



Newborn Screening for Ornithine Transcarbamylase Deficiency (OTCD) Report from the Technical Advisory Committee

Washington State Board of Health
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Presenters

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Technical Advisory Committee for OTCD



Meeting 1 – June 16, 2021

- Available Screening Technology
- Diagnostic Testing and Treatment Available
- Prevention Potential and Medical Rationale
- Public Health Rationale



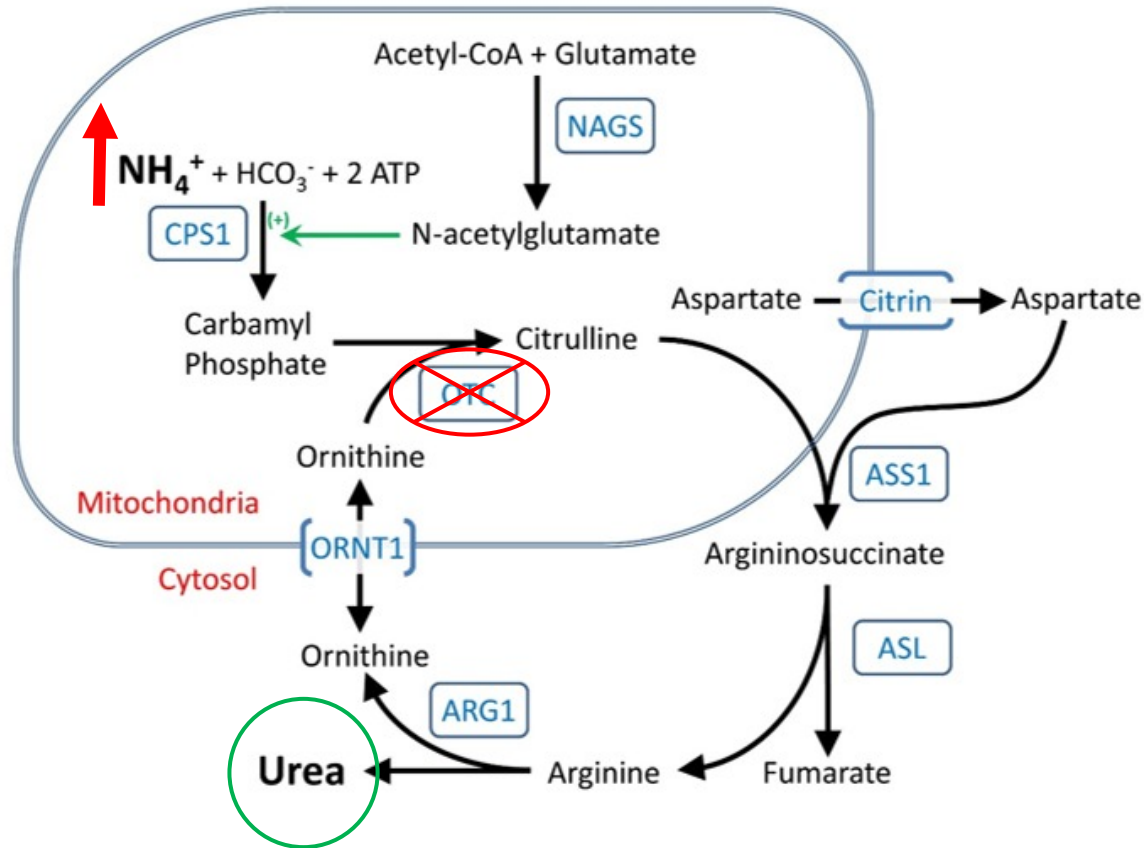
Meeting 2 – July 7, 2021

- Cost-benefit/Cost-effectiveness
- Overall recommendation

Technical Advisory Committee for OTCD

- Advocates
 - March of Dimes Foundation
 - Parents of children with OTCD
 - Save Babies Through Screening
- Biochemical geneticist
- Bioethicist
- Commission on Hispanic Affairs
- Insurance
 - Health Care Authority
 - Office of the Insurance Commissioner
 - Regence
- Public Health
 - SBOH (Dr. Pendergrass – co-chair)
 - DOH (Dr. Lindquist – co-chair)
- WA State Hospital Association
- WA Association of Naturopathic Physicians

