

Wall Street Journal - Expansive Effort Is Begun to Study Rare Diseases

By JENNIFER CORBETT DOOREN

May 16, 2006; Page D3

The National Institutes of Health has started the first of what will eventually be about 50 clinical studies looking into a variety of rare diseases and disorders.

The research involves 10 research consortia studying groups of related rare, and sometimes fatal, diseases that can develop shortly after birth. In most cases, the diseases -- which range from rare blood, liver and lung disorders to a condition that causes temporary paralysis -- lack effective treatments. The NIH is putting \$71 million toward the effort over a five-year period.

The roughly three dozen diseases or disorders being studied are considered rare as they each affect fewer than 200,000 people in the U.S., or less than 1% of the population for each. The NIH has identified about 6,000 rare diseases that affect a total of about 25 million Americans.

All 10 of the research groups will have a longitudinal, or history, study designed to track the disorder's progression over time, aimed at the development of therapies. Some of the studies also will test proposed therapies.

The findings from the NIH-funded research into the rare diseases will be housed in a central location run by the University of South Florida in Tampa. The network is designed to expand collaboration among researchers who in the past tended to conduct their work in isolation.

Stephen Groft, director of the NIH's Office of Rare Diseases, said the hope is not only new treatments or cures can be found, but certain findings might be helpful for broader conditions. For example, brain scans of patients with urea-cycle disorders -- one of the groups of diseases under scrutiny -- might offer new understanding of learning disabilities.

Urea-cycle disorders run in families, and people with the disorders either lack or have a defect in certain enzymes needed to break down ammonia in the body. Ammonia is produced when the body breaks down protein in food.

Trish Hertzog, 35 years old, of Moscow, Pa., in the northeastern part of the state, had never heard of the disorder until 1994 after her son, Matthew, was born. Shortly after birth he became ill, lapsed into a coma and died a few days later. It turns out Matthew had the most severe form of the disorder and couldn't process ammonia, which rose to toxic levels in his blood and damaged his brain.

The discovery of the urea-cycle disorder allowed doctors to later diagnose Trish, her half-sister -- who had suffered debilitating strokes as a toddler in the 1960s -- and her mother with a less-severe form of the disorder that causes a variety of neurological symptoms, sleep disturbances and occasional vomiting. It also likely explained the deaths of two of Ms. Hertzog's grandmother's sons shortly after birth. Ms. Hertzog's two daughters Alex, 13, and Tracy, 10, also were diagnosed with a urea-cycle disorder. So far, they manage it with a diet that limits protein and medication.

Ms. Hertzog says she plans to enroll in the urea-cycle history study and possibly a treatment study so researchers can learn more about the disease. She also is considering enrolling her daughters in the history study because they have a 50% chance of passing the disorder to any potential children.

Mark Batshaw is heading up the urea-cycle disorders research at Children's National Medical Center in Washington, D.C. Unlike many of the rare diseases being studied, there is a Food and Drug Administration-approved drug available. The drug, made by a unit of **Medicis Pharmaceutical Corp.**, helps fight the buildup of ammonia in the body. Along with studying that drug, plus an investigational therapy, Dr. Batshaw and other researchers will use imaging scans to study patients' brains. Many people with urea-cycle disorders have learning disabilities such as dyslexia, which can cause spelling, reading and writing difficulties, Dr. Batshaw said.

While urea-cycle disorders run in families, other disorders, such as Angelman syndrome, might show up only once in a family, said Arthur Beaudet of Baylor College of Medicine in Houston, who is heading research into Angelman as part of the Angelman, Rett and Prader-Willi syndrome consortium.

Angelman is a genetic disorder characterized by mental retardation, severe speech delays and seizures. The condition isn't reversible, and there are no treatments.

Dr. Beaudet will study a therapy for young children along with conducting a history study of the disease.

Terry Jo Bichell, 46, of Chicago plans to enroll son Louie, seven, in the history study because he is too old for the treatment study, although he participated in a previous folic-acid study. While that study wasn't considered an overall success, it suggested folic acid might help certain Angelman patients. Ms. Bichell said of the research, "You can't just sit around and do nothing," although she said she recognizes Louie's condition may not be reversible.

Write to Jennifer Corbett Dooren at jennifer.corbett-dooren@dowjones.com¹