Diagnostic Proficiency Testing Centre: United Kingdom Final Report 2019

prepared by
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Note: This annual report is intended for participants of the ERNDIM DPT UK scheme. The contents should not be used for any publication without permission of the Scientific Advisor.

The fact that your laboratory participates in ERNDIM schemes is not confidential, however, the raw data and performance scores are confidential and will only be shared within ERNDIM for the purpose of evaluating your laboratories performance, unless ERNDIM is required to disclose performance data by a relevant government agency. For details please see the terms and conditions on page18 and the ERNDIM Privacy Policy on www.erndim.org.

In 2019, 22 labs participated to the Diagnostic Proficiency Testing Scheme UK.

1. Geographical distribution of participants

For both surveys all 22 laboratories submitted results.

Country	Number of participants
Australia	1
Czechia	1
Ireland	1
Malaysia	1
New Zealand	2
Spain	1
United Kingdom	15

2. Design and logistics of the scheme including sample information

The scheme has been designed and planned by Joanne Croft as Scientific Advisor and coordinated by Xavier Albe as scheme organiser (sub-contractor on behalf of CSCQ), both appointed by and according to procedures laid down the ERNDIM Board.
CSCQ dispatches DPT EQA samples to the scheme participants and provides a website for on-line submission of results and access to scheme reports. Existing DPT and Urine MPS scheme participants can log on to the CSCQ results submission website at:
https://cscq.hcuge.ch/cscq/ERNDIM/Initial/Initial.php

2 surveys	Round 1: patients A, B and C
	Round 2: patients D, E and F

Origin of patients: all urine samples have been provided by either the DPT scheme organizers or specified participants. One by DPT Switzerland, two by DPT Czech Republic, one by DPT Netherlands, one by Sheffield Children's NHS foundation trust (UK) and one by Birmingham Children's NHS foundation trust (UK).

Patient A: Adenine phosphoribosyltransferase (APRT) deficiency.
Patient B: Barth syndrome.
Patient C: Lysinuric protein intolerance.
Patient D: Normal 13 year old boy.
Patient E: Classical homocystinuria.
Patient F: Mucopolysaccharidosis Type III C.

The samples have been heat-treated. They were pre-analysed in our institute after 3 days incubation at ambient temperature (to mimic possible changes that might arise during transport). In all six samples the typical metabolic profiles were preserved after this process.
Mailing: samples were sent by DHL; FedEx or the Swiss Post at room temperature.

3. Tests

Analyses of amino acids, organic acids, mucopolysaccharides, oligosaccharides and purines/pyrimidines were required in 2019.

4. Schedule of the scheme

- February 5, 2019: shipment of samples
- March 4, 2019: analysis start and website availability of clinical information (Survey 1)
- March 25, 2019: deadline for result submission (Survey 1)
- June 3, 2019: analysis start and website availability of clinical information (Survey 2)
- June 24, 2019: deadline for result submission (Survey 2)
- Sept 3, 2019: ERNDIM participants meeting, Rotterdam
- Nov 21/22, 2019: ERNDIM SAB meeting, Manchester
- January 12, 2020: annual report distributed.

5. Results

22 of 22 labs returned results for both surveys, all by the deadline.

	Survey 1	**Survey 2**
Receipt of results	22	22
No answer	0	0

6. Website reporting

The website reporting system is compulsory for all centres. Please read carefully the following advice:

- Selection of tests: **don't select a test if you will not perform it**, otherwise the evaluation program includes it in the report.
- Results
  - Give quantitative data as much as possible.
  - Enter the key metabolites with the evaluation **in the tables** even if you don't give quantitative data.
  - If the profile is normal: enter "Normal profile" in "Key metabolites".
  - **Don't enter results in the "comments" window**, **otherwise your results will not be included in the evaluation program.**
- Recommendations = **advice for further investigation**.
  - Scored together with the interpretative score.
  - Advice for treatment are not scored.
  - **Don't give advice for further investigation in "Comments on diagnosis"**: it will not be included in the evaluation program.

7. Scoring and evaluation of results

Information regarding procedures for establishment of assigned values, statistical analysis, interpretation of statistical analysis etc. can be found in generic documents on the ERNDIM website.
The scoring system has been established by the International Scientific Advisory Board of ERNDIM. Two criteria are evaluated: 1) analytical performance, 2) interpretative proficiency also considering recommendations for further investigations.

A	Analytical performance	Correct results of the appropriate tests	2
		Partially correct or non-standard methods	1
		Unsatisfactory or misleading	0
I	Interpretative proficiency & Recommendations	Good (diagnosis was established)	2
		Helpful but incomplete	1
		Misleading or wrong diagnosis	0

The total score is calculated as a sum of these two criteria. The maximum to be achieved is 4 points per sample. The scores were calculated only for laboratories submitting results.

