Evidence Supports Screening for Fragile X Syndrome in Prospective Mothers, Says Article in *Genetics in Medicine*

Authors Stress Need for Public Education About Unfamiliar Genetic Disease

Philadelphia, Pa. (June 07, 2010) - There's adequate research data to support population screening of women of childbearing age for fragile X syndrome—the most common inherited cause of cognitive impairment, according to a report in the July issue of *Genetics in Medicine*, the official peer-reviewed journal of The American College of Medical Genetics. The journal is published by Lippincott Williams & Wilkins, a part of Wolters Kluwer Health, a leading provider of information and business intelligence for students, professionals, and institutions in medicine, nursing, allied health, and pharmacy.

Given low public awareness of this very complex genetic syndrome, educational efforts and guidelines for genetic counseling will be essential. The conclusions are based on a review and analysis of previous research evidence on screening for fragile X syndrome, led by Melissa K. Hill, Ph.D., of the Murdoch Childrens Research Institute, Melbourne, Australia.

Evidence Supports Fragile X Screening in Women of Reproductive Age

Fragile X syndrome, which causes cognitive impairment and other abnormalities, affects about 1 in 4,000 males in the United States. (It also occurs in females, but causes less severe impairment.) Fragile X syndrome is caused by relatively common mutations of a gene called *FMR1*. Although estimates vary, 1 in 300 to 400 U.S. couples may be carriers of the abnormal genes. In recent years, accurate and practical tests to identify carriers of the abnormal *FMR1* genes have been developed.

In their review, Dr Hill and colleagues identified eleven studies evaluating the use of fragile X screening in women of reproductive age. Although some of the studies included pregnant women, there are several key advantages to identifying fragile X gene carriers before conception. The women in the studies found fragile X screening acceptable and appreciated having the option of screening, whether or not they chose to be tested.

The studies varied considerably in terms of the percentage of women who agreed to screening, as well as the rate of abnormal *FMR1* gene carriers. Studies that examined the psychological issues involved in screening revealed challenging issues for genetic counseling—especially related to the lack of awareness or personal experience with fragile X syndrome in the general population.

Despite the limitations of the research, fragile X screening in women of reproductive age "clearly meets established criteria" for genetic screening programs, Dr. Hill and colleagues conclude. However, they emphasize the need for "targeted educational and counseling strategies," as well as further research to evaluate the potential impacts of fragile X screening. They write, "It is crucial that future studies offering screening for fragile X syndrome explore a range of psychosocial aspects in addition to looking at uptake of screening and mutation frequency."

More Study Needed on Newborn Screening for Fragile X

In contrast, the review found just one study evaluating the benefits of testing for fragile X syndrome in newborns—far short of the evidence needed to recommend screening. An important consideration is the fact that, unlike some other conditions for which newborn screening is performed, there's currently no early treatment that can improve the outcomes for newborns affected by fragile X syndrome.

Testing for fragile X syndrome later in infancy might be a good alternative to newborn screening, according to an accompanying editorial by Bradford Coffee, Ph.D., of Emory University. He suggests that performing fragile X screening around one year of age would allow early education for affected infants. It would also avoid the "diagnostic odyssey"

experienced by families of children affected by fragile X syndrome—currently, the average age at diagnosis is about three years.

The "unique biology" of fragile X syndrome raises questions different from those of other genetic diseases, Dr. Coffee points out. Screening may detect "premutations" of the *FMR1* gene that don't cause fragile X syndrome—but may cause other health problems later in life, and may lead to fragile X syndrome in future generations. In addition, many girls who test positive for the "full" *FMR1* mutation don't develop fragile X syndrome.

Dr. Coffee agrees that effective public education will be an essential part of any large-scale fragile X screening program. "Given that the vast majority of the general public has never heard of fragile X syndrome, much less are aware of the complexities of screening and predictive testing of premutation-associated disorders, educational and counseling services need to be developed to inform families of the risks and benefits of the screening," Dr. Coffee writes. He adds that any type of fragile X screening program is far more likely to be successful if the process is "voluntary and transparent."

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