ERNDIM PROFICIENCY SCHEME (SCANDINAVIA & UK)

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Dear Colleague

Re: UK/Scandinavia Proficiency Scheme

Samples were despatched on the 26th April (04.1, 04.2 and 04.3) and 22nd July (04.4, 04.5 and 04.6) to the 25 participants in this scheme and returns were requested by 14th May and 13th August respectively. The clinical descriptions were given as:

Patient 04.1 *A female, aged 4 weeks with failure to thrive, serious dysmaturity, infections and hepatomegaly. The parents are consanguineous.*

This sample was obtained from a patient with mevalonate kinase deficiency – this was the Europe-wide common sample.

Patient 04.2 *A female, aged 16 years, unexplained loss of consciousness, bradycardia and reduced respiration rate.*

This samples was obtained from a young girl who had unknowingly been given the recreational drug GHB.

Patient 04.3 *A male, aged 16 years, mental retardation.*

The sample was obtained from a patient with phenylketonuria.

Patient 04.4 *A male, aged 15 years with osteoarthritis and hearing loss.*

This sample was obtained from a patient with Hunter disease (MPS type 2).

Patient 04.5 *A female, aged 10 days, vomiting and lethargy.*

The sample was obtained from a patient with maple syrup urine disease.

Patient 04.6 *A male, aged 3 years, failure to thrive.*

This sample was obtained from a normal child.

Results

Sample 04.1

Results were received from all of the 25 participants.

24/25 noted an increased excretion of mevalonic acid/or mevalonolactone. 13/25 participants noted a moderate dicarboxylic aciduria, 11 of these ascribing this to medium chain tryglyceride supplementation.

All 24 participants who identified the pathognomic metabolites concluded that the patient showed mevalonic aciduria. 19/24 suggesting that this resulted from deficiency of mevalonate kinase. 22/24 participants identifying the metabolites suggested that enzyme confirmation was indicated and 13/24 that mutation analysis should be undertaken. 2/24 suggested that immunoglobin studies should be undertaken to exclude hyperIgD syndrome associated with this condition. 6/24 recommended testing siblings to this index case.

Sample 04.2

Results were received from all of the 25 participants.

All 25 laboratories identified increased excretion of 4-hydroxybutyrate, 7 also commented in the excretion of the dihydroxy-butyrate. 11/25 concluded that these findings were likely to be due to succinic semialdehyde deficiency, 13/25 felt that the findings, linked with the clinical features, suggested that this was more likely to have been caused by GHB intoxication and 1/25 considered that both options were possible. Eight of the 11 who concluded succinic semialdehyde deficiency would have recommended enzyme confirmation and 6 of these would have tested any siblings. Seven of those who raised the possibility of GHB intoxication would have recommended further toxicological investigations.

Samples 04.3

Results were received from 24/25 participants.

21/24 commented upon an increased excretion of phenylalanine on aminoacid analysis. 2/24 considered the sample unsuitable due to bacterial degradation and 1/24 did not perform

aminoacid analysis. On organic acid analysis 22/24 participants reported an increased excretion of phenylalanine related metabolites and 2/24 considered the sample unsuitable for analysis due to bacterial degradation. All 22 participants who identified the key metabolites concluded that this came from a patient with PKU and 19/22 would have recommended plasma aminoacid analysis with 19/22 also recommending biopterin analysis. 6/22 would have suggested family studies.

Sample 04.4

Results were received from 22/25 participants.

18/22 noted an increased excretion of GAGS and/or a pattern suggestive of a mucopolysaccharide disorder. 11/18 commented specifically on the excretion of dermatan sulphate. 3/22 did not perform MPS analysis and 1/22 reported a "normal" result. 17/18 participants who demonstrated an increased excretion of mucopolysaccharides suggested a possible MPS disorder, 15/17 specifically considered MPS2 (Hunter disease) as a possibility. All 18 laboratories that noted an increased excretion of mucopolysaccharides would have recommended enzyme analysis and 3 would have advised testing siblings.

Sample 04.5

Results were received from 22/25 participants.

All 22 commented upon an increased excretion of one or more branched chain aminoacids (BCAA) on aminoacid analysis and 21/22 described an increased excretion of metabolites deriving from BCAA's on organic acid analysis. 21/22 participants concluded that MSUD was the most likely diagnosis with 21/22 going on to recommend plasma aminoacid analysis and 15/22 enzyme confirmation. One laboratory would have recommended testing other siblings.

Sample 04.6

Results were received from 22/25 participants

19/22 reported all investigations as normal or no significant abnormality and 11 of these were confident enough to conclude "no abnormality detected" in this child. The remaining 8 drew no overall conclusion. 3/22 commented on a reduced excretion of serine and/or threonine suggesting that this needed further investigation, all 3 recommended plasma aminoacid analysis.

Conclusions

Samples 04.1

Only one laboratory failed to recognise an increased excretion of mevalonic acid and would have missed the diagnosis.

4/continued

Sample 04.2

While all laboratories identified an increased excretion of 4-hydroxybutyrate almost half incorrectly assumed that this was due to an inherited metabolic disorder. This seems fairly unlikely in a 16 year old with an unexplained loss of consciousness, bradycardia and reduced respiration rate – features known to be associated with GHB intoxication.

Sample 04.3

All participants who analysed this sample recognised that this came from a patient with PKU.

Sample 04.4

Only one laboratory performing MPS analysis failed to detect an increased excretion.

Sample 04.5

While all 22 laboratories identified an increased excretion of branched chain aminoacids or their metabolites, one laboratory failed to conclude that the patient had MSUD.

Sample 04.6

Only 11 of the 22 laboratories submitting reports would have given a clear overall conclusion suggesting that no abnormality could be detected. While EQA schemes do not simulate real conditions this is a little worrying. In a number of reports the clinicians using the service may have been left a little confused and would have been led into additional investigations by three laboratories where the findings (low threonine and serine) could have easily been explained by the age of the sample.

The scores assigned to individual laboratories are shown in the table attached.

Yours sincerely

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Scheme Organiser