Scoring and certificate of participation: scoring is carried by a second assessor who changes every year as well as by the scientific advisor. The results of DPT UK 2019 have been also scored by Dr Christine Saban, from DPT France. At the SAB meeting in November 2019, the definitive scores have been finalized. The concept of critical error was introduced in 2014. A critical error is defined as an error resulting from seriously misleading analytical findings and /or interpretations with serious clinical consequences for the patient. Thus labs failing to make a correct diagnosis of a sample considered as eligible for this category will be deemed not to have reached a satisfactory performance even if their total points for the year exceed the limit set at the SAB. For 2019, the SAB decided that sample C has to be considered as a critical error for any labs who failed to identify an increase of orotic acid.

A certificate of participation will be issued for participation and it will be additionally notified whether the participant has received a performance support letter. This performance support letter is sent out if the performance is evaluated as unsatisfactory. Two performance support letters will be sent by the Scheme Advisor for 2019. Any partial submitters will receive a letter from the ERNDIM Executive Administrator, Sara Gardner.

7.1. Score for satisfactory performance

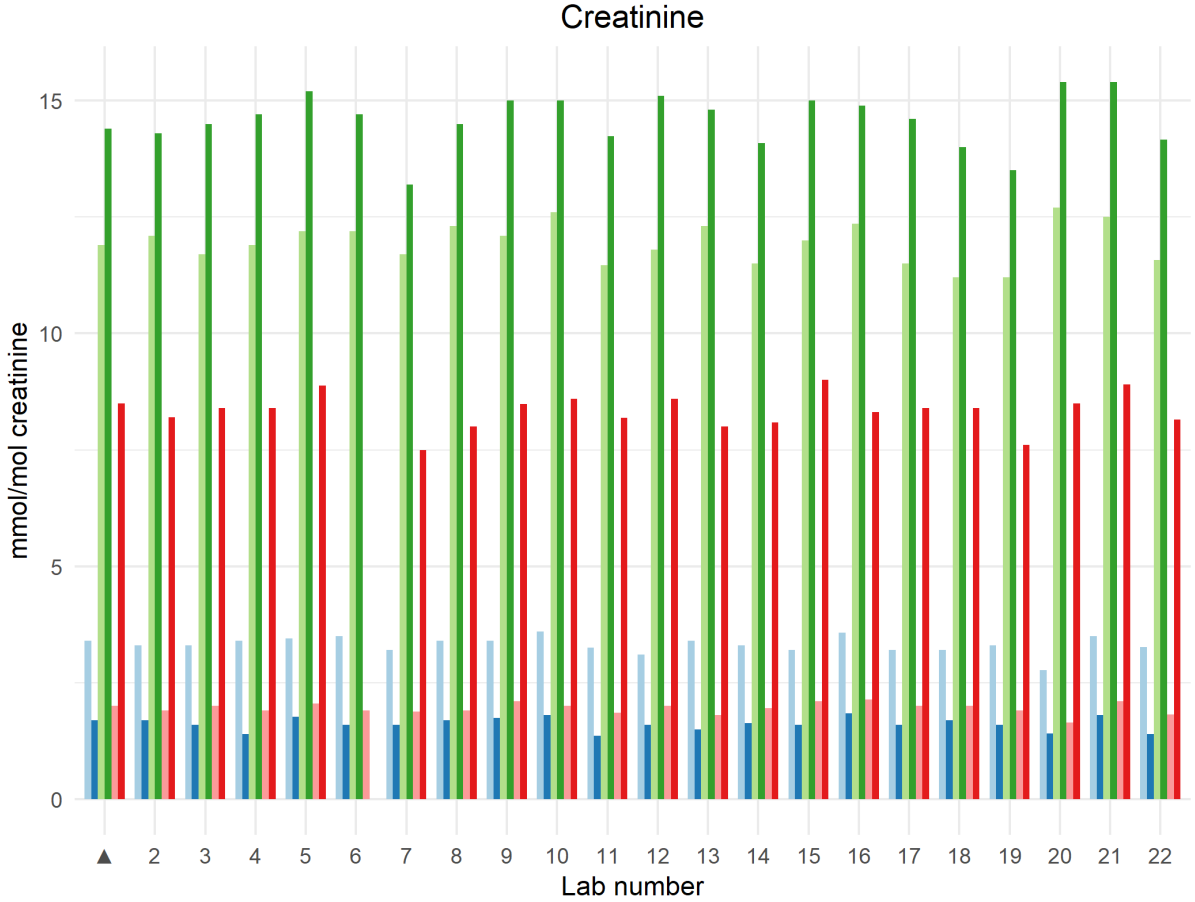
At least 15 points from the maximum of 24 (62%).

8. Results of samples and evaluation of reporting

8.1. Creatinine measurement for all samples

Creatinine analysis was good for all labs this year apart from 1 lab who did not submit a creatinine result for Sample F.

Creatinine concentrations



Sample	A	B	C	D	E	F
Mean	3.32	1.62	11.95	14.58	1.95	8.34
SD	0.18	0.14	0.43	0.57	0.12	0.38

8.2. Patient A

Adenine phosphoribosyltransferase(APRT)deficiency.

Patient details provided to participants

The female was admitted to hospital due to a history of pain on passing urine. Had been treated but urine collected off treatment.

