genetic services in a primary care setting involves specific psychological, familial, social, ethical, vocational, financial, and legal issues that often differ from other areas of medicine.

In 1995, the American Society of Human Genetics (ASHG) published a recommended Core Curriculum in Genetics for medical schools.[11] This curriculum and others have been used to create a list of Core Competencies in Genetics for all health care professionals by the National Coalition for Health Professional Education in Genetics (NCHPEG), a coalition of over 100 health professional organizations.[12] Over half of the 44 competencies included concern the acquisition of communication skills and changes in practice attitudes that speak to the ethical, legal and psychosocial aspects of genetic medicine.

These skills are probably best acquired in the context of specific clinical cases. The accompanying videotape presents three such cases, together with a discussion of the relevant issues by genetic experts, primary care clinicians, ethicists and patient representatives. Watching the tape in conjunction with this viewer's guide, and exploring these issues with colleagues should help clinicians begin to acquire or reinforce the skills and attitudes necessary to initiate pre-test counseling, guide a shared decision-making process about testing, obtain educated informed consent, follow up with post-test counseling, and/or determine when referral to a genetic specialist is indicated.

Challenges Inherent in Information Obtained by Genetic Tests

In general, clinicians have reserved in-depth consultation and patient counseling for difficult therapeutic decisions, and have tended to think of informed consent primarily in the context of treatment. In genetic medicine, however, the most important informed consent discussion is the one that takes place prior to ordering any tests – in the context of diagnosis. Consider some of the challenges that this presents for clinicians:

1. Genetic information does not affect only the individual receiving the test, but other family members as well. While we have always been able to make inferences about the health status of family members from family medical histories and general medical information, genetic testing makes those inferences considerably more precise, bringing some dramatic medical, ethical and psychological side effects into play. For example, the tape depicts, and a number of studies describe, how family members who do not carry a mutation can experience "survivor guilt", demonstrating that even a negative genetic test may have adverse psychological consequences.[13]

A related dilemma concerns whether a clinician has the right, or even the duty, to override her/his patient's wish to keep test results private in order to warn potentially affected family members. As the tape shows, there is disagreement about whether such a duty exists.

2. Genetic information can transform how individuals perceive themselves and are perceived by others. Even in the absence of clinical disease, a positive genetic test result has the potential to transform how a person perceives herself and is perceived by her family, employer, and health care provider. Such "reclassification" of course can have important psychological effects. It may also affect one's chances of getting or keeping a job; one's chances of being promoted; or one's access to health insurance or life insurance coverage. Anecdotal evidence suggests that genetic discrimination is an issue, but as of today, there still are no good data on how often such discrimination actually occurs.[14]

Given that comprehensive federal legislation against genetic discrimination has not been passed (as of January 2002), and that state laws vary, patients are still wise to question the consequences of testing. And in the current health care context, where medical information is shared across huge networks, providers offering tests are faced with the dilemma of being unable to ensure privacy and confidentiality for their patients. It is therefore critical for clinicians to speak explicitly with patients about the prospect that their test results might be disclosed.

3. Genetic information is essentially probabilistic, making it more complex and more difficult to communicate to patients than other types of medical information. As has been shown in numerous studies, effective communication of risk or probabilistic information to patients in the primary care setting is very challenging.[15] Genetic 'information' can paradoxically, seem to create more uncertainty than it resolves. This is seen in the program's first case about BRCA testing. To begin with, there is the phenomenon of incomplete penetrance: even if a person has a mutation associated with a given disease, she will not necessarily have symptoms of that disease. Second, the absence of a mutation does not ensure the absence of disease. Less than 10% of breast and ovarian cancer can be traced to identified inherited mutations, while more than 90% can not be.

Another source of uncertainty in genetic illness is variable expressivity. As illustrated in the tape, even when we know for certain that a fetus is destined to develop cystic fibrosis, we do not know how severe the CF will be or at what age it will first manifest. Moreover, inaccuracy of genetic tests, namely false positive and false negative results, add yet another layer of complexity to genetic medicine. As we saw in our CF case, the lack of standardization in laboratory procedures can easily lead to a false negative result. Finally, as Dr. Giardiello explains in the tape, his study demonstrated that clinicians' lack of familiarity with these tests can, and has led to serious misinterpretation, even when the test results are accurate.[16]

4. Since there are few definitive therapies, the clinical uses of genetic information are often subtle. In genetic medicine today, testing is often far ahead of therapeutics. The utility of these tests may lie either in the psychological benefit of 'knowing' one's status or, in some cases, in the preventive strategies that such testing can promote. The former is highly dependent on individual preferences and coping styles, which need to be carefully explored. The latter depends on a number of complex interacting factors as described by Evans.[17] In particular, each of the following factors tends to increase the utility of genetic testing.

1. *The test is highly predictive*
2. *The disorder involved is serious*
3. *The illness is not easily detected by standard screening or surveillance*
4. *The illness is not easily treated once manifest, and*
5. *Effective preventive and/or screening measures exist, but are too costly or difficult to recommend to the entire population.*

For example, according to Evans, a predictive genetic test for hypertension would not have a high utility, as this condition is easily screened, effectively treated once manifest, and the preventive strategies are relatively inexpensive, and probably beneficial for the entire population – not just for those at high risk. Therefore, population-based genetic testing would probably add little to the overall management of this condition.

The Process of Facilitating Truly Informed Consent

The popular conception of informed consent has rested on a model of patient-physician interaction during which patients ask for, and physicians offer professional recommendations, to which patients then usually consent. Though in the past, informed consent has often been a brief, pro forma "event," collaborative decision-making has recently been gaining ground as an appropriate model for most clinical decisions. Because the risks and benefits of genetic testing are complicated and their evaluation so contingent upon the perspective of the particular patient, the Task Force on Genetic Testing has called for what has been referred to as an expanded informed consent process or an educated consent process.[18] The point is that there are few cases where clinicians can recommend with confidence that a given patient should or should not have a particular genetic test. This is a shared decision, based on a discussion of the individual patient's values and coping styles, as much as it is based on a patient's medical status.

The difficulty, of course, is that conducting an expanded informed consent is a time-intensive process, and the current structure of health care delivery does not encourage clinicians to spend more time with patients. Despite these barriers,

clinicians are finding creative ways of delivering the appropriate genetic services by rethinking their own roles in informed consent, utilizing multiple visits and discussion aids, involving genetic counselors and other health care personnel, and using information technologies.[19] Hopefully, we will also see changes in the structure of health care delivery that address the need for these services and make them easier to deliver.

Conclusion

We began this essay with references to genetics revolutionizing medicine. Most experts who speak of this revolution are referring to a revolution of biotechnology and information science that would make medicine even more highly technological than it is today. While this may come to pass, what we hope to convey in this program is that genetics also has the potential – paradoxically – to reinforce the humanistic, empathic and communicative aspects of clinical care. Clinicians will conceivably become more aware of their patients' values, and more aware of the family, religious and social structures within which these patients live their, still very unpredictable, lives. Genetics will revolutionize medicine. It will send it back to its roots; back to its future.

– Larry Amsel, Diane Dreher, Bruce Jennings, and Erik Parens,
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