

## MEET OUR TEAM

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## Focus on Hyperinsulinism/Hyperammonemia Syndrome

Hyperinsulinism/hyperammonemia (HI/HA) syndrome is extremely rare. One in 25,000 to 50,000 people has HI, and only 20 percent of HI patients also have HA, a metabolic condition where ammonia builds up in the blood to potentially dangerous levels. Normally, ammonia — a byproduct of metabolizing protein — is converted to the less toxic urea and excreted through urine. For patients with HI/HA, which is caused by a mutation in the *GLUD1* gene, the urea cycle doesn't work properly and ammonia concentrations can reach several times the norm. Eating protein triggers this process and also stimulates the pancreas to secrete insulin inappropriately, causing hypoglycemia or low blood sugars. While HI/HA patients are often successfully treated with medication (usually diazoxide) for hypoglycemia, there is no treatment yet for the HA component. Changes in diet can help manage low blood sugars, like eating carbohydrates before protein or limiting protein. More research is needed on the effects of elevated ammonias and potential drug treatments.

## Living Like a Typical Teen — Only with HI/HA Syndrome

Katelyn Hart does everything a typical 17-year-old would do: plays alto sax in her high school marching band, hangs out with her friends and visits college campuses in preparation for her future.



*The Hart Family*

She also does some things a typical 17-year-old doesn't do: tests her blood glucose level up to 10 times a day, takes daily medication, is careful about every bite she eats and participates in clinical trials for hyperinsulinism/hyperammonemia (HI/HA) syndrome, a disease she's had all her life.

"I always carb load at the start of every meal," says Katelyn, who lives in Hillsborough, N.J. "I eat the pasta or rice first, or mashed potatoes, then the chicken. When I was at CHOP for tests, we tried the random order of foods and found this worked the best."

Katelyn's 15-year-old sister, Colleen, and their father, Jeff, also have HI/HA. The trio serves as a genetic resource for CHOP researchers. When Colleen was born, her cord blood was analyzed and helped researchers identify the genes involved with HI/HA. Recently, Katelyn and Jeff participated in a short-term trial of an experimental drug to treat HA.

"I like to participate in research," Katelyn says. "If it can help find answers — or help other families — I'm happy to do it."

Her mother, Randy, sees helping out with research as a way to pay back Children's Hospital for all it has given her family. "We've chosen to help in any way we can because CHOP has helped us in such a tremendous way," she says.

# Notes on Nutrition: Protein Sensitivity

By Linda Steinkrauss, M.S.N., C.R.N.P.

## What is protein sensitivity?

Protein sensitivity means that eating protein will cause a significant drop in blood sugar. Many children and adults with various forms of hyperinsulinism (HI) have protein sensitivity. Children with hyperinsulinism/hyperammonemia (HI/HA) syndrome, which is caused by a mutation in the *GLUDI* gene, almost always have protein sensitivity. We believe this is because the genetic defect in the pancreas that causes HI/HA is stimulated by protein. Eating protein, therefore, causes the pancreas to secrete extra insulin, leading to a drop in blood sugar. Children with other types of HI (such as K-ATP-dominant, diazoxide-responsive patients) may be protein sensitive also.

## How do I know if my child has protein sensitivity?

Protein sensitivity is identified with an oral protein tolerance test (OPTT). This test is typically done during an inpatient admission, after a four-hour fast. The test is

usually done at lunchtime here at CHOP. A child is given a drink containing protein powder mixed with a sugar-free juice. Blood sugar and insulin levels are monitored just before the protein drink and then for the next three hours. Anyone with protein sensitivity will have a rapid drop in blood sugar, typically within those three hours.

## How is protein sensitivity treated?

There are three ways to treat protein sensitivity:

- 1. Diazoxide:** In many children with protein sensitivity, diazoxide works well to eliminate low blood sugar after protein.
- 2. Carbohydrate preloading:** In children who have protein sensitivity that is not completely controlled with diazoxide, taking at least 15 grams of carbohydrate before eating protein can prevent low blood sugar.
- 3. Protein restriction:** Very rarely, if the first two treatments are not successful, protein in the diet may be decreased to prevent low blood sugar.

If your child has protein sensitivity, you may want to consult with a dietician as your child grows for help adjusting his or her meal plan appropriately. Your nurse practitioner or physician can help make sure that this is included in the plan for your follow-up visit if you have concerns.

# Hope on the Horizon: Research News

*The Congenital Hyperinsulinism Center has numerous promising research studies under way. Here are details of two.*

## New Research Drug for HI/HA Patients

**Research Team:** Marc Yudkoff, M.D., Chief/Principal Investigator; and Irma Payan, C.R.N.P., Nurse Practitioner/Study Coordinator, Division of Child Development, Rehabilitation and Metabolic Disease.

We are working to treat individuals who have urea cycle defects, which are genetic conditions. In these conditions there is a problem in converting potentially toxic substances (i.e., ammonia) to the nontoxic form, urea. The drug — called Carbaglu — has been shown to improve the defect in some of these children. Since individuals with hyperinsulinism/hyperammonemia (HI/HA) syndrome can also have a high blood ammonia, CHOP is now testing the drug in people who have HI/HA syndrome.

Our hope is that the medication will lower the high blood ammonia that individuals with HI/HA often display. For information about this study, please contact Irma Payan at 215-590-6236 or [payan@email.chop.edu](mailto:payan@email.chop.edu).

