

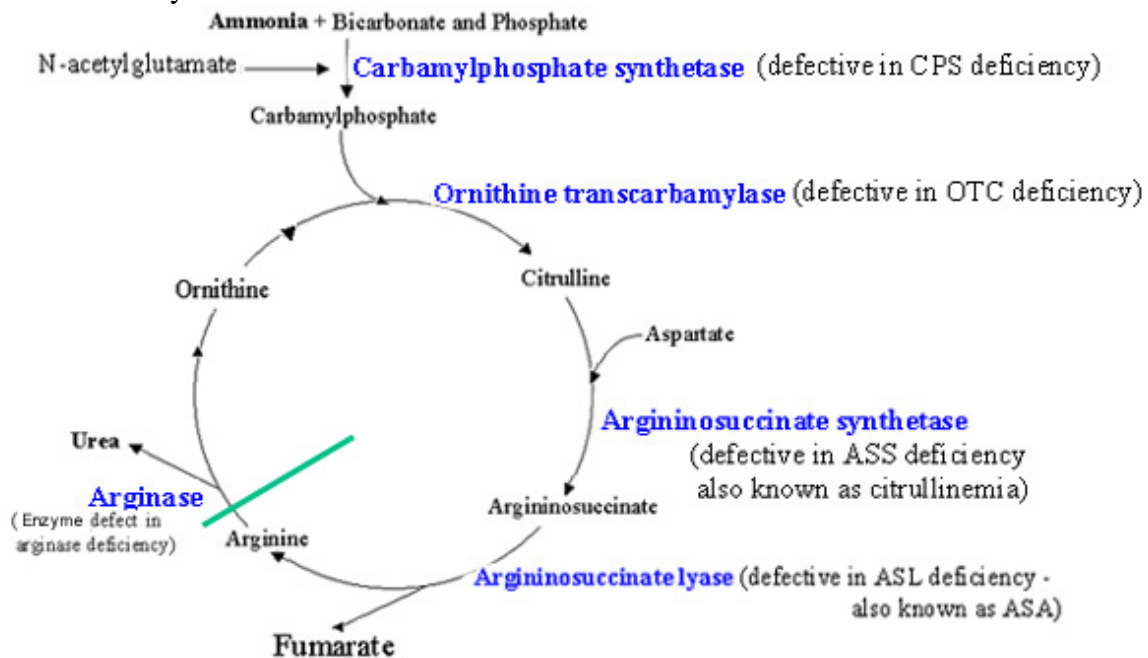
## EMERGENCY PROTOCOL UREA CYCLE DISORDERS ARGINASE DEFICIENCY

### PATHOPHYSIOLOGY

Arginase deficiency usually presents with developmental delay and progressive neurologic features in later childhood. The Arginase isoenzyme associated with the arginase deficiency phenotype, Arginase A1, is cytosolic in location and is found primarily in hepatocytes (the site of activity) as well as red blood cells (utilized for diagnostic assay)

Unlike fats and carbohydrates, the body does not store protein. An excess of protein leads to an excess of liberated nitrogen from the amino acids of protein with a consequent excess of ammonia ( $\text{NH}_3$ ). This additional  $\text{NH}_3$  cannot be metabolized by a defective urea cycle, so the ammonia accumulates. In general, protein overload comes from two sources –

1. Dietary protein intake beyond what is needed for tissue formation and replacement.
2. Any catabolic process, e.g. stresses of the newborn period, infection, dehydration etc...



Characteristically, the amino acid glutamine (containing two nitrogenous moieties and therefore a temporary “repository” for ammonia) accumulates in excessive quantities in affected, untreated individuals. Alanine is also elevated in plasma sampling. Amino acid abnormalities usually precede hyperammonemia and the onset of symptoms.

## Acute management of arginase deficiency

**Plasma ammonia** levels (direct index of toxicity, important for acute management).

1.5 ml blood in sodium-heparin tube (green top tube).

**Plasma amino acids** (glutamine, as an ammonia buffer, reflects direction of control of hyperammonemia, should be checked daily). Require 2 ml blood in green or red top tube.

**Urinalysis**, assessing ketonuria.

**Liver function tests** (specifically transaminases, bilirubin, albumin, PT and PTT)

**Blood gases, lytes+CO<sub>2</sub>**: Alkalosis (associated with respiratory stimulation by the hyperammonemia). Alkalosis is more common than acidosis (as opposed to organic acidemias) but, acidosis can occur, anion gap typically < 20 (but again not always), normal glucose, low ketones more indicative of UCD.

**BUN**: often low but not always, is neither sensitive nor specific for UCDs.

**Newborn screening blood sample**. In neonate carry out at 24 hours of age and call screening lab to track and report results as soon as possible. Though extremely rare arginase deficiency will be picked up in the neonatal variant of arginase deficiency.

### RISING BLOOD AMMONIA

Specimens must be placed immediately on ice and walked to the laboratory. The most common reason for a (mild) elevation in blood ammonia is a delay in this process, necessitating the (unfortunate) drawing of another sample.