Clinical Indications For Amino Acid Analysis

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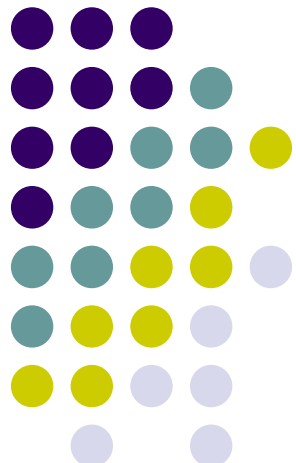


Amino Acid Disorders Workshop

Bristol Royal Infirmary

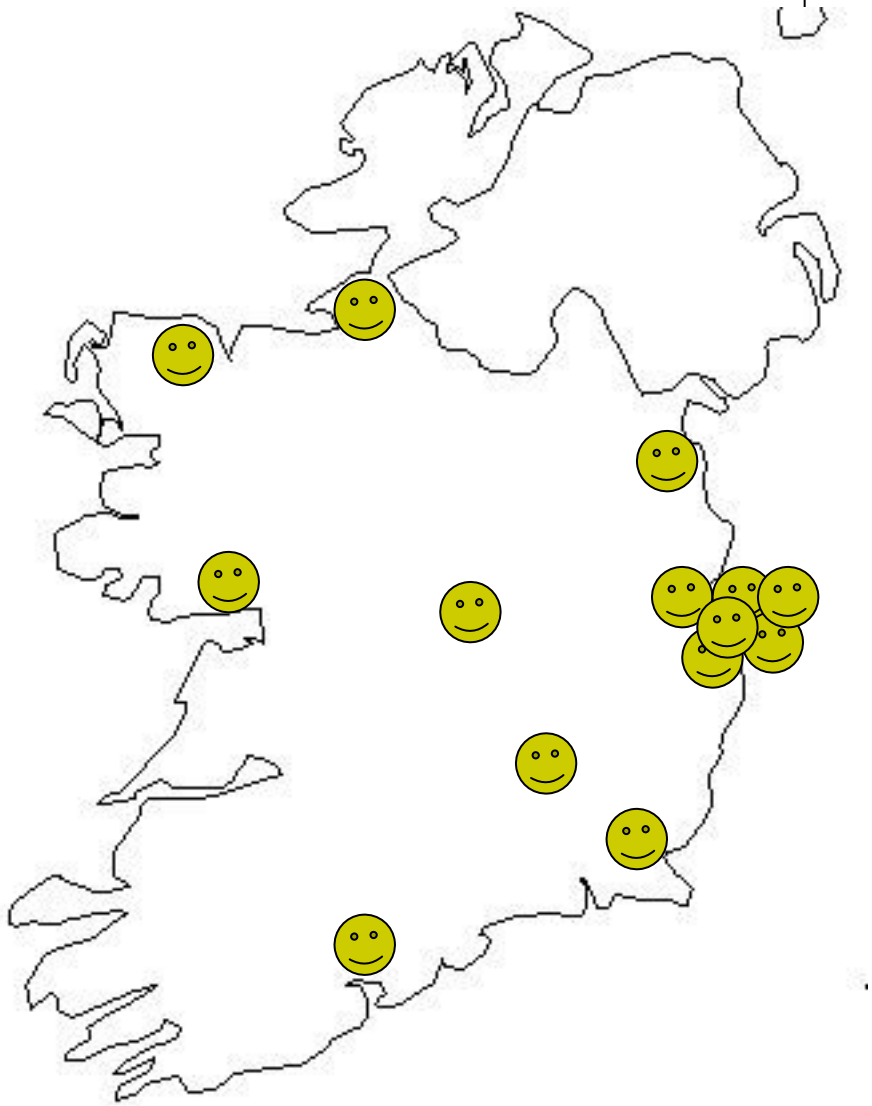
22nd Nov 2005

Presentation Overview

- Interviews with Requesting Physicians
- Audit of AA Analysis Requests
- Conclusions & Recommendations

Physicians Interviewed

- Specialist Metabolic Consultants (2)
- Paediatric Neurologists (2)
- Developmental Consultant
- Paediatric Nephrologist
- General Paediatricians (8)



Q.1 What Clinical Presentations indicated Amino Acid Analysis ?

