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GeneCare

Male infertility and the future of genetics

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Gary and Katie are in their physician's office. After several frustrating years of trying unsuccessfully to have children, the couple recently had an extensive fertility work-up to identify the cause of their problems conceiving. The doctor informs the couple that Gary has a condition known as congenital bilateral absence of the vas deferens (CBAVD). The vas deferens is a tube through which sperm travel from the testis to the ejaculatory duct. A man born with CBAVD, like Gary, typically makes sufficient quantities of sperm but these never reach their intended destination because there is no transport system to get them there. This same transport system is intentionally interrupted when a man chooses to have a vasectomy. At first, Gary feels inadequate and dejected after learning of his condition. Before they leave the office, a blood sample is drawn from Gary for cystic fibrosis (CF) DNA analysis.

Later, a genetic counselor meets with the couple at the fertility clinic. The counselor explains that over 30 years ago it was discovered that men with cystic fibrosis universally have CBAVD. More recently, it was discovered that men with isolated CBAVD often have certain changes in the cystic fibrosis transmembrane conductance receptor (CFTR) gene.

The blood test reveals Gary is a carrier of CFTR mutations associated with CBAVD. The counselor explains that CF is the most common autosomal recessive disorder in North American Caucasians of European ancestry. About 1 in 25 Caucasians carry a CFTR mutation. Gary is somewhat relieved to learn that CFTR mutations are relatively common and that the cause of his infertility is inherited. To him this result means the couple's difficulties having children are not really his fault. In addition, the counselor explains that a procedure, intracytoplasmic sperm injection (ICSI), can enable couples previously infertile due to CBAVD to conceive successfully. ICSI is performed by artificially removing sperm directly from the testis and injecting one directly into an egg to achieve conception, thus by-passing the need for the vas deferens. An egg fertilized by one of Gary=s sperm in this way could then be implanted into Katie=s womb. Such assisted reproductive technologies are widely available.

In 1997 the National Institutes of Health (NIH) convened an independent panel of scientists that recommended CF carrier screening be offered to "adults with positive family history of CF, to partners of people with CF, to couples currently planning a pregnancy, and to couples seeking prenatal care." In 2001 the American College of Medical Genetics issued a statement which reaffirms the NIH recommendation that all couples be offered CF carrier testing, regardless of their ethnic background. Statements with similar positions will follow from other influential organizations which determine the medical standard of care.

CF is an autosomal recessive genetic disorder. "Autosomal" means the gene which causes this disorder is not carried on a sex chromosome so it typically occurs as often in males as in females. "Recessive" means symptoms of this disorder occur when a baby inherits a non-working gene from both parents. If both parents are found to be CF carriers, then they will have a one in four (25%) chance of having an affected baby with each pregnancy.

In individuals affected with CF, thick mucous secretions in the lungs and intestines cause difficulties with breathing and digestion. The respiratory complications of CF may include life-threatening pulmonary infections and lung damage. While some mutations in the CFTR gene cause severe cystic fibrosis symptoms, other milder mutations may cause CBAVD without any of the other classic symptoms of cystic fibrosis.

CF screening identifies carriers of the most common CFTR mutations. However, there are other rare CFTR mutations which are not detectable through routine screening. Because there are many different CFTR mutations that can cause CF, test results are most reliable if the specific mutations in an affected relative or CF carrier are known in cases where there is a family history. If the mutations are not known, carrier testing still may be performed though interpretation of the results is less conclusive. Current DNA testing detects about 97% of CF mutations in individuals of Ashkenazi Jewish ancestry, 90% in North American Caucasians, and less than this in other ethnic groups. In most cases, carrier testing may be completed within one to two weeks and prenatal testing in approximately three weeks.

Individuals who are concerned about their chances of being a carrier of CF or other genetic conditions are encouraged to pursue genetic counseling and also to discuss genetic testing with their physicians. GeneCare Medical Genetics Center, in Chapel Hill, offers genetic counseling and laboratory services, including prenatal screening and diagnostic testing. For more information call (919) 942-0021 or 1-800-277-4363 or visit www.genecare.com.