

Risks and Benefits of Genetic Testing in Persons with Hereditary NMD

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Genetic testing by DNA analysis is becoming a common occurrence in the practice of medicine. It is most frequently being used in the diagnostic evaluation of symptomatic patients. The use of genetic testing is less well understood in the identification of asymptomatic gene carriers, who often may be tested decades before the onset of symptoms. This project addressed an important and timely issue: the risks and benefits of genetic testing of asymptomatic persons in families with hereditary neuromuscular disorders. Nationally, more than 200,000 individuals are at risk for the NMD disorders and could be eligible for genetic testing. The social, psychological and economic fallout from such testing is largely unknown. The impact is likely to vary widely depending on the characteristics of the diseases, the individuals and the local social milieu. It behooves us to carefully measure and evaluate these risks and benefits in order to adjust the testing process appropriately to assist individuals, families and society in coping with the results. It is critical for society and the health care profession to assess and monitor the impact of DNA testing on factors such as general patient well being, family planning, employment and access to insurance in these disorders.

The hereditary neuromuscular disorders provide a broad assortment of diseases on which to assess the impact of genetic testing. This is because they affect several different parts of the nervous system resulting in a wide range of quite variable symptoms and signs, may last many decades, may or may not reduce life span, frequently do not produce cognitive or behavioral deficits and may be perceived quite differently by various family members. In the last seven years genes have been discovered for and testing is available for myotonic dystrophy (MMD), three types of autosomal dominant Charcot-Marie-Tooth neuropathy (CMT) and six types of hereditary ataxia (HA). MMD, CMT and HA have a very broad range of possible degrees of "severity".

The results of testing for myotonic muscular dystrophy, Charcot Marie Tooth dystrophy and hereditary ataxias will likely have different implications than those for other diseases such as colon and breast cancer, where the disease outcomes are different and treatments may be available.

Potential benefits of genetic testing include:

- specific diagnosis of carrier status (positive or negative),
- reduction of anxiety,
- useful information for family planning, financial planning and career plans.

Potential risks of genetic testing include:

- increased anxiety and depression
- threats to insurance, employment
- threats to personal relationships.

The long range goals of this study were to: (a) better understand the motivating factors and decision making processes underlying subject participation or nonparticipation in genetic testing, (b) identify factors influencing both personal and societal responses to genetic testing and (c) develop procedures and strategies to improve the implementation and long-term care and counseling of subjects undergoing genetic testing.

In this study, we found that a common motivation for genetic testing was suspicion that one may be developing early signs of the disease. Many of those with positive tests did show subtle, non-specific signs of the disease on examination. However, some who believed that they had early symptoms of the disease were relieved to discover that they had not inherited the genetic condition. Another important motivation was family planning, making a decision about whether or not to have children.

The response to the testing was generally good. There was a trend for anxiety levels to decrease following testing in both those with a positive test and those with a negative test. An interesting finding was the absence of major depression in the study population. This was in contrast to the findings in Huntington's disease and familial Alzheimer's disease. This is possibly due to the difference in the cognitive effect of the groups of diseases. Those with NMD generally do not exhibit the severe cognitive effects seen in Huntington's and Alzheimer's diseases. Another factor was that those deciding to pursue genetic testing were a highly self-selected group, mainly college-educated, middle-aged females with children. Further study is needed of the psychological make up of this group.

Genetic testing poses a considerable concern over the potential for discrimination in acquiring health insurance. Although in this study we did not find this discrimination, the state in which it was conducted has a law preventing discrimination in insurance. Some of the participants were denied long-term insurance. This aspect also requires further study.

As a part of this study, informational booklets were written:

- ◆ Myotonic Dystrophy: Making an Informed Choice about Genetic Testing
- ◆ Facioscapulohumoral Muscular Dystrophy: Making an Informed Choice about Genetic Testing
- ◆ Spinocerebellar Ataxia: Making an Informed Choice about Genetic Testing

These booklets are designed to provide background information on genetic testing with an emphasis on the issues involved in genetic testing for these three diseases. They are available in pdf format on the Internet at <http://nmdinfo.org/rrtc/publications/genetictesting.asp> or <http://depts.washington.edu/neurogen/>.

These results should not be generalized to other studies and any person considering genetic testing should receive counseling from trained, experienced genetic counselors.