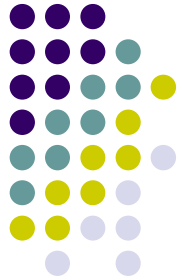
- Unexplained symptoms
- Sick Neonates
- Seizures
- Encephalopathy
- Vomiting
- Hypoglycaemia
- ↑ Ammonia
- ↑ Lactate
- Failure To Thrive
- Abnormal LFTs
- Developmental Delay
- Speech /language Delay
- Eye abnormalities
- Myopathies, ↑CPK
- Energy disturbances
- Psychosis
- Renal tubulopathy
- Renal calculi
- Haemodialysis patients
- Early vascular events

Q.2 Did clinical presentation point to any specific amino acid disorder ?

NO General Paediatricians need to outrule metabolic
Some differentiated conditions which would select AA vs OA

YES Specialist Metabolic /Neurologists /Nephrologist

Clinical Presentation for Specific Amino Acid Requests



• Encephalopathy	Urea Cycle Disorders, MSUD
• Seizures	Non Ketotic Hyperglycinemia, Undiagnosed PKU, HCU, Sulfite Oxidase Def
• Developmental Delay	PKU, HCU, Sulfite Oxidase def
• Eye Abnormalities	HCU, Hyperornithinemia
• Liver Disease	Tyrosinemia
• Renal Stones	Cystinuria, Cystinlysinuria
• Renal Tubulopathy	Fanconi syndrome, Cystinosis
• Vascular Disease	Hyperhomocysteinemia
• Energy Disturbances:	Mitochondrial Disorders

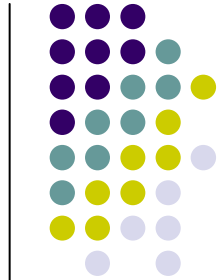
Q.3 What Sample Type Selected ?

Plasma only	Specialists	Specific aminoacidopathies
Urine only	Nephrologist	Renal calculi
	Neurologist	Sulphite oxidase Def
Both	General	To encompass all disorders
	Paediatricians	Not sure which sample type is better
		To prevent follow up request
		Preference for plasma

Q.4 Relevance of Clinical Details?

Awareness - but not always supplied due to circumstances.
Did not realise that some conditions may not be properly investigated in absence of relevant clinical details.

