Washington State Department of Health

NEWBORN SCREENING FOR GUANIDINOACETATE METHYLTRANSFERASE (GAMT) DEFICIENCY

Technical Advisory Committee meeting
September 8, 2023

Presenter

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MPHc

Follow-up Lead

Newborn Screening Program

NBS Criteria

- 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

- Sensitivity – the ability of the screen to correctly identify the babies with GAMT Sensitivity = 1 – false negative rate

- Specificity – the ability of the screen to correctly identify the babies who do not have GAMT
  - Specificity = 1 – false positive rate

- Positive predictive value (PPV) – the percent of babies with a positive screen who have GAMT

- PPV = $\frac{\#\ \text{true(+)}}{\#\ \text{true(+)} + \#\ \text{false(+)}}$

Timely Tests

- 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)

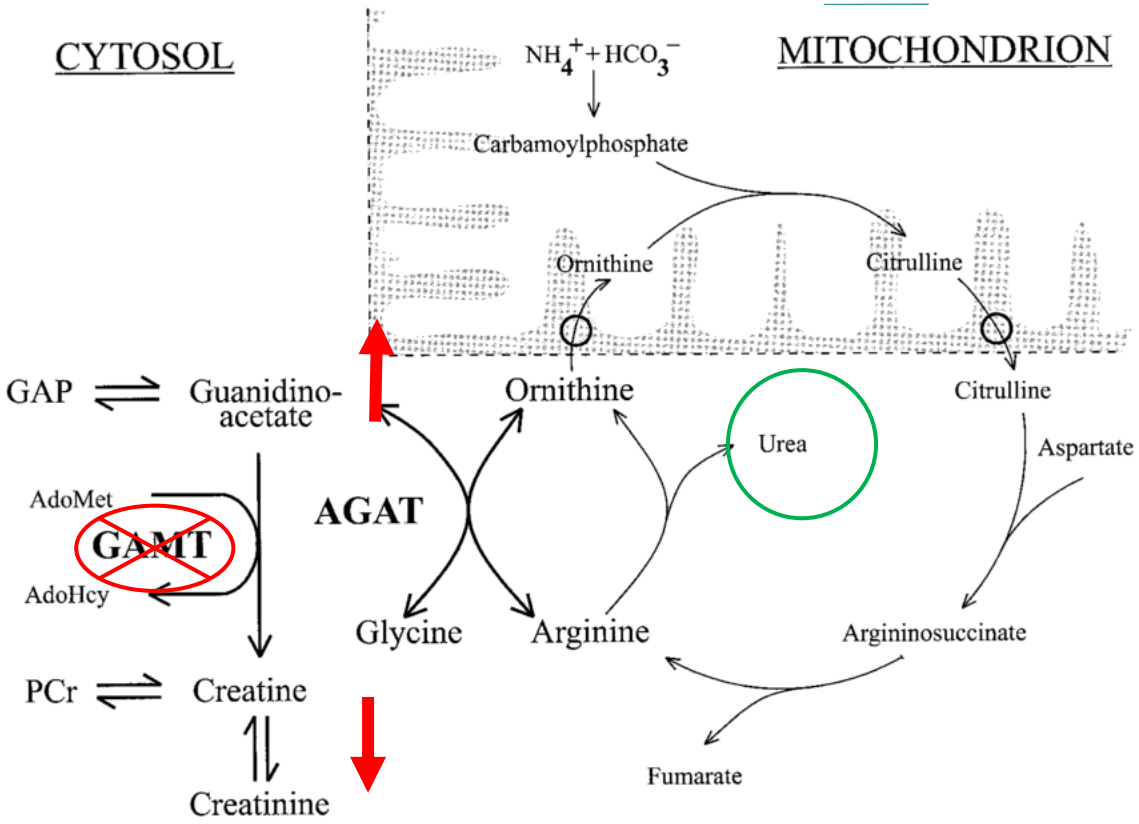
Test for GAMT
Adapted to Mass Screening

- 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 GAMT
Adapted to Mass Screening

