An Educator's Guide to
Urea Cycle Disorders

For Teachers, Nurses and Parents of Students with UCDs

Boston Children's Hospital
Until every child is well™

NUCDF
National Urea Cycle Disorders Foundation

Saving Lives through Awareness,
Education, Research & Support.

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Teachers, nurses, and parents of students who have urea cycle disorders, you asked for information to help your students thrive, and we answered — this guide is for you!

We know that it can be difficult for educators and parents to find evidence-based information about how urea cycle disorders (UCDs) affect a student's classroom experience. We created *An Educator's Guide to Urea Cycle Disorders* for those who work most closely with these students.

In preparing the guide, we interviewed parents and teachers, evaluated data from an established longitudinal study on UCDs, and collected input from physicians, psychologists, nurses, metabolic nutritionists and health communication professionals. Here you'll find accurate, practical information on how to best support students with UCDs.

Suggested ways to use this guide:

- Review the guide in a meeting with parents, teachers, nurses and other school staff involved in the education and care of a child with a UCD. Many parents and teachers find it useful to meet at the beginning of each school year. As you read through the guide, note any questions you may have.
- Use the Communication Plan section to collaborate with parents on a personalized plan for the student, and to streamline communication between home and school.
- Find more detailed clinical information in the special Nurse's Section, and use the note space there to record contact information for the student's healthcare providers.

With your help, students with UCDs can succeed at school and beyond. We hope this Educator's Guide serves as a resource for you to help these students be their best.

Rachel Miller, MA, Emerson College
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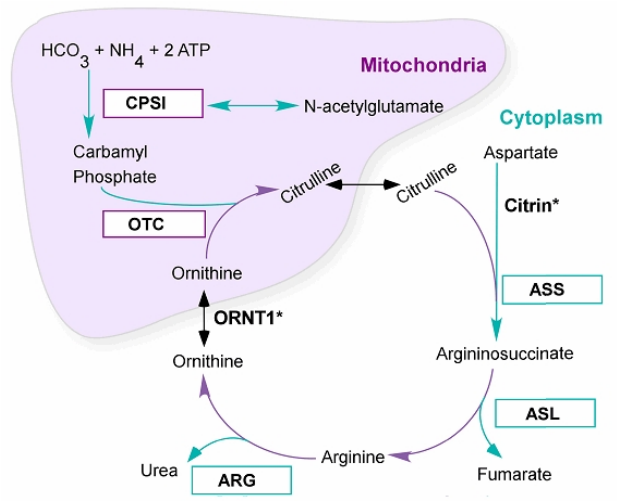
What are UCDs and what causes them?

The urea cycle is a biochemical process that takes place in the liver and kidneys. During the cycle, protein is metabolized (broken down), and nitrogen is released as waste. When the metabolic enzymes of the urea cycle are working correctly, as shown in the figure below, waste nitrogen is removed from the blood and converted to a compound called urea. Urea is then transferred into the urine and removed from the body.

In urea cycle disorders (UCDs), 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. This ammonia buildup, known as hyperammonemia, is highly toxic. Hyperammonemia can cause a range of behavioral and other symptoms. If enough ammonia builds up in the blood, it can affect the brain, and may cause brain damage, coma or death.

UCDs are caused by a genetic mutation. Some people with UCDs are diagnosed as children because they started to show symptoms. Others are diagnosed as infants through newborn screening, which is a blood test for newborns. Children diagnosed with a UCD by screening may receive treatment before they first experience symptoms.

The Urea Cycle



Types of UCDs

There are six different types of UCDs, one for each enzyme in the urea cycle (the enzyme is shown in parentheses):

- NAGS deficiency (N-acetyl glutamate synthetase)
- CPS 1 deficiency (carbamoyl phosphate synthetase)
- OTC deficiency (ornithine transcarbamylase)
- CTLN1 deficiency, also known as citrullinemia type 1, ASD or ASL (argininosuccinate synthetase)
- ALD deficiency, also known as argininosuccinic aciduria, ASA, ASL or AL (arginino succinase)
- ARG deficiency, also called hyperargininemia (arginase)

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

- HHH Syndrome, also called ORNT deficiency (ornithine translocase)
- CTLN2 deficiency, also known as citrullinemia type II (citrin)

"Communication is key—teachers need to be alerted to any changes."

