The Urea Cycle Disorders Consortium: Brought to you by RDCRN

or

“Things I wish my mother had told me before I started a longitudinal study”

Marshall Summar
Children’s National Medical Center
Washington D.C.
“We’re going to be working together for a loooong time.”
How We Started

- Strong and single family organization
- Researchers and clinicians were the same group
- Both groups could stand being in the room together for long periods of time
- We realized after our first “Consensus” meeting that we didn’t really know that much about what we were doing
- We wanted to do a better job and have better information.
This Is Why We Really Started
First: Begin With The End In Mind

- Develop better understanding of outcomes of UCD
- Conduct clinical trials of promising new drugs
- Develop resources with information on UCD for clinicians, researchers, and patients
- Train next generation of investigators in UCD
- Figure out what we are missing.
Second: There’s No Such Thing As A Free Lunch

- Funding is NIH with matching philanthropy
- We are in year 8 and will renew next in 2014
- Each Center receives about 100,000 U.S./year
- Current NIH Funded Protocols
  - 5101 Longitudinal Study of Urea Cycle Disorders
  - 5102 A Randomized, Double-Blind, Crossover Study of Sodium Phenylbutyric
  - 5104 Assessing Neural Mechanisms of Injury in Inborn Errors of Urea Metabolism
  - 5107 Investigation of Brain Nitrogen Metabolism in Partial Ornithine Transcarbamoylase

Third: Diversify Your Portfolio, Be Open to New Ideas

- Vaccine safety
- Seizure frequency
- Cytokine changes
- Neonatal early cycle outcome
- HPN-100 trial
- PYY neuropeptide
- Phenylbutyrate pharmacokinetics
- Pregnancy outcomes
- Cancer surveys
- Menses and stability
- Socioeconomic effects
- Compliance with tx
- Transplant outcomes
- Nitric oxide metabolism
Fourth: Like they say in Real Estate, Location, Location, Location
We meet on a regular basis:
- By phone, once a month
- In person, minimum of once a year
- Coordinators, separate meetings

The More Meetings We Had the Fewer People Showed Up. Mission Fatigue

The Same Is True of Participants. Over the years you have to work hard to keep interest up.
Burden of Study

Pretty high for this study.
- Neurocognitive (1/2 to full day)
- Laboratory
- Physical
- Medications
- Review of systems
- Past Medical Record

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<tr>
<th>Analysis Variable : NUMVISIT</th>
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<td>N</td>
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<td>511</td>
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Dropout or Loss Over 6 Years

- Death: 6
- Lost to Follow Up: 7
- PI Removed from Study: 8
- Parent Patient Requested: 4
- Other: 1

Total: 26

Most withdrew in year 5-6 (except death)
Bromides Lessons We (Re)Learned

• A Good Data Coordinator is more precious than Gold
• There are never as many patients who will enroll as you think (1200 down to 550). The law of additive optimism.
• The paperwork is the rate-limiting step for most things (no patients enrolled til year 2).
• Collecting too much data degrades the quality of the data, wears out the system. The Great is the Enemy of the Good
• The patients fatigue easily and extensive neuropsychological testing wears them out and degrades performance
• It is very hard to capture specific data on intercurrent illnesses
• Dietary data is hard to standardize and reported diet is not always reliable. Patients are often non-compliant with their medications. What’s amazing is we were surprised.
More Lessons We Learned

• Some of your better ideas don’t occur until you are a few years into the process (immunizations, seizures, drug trials)

• Plan as if you will be refunded for a long time. Plan for the desired outcome.

• Consensus of treatment builds over time and outcomes improve.

• Since we started, we’ve lost fewer than 10 (out of 500) patients in the study. Historically should have been about 25%
Suggestions

• Check your coat and your egos at the door

• Collect only what you can consistently get. Revisit this frequently

• Spend some time on defining what the criteria are for having a disease. Harder than you think.

• Involve parent groups and industry early on

• Plan for criteria for opening new sites and closing unproductive ones
A Few More

- Bank DNA
- Work on consensus guidelines which many won’t use……….. At first.
- Agree to disagree
- Include folks you don’t necessarily agree with but who will listen.
- Your Web Page is often your best recruiting tool and best tool for families
- Keep a sense of humor
- Use team building events and socialize. This is very important.
- Listen to the young members of the team. They are the ones still seeing the patients and often make the most interesting observations
Welcome to the Urea Cycle Disorders Consortium!

