ORNITHINE TRANSCARBAMYLASE DEFICIENCY

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Presenters

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Newborn Screening Program
Urea Cycle – how we process nitrogen waste

High ammonia leads to:
- Lethargy
- Sepsis-like symptoms
- Coma
- Death
- Developmental delays
Ornithine Transcarbamylase Deficiency (OTCD)

- X-linked recessive inheritance – greater impact to boys
- Prevalence: ~1:56,000

Boys
- Early-onset: ~50% mortality rate, average age of presentation = 3 days
- Late-onset: 30-40% mortality rate, age at presentation > 30 days
- High rate of intellectual disability in surviving patients

Girls (carriers)
- Second X chromosome is protective
- Onset later in life (20% mortality)
Three guiding principles govern all aspects of the evaluation of a candidate condition for possible inclusion in the Newborn Screening panel:

- **Decision to add a screening test should be driven by evidence.** For example, test reliability and available treatment have been scientifically evaluated, and those treatments can improve health outcomes for affected children.

- **All children who screen positive should have reasonable access to diagnostic and treatment services.**

- **Benefits of screening for the disease/condition should outweigh hard to families, children and society.**
Amino acid analysis
- Low citrulline [CIT] and five other amino acids

Technology: tandem mass spectrometry
- Already being used in Newborn Screening in Washington State

7 states and 1 territory screening for OTCD currently
- CA, CT, MA, ME, NH, PR, RI and VT

Merritt et al. 2018 – retrospective analysis of 11 cases

Low [CIT] may have high false (+) and false (-) rates – needs further research
Access to Diagnostic and Treatment Services

- Patients seen by biochemical geneticists

- Seattle Children’s Hospital has laboratory services to diagnose OTCD

- Biochemical genetics team at Seattle Children’s Hospital treats patients with OTCD
  - Dr. Merritt has special expertise in urea cycle disorders
Treatment Improves Outcomes

- Sudden presentation (3 days of life)
  - Many cases will present before Newborn Screening results are available (5-7 days)

- Treatment
  - Special low protein diet with supplements/restrictions
  - Nitrogen scavengers (medicine to remove nitrogen) - proven effective
  - Partial liver transplant – curative, but does not reverse brain damage

- Diagnosis and treatment of late-onset cases promises to prevent death and disability (no randomized control trials)
Benefits Outweigh Harms

- Potential to save babies from death and disability
- No formal economic analysis performed (yet)
- Low cost to implement
  - DOH already owns and operates instruments
  - Additional repeat testing of abnormal results
  - Additional case load for follow-up
- Harms created by screening?
  - Impact of false (+) and false (-) results
Questions?