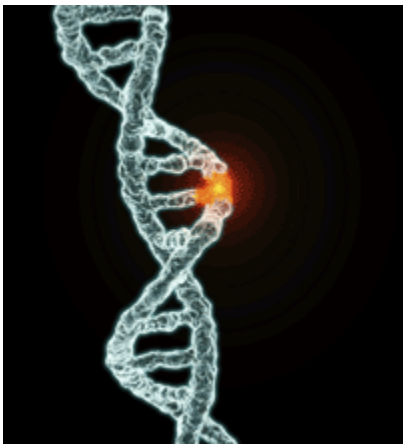
# Genetics in Special Education Series

## May 2011



## Genetic disorders presented in this issue:



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# Cystic Fibrosis

### WHAT DO WE KNOW ABOUT HEREDITY AND CYSTIC FIBROSIS?

Cystic fibrosis (CF) is the most common, fatal genetic disease in the United States. About 30,000 people in the United States have the disease. CF causes the body to produce thick, sticky mucus that clogs the lungs, leads to infection, and blocks the pancreas, which stops digestive enzymes from reaching the intestine where they are required in order to digest food.

### CYSTIC FIBROSIS: A SINGLE GENE DISEASE

Mutations in a single gene - the Cystic Fibrosis Transmembrane Regulator (CFTR) gene - causes CF. The gene was discovered in 1989. Since then, more than 900 mutations of this single gene have been identified.

In normal cells, the CFTR protein acts as a channel that allows cells to release chloride and other ions. But in people with CF, this protein is defective and the cells do not release the chloride. The result is an improper salt balance in the cells and thick, sticky mucus. Researchers are focusing on ways to cure CF by correcting the defective gene, or correcting the defective protein.

## GENE THERAPY RESEARCH OFFERS PROMISE OF A CURE FOR CYSTIC FIBROSIS

Gene therapy offers great promise for life-saving treatment for CF patients since it targets the cause of CF rather than just treating symptoms. Gene therapy for CF had its start in 1990, when scientists successfully corrected faulty CFTR genes by adding normal copies of the gene to laboratory cell cultures.

In 1993, the first experimental gene therapy treatment was given to a patient with CF. Researchers modified a common cold virus to act as a delivery vehicle - or "vector"- carrying the normal genes to the CFTR cells in the airways of the lung.

Subsequent studies have tested other methods of gene delivery, such as fat capsules, synthetic vectors, nose drops or drizzling cells down a flexible tube to CFTR cells lining the airways of lungs. Researchers are now testing aerosol delivery using nebulizers.

But finding the best delivery system for transporting normal CFTR genes is only one problem that scientists must solve to develop an effective treatment for CF. Scientists must also determine the life span of affected lung cells, identify the "parent cells" that produce CFTR cells, find out how long treatment should last and how often it needs to be repeated.

The first cystic fibrosis gene therapy experiments have involved lung cells because these cells are readily accessible and because lung damage is the most common, life-threatening problem in CF patients. But scientists hope that the technologies being developed for lung cells will be adapted to treat other organs affected by CF.

## GENETIC RESEARCH MAY LEAD TO NEW DRUGS TO TREAT CYSTIC FIBROSIS

Another research breakthrough offers a promising approach to treating cystic fibrosis. Researchers at the University of Washington's Genome Center and at PathoGenesis Corporation have completed a genetic map for the Pseudomonas aeruginosa bacterium. This bacterium is the most common cause of chronic and fatal lung infections for people with CF. Scientists hope to use their knowledge of this bacterium's genetic sequence to develop innovative drugs for treating infections caused by P. aeruginosa.

## IS THERE A TEST FOR THE CYSTIC FIBROSIS GENE?

CF has a variety of symptoms, including very salty-tasting skin, a persistent cough and excessive appetite but poor weight gain. The "sweat test" - which measures the amount of salt in sweat - is the standard diagnostic test for those with symptoms. A high salt level indicates CF.

But one in 31 Americans - more than 10 million people - are symptom-less carriers of the defective CF gene and can pass on the defective gene to their children. To develop CF, a child must inherit a defective gene from both parents. If both parents are carriers, there is a 25 percent chance that each child they conceive will have CF, and a 50 percent chance that the child will be a carrier.

The purpose of carrier testing - a laboratory test done on a sample of blood or saliva - is to see if a couple is at risk for giving birth to a child with CF. Carrier testing is not infallible. It cannot detect all of the CF gene mutations. In rare cases, a person can have a normal test result and still be a CF carrier.

If both parents are carriers, they may want to consult with a genetic counselor for help in deciding whether to conceive or whether to have a fetus tested for CF.

Prenatal testing for CF can be done around the 11th week of pregnancy using chorionic villi sampling (CVS). This involves removing a tiny piece of the placenta. Or, the fetus can be tested with amniocentesis, around the 16th week of pregnancy. In this procedure, a needle is used to take amniotic fluid surrounding the baby for testing. Since CF cannot be treated before birth, the purpose of prenatal testing is to prepare parents to care for a baby with special health needs, or to make a decision about terminating the pregnancy.

