



One Mission: End AHC!



YOUR ALTERNATING HEMIPLEGIA OF CHILDHOOD FOUNDATION NEWSLETTER

May 2017

2000 Town Center ■ Suite 1900 ■ Southfield, Michigan 48075

AHCF in ACTION Honoring our American Heroes

This month is full of **important events** for a lot of people: First Communion, prom, graduation, Special Olympics, school ending, Memorial Day, and special birthdays. And, to all who are celebrating this month, our best wishes and congratulations to you and your family.



A **quote by John F. Kennedy** recently struck me as not only relevant to celebrating Memorial Day, but also reminiscent of the **spirit, passion and strength of the AHC community**. I hope you enjoy the upcoming holiday as well as the following words from President Kennedy.

“Let every nation know, whether it wishes us well or ill, that we shall pay any price, bear any burden, meet any hardship, support any friend, oppose any foe to assure the survival and the success of liberty.”

– John F. Kennedy

Lynn Egan, AHCF President



AHC INFO EXCHANGE Important AHC Research Just Published

Five new articles were recently published that will have a significant impact for AHC patients. Be sure to read the summaries in the newsletter or check out the websites for more detail.

The AHC Foundation would like to **express our deep appreciation** to all of the clinicians and researchers for their work on these publications. There are several names familiar to the AHC community that we would like to recognize. Be on the lookout for:

Helen Cross, Suzanne DeBrosse, Thomas Holm, Karin Lykke-Hartmann, Kenneth Silver, Kathryn Swoboda, and Sho Yano.

The Foundation is thrilled to share summaries of all published research as we learn about it. It is through the hard work of **everyone in the AHC community** that will help us reach our **One Mission: End AHC!**



Congratulations to all of those students who have graduated or will be graduating over the next month.

“As you start your journey, the first thing you should do is throw away that store-bought map and begin to draw your own.” –Michael Dell



AHC INFO EXCHANGE

Mouse Model Makes AHC News for those with ATP1A3 Mutation

On May 4th, *PLOS Genetics* published the article, “**Hypothermia-induced Dystonia and Abnormal Cerebellar Activity in a Mouse Model with a Single Disease-mutation in the Sodium Pump.**” It was authored by: Toke Jost Isaksen, Lieke Kros, Natascia Vedovato, Thomas Holm, Ariel Vitenzon, David Christopher Gadsby, Kamran Khodakhah, and Karin Lykke-Hartmann.

In the study, they show that a mouse model with the D801Y disease-mutation ($\alpha_3^{+/D801Y}$ mice)] **displayed severe hypothermia-induced dystonia**, which correlated with abnormal cerebellar neuronal activity in vivo. In vitro pump characterization revealed that **D-to-Y mutant pumps failed to carry out Na⁺/K⁺ exchange, but retained the ability to bind Na⁺**. These data thus provide a heretofore **unknown link between hypothermia and dystonia** that implicates aberrant cerebellar activity in α_3 isoform-related dystonias and **provides functional insight into the disease-causing effects of the underlying Na⁺/K⁺-ATPase dysfunction.**

For more information about what this article means to those with this mutation, Dr. Thomas Holm shared these comments with us.

“The recent paper by Isaksen et al., published in *PLOS Genetics* studies the role of cerebellar Purkinje neurons in fine tuning muscle control in the $\alpha_3^{+/D801Y}$ mouse model. **This mouse model has previously been shown to recapitulate AHC features such as hyperactivity, altered behavior, cognitive deficits and increased risk of seizures.**

The present paper furthermore shows that the $\alpha_3^{+/D801Y}$ **mice displayed ataxia and developed dystonic episodes lasting upwards of 40 minutes when subjected to stress.**



Recordings from individual Purkinje neurons in live **mice revealed that severity of symptoms correlated with increasingly irregular firing patterns.** Functional comparison of the two hotspot mutations, $\alpha_3^{+/D801Y}$ and $\alpha_3^{+/D801N}$, revealed that both mutations permitted H⁺ entry through the channel which is likely to lower the pH of the intracellular environment and in turn will affect a large number of enzymatic reactions in the neurons.

This observation may be central to understanding why Atp1a3 mutant mice with single amino acid mutations may develop much more severe symptoms than heterozygous knockout Atp1a3 mouse models where one Atp1a3 allele is no longer expressed. **This potentially suggests that treatment targeting the mutated allele could help stabilize patients**, as recently shown using exon skipping in Duchenne muscular dystrophy. This paper is the result of collaborative efforts between the laboratories of Drs. Karin Lykke-Hartmann, Kamran Khodakhah and David Gadsby.

Thank you to everyone for this work.



National School Nurse Day

May 10, 2017, was designated National School Nurse Day by the National Association of School Nurses.

