

## National Metabolic Biochemistry Network

### Minutes of Stakeholder meeting held on 14<sup>th</sup> January 2009 at Birmingham Children's Hospital

<b>Present:</b>	Mick Henderson	(MH)
	Steve Krywawych	(SK)
	Helena Kemp	(HK)
	Jim Bonham	(JB Chair)
	Stuart Moat	(SM)
	Mark de Souza	(MS)
	Tim Lang	(TL)
	Mary Anne Preece	(MP)
	Simon Olpin	(SO)
	Lesley Tetlow	(LT)
	Valerie Walker	(VW)
	Jacqui Calvin	(JC)
	Smantina Agalou	(SA)

#### ACTION

#### 1. Apologies

Ann Sheldrake, Mike Badminton, Fiona Carragher, John Fyffe, Peter Galloway, Clodagh Loughrey, George Gray, Paul Newland, Philip Mayne, Janet Stone, Jean Kirk, Hilary Wastell, Ann Brown, David Isherwood

#### 2. Minutes of Meeting held on 16.07.08

Tim Lang apologies were omitted, otherwise accepted as correct.

#### 3. Matters Arising

##### 3.1 Aminoacid reference ranges

A total of 277 paired plasma and CSF AA sample data sets were obtained from 8 different MetBioNet labs. These data were collected by Rachel Carling (Cambridge/Guys). Age related RI's for CSF, Plasma and CSF:plasma ratios have been generated. Data were partitioned into the following age groups: <6months, 6months-1year, 1-5 years and > 5years. Following the correction for age no differences were seen in population means between the 8 different labs. Non-parametric methods were used to calculate the 2.5th and 97.5th percentiles. CSF serine was highly influenced by age and a separate analysis has been performed to partition these data further. These data are to be written up and submitted to the Annals. Rachel Carling to be contacted to discuss writing of manuscript. MetBioNet Amino Acid Working group to be acknowledged.

Plasma ranges were also being prepared with 700 data sets from Cardiff and 1800 from BCH. HK added that the amino acid working group was due to meet in February and would be considering a draft guideline on the measurement of amino acids.

### 3.2 (i) Non lysosomal assay arrangements

SEO presented the findings of a recent meeting where the robustness of arrangements in each centre offering services was discussed. The message from most centres was that the capacity was adequate to meet current demands but was not adequate to allow development and most centres expressed concern about the continuity of services in the event of prolonged staff sickness or retirement. JB suggested that SEO should Email centres to determine if adequate contingency plans were in place and identify the particular services that may be most vulnerable.

### 3.2 (ii) Krabbe reagent

No further update had been received from JK, JB to check

### 3.3 Ammonia Audit

SK summarized the findings from an audit undertaken in 2005 in 80 labs. The results highlighted difficulties in the availability of age matched ranges and action limits. Similarly not all labs were able to provide a 24h service or had back up arrangements in the event of equipment failure. Some labs still used the ammonia checker and not all subscribed to EQA. It was agreed that as the data was now a few years old that SK would contact Annette Thomas at WEQAS to arrange a re-audit with a view to publication. SK would devise the standards against which to audit in conjunction with LT.

### 3.4 Audit

### 3.5 Workforce Planning

MAP agreed to re-circulate the template for completion in March 2009. She would also include last years data. MAP would then use the data when attending the DH workforce planning meeting usually held in May/June

## 4. Reports/Liaison with Other Groups

### 4.1 UKGTN

The last meeting was 11.9.08 and the next 5.3.09. The recent meeting included discussion of the House of Lords enquiry, the gene dossier, the commissioning working group and the laboratory working group. Reports were also usually received from the reference laboratories and various groups including Metbionet, GIG and the Haemophilia centres.

#### 4.2 BSAG

Discussions took place about the PKU referral guidelines and the PKU disease register. A view was expressed that screening for HbE was not a formal part of the sickle program, JB to advise Paul Griffiths.

#### 4.3 JCMG

Next meeting to take place on 20.1.09. Discussions at previous meetings included modernizing scientist careers, the potential of free fetal DNA, the Genetics specialist medical definition..

#### 4.4 GenCAG

Last meeting 8.10.08, next meeting 29.4.09. The last meeting included discussions about the 18 week treatment wait and the 6 week diagnostic wait, recent NICE guidance on FH, developments in specialist commissioning and particularly the development of a specialist medical definition relating to IMD's

#### 4.5 UKNSLN

JC reported that Kate Hall had stepped down as secretary to be replaced by Anthea Patterson. Discussions included the status code implementation and the data collection underlining practical difficulties in achieving all aspects of data collection even with the financial support offered by the program centre.

