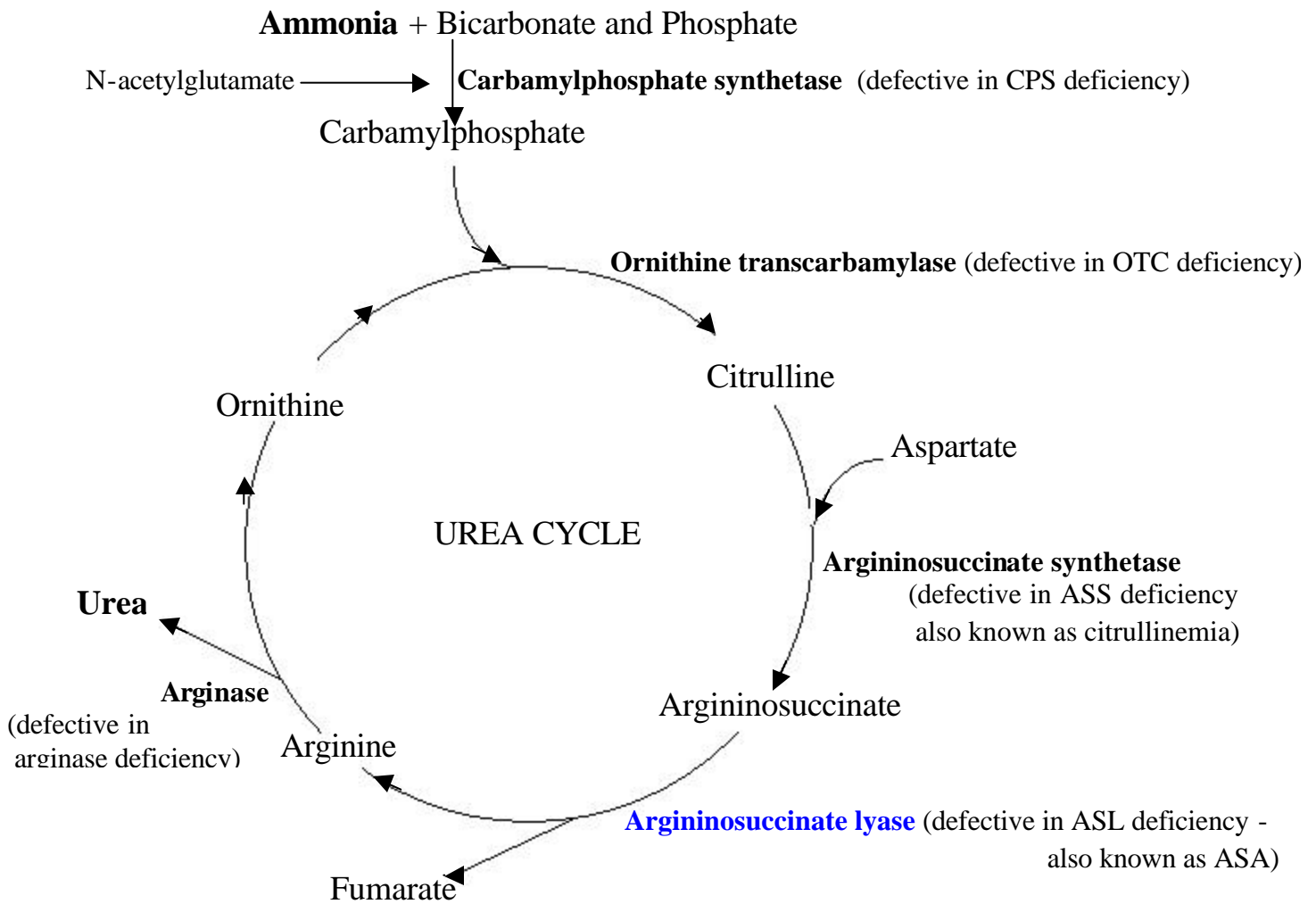


**ACUTE ILLNESS PROTOCOL
 UREA CYCLE DISORDERS
 THE INFANT/CHILD WITH ARGININOSUCCINATE LYASE DEFICIENCY
 (also known as argininosuccinic acidemia)**

PATHOPHYSIOLOGY

Each of the five biochemical reactions within the urea cycle is associated with a known enzyme deficiency and a related clinical disorder as shown in the diagram below



Carbamyl phosphate synthetase (CPS) and ornithine transcarbamylase (OTC) are located in the mitochondria. Arginase, argininosuccinate synthetase (ASS) and argininosuccinic acid lyase (ASL), also known as argininosuccinase, are cytosolic in location. The major site of complete urea cycle activity is the hepatocyte. Argininosuccinic acidemia is autosomal recessive in inheritance; males and females are equally affected.

Unlike fats and carbohydrates, the body does not store protein. Excess protein is catabolized, releasing liberated nitrogen as ammonia (NH_3). This additional NH_3 cannot be metabolized by a defective urea cycle and so accumulates. In general, protein overload comes from either dietary protein intake beyond bodily requirements or secondary to catabolic processes, e.g. stresses of the newborn period, infection, dehydration etc...

Raised ammonia levels appear to be extremely toxic to the central nervous system, causing cerebral edema. It is not clear whether this is a primary effect and/or secondary to elevated glutamine (GLN) which, containing two nitrogenous moieties, functions as a temporary "repository" for ammonia. GLN thus accumulates in excessive quantities in affected untreated individuals, as does alanine (ALA) in the plasma. Amino acid abnormalities may precede hyperammonemia and the onset of symptoms.