Report from the Amino Acids Working Group

Ann Bowron
Anny Brown
Helena Kemp

Introduction

Helena Kemp
Southmead Hospital, Bristol

Where are we now?

- Variation in current practice

Where should we be going?

- Is there a need to change/standardise current practice?
- If so - what areas need to be addressed?
- If so – is there a need to develop Metbionet guidelines?

Existing Guidelines

- Amino acid workshop report
  - 38th Annual Symposium of the SSIEM - Cambridge 2000
  - Mayne, Roche & Deverell (2001). *JIMD* 24: 305-308.
- ERNDIM
  - Recommendations to improve the quality of diagnostic quantitative analysis of amino acids in plasma and urine using cation exchange liquid chromatography with post column ninhydrin reaction and detection. (May 2002)
- American college of Medical Genetics (ACMG)
  - Standards and guidelines for Clinical Genetics Labs (Biochemical Genetics
  - Guidelines for amino acid analysis (updated 2003)

Working Group - membership

- Participation by all Stakeholder laboratories invited
- Representation from 5 laboratories
  - Sheffield Children's Hospital – Claire Hart
  - Dublin Children's Hospital – Dierdre Deverell
  - Birmingham Children's Hospital – Mary Anne Preece
  - North Bristol NHS Trust – Helena Kemp, Anny Brown
  - United Bristol Hospitals Trust – Ann Bowron

Working group - Aims

- 'To collect information to guide the development of recommendations for the provision of a comprehensive, appropriately organised, specialist amino acid diagnostic and monitoring service'.

Work streams

- Repertoire
  - Primary amino acid disorders
  - Other conditions
  - Nutrition
- Analytical methods present and future
- Clinical indications
  - Requesting patterns and practices
- Requirements for monitoring IMD
- International views

Afternoon Session

- CSF amino acid analysis
- Amino acids reporting
  - UKNEQAS amino acids cognitive scheme
  - Clinical Biochemists view
  - The Dietician's experience
  - The requesting doctor

Amino Acid Analysis – What do we need to do?

Ann Bowron, Bristol Royal Infirmary
Anny Brown, Southmead Hospital

Amino Acid Analyser

- Expensive
- Time-consuming
- Interferences (esp urine)
- Increased number of requests
- Demands on staff + budget

Amino Acid Analyser

- Can quantitate > 60 compounds
- Sigma standard 37 amino acids

- Why are we using this technology
- What are we trying to achieve?
- Which amino acids do we need to measure to achieve this?

Why do we measure amino acids?

- Metabolic screen
  - To exclude/diagnose AA disorder
- Information about other diseases
- Assessment of nutritional status
- Monitor treatment

1. Metabolic Screen

- List of amino acid disorders
- How are they diagnosed?

- Spreadsheet of findings (this will be given as a handout)

Established AA disorders

Glutamine
Citrulline
Arginine
Argininosuccinic acid
Ornithine
Valine
Leucine
Isoleucine
Allo-isoleucine
Phenylalanine
Tyrosine
Methionine
Cystine
Taurine
Sulphocysteine
Serine
Glycine
Lysine

18 amino acids

Evidence is unclear

Histidine
Tryptophan
aAAA
OH-lysine
Saccharopine
Proline
OH-proline
cystathionine

Homocystine
Sarcosine
Carnosine
Homocarnosine
Anserine
B-alanine
B-AIBA

- Few cases described
- Same findings in well siblings
- Conditions are ?benign
- Some described before modern methods used
- ?no recent cases as not in routine standards

2. Amino Acids in other disease states

- Spreadsheet – handout

3. Assessment of nutrition status

Amino acids & Nutrition

- From diet
- Continuous exchange between structural muscle protein and free aa's in blood
- Plasma aa levels influenced by timing of meals & their calorie and protein content.
- Muscle proteolysis probably triggered by lowering insulin levels and relate to calorie deprivation.

Dietary requirements

- Mature adult
  - Protein turnover 300g/day
  - ~ 40g/day lost, must be replaced
  - RDA ~ 56g/day
- Growth, pregnancy & convalescence
  - Need extra protein
- Inadequate intake difficult to diagnose unless severe and prolonged

