Study examines implications of genetic screening for disease that can be less serious, treatable

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Some couples in Israel whose fetus screened positive for Gaucher disease, which can range from being mild and treatable to being a severe disease, decided to have the pregnancy terminated, raising questions concerning the appropriateness of certain types of genetic screenings, according to a study in the September 19 issue of JAMA.

“Carrier screening can reduce the burden of genetic disease, especially in populations in which specific diseases are common. Although generally performed for severe, untreatable disorders, carrier screening for less serious yet prevalent conditions is also possible, but there is little information on its implications, even though it is likely to become more common,” the authors write.

Gaucher disease (GD) includes three diseases that are due to deficient activity of a certain enzyme. Carrier screening for GD is controversial because common type 1 GD is often asymptomatic and is usually not severe or untreatable, and the test performed does not fully predict disease severity. It is relatively frequent in Ashkenazi Jews, who have been offered screening worldwide and in Israel since 1995.

Shachar Zuckerman, M.Sc., of Shaare Zedek Medical Center, Jerusalem, and colleagues assessed various aspects of GD screening in Israel, including its scope, the screening process and outcomes. Ten Israeli genetic centers provided data on the number of individuals screened for

GD, the number of carriers identified, the number of carrier couples identified, and the mutations identified in these couples between January 1995 and March 2003. Carrier couples were interviewed via telephone between January 2003 and August 2004.

The researchers found that GD carrier frequency was 5.7 percent and 83 carrier couples were identified among an estimated 28,893 individuals screened. There were 82 couples at risk for offspring with type 1 GD. Seventy of 82 couples (85 percent) were at risk for asymptomatic or mildly affected offspring and 12 of 82 couples (15 percent) were at risk for moderately affected offspring.

Prenatal diagnosis was performed in 76 percent (68 of 90) pregnancies, and terminations were performed in 25 percent (4 of 16) pregnancies of fetuses with GD (2 fetuses predicted to have asymptomatic or mild GD, and 2 fetuses predicted to have moderate GD). There were significantly fewer pregnancy terminations in couples who in addition to genetic counseling had medical counseling with a GD expert (1 of 13 [8 percent] vs. 3 of 3 with no medical counseling [100 percent]).

“With respect to the stated goal of carrier screening programs, the main practical outcome of GD screening was a 66 percent reduction in birth prevalence for moderate type 1 GD, for which the estimated frequency is 1 in 27,000, and a 15 percent reduction in the birth prevalence of asymptomatic or mild type 1 GD for which the estimated frequency is 1 in 1,300. This was achieved through termination of pregnancy of fetuses either treatable or likely to be asymptomatic, and it is debatable whether this represents a true benefit,” the authors write.

“Applying the classic carrier screening paradigm to common, low-penetrance disease leads to inevitable dilemmas, and programs offering such screening should determine whether the true goal is knowledge and presymptomatic risk assessment or pregnancy termination of fetuses

with a specified genetic status. Our results suggest that to avoid termination of pregnancies for generally mild conditions, even in a highly educated population, screening programs would require a combination of traditional, nondirective genetic counseling with medical counseling by professionals familiar with the specific diseases."

Source: JAMA and Archives Journals