Patient details

This was the common sample sent out to all the DPT scheme participants in 2019. The sample was provided by Professor Brian Fowler, Switzerland.

Analytical performance

7/22 laboratories reported increased 2,8 dihydroxy adenine

- Of these, 4 provided quantitative results
  - 0.083 mmol/L (n =1)
  - 0.083 mmol/mol creatinine (n=1)
  - 25 mmol/mol creatinine (n = 2)
- Units issue – it is 0.083 mmol/L which, given a creatinine of 3.4 mmol/l, is 25 mmol/mol

The remaining laboratories did not detect/report either 2,8 dihydroxy adenine or adenine. All participants performed amino acid and organic acid analysis and reported essentially normal results

Diagnosis / Interpretative proficiency

The 7 laboratories who reported the 2,8 dihydroxy adenine correctly diagnosed this as APRT deficiency and scored 2 marks for interpretation (4 marks in total). 7/22 laboratories scored 0 marks for this sample. 6 laboratories scored 1 mark for interpretation (1 mark in total) as they recommended purine/pyrimidine analysis. 2 laboratories scored 2 marks - both suggested a purine/pyrimidine disorder as a diagnosis of exclusion and recommended purine/pyrimidine analysis

Recommendations

- 4/22 - APRT gene mutation analysis
- 8/22 – purine/pyrimidine analysis
- 5/22 – enzyme activity in RBCs
- 5/22 – consider UTI
- 4/22 – refer to specialist
- 4/22 – family studies/genetic counselling

Scoring

- **Analytical results:**
  - Increase of 2,8-dihydroxyadenine (score 2)
  - Increase of adenine without identification of 2,8-dihydroxyadenine (score 1)
- Interpretation of results:
  - APRT deficiency as first or alternative diagnosis (score 2)
  - Advice to perform purine and pyrimidine analysis (score 1)

Overall impression

Overall, performance for this sample was poor within the UK DPT scheme participants (43% proficiency). This may be due to the fact that currently in the UK there is only 1 laboratory performing purine and pyrimidine analysis. Participants are reminded that use of a referral laboratory is allowed under the terms of the scheme but that you must take responsibility for the results you enter.

8.3. Patient B

Barth syndrome

Patient details provided to participants

Patient hospitalised for infection. Tachypnoea was noticed and ultrasound revealed dilated congestive heart failure. Motor milestones were slightly delayed.

Analytical performance

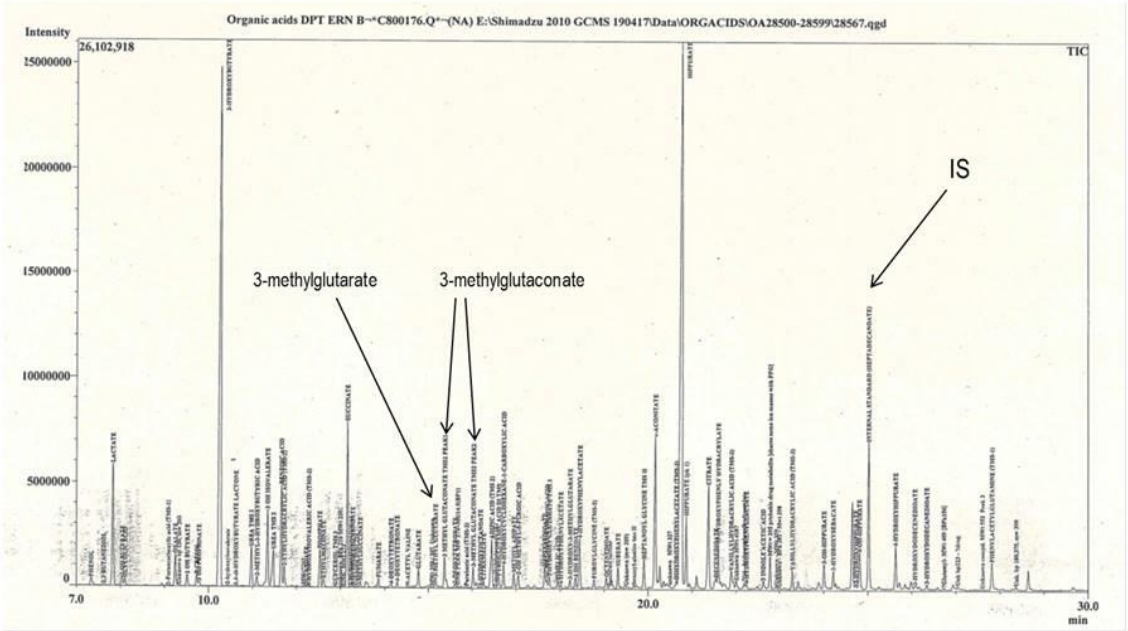
- 20/22 participants scored 2 marks for analysis
  - all detected the increased 3 methylglutaconic acid

- 2/22 participants scored 0 marks for analysis

- both missed the 3 methylglutaconic acid with one reporting a normal profile and the other reporting an increase in 3 hydroxy butyrate

Diagnosis / Interpretative proficiency

- 19/22 participants scored 2 marks for interpretation
- 3/22 participants scored 0 marks for interpretation
  - 1 participant who had detected the increased 3 methylglutaconic acid did not take this into consideration when interpreting the results and concluded SCOT deficiency based on the increased 3 hydroxy butyrate and scored 0 marks for interpretation
  - The other 2 participants did not detect the 3 methylglutaconic acid and both concluded an MPS disorder
    - Both had measured an increased GAG concentration. One reported a borderline fractionation result, the other did not report GAG fractionation.
    - Of all the participants who reported on GAGs, 13 reported a normal quantitative result, 6 an elevated result. However, only these 2 participants concluded an MPS disorder as either primary or other diagnosis.