– Elementary School Speech and Language Therapist

"I have found my student's mother to be a great resource...the standards she has set are very clear cut."

– Teacher of a kindergartner

Hyperammonemia

Hyperammonemia—a buildup of ammonia in the blood—is a major concern for children with UCDs. 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. Talk to parents and school nursing staff about signs to watch for, and what to do if you think a student may be having an episode.

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 one. Some common symptoms include:

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

How are UCDs treated?

Treatment of UCDs usually includes finding the right amount of dietary protein intake for each child—enough so that they have the amino acids necessary for their bodies to grow and develop, but not so much that it overwhelms their impaired urea cycle. Children with UCDs may need to eat a special diet and some may need the help of a feeding tube (gastronomy tube) to make sure they get the nutrition they need. In some children, medications can help keep ammonia levels low.

Illnesses, such as colds, flu, or other infections can stress the metabolic system, so students with UCDs must avoid exposure to people who are sick. If they themselves get sick, they must take extra precautions. Some children with UCDs have had or are recommended to have a liver transplant. However, not every child with a UCD requires treatment. The next section includes additional details about UCD treatment and management.

"It's a group effort to help my daughter succeed in school. The teacher, the school nurse, the social worker, the teacher's aide, all play a big part."

– Parent of a 5th grader

Medications

Children with UCDs may take special medications, known as "ammonia scavengers," to help remove ammonia from their bodies. Some may need to take medication several times per day. Some parents will want to administer medications to their child during the school day, or the school nurse may take care of this.

Ask parents if their child is on any medications, and consult with the parents and school nurse about how these should be given.

Diet

Children with UCDs may need to eat a special diet to help limit how much ammonia their bodies produce. They may need to be carefully monitored to make sure they eat only prescribed foods and in the correct amounts. Most children with UCDs must not consume high protein foods such as meat (beef, chicken, lamb, pork, and fish), dairy products, eggs, nuts, lentils, beans, and soy. Some children may need to take a special formula which has been created specifically for them.

It is important to ask parents if their child has any dietary restrictions or prescribed foods and drinks, and to learn how they would like to manage school meals.

*P*arents may want to prepare their child's school meals instead of having the child participate in the school meal program.

Also, ask parents how they would like to share information about what the child eats during school hours. Some options parents and teachers can use are: email, a quick phone call, or a note sent home with the child.

Most children with UCDs have a diet that is so specialized that it is important that they *not consume foods from another child's lunch*, and that they *not trade foods*. Talk with the student's classmates and school lunch mates about not sharing or trading food.

In some states, there are laws that require schools to make accommodations for special medical diets. For more information, you can contact the National Urea Cycle Disorders Foundation. Check the "Resources" section of this guide for contact information.

Gastrostomy tubes (G-tubes)

Sometimes children with UCDs have trouble eating enough, or don't like to eat. For them, a feeding tube (called a gastrostomy tube or g-tube) can ensure they get the nutrition and medications they need. Some children with g-tubes get all their food through the tube, while others use tube feedings to supplement what they eat orally. Parents of children with feeding tubes may want to administer tube feedings and medications for their child at school, or the school nurse may take care of this. For most kids with feeding tubes, they are a normal part of everyday life.

Ask the student's parents, the student, and the school nurse to tell you more about using a feeding tube.

"Both my children have the same UCD, but it shows up differently in each one. If you didn't know, you'd think they have totally different disorders."

– Parent of a kindergartner and a 2nd grader

"They're just normal kids on a special diet."

– Teacher of a kindergartner

Staying Healthy

It's important that children with UCDs avoid illnesses that may stress their metabolism. If another student is sick, parents of a child with a UCD may ask you to notify them so they can keep their child at home to keep them well.

> *Ask parents if and how they would like to be notified about student illness.*

Liver Transplant

Some children with UCDs have had or may be recommended to have a liver transplant. A liver transplant can prevent further hyperammonemic episodes. A child who has had a liver transplant to treat a UCD no longer needs to eat a restricted protein diet. However, transplantation brings its own set of complications.

