One Mission: End AHC!

INSIDER'S EDGE

YOUR ALTERNATING HEMIPLEGIA OF CHILDHOOD FOUNDATION NEWSLETTER www.ahckids.org MARCH 2015

2000 Town Center ■ Suite 1900 ■ Southfield, Michigan 48075

Foundation Has New Look and New Site

AHCKids.org site is the best place for AHC info

In celebration of spring, the foundation has launched a new website at www.AHCKids.org.

Through the hard work of volunteers within the foundation, our web presence has been updated to reflect a brighter, cleaner, and more streamlined identity.

All of the great information previously hosted on our "blue site" has been transferred and reorganized to better serve the family support aspect of our mission.

ahc 365 The Foundation's blog to connect with, engage, and support the AHC Community.

We have added information too! Our Fundraising tools will continue to expand so our community can continue to do the hard work of raising funds for research.

The community section has been streamlined to make it easier than ever for AHC families to engage with one another. A Patient Care section is planned for completion in the coming months that will be full of both anecdotal and professional advice for the care of AHC patients, their families, and the future of both.

Our resources section has been fleshed out significantly in many categories, and more is coming all the time. These aspects, and the addition of our blog, AHC365, will keep AHCKids.org a valuable resource for the entire AHC community.

Check back regularly, and follow us on Facebook to learn more about the site and new content.

Mollie Erpenbeck & Cate Cohen
CNS Meeting
October 2014

Board of Directors' News

Cohen earns our thanks & gratitude

Please join us in thanking Cate Cohen for her years of service to the foundation as a member of our board.

Cate added wonderful public relations experience to the board and had an incredible energy. She was instrumental in creating our donor video in 2013 and bringing AHC awareness to neurologists at the 2014 CNS Annual Meeting.

We wish Cate well and look forward to working with her on new projects in the future.

AHC Community Clinicians and Researchers Change Institutions

Physicians on the move

Dr. Sandra Reyna recently accepted a position with Massachusetts General Hospital at Harvard University. She is an assistant in neuroscience department and a Clinical Research Operations Scientist at the Neurological Clinical Research Institute.

Dr. Reyna was a long-time researcher at the University of Utah, playing a significant role in the Department of Neurology's receiving of the NeuroNEXT Clinical Trials Award and the StrokeNet Award.

Dr. Reyna has extensive experience in preparation of clinical trials involving multiple sites and the coordination of multiple team members. Dr. Reyna participated in the AHCF workshop in 2014 and has been an active participant at our family meetings as a speaker and clinic physician.

Dr. Laurie Ozelius, PhD., recently accepted a position at Harvard University as an Associate Geneticist in Neurology. Dr. Ozelius is a research scientist performing research in gene discovery in movement disorders and in particular, identifying genes for dystonia and Parkinson Disease.

Dr. Ozelius received her PhD. in Genetics from Harvard Medical School and completed her research fellowship in neurology at Massachusetts General Hospital and Harvard Medical School.

Dr. Ozelius shared her expertise in the 2014 AHCF workshop and will be a valuable collaborator searching for answers for AHC patients.

On January 1, 2015, **Dr. David Goldstein**, joined Columbia University as professor of genetics and development in the College of Physicians and Surgeons and director of a new Institute for Genomic Medicine in partnership with New York-Presbyterian.

Dr. Goldstein, formerly of Duke University, will be responsible for building a program that comprehensively integrates genetics and genomics into research, patient care, and education at Columbia University Medical Center (CUMC) and New York-Presbyterian and that develops programs to prepare students for careers in the expanding field of genomic and personalized medicine.

We wish all of the doctors much success in their new positions at Harvard and Columbia Universities.

We look forward to seeing many wonderful advancements from them in the years to come!

Words of Wisdom: "You gain strength, courage and confidence by every experience in which you really stop to look fear in the face." Eleanor Roosevelt

Researchers Develop Mouse Models with AHC Mutations!

Significant AHC research is published

Dr. Arsen Hunanyan is a senior post-doctoral research associate at Duke University Medical Center, U.S.A.

In January, a team of researchers published an article in the journal *Epilepsia* titled, "Knock-in Mouse Model of Alternating Hemiplegia of Childhood: Behavioral and Electrophysiologic Characterization."

The lead author on the article is Dr. Arsen S. Hunanyan.

The articles discusses how mutations in the ATP1a3 subunit of the neuronal Na+ /K+ -ATPase are thought to be responsible for seizures, hemiplegias, and other symptoms of alternating hemiplegia of childhood (AHC). However, the mechanisms through which ATP1A3 mutations mediate their pathophysiologic consequences are not yet understood.