Sample B - organic acid chromatogram

Recommendations

- 16/22 – cardiolipin investigations
- 17/22 – mutation analysis of the TAZ gene
- 6/22 – reminder that other forms of 3 methyl glutaconic aciduria cannot be ruled out and need to be considered
- 5/22 – check whether patient is neutropaenic
- 6/22 – family screening/genetic counselling

Scoring

- Analytical –
  - detecting increased 3 methyl glutaconate (score 2)
- Interpretation –
  - Barth syndrome (score 2)
  - 3 methylglutaconic aciduria of any type (score 2)

Overall impression

Performance for this sample was good (86% proficiency).

8.1. Patient C

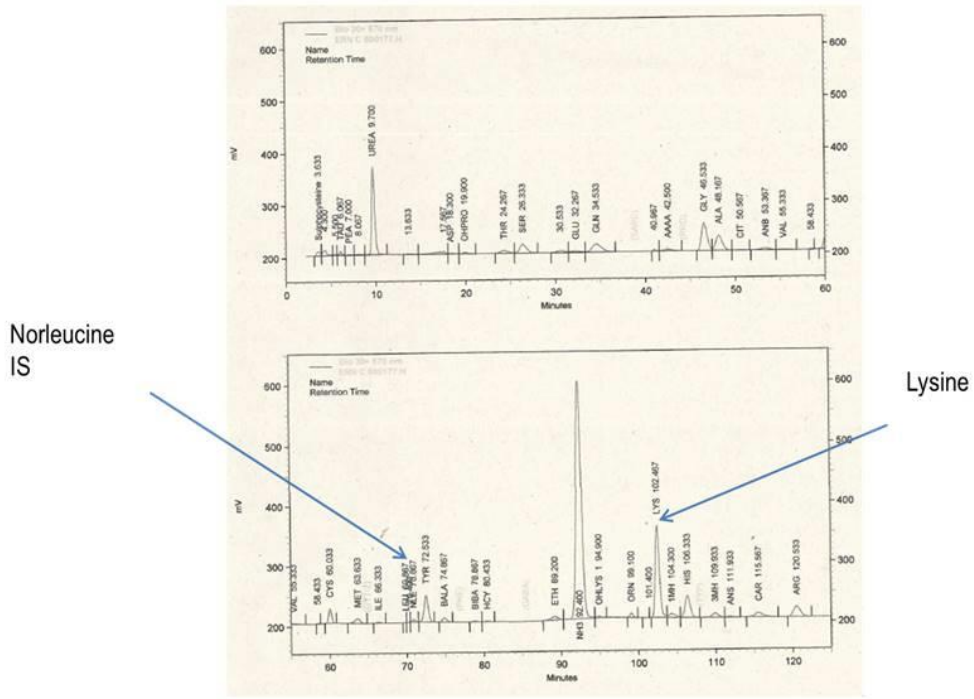
Lysinuric protein intolerance

Patient details provided to participants

A 4 years old boy with splenomegaly,failure to thrive and a special eating behaviour. The sample was collected at the age of 17 years during a routine check-up while receiving specific treatment. The diagnosis was established by molecular analysis.

Analytical performance

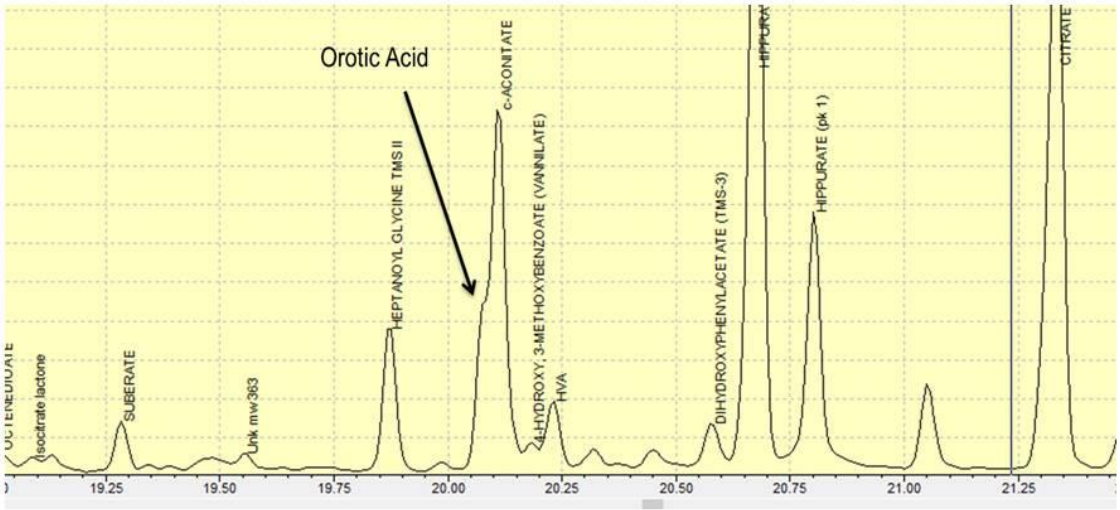
- 21/22 participants scored 2 marks for analysis (1 scored 1 mark)
- Lysine
  - All the participants detected the increased lysine concentration
  - 20/22 provided a quantitative result (in mmol/mol creatinine)
    - Median = 302 SCH result = 275 (ref. 73 – 250)
    - Mean = 371.8
    - Range = 185 – 1790



