NEW/UNDERUTILIZED RESEARCH TECHNIQUES AND THE DRIs (focus on Protein and Amino Acids)

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FUTURE DIRECTIONS

- Know where we come from (what healthy persons eat: Karl Voit about 1900)
- Consider the techniques used to determine the dietary requirements of mono-gastric farm animals
- Farm animals are easier to study and exhibit less genetic variability
- Longer term functional outcomes
USE THE FULL RANGE OF INTAKES TO DEFINE DRI

- The EAR is best established by defining the physiological response both below and above the requirement point.
- This approach also helps define variability and hence the RDA.
- Use of non-linear regression and two-phase linear cross-over regression analysis.

Determination of Amino Acid (Protein) Requirements - Patterns of Response

Dietary Protein Intake in Relation to Health and Disease.
Working paper prepared to FAO (P. Pencharz, 2001)

Breakpoint 147.4 mgN/kg/d

Nitrogen Intake (mg N/kg/d)

Nitrogen Balance (mg N/kg/d)
Adult Protein Requirements Estimated from Linear Regression of N-Balance Data Rand et al 2003 AJCN 77: 109-27

All data:
- Median slope: 0.47
- Median intercept: -48
- Median N requirement: 105 mg/kg/d
- Median Protein requirement: 0.66 g protein/kg/d

THOUGHTS REGARDING THE DRI FOR PROTEIN
- Nitrogen balance is a cumbersome tool.
- Expensive and time consuming
- Failure to include all available data in analysis may have resulted in an underestimation of protein requirements
- Need for longer term feeding studies (e.g. Garza et al. JN 1977; 107:335-52)
- Need for application of new methods

Breath ^13^CO\textsubscript{2} excretion following the oxidation of orally administered L-[1-^13^C]phenylalanine over various protein intakes.
OPTIMAL AMINO ACID PROFILE

AAs are most efficiently used:
Maximize protein synthesis
Minimize amino acid catabolism

A HISTORICAL PERSPECTIVE ON THE DETERMINATION OF ESSENTIAL AMINO ACID REQUIREMENTS IN HUMANS - I

- N Balance studies in men and women
- Generally small number of data points
- Lack of repeated measurements within the same subject
- Neonatal studies by Holt and Snyderman
- Toddler studies by Torun et al.
- School aged studies by Nakagawa et al

A HISTORICAL PERSPECTIVE ON THE DETERMINATION OF ESSENTIAL AMINO ACID REQUIREMENTS IN HUMANS - II

- 1986 - Direct oxidation studies from MIT Group
- 1993 - Indicator Oxidation introduced
- 1994 - 24h Amino Acid Balance
- 1999 - N-balance reanalyzed using non-linear regression
- 2002 - 24h Indicator Amino Acid Oxidation/Balance
AN OVERVIEW OF METHODS TO DETERMINE AMINO ACID REQUIREMENTS

- GROWTH - only useful during rapid growth
- NITROGEN BALANCE - Classical method
- DIRECT OXIDATION
- INDICATOR OXIDATION (IAAO)
- 24 H DIRECT AMINO ACID BALANCE
- 24 H INDICATOR BALANCE (IAAB)

GENETIC VARIABILITY

- Within subject - repeating each subject at every level - results in less variability than between subject variability
- Farm animals with selective breeding have much less variability than humans.
- Recent ongoing studies in dogs is showing a similar degree of variability as seen in humans

INTRAGASTRIC (IG) REQUIREMENT - 2.6 g/kg/d
Relation between phenylalanine oxidation and total BCAA intake

Total BCAA Intake (mg.kg\(^{-1}\).d\(^{-1}\))

Phenylalanine oxidation (m\(\text{mol.kg}^{-1}.h^{-1}\))

**PARENTERAL AMINO ACID SOLUTIONS FOR NEONATES**

- Ideal solution remains unknown
- Composition of commercial AA solutions vary considerably
- Determining AA requirements
- Expensive, invasive, time consuming

**OBJECTIVES**

To use the indicator AA oxidation technique (IAAO) as a direct reflection of protein synthesis to:

- Compare a commercially available parenteral AA solution (Vaminolact) to a new parenteral solution
- Identify limiting AA in both parenteral solutions
Amino Acid Formulations

<table>
<thead>
<tr>
<th>AA (g/100 g)</th>
<th>Vaminolact</th>
<th>New Profile</th>
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</thead>
<tbody>
<tr>
<td>Lysine</td>
<td>8.6</td>
<td>3.6</td>
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<tr>
<td>Phenylalanine</td>
<td>4.2</td>
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<tr>
<td>Tyrosine</td>
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<td>0</td>
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<tr>
<td>Aspartate</td>
<td>6.3</td>
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</table>

N-acetyl cys L-tyr and gly-tyr Ala-gln

SUMMARY - AROMATIC AA

1. AAA provided at 4.9% with 0.7% as tyr was inadequate

2. Additional AAA reduced lysine oxidation by >30%

3. AAA provided at 5.6% with 2.0% as tyr is adequate

4. Additional AAA did not improve AA utilization

* P < 0.05
SUMMARY - SULFUR AA

- SAA provided at 2.7% with 0.7% as cys is inadequate
- Additional SAA reduced lysine oxidation by almost 30%
- SAA provided at 3.5% with 1.5% as cys is adequate
- Additional SAA did not improve AA utilization

NEED TO RELATE SHORT DETERMINATION OF DRIs TO LONG TERM DIETARY INTAKES

- Do short term balance studies relate to long term health?
- Functional studies of exercise performance have worked well for iron
- Conversely how do studies which show a suppression of PTH level with increased 25OH-Vitamin D levels relate to bone health and hence vitamin D requirements?