

## UREA CYCLE DISORDER GLOSSARY

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### **A**

**Allele:** One of a pair of genes, situated on the same site on paired chromosomes, containing specific inheritable characteristics.

**Ammonia:** A by-product of protein metabolism.

**Amino Acids:** When proteins are digested in the diet, amino acids remain – amino acids are either **essential** (obtained through the diet) or **non-essential** (made by the body from the essential amino acids).

**Arginine:** Non-essential amino acid (made only by the urea cycle). An amino acid produced by the digestion of proteins, formed during the normal urea cycle by the transfer of a nitrogen atom from aspartate to citrulline. Supplemented (pharmaceutical grade only) in all the urea cycle disorders except arginase deficiency, which is characterized by high levels of arginine in the blood.

**Argininosuccinate or Argininosuccinic Acid:** A molecule made by the urea cycle.

**Aspartate:** Non-essential amino acid (made only by the urea cycle).

**Assay:** Assessment of characteristics (as weight, measure, or quality).

**Asymptomatic:** Showing no symptoms, as in asymptomatic carriers for OTC deficiency.

**Autosomal Recessive Inherited Disorder:** A characteristic or disorder occurring when an individual receives two copies of a gene for that condition, one from the mother and one from the father.

### **B**

**Biochemical Pathways:** Systems in the body for processing molecules for useful purposes.

**Branched chain amino acids (BCAA):** L-Leucine, L-Isoleucine, L-Valine are essential amino acids. They are easily converted to ATP, critical to energy and muscle metabolism. They aid in hemoglobin formation, which helps to stabilize blood sugar and lower elevated blood sugar levels. L-Leucine decreases blood sugar and boosts tissue healing, including bone. L-Isoleucine is essential for hemoglobin formation and regulates blood sugar and energy levels. L-Valine acts as a natural stimulant and is involved in tissue regeneration and nitrogen balance.

### **C**

**Carrier:** Individuals with one abnormal gene in their gene pair. These individuals do not show evidence of the disorder.

**Catabolism:** The breakdown of lean muscle mass to obtain amino acids (for growth and development) and energy, resulting from inadequate supply in the diet. Results in excess production of ammonia.

**Cerebral edema:** Accumulation of fluid in the tissues of the brain, ultimately causing coma.

**Chronic (or Chronically):** A situation or disease with a long duration.

**Citrulline:** An amino acid produced from ornithine during the normal urea cycle and subsequently transformed to arginine by the transfer of a nitrogen atom from aspartate. Sometimes used in place of arginine supplementation in OTC deficiency.

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**Cofactor:** Interaction between two substances that to bring about changes.

**Cytoplasm:** Area of the cell that most of the chemical actions occur.

## D

**Deficiency:** A lower amount than necessary for functioning.

**De novo mutation:** A genetic change in the DNA that happens for the first time in a patient, i.e., the parents do not carry the change.

**Developmental Disabilities:** A chronic mental or physical impairment that results in decreased ability of an individual to reach appropriate age-level developmental goals.

**DNA:** Deoxyribonucleic acid (DNA) is the chemical inside the nucleus of all cells that carries the genetic instructions for making living organisms.

## E

**Encephalopathy:** Caused by an abnormal condition of the structure or function of the tissues in the brain, especially chronic, destructive or degenerative conditions such as hyperammonemia, metabolic or mitochondrial disorders.

**Enzyme:** Proteins produced by cells in the body and assists the body's processes.

**Enzymatic Assay:** Examination of the enzyme.

**Etiology:** The origins of a disease.

## F

**Fibroblasts:** A cell that is always present in connective tissue and active in making and secreting collagen.

## G

**Glutamine:** A nonessential amino acid; also a "storage" form of ammonia. Elevated glutamine levels are sometimes a harbinger of elevation of ammonia levels.

## H

**Hepatic:** Pertaining to the liver.

**Hepatocytes:** Cells in the liver.

**Heterozygote:** An individual who has carries a gene with a particular characteristic (like OTC deficiency).

**Hyperammonemia:** Abnormally high levels of ammonia in the blood; if untreated, causing severe agitation, vomiting, lethargy, coma and death.

**Hypertremia:** Abnormally high levels of sodium in the blood.

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**Hypothermia:** Abnormally low body temperature, below 95 degrees F, causing heart and respiration slowing and paleness, a classic symptom of urea cycle disorders in infants.

## I

**In vivo:** Occurring in a living organism. In vivo experiments are therefore performed on living organisms.

**Intellectual Development:** The ability to gain knowledge.

**Intramitochondrial:** Within the cell, produces energy for the cell.

## L

**Late-onset disorder:** Characterized by mild, moderate or severe symptoms occurring in early or late childhood resulting from mutations allowing varying degrees of partial enzyme activity. Also sometimes referred to as “partial” defects.

**Lethargy:** Sleepiness.

**Liver:** A large vascular organ in the body that causes important changes in substances in the body in order for the body to use these substances.

