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# Diagnostic Proficiency Testing
# Centre: Switzerland

## Final Report 2020

prepared by
Brian Fowler and Deborah Mathis

**Published:** 17 February 2021[1]

**Note**: This annual report is intended for participants of the ERNDIM DPT Switzerland 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 ERNDIM Privacy Policy on www.erndim.org.
In 2020, 22 labs participated in the Proficiency Testing Scheme Switzerland.

### 1. Geographical distribution of participants

For both the first and second survey 22 laboratories submitted results.

| Country | Number of participants | Country | Number of participants |
|---|---|---|---|
| Australia | 3 | Norway | 1 |
| Austria | 2 | Sweden | 2 |
| Canada | 3 | Switzerland | 2 |
| Estonia | 1 | United Kingdom | 1 |
| Germany | 3 | United States of America | 3 |
| Hong Kong | 1 | | |

### 2. Design and logistics of the scheme including sample information

The scheme has been designed and planned by Brian Fowler and Déborah Mathis as Scientific Advisors 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 |

1 If these scheme instructions are not Version 1 for this scheme year, go to APPENDIX 1 for details of the changes made since the last version of this document

**Origin of patients**: Three of the urine samples were provided by the scheme organizers themselves, and one each by Christine Saban, Lyon: Jurgita Songailiene, Vilnius and George Ruijter, Rotterdam.

Patient A: PKU
Patient B: α-Mannosidosis
Patient C: No IEM
Patient D: SSADH deficiency
Patient E: SCAD deficiency
Patient F: HHH Syndrome

The samples have been heat-treated. They were pre-analyzed 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 2020.

## 4. Schedule of the scheme

Feb 11, 2020: shipment of samples of survey 1 and survey 2.
Mar 9, 2020: clinical details given and start of analysis of survey 1.
Mar 30, 2020: deadline for result submission (survey 1)
May 20, 2020: interim report of survey 1 by e-mail
Jun 8, 2020: clinical details given and start of analysis of survey 2.
Jun 29, 2020: deadline for result submission (survey 2)
Aug 18 2020: interim report of survey 2 by e-mail
Sept 1, 2020: Annual meeting of participants by Web-Seminar.
Feb 2021: Annual report with final scoring by e-mail. The final report will be confirmed by the SAB.

## 5. Results

All labs returned results for both surveys by the deadline.

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

## 6. Web site 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 out by a second assessor who changes every year as well as by the scientific advisor. The results of DPT Switzerland 2020 were also scored by Dr Christine Saban, DPT-Lyon. At the SAB meeting on November 20-21, the definitive scores were 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.

**Evaluation of critical errors** for 2020, was as follows:

Sample A, missing diagnosis (no lab); sample B, missing diagnosis or no appropriate recommendation (no lab); sample C, not valid; sample D, missing metabolites/diagnosis (no lab); sample E, missing key metabolites (no lab); sample F, missing abnormalities (no lab).

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. No performance support letters will be sent by the Scheme Advisor for 2020. Any partial submitters will receive a letter from the ERNDIM administrative office.

### 7.1. Score for satisfactory performance

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

If your laboratory is assigned poor performance and you wish to appeal against this classification please email the ERNDIM Administration Office (admin@erndim.org), with full details of the reason for your appeal, within one month receiving your Performance Support Letter.

## 8. Results of samples and evaluation of reporting

### 8.1. Patient A

Phenylketonuria due to phenylalanine hydroxylase deficiency, OMIM #261600

**Patient details provided to participants**

Adult patient investigated due to spastic paraparesis, leukodystrophy and hemolytic uremic syndrome

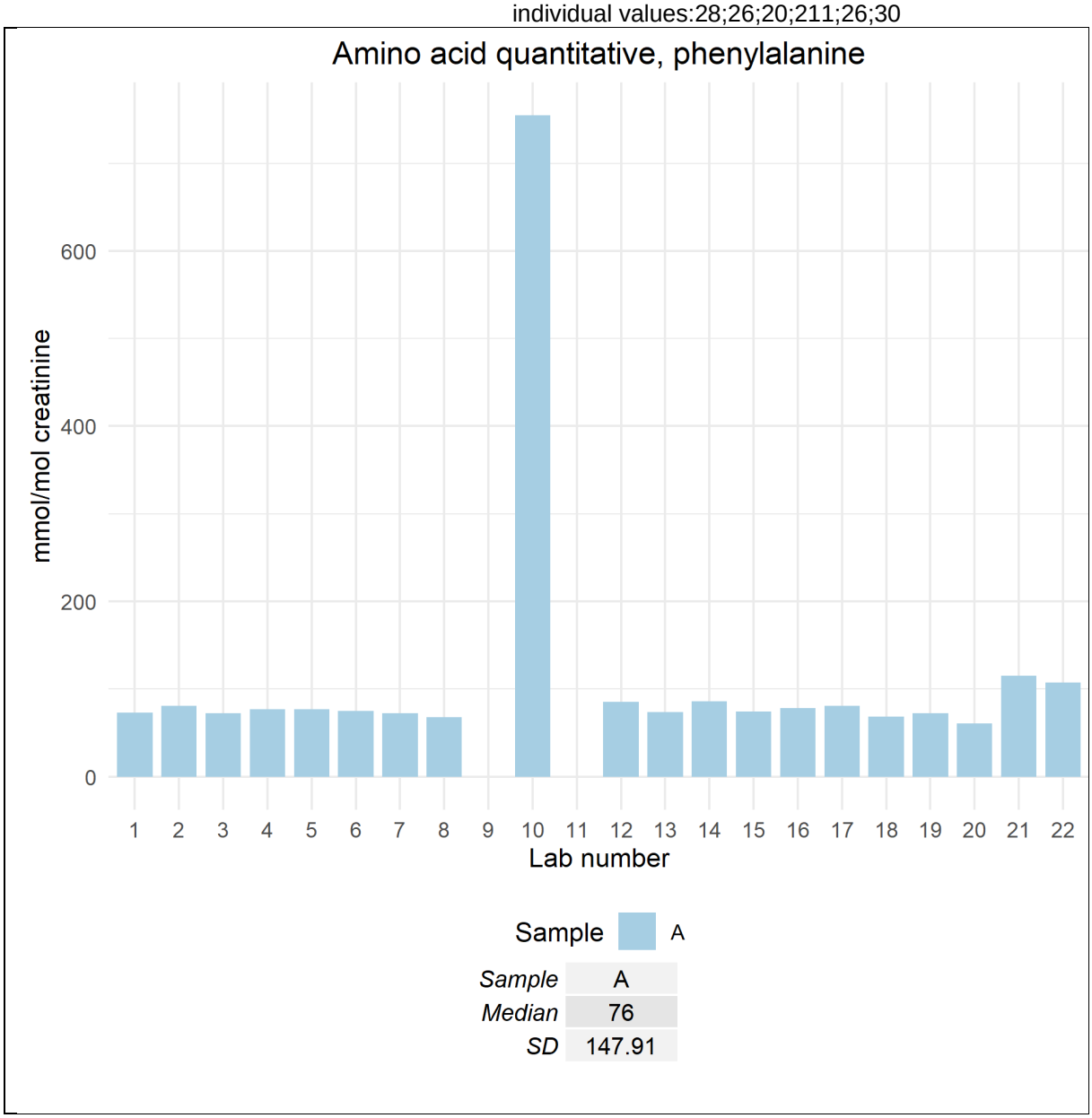
**Patient details**

An untreated adult patient with phenylketonuria. Adult patient investigated due to spastic paraparesis, leukodystrophy and hemolytic uremic syndrome. Undiagnosed (and untreated) patient with phenylketonuria (PKU) : he did not benefit from neonatal screening, No further information

**Analytical performance**

Increase of phenylalanine scored one point (21/22 labs). The median for the phenylalanine level is 76 mmol/mol creat. Increase of at least 1 abnormal organic acid e.g. phenyllactic, phenylpyruvic, mandelic, phenylacetic, N-acetylphenylalanine scored 1 point (22/22 labs).

