



## NEWBORN SCREENING FOR ORNITHINE TRANSCARBAMYLASE DEFICIENCY (OTCD)

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# Presenter



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Newborn Screening Program

# NBS Criteria

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- Available Screening Technology
  - Sensitive, specific and timely tests are available that can be adapted to mass screening
- Diagnostic Testing and Treatment Available
- Prevention Potential and Medical Rationale
- Public Health Rationale
- Cost-benefit/Cost-effectiveness

# Available Screening Technology

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- Sensitivity – the ability of the screen to correctly identify the babies with OTCD
  - Sensitivity = 1 – false negative rate
- Specificity – the ability of the screen to correctly identify the babies who do not have OTCD
  - Specificity = 1 – false positive rate
- Positive predictive value (PPV) – the percent of babies with a positive screen who have OTCD
  - $PPV = \frac{\# \text{ true}(+)}{\# \text{ true}(+) + \# \text{ false}(+)}$

# Timely Tests

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- Timeliness

- Aim: Identify and treat prior to onset of symptoms
- Each step important
  - Specimen collection
  - Specimen Transport
  - Testing
  - Result reporting
- Goal: time-critical results reported by 5 days of life

Source: Sontag et al. PLoS ONE 15(4):e0231050 (2020 – funded by HRSA)

# Test for OTCD

## Adapted to Mass Screening

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- Technology – tandem mass spectrometry (MS/MS)
- Uses one 1/8" hole punch from dried blood spot to test for 19 congenital disorders simultaneously
  - Amino acids
  - Acylcarnitines (fat transporters)
- In WA NBS Program since 2004



# Test for OTCD

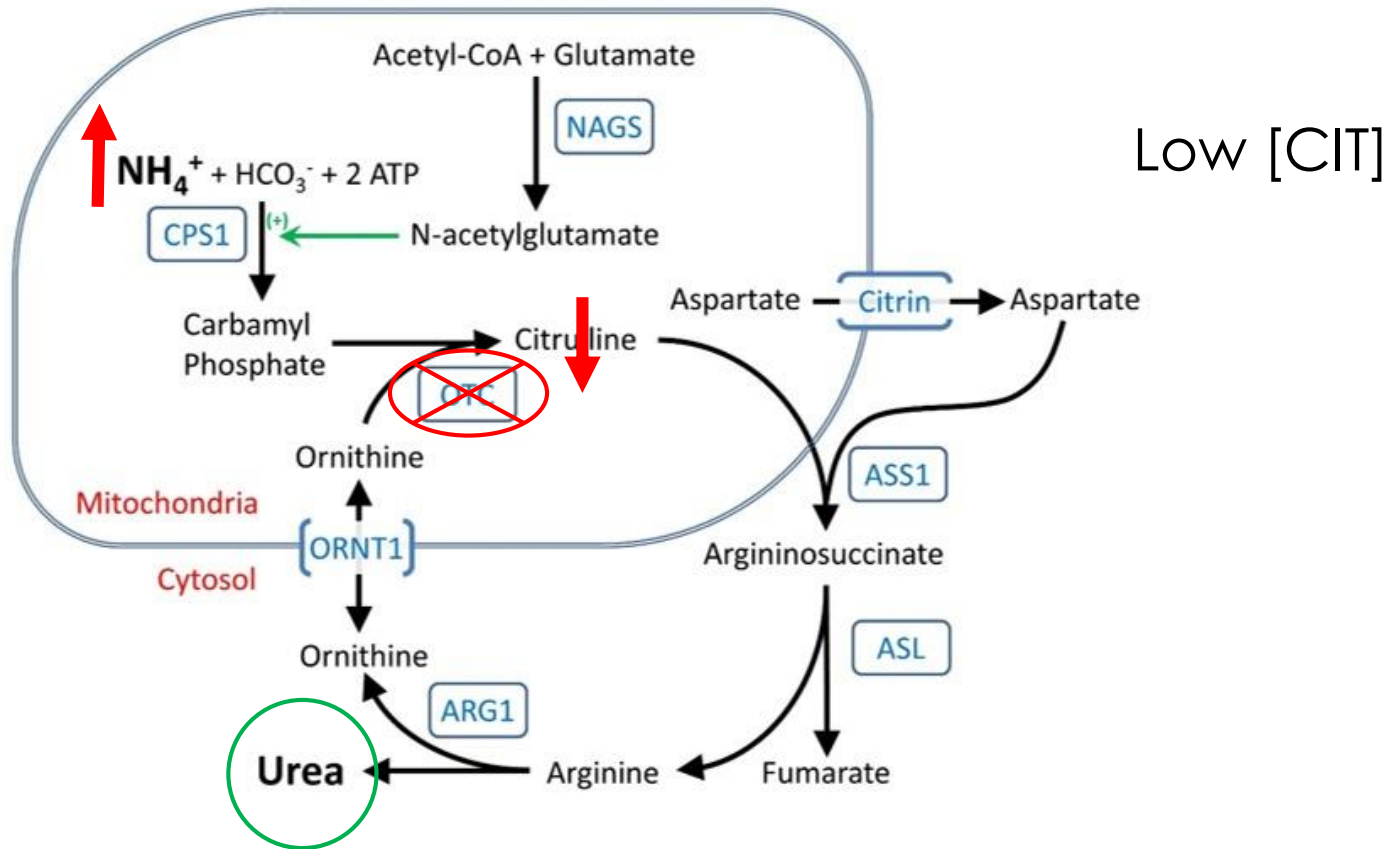
## Adapted to Mass Screening

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- Amino acid analysis
  - Primary target: low citrulline [CIT]
  - Secondary markers may be helpful to reduce false(+) results

