

# SOUTHWESTERN NEWS

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## **LEPTIN REPLACEMENT THERAPY REDUCES METABOLIC ABNORMALITIES IN PATIENTS WITH RARE FAT DISORDERS, RESEARCHERS REPORT**

DALLAS – Feb. 21, 2002 – Leptin replacement therapy drastically reduces triglyceride levels and controls diabetes in patients with rare fat disorders known as lipodystrophies, according to researchers at UT Southwestern Medical Center at Dallas and the National Institute of Diabetes and Digestive and Kidney Diseases.

Leptin is a protein produced by fat cells and is nearly absent in patients with generalized lipodystrophies – disorders which result in extreme loss of body fat. Generalized lipodystrophies are associated with metabolic abnormalities such as diabetes, high blood cholesterol and an accumulation of fat in the liver. Current treatment consists of high-dose insulin plus triglyceride- or lipid-lowering medications.

Results of the study, published in today's issue of *The New England Journal of Medicine*, indicated that leptin replacement therapy not only controlled severe insulin resistance and lowered triglyceride levels but also decreased fat accumulation in the liver, an abnormality for which there has been no effective therapy.

Dr. Abhimanyu Garg, professor of internal medicine and chief of nutrition and metabolic diseases at UT Southwestern, and Dr. Elif Arioglu Oral of the National Institute of Diabetes and Digestion and Kidney Diseases were the principal investigators at the two sites.

"It's very frustrating to treat patients with generalized lipodystrophies," said Garg, who has been studying patients with lipodystrophies referred from all over the world for the past 16 years. "Diabetes is so severe and very difficult to manage. Extremely high blood fat levels can cause recurrent abdominal pain due to pancreatic inflammation.

"We have shown that leptin replacement therapy is an effective treatment for patients with lipodystrophies," said Garg, senior author of the study.

Nine females participated in the 17-week study. Eight of the participants were diabetic

(MORE)

## LEPTIN REPLACEMENT - 2

and all nine participants had high triglycerides levels ranging from 445 to 9,560 milligrams per deciliter. Normal triglyceride levels are 150 mg/dL or below.

The study participants received leptin injections under the skin twice a day for four months. After four months of the therapy, they experienced a 60 percent decrease in blood triglyceride levels and a 28 percent decrease in liver volume. Blood glucose levels also showed marked improvement. Six of the eight patients no longer required insulin therapy to control their diabetes. Two required much lower dosages of insulin, and only one continued to require additional triglyceride-lowering medication.

"This is a very dramatic effect to go from 3,000 units of insulin a day to none," Garg said.

"This study shows that leptin provides some hope for treatment specifically for the complications that result from lipodystrophies. It may not be a cure all for lipodystrophies, because there are several forms of the condition, but we've shown that leptin therapy is effective in diabetes control and decreases triglycerides and the accumulation of fat in the liver."

The researchers have initiated a second study to determine the long-term benefits and possible side effects of leptin replacement therapy.

Other researchers involved in the study include Dr. Peter Snell, associate professor of internal medicine; Dr. Vinaya Simha, a postdoctoral fellow in endocrinology and metabolism at UT Southwestern; and researchers with the Diabetes Branch of the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health and Amgen Inc.

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