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PEARLS OF LABORATORY MEDICINE

Biotinidase Deficiency

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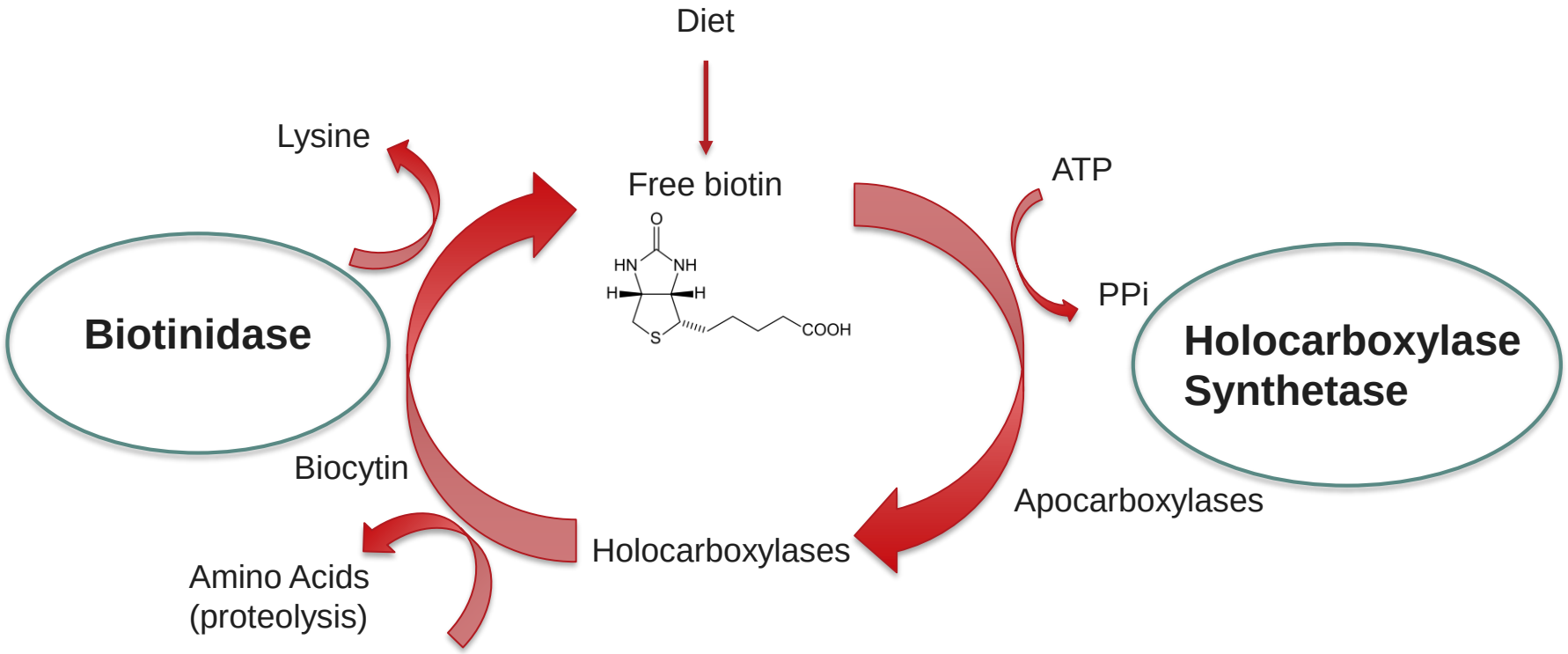
CCTC Clinical Chemistry Trainee Council

Biotinidase Deficiency- Lecture Overview

- Background
  - metabolic role and clinical features
- Clinical Testing
  - Targeted and screening tests
- Newborn screening- changing patient outcomes!

