Diagnostic Testing for OTCD

Anna Scott, PhD, FACMG

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Ornithine Transcarbamylase Deficiency

A defect of the urea cycle

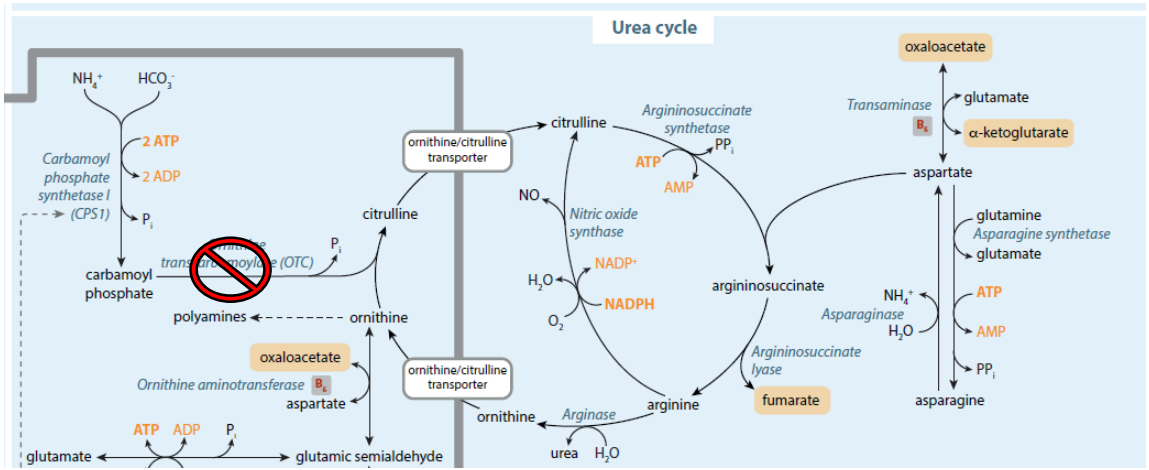
X-linked metabolic disease

Diagnostic tests:

-Blood ammonia

-Plasma amino acids

-Urine organic acids



[Ornithine Transcarbamylase Deficiency - GeneReviews® - NCBI Bookshelf (nih.gov)]

https://www.acmg.net/PDFLibrary/Decreased-Citrulline.pdf

Blood Ammonia

Sample type: Peripheral blood
Sodium heparin venous or arterial blood, stable RT <15 min, 4°C <3 hours

TAT: 1 hour

Cost: $100-200

Typical OTC finding: >500-1,000 µM

Normal Values
0- 3 days old, <107 µM
>2 months old, <35 µM

Colorimetric assay on automated analyzer (Core Chemistry)

Plasma Amino Acid Analysis

high pressure liquid chromatography

Light absorption (Beer's law of A = εlc)

Sample type: Peripheral blood

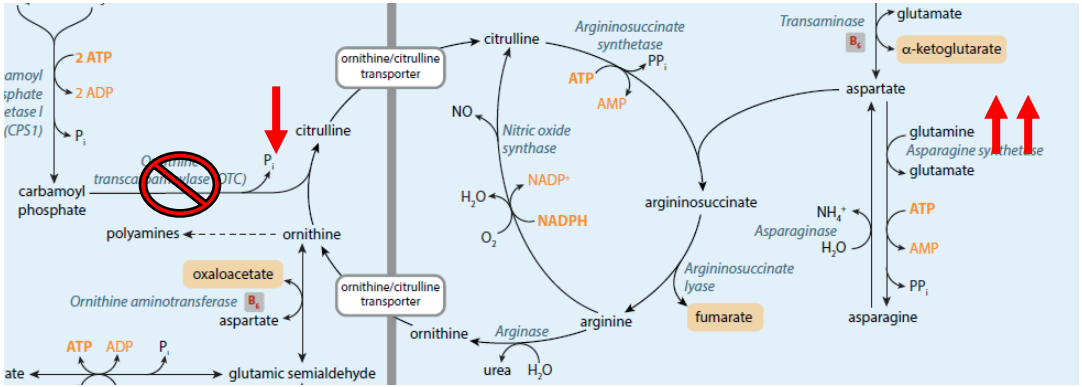
Na Heparin, plasma, frozen

TAT: 1-2 days (instrument run time is ~4 hours/sample)

