This issue of the *Journal* carries a report by Shah et al\(^1\) in which they characterized the genetic mutation in the MEN1 gene in a proband with multiple endocrine neoplasia type 1 and a family history of endocrine neoplasia, and then used this information to screen eight, apparently healthy, family members.

The information available on genetic mutations in a variety of conditions, and the ease of performance and reducing costs of molecular biology tests suggest that this is a tool that will increasingly be used to clarify the nature of the genetic defect in individuals with heritable diseases and that this information can be used for primary prophylaxis of disease in individuals carrying the mutated gene. The greatest experience in genetic testing for susceptibility to specific cancers has been in the area of breast cancer, where clinical testing for BRCA1/BRCA2 mutations has been available for over a decade now.

The technology to sequence the human genome has rapidly evolved to the extent that an individual desirous of knowing his or her whole genome data can get this done at a cost of approximately US$ 50,000 today, a cost expected to drop to US$10,000 in the very near future. Utilizing this information provides a potentially powerful tool for health care workers to deliver preventive medicine. Prevention of disease in at-risk individuals can involve periodic screening for early markers, institution of preventive medication, or alteration of lifestyle. Particularly when the disease affects the gastrointestinal tract, prevention can take the form of personalized nutritional intervention; this has led to the emergence of the field of nutrigenomics. In the present case series, Shah et al used the genetic information to screen 8 family members at risk for MEN1 and successfully identified a child who had asymptomatic endocrine tumors. It is likely that such intervention will prevent morbidity, at least in the short to intermediate term. The case series reported in this issue is thus an elegant demonstration of the power of modern molecular biology to aid preventive medicine and improve human health.

For a variety of reasons, genetic testing of asymptomatic individuals is not to be undertaken lightly. Psychological impacts of such testing need to be considered before we begin to offer such testing to healthy individuals with a family history of cancer or other heritable disease. The identification of a genetic defect in an asymptomatic individual leads to a variety of effects including depression, anxiety, cancer-related worries, and family stresses, and may significantly impair the quality of life in a proportion.\(^2\) Some studies have distinguished between the effects of risk assessment versus genetic testing, finding increased scores of depression and anxiety following genetic testing, whereas scores decreased when risk assessment was performed.\(^3\) A Cochrane review in 2007 of the impact of genetic screening for individuals at risk of familial breast cancer found only 3 evaluable studies comprising 1251 participants, and concluded that there was no significant adverse psychological outcome of such testing.\(^4\) A more recent meta-analysis included 30 studies covering hereditary non-polyposis colorectal cancer, hereditary ovarian and breast cancer and Alzheimer’s disease and found that negative affective reactions were a common, but short-lived, response to testing positive for a mutation, and that overall there was no significant impact on psychological outcome.\(^5\)

Genetic testing and identification of individuals at risk is expected to lead to measures that will prevent cancer, including frequent screening for cancer, chemoprophylaxis, and prophylactic surgery. Unfortunately, identification of a genetic predisposition to cancer does not necessarily translate to regular screening. Although an increase in screening behavior is reported, the change in behavior is less than expected and up to 40% of individuals identified with mutations do not turn up for regular screening.\(^5,6\) Chemoprophylaxis for cancer carries significant adverse effects and is not usually a satisfactory solution. Prophylactic surgery reduces cancer risk in conditions such as breast cancer (mastectomy) or colorectal cancer (colectomy), but these individuals are also often at risk for cancer in other organs.

Yet another concern with genetic testing is its likely influence on costs of medical care. As our society progressively moves away from state-provided free medical care to health care that is dependent on insurance, this issue is likely to pose significant problems. Medical insurance providers in some countries insist on disclosure of personal genetic information if available, and this will impact on cost of health care for the individual. Genetic information can also potentially be used by some employers to deny employment to individuals. Finally, it is not clear for most cancers that the simple presence of a genetic mutation is sufficient to lead to disease, and this is due to the variable
penetrance of the gene effect. This is an additional factor to be considered before beginning the process of genetic counseling and testing.

The available evidence for genetic testing in screening for cancer has been derived from highly selected populations. Further data on the predictive value of positive tests, and an understanding of the role of the physician in maintaining confidentiality and the rules governing disclosure, are necessary to understand the consequences of such testing in countries such as India. In the meantime, careful consideration must be given to the individual and family circumstances, the nature of the defect being probed, the natural history of the disease, and the possibility of practical interventions before genetic testing is offered to individuals judged to be at risk of having genetic predisposition to cancer.

B S Ramakrishna
Professor and Head, Clinical Gastroenterology and Hepatology, Christian Medical College, Vellore, India

References


E-mail: rama@cmcvellore.ac.in

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