editorial

Alzheimer's disease and testing

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The article, "Who seeks genetic susceptibility testing for Alzheimer's Disease? Findings from a multisite, randomized clinical trial," published in this issue of *Genetics in Medicine* is a significant study in that it begins to address our understanding of who would want susceptibility testing for common complex diseases.[1] The information learned from this study is important not only for genetics professionals but also for primary care providers who will likely be in the position of responding to the majority of patient requests for such testing. How genetic susceptibility testing fits into current medical care will likely impact the type of services genetics professionals will provide. The risks and benefits of such testing remain unclear.

Genetic susceptibility testing is a recently emerging service for individuals with known risk factors for common complex diseases. The authors of this article rightly assert that one of the reasons why they believe their study is important is that this type of testing will become more common in the near future and we have little understanding of who would want such testing and why. This particular study is most helpful in trying to answer these questions in that the investigators used "real-life" situations. Individuals with factors placing them at a higher risk for Alzheimer's disease participated in the study and one group actually underwent susceptibility testing.

The authors correctly identify one of many major issues inherent in susceptibility testing; that is the incredible uncertainty of the meaning of the results. This uncertainty greatly complicates the value of the testing as well as the meaning of the results to both the clinician and the patient. As is stated in the article, the finding of an allele for APOE 4 does not mean that an individual will develop Alzheimer's disease and absence of this allele does not mean that the individual will be disease free. In addition, other risk factors that are likely involved have not yet been clearly identified. In comparing this type of testing to predictive genetic testing, the limitations of genetic susceptibility testing become more apparent. The major difference is the limited predictive value of the test results. For example, if you are an individual at risk for Huntington disease, you might want predictive testing because learning that you have two normal alleles means that you will not develop the disease. This is not the case with susceptibility testing. You can never be sure that you will not develop the disease in question. As a matter of fact, your risk could still be quite significant. Again looking at Huntington disease, if you are at risk and you learn that you have an abnormally expanded allele, you know that you will likely develop Huntington disease if you live long enough. You can then make life decisions based on this information. In the case of predictive cancer testing, you can even think about increased surveillance or having prophylactic procedures. Once more, this is not the case with susceptibility testing. The results of the testing indicate that you are more likely or less likely to develop the disease than you originally thought based on your family history and other known risk factors alone. You are still left with many of the same questions you had before the testing. This high level of uncertainty makes susceptibility testing especially daunting particularly in light of the fact that so many people will be at risk for Alzheimer's disease and other common complex diseases. It also suggests that involvement from genetics professionals is more important than ever before. Results from susceptibility testing are much more difficult to make use of than are the results of direct gene testing. Likely clinicians as well as patients will be confused as to what to do with them.

When thinking about the possible outcomes of the availability of mass susceptibility testing, one might consider the triple screening situation in the prenatal arena. Here we have a test designed to identify those individuals at a higher risk for having a child with a birth defect than would be expected based on maternal age alone. This is similar to the Alzheimer's disease situation in that the testing for Alzheimer's disease identifies individuals at a higher risk for developing the disorder than would be expected based on their family history alone. In addition, the testing would likely be offered outside of the traditional medical genetics setting and the results would likely be interpreted and given to the patient by a health care professional not specifically trained in genetics or genetic counseling. Although the triple screen has helped many patients decide whether or not to have invasive testing by providing better and more specific risk information, the results are often misinterpreted or misrepresented leading to much unnecessary stress and fear. Everyone in the genetics community is aware of the multitude of patients who got the phone call telling them that their blood test is "positive for Down syndrome." This is quite an inappropriate interpretation of these test results and patients then often feel compelled to have an amniocentesis to alleviate their fears. In my experience, many have the amniocentesis not knowing what they will do with those test results but they do not feel as though they have an option because the chance of a problem has been identified and they have a piece of paper saying so. The same scenario is very possible with susceptibility testing for Alzheimer's disease and other common diseases. One can almost hear the statement, "your test is positive for Alzheimer's disease." Again, this would not exactly

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be an appropriate interpretation and would not be very useful to the patient. However, it may place the patient at a higher risk for genetic discrimination and increase the potential for long-term psychological harm and have a damaging impact on the family.

So how could medical genetics play a helpful role in this developing testing arena? Medical genetics is poised to become a necessary educational and consultative service as susceptibility testing programs develop. It is more important than ever for genetics professionals to partner with neurologists, cardiologists, dermatologists, and other practitioners who see patients with common complex diseases. For many years, geneticists have been saying that genetics will move into all areas of medicine. The development of susceptibility testing suggests that this prediction was quite correct. Studies such as this are critical to our understanding of how to best provide susceptibility testing. More information is needed about how the participants in this study used the information to make changes in their lives. More studies are needed so that we can learn how to help other medical specialties best provide this service.

Furthermore, appropriate counseling may obviate the need for testing that may actually add little information for the patient. For example, in a related study by the same authors cited in this article, it was found that participants gave many reasons for wanting susceptibility testing for Alzheimer's disease including to set personal affairs in order, make arrangements for long-term care, help prepare their family for their possible future illness, and to do things sooner than they had otherwise planned.[2] For some individuals, these stress issues could well be addressed with appropriate genetic and psychological counseling. Many of the questions posed by patients before testing, such as how do I plan my life, how do I prepare my family, and how do I get the most out of life, will still be there after testing. In other words, the testing will not answer these questions for many people but appropriate counseling may help people deal with issues. For conditions such as heart disease, stroke, and type II diabetes, it has been suggested that patients could make lifestyle changes in response to susceptibility testing results that indicate a higher risk. However, one could argue that everyone should be encouraged to live the healthy lifestyles that could help prevent these diseases. In the absence of proven treatment options, susceptibility testing today may not help patients and their families as much as appropriate counseling and support.

References

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