Audit of Requests

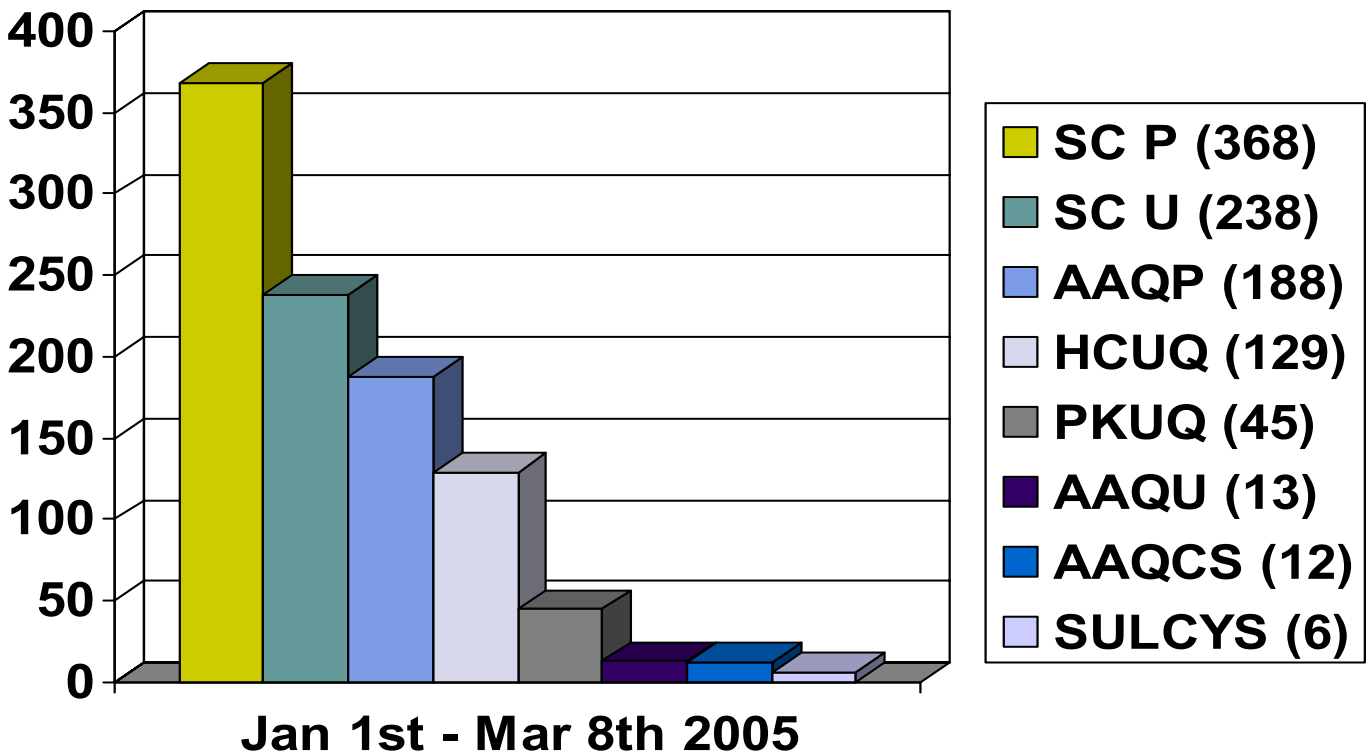


- 1,000 requests (Excludes 1052 PKU/150 MSUD monitors)
- Results reported from 1st Jan 2005 – 8th Mar 2005
- Information logged on Access database
  - Name, date of birth, laboratory identification no.
  - Location, requesting physician
  - Clinical details if supplied
  - Sample type and tests requested
  - Whether diagnostic screen or monitoring
  - Results category