Why am I here?
The UCDC exists to bring together physicians and patients for the sake of Urea Cycle Disorders research.

What can I do?

Take Action
Take an active role in Urea Cycle research...

Receive the most current information on:
- open recruitment for clinical studies of your disease
- opening of new clinical sites doing research on rare diseases
- activities from affiliated awareness and advocacy groups
- information future opportunities to participate in research

Learn More
N-Acetylglutamate Synthase (AGS) Deficiency
Carbamyl Phosphate Synthetase (CPS) Deficiency
Ornithine Transcarbamylase (OTC) Deficiency
Argininosuccinate Synthetase Deficiency (Citrullinemia I)
Citrullinemia (Citrullinemia II)
Argininosuccinate Lyase Deficiency (Argininosuccinic Aciduria)
Arginase Deficiency (Hyperargininemia)
Ornithine Translocase Deficiency (HH) Syndrome
Glossary of Terms
Frequently Asked Questions

Resources For Physicians:
Learn More About Urea Cycle Disorders
Other Useful Resources
Treatment Guidelines
Download Contact Registry Paper Form
New > UCDC Publications

UCDC Events | UCDC Publications

2011 National Urea Cycle Disorders Foundation Annual Conference

Children’s National Division of Genetics & Metabolism
Improving the quality of diagnosis, information, research and treatment for individuals affected with an organic aciduria (OAD) or with a urea cycle defect (UCD).

Patients and families

- For younger persons
- For patients, parents and family

Select a language:

- [English](#)

General introduction

European patient registry

E-IMD has been funded by the European Commission through its Public Health and Consumer Protection Directorate (DG SANCO), PHEA programme (more information).

Survey for patients

E-IMD is currently conducting a survey to patients and parents in order to better understand their healthcare needs and services. To participate in this survey please click below:

- [English version: Click here to take survey](#)

Guideline development

Consensus care protocols for OADs and UCDs are currently being developed.

Subscribe to the Newsletter

E-mail
Old Joke

What’s so special about Fred Astaire……
Ginger Rogers did everything he did backwards wearing high-heels.

Translation, In the States, we only have to deal with English (American to my British colleagues). In the EU it is about 16+ languages
How Europe Might Theoretically View American Science

Children’s National Division of Genetics & Metabolism
# Cognitive and Adaptive Outcome in Children ages 3-16*, Mean (SD) in UCDC data

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<thead>
<tr>
<th></th>
<th>Neonatal Ages 3-5</th>
<th>Late Onset Ages 3-5</th>
<th>Neonatal Ages 6-16</th>
<th>Late Onset Ages 6-16</th>
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<td><strong>WASI/WPPSI-3 Composite Scores</strong>*</td>
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<tr>
<td>Verbal IQ</td>
<td>81.3 (16.6)</td>
<td>101.7 (24.4)</td>
<td>72.9 (14.3)</td>
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<td>Performance IQ</td>
<td>77.7 (15.0)</td>
<td>95.6 (17.4)</td>
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<td>89.5 (20.4)</td>
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<tr>
<td>Full Scale IQ</td>
<td>77.7 (16.3)</td>
<td>99.6 (22.6)</td>
<td>71.4 (12.8)</td>
<td>94.1 (22.0)</td>
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<tr>
<td><strong>ABAS-II</strong>*</td>
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<tr>
<td>General Adaptive Composite</td>
<td>73.2 (31.2)</td>
<td>91.4 (23.6)</td>
<td>66.0 (17.9)</td>
<td>84.4 (21.6)</td>
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*Clinically significant difference between the groups for IQ and adaptive

Children’s National Division of Genetics & Metabolism
Full Spectrum IQ in OTC Carriers and controls

FSIQ by Group

- Symptomatic
- Nonsymptomatic
- All Cases
- Control

Mean FSIQ

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THE SECRET OF SUCCESS

WHAT IS THE SECRET? PRETEND YOU’VE ALREADY ACHIEVED IT—THEN OFFER TO SELL THE SECRET TO OTHERS.

Children’s National Division of Genetics & Metabolism