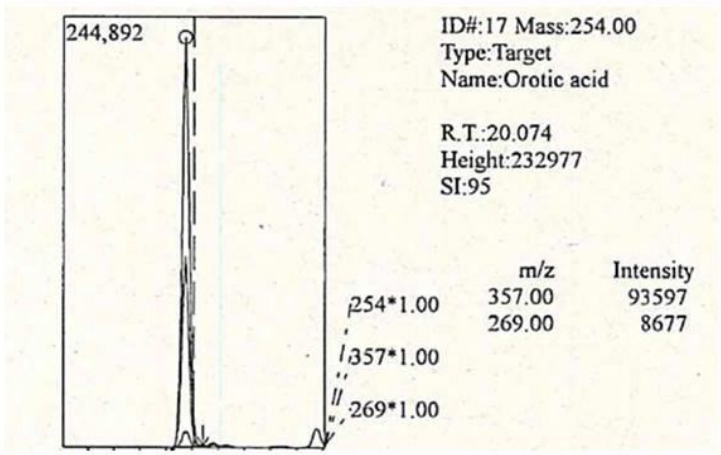
Sample C - Biochrom amino acid analyser trace

- Orotate
  - 1 participant did not detect the orotic acid (gave a quantitative value of 0.1 mmol/mol creatinine)
  - Meaning that 21 participants did
  - 11/21 provided a quantitative result (excluding the 0.1 mmol/mol result)
    - Median = 47.5 mmol/mol creatinine SCH result = 41.9 (ref.< 3.5)
    - Mean = 55.2
    - Range = 25 – 138

Failure to detect the increased orotic acid has been deemed to be a critical error by the Scientific Advisory Board.



Sample C - orgnic acid chromatogram showing presence of orotic acid



Sample C - extracted ions for orotic acid

Diagnosis / Interpretative proficiency

- 21/22 participants scored 2 marks for interpretation
    - Gave LPI as the diagnosis
- 1 participant scored 0 marks

  Despite detecting a clearly elevated lysine (reported 308 mmol/mol) this lab felt the most likely diagnosis was an MPS disorder. This lab did not detect the orotic acid (gave a quantitative value of 0.1 mmol/mol)

Recommendations

- 18/22 – Mutation analysis of the SLC7A7 gene
- 16/22 – Urgent plasma ammonia
- 17/22 – Plasma amino acids
- 16/22 – Metabolic referral
- 5/22 – Repeat urine
- 7/22 – Genetic counselling/family testing
- 6/22 - FBC/LDH/Ferritin
- 1/22 - Periodic evaluation of renal function and lung involvement
- 1/22 - Enzyme studies (liver) – this seems an unnecessary and invasive test given that the diagnosis can be confirmed by genetics. They also suggested molecular testing.

Scoring

- Analytical –
    - Detecting increased lysine concentration (score 1)
    - Detecting orotic acid (score 1)
- Interpretation
    - Concluding lysinuric protein intolerance (score 2)
    - Normal or wrong diagnosis – (score 0)

Overall impression

Performance for this sample was very good with overall proficiency of 97%. There were fewer laboratories who failed to detect the orotic acid than seen in previous years.

8.1. Patient D

Sample from a normal healthy boy

Patient details provided to participants
Teenager with deteriorating performance at school.

Patient details
This sample was obtained from a healthy boy with no suspected inborn error of metabolism.

Analytical performance

- 19/22 participants scored 2 marks for analysis
- 2/22 participants scored 1 mark for analysis
  - 1 laboratory detected possible ASA and anhydrides on amino acid analysis though they couldn't confidently report as ASA. Would ask for plasma sample for confirmation
  - 1 laboratory obtained equivocal results on their oligosaccharide analysis and stated that they couldn't exclude aspartylglucosaminuria
- 1/22 participants scored 0 marks for analysis
  - they found an increased concentration of glycosaminoglycans (gave a result of 15, mean result of all labs = 6.2, n = 21). They concluded to an MPS disorder.

