



FACT SHEET

What is H-ABC?

Hypomyelination with Atrophy of Basal Ganglia and Cerebellum (H-ABC) is a genetic disorder that affects the myelin, the white, fatty insulation that nerves need to carry electrical signals of the brain, and is progressive in nature. The deterioration of myelin in the brain also causes the common neurologic disorder multiple sclerosis. Myelin defects are also at the root of the leukodystrophies — genetic disorders that include H-ABC and affect 1 out of every 7,000 children annually.

How many are affected by it?

H-ABC is newly recognized and to date fewer than 100 individual cases have been published in the medical literature. Due to the mortality rate that results from the disease, the majority of cases are children. However, it is emerging as one of the most common genetic disorders of hypomyelination (lack of myelination development.)

How do children get this disorder?

H-ABC is genetic but most often not inherited, resulting from spontaneous genetic mutations. It is caused by changes in the gene TUBB4A, although it is not yet completely understood how these changes cause H-ABC.

How does H-ABC affect children with this disorder?

Children with H-ABC typically develop normally until early childhood (about age 3) when various symptoms begin and affect each child differently. These symptoms may range from speech difficulties to mobility challenges, balance issues and involuntary muscular contractions. Children with H-ABC need specialized supportive care, including neurology, physiatry (rehabilitation), speech therapy, physical therapy, occupational therapy, pediatric and orthopedic care, and surgery.

Is there a cure?

There is currently no cure for this disabling and life threatening condition. Unfortunately, H-ABC is most likely irreversible, but progression of the disease can be stopped.

What is being done to find a cure?

Children's Hospital of Philadelphia (CHOP) is leading H-ABC research. As a member and leader of the Global Leukodystrophy Initiative (www.theGLIA.org) consortium, CHOP participates with other clinicians, researchers and advocacy groups to improve both clinical care and research for children with myelin disorders. Genetic research is going on at CHOP and is being led by Adeline Vanderver, M.D., program director of CHOP's Leukodystrophy Center for Excellence. To date, Dr. Vanderver has completed cellular level research to understand the disease and is now collaborating internationally to

develop next steps. The Universities of Pittsburg and Yale have joined in the research and are actively conducting mice modeling to characterize the disease in mice with hopes to molecularly engineer the mouse genome to target and destroy the defective protein that is causing the disease. "A Natural History of HABC" is also in full swing, a multi-site, two-year pilot study to chronicle the timeline and individual variations of H-ABC. The goal of the study is to clinically determine the exact progression of H-ABC so that the best therapeutic interventions may be identified and implemented.

Existing evidence suggests that the gene therapy approach might be effective in H-ABC: finding and masking the bad copy in the gene while allowing good components of the cell to function normally.

What is the next step in the research?

The next step is to confirm the gene approach in mice, then apply it to primates, all of which is critical to developing an effective and safe gene therapy approach eventually in humans.