UREA CYCLE DISORDERS CONSORTIUM

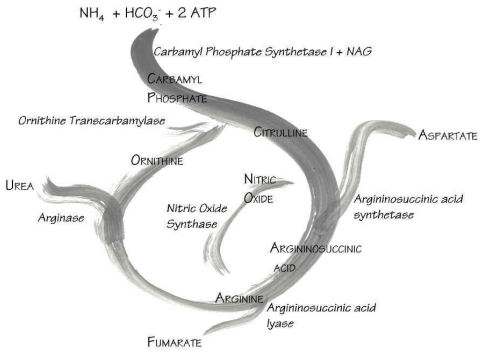
UCDC Update

Inside:

Issue 2 **Spring 2013**

Greetings from the Urea Cycle Disorders Consortium (UCDC)

This newsletter is being sent out to all of you who are participating in the UCDC Longitudinal Study, one of the UCDC clinical studies, the "Contact Registry" (page 5), or are members of the National Urea Cycle Disorders Foundation (NUCDF). If you did not receive a copy of our first newsletter from February 2012 and would like one, please contact Jennifer Seminara (contact information is on the last page) and she will send a copy to you.



The Urea Cycle

Enrollment continues for our Longitudinal Study and we now have more than 600 participants. We are learning many things about the natural history of UCDs by looking at the data collected in this study. A comparison of cognitive outcomes across the eight UCD subtypes is being conducted using the Longitudinal Study data and initial results were published in 2012 (see abstract on page 6); several other papers will be publishing later this year—results are discussed in this newsletter. We are pleased that European and Japanese metabolism groups have followed our lead and have initiated longitudinal studies of UCD of their own and in collaboration with us. We look forward to sharing and comparing data in the next few years, making this an international effort to better understand UCDs and to help improve the treatments and outcomes of affected individuals.

There are a number of UCDC research studies that are open and you may wish to participate in. Dr. Gropman is currently enrolling patients with OTCD in a neuroimaging study that helps to identify biomarkers of disease. We also continue to enroll participants in: 1) the N-acetylglutamate (Carbaglu) in the Treatment of Hyperammonemia (CPSID and females with OTCD), 2) the Carbaglu Surveillance Protocol (NAGSD); 3) Oxidative Stress, Inflammation and Acute Decomposition Study (all UCD), and 4) a study of Nitric Oxide Flux and Ureagenesis in ASSD. If you are interested in knowing more about any of these studies please contact the UCDC site coordinator at your site or Jennifer Seminara who can put you in touch with the site.

In this newsletter we focus on neuroimaging studies and some of the questions we are starting to be able to answer through the Longitudinal Study. Summaries of several other recent publications are also included in this newsletter. The full articles are available on our website (www.RareDiseasesNetwork.org/ucdc). If you have any questions about the summaries or the articles, don't hesitate to talk to the physician or coordinators at your clinical site. We are happy to discuss the findings with you and answer any questions you might have.

We are very excited about what we have learned from these important studies so far and look forward to continuing our work with you to discover and test more effective treatments. Our goal is to improve the outcome of all individuals with UCDs and to spread knowledge about these disorders so physicians can treat them more rapidly and effectively. We thank you for your help in making this possible by participating in the UCDC.

Mark Batshaw, MD, Mendel Tuchman, MD, and Marshall Summar, MD
Principal Investigators, Urea Cycle Disorders Consortium

A Message from the National UCD Foundation (NUCDF)

We are so pleased to report the research findings of the Urea Cycle Disorders Consortium to you. You are helping our researchers begin to unlock many of the mysteries of UCD. Together, as a UCD community, we are increasing knowledge about UCD and reaching milestones that improve care and quality of life.