## HI/HA: Tracking Neurological Symptoms

The HI team recently started to collaborate with Daniel J. Licht, M.D., and Nicholas Abend, M.D., in the Division of Neurology at CHOP to formally evaluate our HI/HA patients who demonstrate neurological symptoms, such as seizures and attention problems. Evaluations are done during elective inpatient admissions and typically include a neurology consult, video EEG monitoring and MRI imaging if indicated. In the short term, our goal is to assist patients to find the best treatment for their neurologic symptoms. In the future, we hope this collaboration leads to research studies that will help us better understand the biochemical pathways in the brain and causes of neurologic features seen in HI/HA, leading to better treatments and, potentially, to the prevention of these issues altogether.

We are planning to make this a formal research project. Andrea Kelly, M.D., will lead the HI team as primary investigator. We invite current and new HI/HA patients to contact us at 215-590-7682 or at [hyperinsulin@email.chop.edu](mailto:hyperinsulin@email.chop.edu) to be added to our database of HI/HA patients.

## HI Hope: Family Story

### Tapping into CHOP's Expertise from Far and Near



*Natalie Tenen*

Even before Michael and Michelle Tenen and their 4-year-old daughter, Natalie, stepped foot inside The Children's Hospital of Philadelphia last fall, they had benefited from the expertise of the Congenital Hyperinsulinism (HI) Center.

From the first days of Natalie's diagnosis of hyperinsulinism/hyperammonemia (HI/HA) syndrome, their doctor back in Orange County, Calif., had conferred frequently with CHOP doctors, and they'd read articles from CHOP physicians and researchers on the latest treatments.

They came to CHOP for a series of tests to make sure Natalie's current treatment plan was the optimal one for her. "We always wanted to come here to have her tested," Michael says. "This is *the* place for HI/HA."

“We'd be happy to join any study that's appropriate for Natalie,” Michelle says.

The Tenens' experience with Natalie's diagnosis was, unfortunately, not that uncommon. "When she was about 6 weeks old, when I fed her, I noticed rapid eye movements," Michelle says. "We went to the ED, but they couldn't find anything. Every day for two weeks there was something else that looked wrong, so we kept going to the hospital or the pediatrician. Finally, they tested her blood, and she had a glucose level of 10 — extremely low."

Natalie was started on diazoxide, which controlled her glucose. But her parents believe there was some brain damage during the two weeks she went undiagnosed. At 3 years old, Natalie started to have infrequent blank stare (or absence) seizures. At 4, she began having grand mal epileptic seizures and was diagnosed with secondary, focal seizures. She now has an emergency med, Diastat, to stop the seizures before they can do damage, as well as a daily seizure medication to try to prevent or decrease their frequency.

For reasons doctors don't fully understand, HI/HA patients frequently suffer seizures; some are misdiagnosed as having epilepsy and their condition can go untreated for years.

Natalie has experienced some delays in development. She didn't walk until 21 months and had delayed speech. Natalie qualified for early intervention and receives speech, physical and occupational therapy.

The Tenens' trip to CHOP involved an 18-hour fasting test, an oral protein tolerance test and a video EEG (with electrodes attached to Natalie's head to monitor brain activity) that ran concurrent with the other tests. The Tenens met with a CHOP neurologist to discuss Natalie's seizures and to discuss seizure medication options. The family also contributed DNA to further CHOP HI/HA research. "We'd be happy to join any study that's appropriate for Natalie," Michelle says. "The more doctors learn about this disease, the more they can help children like Natalie."

The Tenens deal with the challenges with positive resolve. They coax their protein-loving daughter to eat her carbohydrates, carry her three medicines at all times and are vigilant about checking Natalie's blood sugars.

"Like all parents who've had a close call, we're so grateful to have her and see her improve," Michael says. "We don't take anything for granted. Natalie is so happy. She really enjoys life and appreciates the small things."

Childhood is  
a *gift* and you  
can *give it*.

*For information about giving to the  
Hyperinsulinism Program, contact*

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## Keep Us Updated

We want to keep in touch, but we need your help. If your contact information changes, please let us know by e-mail at [hyperinsulin@email.chop.edu](mailto:hyperinsulin@email.chop.edu) or phone at 215-590-7682. If you no longer want to receive this newsletter, we will remove your name from our list. We do not sell or give out our mailing list, but we may occasionally send out HI-related information from groups we collaborate with. To ensure your privacy and to comply with HIPPA regulations, we never share contact information.

**Save the dates:  
June 18 – 19**

**Congenital Hyperinsulinism International  
(CHI) Family Conference in San Diego.**  
For more information go to:  
[www.congenitalhi.org/famConference.php](http://www.congenitalhi.org/famConference.php)

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## A Distinguished Ranking

The Children's Hospital of Philadelphia has been ranked first in Diabetes and Endocrine Disorders in U.S. News Media Group's edition of America's Best Children's Hospitals, featured in the August issue of *U.S. News & World Report*. CHOP was ranked No. 1 in more specialties, including Neonatal Care, than any other hospital and is the only hospital that scored in the top three in all 10 of the specialties ranked.

## Don't Forget! Reminders for HI Parents

Because of the risks associated with hypoglycemia, we recommend that every child with HI undergo formal developmental assessments at 2 and 5 years of age. Your pediatrician should be able to recommend a developmental pediatrician or specialist for you to see. We would love to hear the results of this testing and how your child is doing!

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