Genetic test for spinal muscular atrophy should be offered to all couples, says the ACMG

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Carrier screening for spinal muscular atrophy (SMA)—a serious genetic disease affecting approximately 1 in 10,000 infants that causes progressive muscle weakness and death—should be made available to all families, according to a new practice guideline issued by the American College of Medical Genetics (ACMG). The statement appears in the November 2008 issue of Genetics in Medicine, the official peer-reviewed journal of the American College of Medical Genetics. In the past, tests to identify carriers of the gene responsible for SMA have generally been offered only to people with a family history of the disease.

According to new recommendations from the ACMG's Professional Practice and Guidelines Committee of the ACMG, "Because SMA is a common genetic disorder in all populations, carrier testing should be offered to all couples regardless of race or ethnicity." Thomas W. Prior, Ph.D., professor at The Ohio State University, is the author of the new statement.

Spinal muscular atrophy is a severe neuromuscular disease caused by mutations in the SMN1 gene. The mutations cause degeneration of a specific type of nerve cell (motor neurons) in the spinal cord, leading to progressive muscle weakness and paralysis. Children with the most common and severe type of SMA (type I, also called Werdnig-Hoffman syndrome) have severe, generalized muscle weakness, usually leading to

death from respiratory failure before age 2. Other types of SMA are less severe, but are still serious and disabling.

Spinal muscular atrophy is a recessive genetic disease, meaning that both parents of an affected child are usually carriers of an abnormal SMN1 gene. It is the second most common recessive disease, after cystic fibrosis. It is estimated that between 1 in 40 to 1 in 60 individuals carry an abnormal SMN1 gene, and about 1 in 10,000 infants are born with SMA.

An accurate genetic test is available for detecting the SMN1 gene mutation that causes SMA. In the past, these tests have been primarily offered to families with a child affected by SMA—whereas individuals without a history of the disorder were not tested. There is no way to identify couples at high risk of carrying the abnormal SMN1 genes, other than DNA testing. Furthermore in contrast to some other genetic diseases for which carrier testing has been extremely important—for example, Tay-Sachs disease, which occurs at high rates among people of Ashkenazi Jewish ancestry—SMA seems to affect all populations.

According to the new ACMG guidelines, SMA meets established criteria for population-based genetics screening. It is a severe disease, there is a relatively high frequency of gene carriers in the population, and an accurate genetic test is available, along with prenatal diagnosis and genetic counseling.

"The goal of population based SMA carrier screening is to identify couples at risk of having a child with SMA," said Prior, the Guideline's author. Ideally, testing should be performed early in pregnancy or before conception: "Preconception carrier screening allows carrier couples to consider the fullest range of reproductive options."

A key stipulation is that formal genetic counseling must be made

available to anyone requesting SMA testing. "It is important that all individuals undergoing testing understand that a carrier is a healthy individual who is not at risk of developing the disease, but has a risk of passing the gene mutation to his/her offspring," according to the statement. Couples with positive tests need to be provided with information on the risks of any current or future pregnancies, as well as all available reproductive options.

Counseling must also include information on the limitations of carrier screening. Because of the complexity of the genetic abnormalities causing SMA, about ten percent of carriers of abnormal SMN1 genes are not detected by the current test. Couples must also understand that the test cannot predict how severe the disease will be—although the type 1 SMA occurs in about 70 percent of cases, and milder types of SMA account for 30 percent.

As for any type of gene carrier screening, testing is voluntary. The statement also addresses the need for informed consent, as well as issues of confidentiality, social and psychological, and cost issues common to all genetic tests. "The new recommendation to extend SMA carrier screening to the general population is a good example of the way in which technical capabilities and knowledge in the field of genetics are advancing to the point that entire populations stand to benefit," comments Dr. James P. Evans, Editor-in-Chief of Genetics in Medicine.

Source: American College of Medical Genetics