Gene testing in the biotech century: Are physicians ready?

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Few technological developments have elicited as much public interest, excitement and concern as the rapid advances in human genetics. Indeed, *Time* magazine recently declared genetics to be the "future of medicine."[1] The introduction of an increasing number of molecular genetic tests (gene tests) with relevance to an ever-broadening spectrum of the public will be a significant part of this future. Although there has been a tremendous amount of commentary on whether, when and how gene testing services should be offered to patients,[2] many physicians may not be prepared for the challenges linked to this technology. As the public demand for gene testing increases, physicians will need to acquire more knowledge about the benefits, costs, limits and possible legal and ethical ramifications of these tests to assist their patients to make informed decisions about their use.

Medical genetics has played an important role in the diagnosis of disorders for many decades (e.g., clinical cytogenetics emerged in the early 1960s).[3] However, gene tests, which involve direct analysis of the DNA molecule, are the most recent and sophisticated genetic testing technologies[4] and, unlike earlier testing techniques, have the potential to be relevant to a significant portion of the population. There are already many gene tests available throughout Canada. (For a comprehensive list of research and service laboratories and available gene tests visit the Web site of the Canadian College of Medical Genetics (http://ccmg.medical.org). Basic information about gene testing can be found at Human Genome Project Information.[4]) Gene testing can be used to assist patients to make reproductive decisions by identifying those who carry a mutation for an autosomal recessive disease (e.g., cystic fibrosis), confirm a clinical diagnosis (e.g., fragile X), make a prenatal or preimplantation diagnosis of a genetic condition (e.g., Tay Sachs), determine if a patient is presymptomatic for a late-onset genetic disease (e.g., Huntington's disease) and help to estimate the risk of adult-onset cancer.[2,3,5,6] A multitude of new tests, particularly for mutations that increase susceptibility to diseases such as cancer and heart disease, seem likely to become available in the near future.[7]

Currently, almost all gene testing is provided as part of a clinical research program or through existing health care structures (e.g., pediatric, obstetric, clinical genetic or cancer genetic programs)[5,8] and costs are generally covered by the health care system. There seems to be growing pressure from patients for provincial governments to cover gene testing services, as highlighted by a recent Ontario decision that compelled the Ontario Health Insurance Plan to cover testing for the *BRCA1/2* mutations for susceptibility to breast and ovarian cancer.[9] For a limited number of tests, however, patients may also access private commercial services. The American company Myriad Genetics, for instance, provides commercial testing (at US$2400) for *BRCA1/2*.[10] While Myriad will test anyone, the test must still be carried out through a physician.[5,10]

Whether a service is offered through the public system or by a commercial company, the recommended approach to genetic testing is generally one of caution and restraint.[11–15,16–18] For example, it has been noted that *BRCA1/2* testing should only be offered to patients at a high risk for carrying the mutation and even with this population testing should be undertaken with great care.[17,19] Ethical, legal and psychosocial issues have been a significant motivating factor in the development of these conservative testing policies. Indeed, a number of commentators have gone so far as to suggest that there should be a moratorium on gene testing until the many complex social and legal dilemmas have been sufficiently addressed.[20] Concerns include the effect of test results on the insurability of patients, on family relationships and on self image.[5,18,19]

Physicians will inevitably play a central role in the implementation of these cautious testing and referral policies.[21] However, given the unending media attention,[18,20,22,23] the anticipation of the research community, growing pressure from companies selling the tests to use their products[24] and public interest it may prove difficult for physicians to meaningfully mediate access to genetic technologies.[5] As investment in genetic technology increases so too does the pressure to produce financial returns.[25] There is concern that pressure from the growing biotechnology industry, coupled with understandable public excitement, will induce premature implementation and inappropriate use of some testing services.[25–31]

Numerous studies have suggested that both the general public[1,32] and patients in at-risk populations[33–35] already have a high initial interest in accessing genetic testing technologies, and many believe they are entitled to unencumbered access to such services. Benkendorf and colleagues found that 95% of the women in their study thought they should be able to get testing despite a physician's recommendation to the contrary.[36] Similarly, a North American study found that 60% of those surveyed thought that they were "enti-

tled to any [genetic] service they can pay for out of pocket" and 69% thought that "withholding any service was a denial of the patient's rights."[37]

As demonstrated by experience with Huntington's disease and cystic fibrosis, a stated initial interest will not necessarily translate into the uptake of the genetic test.[38,39] Nevertheless, it seems safe to conclude that physicians — particularly family practitioners — are going to face an increasing number of inquiries about and, perhaps, demand for genetic testing. Physicians must be equipped with a knowledge base sufficient to help patients balance this "genetic enthusiasm"[20] against the concerns and uncertainties associated with gene testing.

An increase in public interest in genetics portends enormous legal challenges for Canadian physicians, to say nothing of the ethical dilemmas.[18] Even basic legal obligations take on a unique spin in this context. For example, because genetics is such a rapidly evolving area, it may be difficult for physicians to maintain the knowledge base they need to appropriately fulfill their informed consent obligations. Studies have shown that a significant proportion of physicians have a poor understanding of human genetics.[40–42] As noted by L.B. Andrews, "Malpractice suits in this area are inevitable because physicians are unprepared for the onslaught of genetic information."[43]

The problems with disclosure are magnified by the complexity of the information that will be generated by future genetic tests, particularly if multiplex tests (tests for multiple conditions simultaneously) become common.[40] With the exception of tests for single gene disorders, most of the genetic information generated by testing will be probabilistic risk information.[44] Communicating information about susceptibility to a disease, carrier status and potential risk will not be easy,[4] but this is precisely the type of information that the law requires physicians to disclose and to ensure patients understand.[45] In addition, physicians have an obligation, both ethically and legally, to communicate information about the potential legal, ethical, familial and social ramifications of testing.[18]

There is almost uniform agreement that genetic testing — be it prenatal, carrier or individual testing — should only be done after appropriate counselling is provided.[11–14,19] Unfortunately, few (if any) provincially funded genetic centres have the counselling resources to meet the anticipated demand. The counselling provided by commercial services may be insufficient.[6] Regardless of the availability of counselling, many of the initial inquiries and assessments will undoubtedly take place in a family physician's office.[12,46] Minimally, then, physicians will need sufficient knowledge about genetics to answer questions, identify at-risk patients and refer appropriately.

The recent increase in wrongful birth actions is a harbinger of the type of lawsuits that may soon become common.[47–49] In these cases the plaintiff(s) allege(s) that "but for" the negligence of a physician, a child with a given genetic condition, for instance, would not have been born. While they remain controversial, there seems little doubt that wrongful birth actions can succeed in Canada.[50] In the case of *H (R)* v. *Hunter*, for example, the parents of 2 children with Duchenne muscular dystrophy successfully argued that the defendant physicians should have referred the plaintiff mother for additional genetic counselling.[51] The plaintiffs were awarded nearly $3 million.

While genetics may very well be the future of medicine, it is a future for which many physicians may not be prepared. Although a wide range of health professionals will undoubtedly be involved in providing genetic services, physicians will meet the brunt of patient inquiries, be the focus of commercial marketing and be the primary target of genetic malpractice claims. How physicians respond to these pressures will play a large role in determining future utilization patterns. Medical schools, family physicians, medical geneticists and other genetic professionals need to work together to ensure that Canadian physicians have the knowledge base necessary to thoughtfully consider emerging policies and to help patients make informed decisions about gene testing.

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