

Treating Genetic Disease

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The focus for the front cover of *CJHP* in 2002 will be the Human Genome Project and advances in science, medicine, and technology related to this project.

Colon cancer,¹ specifically hereditary nonpolyposis colorectal cancer,² and breast cancer³ are malignant diseases that show some degree of genetic inheritance, as do cystic fibrosis,⁴ Duchenne muscular dystrophy,⁵ and neurofibromatosis.⁶ In fact, humans are afflicted by nearly 4000 genetic diseases, and the possibility exists that knowledge of a person's genetic code could allow us to prevent or cure some of them.

Cancers arise from a multistep process involving the interplay of multiple changes, or mutations, in several different genes, in combination with environmental factors such as diet or lifestyle. In the most common, noninherited forms of cancer, the genetic changes are acquired after birth. But people who have a hereditary risk for cancer are born with one or more altered genes — in other words, they are one step along the road to cancer from birth.

Women in general have a 10% risk of breast cancer and a 2% to 3% chance of ovarian cancer sometime in their lifetime.³ With regard to breast cancer, mutations in the *BRCA-1* and *BRCA-2* genes are present in only a small portion (5% to 10%) of all cases, but carriers of mutations in these genes have a greater risk of cancer, especially before menopause.³

Similarly, in hereditary nonpolyposis colorectal cancer, children who inherit an altered gene from either parent face a 70% to 80% chance of developing this disease,¹ usually at an early age.

In treating a genetic disease, the first question that must be answered is, Which altered gene causes the disease?⁷ Two related questions are, What protein does this gene normally produce? and Can the altered protein or gene be fixed or replaced?⁷ Determining the answer to the first question is often difficult, because few clues exist as to where, on any of the 23 pairs of chromosomes, the altered gene resides. However, as a result of the Human Genome Project, the altered genes



The results of the Human Genome Project are expected to drastically change the way we think about and treat disease. Graphic courtesy of US Department of Energy Human Genome Program (<http://www.ornl.gov/hgmis>).

for many genetic diseases have now been identified.

These discoveries offer a preview of how the Human Genome Project is likely to transform medicine by opening up new approaches to prevention. The earliest beneficiaries will be individuals and families who face a very high risk of cancer. First, for those who choose to take it, will come a simple blood test to determine if they carry the altered gene or genes. In the case of hereditary nonpolyposis colorectal cancer, individuals found to carry an altered gene would likely receive counselling to adopt a high-fibre, low-fat diet in the hope of preventing the cancer. They would also be advised to undergo yearly colon examinations starting at about age 30. Such exams should help to detect any

continued on page 100

benign polyps early in the disease process so they can be removed before they become malignant. For those who do not carry the altered genes, the diagnostic test may be a source of huge relief, removing any fears they have had and sparing them from frequent colonoscopies.⁷

Despite the life-saving potential of such diagnostic tests, ethical and practical issues must be answered. The dark side of many of these issues was presented in the 1997 Sony film entitled *Gattaca*, in which employment and mate selection in a futuristic society were based largely on nonconfidential genetic information. Careful attention to these social and ethical issues now will help prepare the public and the medical profession for the choices that lie ahead.

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