In February, our community reached a major milestone with the FDA approval of Ravicti™ (by Hyperion Therapeutics) for chronic treatment of UCD. It took almost eight years of effort driven by all of us standing together as the National Urea Cycle Disorders Foundation to achieve this goal. This is pretty amazing—the average time it takes to get a drug from discovery to approval is more than 12 years. It would not have been possible without the participation of our families and the UCDC research sites that were critical to the success of the trials. Since we had established research sites and our UCD community is so engaged, we were able to quickly enroll the trials and reduce the timeline. Our UCDC research investigators and coordinators ensured we had high-quality, efficient trials. Less than 5% of the over 7,000 rare diseases has a drug treatment. Our rare disease now has three! Findings from the trials are being published that may lead to new management recommendations, further improving patient care.

Our UCD community is also catalyzing research critical to developing new interventions and treatments to protect the brain from the effects of UCD. As you will read in this newsletter, Dr. Gropman's work is focused on answering questions that will help us move forward with those goals. Your participation in these critical studies is the key to accelerating this critical research.

If you would like to discuss the research studies and what they may mean to your family, need help or support with UCD issues, or have questions or concerns, please email us at cureucd@nucdf.org.

Warm regards,
Cynthia Le Mons
Executive Director, NUCDF

UCD Subtype Abbreviations

OTCD
Ornithine transcarbamylase deficiency

ASLD
Arginosuccinate lyase deficiency, arginisuccinic aciduria, ASA

ASSD
Argininosuccinate synthetase deficiency, argininosuccinic acid synthetase deficiency, citrullinemia

ARGD
Arginase deficiency

CPSID
Carbamylphosphate synthetase I deficiency

HHH/ORNTD
Hyperornithinemia, hyperammonemia, homocitrullinuria syndrome or ornithine deficiency

CITRD
Citrulline deficiency, citrullinemia type II

NAGSD
N-acetylglutamate synthetase deficiency

Enrollment in the Longitudinal Study of Urea Cycle Disorders

Data current as of April 8, 2013

By Subtype and Onset

UCD Subtype	Neonatal Onset	Late Onset	Total
OTCD	46	317	363
ASLD	45	48	93
ASSD	53	30	83
ARGD	1	21	22
CPSID	11	5	16
HHH/ORNTD	1	7	8
CITRD	1	1	2
NAGSD	0	3	3
Diagnosis pending	2	8	10
Total	160	440	600*

*600 participants have enrolled in the Longitudinal Study. 45 of these are "off study" due to death, being lost to follow up, or being withdrawn for other reasons. 555 participants are currently "on study".

By Institution

UCD Subtype	Currently On Study
Baylor College of Medicine, Houston	60
Children's Hospital of Philadelphia	38
University of California at Los Angeles	57
Mount Sinai School of Medicine, New York	38
Children's National Medical Center, Washington DC	88
Rainbow Babies and Children's Hospital (Case Western Reserve University), Cleveland	49
Hospital for Sick Children, Toronto	29
University Children's Hospital, Zurich	41
Seattle Children's Hospital	26
Oregon Health and Sciences University, Portland	14
The Children's Hospital, Colorado	27
University of Minnesota	22
University of Heidelberg	26
Closed sites (Vanderbilt, Yale)	0
Total	555*

Neuroimaging in Urea Cycle Disorders, Andrea Gropman, MD

There is more to MRI (magnetic resonance imaging) than just a routine look at anatomy. Did you know that with advanced MRI technology, one can look at biochemicals in the brain, pathways involved in thinking and movement, and tracks connecting various important functions in the brain?

Neuroimaging studies led by Dr. Gropman's team are investigating how people with a UCD think and what their brain biochemistry looks like. Focusing on OTCD, her studies suggest that hyperammonemia and high brain glutamine levels can cause changes both in the structure of the brain (neural networks and fiber tracts) and brain biochemistry (neurochemicals) that can affect cognition and problem solving.

