Before, Between & Beyond Pregnancy
The National Preconception Curriculum and Resources Guide for Clinicians

Guidance for Preconception Cystic Fibrosis Carrier Screening

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Moskowitz SM, Chmiel JF, Sternen DL, Cheng E, Gibson RL, Marshall SG & Cutting GR. 2008. Clinical practice and genetic counseling for cystic fibrosis and CFTR-related disorders. Genet Med. 2008. Dec;10(12):851-868.

Cystic fibrosis is the most common life-shortening autosomal recessive condition in the Caucasian population. It occurs in approximately 1/2000-1/4000 live births and currently has a prevalence of approximately 30,000 people in the United States. The disorder affects the epithelia of the respiratory tract, exocrine pancreas, intestine, hepatobilary system, male genital tract, and exocrine sweat glands, resulting in complex multi-organ disease. The major cause of morbidity and mortality is pulmonary disease, with an overall mean survival of 36.9 years as of 2006.

Cystic fibrosis is caused by the presence of two disease-causing mutations in the CFTR gene, located on chromosome 7q31.2 and containing 27 coding exons spread over 230 kb. The CFTR protein is an integral membrane protein that functions as a regulated chloride channel in a number of epithelial cells. Mutations can affect the protein quantitatively, qualitatively or both.

Over 1600 disease causing mutations have been identified. The most common mutation, delta F508 (ΔF508), accounts for 30-80% of mutant alleles depending on the ethnic group. Genotype-phenotype correlation is best seen in the context of pancreatic symptoms and is generally of limited utility in the prediction of pulmonary disease.

Testing of the 5T allele, a shortening of the string of thymidine bases located in intron 8 of the CFTR gene, is appropriate in the presence of the R117H mutation, when an adult male is being evaluated for CBAVD, or when adults with non-classical CF wish to refine their reproductive risks. Testing of the 5T allele is not otherwise recommended for routine evaluation.

The combination of a severe CFTR mutation on one chromosome and a mild CFTR mutation or the 5T allele on the other chromosome can result in congenital bilateral

absence of the vas deferens (CBAVD) and/or mild respiratory or pancreatic symptoms. Therefore, caution must be used when using genotype to predict a mild CF-like phenotype.

CBAVD accounts for 1.2-1.7% of male infertility. It may be isolated or part of a syndrome. Approximately 80% of men with CBAVD have at least one CFTR mutation.

The optimal time for determination of risk, carrier testing and the discussion of prenatal testing is before pregnancy. In order to perform prenatal diagnosis, disease-causing CFTR mutations must be identified in both parents. If a mutation is identified in only one parent, prenatal diagnosis is less effective and may not be available. If an echogenic bowel is noted on ultrasound, genetic counseling followed by CFTR testing of the parents and/or fetus is appropriate.