The genomification of medicine

Fifty years ago this month a famously terse article in *Nature* proposed a model for the molecular structure of DNA.[1] The double helix "suggested" by Watson and Crick — 50 years after Archibald Garrod first applied Mendelian principles to human disease — set in motion a new science that would lead to the sequencing of the entire human genome[2,3] and turn genetics, the study of single genes, into genomics, the study of the interaction of all genes with one another and with their environments.

If molecular biologists and clinical geneticists once occupied the dimly lit anterooms of medical science, they now capture the lion's share of research funding and have moved with teams of computer and information scientists, epidemiologists, biochemists and others into the corner office. A search with the MeSH major topic heading "genome" (not used in MEDLINE until 1992) generates citations to almost 8000 publications for each of the past 2 years. In 2001 more than 92 000 articles were indexed under the term "genetics," a growth of 52% since 1995.

The field of medical genetics used to cover a relatively limited range of single-gene disorders, such as Garrod's congenital alkaptonuria. Now, disease-causing mutations have been identified in roughly 1000 of the estimated 30 000 chromosomal genes. (A complete inventory is housed in the Online Mendelian Inheritance in Man databases at www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM.) Our understanding of disease causation is changing, along with our view of prognostication and treatment. We are witnessing a radical shift with immediate and important implications for clinical practice, health policy and financing, education, ethics and law.

What may well be a tidal wave of genomics will bring new choices for screening, diagnosis and risk stratification, and treatment. Randomized trials are necessary to evaluate these new options. For example, the knowledge that mutations in the connexin 26 gene account for 40% of cases of childhood hearing deficit should alter our approach to screening for deafness in children. As our understanding of multifactorial disorders increases, we will see increasingly legitimate, evidence-based demands for population screening and early detection of single- and multiple-gene mutations, now understood as risk factors for adult disease. As oncologists, for example, guide breast cancer patients through treatment decisions, they will be aware of newly discovered metastasis suppressor and enhancer genes[4] and of research that has identified a veritable orchestra of 70 genes that are highly predictive of metastatic disease (or its absence) and death (or survival).[5] Pharmacogenomics will profoundly change how drugs are designed and prescribed.[6]

In health policy and financing, genomic screening will compete with CT and MRI scanners in our technology priority lists. In this issue (see page 989) Steve Morgan and colleagues examine some of these policy issues.[7] New ethical questions will be posed; our laws will be found wanting.

Medical schools, slow to recognize the profound implications of genomics for clinical medicine, have been lurching, if not stumbling, forward to embrace the genomification of medicine. There is inadequate time in the crowded curriculum and insufficient faculty to teach the new science at the necessary cellular, clinical, epidemiologic and ethical levels. Those already in practice will need continuing education in order to respond wisely to requests for genetic testing and to help patients understand their specific health risks through genomic analysis.

As they strive to understand, diagnose, counsel, encourage or dissuade, physicians will need practical and just-in-time information to help their patients translate new knowledge into personal interpretations of hope and of risk. And, while genetic testing becomes ever more refined, physicians will need to maintain their clinical acumen: genetic tests, like all tests, have imperfect sensitivity and specificity and are not exempt from biological variation and laboratory and clerical error.

It is a tall order to adapt our practice of medicine to the genomic revolution. But to do so will help us get the right diagnosis sooner, improve our predictive abilities and individualize a large amount of patient decision-making. — *CMAJ*

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