

Urea cycle disorder (UCD) *At a Glance*

Urea cycle disorders are a group of genetic conditions that fall under the broad category of metabolic disorders. The urea cycle is a biochemical process that occurs in the liver. Through this process, body waste from the metabolism of protein (in the form of nitrogen) is removed from the blood and converted to a compound called urea. There are eight enzymes that complete this process, and normally the urea is transferred into the urine and removed from the body.

However, in urea cycle disorders, one of the enzymes in the cycle is deficient. Without the proper enzymes, the process can't be completed, and nitrogen accumulates in the blood in the form of ammonia, a highly toxic substance. The accumulation of ammonia in the blood is called hyperammonemia. Hyperammonemia is especially toxic to the brain and can cause brain damage, coma or death.

UCDs are caused by a genetic mutation. Some children are diagnosed as children because they show symptoms. Other children are diagnosed as infants through new-born screening (NBS). Children diagnosed by NBS may receive treatment before they first experience symptoms.

Learn more about features of UCDs (NOTE: not all people with UCDs will have all of these features).

Types of UCDs

There are six different types UCDs, one for each enzyme in the urea cycle:

- NAGS (N-acetyl glutamate synthetase) deficiency
- CPS 1 (carbamoyl phosphate synthetase) deficiency
- OTC (ornithine transcarbamylase) deficiency
- CTLN1 (Citrullinemia type 1, ASD or ASL deficiency)
- ALD (Argininosuccinic Aciduria, ASA, ASL or AL) deficiency
- ARG deficiency (hyperargininemia)

There are also two enzyme transporter deficiencies, which are often considered UCDs:

- HHH Syndrome (ORNT deficiency)
- CTLN2 (Citrullinemia Type II or Citrin deficiency)

Things to Think About

1. Medical / Dietary Needs

What you need to know

Treatment of UCDs usually involves finding the right balance of dietary protein intake- enough so that the individual has the protein building blocks necessary for their cells to grow and develop, but not so much that it overwhelms the broken urea cycle.

- They may need to eat a special diet and some may need the help of a feeding tube to make sure they get the nutrition they need.
- There are also medications that can help keep ammonia levels low.
- Further, because illness can cause stress on the metabolic system, they need to avoid being exposed to people who are sick, and if they get sick they need to take extra precautions.
- Some children with UCDs have had or may be recommended to have a liver transplant.
- **These children often no longer need to follow a special diet, but may be on medications for their transplant.**

Not every child with a UCD requires treatment.

What you can do

Teachers of students with UCDs find that parents are an excellent resource when it comes to understanding the child's treatment.

- Ask parents if their child is on any medications, and consult with the nurse and parents about how medications should be administered at school.
- Ask the parents if the student has any dietary restrictions and how they would like to manage school meals.
- If the student uses a feeding tube, ask the student's parents, the student and the school nurse to tell you more about what it's like to use a feeding tube.
- Ask parents if and how they'd like to be notified about student illnesses.

If your student is not on any treatment, ask parents how you can help make sure the child stays healthy

2. Education Supports

Many children with UCD's have no intellectual disability. It is important to have high expectations for all children who have UCDs.

What you need to know

- A child with a UCD may have developmental delays or cognitive deficits due to higher than normal levels of ammonia in the brain
 - They may have had a hyperammonemic episode earlier in life
 - They may have on going problems with chronic or occasional high ammonia levels
 - The learning issues may become more apparent if the child's ammonia level rises.
 - Most children regain prior levels of function after a hyperammonemic episode.
- Specific challenge areas
 - Deficits in working memory, attention and fine motor coordination.
 - Many children with UCDs take longer to develop social and self-care skills.
 - Your student may have difficulty in areas that are different than what is shown here

What you can do

- Ask the parents about concerns about their child's academic performance
- Make sure that the child receives a developmental evaluation when appropriate
- If there is regression in a child's abilities, discuss this with the child's parents

3. Behavioral and Sensory Support

What you need to know

UCDs show up differently in different children. Some children have no behavior or sensory impacts, while others have behaviors that mimic autism or Attention Deficit Hyperactivity Disorder (ADHD) and need similar sensory support.

What you can do

Talk to parents about any special accommodations or needs that their child may need.

4. Physical Activity, Trips and Events

What you need to know

Students with UCDs can go on field trips and participate in school events along with the other students. They may need additional supports or accommodations to do so.

Students with UCDs may not be as active or agile as other students. It is good to encourage children to be active and to make accommodations if physical activity is difficult or uncomfortable.

What you can do

Talk to the student's parents about how they would like to handle field trips:

- If the student is on a restricted diet, they may need to bring along food that they can eat. The child may need to be watched to make sure he or she doesn't eat restricted food.
- If the child uses a feeding tube, a parent or aide may need to accompany the child.
- Make sure that school staff has a copy of the child's emergency plan on hand at the event.

5. School Absences and Fatigue:

What you need to know

Children with UCDs need to avoid illnesses, and may need to stay home when other students are ill. If a student with a UCD gets a virus, he or she may need to stay home and take extra precautions to get well. If a student experiences a hyperammonemic episode, they will need to be hospitalized for one or more weeks.

For all these reasons, a child with a UCD may be absent from school frequently or for extended periods of time.

What you can do

Good communication is key when helping a child with a UCD who is absent from school. Talk to parents about what you can do to support the child during an absence. They may benefit from a home visit by a teacher or utilizing online technology to be present in class from home.

6. Emergency Plan Considerations:

What you need to know

Hyperammonemia is a major concern for children with UCDs. Symptoms of hyperammonemia can vary from child to child. Parents of children who have hyperammonemic episodes are often able to tell early on when their child is starting to have an episode. Some common symptoms of hyperammonemia include:

- Feeling fatigued or listless
- Staring or 'zoning out'

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- Nausea or vomiting
- Eyes rolling back into the head, 'glassy-eyed' look
- Losing touch with reality, hallucinating
- Being unusually irritable or uncooperative

If you see these symptoms in your student, call 911 and contact parents and the school nurse.