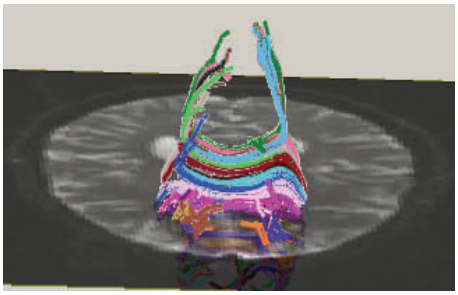


Figure 1

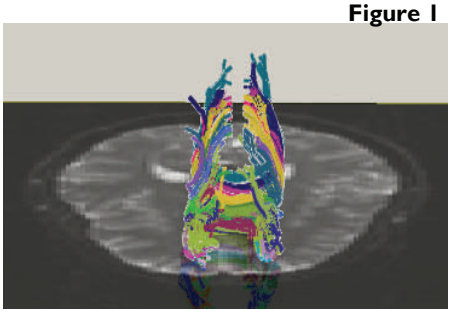


Figure 2

Patterns of Brain Injury in Inborn Errors of Metabolism

Imaging studies show that there are changes in the fiber tracks which are comprised of myelin, a substance that coats the nerve cells and speeds conduction of impulses. By using a technique known as diffusion tensor imaging or DTI, small disruptions in myelin can be measured and are correlated with changes in cognitive and motor function.

Findings of routine magnetic resonance imaging in OTCD are often normal in patients with late-onset disease, carriers, or in those not having a hyperammonemic crisis. However, analyzing an MRI scan using DTI is more sensitive for detecting abnormalities in normal-appearing white matter fiber tracks. Using DTI Dr. Gropman found that the extent of abnormality in the fiber tracks correlated with cognitive deficits. The location of the white matter track abnormalities was in the front of the brain. This is important because the frontal white matter contains fibers that are vital for performing executive function, attention, and working memory, areas of weakness in patients with OTCD. In Figures 1 and 2 DTI shows blunting of fibers in patients with late onset/carrier OTCD (Fig. 1) as compared to a non-affected controls (Fig. 2).

An fMRI Study of Altered Neural Activation during Executive Cognition

A second new approach to neuroimaging is called functional MRI. Here a subject performs a thinking or motor task in the scanner, and imaging show what parts of the brain are activated during the task. Our research has shown that brains of people with OTCD have to work harder and involve more areas to assist in these tasks than subjects without OTCD. The time to make a response is longer, although accuracy may still be good. There is in a sense a time-to-accuracy tradeoff and the brain is less efficient in these tasks. This has implications for school function as it may take longer for the child to understand or answer a question verbally or in writing.

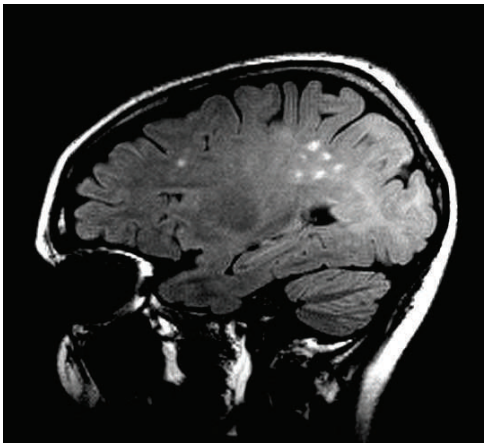


Figure 3: T1 Weighted FLAIR image in a female with partial OTCD showing abnormal white matter signal in the deep white matter of the centrum semiovale and motor association cortex. Such white matter findings may be reversible and are felt to be markers of recent hyperammonemia. There is also cortical atrophy with widened sulci.

1H MRS Identifies Symptomatic and Asymptomatic Subjects with Partial OTCD

A third novel approach to neuroimaging is called magnetic resonance spectroscopy (MRS) which allows the measurements of certain biochemicals in the brain, including glutamine, a storage form of ammonia and myoinositol, a buffering molecule. When glutamine increases in the brain it causes swelling. A counter regulatory molecule, called myoinositol tries to diminish swelling. This is an adaptive, protective function. One question is whether the amount of brain myoinosital that remains after hyperammonemia can predict the severity of a future hyperammonemic episode. If it can, MRS can be a useful way to monitor patients who

(Continued on page 4)

Neuroimaging—Key Points:

Despite the fact that the whole brain "sees ammonia" when it is elevated, only certain parts of the brain appear to be sensitive to those effects. This can be revealed by these studies.