Background

- Inborn error of vitamin B7 (biotin) metabolism



Clinical Symptoms and Therapy

classic biotinidase deficiency- age of onset 2-5 months

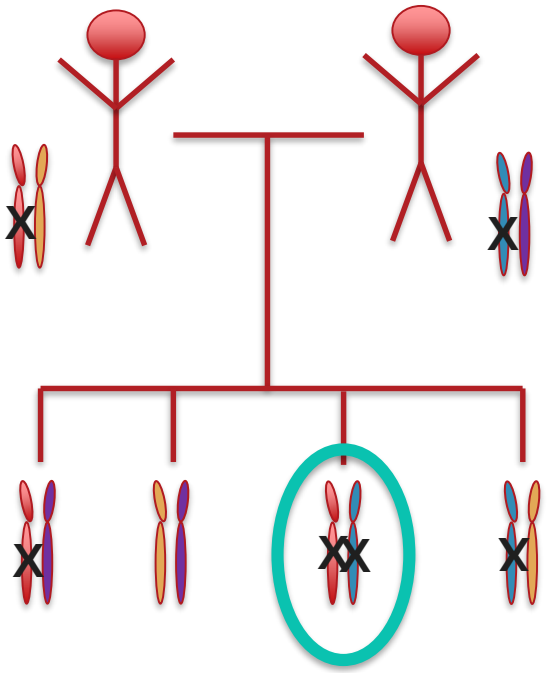
- Alopecia
- Eczema
- Hearing/vision loss
- Acidosis
- Hyperammonemia
- Seizures
- Coma

Treat with high dose oral biotin!