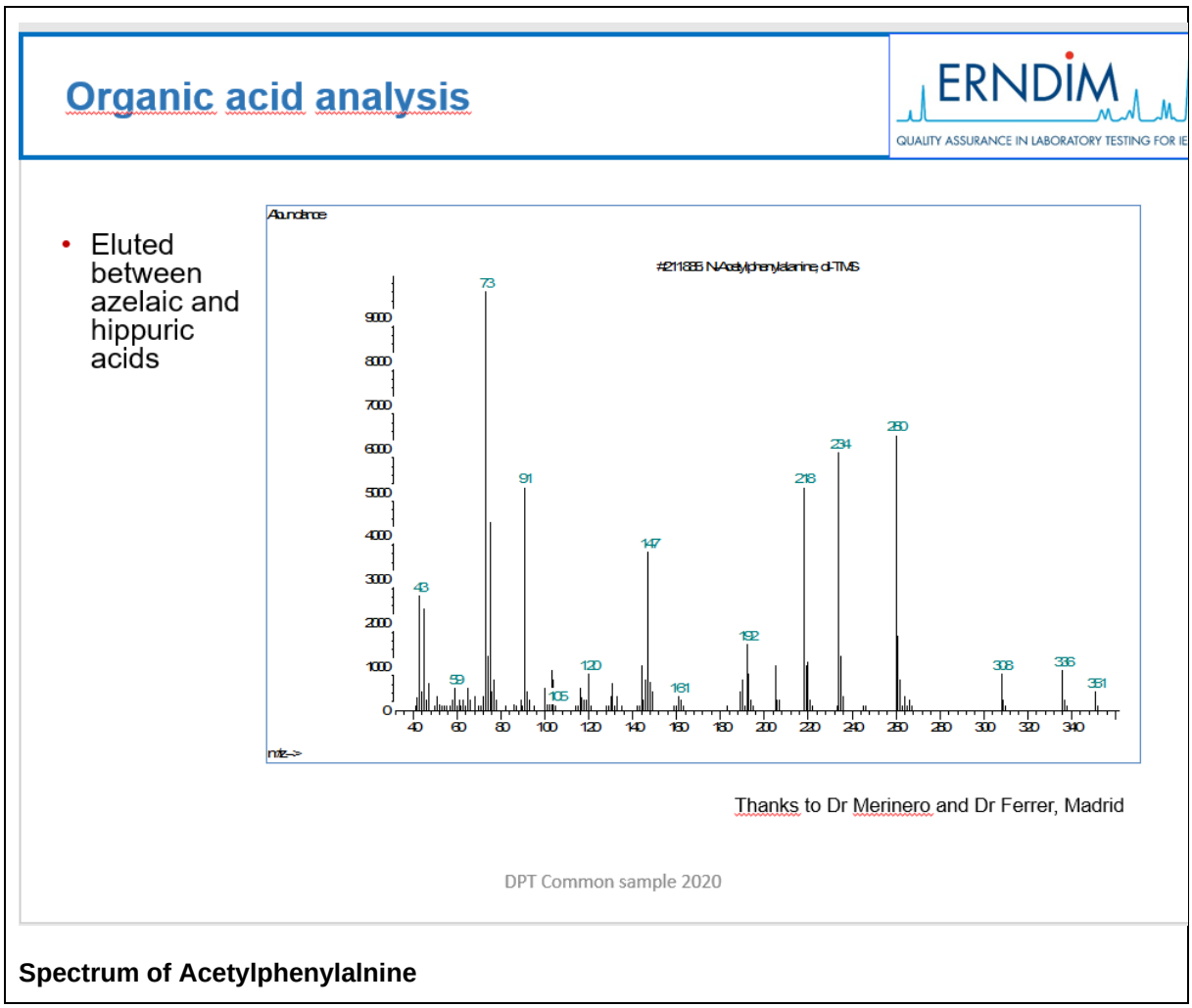
| | | | |
|---|---|---|---|
| **Creatinine** (mmol/L): | n 21 | median 4.5 | range 3.97 – 4.8 (one outlier with 0.66) |
| pH: | 13 | median 5.0 | range 5.0 – 6.0 |
| **Organic acids** (mmol/mol Creat.) | | | |
| | Phenyllactic acid | n 5 | median 509 range 341-763 |
| | Phenylacetic acid | n 6 | median 27 range 20-211 |
| | | individual values:28;26;20;211;26;30 | |



**Diagnosis / Interpretative proficiency**
Phenylketonuria as first or alternative diagnosis received a score of 2 points (22/22 labs).

**Recommendations**
Appropriate: plasma amino acids (20 labs); pterin defect testing (17 labs); PAH gene (14 labs).
Other: “genetic” testing (4 labs); DHPR (1 lab).

**Overall impression**
Very high proficiency of 98% and 100% for analytical findings and interpretation, respectively




**Spectrum of Acetylphenylalnine**

**SampleA: General aspects and summary of results from the five centres (Christine Saban, DPT-France)**

# Untreated PKU

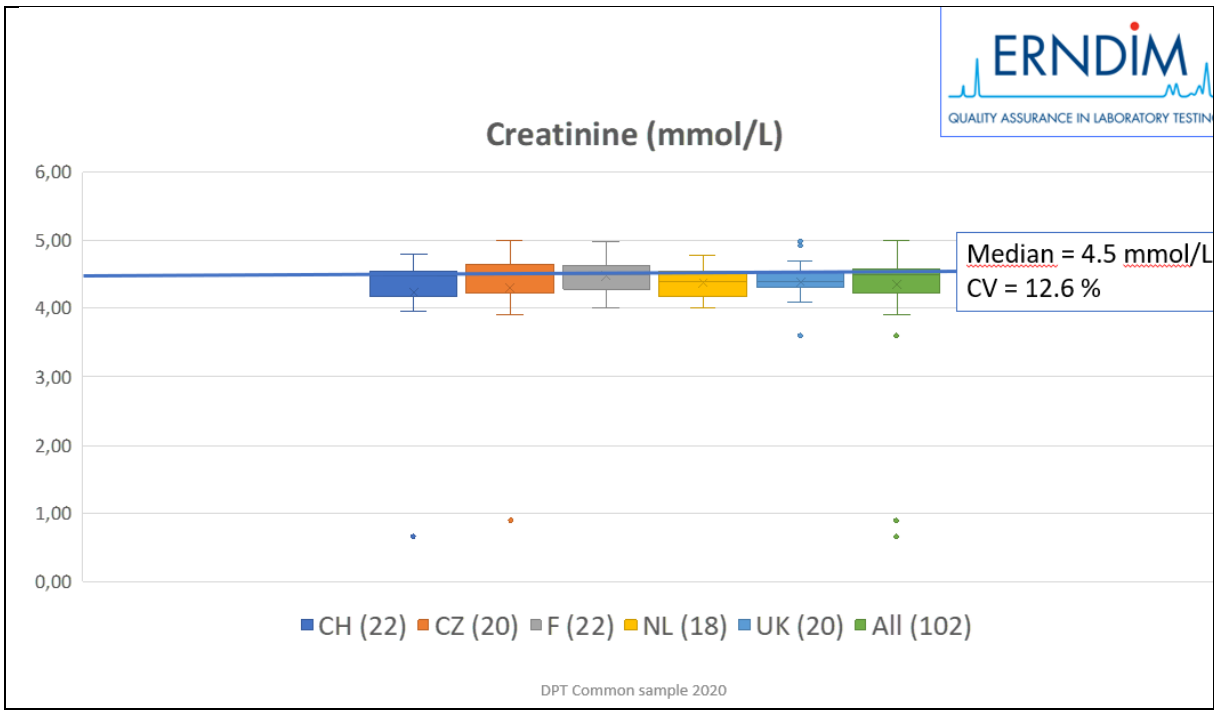
- Clinical presentation
  - Natural history of PKU: mental, behavioural, neurological and physical impairments
  - Moderate to profound mental retardation (IQ generally <50)
  - Hyperactivity, aggressiveness
  - Epilepsy, tremor, spasticity of limbs
  - Reduced hair, skin and iris depigmentation (due to reduced melanin synthesis)
  - Haemolytic uremic syndrome is not a clinical sign of PKU: other aetiology for this patient?
- Pathophysiology
  - Although the pathogenesis of brain damage is not fully understood, it is related to increased level of Phe
  - Tyr becomes a semi-essential amino acid: reduced levels leads to impaired synthesis of biogenic amines, such as dopamine, norepinephrine, serotonin

DPT Common sample 2020

# DPT centers

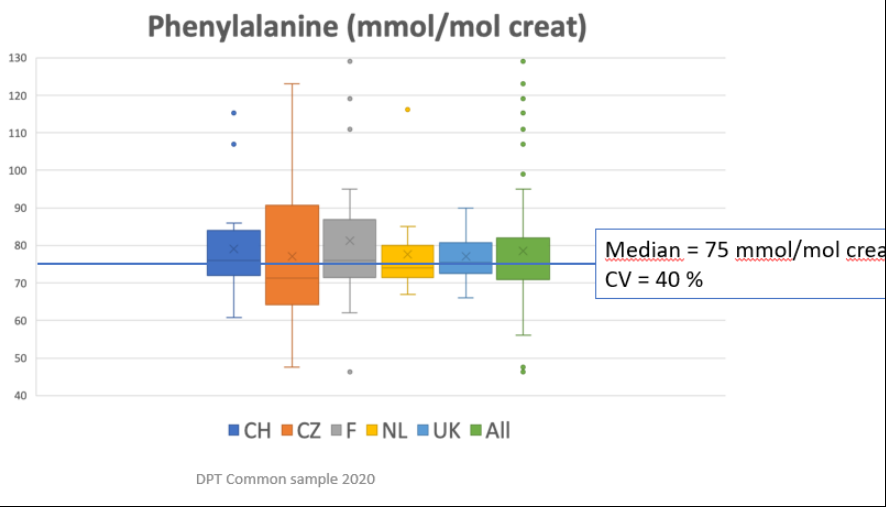
| | |
|---|---|
| • DPT CH (Switzerland) | 22 participants |
| • DPT CZ (Czech Republic) | 20 participants |
| • DPT F (France) | 22 participants (1 no answer) |
| • DPT NL (Netherlands) | 19 participants |
| • DPT UK (United Kingdom) | 20 participants (1 no answer) |
| • **Total** | **103 participants** (among 105 registered) |

DPT Common sample 2020




# Amino acid analysis

- 96 / 103 participants
- Increase of Phe: 95 / 96
- Phe quantification n = 87
- Exclusion of 2 wrong values: 21 & 318 mmol/mol creat (DPT CZ)



# Organic acid analysis

- 103 / 103 participants : all but one identified organic acid(s) indicative of PKU