Diagnosis / Interpretative proficiency

- 20/22 participants scored 2 marks
  - the participant who had detected possible ASA and anhydrides concluded to no diagnosis and therefore scored 2 marks for interpretation
- 2/22 participants scored 0 marks
  - the participant who reported an elevated GAG result and concluded an MPS disorder
  - the participant who concluded aspartylglucosaminuria

Recommendations

- 4/22 – no further recommendations at this time/none
- 2/22 – section left blank
- 5/22- ask for full history/further clinical information
- 2/22 - suggest contact lab to discuss
- 6/22 – urine for purine/pyrimidine analysis
- 6/22 - plasma very long chain fatty acids
- 3/22 – lysosomal screen
- 2/22 - plasma amino acids
- 1/22- plasma ammonia (participant who mentioned ASA)
- 5/22 – refer to metabolic team/discussion with consultant inIMD

Scoring

- Analytical
  - Performing at least 3 analyses (not including the 'pre-investigations') and finding no significant abnormality (score 2)
- Interpretation
  - Concluding no significant abnormality (or similar) (score 2)
  - Concluding the wrong diagnosis (score 0)
  - Leaving diagnosis section blank or putting n/a (score 0)

Overall impression

Overall proficiency for this sample was 91%. This is comparable to previous years when urine from a healthy child has been used (2018 – 92.9%, 2017 – 95.5%).

8.1. Patient E

Classical homocystinuria

Patient details provided to participants

Patient presented with subluxed lenses, high arched palate and learning difficulties. She had long standing joint problems including scoliosis.

Patient details

She was diagnosed at 13 years of age and has been shown to be pyridoxine responsive.

Analytical performance

- 20/22 participants scored 2 marks for analysis
  - all participants detected the homocystine
  - SCH homocystine result = 65 µmol/mmol creatinine (ref. 0 – 3)
- 2/22 participants scored 1 mark for analysis
  - 1 lab did not perform quantitative methylmalonic acid (MMA) or organic acid analysis
  - 1 lab reported an increased MMA concentration

Diagnosis / Interpretative proficiency

- 21/22 participants scored 2 marks
  - 1 lab did not recommend performing either total homocysteine or CBS gene analysis

Recommendations

- 21/22 – total homocysteine in plasma *
- 19/22 – plasma amino acids
- 15/22 – genetic testing (CBS and MTHFR genes mentioned)
- 14/22 – refer to metabolic team
- 10/22 – measure folate, Vitamin B12
- 8/22 – assess for pyridoxine responsiveness
- 6/22 – measure plasma/urine MMA
- 8/22 – sibling/family studies
- * 1 lab gave no recommendations

Scoring

- Analytical
  - Increased homocystine or homocysteine-cysteine mixed disulphide (score 1)
  - No increase in methylmalonic acid or normal organic acid profile (score 1)
- Interpretation
  - CBS deficiency, homocystinuria with recommendation to perform plasma amino acids and total homocysteine or CBS gene analysis (score 2)
  - Homocystinuria without recommendation (score 1)

Overall impression

Overall proficiency for this sample was 97%. Measurement of plasma total homocysteine in plasma should be mandatory after finding homocystine in urine.

8.1. Patient F

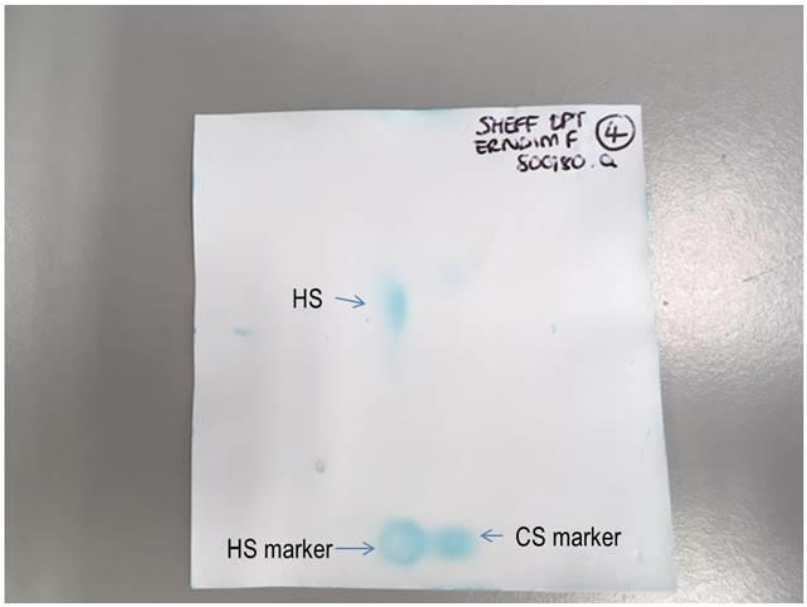
Mucopolysaccharidosis Type III C

Patient details provided to participants

Patient born after a complicated pregnancy. Since the age of 7 years a regression in psychomotor development was observed. The sample was obtained at the age of 19 years when the patient was receiving treatment. The diagnosis was established by molecular analysis.