5-20 mg/day

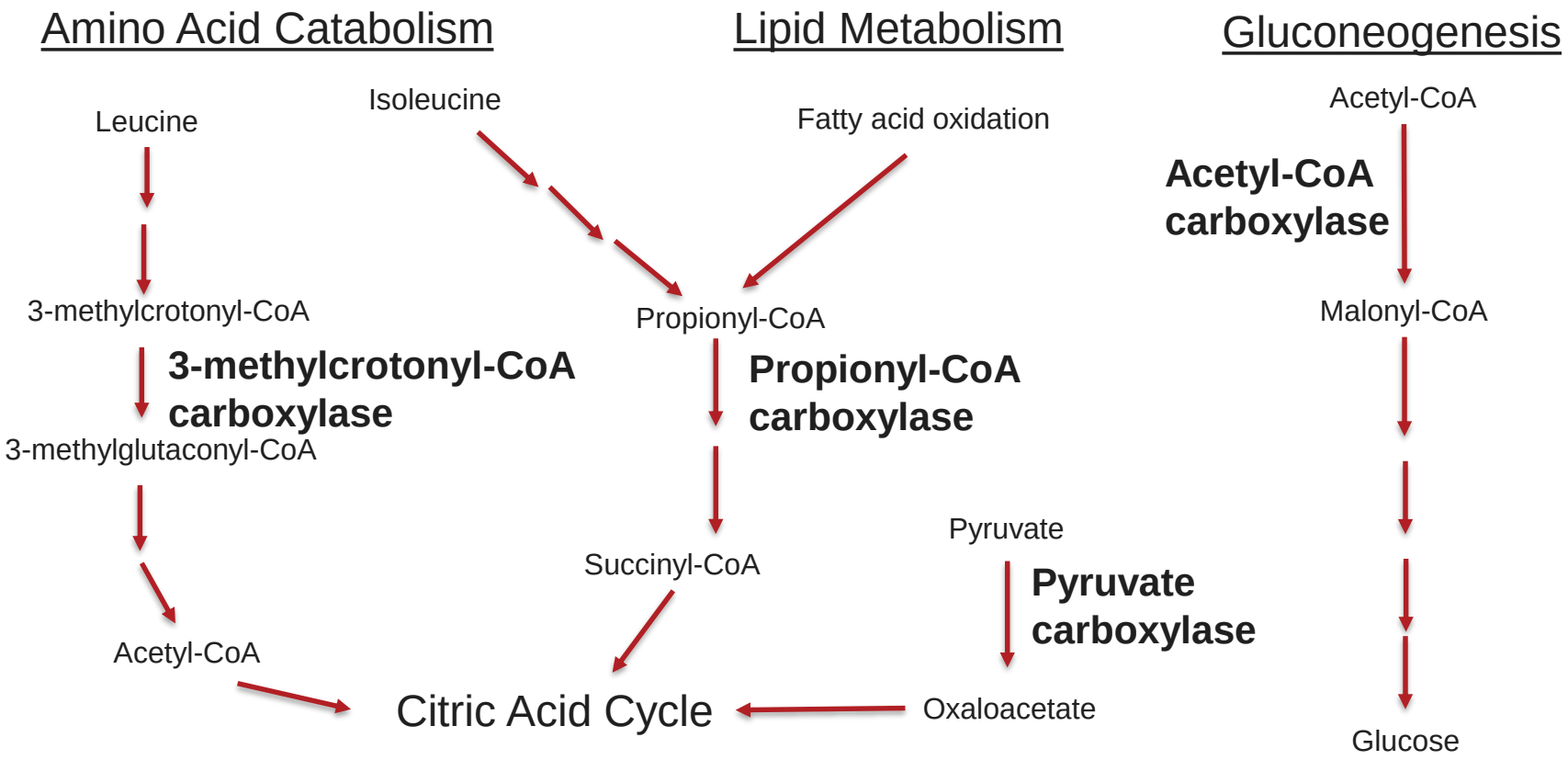
Inheritance and Disease Variation

- Autosomal recessive inheritance
- 1:30,000-80,000 estimated incidence
- Classic/profound deficiency <10%
- Partial deficiency 10-30%
  - Need to treat varies by patient