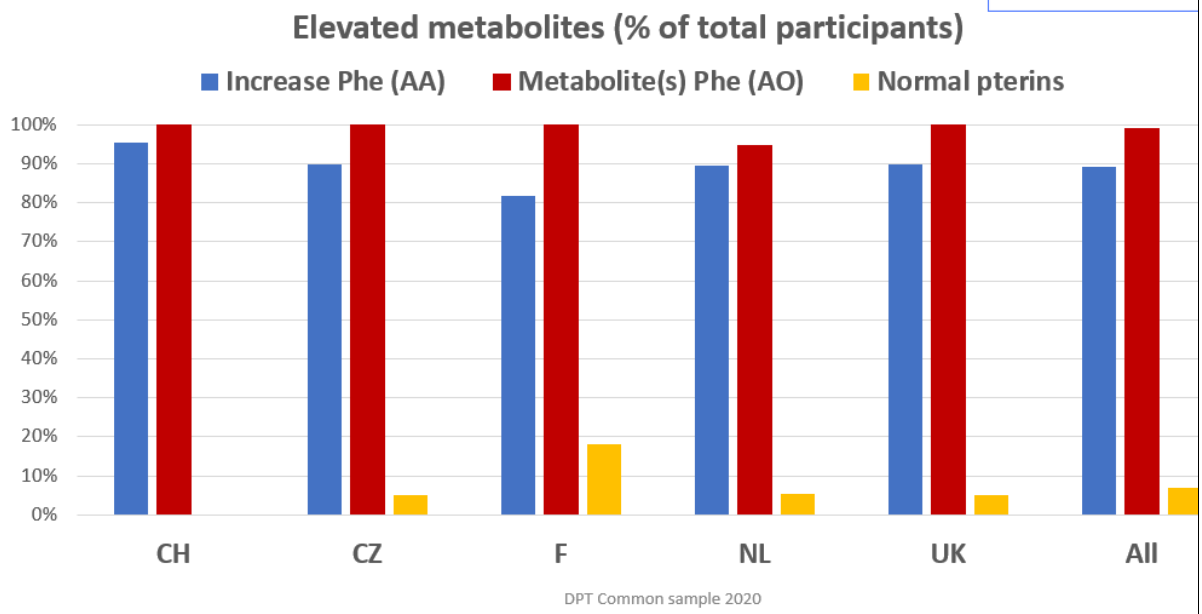
| Organic acid | n | Quantification | | | |
|---|---|---|---|---|---|
| | | Median (mmol/mol creat) | Range (mmol/mol creat) | CV | n |
| Phenyllactic | 91 | 571 | 124 - 1123 | 48 % | 21 |
| Phenylpyruvic | 80 | 172 | 48 - 515 | 70 % | 15 |
| 2-Hydroxyphenylacetic | 78 | 148 | 103 - 200 | 19 % | 12 |
| Phenylacetic | 71 | 35 | 20 - 211 | 186 % | 14 |
| Mandelic | 55 | 65 | 41 - 80 | 24 % | 6 |
| N-acetylphenylalanine | 26 | | 40 - 51 | | 3 |
| 4-hydroxyphenyllactic | 57 | 34 | 26 - 138 | 86 % | 13 |

DPT Common sample 2020

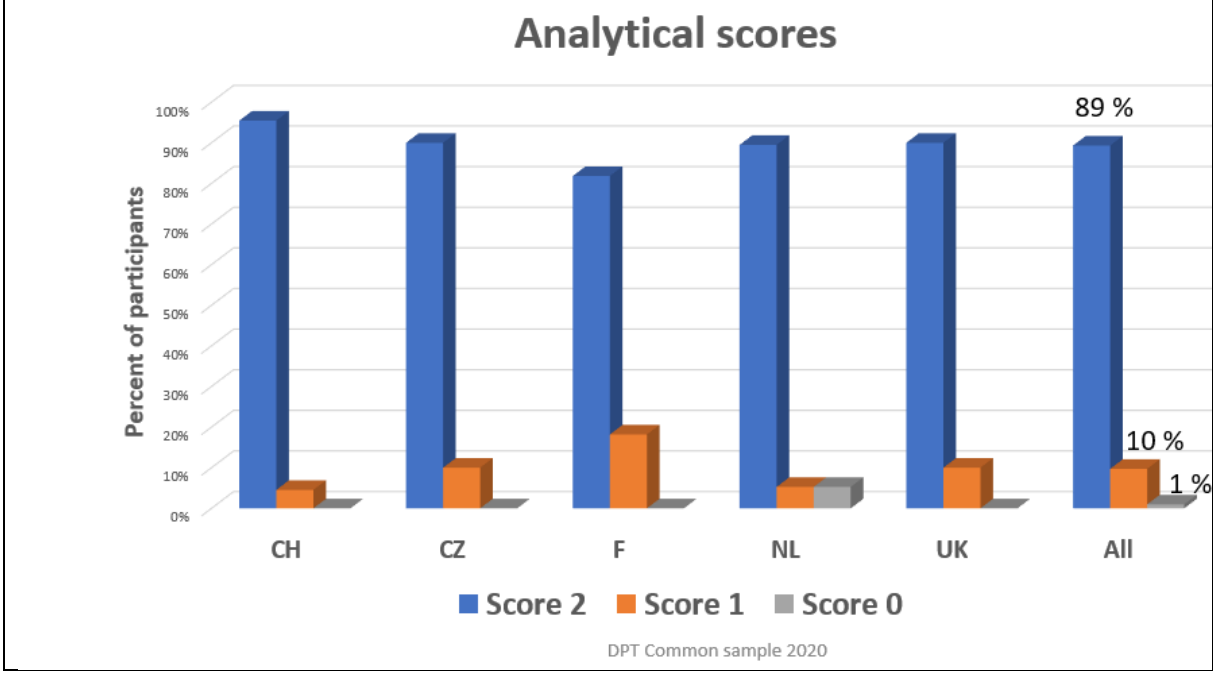
# Pterins analysis

- Performed by 7 / 103 participants
  - DPT Switzerland 0
  - DPT Czech Republic 1
  - DPT France 4
  - DPT Netherlands 1
  - DPT United Kingdom 1
- All concluded to a normal profile

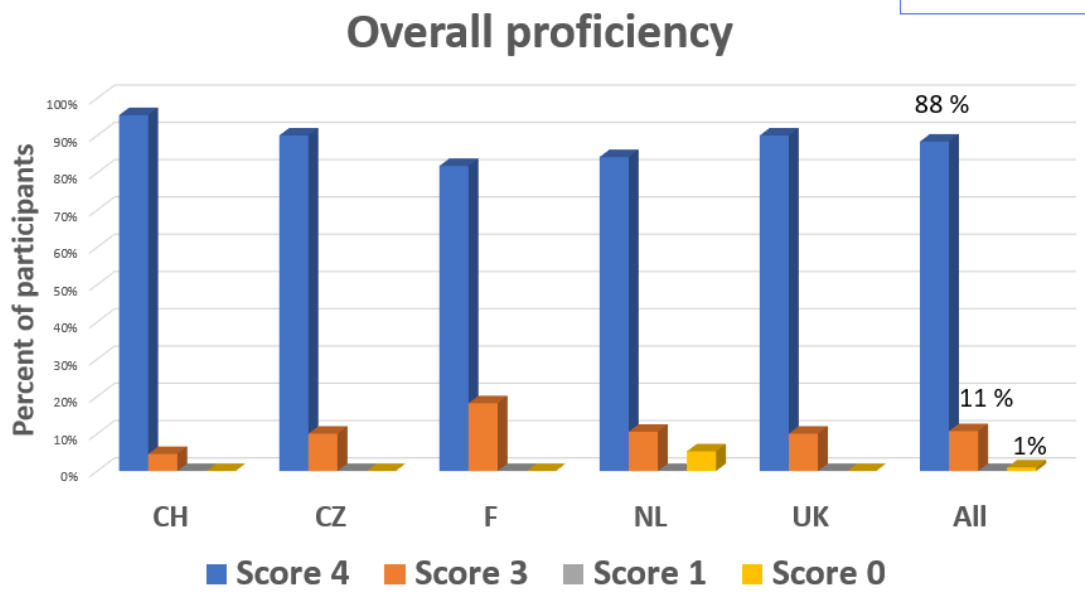
# Analytical proficiency




# Analytical interim scores



# Overall interim scores




DPT Common sample 2020

# Summary

- Easy DPT sample
- Excellent analytical performance
  - 95 / 96 participants who performed amino acids (96) reported an increase of Phe
  - 102 / 103 participants who performed organic acids (103) reported an increase of at least one organic acid present in PKU
- Excellent interpretation
  - 100 / 103 participants concluded to PKU as first or alternative diagnosis
  - 2 concluded to hyperphenylalaninemia
  - Only 1 participant concluded to “no IEM” (most probably critical error)

DPT Common sample 2020

## 8.2. Patient B

Alpha-mannosidosis due to alpha-mannosidase deficiency (OMIM 248500)

**Patient details provided to participants**

Congenital bilateral hip dislocation at birth, frequent infections and spinal deformation noted at 7months. Further symptoms included psychomotor retardation, macroglossia and hepatomegaly.