#### 4.6 RCPATH SAC

No report

#### 4.7 SAGE

No report

### 5. Expanded Newborn Screening

JB outlined the progress with the expanded screening research project with meetings held in September and November, the next project team meeting is planned for 6<sup>th</sup> Feb 2009. Five conditions to be included (IVA, MSUD, GA1, LCHAD, Hcys (non-pyridoxine responsive)) had been agreed with work plans to undertake investigation related to informed choice and the effects of false positive results. Research ethics submission is planned for April and the size of the study and therefore the centres to be included is likely to be dictated by the requirements concerning consent. It is planned that screening will begin in 2010.

### 6. Training and Education

MH outlined the recent training report of the HST workshop held in Birmingham which is attached. MH to clarify copyright issues. Prompted by a recent RCPATH question addressing the utility of biochemical tests as a complimentary approach to molecular genetics, Sarah Ball suggested the benefits of a biochemical genetic component to foundational training in molecular genetics. It was

agreed that input during the first two years of training would be helpful and that this should include a visit to a biochemical genetics laboratory. GG and Sarah to collaborate in the development of a module to be used in induction, this will include the development of a syllabus for Biochemical Genetics as part of molecular genetic training.

## 7. Report from the BMS Group

MdH reported that 60 delegates attended the annual symposium held in September and that the meeting was very well received. In the coming year a GCMS workshop is planned for 25 in Birmingham in June and that there will be a meeting at the IBMS annual symposium also to be held in Birmingham in October. Worries continuing with the IBMS to establish a diploma in expert practice related to newborn screening, a decision from the IBMS is expected by September.

MdH requested all HoD's to encourage relevant staff in the junior grades to attend training courses.

MAP drew attention to a very useful lab skills training document available in electronic form, MH added that elements of this were in use in Leeds.

## 8. Web Review

### 8.1 Update

Continuing concerns were expressed about the presentation and content of the website. Much information seemed dated and required pro-active regular review. JB commented that the group looked to GG to review and update the website and MH felt that it may be profitable to align the form and content with the BIMDG website. This was agreed and MH was asked to contact the BIMDG website provider.

### 8.1 Assay Directory

JS was not able to be present to provide a report. JC commented that it would be useful to include reference to creatine synthesis defects and the measurement of guanidinoacetate.

## 9. Audit

TL had tried to publish the findings of the pyruvate audit in the ACB Newsletter but Jonathan Berg did not feel that the content was suitable. The group felt that publication in the BIMDG newsletter may be helpful.

TL had engaged in discussion with the ACB audit committee regarding the organization of hypoglycaemia sample collection, he had also contacted laboratories in Australia/New Zealand and from the responses received together with those from MetBioNet stakeholders he would produce guidelines suitable for future audit.

## 10. Workforce Planning

MAP confirmed that she would re-circulate the group in March/April to obtain updated information.

## 11. Quality Assurance schemes

Finlay Mackenzie continued to express concern about the EQA performance of laboratories offering orotic acid measurement. While the group felt that these differences may not necessarily be a clinical risk, it would be helpful to hear from Finlay at the annual QA workshop.

## 12. Guidelines

PN could not attend the meeting but has expressed his desire to be replaced as the guideline lead. TL volunteered to replace him and LT was also considering this role as part of a "trainer" function. This is to be agreed following further discussion with LT. These seemed to be a certain degree of confusion around guideline production with both TL and Camilla Reed undertaking hypoglycaemia guideline review. In addition, many authors had work outstanding and this important area needed a pro-active approach to ensure that authors completed work in a reasonable timescale. The offer of honoraria to encourage guideline submission was also discussed but no conclusion was reached.

## 13. Finance

JB confirmed that the finances were healthy but that trainer income would cease in March 2010. The group needed to ensure that the maximum value was obtained from this limited, non recurrent funding stream. LT and MH were currently considering their time allocation and JB would seek reassurance that GG was engaged in MetBioNet business 2 days per week. It seemed likely that as the only paid officers, these posts would have to ensure delivery on the key activities of MetBioNet including: Audit, Guideline creation and Website review, activities that were all directly relevant to training.

#### **14. Meetings planned**

##### **14.1 Future workshops**

An intermediary metabolite workshop is planned for April 22nd in London - SK to organize MAP/SM confirmed their intention to arrange a B12/propionate workshop in early summer in Birmingham.