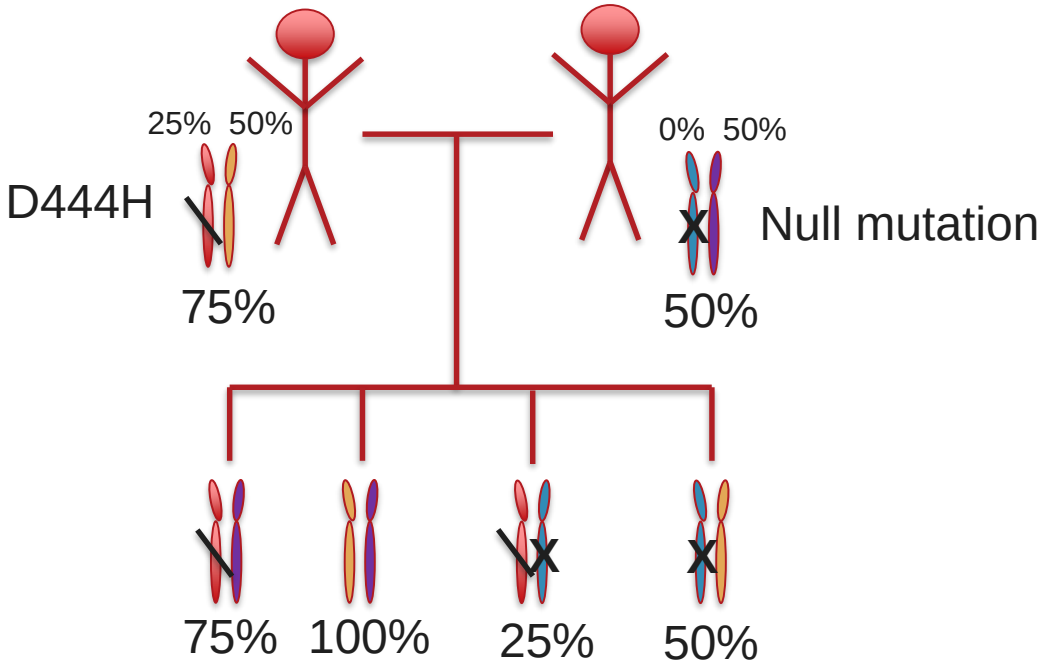
Metabolic Role

- Cofactor for 4 carboxylase enzymes



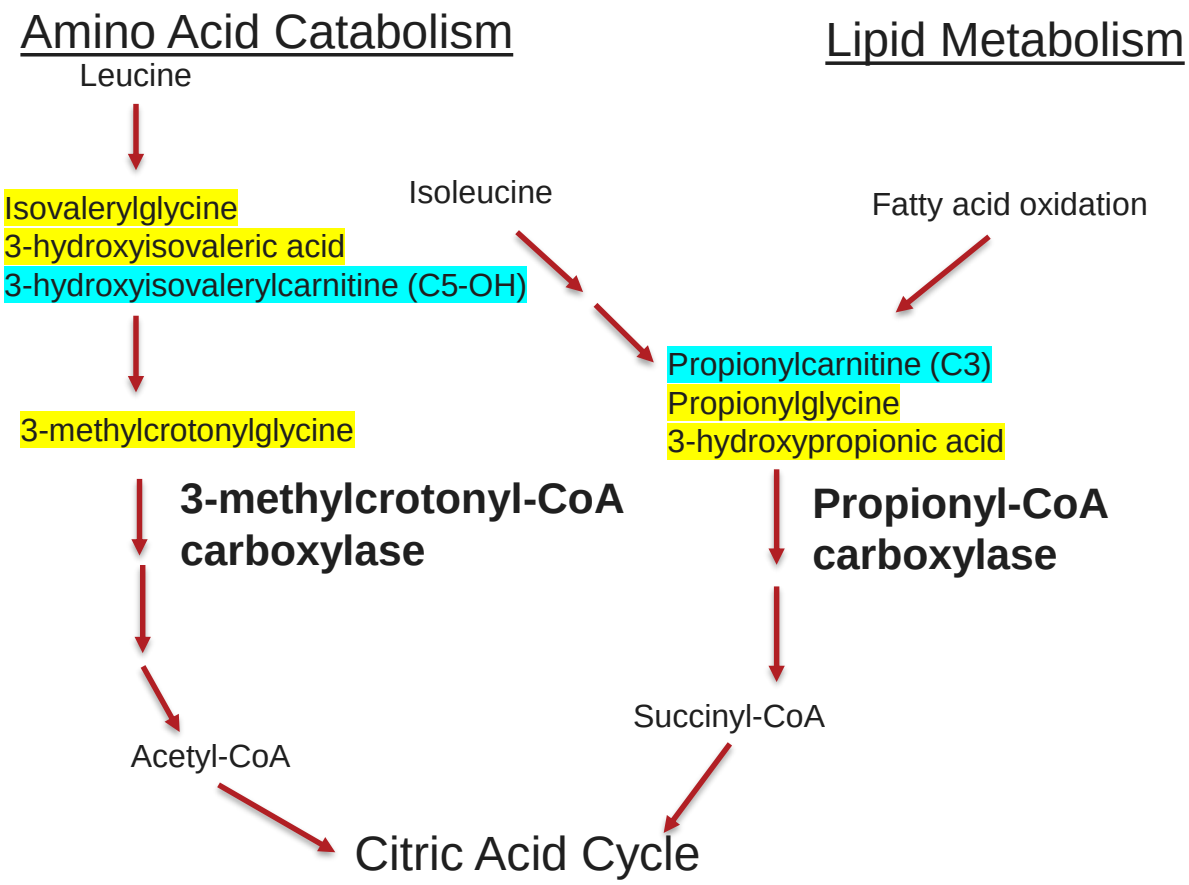
Clinical Testing

- Biotinidase enzyme analysis
- Urine organic acids
- Plasma acylcarnitine profile
- DNA sequencing
  - Common variant (Asp444His) -> 50% activity