For the first time, it has been shown that carriers who may not have full blown symptoms of hyperammonemia still have changes in their brain chemistry, neural networks and fibers, although milder than those who have had symptomatic hyperammonemia.

It suggests that MRI is a valuable tool for monitoring patients after HA episodes, especially if they have not returned to baseline function.

(Continued from page 3)
might have elevated brain glutamine levels despite normal blood labs.

To Learn More

To read the full articles summarized here and more about Dr. Gropman's research, visit the UCD website at : www.RareDiseasesNetwork.org/ucdc

Gropman AL. Patterns of Brain Injury in Inborn Errors of Metabolism. Seminars in Pediatric Neurology. 2012 Dec;19(4):203-10. doi: 10.1016/j.spen.2012.09.007. PMID:23245554

Gropman AL, Gertz B, Shattuck K, Kahn IL, Seltzer R, Krivitsky L, Van Meter J. Diffusion Tensor Imaging Detects Areas of Abnormal White Matter Microstructure in Patients with Partial Ornithine Transcarbamylase Deficiency. American Journal of Neuroradiology. 2010 Oct;31(9):1719-23. doi: 10.3174/ajnr.A2122. PMID:20488904

Gropman AL, Shattuck K, Prust MJ, Seltzer RR, Breeden AL, Hailu A, Rigas A, Hussain R, Vanmeter J. Altered Neural Activation in Ornithine Transcarbamylase Deficiency During Executive Cognition: An fMRI Study. Human Brain Mapping. 2013 Apr;34(4):753-61. doi: 10.1002/hbm.21470. Epub 2011 Nov 23. PMID: 22110002

MRI lab at Georgetown University: left to right, Ileana Pacheco-Colon, research assistant, Dr. Andrea Gropman, Principle investigator, Courtney Sprouse, research assistant

Gropman AL, Fricke ST, Seltzer RR, Hailu A, Adeyemo A, Sawyer A, van Meter J, Gaillard WD, McCarter R, Tuchman M, Batshaw M; Urea Cycle Disorders Consortium. 1H MRS Identifies Symptomatic and Asymptomatic Subjects with Partial Ornithine Transcarbamylase Deficiency. Journal of Molecular Genetics and Metabolism. 2008 Sep-Oct;95(1-2):21-30. doi: 10.1016/j.ymgme.2008.06.003. Epub 2008 Jul 26. PMID: 18662894

Drug Trial Results

A Randomized Controlled Trial to Evaluate the Effects of High-Dose Versus Low-Dose of Arginine Therapy on Liver Function Tests in Argininosuccinic Aciduria

The objective of this study was to compare the effects of combinatorial therapy with low-dose arginine plus a nitrogen scavenging agent (Buphenyl) vs. conventional therapy using high-dose arginine in patients with argininosuccinic aciduria (ASA or ASLD). Twelve patients with argininosuccinic aciduria were enrolled. Subjects were assigned at random to receive either low-dose of arginine therapy combined with Buphenyl or a high-dose of arginine alone for one week. At the end of one week of therapy, liver function tests were measured. The results of the study showed that patients had significantly increased levels of ASA, and AST levels (measure of abnormal liver function) after treatment with high-dose arginine. In subjects with elevated liver enzymes to begin with, treatment with high-dose of arginine was associated with further increases in plasma levels of liver enzymes. Hence, low-dose arginine sufficient to normalize arginine levels in plasma combined with nitrogen scavenging therapy (Buphenyl or Ravicti) should be considered as a therapeutic option for treatment of ASA in patients with abnormal liver function tests.