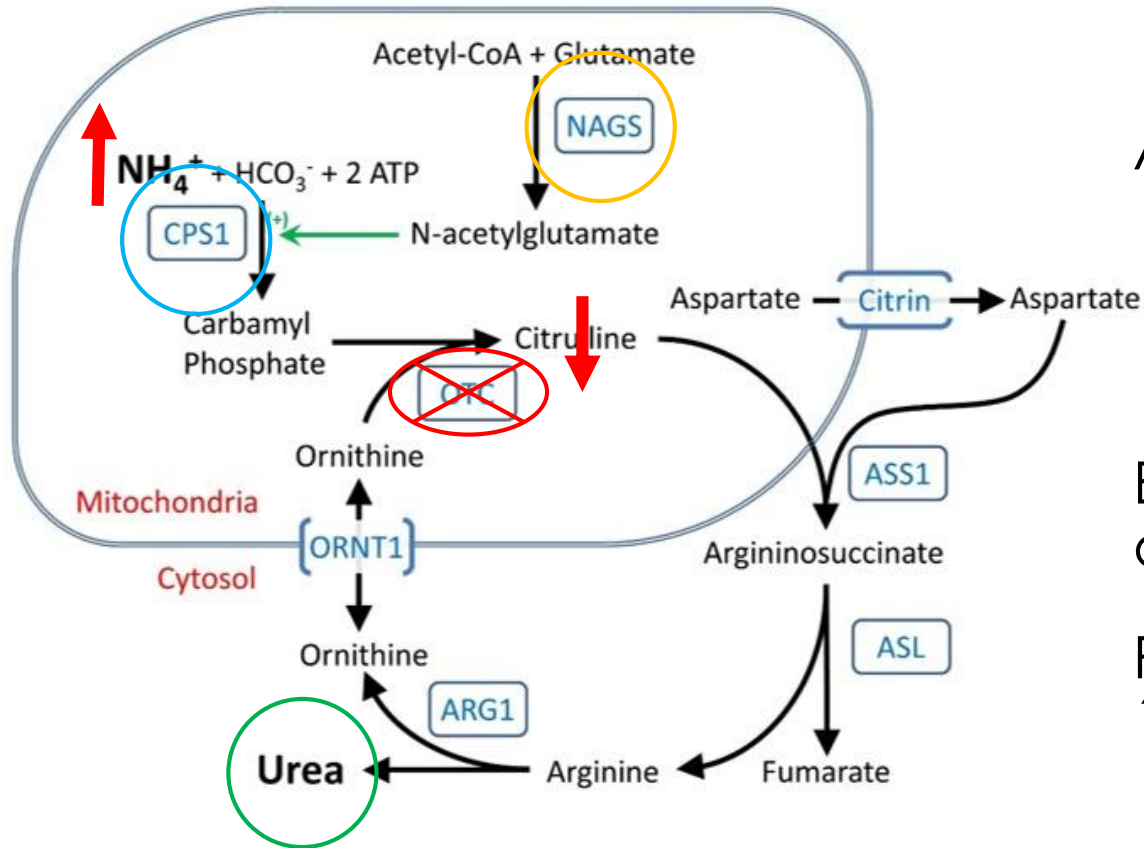


# Test for OTCD Adapted to Mass Screening





# Test for OTCD Adapted to Mass Screening



Also have low [CIT]

- NAGS deficiency
- CPS1 deficiency

Both are ultra rare diseases

Prevalence: less than 1 per million births

# Newborn Screening - California

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- 10y of screening – 4.735 million babies
  - 30 cases of OTC (prevalence = 1:157,000 births)
    - 26 true positives (sensitivity = 86.7%)
    - 4 false negatives
  - 937 false positives (specificity = 99.98%)
  - PPV = 2.7%

# Newborn Screening - California

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- 10y of screening – 4.735 million babies
  - 19/26 were symptomatic at time of NBS report
    - Avg. age at report = 4.5d (range 3-8d)
  - 9 deaths (9/30 = 30%)
    - 8 early deaths
      - ◆ Avg. age at death = 4.5d (range 3-6d)
    - 1 death at 3m

# Newborn Screening - New England

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- Regional program (CT, MA, ME, NH, RI & VT)
- 15 years of screening – > 1 million babies screened
- No known missed cases (presumed 100% sensitivity)
- Specificity = 99.9%
- PPV = ~15%
  
- Most low CIT results were from babies in the NICU
- Confirmed CA experience of babies being sick or deceased at time of NBS reporting

# Newborn Screening - Puerto Rico

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- 9 years of screening – ~280,000 babies screened
- 1 presumed case
  - No diagnostic testing was done because the baby was already deceased at time of NBS report

# Timing to results – Washington State

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- Turnaround time (TAT) in Washington State NBS Lab
  - Preliminary results within 24 hours of receipt = 59%
  - Preliminary results within 48 hours of receipt = 91%
  - Avg. turnaround time (preliminary) = 1.6d
- Abnormal results are typically repeated in duplicate the same day
- Urgent values can be reported immediately after the preliminary results are released to speed up diagnosis

## Timing to results – Washington State

- State law requires that NBS specimens are
  - Collected  $\leq 48$ h of birth (98.8% compliance)
  - Delivered to PHL  $\leq 72$ h of collection (85.5% compliance)

Age at initial [CIT] result	Percent reported	Cumulative percent
Day 3 of life	16%	16%
Day 4 of life	32%	48%
Day 5 of life	27%	75%
Day 6 of life	14%	89%
Day 7 of life	5%	96%

Questions?

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