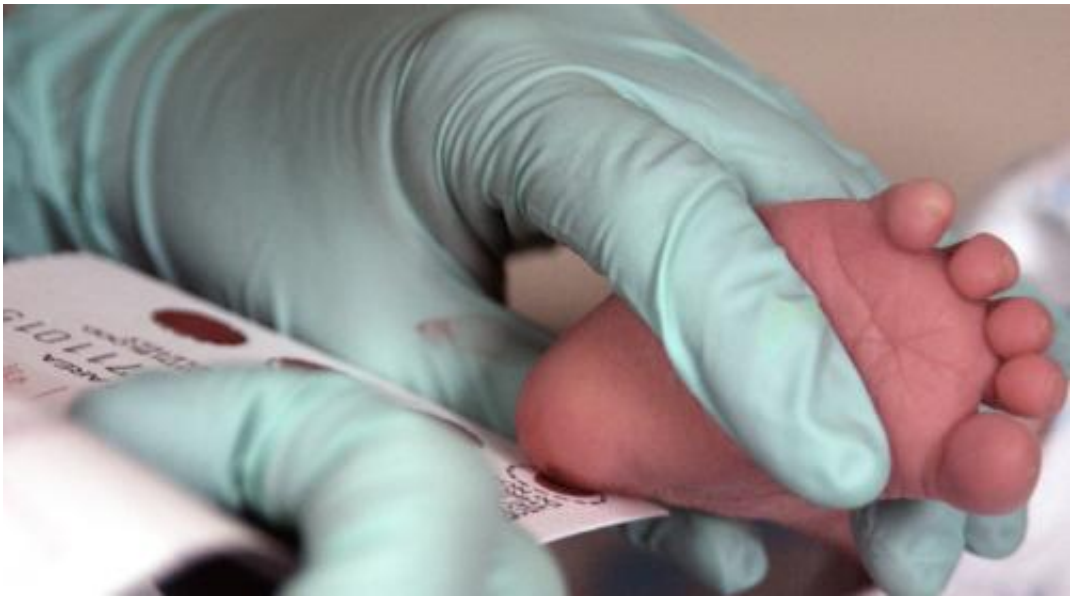
Infant tests for debilitating diseases set for mainstream

April 2 2013, by Vince Stricherz



Credit: U.S Air Force/Staff Sgt. Eric T. Sheler

(Medical Xpress)—Michael Gelb and František Tureček have worked more than a decade to devise and implement newborn screening for some debilitating, often-fatal conditions that show up in the first year to several years of a child's life.

The idea is to detect the conditions as early as possible, before symptoms begin to appear, so treatment can lessen the physical damage.

Now the University of Washington chemistry professors' methodology is

drawing interest from companies that could use it in tests distributed nationally and around the world.

"It's the ultimate analytical device to find a needle in a haystack, when you know what you are looking for," Gelb said.

Currently, the screening can detect six diseases—Krabbe, Pompe, Niemann-Pick, Gaucher, Fabry and Hurler syndromes—that are associated with enzyme deficiencies within lysosomes, structures that break down large molecules and eliminate waste in most cells. Three others are likely to be added to the screening soon, and more can be added as treatments for the conditions are developed.

One question – whether the UW-developed test, which uses a method called tandem mass spectrometry, could be integrated into routine newborn screening – was tested at the Washington State Newborn Screening laboratory.

A new research paper in press with the *Journal of Pediatrics* shows that not only can the lysosomal storage disease testing be integrated with other newborn screening, but that it is a better predictor than the methods currently used for non-lysosomal disorders, said Dr. Ronald Scott, the paper's lead author and a UW professor of pediatrics.

There are more than 40 lysosomal storage diseases, but there are effective treatments for fewer than a dozen. "Those are the ones we focus on," said Scott, who serves as an adviser to the Washington Health Department on newborn screening and has worked closely with Gelb and Tureček in their research (they are coauthors of the *Journal of Pediatrics* paper).

Newborns are routinely screened for a variety of disorders. In Washington state those range from maple syrup urine disorder to cystic

fibrosis. But screening for lysosomal storage diseases is just now being added by a few states. New York, with efforts led by Hunter's Hope Foundation, tests for Krabbe disease, the condition that claimed the life Hunter Kelly, son of former Buffalo Bills quarterback Jim Kelly.

New Jersey has passed legislation to screen for several disorders as soon as testing has passed federal approval and is readily available. Similar significant efforts, led by the Evanosky Foundation, are under way in Illinois and Missouri, and there have been inquiries from other states.

The screening developed by Gelb and Tureček is similar in some ways to newborn screening for other disorders – a spot of blood drawn from a baby's heel is dried on a paper card, a small section of the blood spot is punched out and rehydrated, then target enzymes are incubated and measured using tandem mass spectrometry, a means of determining a substance's chemical makeup and quantity.

"In the sense of making it to the real world, it's very far along," Gelb said of the technique. "But in terms of worldwide use, it's still very early."

Lysosomal disorders have a variety of effects and treatments. In Gaucher and Fabry disorders, for example, enzyme therapy can help to alleviate symptoms, Scott said. Enzyme therapy is not effective for Krabbe disease, an often-fatal disorder that affects the myelin sheath of nerves, and it is treated instead with a bone marrow transplant.

A condition called Mucopolysaccharidosis II – with symptoms ranging from a complete halt to development at an early age to learning disabilities, psychiatric problems or aortic valve disease at a later age – has not yet been added to the testing regimen. But testing can detect it early enough that an infant can be treated and kept stable until the age of 2, when a bone marrow transplant can be performed to treat symptoms that affect the central nervous system.

"Depending on the mutation, some affected individuals will develop a severe infantile form of the disease and be treated as soon as possible," Tureček said. "Others will have milder forms that may cause associated health problems later in life, but there is no need for early treatment."

Besides the growing U.S. interest, some in other countries – ranging from individual doctors to government officials – have expressed an interest in learning more. And there are concerns. Cost is an issue for some, Gelb said, while for others it's that testing and early treatment aren't necessarily a perfect answer.

"Many of these babies are not saved from illness," he said. "They're better, but they're not perfect. Some are better than others."

But Scott, who has spent his career leading research at UW and Seattle Children's on a variety of pediatric genetic disorders, has been heartened by the advances in detection and treatment that have come in a relatively short time.

"I am absolutely enthralled with the changes that have been made for some of the lysosomal storage diseases in the last decade," he said. "I have patients who in the past would have been seriously debilitated but who are now leading normal lives, going to college, raising families, and for the most part with no symptoms."

Provided by University of Washington