Nagamani SC, Shchelochkov OA, Mullins MA, Carter S, Lanpher BC, Sun Q, Kleppe S, Erez A, O'Brian Smith E, Marini JC; Members of the Urea Cycle Disorders Consortium, Lee B. Mol Genet Metab. 2012 Nov;107(3):315-21. Epub 2012 Sep 17. PMID: 23040521

From left: Sandesh C. Sreenath Nagamani, MD, Oleg Shchelochkov, MD, and Brendan Lee, MD, PhD

Ammonia Control in Children with Urea Cycle Disorders; Phase 2 Comparison of Sodium Phenylbutyrate (Buphenyl) and Glycerol Phenylbutyrate (Ravicti)

Twenty four hour ammonia profiles and correlates of drug effect were examined in a comparison of Buphenyl and Ravicti. No statistically significant differences were observed in plasma phenylacetic acid and phenylacetylglutamine (PAGN) exposure during dosing with the two drugs, and the percentage of orally administered phenylbutyric acid excreted as PAGN (66% for Ravicti vs. 69% for Buphenyl) was very similar. These findings suggest that Ravicti is at least equivalent to Buphenyl in terms of ammonia control and that urinary PAGN is a clinically useful biomarker for dose selection and monitoring.

Lichter-Konecki U, Diaz GA, Merritt JL 2nd, Feigenbaum A, Jomphe C, Marier JF, Beliveau M, Mauney J, Dickinson K, Martinez A, Mokhtarani M, Scharschmidt B, Rhead W. Ammonia control in children with urea cycle disorders (UCDs); phase 2 comparison of sodium phenylbutyrate and glycerol phenylbutyrate. Journal of Molecular Genetics and Metabolism. 2011 Aug;103(4):323-9. doi: 10.1016/j.ymgme.2011.04.013. Epub 2011 May 5. PMID:21612962

What Have We Learned From the Longitudinal Study So Far?

When we developed the UCDC back in 2003, we had some questions in mind that we hoped our Longitudinal Study would be able to answer. Now, with 7 years of data and 600 of you enrolled we are able to answer some of those questions thanks to your dedication and support of these studies. We have published some of this data and other publications are on the horizon. We would like to share some of these answers with you.

How common are urea cycle disorders (Incidence)?

Like all rare diseases, it has been difficult to assess the frequency with which children are born with urea cycle disorders. Using highly sensitive newborn screening data for argininosuccinic aciduria (ASLD) and citrullinemia (ASSD) from over 6 million births in seven large diverse states we found that the frequency of these two disorders was 1/117,000 births. We examined data from the UCDC longitudinal study looking at the ratio of patients with these two disorders in relationship to the other UCDs and found that 30% of all urea cycle disorders in the longitudinal study were accounted for by these two disorders. We compared this to NUCDF data and to our European sister organization and found the same thing. Using this ratio we calculated that the overall incidence of UCDs in the United States should be 1/35,000. (OTC 1/63,000 , NAGS/CPSI 1/975,000, ASS 1/278,000, ASL 1/243,000, and Arginase < 1/1,000,000). With a birthrate of about 4 million in the U.S. that should result in about 113 newborns being born with a UCD each year. From the UCDC Longitudinal Study we find that 26% of participants presented with hyperammonemia in the newborn period (first month of life) and 69% presented with symptoms sometime later in life. This would result in about 30 symptomatic newborns being born in the U.S. per year and about 75 new UCD patients presenting at all ages each year.

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Take Action

Take an active role in Urea Cycle research...

Join the RDCRN Contact Registry

Many of you are already registered with the RDCRN Contact Registry*. If you haven't registered, consider doing so, so that you can **receive the most current information on:**

- Open recruitment for clinical studies of your disorder
- Opening of new UCDC clinical sites
- Awareness and advocacy group activities
- Information about future opportunities to participate in UCD research

Contact Registry Link: http://rarediseasesnetwork.epi.usf.edu/ucdc/takeaction/registrymenu.htm

*The Contact Registry is a way for you to provide your contact information so that the UCDC can contact you to keep you informed about UCDC research. It does not facilitate contact between individuals with UCD.