##### **14.2 Quality assurance day**

MH agreed to host the annual QA day in Leeds in October 2009

#### **15. Any Other Business**

None noted

#### **16. Date and time of next meeting**

It was agreed that the next meeting would be planned for Wednesday 15<sup>th</sup> July 2009 to begin with coffee at 10.00 am in the Pan Pathology Seminar room at Birmingham Children's Hospital

**The meeting closed at 15:10**

## Grade A Syllabus in Clinical Biochemistry – IMD Component

### Knowledge Sessions (Mini-Modules) (20 mins)

#### 1 The Effects of a Metabolic Block

A description of how metabolic pathways can be disturbed by metabolic disease and the pathogenesis of the disease. The importance of cofactors and vitamins.

#### 2 Amino Acid Disorders

A short description of the major amino acid disorders that can present at a DGH and the methods used to detect them.

Hyperglycinaemia, Maple Syrup Urine Disease, Tyrosinaemia, Homocystinuria, Cystinuria, Phenylketonuria

#### 3 Organic Acid Disorders

A short description of the major organic acid disorders that can present at a DGH and the methods used to detect them.

Methylmalonic Aciduria, Propionic Acidemia, Glutaric Aciduria Type Biotinidase Deficiency

#### 4 Carbohydrate Disorders

A short description of the major disorders of carbohydrate metabolism that can present at a DGH and the methods used to detect them.

Glycogen Storage Diseases, Gluconeogenic Disorders, Galactosaemia, Hereditary Fructose Intolerance. G6PDH deficiency

#### 5 Lysosomal Storage Disorders

A short description of the major lysosomal disorders that can present at a DGH and the methods used to detect them.

Mucopolysaccharidoses, Oligosaccharidoses, Gauchers Disease, Tay - Sachs disease, Metachromatic Leucodystrophy

#### 6 Urea Cycle Defects

A short description of the major disorders causing hyperammonaemia that can present at a DGH and the methods used to detect them.

OTC Deficiency, CPS Deficiency, Argininosuccinic Aciduria, Citrullinaemia.

#### 7 Lactic Acidaemias

A short description of the major disorders affecting lactate metabolism that can present at a DGH and the methods used to detect them.

Respiratory Chain Disorders, PDH Deficiency

#### 8 Fatty Acid Oxidation Defects

A short description of the major fatty acid oxidation disorders that can present at a DGH and the methods used to detect them.

MCADD, Long chain fatty acid oxidation defects, Multiple Fatty Acid Oxidation Defects, carnitine deficiency

## **9 Other Metabolic Disorders**

A short description of the other inherited metabolic disorders that can present at a DGH and the methods used to detect them.

Peroxisomal Disorders (X-ALD, Zellwegers Syndrome), Menkes & Wilson's Disease, Lesch Nyhan Syndrome

## **10 Treatments and Monitoring**

The current strategies available for the treatment and monitoring of inherited metabolic disease

Dietary control, Vitamin-responsive disorders, Pathway Inhibition, Chelation, Transplantation (Liver, Kidney Bone Marrow), Enzyme Replacement Therapy

## **11 Prenatal Diagnosis**

A brief description of the techniques used for sample collection and the types of testing available for the prenatal diagnosis of inherited metabolic disease.

Foetal Sexing Chorionic Villous Biopsy, Amniocentesis, Foetal Blood Sampling. Metabolite, enzymological and molecular genetic analysis.

## **12 Newborn Screening**

The current services and tests for Newborn Screening in the UK

PKU, Hypothyroidism, Cystic Fibrosis, Sickle Cell Anaemia, MCADD

Total time of course = 240 mins i.e. equivalent to 4 hours lectures

## Pathopaedia Topics

Chitotriosidase  
Cellulose acetate electrophoresis of mucopolysaccharides  
Very long chain fatty acids.  
Galactosaemia screening tests  
Free and total homocysteine  
Rhabdomyolysis  
Reyes Syndrome  
Leigh's Syndrome  
NTBC  
Cherry Red Spot  
Post mortem biochemical investigations  
Tandem mass spectrometry  
Sulphocysteine  
Metabolome  
Acylcarnitines  
Newborn bloodspot screening  
Leukocyte cystine measurement  
Fanconi syndrome

*This is merely a start of a list. As the various knowledge sessions are written more instances of topics suitable for inclusion in the Pathopaedia will appear.*

## Case Sessions

- 1 The child with the raised ammonia
- 2 The child with lactic acidemia
- 3 The hypoglycaemic child.