If your student has had a liver transplant, talk with parents or the student's physician about the student's care during the school day.

Observation

Not every student with a UCD will have special health care needs. Thanks to advances in diagnosis and treatment, many children do not need all the interventions described in this guide.

Often, a child's blood ammonia levels will be monitored by their physician, and parents will watch their behavior for symptoms of rising ammonia levels. For these students, you can play an important role in making sure parents and physicians are notified quickly of any change in behavior or cognition.

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

"My daughter comes home with an 83 on a spelling test, and we're over the moon. She's got a work ethic like I've never seen in a kid."

– Parent of a 1st grader

Current Research on UCDs

A child with a UCD may have chronic or occasional elevated blood ammonia levels (hyperammonemia), exposing the brain to higher than normal levels of ammonia. As a result, the student may have cognitive or developmental deficits. These deficits may become more apparent if the child's ammonia level rises during what is known as a *hyperammonemic episode*. Most children regain prior levels of function after the episode. If you notice the student losing abilities or regressing, it is important that you talk with their parents and metabolic doctor.

Recent research has shed light on areas where children with UCDs may struggle in school. Generally, these students experience deficits in working memory, attention and fine motor coordination. Many children with UCDs take longer to develop social and self-care skills. However, it's important to note that many children with UCDs *do not* experience these difficulties.

This table summarizes areas in which children with UCDs typically struggle. Children may show none, one, or several of these deficits:

- 43-55% have difficulty paying attention
- 40-49% have a hard time with self-direction skills, such as goal setting and planning
- 33-79% have delays in learning and adopting self-care skills
- 38-62% show deficits in working memory
- 30-54% have difficulty with social skills
- 26-50% have a hard time assessing their own performance and the impact of their behavior on others
- 33-35% are slow or unable to initiate activities
- 32-34% have difficulty with organization
- 27-33% have difficulty shifting from one activity to another
- 15-19% struggle with regulating their emotions (Note: 0% of children with ASA show this)

These percentages were derived from studies of students with OTC, CTLN1 and ASL. Data on students with other UCDs are not yet available. However, our metabolic experts report that the data above can be generalized to include children with ARG, CPS1, ALD, HHH and CTLN2.

"He is a constant reminder that kids learn differently, but they can still learn. If we can meet his needs, he'll go far."

– Teacher of a 1st grader

Children with UCDs may also have IQs below the normal range. An average IQ score is 100. About one third of the general population of students has IQ scores between 85 and 100, and one third has scores between 100 and 115.

This table shows the percentage of children with UCDs with IQs below 85:

Type of UCD	Full Scale IQ	Verbal IQ	Performance IQ
ALD	76%	70%	84%
ASD	48%	42%	53%
OTC	24%	19%	27%
All UCDs	38%	33%	43%

Full Scale IQ is a measure of overall intellectual ability and incorporates scores from both Verbal and Performance subtests. The Verbal IQ reflects verbal reasoning, expression and comprehension. The Performance IQ measures nonverbal reasoning, visual spatial understanding and fine motor and visual processing speed.

UCD affects different children in different ways, and IQ scores are one of many measures of skill and ability. While many children with UCD experience learning or behavioral issues, many others do not. Your student may have difficulty in areas different than those discussed here. Many teachers have found parents to be an excellent resource for identifying the best way to support the student academically.