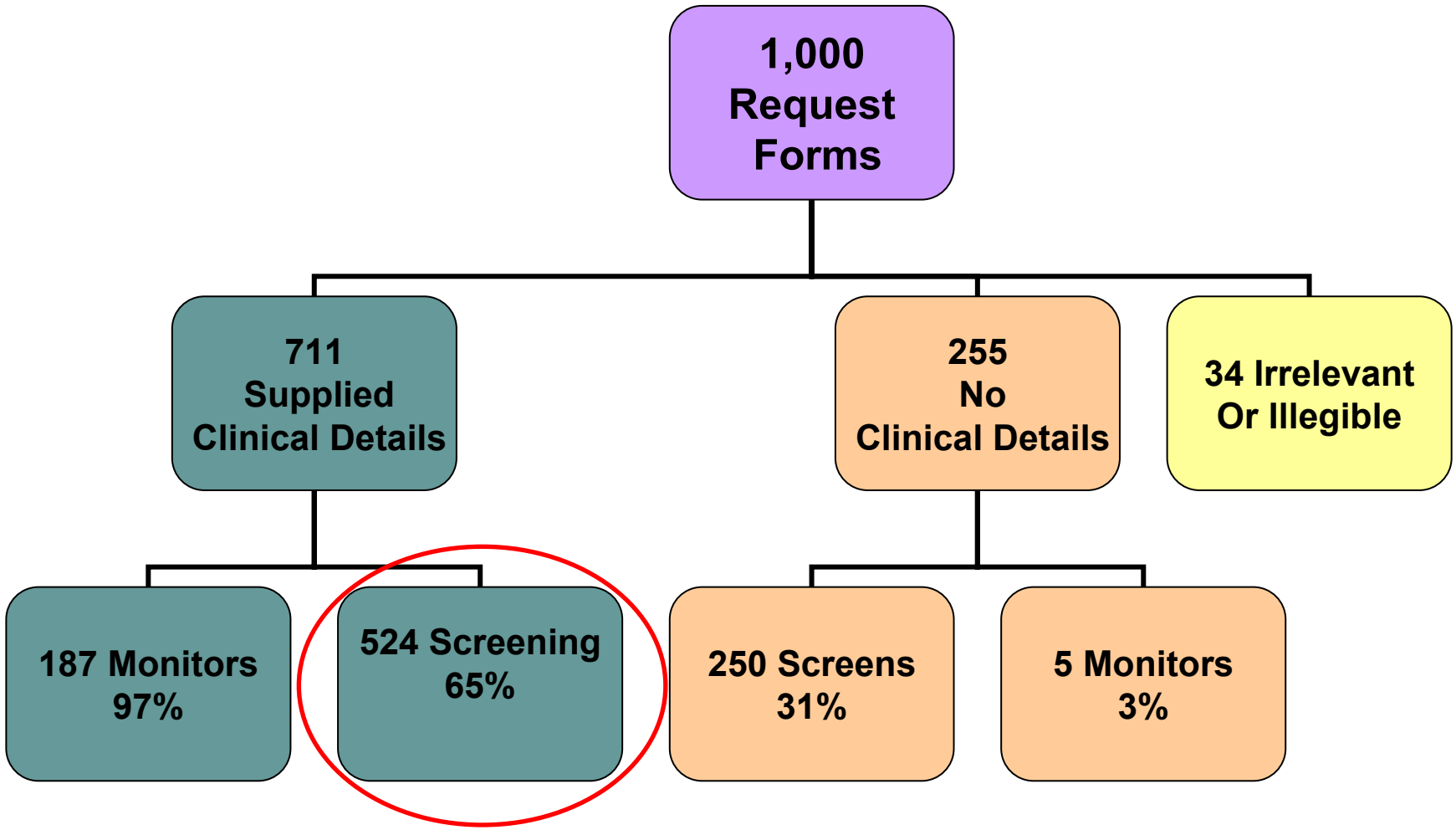
Amino Acid Requests

- 808 Screening / 192 Monitoring
- 35 Locations
  - Children's University Hospital 319, External 681
- Age Range 1day – 75yrs
  - Neonates 0 – 3m 228 samples
  - Infants 3m – 2yr 235 samples
  - Children 2yr – 16yr 376 samples
  - Adults >16yr 161 samples
- Sample Type
  - 731 Plasma, 257 Urine, 12 CSF

