Editorials

Individualized medicine

What the genetic revolution will bring to health care in the 21st century

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Part of the joy of family practice is getting to know the people who are part of your practice. It is important to understand them as whole people—their jobs; their stresses; their lifestyles; their family, friends, and companions; and their family histories—in order to determine their risk factors and predispositions.

Major health advances were made in the last century through providing simple public health measures to all Canadians, eg, clean water, sanitation, and immunizations. In Canada, life expectancy went from the late 40s (47 years old in 1900) to about 80 years by the end of the century. But what does this new century hold?

As our Canadian health system undergoes reform, we worry about the costs of technology; waiting lists; and how to keep our universal, publicly funded system viable. So what is new? The sequencing of the human genome! Said to be the "book of life," knowledge of DNA sequences in human beings means that all the building blocks (proteins) that are needed to construct the human body can actually be known and catalogued. Genetic studies also show that one of the things that makes each person individual (aside from monozygotic twins, who are said to be genetically identical) is that each person's DNA is totally unique. Although the DNA of human beings is 99.9% identical, one in every 1000 base pairs is different. Because there are 3 billion base pairs in the human genome, on average there are 3 million base pair differences between individuals. We are each truly unique!

Soon we will be able to identify those DNA differences that predispose to illness (and health). For physicians, this means tailoring health care to individuals: identifying which environmental, nutritional, and occupational factors could be a problem in order to write prescriptions for lifestyle and appropriate medications. The option of knowing your genetic risk factors is becoming a reality. Researchers predict that, in 10 years, you will be able to get a printout (blueprint) of your personal genetic differences and susceptibilities for $1000. It will be in the form of a credit card–size chip that you can carry in your wallet along with your provincial health card. Are you interested? Do you want to know how you are different? Do you want to know what makes each of your patients genetically unique? Will you be able to apply all this new knowledge effectively and appropriately?

Saving time and money

Family physicians will need to be aware of these developments not only to be knowledgeable, but to offer their patients options. Pharmaceutical companies will probably develop genetic screening tests to be used before prescribing medications. Theoretically, such tests will be able to predict who will react badly to a drug, who will have a beneficial reaction, and who will get no effect. Clinical guidelines for drug use are likely to require this type of screening (based on knowledge of biochemical pathways and genetically based responses to a drug action) in order to avoid adverse reactions. Treatments for everything from hypertension to cancer will be more appropriate, based on known genetic mutations in known metabolic pathways. It is likely that prescribing appropriate, effective medications tailored to individuals will save the system a lot of money because only medications that are appropriate and effective for a specific individual will be prescribed.

Biology is complex, and the many genetically heterogeneous and complex disorders, such as hemochromatosis, hypertension, diabetes, autism, cancer, heart disease, and stroke (see related articles in this issue) are lining up for clarification. Family history and ethnic predisposition are important pieces of information for family physicians. Patients are more likely to have or develop disorders that run in their families. Each ethnic group has specific disorders for which they are at increased risk. Even infectious disorders, such as HIV, have predispositions and resistance. One percent of people with European ancestry are resistant to HIV, while only 0.1% of those of African ancestry are resistant. This is probably due to the selective forces at work during the Middle Ages in Europe, eg, the same gene(s) that kept people from dying of the plague, which swept through Europe but not Africa, make descendents resistant to HIV.

Imagine that a young child with fever comes to your office. Today you find a bulging red eardrum and decide to prescribe broad-spectrum antibiotics to avoid the risk of the infection becoming generalized. Tomorrow you

will determine by an office-based 5-minute DNA test whether the infection is caused by a virus or a bacteria. Then you will determine antibiotic (or anti-viral agent) resistance on the same sample. Next, you will determine by a DNA test whether the child will have an adverse reaction to the suggested medication by using a buccal smear of the child's cells. If you find the child would have an adverse reaction, you will alert the family so that they can be aware that they might be at risk of a genetically based adverse drug reaction. Then you will select an effective medication that will not cause an adverse reaction—all this in 10 minutes using easy, inexpensive, office-based tests.

Patenting human genes

Individualized? Yes. Better medical care? Yes. Can we afford it? Not clear. The recent flap about breast cancer testing suggests that using individualized testing is not straightforward. An American company patented two genes for inherited forms of breast cancer. Having patented the genes, they then developed a diagnostic screening test for which they charge several thousand dollars. Medical molecular diagnostic laboratories across Canada developed their own screening tests (once a gene's nucleotide sequence and disease-causing mutations are known, it is very simple to do) to be used in their home provinces for as little as one tenth the price. The American company has threatened to sue because they hold the patent for the genes. The issue is whether human genes can be patented (after all, we all have them as part of our own bodies) or whether only diagnostic and therapeutic applications of genes should be patentable.

Canada must think carefully about patenting human genes (as well as those of other species) if we are to be able to afford to apply the new genetic knowledge to treat disease in such a way as to improve human health outcomes in the 21st century. The application of genetic knowledge must be at a competitive, realistic price within our universal, transportable, accountable health care system if we are to enjoy its benefits. The potential for individualizing testing for genetic predispositions to illness does exist and will increase. The disorders you read about in this issue of *Canadian Family Physician* are just the tip of the iceberg.

Newfangled medicine

Another important consideration is whether your patients will want this "newfangled" type of individualized medicine. Some people would rather live in blissful ignorance than think they are destined to develop the same type of heart disease as their fathers or arthritis that disabled their grandmothers. They hold to a fatalistic and deterministic perspective that there is nothing they can do to make a difference. Others want to know their risks, to educate themselves and to use whatever prevention is available. Their perspective is that they can do things to modify the effect of their inherited endowment. And, of course, others will change their minds over time as they watch the consequences in their families and new options develop. Fortunately, ethicists are vocal in helping us think through applications of the new genetic tools. What is clear is that patients have the right to decide for themselves whether they want genetic testing (both predictive and diagnostic). The results might have very powerful effects, both positive and negative, upon their lives and the lives of those around them.

Nevertheless, there is a distinction between predisposition and predestination. Each disease, disorder, and predisposition has its own natural history and complex biology. As more is learned each year, knowledge and understanding are likely to make it possible to change outcomes. All this seems like a huge amount of information for family physicians to track. Fortunately, the revolution in informatics will help. But it does mean that each patient must be thought of as an individual, and an approach that allows for individualized care is needed. Automation will not do.

For your own sake, the sake of your family, and the sake of your patients and their families, "listen up" and learn about the applications of genetics to common disorders. It will make your days more exciting, you will learn to take family histories avidly, and you will appreciate the remarkable nature of our genetic endowment. You do not have to memorize mutation jargon to understand the applications. You can always call a hospital-based clinical geneticist if you are confused.

I would like to think that the part of family practice that leads you to want to know your patients as individuals so that you can understand their risk factors and predispositions will include understanding the application of genetic knowledge about their individuality. I hope that you will see the importance of individualizing medical care in the Canadian health care system of the 21st century.

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