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AN ALTERNATIVE TEST FOR CYSTIC FIBROSIS SCREENING FROM THE PAP TEST VIAL

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What is Cystic Fibrosis?

With over 25 years of experience as a respiratory care practitioner, the patients I have cared for with cystic fibrosis have all but become family. Some you treat from the moment they are diagnosed, or from the moment they are born, some unfortunately to the moment that they die. You sit with them, you cry with them, you give them therapy with a passion to help them fight for every breath. You see, they are the soldiers that fight the fight every day just to stay alive. If you are born with CF, your average lifespan is approximately 30 years. CF is a chronic, progressive genetic disease of the body's mucous glands. CF primarily affects the respiratory and digestive systems in children and young adults, involving the sweat glands and the reproductive system as well. CF-like disease has been known for well over two centuries, first considered back in 1938 as a disease of the pancreas. It is the most common autosomal recessive genetic disorder in Caucasian populations (*1*).

Carrier Testing

ACOG (American College of Obstetricians and Gynecologists), ACMG (American College of Medical Genetics), and NHGRI (National Human Genome Research Institute) have recommended that all Caucasian couples who are pregnant or are considering pregnancy be offered carrier screening for cystic fibrosis, and that non-Caucasian couples be made aware of the availability of the screening test (*2*). This enables the earlier identification of at-risk couples who would have the ability to exercise their reproductive options, including prenatal diagnosis, as well as earlier diagnosis and treatment of affected children. One in 25 Caucasians alone are unaffected carriers, while one in every 20 Americans are unaffected carriers of an "abnormal CF gene." The delta F508 gene is accountable for 70—80% of all cystic fibrosis (*1*). Because phenylanine is located in position 508 of the protein chain, this mutant protein is called delta508 CFTR (cystic fibrosis transmembrane regulator), located on chromosome number seven (*2*).

Couples, both of whom carry the CF mutation, have a 1-in-4 chance of having a child with CF in each pregnancy, a 25% rate of inheritance. There is then a two-thirds chance that unaffected children will be CF carriers.

Advanced Molecular Technology

There are more than 900 documented mutations for cystic fibrosis. However, there are 25 that show up more often than 1:1,000 in Caucasians or people of Northern European and Ashkenazi Jewish descent. The **AmeriPath Cystic Fibrosis Test** consists of multiplex PCR amplifications of selected regions of the CF gene, followed by the probe-specific detection of wild-type and mutant alleles, using the Roche CF Gold 1.0™ Linear Array Panel, which detects the 25

mutations and polymorphisms, as recommended by the American College of Obstetricians and Gynecologists. It can also be done directly from the Pap test using ThinPrep or Sure-Path testing from DNA with PCR amplification and CF genotyping. Polymerase chain reaction allows very small amounts of genetic material to be amplified into billions of copies in just a few hours, thus facilitating the detection of target DNA. DNA also can be extracted from buccal cells collected from the inner cheeks of patients for testing of the CF mutations.

What is the Benefit of Knowing?

If you are planning a family or have already been confirmed that you are pregnant, there are diagnostic tests that can be performed at very low risk, such as PCR testing from your pap test.

The socio-economic burden of caring for a child with a life-long disease could be emotionally and economically draining. It is a matter of preparing and educating yourself, both at the same time. More than 12 million people are unaffected carriers of the CF gene, who are unaware that they are carriers (*1*).

How is Cystic Fibrosis Diagnosed?

The most common test is called a sweat chloride test, which measures the amount of salt (sodium chloride) in the sweat. An area of the skin is made to sweat by stimulating the sweat gland by using a chemical called pilocarpine and applying a mild electric current. The sweat is collected in a coil type device and analyzed for higher than normal amounts of sodium and chloride, suggesting CF. In the case that not enough sweat can be collected, another test called an IRT (immunoreactive trypsinogen test) may be used. Blood drawn 2 to 3 days after birth is analyzed for a specific protein called trypsinogen.

CF can be detected in an unborn fetus by two special prenatal tests. Either an amniocentesis or a chorionic villus biopsy can be performed. Cells in the amniotic fluid are tested to see if the CF genes common to the parents are present. In a chorionic villus biopsy, cells from the tissue that form the placenta are tested for CF.

Can Cystic Fibrosis be Prevented?

In babies with two abnormal CF genes, the disease is already present at birth in some organs such as the pancreas and liver. The next best thing to prevention is detection. Here at AmeriPath, we offer a DNA test by PCR, using Roche Amplicor Gold 1.0 LAP™ detection from the Pap test from one vial, along with other diagnostic testing such as HPV, HSV, *Chlamydia*, gonorrhea, and now, Group B Strep, another essential test for delivering a healthy baby. Although there is no cure for CF, just knowing that one is an unaffected carrier of the gene is important in the management of the disease.

Quality Diagnostics

The diagnostic quality and superior turn-around times at AmeriPath, along with enhanced pathology reports featuring color-coding and photomicrographs, complement each case and provide excellent diagnostics. In addition to Pap-to-biopsy correlation, we also provide complimentary patient education materials and a Pap test hotline to notify patients of normal Pap test results.

The advanced diagnostic quality of **AmeriPath Diagnostics** is the highest in the industry. Over 70 board-certified cytopathlogists, along with more than 400 board-certified pathologists, consistently use their medical expertise and skills in diagnosing each case and provide personal consultations regarding treatment plans and disease management.

For more information concerning AmeriPath's tests for CF, call AmeriPath at 1-800-330-6565 ext. 7310; or visit the company's Web site at www.ameripath.com.

References:

1. The National Cystic Fibrosis Foundation and ACOG Web site: HealingWell.com/NHLBI.
2. American College of Obstetricians and Gynecologists; American College of Medical Genetics. *Preconception and Prenatal Carrier Screening for Cystic Fibrosis: Clinical and Laboratory Guidelines.* Washington DC: ACOG, 2001.