- Acylcarnitine/Amino acid analysis
  - Primary target: high guanidoacetate [GUAC]
  - Secondary markers may be helpful to reduce false(+) results

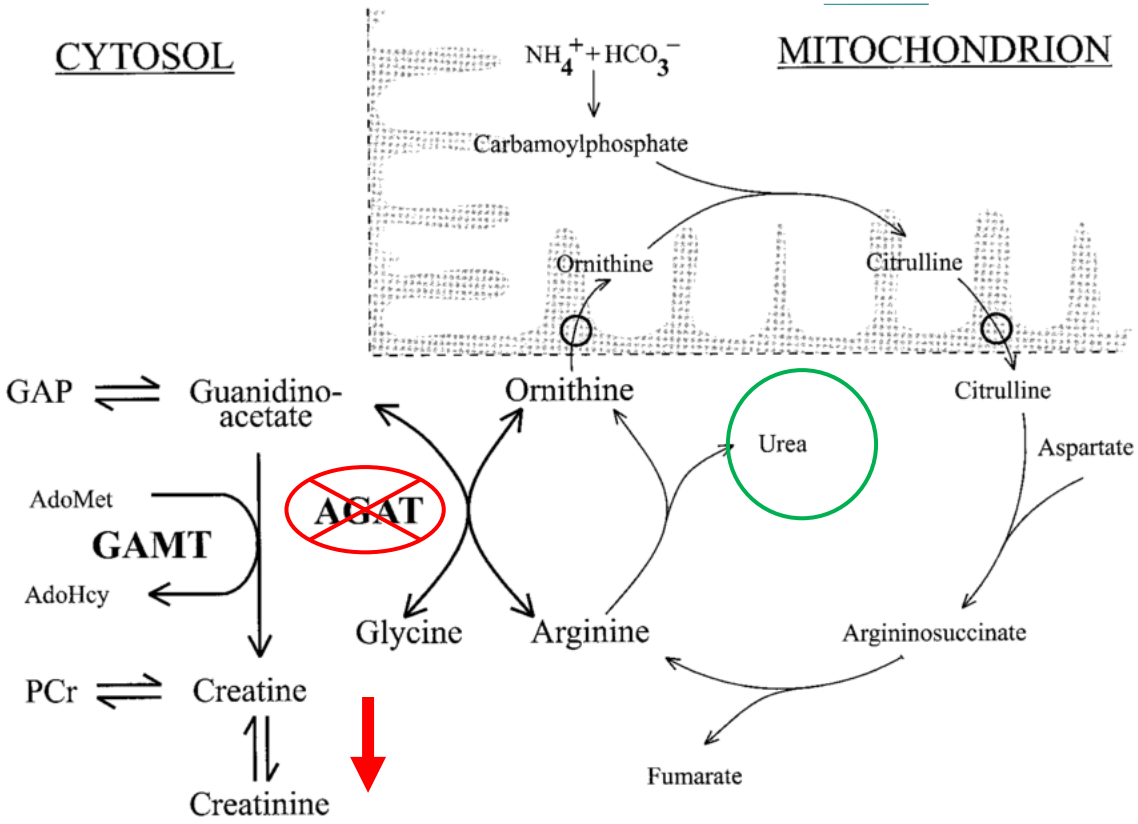
Test for GAMT
Adapted to Mass Screening



High [GUAC]

Low [Creatine]

Test for GAMT
Adapted to Mass Screening



Also has low [Creatine]

- AGAT deficiency

Only GAMT has high [GUAC]

AGAT Prevalence: less than 20 cases ever reported

CCDS caused by transporter defects = normal GUAC and Creatine in blood

Newborn Screening - GAMT

- Across 4 screening jurisdictions– 3.07 million babies
  - 3 cases of GAMT (prevalence = 1:1,000,000 births)
    - 3 true positives (sensitivity = 100.0%)
    - 0 false negatives
  - False positive rate (NY+UT) 2.1/100,000 (specificity = 99.99%)
  - PPV = 99.99%

Questions?

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