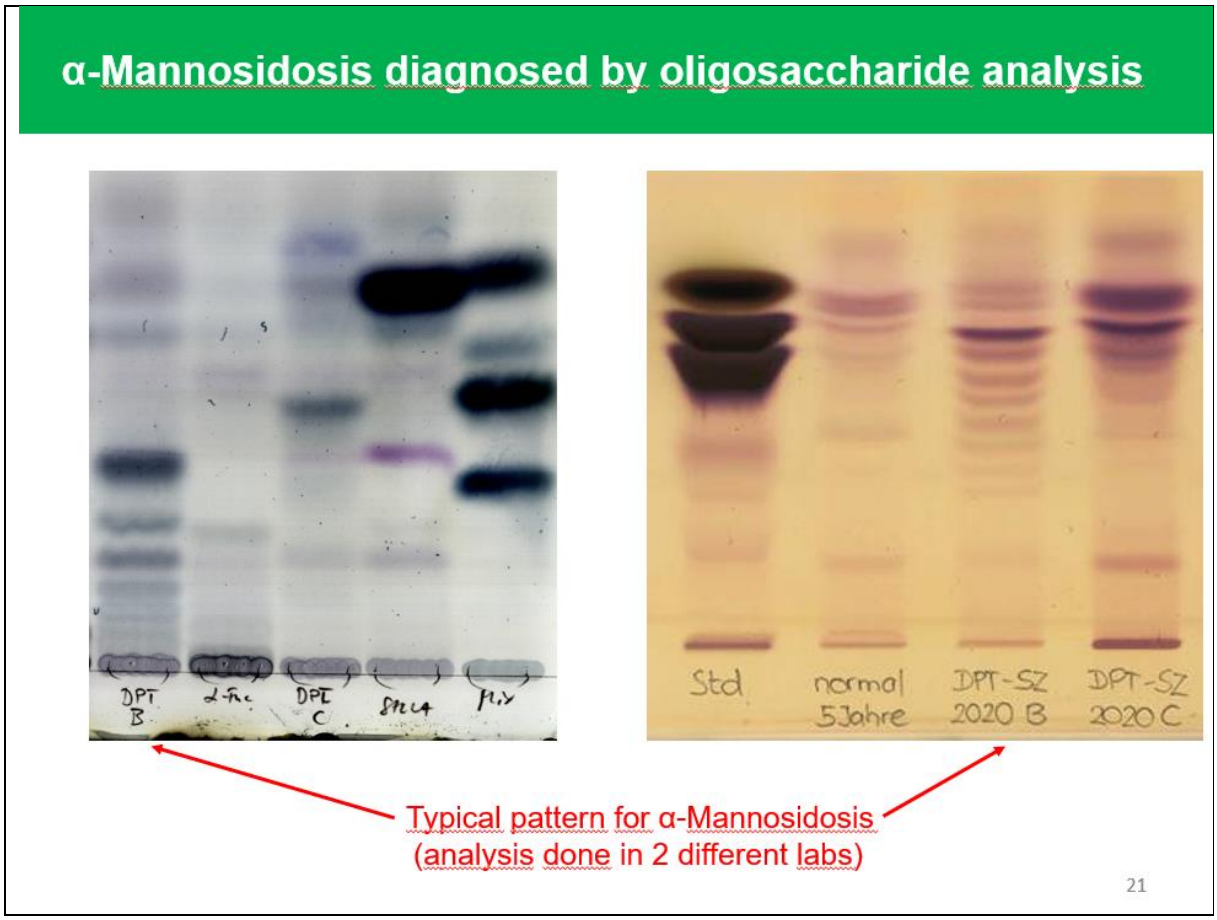
**Patient details**

Congenital bilateral hip dislocation at birth. Frequent respiratory and intestinal infections, permanent nasopharangeal secretions in early infancy. Spine deformities from seven months, lumbar hyperlordosis, bilateral genu valgum and arthritic features in both knees developed later. Other symptoms were psychomotor retardation, coarse facial features, macroglossia, hepatomegaly, macrocephaly, umbilical hernia, mitral valve insufficiency, severe caries, muscular hypotonia, myopia and strabismus. Thin layer chromatography of oligosaccharides in urine showed characteristic pattern. Diagnosis confirmed by finding of marked alpha-mannosidase deficiency and homozygosity for a mutation in the LAMAN gene.

**Analytical performance**

Oligosaccharide analysis was needed to make the diagnosis, performed by 16/22 labs. Finding of abnormal pattern characteristic of alpha-mannosidosis was scored with 2 points (15 labs) and non-specific abnormality was scored with one point. Overall proficiency 70%.

| | | | |
|---|---|---|---|
| Creatinine (mmol/L): | n 22 | median 7.54 | range 3.12 – 8.13 |
| pH: | n 13 | median 5.5 | range 5.0 – 6.0 |



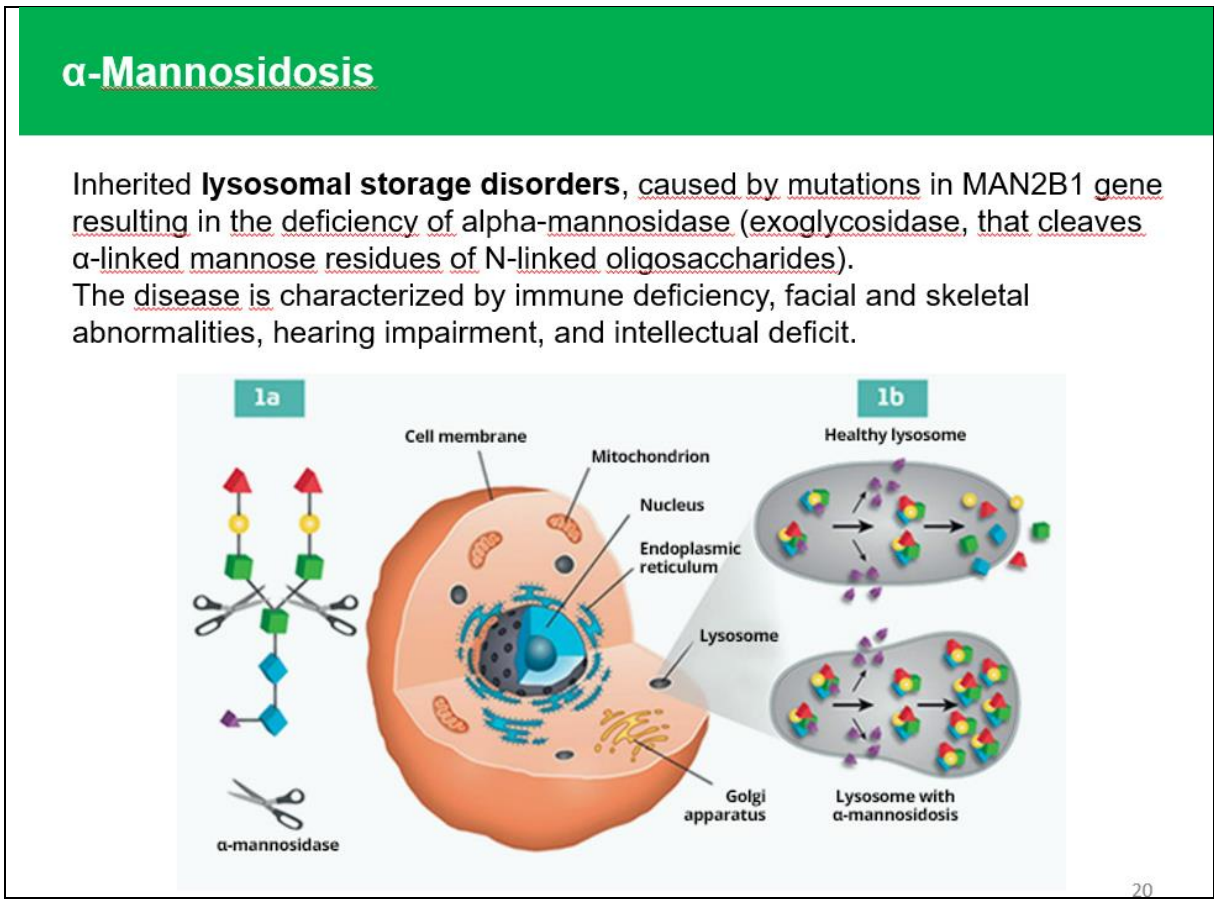

DPA stain (left of picture)

Anderson et al. (2000) Diphenylamine-Aniline-Phosphoric Acid Reagent, a Versatile Spray Reagent for Revealing Glycoconjugates on Thin-Layer Chromatography Plates, Anal Biochemistry 287: 337–339

**Diagnosis / Interpretative proficiency**
The correct diagnosis was scored with two points (17 labs). Mention of alpha-mannosidosis without relevant analytical findings or recommendation for appropriate further testing was scored with one point (5 labs). Overall proficiency 80%.

**Recommendations**
Appropriate: leucocyte alpha-mannosidase (13 labs); MAN2B1 gene (11 labs), oligosaccharides, first or repeat (4 labs), general lysosomal enzymes (3 labs).
Other: “genetic” testing (4 labs); vacuolated lymphocytes (1 lab); I-cell disease testing (1 lab); MPS testing (1 lab).

**Overall impression**
Good proficiency for those labs that performed oligosaccharide analysis. Overall proficiency of 75%.



### 8.1. Patient C

No known inherited metabolic disorder.

**Patient details provided to participants**

Feeding difficulties and vomiting, failure to thrive with hypotonia and poor head control.