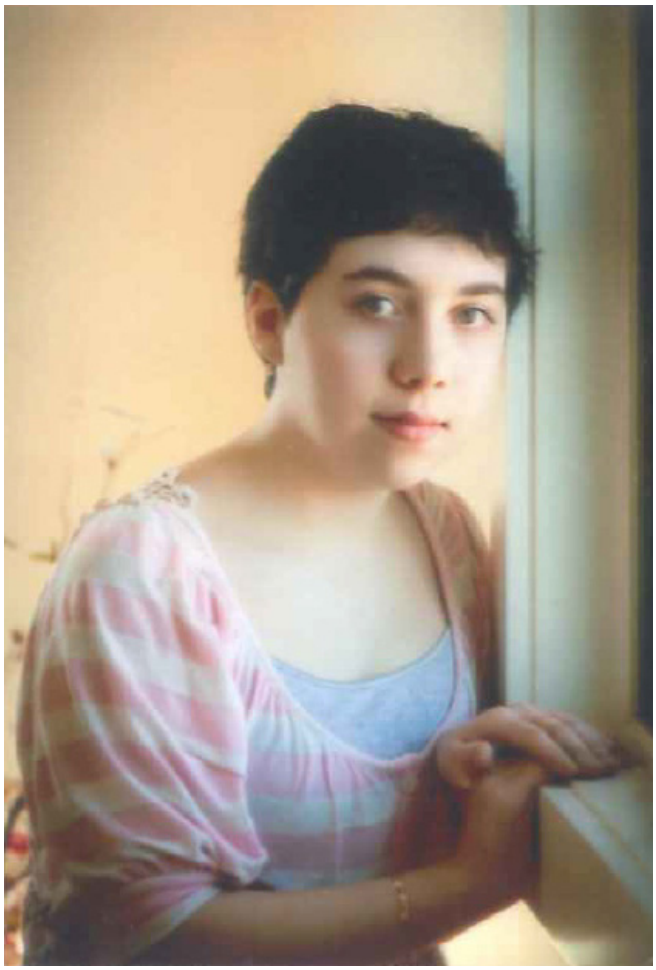
Ask the student's parents if they have any concerns about their child's academic performance.

Meet a Child with a UCD

Fourteen years ago, when Ashley was an infant, she developed the hiccups, wasn't eating, and her body temperature became alarmingly low. After a series of medical tests and an emergency transfer to Boston Children's Hospital, she was diagnosed with ASA (argininosuccinic aciduria) which is a urea cycle disorder (UCD).

At first, as part of her treatment, Ashley had a nasogastric feeding tube, then later a gastrostomy tube called a MIC-KEY® to ensure that she received proper nutrition and medicines. She also developed seizures at that time.

When she was 4 years old, Ashley had a liver transplant. She has just celebrated her 10-year anniversary of getting her new liver. Her health has improved greatly since the transplant. Ashley is a very lovable, talkative teenager who will "talk your ear off" according to her mother, Dina.



Ashley at age 14

As a transplant recipient, Ashley must take drug therapy to suppress her immune system and keep her body from rejecting the donor liver. Because of this, she can get sick very easily. For example, if she catches a typical cold, she may be out of school for 5 days. To reduce her exposure to germs, Ashley is in a small seventh grade class. Her school team and nurse know her well and help communicate any health issues immediately to Dina so they can determine next steps.

Ashley's teachers and family help her do well in school, including helping her learn to read the social cues of others. She does her homework every night but likes her mother to sit right beside her when she does it. She gets speech therapy at school to help her with expressing herself and developing social skills. As part of preparing Ashley for a transition to a more independent school environment, her family is considering moving her into larger classes. 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 is: trust your instincts and detect issues early. She says the teachers and administrators at Ashley's school have been very understanding of her health needs and frequent absences.

Dina says that Ashley no longer has ASA and that they identify more with families of children 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!

This section adapted with permission by Genetic Education Materials for School Success

Nurses' Section

The urea cycle involves the metabolism of protein in the body, and the generation of nitrogen as a waste product. Urea cycle disorders (UCDs) result from an absence or deficiency in one of the first four enzymes in the cycle: carbamyl phosphate synthetase I (CPSI), ornithine transcarbamylase (OTC), argininosuccinate synthetase (ASS), or argininosuccinate lyase (ASL). UCDs may also result from the absence or reduced functioning of the co-factor enzymes, N-acetyl glutamate synthetase (NAGS) or arginase (ARG).

These enzyme abnormalities are associated with 8 UCDs:

- CPS 1 deficiency (carbamoyl phosphate synthetase)
- OTC deficiency (ornithine transcarbamylase)
- CTLN1 deficiency, also known as citrullinemia type 1, ASD or ASL (argininosuccinate synthetase)
- ALD deficiency, also known as argininosuccinic aciduria, ASA, ASL or AL (arginino succinase)
- NAGS deficiency (N-acetyl glutamate synthetase)
- ARG deficiency, also called hyperargininemia (arginase)
- HHH Syndrome, also called ORNT deficiency (ornithine translocase)
- CTLN2 deficiency, also known as citrullinemia type II (citrin)

Except for OTC deficiency which is an X-linked disorder, urea cycle disorders are of autosomal recessive inheritance.

