SCRIPPS CLINIC RESEARCHERS DEVELOP METHOD TO PREDICT SEVERITY OF GAUCHER'S DISEASE

LA JOLLA, CA Aug. 11, 1989 -- Researchers at Scripps Clinic and Research Foundation in La Jolla, CA have developed a method to predict the severity of Gaucher's Disease, a disorder particularly common among the Jewish population, but found in others, as well.

The results, based upon studies of 47 patients, will be published in the Aug. 12 issue of the medical journal, The Lancet.

One of the authors, Ernest Beutler, M.D., chairman of the Scripps Clinic Department of Molecular and Experimental Medicine, explains that the manifestations of Gaucher's Disease vary from a rapidly fatal disease, with death occurring in the first year of life, to a disease so benign that it is diagnosed quite by accident.

Because physicians have been unable to identify the severity of the disease in its early stages, prognosis and genetic counseling have been difficult.

"We've suspected for some time that the disease is variable due to different mutations of the same gene," Dr. Beutler says. "In our laboratories, we've now worked out a means of actually looking at the mutation and classifying it to see how severe the disease will become in the patient."

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Dr. Beutler gives two examples of how the prediction of severity directly affected patients who were tested in an NIH (National Institutes of Health) supported program at the Sam and Rose Stein General Clinical Research Center of Scripps Clinic.

"One family had a child with Gaucher's Disease, and the mother was pregnant with a second child. From an amniocentesis, we were able to determine that the second child would also have the disease, but that it would be a relatively mild form, with a good prognosis," he says.

In a second case, a one-year-old child was diagnosed by the Center as having the severe form of Gaucher's Disease, with a prognosis for serious liver, spleen, bone and neurologic involvement. Although bone marrow transplantation carries a 30 percent mortality rate, Dr. Beutler says this radical treatment would have to be considered for a child so severely affected.

What is also significant about the study published in The Lancet is that it represents an example of the use of molecular biology techniques to narrow down the type of genetic disease.

"In 1985, Scripps Clinic was the first to report the cloning of the gene involved in Gaucher's Disease," Dr. Beutler says, adding that scientists then worked out the method to look at the gene mutation and classify it.

"However, just a few years ago, each patient would have been a major research project. We could have found 60 patients, but we'd be working on them until the year 2001," he notes. "Now we can get reliable data within a few hours."
He credits the development of modern DNA technology, such as the Polymerase Chain Reaction (PCR), which allowed the researchers to study the genes in many people in a matter of hours, rather than months.

Of the 47 patients mentioned in The Lancet article, 22 were determined to have a mild form of the disease, 22 had a moderate disorder, and three were diagnosed as severe. The authors note that one of the three severely affected patients died at the age of 32 due to complications of liver and lung disease.

Of the 22 patients with mild disease, eight were entirely asymptomatic, with the remaining 14 experiencing enlarged spleens and lower platelet count.

The patients with moderate disease were usually diagnosed early in life and had significant enlargement of the liver, abnormal liver function tests, significant bone involvement, and many had undergone splenectomy.

Of the severe cases, manifestations included renal and lung involvement, plus severe liver disease.

Additional authors of The Lancet article include Ari Zimran, M.D., a post-doctoral fellow at Scripps Clinic for three years, who has now returned to the Shaare Zedek Medical Center in Jerusalem, Israel to continue his research on Gaucher's Disease; and Joseph Sorge, M.D., an adjunct associate member of the Research Institute of Scripps Clinic and president of the La Jolla firm Stratagene.

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Note: Gaucher is pronounced Go Shey.