UCDC Research Team in Zurich, clockwise from top left: PI Matthias Baumgartner, MD, co-PI Tamar Stricker, MD, neuropsycologist Fabienne Dietrich, PhD, and study coordinator Ursina Spörri, MSc

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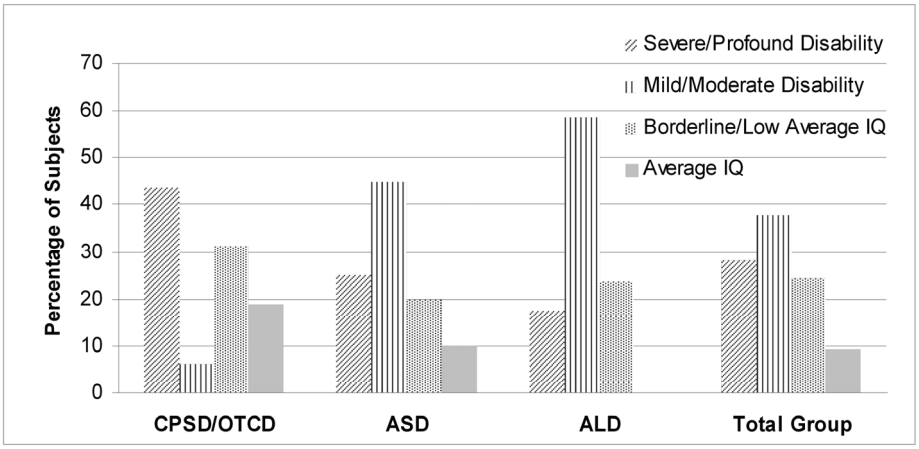
Do clinical outcomes of neonatal onset disease differ among the different UCDs?

The objective of this analysis was to compare the clinical course and outcome of patients diagnosed with one of 4 neonatal-onset forms of UCDs: complete deficiencies of carbamyl phosphate synthase I (CPSID), ornithine transcarbamylase (OTCD), argininosuccinate synthase (ASSD), or argininosuccinate lyase (ASLD). We looked at clinical, biochemical, and neuropsychological data from 103 participants with neonatal-onset UCDs who are enrolled in the Longitudinal Study. 88% of the subjects presented clinically with UCD symptoms by 7 days of age. Peak ammonia level was 963 μM (micromoles/liter) in patients with proximal UCDs (CPSID or OTCD), compared with 589 μM in ASSD and 573 μM in ASLD. Roughly 25% of subjects with CPSID or OTCD, 18% of those with ASSD, and 67% of those with ASLD had a "honeymoon period" of 1 year or more. A "honeymoon period" is defined as the time interval from discharge from the NICU (newborn intensive care unit) to subsequent admission for hyperammonemia. The proportion of patients with a poor outcome (Intelligence Quotient/Developmental Quotient <70, normally 100 in the general population) was greatest in ASLD (68%), followed by ASSD (54%) and CPSID/OTCD (47%). This trend was not significant, but was observed in both patients younger than 4 years old and those 4 years and older. Poor cognitive outcome was not correlated with peak ammonia level or duration of the initial admission for hyperammonemia.



Ah Mew N, Krivitzky L, McCarter R, Batshaw M, Tuchman M; Urea Cycle Disorders Consortium of the Rare Diseases Clinical Research Networ. Clinical Outcomes of Neonatal Onset Proximal Versus Distal Urea Cycle Disorders Do Not Differ. Journal of Pediatrics. 2013 Feb;162(2):324-9. Epub 2012 Aug 15. PMID: 22901741

Figure 4: Neurodevelopmenatal outcome of subjects 4 years or older by diagnosis.