The AHC Foundation wishes to honor and recognize the women and men charged with caring for the health of the students in their schools.

AHC INFO EXCHANGE

AHCF Medical Advisory Board Members Publish Article in May

**PEDIATRIC
NEUROLOGY**

In the May issue of *Pediatric Neurology*, the article, “Fever-induced Paroxysmal Weakness and Encephalopathy, a New Phenotype of ATP1A3 Mutation,” was published. Many of the authors will be familiar to the AHC Community. They include: **Sho T. Yano, MD, PhD, Kenneth Silver, MD**, Richard Young, MD, **Suzanne D. DeBrosse, MD**, Roseanne S. Ebel, MS, **Kathryn J. Swoboda, MD**, and Gyula Acsadi, MD, PhD.

The objective of the project included identifying a group of patients with ATP1A3 mutations at residue 756 who **display a new phenotype** distinct from alternating hemiplegia of childhood (AHC), rapid-onset dystonia-parkinsonism (RDP), and cerebellar ataxia, areflexia, pes cavus, optic atrophy, sensorineural hearing loss (CAPOS) syndromes.

Patients with ATP1A3 R756H **have onset in childhood of infrequent, fever-triggered paroxysms of encephalopathy and weakness with slowly improving but persistent deficits**. Motor findings of weakness are mostly generalized, and patients may also have bulbar or oculomotor problems. Longer-term outcomes range from mild motor apraxia with near-normal function to persistent dysphagia, dysarthria, cognitive deficit, motor apraxia, and inability to walk due to ataxia. Patients with ATP1A3 R756L have a similar phenotype that includes **paroxysmal, stepwise progression of ataxia associated with infections**.

To read the journal abstract, go to: [http://www.pedneur.com/article/S0887-8994\(17\)30121-2/pdf](http://www.pedneur.com/article/S0887-8994(17)30121-2/pdf)

AHCF in ACTION

Webinar Turns into Quarterly Resource for Families!

The AHCF held a “**call to action**” webinar May 1st for all AHC families to discuss what we can do to urge our congressional leaders to **support the 21st Century Cures Act**.

Dr. Al George, from Northwestern University, accompanied by **Dr. Kevin Ess**, from Vanderbilt University, first gave a synopsis of their current research and then discussed **how the families could lobby congress to continue funding the National Institute of Health programs**.



Without this funding rare disease research will be severely limited. **Everyone is urged to keep the pressure up** by calling your representative and senator until the bill is voted on in the senate this fall!

The webinar was very well received, yet at the same time it became clear that parents were eager to take this **opportunity to ask medical questions important to their children’s care**.

To help answer your questions, the Foundation has decided to **host quarterly webinars on various topics** for the families. The first will be held this summer.

Do you have a topic suggestion? Send requests to: sharon@ahckids.org.

Thank you to AHCF Board member Bill Gerber for volunteering to host the webinars.

AHC INFO EXCHANGE

More to Consider about Synthetic Cannabinoids

In the March issue of the *Journal of Clinical Neuroscience*, **Dr. Sho Yano (AHCF MAB)** was one of the authors on the article, “Buzz Juice: Neurological Sequelae of Synthetic Cannabinoids.”

The article discusses that the use of synthetic cannabinoids is becoming more widespread. **Familiarity with the potential toxicities associated with these agents will grow in importance.**

They presented a case of a woman who **developed onset of confusion, visual hallucinations, and ataxia** after vaporizing synthetic cannabinoids. MRI imaging demonstrated restricted diffusion and increased T2/FLAIR signal in the corpus callosum and cerebellar peduncles.

The research conducted at the University of Chicago is one of many projects looking at the efficacies of cannabinoids and “medical marijuana.” Please always defer to discussions with your physicians and specialists.

AHC ANSWERS

AHCF Medical Advisory Board Answers Your Questions

The AHC Foundation is incredibly fortunate to have **12 internationally recognized AHC experts** serving on our Medical Advisory Board (MAB) **from four different countries.** In this column, your questions are answered by one or more members of the MAB.



To have your question answered, contact sharon@ahckids.org

Question posed to our AHC experts: “How do you feel about birth control medication for our girls and do you feel it is safe for them?” “Please address hormone levels and their effect on AHC.”

Response: From Dr. Marcio Sotero: Only one of my patients used, and no problems.

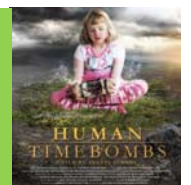
Response: From Dr. Matt Sweney:

As with many issues related to AHC, there is no satisfactory answer. The best model to base any preliminary conclusions would be from the role of hormones in epilepsy.