**Lysine:** An essential amino acid.

## M

**Metabolite:** A substance produced by metabolic action or necessary for metabolic process. In UCDs, certain metabolites can reach toxic levels, others can be abnormally low.

**Metabolic Pathway:** The sequence by which the chemical changes in living cells provide energy for vital processes in the body, resulting in new material mitochondria – found inside the cell and produce energy for the cell.

**Molecule:** A combination of tiny, invisible particles in the body that are bonded together.

**Mosaicism:** When different cells in the same body or tissue has different genetic make up. This could be, for example, some cells carrying a mutation in the OTC gene, but other cells in the same body do not.

**Mutation:** An unusual change in genetic material occurring spontaneously or by induction, which changes the original expression (function or purpose) of the gene.

## N

**N-acetylglutamate:** A coenzyme that assists in processing the first step of the urea cycle and activates carbamoyl phosphate synthetase I.

**Nitrogen:** An atmospheric gas that forms many compounds in the body (such as proteins) and is a component of all living cells.

**Neonatal-onset disorder:** Severe, catastrophic disorder with life-threatening symptoms occurring in the neonatal period resulting from null/zero enzyme mutations or severely impaired enzyme activity.

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#### O

**Ornithine:** Functions in the urea cycle and acts as a carrier by changing from citrulline to arginine.

#### P

**Partial Activity:** Not completely active, may be missing vital components.

**Phenotype:** The complete observable characteristics of a group, including anatomical, physiologic, biochemical traits as determined by genetic makeup.

**Phenylacetylglutamine:** Normally formed from phenylacetate and glutamine and excreted in the urine.

**Plasma:** Liquid part of the blood in which blood cells are suspended.

**Proband:** An individual with a particular disorder who causes a study of his hereditary and genetic factors to determine if other members of the family have the same disease or carry it.

**Prenatal:** Before birth.

**Protein:** Essential to all living cells, simplified by body processes to simple alpha-amino acids.

**Proximal:** Nearest to the point of reference.

#### Q

**Quantitative plasma amino acids:** Measures levels of various amino acids, like glutamine, alanine, glycine, citrulline, arginine, in individuals with UCDS.

#### R

**Rapid-onset:** Beginning quickly without warning.

**Red blood cells:** A type of cell in the body that carries oxygen to the body's tissues.

#### S

**Scavenger:** Collects excess particles.

**Seizures:** A temporary change in brain performance due to abnormal electrical activity of a specific group of cells in the brain that either present with sudden muscle contractions, decreased level of consciousness, and several other symptoms.

**Self-select:** To determine on one's own, either consciously or subconsciously.

**Serum or plasma ammonia level:** Amount of ammonia concentration present in blood or plasma, used to monitor ammonia levels in UCDS.

**Sodium benzoate:** A compound used in urea cycle disorders to create an alternative pathway for removal of ammonia by conjugating with glycine to form hippurate.

**Sodium phenylacetate:** Ammonia scavenging compound, used in combination with sodium benzoate in intravenous form to treat critically elevated ammonia levels, trade name Ammonul.

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**Sodium phenylbutyrate:** Ammonia scavenging drug used in treatment of urea cycle disorders, trade name Buphenyl. Removes ammonia by conjugating to phenylacetylglutamine, which is then excreted from the body.

**Spasticity:** Continuous contraction of certain muscles.

**Substrate:** A substance acted on and changed by an enzyme in any chemical reaction.

**Supplementation:** A substance added to counteract a deficiency or potential deficiency.

### T

**Transaminases:** The addition of an amine group.

**Transport:** To carry from one area to another in the body or within a cell.

**Tremor Ataxia:** Trembling or shaking and lack of control of voluntary muscles.

**Trichorrhexis Nodosa:** A node-like appearance of fragile hair.

**Triggering Event:** An episode that causes a reaction or illness.

### U

**Urea:** A product of protein breakdown of amino acids, excreted in the urine.

**Urea Cycle:** A metabolic process in which waste (nitrogen) from the breakdown of proteins in the body is changed by the urea cycle enzymes in the liver into urea in the bloodstream, which is then excreted in the urine.

**Ureagenesis:** The transformation of proteins to a urea compound that can be excreted in the urine.

### V

**Vector:** A retrovirus (retroviruses are a class of RNA viruses that are capable of converting their RNA into DNA, and integrating into the host genome) or adenovirus (carrier of common viruses) that has had its own genetic material modified or removed and replaced by other genes (like those that contain instructions to make OTC enzyme). The vector can then be introduced into a patient who suffers from an enzyme deficiency, carrying the new needed genetic material into that individual.

### W

**Waste:** Unusable or excess material, lost by breaking down of the body's tissues.

### X

**X-Chromosome:** A sex chromosome in both males and females (males have one X-chromosome and one Y chromosome, XY=male, and females have two X-chromosomes, XX=female).

**X-linked disorder:** A disorder occurring when an individual receives an affected X chromosome (carrying the disorder) from the mother.