

Urea Cycle Disorders (UCD) *For Healthcare Providers*

This is a customized health care provider version of our website. Please visit the main website to find more comprehensive information for families and schools (www.gemssforschools.org).

Urea Cycle Disorders (UCD) Introduction

Urea cycle disorders are a group of inborn errors of metabolism disorders in which the breakdown of protein is inhibited by the lack of an enzyme in the urea cycle. 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) or (ASD or ASL) deficiency
- ALD (Argininosuccinic Aciduria) or (ASA, ASL or AL) deficiency
- ARG (Arginase) deficiency

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

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

All of the UCDs except for OTC deficiency, are inherited in an autosomal recessive manner. OTC is inherited in a sex-linked or X-linked manner. While newborn screening has the ability to detect many of these abnormalities, some of these conditions are associated with rapid onset of a metabolic crisis in the newborn period and therefore will be symptomatic before the newborn screening results are obtained.

Physical characteristics and/or symptoms

Note: not all people with UCD will have all of these features.

Children with a UCD do not have any distinct physical features, but can have symptoms during times of fasting, illness, stress, or prolonged physical activity. They can have recurrent episodes of hyperammonemia, which can lead to multiple emergency room visits or hospitalizations, particularly within the first years of life. Hyperammonemia can present with the following symptoms:

- Loss of appetite
- Vomiting

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- Lethargy
- Behavioral changes
- Seizures

They may also have developmental delay or cognitive deficits related to their history of metabolic crises that may have occurred prior to diagnosis

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

Recommended Routine Surveillance

Because of the specialized diet and need for biochemical monitoring, many children with a UCD have frequent blood draws and may have an indwelling port to facilitate blood draws. They may also have a feeding tube.

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- Routine growth monitoring
- Routine monitoring of amino acid levels
- Regular assessment of diet
- Monitoring of port site a gastrostomy tube site
- Developmental evaluation and therapies as needed

Emergency Protocols

- Individuals should have an emergency letter for health care providers who may not be familiar with UCDs. This letter should include recommendations for emergency labs to be drawn with any signs of hyperammonemia, as well as instructions for IV fluid management
- See the examples listed below in sample forms. Note the emergency protocol should be reviewed by the metabolic specialist following the child.
- The emergency protocol should be in the child's electronic medical record

Specialists Who May Be Involved

Follow up is need on a case-by-case basis. A multidisciplinary team approach to best meet the child's individual needs is recommended. The specialists for a UCD may include:

- Developmental Specialist
 - Speech therapy
 - Physical therapy
 - Occupational therapy
- Feeding team
 - Address feeding issues including aversions
- Gastroenterologist/Transplant specialist
 - To treat feeding disorders related to diet therapy
 - To manage gastrostomy tube
 - To work together to monitor after liver transplantation
- Geneticist/Genetic Counselor:
 - Diagnosis
 - Coordination of care
 - Genetic risk to the family
 - Clinical trials
- Metabolic Multispecialty Clinic
 - Clinical follow-up as needed with a metabolic specialist
 - Dietician familiar with VLCAD
 - Social Worker
 - Nurse specialist
- Neurologist
 - Seizures

Sample Forms

Acute Illness protocols are important for all children with urea cycle defects. Parents may have an emergency protocol that they have been given from the Metabolic Specialist. At the reference below are examples of acute illness protocols that can be adapted to your patient.

The New England Metabolic Consortium

<http://newenglandconsortium.org/for-professionals/acute-illness-protocols/urea-cycle-disorders/>

Seven Important Aspects of School Life

“[Urea Cycle Disorders at a Glance](#)” will help you talk with parents and schools about:

- Medical / Dietary Needs
- Education Supports
- Behavior & Sensory Supports
- Physical Activity, Trips, Events
- School Absences & Fatigue
- Emergency Planning
- Transitions



Resources

Gene Reviews

Urea Cycle Defects Overview

<https://www.ncbi.nlm.nih.gov/books/NBK1217/>

Some of the UCDs have individual Gene Review entries:

OTC (ornithine transcarbamylase) deficiency

<https://www.ncbi.nlm.nih.gov/books/NBK154378/>

CTLN1 (Citrullinemia type I)

<https://www.ncbi.nlm.nih.gov/books/NBK1458/>

ALD (Argininosuccinic Aciduria)

<https://www.ncbi.nlm.nih.gov/books/NBK51784/>

ARG (Arginase) deficiency

<https://www.ncbi.nlm.nih.gov/books/NBK1159/>

HHH syndrome (ornithine translocase deficiency)

<https://www.ncbi.nlm.nih.gov/books/NBK97260/>

CTLN2 (Citrullinemia Type II or Citrin deficiency)

<https://www.ncbi.nlm.nih.gov/books/NBK1181/>

Genetic Home Reference

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 I) (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 (Arginase) deficiency

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

HHH syndrome (ornithine translocase deficiency)

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

CTLN2 (Citrullinemia Type II or Citrin deficiency)

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

The New England Metabolic Consortium

<http://newenglandconsortium.org/for-professionals/acute-illness-protocols/urea-cycle-disorders/>

National Organization for Rare Disorders (NORD) Physician Guide for UCDs

<http://www.nordphysicianguides.org/urea-cycle-disorders/>