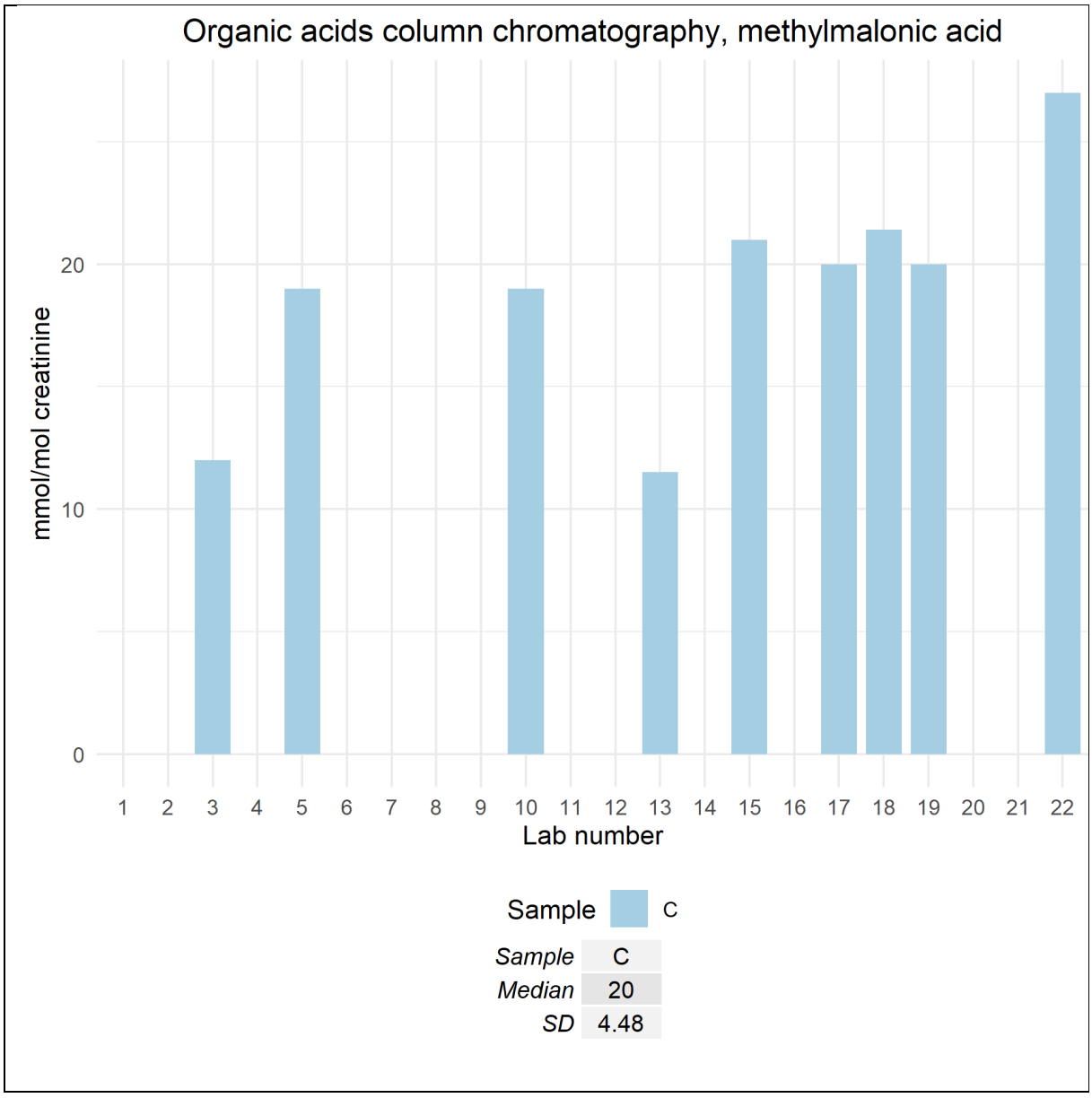
**Patient details**

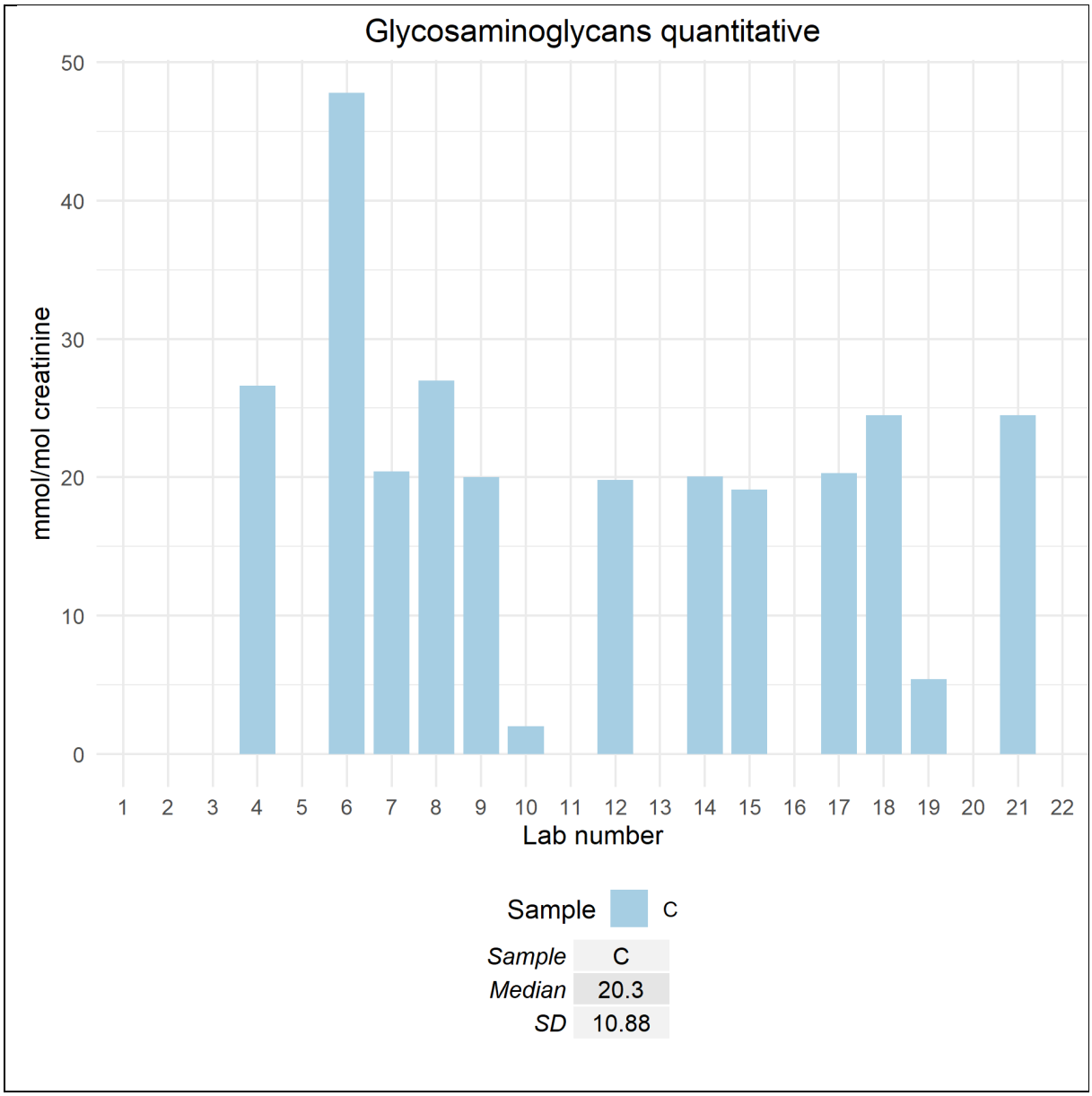
Feeding difficulties and vomiting, failure to thrive with hypotonia and poor head control at 6 months. A reflux disorder was excluded. A suspected demyelination disorder on MRI led to extensive studies for a storage disease, all negative.

**Analytical performance**

Points were given for none specific elevation of amino acids, organic acids with slight increase of methylmalonic acid or total GAGs and performing more than three tests with no evidence of a specific disorder scored 2 points (17 labs). Incomplete analytical results scored one point (5 labs). Overall proficiency of 89%.

| | | | |
|---|---|---|---|
| Creatinine (mmol/L): | n 22 | median 1.93 | range 0.25 – 2.19 |
| pH: | n 13 | median 7.0 | range 6.5 – 7.5 |






**Diagnosis / Interpretative proficiency**
An inconclusive diagnosis or no evidence of an inborn error scored one point (9 labs), appropriate recommendations for further testing scored one point (14 labs), two points were scored by 7 labs. A conclusion of a specific disorder such as a purine/pyrimidine disorder, a genetic cobalamin disorder or other specific disorder was scored as 0 points. The elevation of amino acids was not considered to be sufficiently high for Fanconi Syndrome.
Interpretative proficiency of 59%.

**Recommendations**
Appropriate: exclusion of B12 deficiency (9 labs); plasma MMA (4 labs); repeat urine for various analytes (9 labs); plasma amino acids (7 labs); acyl carnitines (3 labs); SUCLA genes (2 labs); NGS panel (1 lab).
Other: enzyme activities (2 labs); inappropriate genetic testing (3 labs); medication information (1 lab); renal tubular function (3 labs); white blood cell cystine (1 lab).

**Overall impression**
Some changes may be related to deterioration of the sample. This child had been extensively investigated for an inherited metabolic disease but none was found. Unspecific minor changes were slight elevations of methylmalonic acid and total glycosaminoglycans with a mild hyperaminoaciduria. Overall proficiency rather low at 74% mainly due to a tendency to over-interpret only minor findings.

### 8.1. Patient D

Succinic semialdehyde dehydrogenase deficiency (OMIM #271980)

**Patient details provided to participants**

A 7 months old boy with delayed psychomotor development Investigation revealed a marked suint and Strabismus convergence was observed and cranial ultrasound showed ventricular CSF accumulation .