Is there unrecognized acute liver failure and hepatocellular injury in OTCD? (Renata Gallagher, MD, PhD)

We studied whether acute liver failure and liver cell injury may be under-recognized complications in OTCD. Hepatocellular injury and liver failure have been reported occasionally in patients with a UCD, but there has been no systematic study of the frequency of hepatic injury or dysfunction in UCDs. To address this issue, charts were reviewed at two UCDC centers to assess the proportion of 71 individuals with OTCD who had evidence of acute liver failure, liver dysfunction, or hepatocellular injury. We found that 57% of the 49 patients with symptomatic OTCD had liver abnormalities: 29% met the criteria above for acute liver failure, 20% had liver dysfunction, and 8% had isolated hepatocellular injury. The proportion with acute liver failure was greatest in those with more severe OTCD, including neonates with markedly elevated ammonia levels (> 1,000 μmol/L). However, some late onset/carrier OTCD patients with severe liver involvement had only moderate hyperammonemia (100 - 400 μmol/L). Acute liver failure was the initial presenting symptom of OTCD in at least 3 of 49 symptomatic OTCD patients. We conclude that episodes of hepatocellular injury, liver dysfunction, and acute liver failure occur in a high proportion of individuals with symptomatic OTCD. The more severely affected OTCD patients had a higher likelihood of acute liver failure.

How do children with UCD who undergo liver transplantation do compared with those treated with conventional medication? (Philippe Campeau, MD, FCCMG)

- Overall 42/66 patients were transplanted before 2 years of age. In the last two years, 8 patients were transplanted and all but one were younger than 2 years of age, suggesting liver transplantation is happening earlier in life.
- 7 patients with CPS1 deficiency, presenting on average at 2 days of age, were transplanted on average at 1 year of age. An additional patient presented at 32 years and was transplanted at 34 years. Formal psychological testing after transplantation was available for 3 of these individuals. Results on their latest evaluations showed IQ/DQ scores in the average range (defined as an

(Continued on page 7)

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IQ of 85-115) up to 10 years after transplantation.

- 27 boys with neonatal onset OTC deficiency were transplanted on average at 1 year of age. Formal psychological testing after transplantation was available for 19 of them. Results on their latest evaluations showed IQ/DQ scores with an average IQ of 78 at 5 years of age, 3 years after transplantation.
- 6 girls with OTC deficiency, presenting on average at 17 months of age, were transplanted on average at 6 years of age. Formal psychological testing after transplantation was available for 5 of them. Results on their latest evaluations showed IQ/DQ scores in the average range at 14 years of age, 7 years after transplantation.
- 10 patients with neonatal onset argininosuccinic aciduria, presenting on average at 5 days of age, were transplanted on average at 5 years of age. Formal psychological testing after transplantation was available for 7 of them. Results on their latest evaluations showed IQ/DQ scores in the mild range of intellectual disability (defined as IQ 55-70) at 12 years of age, 5 years after transplantation.
- 13 patients with neonatal onset citrullinemia, presenting on average at 13 days of age, were transplanted on average at 2 years of age. Formal psychological testing after transplantation was available for 8 of them. Results on their latest evaluations showed IQ/DQ scores in the average range at 6 years of age, 4 years after transplantation.
- After liver transplantation, there were only 5 HA events reported in 2 subjects (both neonatal OTC males). There were 4 events for 1 patient and 1 event for the other. The other 64 patients had no further HA episodes after transplantation. These results suggest that liver transplantation appears to be curative and that the intellectual outcomes are mainly good. This study, however, did not look at mortality and morbidity associated with liver transplantation.
- See the summary in Table 1.

	Number trans-planted	Age at presentation	Age at transplanta-tion	Number with psy-chological testing	IQ/DQ scores	Age at last psychological testing	Time after transplanta-tion
CPS1D (early onset)	7	2 days (± 1 day)	1 year (± 1 year)	3	97 (+/-16)	21 years (± 13 years)	10 years (± 10 years)
OTC males	27	1 month (± 3 months)	1 year (± 2 years)	19	78 (+/-19)	5 years (± 5 years)	3 years (± 4 years)
OTCD females	6	17 months (± 16 months)	6 years (± 8 years)	5	87 (+/-23)	14 years (± 9 years)	7 years (± 3 years)
ASLD	10	5 days (± 6 days)	5 years (± 5 years)	7	63 (+/-11)	12 years (± 6 years)	5 years (± 2 years)
ASSD	13	13 days (± 3 days)	2 years (± 3 years)	8	87 (+/-14)	6 years (± 3 years)	4 years (± 3 years)

Table 1: Information about longitudinal study participants with liver transplants.

