At a Glance
Urea Cycle Disorders (UCD)

Deficient enzyme: NAGS- N-acetylglutamate synthetase
CPS- Carbamoyl phosphate synthetase
OTC- Ornithine transcarbamylase
ASS (Citrullinemia I)- Argininosuccinic acid synthetase
ASL- Argininosuccinic acid lyase
Argininemia- Arginase

Toxic Metabolites: Ammonia
Argininosuccinic acid- in ASL deficiency
Arginine- in arginase deficiency

Treatment: prevent catabolism, limit intact protein and provide essential amino acid medical food, supplement citrulline or arginine (except in arginase deficiency), provide nitrogen scavenging medications

Clinical presentation in untreated patients: hyperammonemia caused neurotoxicity, poor feeding, growth failure vomiting, seizures, lethargy, liver dysfunction, coma, death; late identified adolescents/adults- chronic neurological symptoms and dietary history of self-restricting dietary protein.

Goal Treatment Range*: Ammonia- normal (<35 µmol/L; <60 mcg/dL)
Plasma amino acids- maintain all within normal range

*MacLeod, E. Nutrition Management of Urea Cycle Disorders. In LE Bernstein, F Rohr, S van Calcar (Eds.) *Nutrition Management of Inherited Metabolic Diseases* (2nd Edition). Springer: 2021

Nutrient Needs by Age*

Age	Intact Protein g/kg/d	Essential Amino Acid (medical food; g/kg/d)	Total Protein g/kg/d
0-1 yr	0.8-1.1	0.4-1.1	1.2-2.2
1-7 yr	0.7-0.8	0.3-0.7	1.0-1.2
7-19 yr	0.3-1.0	0.4-0.7	0.8-1.4
>19 yr	0.6-0.7	0.2-0.5	0.8-1.0

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Starting a Diet

1. Determine goals for total protein (g) and percentage to be provided by intact protein vs essential amino acids (medical food). Consider 30-50% from essential amino acids for initial diet.
2. Calculate amount of intact protein source (breast milk, infant formula, food) and amount of medical food required to meet total protein (g) goal.
3. Calculate energy (kcals) provided by intact protein and medical food sources to ensure DRI for energy needs are met. Consider addition of protein-free calorie modular as needed to meet energy needs.
4. Consider use of enteral nutrition support in this population as anorexia is a common complication.
5. Patients with severe forms of UCD may require placement of a gastrostomy tube.

Urea Cycle Disorders (UCD)

Medical Food Therapy

	Abbott abbottnutrition.com	Mead Johnson hcp.meadjohnson.com	Nutricia NutriciaMetabolics.com	Vitaflo www.VitafloUSA.com
Infant (0-1 yr)	Cyclinex-1®	WND 1		
Toddler & Young Children	Cyclinex-1® Cyclinex-2®	WND 1 WND 2	UCD Anamix® Junior Essential Amino Acid Mix	UCD trio™ EAA supplement™
Older Children & Adults	Cyclinex-2®	WND 2	UCD Anamix® Junior Essential Amino Acid Mix	UCD trio™ EAA supplement™
Protein Free Modular	Pro-Phree®	PFD Toddler PFD 2	Duocal® Polycal™	S.O.S™ 20, 25

Supplementation*

L-Arginine (ASS and ASL deficiency): 100-300 mg/kg/d (100 mg/kg/d may be sufficient in ASL)

L-Citrulline (OTC and CPS deficiency): 100-200 mg/kg/d

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Medical Therapy*

Nitrogen scavenging medications – use alternative pathways to remove nitrogen to prevent hyperammonemia while allowing for greater protein tolerance. Monitor branched chain amino acids.

Sodium Benzoate- binds with glycine to form hippurate, removes one nitrogen atom, then is excreted in urine

Sodium Phenylacetate- binds with glutamine to form phenylacetylglutamine, removes two nitrogen atoms, then is excreted in urine

Buphenyl ® (Horizon Pharma- www.horizonpharma.com)

Glycerol Phenylacetate- same mechanism of action as sodium phenylacetate

Ravicti® (Horizon Pharma- www.horizonpharma.com)

Sodium Phenylacetate + Sodium Benzoate (IV only)

Ammonul® (Ucyclyd Pharma, Inc- www.ucyclyd.com)

Carglumic acid- a synthetic form of N-acetylglutamate synthase used for NAGS deficiency

CARBAGLU® (www.recordati.com)

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Laboratory Monitoring

Plasma Amino Acids[1] (especially glutamine)
Ammonia[1]
Prealbumin[2]
25-OH Vitamin D[2]
CBC[2]
Ferritin, iron, folate, zinc[2]

[1] Weekly in infancy, monthly thereafter
[2] At least annually

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