Analytical performance

- 18/22 participants scored 2 marks
  - Detected the heparan sulphate
- 4/22 participants scored 1 mark
  - 3 detected increased GAG concentration but did not perform GAG fractionation
  - 1 detected increased heparan but also increased dermatan
  - SCH GAG result = 18.4 mg/mmol (ref. 1.7 – 4.4)



Sample F - glycosaminoglycan electrophoresis showing heparan sulphate

Diagnosis / Interpretative proficiency

- 16/22 scored 2 marks for interpretation
- 5/22 scored 1 mark for interpretation
  - 3 who had not performed GAG fractionation
  - 1 lab who had concluded to MPS I,II, III or VII
  - 1 lab who had concluded to MPS Type 2
- 1/22 scored 0 for interpretation
  - they had detected the increased heparan sulphate but concluded no clear diagnosis without further investigation

Recommendations

- 8/22 – fresh urine for repeat GAG analysis
- 16/22 – enzyme assays
- 11/22 – molecular analysis in the gene for deficient enzyme
- 14/22 – refer to metabolic team
- 5/22 – exclude heparin therapy as cause of MPS screen results
- 7/22 – family testing
- 1/22 – refer to clinical genetics
- The lab who gave MPSII as their diagnosis stated 'since it is a known case and already confirmed by molecular analysis, no further recommendation'. In the future I will not state whether there is already molecular confirmation of the case with the clinical details you are provided. DPT urines should be treated as though they are diagnostic samples.

Scoring

- Analytical
  - Detecting increased heparan sulphate - (score 2)
  - Increased GAG quantitation if electrophoresis not done (score 1)
- Interpretation
  - MPS IIIC (score 1)
  - MPS disorder (score 1)

Overall impression

Proficiency for this sample is good (88% overall).

9. Scores of participants

All data transfer, the submission of data as well as the request and viewing of reports proceed via the DPT-CSCQ results website. The results of your laboratory are confidential and only accessible to you (with your username and password).The anonymous scores of all laboratories are accessible to all participants and only in your version is your laboratory highlighted in the leftmost column.

Detailed scores – Round 1

Lab n°	Patient A Adenine phosphoribosyltransferase (APRT) deficiency.			Patient B Barth syndrome			Patient C Lysinuric protein intolerance.			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	2	2	4	2	2	4	12
2	0	0	0	2	2	4	2	2	4	8
3	2	2	4	1	1	2	2	2	4	10
4	0	1	1	2	2	4	2	2	4	9
5	0	1	1	2	2	4	2	2	4	9
6	2	2	4	2	2	4	2	2	4	12
7	2	2	4	0	0	0	2	2	4	8
8	0	0	0	0	0	0	2	2	4	4
9	0	0	0	2	2	4	2	2	4	8
10	0	0	0	2	2	4	2	2	4	8
11	0	1	1	2	2	4	2	2	4	9
12	0	1	1	2	2	4	2	2	4	9
13	2	2	4	2	2	4	2	2	4	12
14	0	2	2	2	2	4	2	2	4	10
15	0	0	0	2	2	4	2	2	4	8
16	0	0	0	2	2	4	2	2	4	8
17	0	0	0	2	2	4	2	2	4	8
18	0	1	1	2	2	4	2	2	4	9
19	0	2	2	2	2	4	1	0	1	7
20	2	2	4	2	2	4	2	2	4	12
21	2	2	4	2	2	4	2	2	4	12
22	0	1	1	2	0	2	2	2	4	7

Detailed scores – Round 2

Lab n°	Patient D Normal 13 year old boy.			Patient E Classical homocystinuria.			Patient F Mucopolysaccharidosis Type III C			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	2	2	4	2	2	4	12
2	2	2	4	2	2	4	2	2	4	12
3	2	2	4	2	2	4	2	0	2	10
4	2	2	4	2	2	4	2	2	4	12
5	2	2	4	2	2	4	2	2	4	12
6	2	2	4	2	2	4	2	2	4	12
7	2	2	4	2	2	4	1	1	2	10
8	1	0	1	2	2	4	2	2	4	9
9	2	2	4	2	2	4	2	2	4	12
10	2	2	4	2	2	4	2	1	3	11
11	2	2	4	2	2	4	2	2	4	12
12	2	2	4	1	2	3	2	2	4	11
13	2	2	4	2	2	4	2	2	4	12
14	0	0	0	2	2	4	1	1	2	6
15	2	2	4	2	1	3	2	2	4	11
16	2	2	4	2	2	4	1	1	2	10
17	2	2	4	2	2	4	2	2	4	12
18	2	2	4	2	2	4	2	2	4	12
19	2	2	4	1	2	3	2	2	4	11
20	2	2	4	2	2	4	2	2	4	12
21	1	2	3	2	2	4	2	2	4	11
22	2	2	4	2	2	4	1	1	2	10

