UREA CYCLE DEFECTS (UCD)

What are Urea Cycle Defects?

The urea cycle is the main pathway of the body to dispose of excess nitrogen. It allows for the conversion of ammonia into urea that can be excreted into the urine. Citrullinemia and Argininosuccinic Aciduria are inherited in an autosomal recessive manner. Citrullinemia occurs as a result of argininosuccinic synthase deficiency while argininosuccinic aciduria is due to a deficiency of argininosuccinic lyase. Both conditions may manifest with tachypnea, lethargy, vomiting, irritability, seizures, coma and ultimately death if left untreated. The increased levels of ammonia may cause brain damage.

Due to blocks in the urea cycle owing to the enzyme deficiency, patients with UCD have low levels of arginine. This makes arginine an essential amino acid among patients with UCD.

Urea Cycle Defects include:

- Citrullinemia (CIT)
- Argininosuccinic Aciduria (ASA)

Urea Cycle Defects	Confirmatory Testing
Citrullinemia (CIT)	Plasma amino acids and urine organic acids
Argininosuccinic Aciduria (ASA)	Plasma amino acids and urine organic acids

Further confirmatory testing may be required after referral to a metabolic specialist.

Treatment of Urea Cycle Defects

Treatment is through the dietary restriction of protein and the supplementation of a protein free formula. Sodium benzoate, an ammonia scavenger, is given as well as arginine supplementation.

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by an excess intake of protein, illness, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to reverse the catabolic state and prevent essential amino acid deficiency.

UREA CYCLE DEFECTS (UCD)

Citrullinemia (CIT)

What is Citrullinemia (CIT)?

Citrullinemia is an inborn error of metabolism resulting from the deficiency of arginosuccinate synthetase, an enzyme pre- sent in all tissues but the level of which is highest in the liver where it functions in the urea cycle.

CLINICAL MANIFESTATIONS

Following a brief hiatus in which the newborn appears normal, anorexia, vomiting and therapy develop followed rapidly by progression to deep coma. The symptoms mimic that of sepsis and affected newborns present with severe lethargy, poor feeding to respiratory distress, jitteriness and seizures.

A late onset form may occur as late as 20 years old and present as symptoms such as slurred speech, irritability, insomnia or delirium.[3]

PATHOPHYSIOLOGY

Argininosuccinate synthase is an enzyme that converts citrulline to arginosuccinate, the absence of which causes an increase in plasma citrulline and ammonia levels.

Inheritance: autosomal recessive

CONFIRMATORY TESTING

Plasma amino acids and urine organic acids. Further confirmatory testing may be required once referral to a metabolic specialist is done.

Overview of Disease Management

Long-term steady state management can usually be provided with arginine (250 mg/kg/day in divided doses), sodium benzoate (250 mg/kg/day in divided doses), and a diet modestly restricted in protein.[3] Initiation of management should be done in consultation with an attending physician/ metabolic specialist.

Prognosis

Prognosis for intellectual development depends on the nature of the initial hyperammonemia especially its duration or those of recurrent episodes.[3]

Preliminary / Initial Management During Metabolic Crisis

Metabolic crises may be caused by illness, prolonged fasting or stressful situations such as surgery and severe infection. The goal of treatment is to reverse the catabolic state, correct the acidosis and prevent essential amino acid deficiency.

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UREA CYCLE DEFECTS (UCD)

Citrullinemia (CIT)

WHAT TO DO

If unwell and cannot tolerate oral intake:

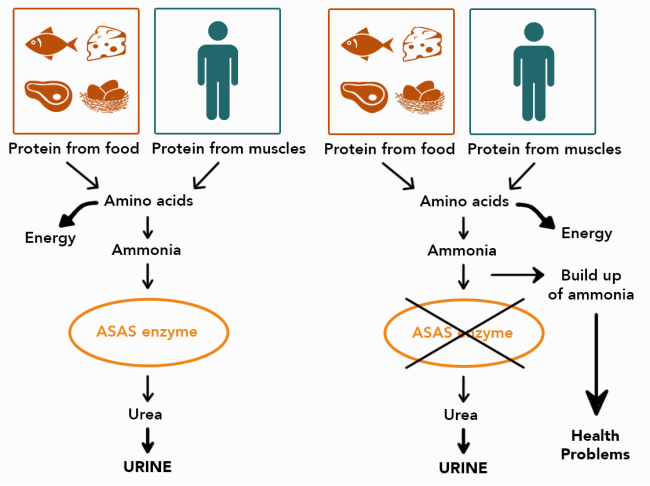
- Nothing per orem
- Ensure patient's airway is secure
- Insert IV access. Collect sample for serum ammonia. May request for investigations (i.e. CBC, etc.) as needed.
- May give fluid boluses if patient requires.
- Start D12.5% 0.3NaCl at full maintenance. Assess patient clinically, if there is need to increase fluid, may do so up to 1.2 or 1.5x the maintenance.
- Start IV sodium benzoate loading dose (250mg/kg) to run for 1-2 hours
- Start IV arginine loading dose (250mg/kg) to run for 1-2 hours
- Monitor input and output strictly (q6 hours).

If unwell and can tolerate oral intake:

- Insert oro- or nasogatric tube and start continuous feeding with protein free formula at maintenance rate
- Insert IV access. Collect sample for serum ammonia Monitor glucose levels. May request for investigations as needed.
- Start D12.5% 0.3NaCl at 5-10 cc/hr
- Start IV sodium benzoate loading dose (250mg/kg) to run for 1-2 hours
- Start IV arginine loading dose (250mg/kg) to run for 1-2 hours
- Monitor input and output strictly (q6 hours).

**Children should not be protein restricted for longer than necessary (24-48 hours)*
**If the patient does not improve with the initial management (within 12 hours), hemodialysis may be indicated. Monitor pa- tient clinically, the necessity of hemodialysis will depend on the patient's clinical status.*
**Inform the metabolic doctor on call for further guidance regarding on-going management*
**If the patient is well, coordinate with a metabolic specialist regarding further management.*

Normal breakdown of protein vs Citrullinemia patient's breakdown of protein



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