Cost: $200-300

OTC Finding: Citrulline 0-4 µM (normal >6 µM)

Glutamine ~2,000 µM (normal <825 µM)



Urine Organic Acid Analysis

gas chromatography- mass spectrometry

Semi-quantitative analysis of all metabolites/compounds in urine

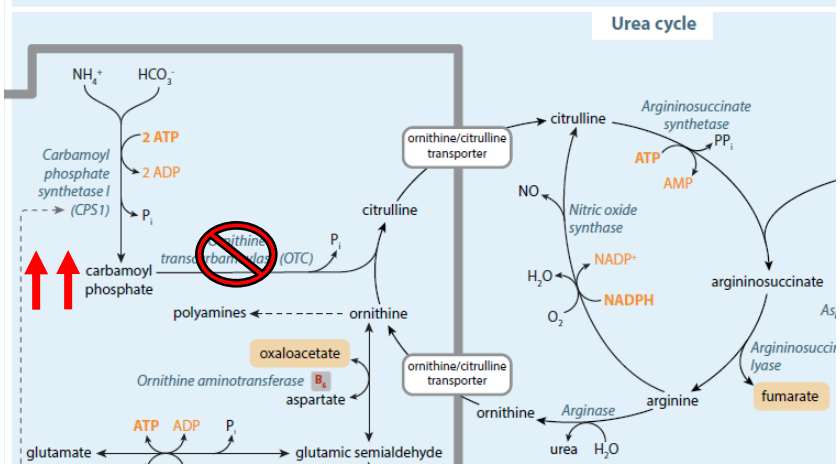
Sample type: urine

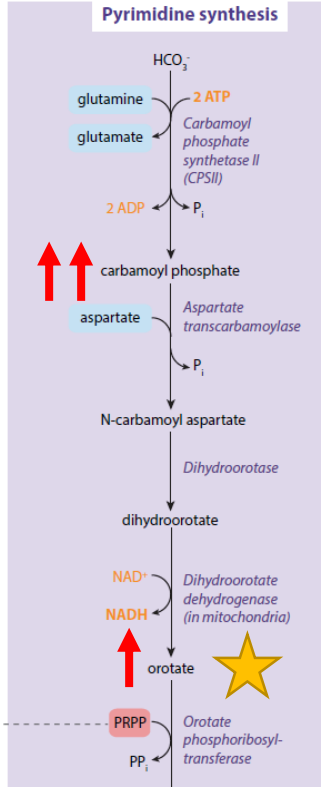
Clean catch, frozen

TAT: 1-2 days

Cost: $286-668

OTC finding: elevated orotic acid





Sensitivity and Specificity?

Unknown for diagnostic tests

Biochem Markers

- High ammonia and glutamine, with low citrulline, and excretion of orotic acid are “text-book” diagnostic findings
- Females may or may not have abnormal findings
- Many cases of affected individuals (male and female) have normal citrulline and orotic acid.

DNA Analysis

Sequencing and deletion/duplication studies find pathogenic variants in ~90% of cases.

Diagnostic Testing

If neonate is symptomatic and NBS has low citrulline…

1) STAT Blood ammonia; start treating clinical symptoms!

2) Plasma amino acids; prioritized by BCG lab, goal of results out same day that specimen is received.

Best test to diagnose urea cycle defects or suggest organic acidemia.

Organic acidemias are best diagnosed by urine organic acid analysis and plasma acylcarnitines.

3) Urine organic acids; also prioritized by BCG lab.

May provide supporting evidence for OTCD or identify organic acidemia (alternative causes of hyperammonemia).

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