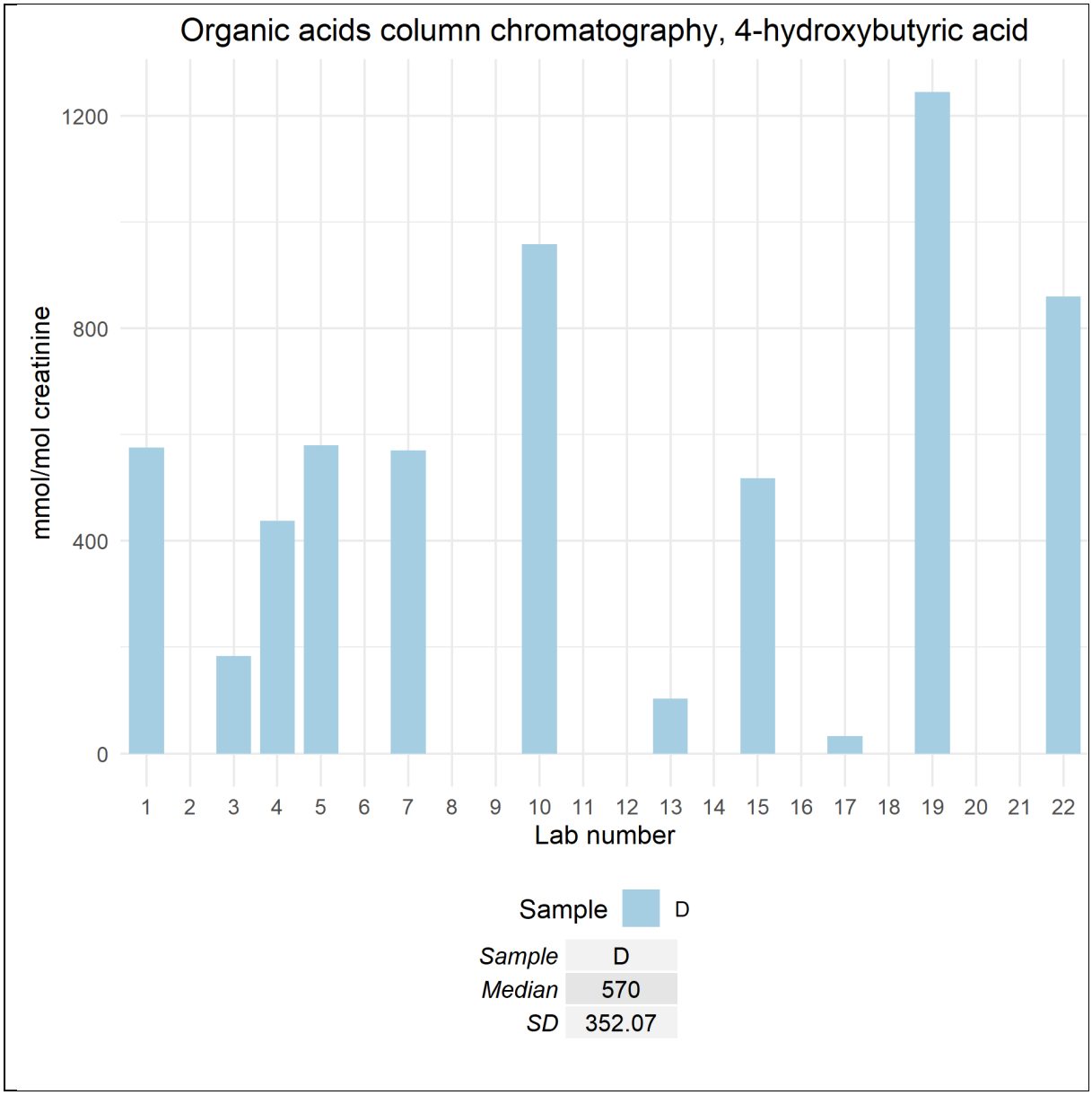
**Patient details**

The urine was collected from a 7 months old child with delayed motor development as indicated by poor head control, absence of trunk control and inability to roll over. Strabismus convergence was observed and cranial ultrasound showed internal hydrocephaly. The diagnosis SSADH deficiency was confirmed.

**Analytical performance**

The finding of 4-hydroxybutyric acid with or without other key metabolites such as 3,4-dihydroxybutyric acid was considered to be correct and scored two points (22/22 labs). The median for 4-OH-butyric acid level is 570 mmol/mol creat.

| | | | |
|---|---|---|---|
| Creatinine (mmol/L): | n 22 | median 2.48 | range 2.08 – 2.77 |
| pH: | n 12 | median 6.5 | range 6.0 – 7.0 |

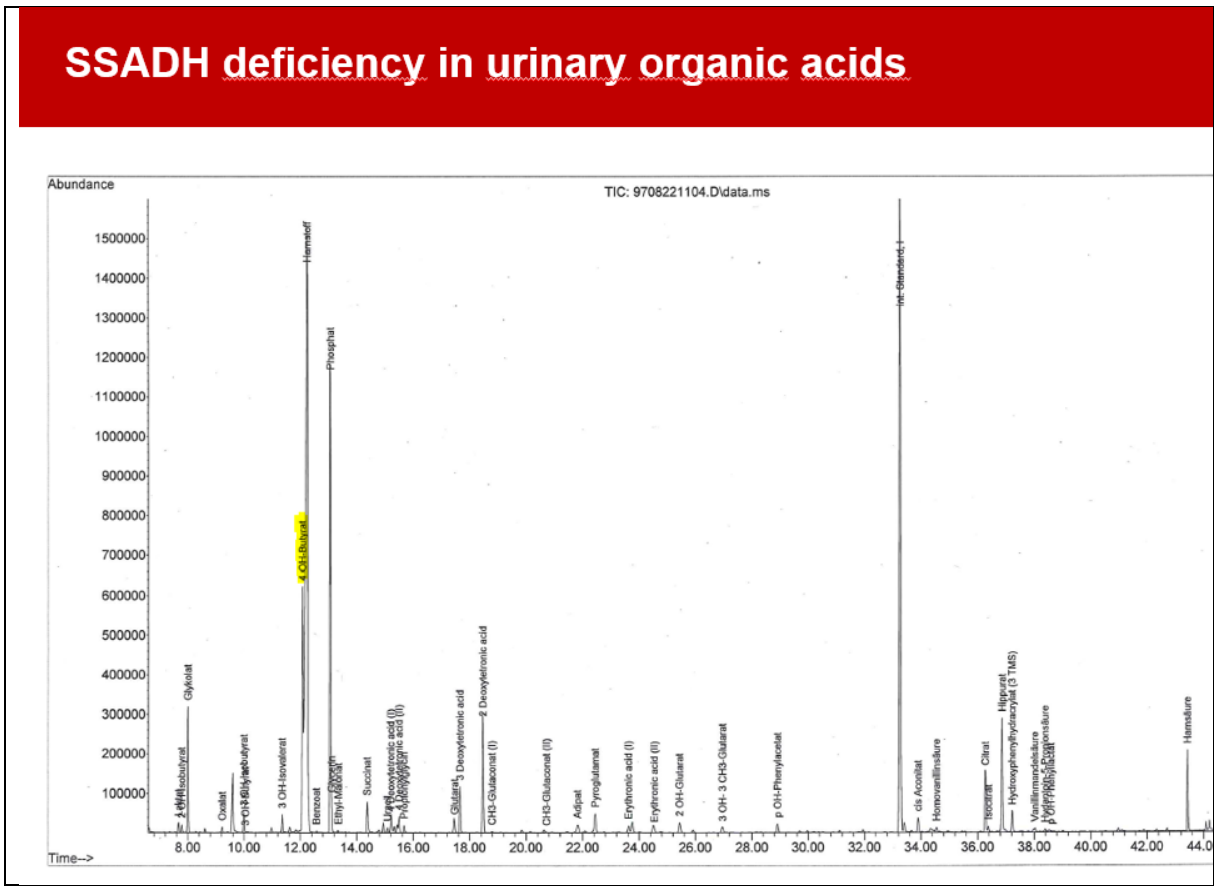


**Diagnosis / Interpretative proficiency**
The correct diagnosis - SSADH deficiency - was scored with two points (21/22 labs). The correct diagnosis stated as other possible diagnosis scored 1 point (1 lab).

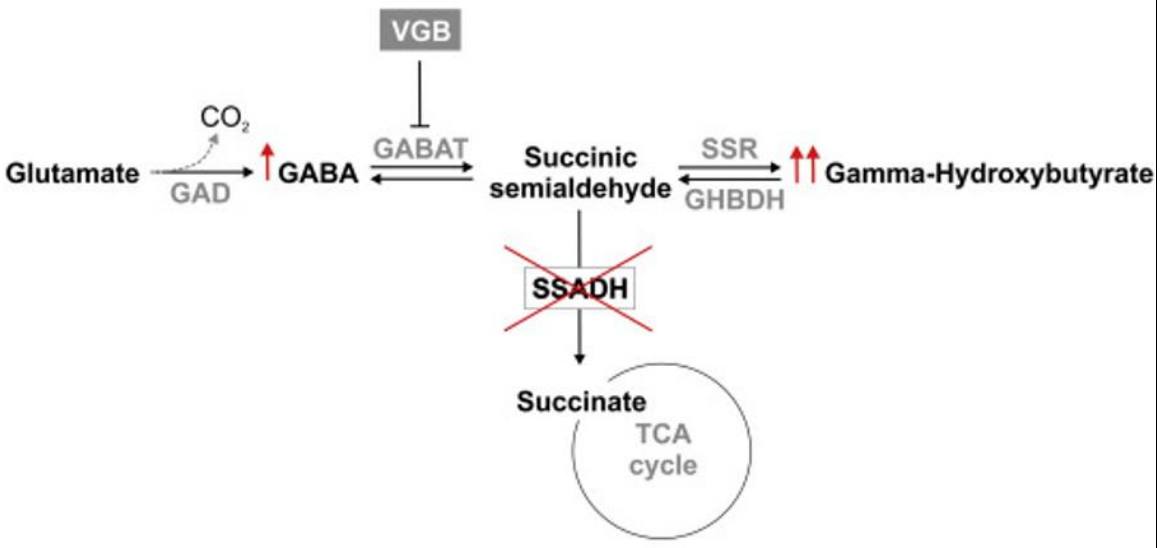
**Recommendations**
Appropriate: repeat urinary organic acids (6 labs). Genetic analysis of the ALDH5A1 gene (22 labs). Enzyme assay (6 labs).
Other: Free GABA and homocarnosine in CSF (3 labs). Plasma amino acids(2 labs). Organic acids in CSF (1 lab). Acylcarnitines in DBS (1 lab). Creatine/creatinine ratio in urine (1 lab). Neuroimaging (1 lab). EEG (1 lab). Glycosaminoglycans in urine (1 lab).