Untargeted Evaluation

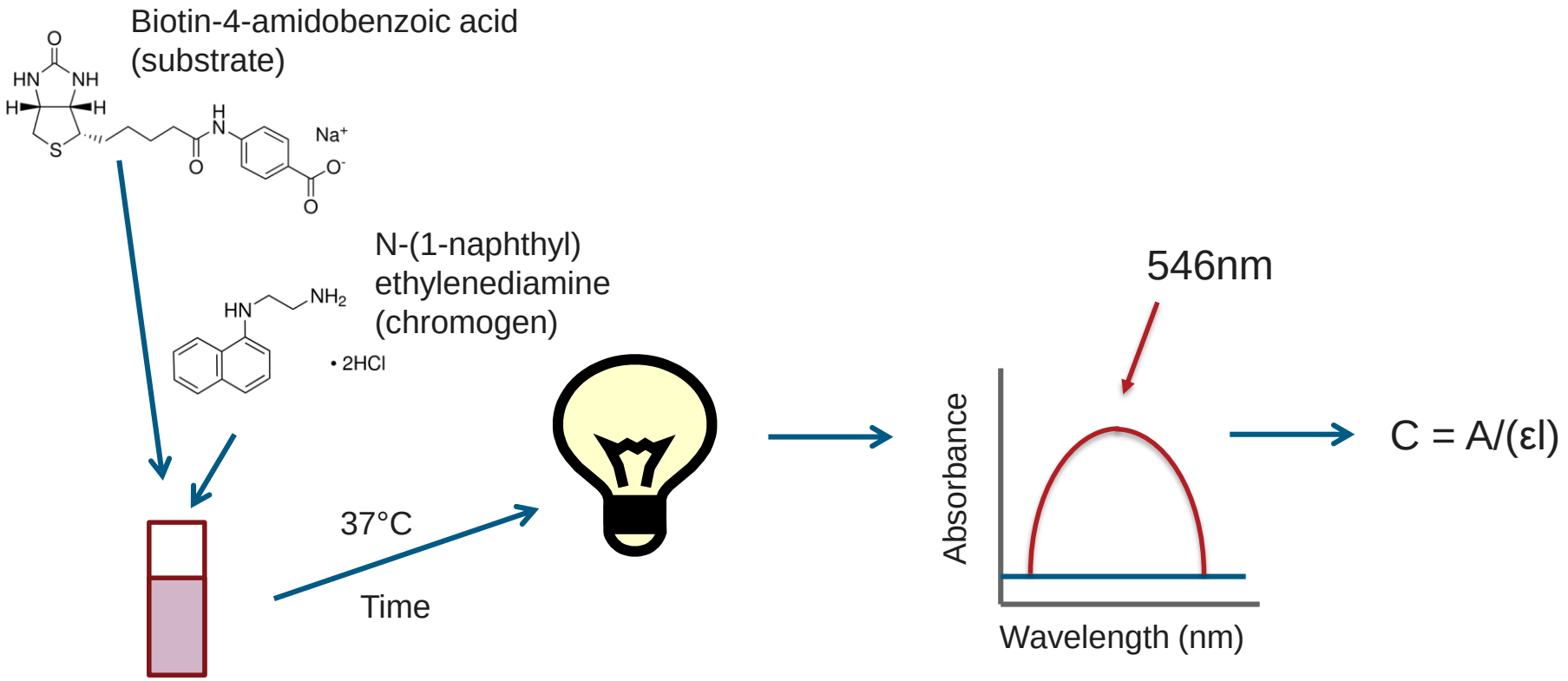
- Urine organic acid analysis and Plasma Acylcarnitine Profile



Enzyme Activity

Biotin-4-amidobenzoic acid + biotinidase → 4-amidobenzoic acid

4-amidobenzoic acid+ Na nitrite + N-(1-naphthyl)ethylenediamine dihydrochloride → Mauve color!



Assay Controls

- Batch controls
  - Normal
  - Deficient
  - Patient blanks (endogenous interference)

- Shipping/Sample Controls
  - 2nd individual (presumably normal)
  - Test 2nd enzyme

Interference Effects

- Sample Handling
  - Excess heat/humidity
  - Incomplete drying of blood spot card
  - Delayed plasma processing
  - Repeat freeze/thaw cycles
- Artificially normal results
  - Blood transfusions
  - Sulfa drugs (sulfonamides)
- Fluorescence assay specific interference
  - Ampicillin
  - Bilirubin
  - Hemoglobin
  - Glutathione

Beware!!! High dose biotin supplementation interferes with other chemistry assays!!!

Biotinidase Deficiency is Ideal for Newborn Screening

Guiding Principles for Population Screening

1. Important health problem with known natural history
2. Suitable (aka easy) test
3. Accepted treatment for identified patients
4. Infrastructure to diagnose and treat
5. Cost effective
6. Testing acceptable to population

Main Points

- Biotinidase deficiency is a systemic enzyme defect that results in a variety of clinical features.
- The disease is completely treatable with oral biotin (vitamin B7) supplementation.
- Measuring enzyme activity in plasma is the most rapid and specific means of diagnosing a patient.

References

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Disclosures/Potential Conflicts of Interest

Upon Pearl submission, the presenter completed the Clinical Chemistry disclosure form. Disclosures and/or potential conflicts of interest:

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