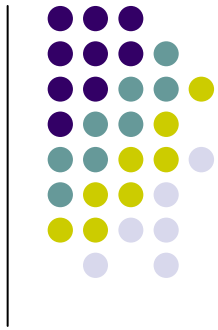
AA Profiles for 1,000 Requests



Clinical Details Supplied

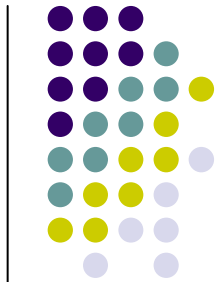


Clinical Details Supplied



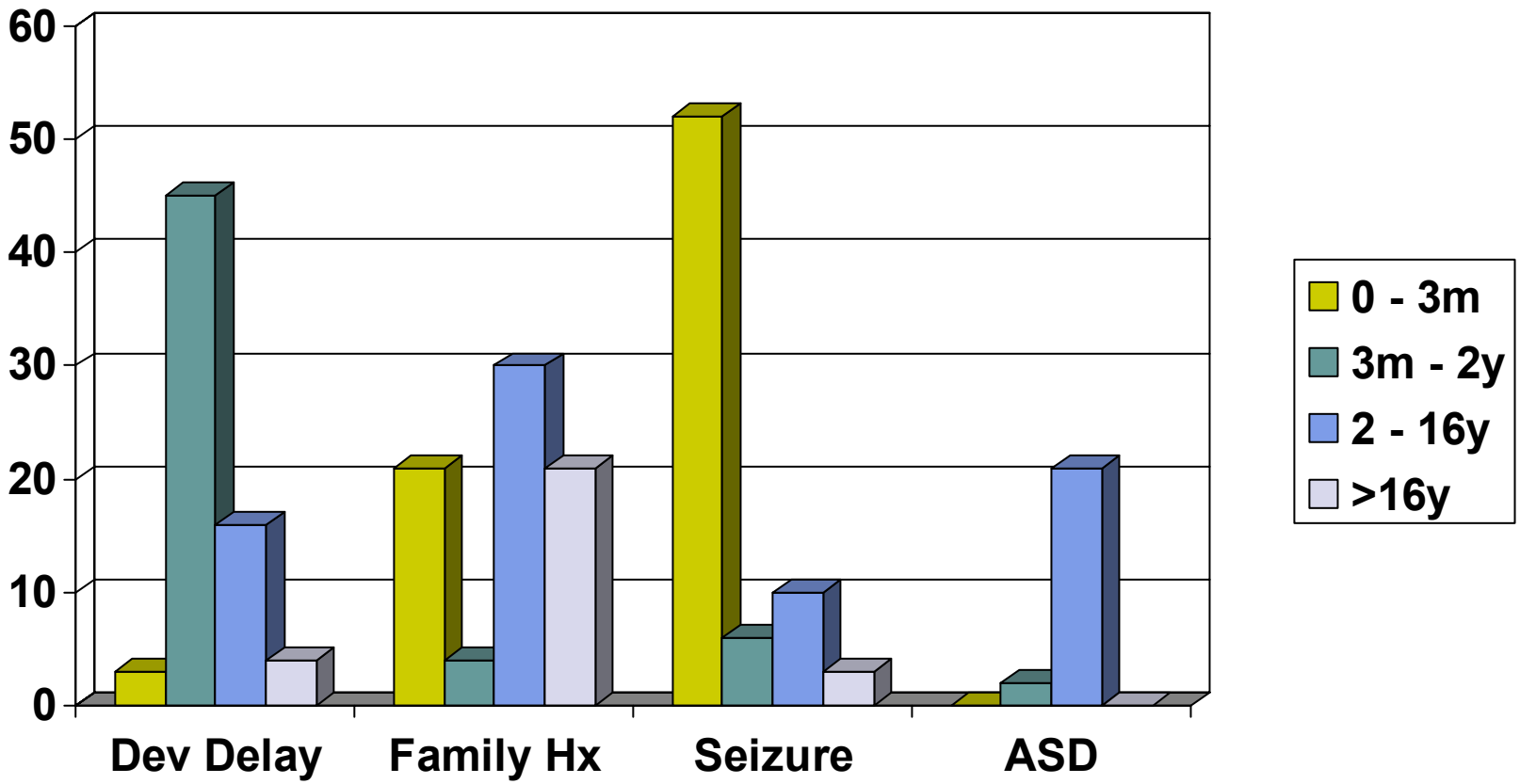
• Developmental Delay	75
• Family History	62
• Seizures	59
• Failure To Thrive	28
• Autism / Aspergers	28
• Hypoglycaemia	26
• Previous Elevated AAs	24
• Speech and Language Delay	23
• Learning Difficulty	23
• Apnoeic Episode	15

Clinical Details Supplied



• Hypotonia	13
• ADHD	13
• Microcephaly	13
• Vomiting	10
• Cardiovascular Disease	10
• Dysmorphic Features	9
• Cardiomyopathy	8
• Mitochondrial Dysfunction Query	7
• Renal Calculi	6
• Prolonged Jaundice	6
• ALTE	6

Age Related Clinical Indication



Screening Samples Results

Result	No.	Clinical Details	Action
Unsuitable	37	21	Repeat (e.g. Dilute or rotten urines, grossly haemolysed plasmas)
Normal	607	399	No further action indicated
Slightly Abnormal	97	66	May need repeat (e.g. Generalised AAs or slightly elevated /non specific AAs, Deficient patterns….)
Abnormal	62	40	Further tests (Plasma AAs, Csf AAs, Ammonia, Lactate, Organic Acids, LFTs)
Diagnostic	6	6	Refer to Metabolic Consultant

Diagnostic Samples

Condition	Clinical Details Supplied
PKU (3 days)	Family History of PKU
2x PKU (5/6 days)	Elevated Phenylalanine on Newborn Screening
Histidinemia (4yrs 5m)	Global Developmental Delay / Mild Dysmorphism
Hyperprolinemia (13yrs)	Learning Disability
Hyperornithinemia (53yrs)	Family Hx Gyrate Atrophy of Choroid & Retina

Conclusions

- Why we Measure Amino Acids
  - In patients presenting with a very wide range of otherwise unexplained clinical symptoms, there is a need to outrule, or aid in the diagnosis of, a metabolic disorder
  - Monitor of known patients with IEMs
- Requirement for Relevant Clinical Details
  - Ensure correct tests are performed
  - Aids interpretation and reporting of results

Recommendations

- Updated Guide to Metabolic Investigations
- Educational / Information sessions for non specialist paediatricians
- Improved Communications
- Metabolic Request Form, with tick box for clinical details, to be attached to requests
- Useful interpretative comments on reports with suggestions for further investigations

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