UREA CYCLE DISORDERS

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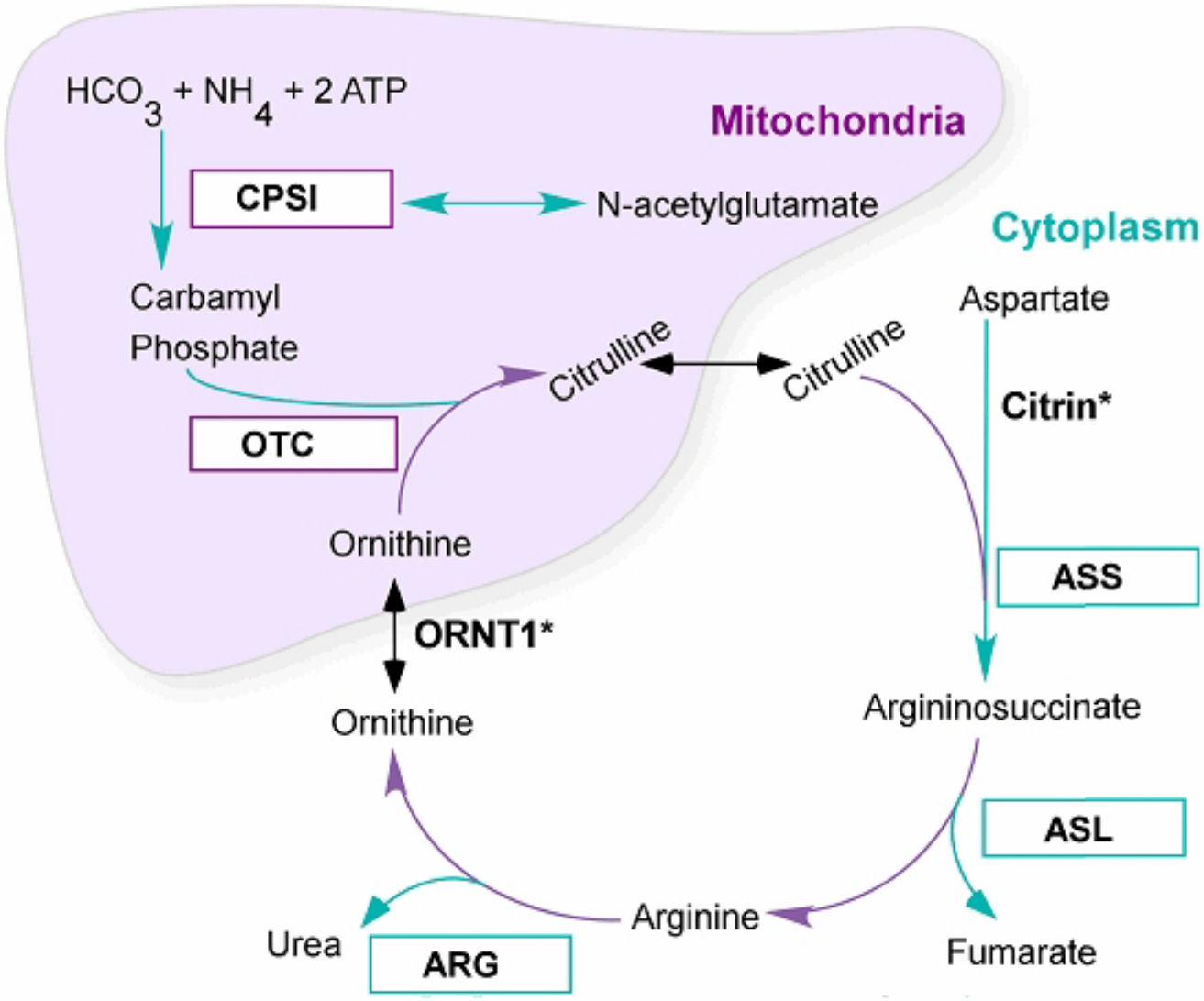
OVERVIEW OF UREA CYCLE



Slide from Urea Cycle Disorders Overview, by Marshall L. Summar, MD

SYMPTOMS OF UCD

- Somnolence to Lethargy
- Poor feeding/Anorexia
- Breathing problems (Hyper or Hypoventilation)
- Hypothermia
- Seizures
- Neurologic posturing
- Cerebral Edema
- Coma

DIAGNOSIS OF UCD

- Hyperammonemia
- Anion Gap and Glucose
- Plasma amino acids (tentative dx)
- Urine Orotic Acid
- Liver Biopsy
- Genetic testing
- Fibroblast enzyme assay
- Red cell enzyme assay

UCD MANAGEMENT AT INITIAL DX

- Dialysis to reduce plasma ammonia
- Pharmacologic management
  - IV administration of Arginine HCL
  - Other Nitrogen scavenging drugs
    - Allows alternate pathway to excrete excess Nitrogen
- Restriction of protein
- Carbohydrate intake (IV glucose)
- Fat intake (intra-lipids/protein free formula)

OTC DEFICIENCY

- Most commonly occurring UCD
- Incidence = 1:80,000
- Only X-linked UCD disorder. Remainder are autosomal recessive
  - Females with one altered copy of OTC gene can show signs and symptoms of OTC deficiency
- Symptoms evident in 1st few days of life

OTC CASE
MALE 40 WKS GA/ 2826 G

1st specimen

- Collected at 36 hours old
- Pre-transfusion
- Feeds (Breast, Lactose)
- MS/MS results
  - Cit = 2.3 µmol/L
    - Low Cit cutoff <4 µmol/L
  - Arg = 8.4 µmol/L
    - Low Arg cutoff not set
  - Orn/Cit ratio = 32
    - Cutoff <26.8

2nd Specimen

- Collected at 2 days and 7 hours old
- Transfused w/ WB, FFP and PIts and AB admin
- Feeds (NPO)
- MS/MS Results
  - Cit = 2.9 µmol/L
  - Arg = 21.4 µmol/L
  - Orn/Cit ratio = 41.4

OTC CASE

- Bedside glucose = 76 mg/dL
- Ammonia = 2513 umol N/L
- Anion gap = 17
- Plasma amino acids
  - Citrulline 9 µmol/L (normal 10-45)
  - Arginine 60 µmol/L (normal 6-140)
- No Urine Orotic Acids performed
- Fibroblast specimen sent to Reference lab
  - DX OTC with common mutation detected

REFERENCES

- Nitrogen Metabolism and the Urea Cycle, Available at: http://web.indstate.edu/thcme/mwking/nitrogen-metabolism.html . Accessed 4/2007
- Ornithine Transcarbamylase Deficiency, Genetics Home Reference, Available at: http://ghr.nlm.nih.gov/condition/ornithine-transcarbamylase-deficiency. Accessed 8/2010.
- Summar, Marshall L., *Urea Cycle Disorders Overview*, Gene Review, 4/2003.