When the urea cycle is disrupted, ammonia or other precursor metabolites build up in the blood and brain. In the newborn this can lead to cerebral edema. Hyperammonemia is associated with lethargy, anorexia, hypothermia, seizures, coma and death.

Talk to parents and the student's metabolic team to learn more about the child's treatment and how you can help accommodate his or her needs at school.

Help teachers to understand treatments and emergency procedures.

Survivors often experience recurrent hyperammonemia, motor delays and intellectual disability. In the milder forms of UCDs and in arginase deficiency (ARG), high ammonia may only first occur at times of illness or extreme physical stress.

Long-term treatment of UCDs involves a protein-restricted diet, special medical foods (formulas), and nitrogen-scavenging medications. To prevent a hyperammonemic episode, individuals with UCDs may be hospitalized for monitoring and additional treatments when they become sick with respiratory or gastrointestinal illnesses. In many cases (but not all), liver transplantation "cures" most of the urea cycle disorder, prevents hyperammonemia, and results in maintenance or improvement of the child's neurocognitive functioning.

The somewhat varied outcomes associated with the different disorders and the heterogeneity even within a single diagnostic category prevent simple explanations related to genotype or hyperammonemia. Outcome may depend on the level of enzyme block, timing of detection and treatment, age of symptom onset, number and severity of hyperammonemic episodes, educational interventions (e.g., early intervention), treatment strategies (including medications, liver transplant, medications, use of a gastrostomy tube), treatment adherence, and other psychosocial variables.

Students with UCDs may need special accommodations. For example, a parent may need to bring in pre-mixed formulas for the child to drink while at school, or the child may need medication administered by gastrostomy tube.

Teachers may also have concerns or questions about the disorder, treatment and how to respond to an emergency.

Communication Plan

Many parents and teachers find it helpful to develop a communication plan together. This plan details how parents, teachers and nurses will communicate with each other about academic, behavioral and medical issues that the student may experience while at school. It also helps to organize contact information and clarify any questions teachers may have for parents.

Use the space here to document information from parents, or use a separate sheet to create your own document. Some questions may not apply to your student, or you may have other questions. Use these questions as a guide to your discussion with parents.

Information Request and Questions for Parents of a student with a UCD:

Contact Information

Student Name: _____

Date of Birth: _____ Year/Grade in School: _____

Parent/Guardian Name: _____

Home phone: _____

Work phone: _____

Cell phone: _____

Email: _____

Parent/Guardian Name: _____

Home phone: _____

Work phone: _____

Cell phone: _____

Email: _____

Other Emergency Contact: _____

Home phone: _____

Work phone: _____

Cell phone: _____

Email: _____

Contact Information for School Nurses

Parents can supplement this plan with other documents, such as a doctor's letter, medical note, etc. Be sure to fill out your school's release of information form before contacting the clinic.

Child's Metabolic Physician: _____

Tel: _____

Location: _____

Child's Primary Care Physician: _____

Tel: _____

Location: _____

Hyperammonemic Episode or Other Health Emergency

What might trigger a hyperammonemic episode in your child?

Are there any signs or warnings to watch for that may be early signs of a hyperammonemic episode?

How should I respond if I suspect a hyperammonemic episode?

Who should I contact if I suspect a hyperammonemic episode?

Other health emergency questions or concerns:

Communication Plan (continued)

Treatment

Is your child on any treatment for his or her UCD?

Does your child have any dietary restrictions?

How should we communicate about any dietary concerns that come up during the school day (for example, if your child eats food from another student's lunch, or if your child needs to be encouraged to eat during the day)?

Does your child have a feeding tube (g-tube)? What should I know about his or her g-tube?

Do you want to be notified when other students in your child's class are sick? How should I notify you?

Will your child need to take medication while at school? If yes, how should the medication be administered?

If your child is not on any treatment, what can I do to make sure he or she stays healthy?

Academics and Skill Development

Tell me about your child's academic history. What is important for me to know?

What skills does your child have?

What does he or she need to work on?