Total scores

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score (%)	Critical error
1	4	4	4	4	4	4	24	100	
2	0	4	4	4	4	4	20	83	
3	4	2	4	4	4	2	20	83	
4	1	4	4	4	4	4	21	88	
5	1	4	4	4	4	4	21	88	
6	4	4	4	4	4	4	24	100	
7	4	0	4	4	4	2	18	75	
8	0	0	4	1	4	4	13	54	
9	0	4	4	4	4	4	20	83	
10	0	4	4	4	4	3	19	79	
11	1	4	4	4	4	4	21	88	
12	1	4	4	4	3	4	20	83	
13	4	4	4	4	4	4	24	100	
14	2	4	4	0	4	2	16	67	
15	0	4	4	4	3	4	19	79	
16	0	4	4	4	4	2	18	75	
17	0	4	4	4	4	4	20	83	
18	1	4	4	4	4	4	21	88	
19	2	4	1	4	3	4	18	75	CE
20	4	4	4	4	4	4	24	100	
21	4	4	4	3	4	4	23	96	
22	1	2	4	4	4	2	17	71	

Performance

	Number of labs	% total labs
Satisfactory performers (≥ 60 % of adequate responses)	20	91
Unsatisfactory performers (< 60 % adequate responses and/or critical error)	2	9
Partial and non-submitters	0	0

Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
DPT-US-2019-A	Adenine phosphoribosyltransferase (APRT) deficiency.	32	55	43
DPT-US-2019-B	Barth syndrome	89	84	86
DPT-US-2019-C	Lysinuric protein intolerance.	98	95	97
DPT-US-2019-D	Normal 13 year old boy.	91	91	91
DPT-US-2019-E	Classical homocystinuria.	95	98	97
DPT-US-2019-F	Mucopolysaccharidosis Type III C	91	84	88

10. Annual meeting of participants

This took place in Rotterdam on September 3rd 2019, before the SSIEM Meeting.

Participants

We remind you that attending the annual meeting is an important part of the proficiency testing. The goal of the program is to **improve** the competence of the participating laboratories, which includes the critical review of all results with a discussion about improvements.

11. Information from the Executive Board and the Scientific Advisory Board

- New **reference materials** are now provided by SKML: they are not related to EQA samples anymore. There are two concentration levels for each group of analytes. The most suitable low and high concentration levels are defined by the respective scientific advisors. Analytes and their concentrations will be approximately the same in consecutive batches of control material. These reference materials can be ordered through the ERNDIM website. Participants are encouraged to use them as internal control, but they cannot be used as calibrants. On the website a new section for data management completes the ERNDIM internal Quality Control System. Laboratories have the option to submit results and request reports showing their result in the last run in comparison to defined acceptance limits, their own historical data and the mean of all laboratories using the same batch control material.

- A set of **organic acid mixtures** has been developed by Dr Herman ten Brink in Amsterdam, following request and advice from ERNDIM. The product is currently available at: HJ.tenBrink@VUmc.nl
- **Urine samples**: we remind you that every year, each participant must provide to the scheme organizer at least 300 ml of urine from a patient affected with an established inborn error of metabolism or "normal" urine, together with a short clinical report. If possible, please collect 1500 ml of urine: this sample can be sent to all labs participating to one of the DPT schemes. Each urine sample must be collected from a single patient (don't send urine spiked with pathological compounds). Please don't send a pool of urines, except if urine has been collected on a short period of time from the same patient. For "normal" urine, the sample must be collected from a symptomatic patient (don't send urine from your kids!). As soon as possible after collection, the urine sample must be heated at 50 °C for 20 minutes. Make sure that this temperature is achieved in the entire urine sample, not only in the water bath. Then aliquot the sample in 10 ml plastic tubes (minimum 48 tubes), add stoppers and freeze. Be careful to constantly homogenize the urine while aliquoting the sample. Send the aliquots on dry ice by rapid mail or express transport to:

  Mrs Joanne Croft
  Dept of Clinical Chemistry
  Sheffield Children's NHS Foundation
  Trust, Western Bank
  Sheffield, S10 2TH
  United Kingdom
  Tel: +44(0)114 271 7000 Ext 17267
  Fax: +44(0)114 276 6205
  Email: Joanne.Croft@sch.nhs.uk

  Please send us an e-mail on the day you send the samples.

12. Reminders

We remind you that to participate to the DPT-scheme, you must perform at least:
- Amino acids
- Organic acids
- Oligosaccharides
- Mucopolysaccharides

If you are not performing one of these assays, you can send the samples to another lab (cluster lab) but you are responsible for the results.
Please send quantitative data for amino acids and, as much as possible, for organic acids.

13. Tentative schedule in 2020

Sample distribution	11 February 2020
Start of analysis of Survey 2020/1 Website open	March 9
Survey 2020/1 - Results submission	March 30
Survey 2020/1 - Reports	April
Start of analysis of Survey 2020/2	June 8
Survey 2020/2 – Results submission	June 29
Survey 2020/2 - Reports	July
Annual meeting of participants	Sept 1st Freiburg, Germany SSIEM
Annual Report 2020	December

14. ERNDIM certificate of participation

A combined certificate of participation covering all EQA schemes will be provided to all participants who take part in any ERNDIM scheme. For the DPT scheme this certificate will indicate if results were submitted and whether satisfactory performance was achieved in the scheme.

Date of report, 2020-03-03

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