**Overall impression**
Very high proficiency of 100% and 98% for analytical findings and interpretation, respectively.

The sample has been circulated in 2010 with overall proficiency of 90%.



# SSADH deficiency



## 8.1. Patient E

Short-chain acyl-CoA dehydrogenase deficiency (OMIM #201470)

**Patient details provided to participants**

at age 7 years, patient was referred for chronic fatigue, urine was collected as part of selective screening from this cognitively normal patient

**Patient details provided to participants**

at age 7 years, patient was referred for chronic fatigue, urine was collected as part of selective screening from this cognitively normal patient

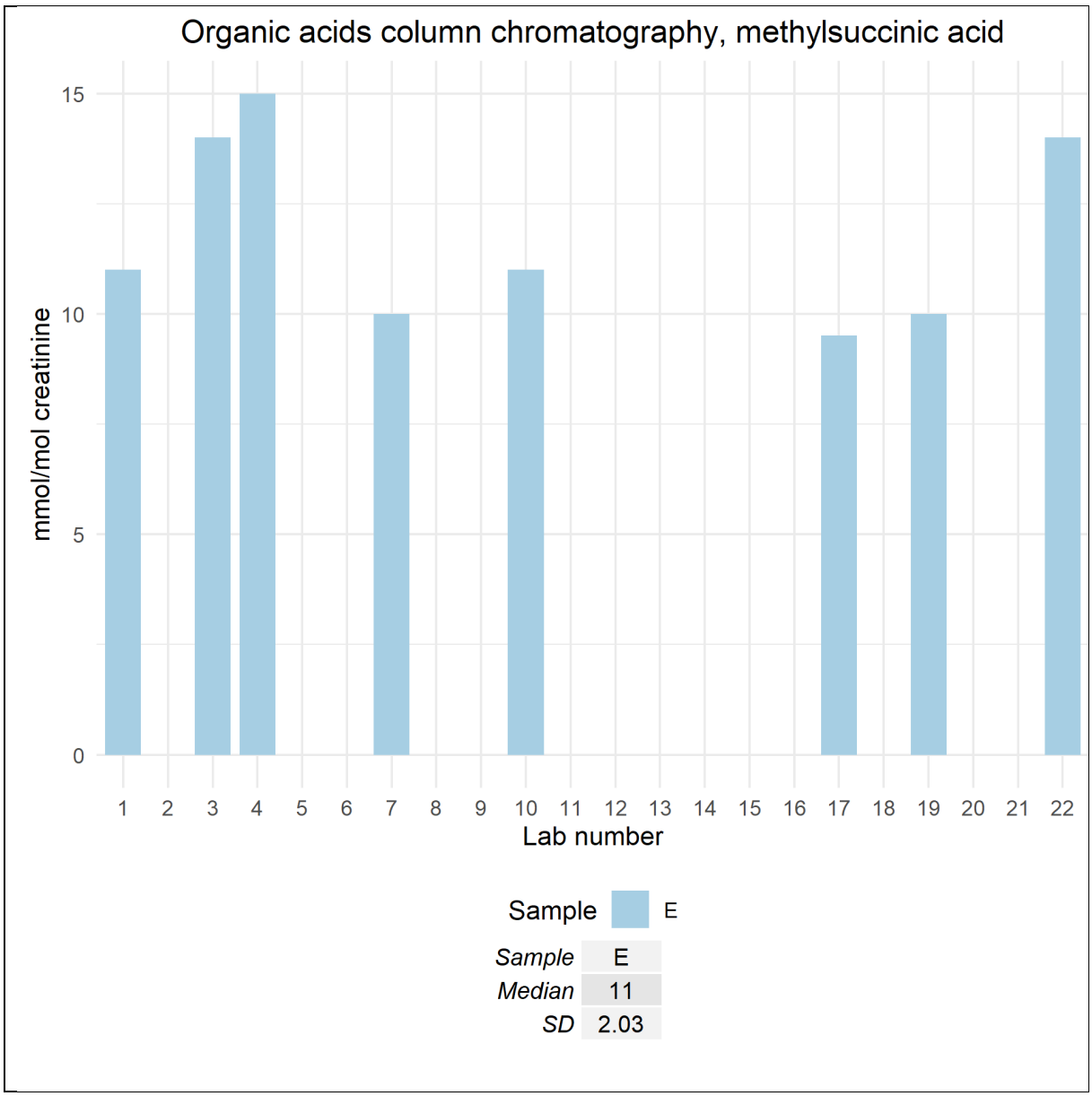
**Patient details**

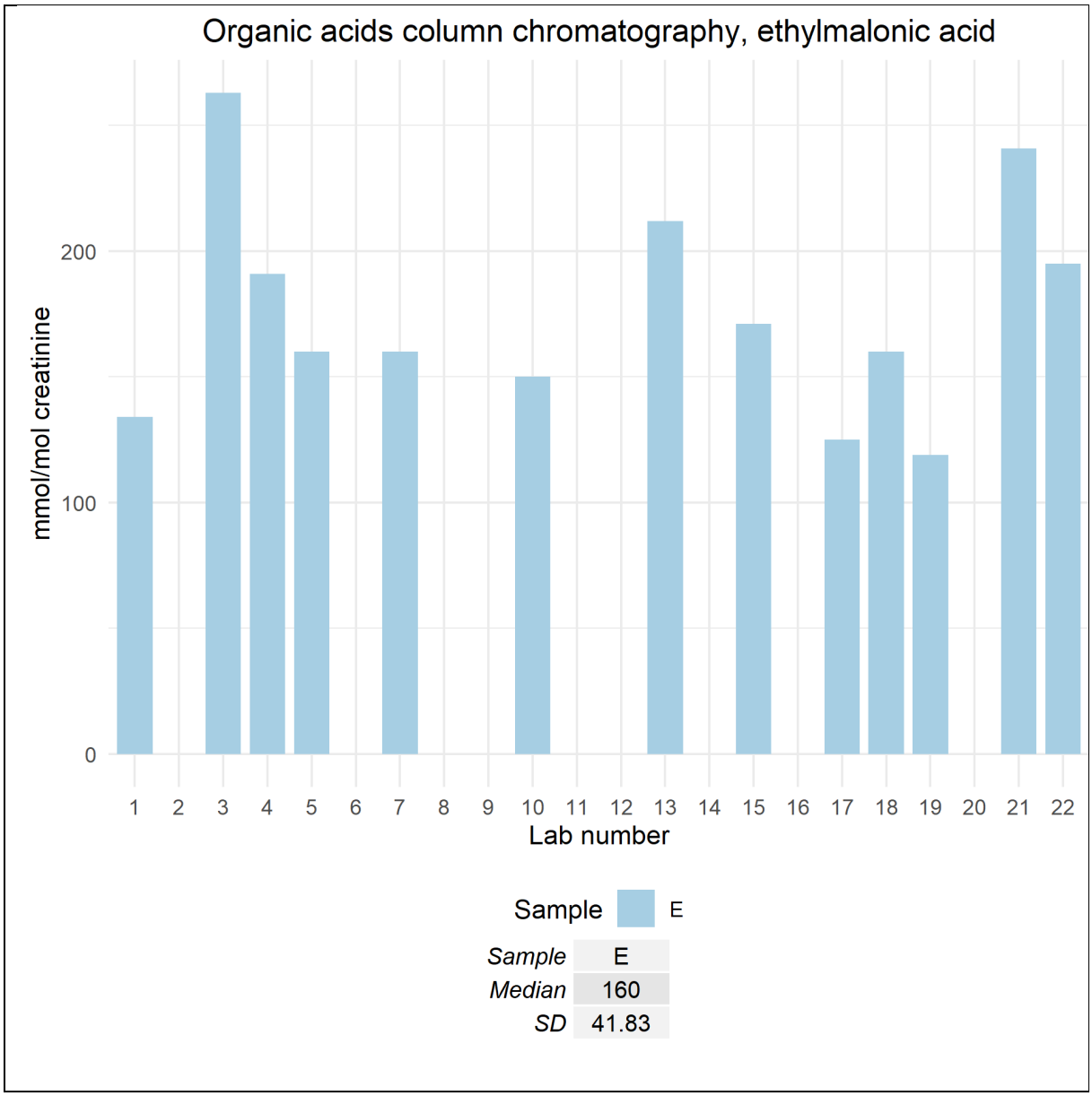
At age 7 years, this cognitively normal patient was referred for chronic fatigue and urine was collected as part of selective screening. The diagnosis was confirmed by mutation analysis.

