

Transplanting fat may be effective treatment for metabolic disease

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(Medical Xpress)—Transplanting fat may treat such inherited metabolic diseases as maple syrup urine disease (MSUD) by helping the body process the essential amino acids that these patients cannot, according to Penn State College of Medicine researchers.

The researchers are targeting maple syrup urine disease because it disproportionately affects the Amish and Mennonites who reside in the central Pennsylvania communities surrounding the College of Medicine and its hospital, Penn State Milton S. Hershey Medical Center.

The team transplanted up to two grams of [fat](#) into either abdomens or backs of mice genetically engineered to have MSUD. When fat was transplanted in the back of the MSUD mice, amino acids levels decreased considerably compared to non-transplanted MSUD mice. The fat was either cut into small pieces or minced into fine pieces, with no noticeable difference in results.

The procedure does not work in the abdomen and instead resulted in inflammation and the transplanted fat not forming blood vessels or attaching properly.

Results were published recently in the journal *Molecular Genetics and Metabolism*.

The procedure may be effective for other inherited [metabolic diseases](#), including phenylketonuria and organic acidurias, said Christopher

Lynch, professor of cellular and [molecular physiology](#), lead researcher.

"While individually these diseases are relatively rare, inherited metabolic diseases are sufficiently common that they are part of [newborn screening](#) in Pennsylvania and most other states," Lynch said.

The body uses amino acids to make proteins and breaks down amino acids to create energy. Patients with maple syrup urine disease cannot fully metabolize three branched chain amino acids. In MSUD patients, the process of breaking down the amino acids begins but cannot be completed.

This leads to accumulation of the amino acids and their initial metabolic by-products to toxic levels resulting in, without treatment, to loss of appetite, crying, seizures, coma and death. These products build up to such levels in these patients that they form crystals in the urine and give the urine a burnt sugar smell, hence the name of the disease.

Since amino acids are needed and cannot be fully removed from the diet, standard treatment for MSUD requires a specialized diet that limits meat and dairy. Even with careful diet, patients with MSUD are in danger of experiencing coma or seizures in response to stressful situations or when they have an infection.

A recent advance in the treatment of this disease is liver transplant, which provides sufficient metabolic capacity for many patients to resume a normal diet. While this experimental therapy works well, there is a shortage of donor livers and the cost is estimated to be upward of \$500,000 during the first year of treatment.

Researchers will now try to refine the use of fat for the best results.

"We're taking lessons from plastic surgeons to see how much and how

best to transplant the fat," Lynch said. "We found that injecting more fat didn't mean better results. When we increased the fat injected from one to two grams, it did not lower the amino acid levels further. So injecting less fat may help blood vessels develop through the fat, helping to circulate more of the [amino acids](#) through the transplanted tissue."

Researchers are also looking into the use of adult stem cells mixed with the transplanted fat to help with replenishment. In other kinds of transplants, stem cells also reduce rejection.

"We now need to look through the existing arsenal of transplant drugs to see which ones are most compatible with fat transplant and adult adipose regenerative stem cell growth and fat cell conversion," Lynch said.

Lynch's team believes that it may be easier to get fat donors compared to other organs and that fat transplant operations would be far less expensive than other kinds of transplants. Alternatively, it could be a bridging therapy before liver transplant.

Other researchers on this project are Heather Zimmerman, Department of Comparative Medicine; Kristine Olson, Department of Cellular and Molecular Physiology; and Gang Chen, from the Department of Public Health Sciences.

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