Nearly 1/3 of women with epilepsy may have some synchronization of seizures to their menstrual cycle (although the timing may be very individualized). There is good literature to suggest that estrogen may have pro-seizure effects in women and men (even men have some amounts of estrogen, albeit small). As a result, progesterone-only formulations may prove beneficial in oral contraceptive formulations; however the complex hormonal dynamics make it difficult to come up with scientifically-based recommendations.



For all of you folks out east, plan on attending a local screening of the AHC documentary, “Human Timebombs.” The event is hosted by Karen & Matt Shubert and will take place on June 11th.



“Like us on Facebook” <https://www.facebook.com/AHCKids>

AHC INFO EXCHANGE

SUDEP Practice Guideline Summary Published



The **sensitive nature of discussions** of this infrequent but important risk with patients and families has prompted the need for **evidence-based information** about Sudden Unexpected Death in Epilepsy, or SUDEP.

A Subcommittee of the **American Academy of Neurology and the American Epilepsy Society** jointly created a document to examine evidence for the SUDEP incidence rate in epilepsy populations and for prognostic factors for SUDEP occurrence. This in turn will **inform an honest and balanced discussion** when clinicians counsel people about SUDEP, and provide insight into areas where more clinical research is needed.

The full-text of the article can be found at: <http://www.neurology.org/content/88/17/1674.full.pdf+html>

We would also like to **acknowledge J. Helen Cross for her contributions** to this work. Thank you for your service to the AHC Community as well as those with epilepsy.



AHC COMMUNITY CONNECTIONS Dr. Silver Goes Back to School at NU

Adult and pediatric researchers and clinicians from **Northwestern Memorial Hospital and Lurie Children's Hospital** came together on Monday, May 15th, for a continuing education conference on epilepsy and related neurological disorders.

Dr. Al George, Chair, Department of Pharmacology Director, Center for Pharmacogenomics, **invited AHC expert Dr. Kenneth Silver** to present an overview of clinical aspects of AHC to the group. **The goal of the presentation was to help expand interest in AHC.** Dr. Silver was also able to meet with research fellows.

Thank you Dr. Silver and Dr. George for helping educate the medical community including future researchers and clinicians about AHC!

Keep up to date with the AHC community.

So, make sure we have your current email address,

Like us on Facebook <http://www.facebook.com/AHCKids/>

Join the AHC Support Group (a private chat site for parents only)

www.facebook.com/groups/1436035426663331/

And follow us on twitter @AHC Kids.

AHC INFO EXCHANGE

Lessons about ATP1A3 and Brain Development

In the upcoming July 2017 issue of *Brain Research*, an article from researchers in Japan will be published under the title, “**Knockout of Sodium Pump $\alpha 3$ Subunit Gene (*Atp1a3*^{-/-}) Results in Perinatal Seizure and Defective Respiratory Rhythm Generation.**”

The article discusses how three ATP1A3 disorders, AHC, apnea, and severe infantile epileptic encephalopathy often appear shortly after birth.

To gain insight into these disorders **and** to understand the functional roles of the sodium pump $\alpha 3$ subunit in **the brain during this period of development**, they examined the phenotype of *Atp1a3* knockout homozygous mouse fetuses (*Atp1a3*^{-/-}).

Highlights from the study include:

- The mRNA of *Atp1a3* is expressed in almost all regions in the neonatal mouse brain.
- About half of *Atp1a3*^{-/-} fetuses showed seizures immediately after birth.
- Expression of c-Fos signal in the cerebellum was unique in *Atp1a3*^{-/-}.
- Increased monoamine content was observed in the *Atp1a3*^{-/-} brains.
- *Atp1a3*^{-/-} showed various abnormal respiratory rhythms as recorded from phrenic nerve.

We expect more information about this study will be shared at the next ATP1A3 Symposium in Japan this September. Keep watching the newsletter for more developments regarding this work.



AHCF FUNdraising New England Walk Huge Success

The AHCF New England Walk took place on Sunday, May 21st and was hosted by Olga and Bill Gerber in honor of their son Sean.

It was a family fun-filled day with a bounce house, face painting, **Bad Penny** playing live music, food trucks and oh yes, shopping. There were **even various prizes** for Best Team Spirit supporting AHC; Best Individual Spirit supporting AHC and Most Funds raised by a Team or Individual

Thank you to the entire Gerber clan for making this event a huge success!

Join in on the fun with your friends or family at one of our upcoming events

Friday, July 28th
Illinois Golf Outing
Contact:
Gene Andrasco
gene@ahckids.org

Sunday, August 6th
Michigan Golf Outing
Contact:
Rik Greenwood
rik@ahckids.org

Saturday, August 26th
5K for Kathryn (IN)
Contact:
Josh Marszalek
joshua@ahckids.org

Sunday, September 17th
12th Chicago Walk
Contact:
Vicky Platt
vicky@ahckids.org