Tay-Sachs Disease

Tay-Sachs is an autosomal recessive disease, meaning for a person to develop it they must receive two copies of a defective gene, one from their father and one from their mother. The condition causes progressive destruction of the central nervous system in affected children and is ultimately fatal. Tay-Sachs Disease (TSD) is caused by a defective gene which stops the production of a vital enzyme that is needed to break down a fatty substance that builds up in nerve cells. As the disease progresses the affected child is made blind and deaf and becomes unable to swallow. Their muscles begin to dysfunction and paralysis eventually sets in.

Tay-Sachs disease is named after Warren Tay (1843-1927) and Bernard Sachs (1858-1944) Tay was a British ophthalmologist who in 1891 described a patient with Tay-Sachs that had a cherry red spot on their retina. Bernard Sachs was a New York neurologist who's work several years later gave the first descriptions of the cellular changes in TSD. He also recognized the inherited nature of the disease. Sachs also observed that most of the children affected were of European Jewish origin.

Cause of Tay-Sachs Disease

TSD is caused by the absence of an enzyme called beta-hexosaminidase A (Hex-A). This enzyme, which is found in organelles that break down large molecules for recycling, is vital for breaking down a lipid (fatty substance) called GM2 ganglioside. In people with TSD GM2 builds up in nerve cells in the brain and in the spine. This build up causes progressive damage to the cells, the amount of damage caused depends on the amount of Hex-A in the patients body. The damage to the cells normally begins early in pregnancy, however, the disease is not clinically present until the child is several moths old. By the age of three or four the affected child's nervous system is so badly affected the it can no longer support the child's life. All children with TSD die by about the age of five years old.

Symptoms

A baby affected by Tay-Sachs disease will appear to develop normally up to about the age of six moths. After that time the first signs of TSD can be seen, these include loss of peripheral vision, a reduction in development and an abnormal startle response. By the age of two most children with TSD have recurring seizures and diminishing mental function. Affected babies lose one skill after another and are eventually unable to crawl, turn over, sit or reach out. They also suffer loss of coordination, inability to swallow and difficulty breathing. Children with TSD eventually go blind developing a cherry red spot on their retina, become mentally retarded, paralyzed and non-responsive to the environment around them.

Late Onset Tay-Sachs Disease

There is another rarer form of Tay-Sachs disease that occurs later in a patients life. The first symptoms are usually visible between adolescence and the patient's mid-thirties. However, there can be very subtle signs before adolescence such as clumsiness, tremors, falls and mood changes. This form of the disease is caused by the same missing Hex-A enzyme activity as in the classical form of TSD. Because there is still some Hex-A activity unlike the other version of the disease the GM2 is slower to accumulate in the body's nerve cells which leads to the later onset and slower progression of the disease. The symptoms and the severity of them can vary quite a lot.

They can range from muscle weakness, cramping and wasting to lack of coordination, hand tremors, slurred speech and sensory impairment. This form of the disease can also affect the intellectual function of the patient. They can suffer from memory impairment, difficulty comprehending and a downturn in their school performance. Short attention spans and personality changes have also been reported from some patients. Unlike the classical form of TSD late onset TSD is not always fatal.

Transmission of Tay-Sachs

Tay-Sachs Disease is transmitted through genes from parents to their children. For a child to be affected by Tay-Sachs disease they have to receive a defective Hex-A gene from both their mother and their father. If they inherit only one gene they will become a carrier of the disease but will not be affected by it. Approximately one in three hundred people are carriers of the defective gene which is found in chromosome fifteen. When both parents are carriers there is a twenty five percent chance with each pregnancy that the child have TSD and a fifty percent chance that they will be a carrier and a twenty five percent chance that they will be a non carrier. Carriers of the defective gene produce less Hex-A than normal but are in no way affected by this. A Hex-A blood activity test can detect weather a person has TSD or if they are a carrier. If a couple have the test and are both found to be carriers a genetic counselor can help them to comprehend the risks involved in having children.

Tay-Sachs disease occurs mostly in people of central and eastern European (Ashkenazi) Jewish origin or French Canadians of Southeastern Quebec. There are also other nationalities that carry the defective gene. One in twenty seven Jews in the United States is a carrier of the defective gene and approximately one in sixty seven thousand of the US Jewish population are affected by the late onset form of the disease.

Cure for Tay-Sachs Disease

At the moment there is no cure of Tay-Sachs disease. However, there is promise being shown in treatment of late onset TSD with a GM2 synthesis inhibitor. The effectiveness of this treatment in the classical form of TSD is limited because of the amount of irreversible neurological damage that has already occurred before and after birth. Because of the amount of damage it is hard to develop an effective treatment for this form of the disease. It is hoped that the late onset form of TSD will be responsive to treatment and that this combined with the DNA and enzymatic screening programs already in place will lead to the disease being controlled.

The other form of Tay-Sachs may be able to be treated with enzyme replacement or gene replacement therapy. In enzyme replacement therapy a manufactured enzyme is injected into the patient. This enzyme is supposed to do the job of the missing enzyme in the patient's body much like people with diabetes injecting insulin. Gene replacement therapy is where a replacement gene is introduced into the patient so that the missing enzyme will be produced. These treatments will rely on early diagnosis of the disease so the therapies can be commenced quickly and so that their benefits will be maximized. Enzyme replacement therapy has been successful in the treatment for Gaucher disease and this has given hope to those who are affected by other genetic diseases such as Tay-Sachs.

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