Multiple endocrine neoplasia type 2 (MEN-2) may be the ideal disease for presymptomatic genetic testing. The syndrome has an autosomal dominant pattern of inheritance and includes medullary thyroid carcinoma, pheochromocytomas, and, sometimes, parathyroid adenomas. The risk of medullary thyroid carcinoma in affected persons is extremely high.

The Netherlands group previously found that all persons diagnosed by genetic testing harbored small foci of medullary thyroid carcinoma, whether or not their plasma calcitonin level was abnormal. Furthermore, the cancer was curable in each case. This represents a significant advance over periodic biochemical testing, which does not detect some thyroid cancers early enough for cure. Also, half of those who undergo periodic testing are not carriers of the mutant gene at all.

Multiple endocrine neoplasia type 2 is caused by missense mutations in the RET proto-oncogene. Carriers of the mutant gene can be identified by genetic testing once the specific disease-causing mutation for an affected family has been identified. Non-gene carriers can then be spared further testing and concern for themselves and their offspring. Gene carriers can undergo curative thyroid surgery and appropriate observation and screening for other possible tumors; these individuals also will know that testing is necessary for their offspring.

The present study addresses the psychological and social consequences of genetic testing for MEN-2. The investigators were careful to follow the accepted ethical approach to testing, which includes education and counseling before testing, at the time results are given, and after disclosure. The most notable results of the study included feelings of anxiety and depression, mixed with relief, in subjects who tested positive, and relief coupled with worry in those who tested negative. Most important, subjects usually received appropriate support from family members, and any early negative psychologic impact had resolved by 1 year after testing. Adverse social impact, such as insurance discrimination, was not apparent, but could not really be judged without longer follow-up.

How Does Genetic Testing Differ From Presymptomatic Disease Diagnosis?
This study is a careful, meaningful examination of the psychological and social risk issues associated with genetic testing. But what is all the fuss about these issues anyway? For years physicians have been involved in the diagnosis of presymptomatic disease. Measurement of blood pressure is a good example. High blood pressure usually is not considered a disease by itself, but it predicts the development of cardiovascular and cerebrovascular problems. Cholesterol measurements are similar in this regard. There certainly are psychological and social consequences of having high blood pressure or high cholesterol, and their presence always affects insurance. But we never give counseling or obtain informed consent about the possible consequences of measuring blood pressure or cholesterol. If, however, a genetic test became available that identified those who would develop essential hypertension (a likely event), then counseling and informed consent for testing would become ethically necessary. What's the difference?

Several factors have focused critical attention on the psychological and social impact of genetic testing. First, an aura and mystique surround any new technology. These result in increased critical scrutiny. Second, there has been a heightened concern about ethics and informed consent in general. Some of this concern derives from an improved ability to quantitate such issues, as the present study illustrates. However, there is also a genuine increased awareness of these matters. It is unlikely that today's health-care workers are more ethical or patient-oriented than their predecessors. Rather, the patient-physician relationship has evolved from a relationship based on authority to one based on education and interaction.
Third, there are, indeed, some very real differences between genetic testing and traditional disease assessment. Genetic testing is extremely precise; who does and does not have a predisposition is determined with near certainty. Genetic testing is also very personal; it derives from the very stuff, DNA, that determines who and what we are. We can't change our genes like we can treat blood pressure or cholesterol.

Most important, genetic testing is almost always applied presymptomatically, while most traditional medical testing is done to evaluate symptoms. It is assumed that a diagnosis is important once symptoms develop. But how crucial is it to reach a diagnosis before symptoms of a disease occur? It may be important for some conditions but unimportant and even harmful for others. Genetic testing, by itself, ignores how important or unimportant, and how beneficial or harmful, knowledge of a presymptomatic diagnosis may be.

The genetic causes of disease are being studied because the requisite technology is now available and because genetic treatment may eventually become possible. As the field has progressed, however, genetic diagnosis has become a reality for many diseases, but genetic treatment, so far, has become possible for almost none. Available treatments or the lack thereof remain unchanged. Traditional medical approaches have usually developed for conditions in which a difference can be made. Population screening is done for cervical cancer, for example, because it can be cured, but not for lung cancer, because it cannot. Blood pressure and cholesterol are routinely measured because they can be treated and their consequences minimized. Genetic testing again ignores whether anything clinically useful can come of the test.

Making the Decision

For the above reasons, the decision to use genetic testing must weigh the existing medical benefits of testing against the psychological and social risks (or benefits). It is most important to recognize that these risks and benefits differ markedly for each disease or disease predisposition under consideration. At one extreme, if successful prevention and treatment are already available for the disease in question, and only earlier diagnosis is needed, then genetic testing is a welcome addition. The medical benefit of testing in such a situation is so great that the psychological and social issues are of minimal consequence and may well take care of themselves. The article by Grosfeld et al represents a situation close to this extreme.

At the other extreme are severe diseases for which there currently is no prevention or treatment. In such instances, genetic diagnosis serves only to relieve worry in the unaffected person, but at the probable expense of those who are found to be affected. Social and psychological concerns in this situation become paramount. They are the determining factors in the decision of whether or not to undergo the genetic test. Huntington's disease is the obvious example of this situation.

Most diseases fall between these two extremes.

Problems of Genetic Testing Compounded in Children

The problems of genetic testing are further compounded in children. Parents almost always want their children to be tested, but what they really want to know is that their children are unaffected. Children's rights must sometimes be invoked to avoid potentially dire social consequences. Parents' intentions cannot be questioned, but their understanding of the consequences of testing is often incomplete. The testing of children was of little question in the present study in which the parents clearly understood the medical benefit of such testing.

In summary, the medical benefits of genetic testing must be weighed against the psychological and social consequences for each disease individually. The authors carefully identify the social and psychological issues that need to be considered. The degree of benefit or harm will differ for each disease, as will the medical consequences.

Patients, physicians, and genetic counselors must all be aware of these issues. Patients ultimately decide whether or not to undergo genetic testing, but that decision is influenced greatly by how the issues are presented. Significant responsibility, therefore, rests with health-care workers to be aware of the positive and negative consequences of testing and how to explain them. Patients almost always have an inherent interest in knowing whether they have a disease predisposition, but they must be able to answer the question, "Is it in my best interest to know?"

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