What academic plans or interventions are in place for your child?

Other Thoughts or Concerns

Please let me know any additional thoughts or concerns you may have about your child's school experience:

Additional Resources

The New England Consortium of Metabolic Programs

The Consortium offers information and resources developed by a group of renowned medical and health professionals working together to provide the best possible care for people with metabolic disorders.

http://newenglandconsortium.org/

The National Urea Cycle Disorder Foundation (NUCDF)

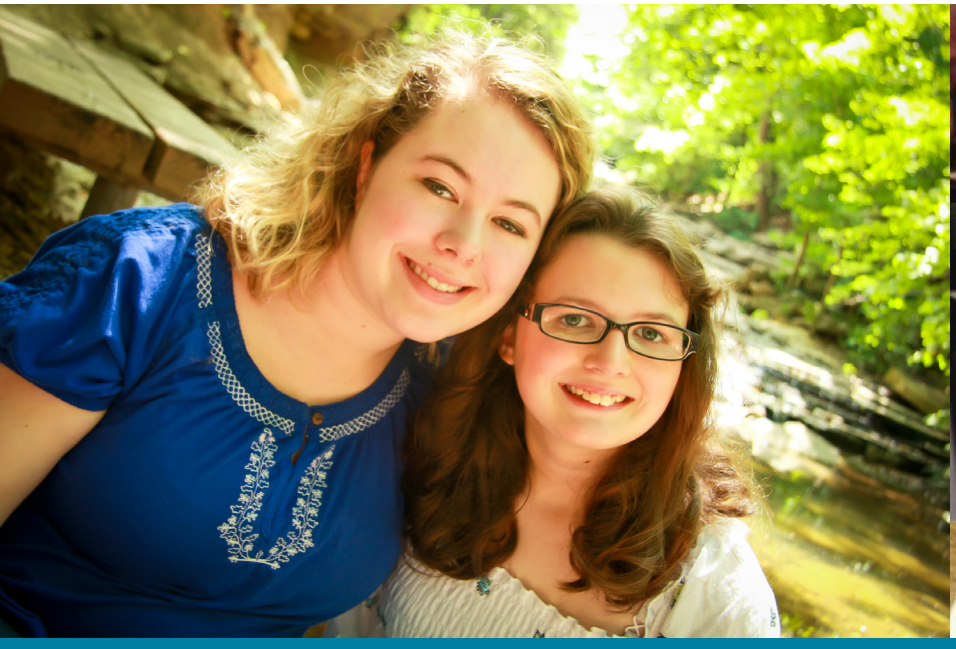
The National Urea Cycle Disorders Foundation is a non-profit organization dedicated to the identification, treatment and cure of urea cycle disorders. NUCDF is a nationally-recognized resource of information and education for families and healthcare professionals.

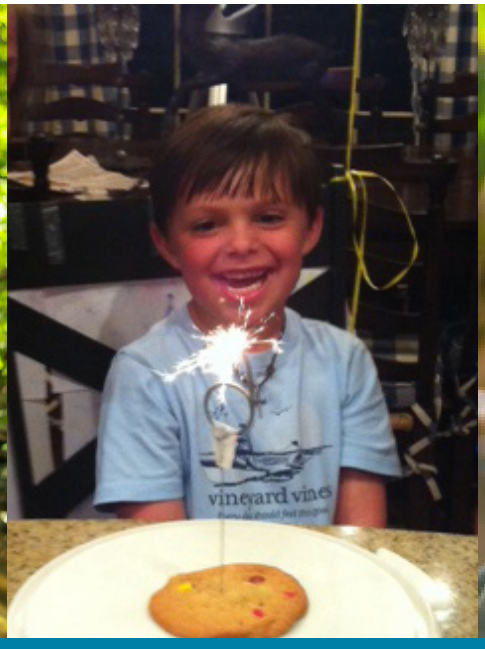
http://cureucd.org/

Genetics Education Materials for School Success (GEMSS)

GEMSS offers a large collection of information about genetic conditions, including metabolic disorders. The web site provides parents and teachers with information and resources to help children with genetic conditions succeed at school.

http://gemssforschools.org/





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An Educator's Guide to Urea Cycle Disorders

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