Urea Cycle – how we process nitrogen waste



High ammonia leads to:

- Lethargy
- Sepsis-like symptoms
- Coma
 - Death
 - Developmental delays

OTCD – Available Screening Technology

- Testing technology is available at DOH NBS
 - Low citrulline concentrations
 - Not specific to OTCD
 - Can use secondary markers to reduce false positives
 - Expect a large case load for follow-up team
- Test performance
 - Sensitivity – 87% CA; 100% MA (probably somewhere in between)
 - Specificity – 99% (high)
 - Positive predictive value – 2.5-15% (CA & MA)

OTCD – Available Screening Technology

- What proportion of babies with OTCD will benefit?
- What percent of babies with OTCD will be identified through NBS?
 - Prevalence in NBS programs is less than expected

Form of OTCD	Proportion of cases	ID through NBS?	Impact of early ID/tx
Neonatal	30%	Yes	Life-saving, if found quickly
Childhood	60%	Unsure	Potentially life-saving
Adolescent/Adult	10%	No	Quality of life

OTCD – Available Screening Technology



Time for Board discussion

OTCD – Diagnostic Testing Treatment Available

- Specialized treatment is available for babies with OTCD in Seattle, Tacoma, Spokane and Portland
 - Emergency treatment of high blood ammonia levels
 - Dietary modifications
 - Medications
 - Liver transplant
- Will the clinical system be able to handle the high positive rate?

OTCD – Diagnostic Testing and Treatment Available

Time for Board discussion

OTCD – Prevention Potential and Medical Rationale

- Patient outcomes are improved if treatment starts before symptoms
- 50-75% of cases of OTCD are expected to be sick or deceased at the time of reporting NBS results
 - Time to negative outcomes is faster than diagnostic testing
 - It won't identify all babies with OTCD, but it will identify some
- Treating patients while diagnostic testing is done does not harm the baby

OTCD – Prevention Potential and Medical Rationale



Time for Board discussion

OTCD – Public Health Rationale

- Rare condition
- Many individuals are unaware of their own carrier status
 - Wouldn't know to seek risk-based screening

OTCD – Public Health Rationale

Time for Board discussion

OTCD – Cost-benefit/Cost-effectiveness

	Babies/Year	Value/Year
Deaths averted	0.039	\$ 447,552.89
Long-term disability averted	0.043	\$ 64,303.58
Less treatment costs		\$ (75,580.28)
Total benefits		\$ 436,276.19
Total costs		\$ 633,179.55
Benefit/cost ratio		0.69
Net benefit		\$ (196,903.37)

OTCD – Cost-benefit/Cost-effectiveness

- Model parameters are based on limited experience
- Model sensitive to prevalence
 - Lower prevalence than expected – is NBS catching all cases?
- Unintended consequences of screening
 - Ambiguous results when using low citrulline as marker
 - Screening program “fails” 50% of the time

OTCD – Cost-benefit/Cost-effectiveness



Time for Board discussion

OTCD TAC voting

Criteria	Yes	No	Unsure
Available Screening Technology	12	0	1
Diagnostic Testing and Treatment Available	12	0	1
Prevention Potential and Medical Rationale	11	0	2
Public Health Rationale	12	0	1
Cost-benefit/Cost-effectiveness	7	4	2
Overall	9	3	1

Based on the voting data, TAC members were told that this was not a slam dunk that the Board would add OTCD.

OTCD – Implementation Challenges

- Need to improve timeliness of specimen collection and delivery
 - Ensure overnight delivery of NBS specimens (requires fee increase to establish statewide courier service)
 - Reevaluate NBS timing requirements/recommendations
 - Goal: earlier identification and treatment of affected babies = improved outcomes
- Improve communications
 - Messaging to medical partners and parents that the NBS will not identify 100% of babies
- Expand internal laboratory quality assurance efforts to improve turn-around-time of results

Questions?



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