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# Tay-Sachs

## WHAT DO WE KNOW ABOUT HEREDITY AND TAY-SACHS DISEASE?

Tay-Sachs disease (TSD) is a fatal genetic disorder, most commonly occurring in children, that results in progressive destruction of the nervous system. Tay-Sachs is caused by the absence of a vital enzyme called hexosaminidase-A (Hex-A). Without Hex-A, a fatty substance, or lipid, called GM2 ganglioside accumulates abnormally in cells, especially in the nerve cells of the brain. This ongoing accumulation causes progressive damage to the cells.

In children, the destructive process begins in the fetus early in pregnancy. However, a baby with Tay-Sachs disease appears normal until about six months of age when its development slows. By about two years of age, most children experience recurrent seizures and diminishing mental function. The infant gradually regresses, and is eventually unable to crawl, turn over, sit or reach out. Eventually, the child becomes blind, cognitively impaired, paralyzed and non-responsive. By the time a child with Tay-Sachs is three or four years old, the nervous system is so badly affected that death usually results by age five.

A much rarer form of Tay-Sachs, Late-Onset Tay-Sachs disease, affects adults and causes neurological and intellectual impairment. Only recently identified, the disease has not been extensively descried. As for the childhood form of Tay-Sachs, there is no cure. Treatment involves managing the symptoms of the disease.

## DEFECT IN HEX-A GENE CAUSES TAY-SACHS

Tay-Sachs disease results from defects in a gene on chromosome 15 that codes for production of the enzyme Hex-A. We all have two copies of this gene. If either or both Hex-A genes are active, the body produces enough of the enzyme to prevent the abnormal build-up of the GM2 ganglioside lipid. Carriers of Tay-Sachs - people who have one copy of the inactive gene along with one copy of the active gene - are healthy. They do not have Tay-Sachs disease but they may pass on the faulty gene to their children.

Carriers have a 50 percent chance of passing on the defective gene to their children. A child who inherits one inactive gene is a Tay-Sachs carrier like the parent. If both parents are carriers and their child inherits the defective Hex-A gene from each of them, the child will have Tay-Sachs disease. When both parents are carriers of the defective Tay-Sachs gene, each child has a 25 percent chance of having Tay-Sachs disease and a 50 percent chance of being a carrier.

## EASTERN EUROPEAN (ASHKENAZI) JEWS AT GREATER RISK FOR TAY-SACHS DISEASE:

While anyone can be a carrier of Tay-Sachs, the incidence of the disease is significantly higher among people of eastern European (Ashkenazi) Jewish descent. Approximately one in every 27 Jews in the United States is a carrier of the Tay-Sachs disease gene. Non-Jewish French Canadians living near the St. Lawrence River and in the Cajun community of Louisiana also have a higher incidence of Tay-Sachs. For the general population, about one in 250 people are carriers.

There is no cure or effective treatment for Tay-Sachs disease. However, researchers are pursuing several approaches to finding a cure. Scientists are exploring enzyme replacement therapy to provide the Hex-A that is lacking in babies with Tay-Sachs. Bone marrow transplantation has been attempted also, but to date has not been successful in reversing or slowing damage to the central nervous system in babies with Tay-Sachs. Another avenue of research is gene therapy in which scientists transfer a normal gene into cells to replace an abnormal gene. This approach holds great promise for future Tay-Sachs patients.

## IS THERE A TEST FOR TAY-SACHS DISEASE?

A simple blood test can identify Tay-Sachs carriers. Blood samples can be analyzed by either enzyme assay or DNA studies. The enzyme assay is a biochemical test that measures the level of Hex-A in a person's blood. Carriers have less Hex-A in their body fluid and cells than non-carriers.
DNA-based carrier testing looks for specific mutations or changes in the gene that codes for Hex-A.

Since 1985, when the Hex-A gene was isolated, more than 50 different mutations in this gene have been identified. Nevertheless, some mutations are not yet known. The current tests detect about 95 percent of carriers of Ashkenazi Jewish background and about 60 percent of carriers in the general population.

If both parents are carriers, they may want to consult with a genetic counselor for help in deciding whether to conceive or whether to have a fetus tested for Tay-Sachs. Extensive carrier testing of Ashkenazi Jews has significantly reduced the number of Tay-Sachs children in this population group. Today most cases of Tay-Sachs disease occur in populations thought not to be at high risk.

Prenatal testing for Tay-Sachs can be performed around the 11th week of pregnancy using chorionic villi sampling (CVS). This involves removing a tiny piece of the placenta. Alternatively, the fetus can be tested with amniocentesis around the 16th week of pregnancy. In this procedure, a needle is used to remove and test a sample of the fluid surrounding the baby.

Assisted reproductive therapy is an option for carrier couples who don't want to risk giving birth to a child with Tay-Sachs. This new technique used in conjunction with in-vitro fertilization enables parents who are Tay-Sachs carriers to give birth to healthy babies. Embryos created in-vitro are tested for Tay-Sachs genetic mutations before being implanted into the mother, allowing only healthy embryos to be selected.