The following hypotheses were investigated: (1) Our novel knock-in mouse carrying the most common heterozygous mutation causing AHC (D801N) will exhibit the manifestations of the human condition and display predisposition to seizures; and (2) the underlying pathophysiology in this mouse model involves increased excitability in response to electrical stimulation of Schaffer collaterals and abnormal predisposition to spreading depression (SD).

Methods used during the research included generating the D801N mutant mouse (Mashlool, Mashl+/□) and compared mutant and wild-type (WT) littermates. Behavioral tests, amygdala kindling, flurothyl-induced seizure threshold, spontaneous recurrent seizures (SRS), and other paroxysmal activities were compared between groups. In vitro electrophysiologic slice experiments on hippocampus were performed to assess predisposition to hyperexcitability and SD.

Results found that Mutant mice manifested a distinctive phenotype similar to that of humans with AHC. They had abnormal impulsivity, memory, gait, motor coordination, tremor, motor control, endogenous nociceptive response, paroxysmal hemiplegias, diplegias, dystonias, and SRS, as well as predisposition to kindling, to flurothyl-induced seizures, and to sudden unexpected death.

Hippocampal slices of mutants, in contrast to WT animals, showed hyperexcitable responses to 1 Hz pulse-trains of electrical stimuli delivered to the Schaffer collaterals and had significantly longer duration of K+ -induced SD responses.

The Significance of this work is that their model reproduces the major characteristics of human AHC, and indicates that ATP1a3 dysfunction results in abnormal short-term plasticity with increased excitability (potential mechanism for seizures) and a predisposition to more severe SD responses (potential mechanism for hemiplegias).

This model of the human condition should help in understanding the molecular pathways underlying these phenotypes and may lead to identification of novel therapeutic strategies of ATP1a3 related disorders and seizures.

THANK YOU TO ALL OF THE RESEARCHERS
WHO WORKED ON THIS IMPORTANT PROJECT!

To view the full text of this article, go to: http://onlinelibrary.wiley.com/doi/10.1111/epi.12878/full

Five Part Series on Getting Diagnosed with AHC by Doug Morris

Part three: What is wrong with my child?

This is the story of how one family went through various phases of learning about their children's AHC diagnosis to thriving in life.

Many of you may relate to their experience while others of you may see hope for all of our AHC community.

By the end of the series we hope you all will see that our kids can lead a fulfilling life as we all work towards ultimately finding a cure.

PHASE 3 BARGAINING

Our first child, Haley, was diagnosed with AHC in January 1994. Six weeks later, our second child, Caroline was born. Within 18 months, she too was diagnosed with AHC.

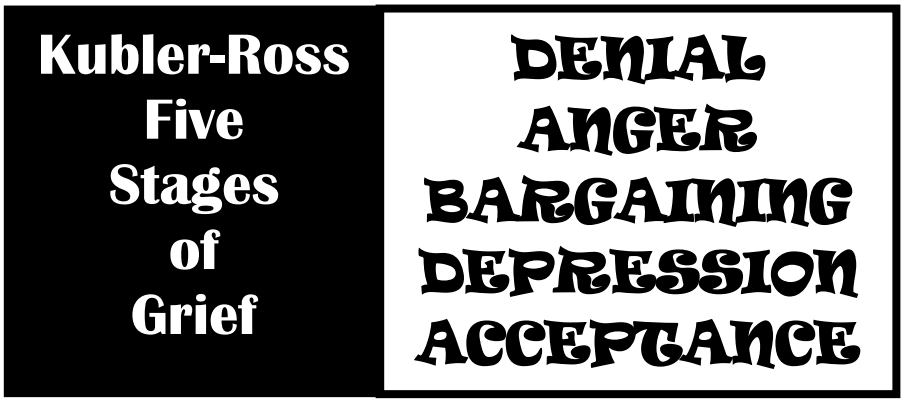
In the first part of this series, I discussed how my wife and I initially we went through denial. As parents we searched for every piece of information we could find on AHC and talked to various doctors to understand the symptoms better. We wanted to be able to predict and provide a better future for Haley and Caroline.

After denial came anger. Why me? What did I do in the past to bring this on to our first child? Why did Haley come genetically into this world with AHC? Why did Caroline come with AHC too? It's not fair to our kids, their mother, or to me.

Anger subsided and I started bargaining. I bargained to influence more positive outcomes for the kids.

Nothing I offered changed the kids. Then, when I started acting like a normal father, they seemed to start acting like normal kids. The more they acted normal, then the more normal I acted. We zigged-zagged to find the new normalcy in a positive outcome. While this was better, I was still not happy.

Next month, I'll share more about how AHC weighed on me as a parent.



Be sure to join us next month as Doug talks about depression and how it played a role in dealing with the diagnosis of AHC for his family.

Donors: Your gifts fund 100% of our effort to help children with AHC. It is our privilege to coordinate the support and services you find critical to improving their quality of life. Thank you for your steady support. Everything we achieve depends on you.