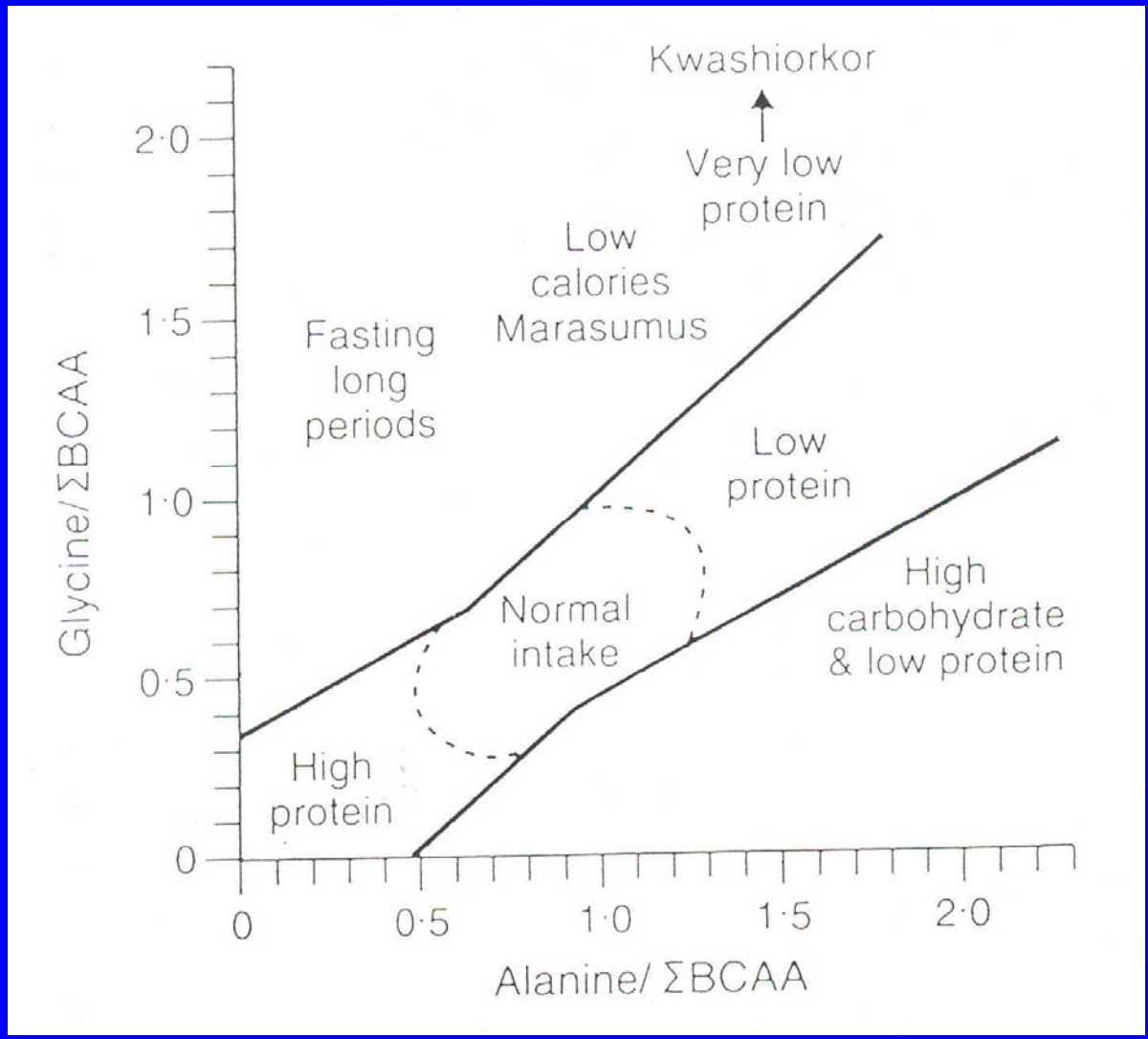
Total calorie vs isocaloric protein deprivation

- Key aas; glycine, alanine & BCAAs
- Isocaloric protein deprivation
  - BCAA ↓ (particularly valine)
  - Alanine ↑, Glycine ↑
- Total calorie deprivation (starvation)
  - BCAA ↑
  - Alanine ↓, Glycine ↓

Use of aa ratios

- Indicator of muscle breakdown
- Monitor patients on restricted diets
  - Increase dietary protein indicated
  - Proteolysis may stress liver in UCD
  - Val chronically low in PA
    - ? Patients very sensitive to protein deprivation

Ratiogram



Proc 1st International Conf Amino Acids, Vienna, 1989

Interpretation

- Timing of sample - IMPORTANT
- What control data are we using?
  - Fasting levels / 8 hours
  - 4 hrs post-meal
  - ? Protein ingested
- Interpretation with care!

Conclusion

- Current methods may not be sustainable
- Number of *AAs* routinely measured can be reduced
- ? *Alternative methods*
- ? Other *AAs* as second line tests

Obstacles

- Lack of evidence for some amino acid disorders
- Resistance to change
- Specific requirements for individual labs