What you can do

It's a good idea to be prepared and know how to respond to a hyperammonemic episode before it occurs, even if your student has never had one. Because hyperammonemia looks different in every child, it's important to talk to parents and school nursing staff about signs to watch for. Make sure you understand what to do if you think a student may be having a hyperammonemic episode.

7. Resources

An Educator's Guide to UCDs

From the New England Consortium of Metabolic Programs, has been created for teachers to help support children with UCD at school. The guide includes information about UCDs, new research on the most common learning challenges in UCD, guidance for educators on what they can do to help, and a guide to create a communication plan for parents and teachers.

The New England Metabolic Consortium

Brings together healthcare professionals at all levels involved in identifying and treating individuals with metabolic disorders.

The goals of the Consortium are to disseminate information, collaborate in the development of social support programs and educational materials, support organizations for parents and adults with metabolic disorders, provide training for students in medicine and related fields, jointly develop and conduct research projects, and establish uniform treatment protocols for individuals with metabolic disorders.

The National Urea Cycle Disorders Foundation (NUCDF)

The National Urea Cycle Disorders Foundation is a non-profit organization dedicated to the identification, treatment and cure of urea cycle disorders. NUCDF is a nationally-recognized resource of information and education for families and healthcare professionals.

Our organization was formed in 1988 by a handful of parents whose children were affected. The Foundation is operated and supported by the volunteer efforts of families with children suffering from UCDs and is a supportive network of families, friends, and medical professionals.

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Genetics Home Reference

Consumer-friendly information about human genetics from the U.S. National Library of Medicine

Although there are other variations in this group, we're including the most common:

NAGS (N-acetyl glutamate synthetase) deficiency

<https://ghr.nlm.nih.gov/condition/n-acetylglutamate-synthase-deficiency>

CPS 1 (carbamoyl phosphate synthetase) deficiency

<https://ghr.nlm.nih.gov/condition/carbamoyl-phosphate-synthetase-i-deficiency>

OTC (ornithine transcarbamylase) deficiency

<https://ghr.nlm.nih.gov/condition/ornithine-transcarbamylase-deficiency>

CTLN1 (Citrullinemia type 1, ASD or ASL) deficiency

<https://ghr.nlm.nih.gov/condition/citrullinemia>

ALD (Argininosuccinic Aciduria, ASA, ASL or AL) deficiency

<https://ghr.nlm.nih.gov/condition/argininosuccinic-aciduria>

ARG (hyperargininemia) deficiency

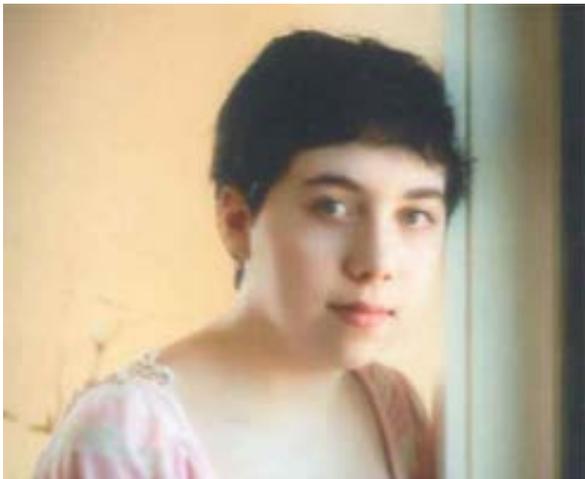
<https://ghr.nlm.nih.gov/condition/arginase-deficiency>

Note: This printable version does not include the information found under the green button marked "Transitions" on the website. Those general pages may be printed separately.

8. Meet a Child with UCD

Ashley's Anniversary!

GEMSS would like to thank Ashley and her mother for their generosity in sharing this story with us. You have made the site come to life with the addition of your thoughts and feelings. Thank you so much!



Fourteen years ago, Ashley was an infant who developed the hiccups, wasn't eating, and her body temperature became alarmingly low. After a workup and emergency transfer to Boston's Children's Hospital, she was diagnosed with ASA (Argininosuccinic Acidemia) which is a Urea Cycle Disorder. Eventually, Ashley had an NG feeding tube (nasogastric) and then a Mickey button (G-tube) to help her eat her special diet. She also developed seizures at that time. When she was 4

years old, she had a liver transplant and has just celebrated her 10- year anniversary of getting her new liver! Her health is much improved since the transplant.

Ashley is a very lovable, talkative teenager who will 'talk your ear off' according to her mother Dina! Since she is immune-depressed and can very easily get sick, Ashley is in a small class in seventh grade to eliminate exposure to germs. For example, if she gets a common cold, she may be out of school for 5 days. Her school team and nurse know her well and help communicate any health issues immediately to Dina so they can determine next steps.

Her teachers and family are helping her learn to read social cues of others, and helping her do well in school due to her learning issues. She does her homework every night but likes her mother to sit right beside her when she does it. As they think of transition to the next grade, they are considering the idea of moving her into larger classes. She gets speech therapy at school to help her with expressing herself and developing social skills. Ashley loves her family members and also young children. She has a special spot in her heart for her two grandmothers.

Dina's advice is for parents to trust their instincts and detect issues early. She says that the teachers and school administrators are very understanding of Ashley's health needs and even her frequent absences.

Dina says that Ashley no longer has ASA and that they identify more with children and families who have had a liver transplant. "We have had smooth sailing for the past 10 years since the transplant," says Dina and that is a wonderful reason to celebrate this young woman's anniversary!