# ERNDIM PROFICIENCY SCHEME (NORTHERN EUROPE)

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Dear Colleague

**Re: ERNDIM Proficiency Scheme Report – Samples 07.1, 07.2, 07.3, 07.4, 07.5, 07.6**

Six samples were distributed in two batches to 21 participants, returns were received from 21 participants for samples 07.1, 07.2 & 07.3 and from 21 participants for samples 07.4, 07.5 & 07.6.

## Patient 07.1

*Male, aged 5 years with dysmorphia and speech delay*
**This sample was obtained from a patient with MPS type 2**

**Findings**

19/21 laboratories identified an increased excretion of dermatan and/or heparan sulphate.

**Conclusions**

All participants who identified an increased excretion of dermatan and/or heparan sulphate concluded that a mucopolysaccharide disorder was likely. 16/19 indicated that MPS type 2 was either likely or possible.

**Further investigations**

All 19 laboratories identifying an increased excretion of dermatyan/heparan sulphate would have recommended leucocyte enzyme assay.

**Comment**

It is reassuring that all laboratories undertaking MPS analysis identified an increase in either dernatan or heparan sulphate or both. The laboratory not identifying this increase did not report on MPS analysis.

## *Patient 07.2*

*Male, aged 5 years, unexplained seizures*
**This sample was obtained from a 5 year old male relative of laboratory staff**

**Findings and Conclusions**

17/21 participants reported no diagnostic findings and clearly concluded that no metabolic disorder was indicated. Three laboratories did not make this

clear conclusion and one felt that the findings suggested possible pyridoxine deficiency.

**Further investigations**

On this basis of these studies nine of the sixteen laboratories concluding that no metabolic disorder was present would not have recommended any further investigations.

**Comment**

It is understandably difficult in an EQA scheme for participants to have the confidence to conclude that a sample is "normal" and refrain from recommending unnecessary additional investigations.

## *Sample 07.3*

*A female, aged 18 years, learning difficulties and behavioural problems since 5 years of age. She also has short stature.*

**This sample was obtained from a 18 year old woman with saccharopinuria**

**Findings**

16/21 laboratories noted an increased excretion of lysine (mean concentration 289µmol/L, range 240-516 µmol/L). Seven of these identified the additional excretion of saccharopine. Five laboratories reported no significant abnormality on aminoacid analysis.

**Conclusions**

5/6 laboratories identifying the excretion of saccharopine concluded that deficiency of a-aminoadipic semi-aldehyde synthase was the most likely cause. In addition, three other laboratories who failed to identify the saccaropine excretion, nevertheless considered that this enzyme deficiency was the likely diagnosis.

Four laboratories concluded that lysinuric protein intolerance was the probable diagnosis and five others felt that this was possible.

All four laboratories who failed to report any significant abnormality of aminoacids concluded that no metabolic disorder could be diagnosed.

**Further investigations**

14/16 laboratories reporting an increased excretion of lysine indicated the need for plasma aminoacid analysis to help determine its significance.

Of the five participants who identified an excretion of saccharopine and correctly suggested a diagnosis of a-aminoadipic semi-aldehyde synthase deficiency, three would have recommened enzyme analysis or molecular genetic analysis to help confirm the defect. One of the five felt that this was unesesary and the other did not comment.

**Comment**

It is disappointing that only five participants identified an excretion of saccharopine in this sample and a little surprising that four laboratories concluded that lysinuric protein intolerance was the most probable diagnosis despite the relatively normal extretion of ornithine and arginine.

## *Sample 07.4*

*Female, 5 years of age with developmental delay*

**This sample was collected from a 5 year old female relative of laboratory staff**

**Findings**

No participants identified any significant findings in this sample.

**Conclusions**

19/21 laboratories who returned results concluded that no metabolic disorder was indicated in this patient. The remaining laboratories failed to state a clear conclusion.

**Further investigations**

Three laboratories would have advised additional investigations.

**Comment**

It is reassuring that all but two laboratories would have clearly concluded that no metabolic disorder was indicated from these investigations.

## *Sample 07.5*

*Male, aged 3 years with motor and psychosomal retardation*

**This sample was obtained from boy aged twelve years with Lesch-Nyhan syndrome (HPRT deficiency)**

**Findings**

Only 3/21 participants identified an increased urate : creatinine ratio. 2/21 reported an increased excretion of GAGS; 10/21 reported some abnormalities on aminoacid analysis, although four of these commented that they were unlikely to be significant; 16/21 reported some abnormalities on organic acid analysis, 10 of these commenting on the presence of paracetamol and 9 considering that lactate excretion was increased. Only one laboratory reported uniformly normal findings.

**Conclusions**

Two of the laboratories who identified an increased urate:creatinine ratio considered that HPRT deficiency was the probable diagnosis. 9/21 raised the possibility of other diagnoses including two who considered that an MPS disorder was likely or possible. 8/21 considered that no metabolic disorder was indicated and 2/21 failed to draw any conclusion from the findings.

**Further investigations**

5/21 participants would have recommended analysis for purine/pyrimidine metabolites with 11 others recommending a range of additional investigations.

**Comment**

Participants found this a difficult sample. The ratio of urate:creatinine was increased but only slightly (in our laboratory 0.98 mmol/mmol cr, ref range 0.3-0.8) as the child was receiving allopurinol. Hypoxanthine and xanthine were significantly elevated secondary to the enzymic inhibition. This case emphasises both the value and limitations of urate measurement as part of a metabolic screen.

## *Sample 07.6*

*Female, aged 3 years with delayed motor development, sitting at 9 months, walking at 2 years*

**This sample was obtained from a girl of 5 yrs with glutaric aciduria type 1**

**Findings**

All 21 participants returning results identified an increased excretion of glutarate. 19/21 also commented on an increased excretion of the pathogonomic metabolite 3-hydroxyglutarate. 5/21 specifically noted the absence of acylglycine excretion. 6/21 reported a ketonuria in association with the other findings.

**Conclusions**

All 21 participants returning results concluded that the sample was obtained from a patient with glutaric aciduria type 1

**Further investigations**

17/21 participants recommended enzyme confirmation and 17/21 acylcarnitine analysis. Only 6/21 commented on the need to test other siblings.

**Comment**

It is reassuring that all participants returning results identified an increased excretion of glutarate and concluded that the patient had glutaric aciduria type 1. It is surprising that two did not comment on the presence of 3-hydroxyglutarate and that less than one third would have advised that other siblings should be tested.

Overall this was quite a challenging set of samples, the scores are attached.

**Sample receipt and results return**

*Circulation 7.1,7.2,7.3*

Nine participants received the samples on the day following dispatch; four, 2 days later; two, 3 days later; three, 4 days later; two, 8 days later and one did not report.

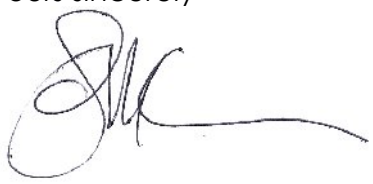
Eighteen reported on time, one was 11 days late and one 24 days late.

*Circulation 7.4,7.5,7.6*

Fourteen participants received the samples on the day following dispatch; three, 2 days later; one, 8 days later and two did not report. One sample set was lost in the post and had to be re-issued.

All participants submitted reports on time.

Yours sincerely



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