What are the precipitants of acute hyperammonemic (HA) episodes in UCD? (Peter McGuire, MS, MD)

We sought to characterize acute hyperammonemic (HA) episodes in terms of types of precipitants and utilization of medical resources. In addition, we examined indicators of increased morbidity for infectious precipitants. A total of 128 patients studied in the UCDC experienced 413 HA events. Most patients experienced between 1-3 (65%) and 4-6 (23%) HA events since the study inception 6 years ago, averaging less than 1 HA event/year. The most common precipitant was infection (33%). 24% of infections were due to upper/lower respiratory tract infections. Increased morbidity was seen with infectious precipitants that resulted in increased hospitalization rates, longer hospital stays and increased use of intravenous ammonia scavengers. So infections should be identified and treated early to avoid precipitating a HA episode in patients with UCD.

Your Feedback Is Important To Us

Please let us know what you think about this issue of *UCDC Update*.

Please go to https://www.surveymonkey.com/s/UCDCUpdate_Spring2013 to complete the newsletter survey on-line.

NUCDF invites you to the

2013 NUCDF Annual Conference

Featuring speakers from the UCDC

For the first time, the conference will be an online as a virtual webinar. For information, visit the NUCDF website at www.CureUCD.org

Improving the lives of individuals and families affected by urea cycle disorders

UREA CYCLE DISORDERS CONSORTIUM

Contact the UCDC
For questions about the Urea Cycle Disorders Consortium, please contact:
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UCDC Program Manager
Phone: 202-306-6489
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111 Michigan Avenue, NW
Washington, DC 20010

Visit our website:

www.RareDiseasesNetwork.org/ucdc

The Urea Cycle Disorders Consortium (UCDC) is a team of doctors, researchers, and patient advocates, working together to improve the lives of individuals and families affected by urea cycle disorders through research and education. The consortium provides a way for patients to join doctors and researchers in developing new and better treatments for urea cycle disorders by participating in research studies. The greater the collaboration between doctors and patients, the more we can learn about urea cycle disorders. This important first step is necessary if we are to find new and better treatments.

The goals of the UCDC are to:

- Develop better treatments and a deeper scientific understanding of the causes of UCD.
- Understand how UCDs can cause brain damage and develop protection against this.
- Conduct clinical trials of promising new drugs for the treatment of UCD.
- Work with the National Urea Cycle Disorders Foundation, the UCD patient advocacy group, to understand the research priorities of the UCD community and to help patients who wish to be involved in research connect with doctors conducting UCD research.
- Construct and maintain resources with significant information for clinicians, researchers, and patients.
- Train a new generation of physicians to become experts in providing care for and treating those with UCD.

The Urea Cycle Disorders Consortium is part of the Rare Diseases Clinical Research Network (RDCRN) funded by the National Institutes of Health and through philanthropic support from the O'Malley Foundation, the Rotenberg Family Fund, the Dietmar-Hopp Foundation, and the Kettering Fund.

Participating Centers

Children's National Medical Center
(lead institution)
Washington, DC

Baylor College of Medicine
Houston, Texas

The Children's Hospital
Aurora, Colorado

Children's Hospital of Philadelphia
Philadelphia, Pennsylvania

The David Geffen School of Medicine at UCLA
Los Angeles, California

The Hospital for Sick Children
Toronto, Ontario, Canada

Mount Sinai School of Medicine
New York, New York

Boston Children's Hospital
Boston, Massachusetts

Oregon Health and Science University
Portland, Oregon

Rainbow Babies and Children's Hospital
Cleveland, Ohio

Seattle Children's Hospital
Seattle, Washington

University Children's Hospital
Zurich, Switzerland

University of Heidelberg
Heidelberg, Germany

University of Minnesota Amplatz Children's Hospital
Minneapolis, Minnesota

UCDC investigators, study coordinators, and administrators