**Analytical performance**

Increase of ethylmalonic acid scored one point (median 160 mmol/mol creat, 22/22 labs). Increase of methylsuccinic acid scored one point (median 11 mmol/mol creat) (17/22 labs).

| | | | |
|---|---|---|---|
| Creatinine (mmol/L): | n 22 | median 6.08 | range 4.06 – 6.9 |
| pH: | n 12 | median 5.5 | range 5.0 – 6.0 |



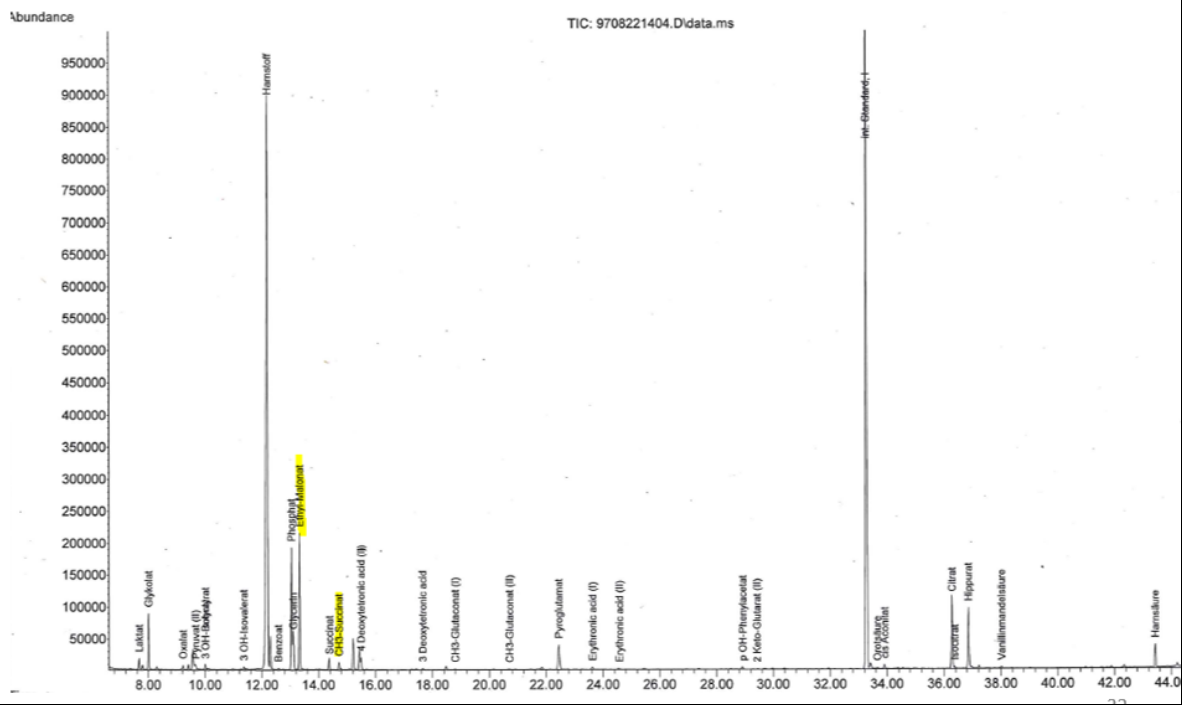



**Diagnosis / Interpretative proficiency**
The correct diagnosis was scored with two points (22/22 labs).

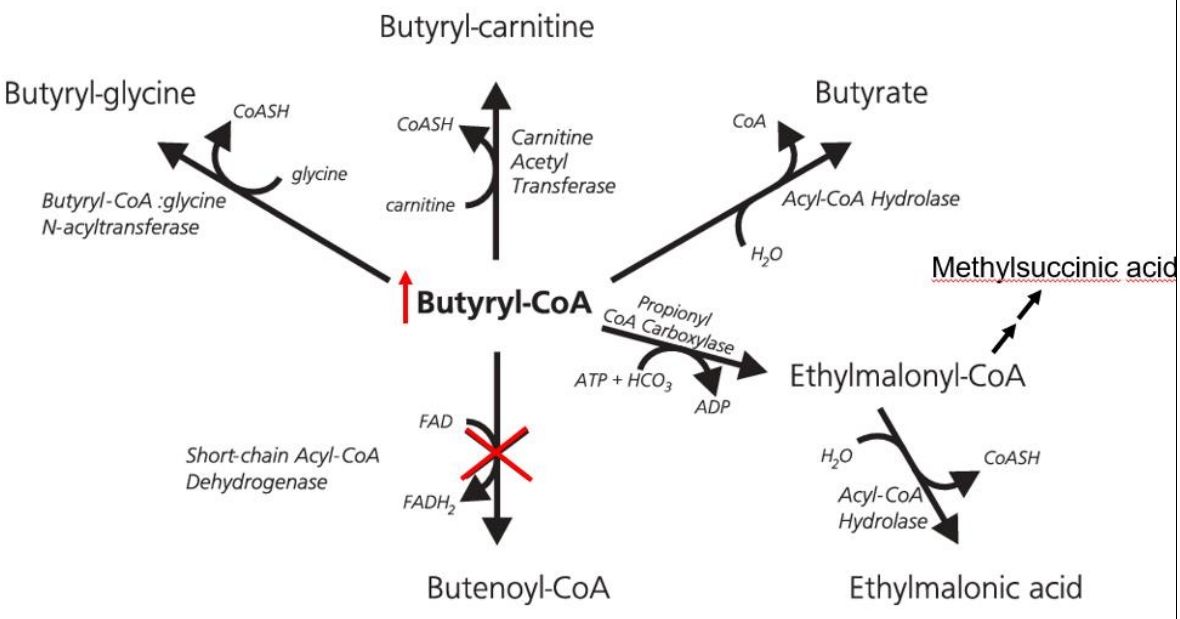
**Recommendations**
Appropriate: Repeat urinary organic acids (3 labs). Analyse acylcarnitines in DBS or plasma (20 labs). Confirm diagnosis with molecular analysis of the ACADS gene (20 labs).
Other: Analyse plasma amino acids and lactate (1 lab).

**Overall impression**
Good proficiency of 91% for analytical findings and very high proficiency of 100% for interpretation.

# SCAD deficiency in urinary organic acids




# SCAD deficiency



### 8.1. Patient F

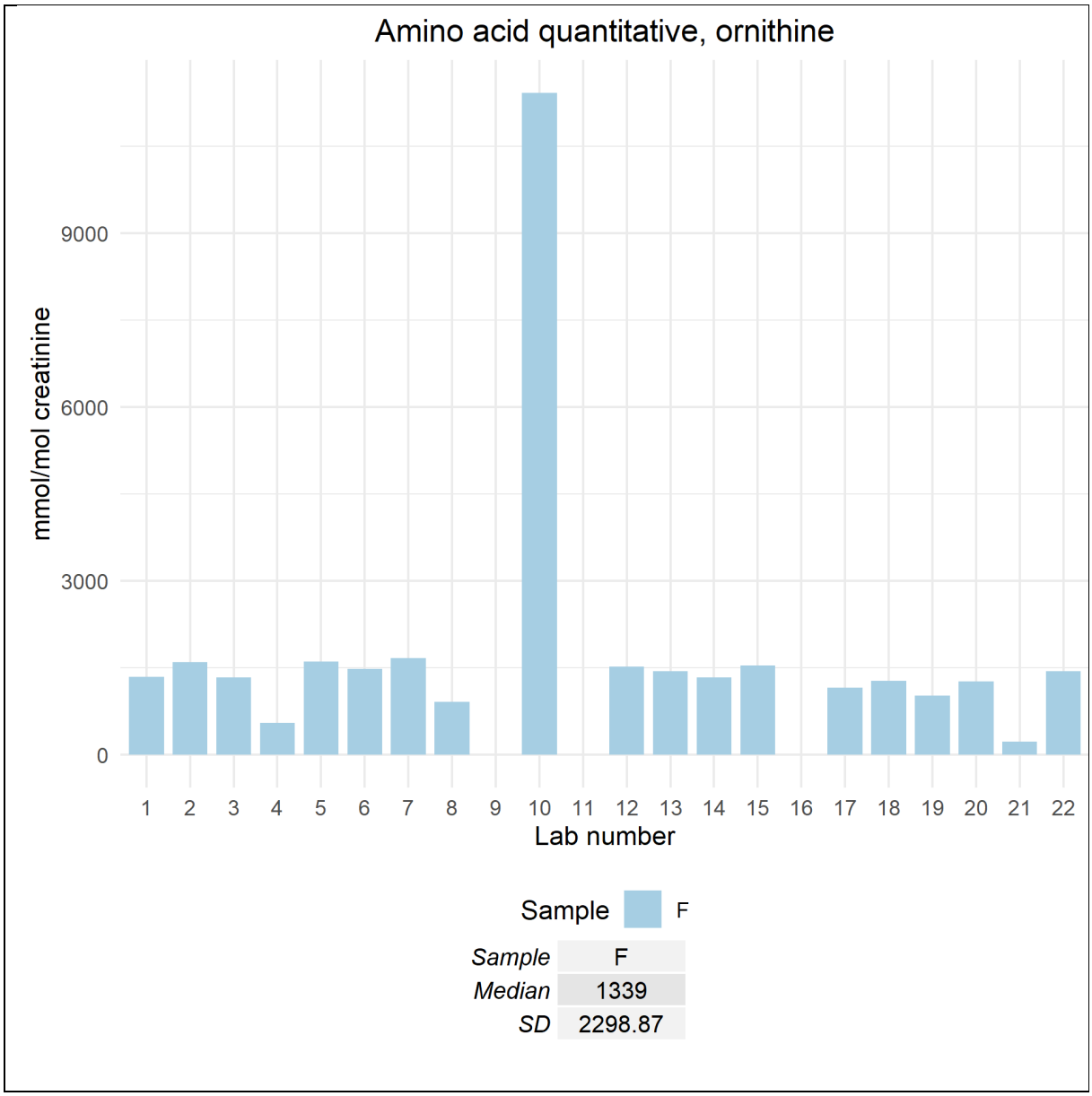
Hyperornithinemia-hyperammonemia-hmocitrullinuria syndrom (OMIM #238970)

**Patient details provided to participants**

was discharged from birth clinic on day 3 of life despite tiredness and poor feeding, deteriorated at home and was brought back to the hospital on day 6. On admission, he was lethargic and treatment was started immediately. Discharged home on therapy on day 20.

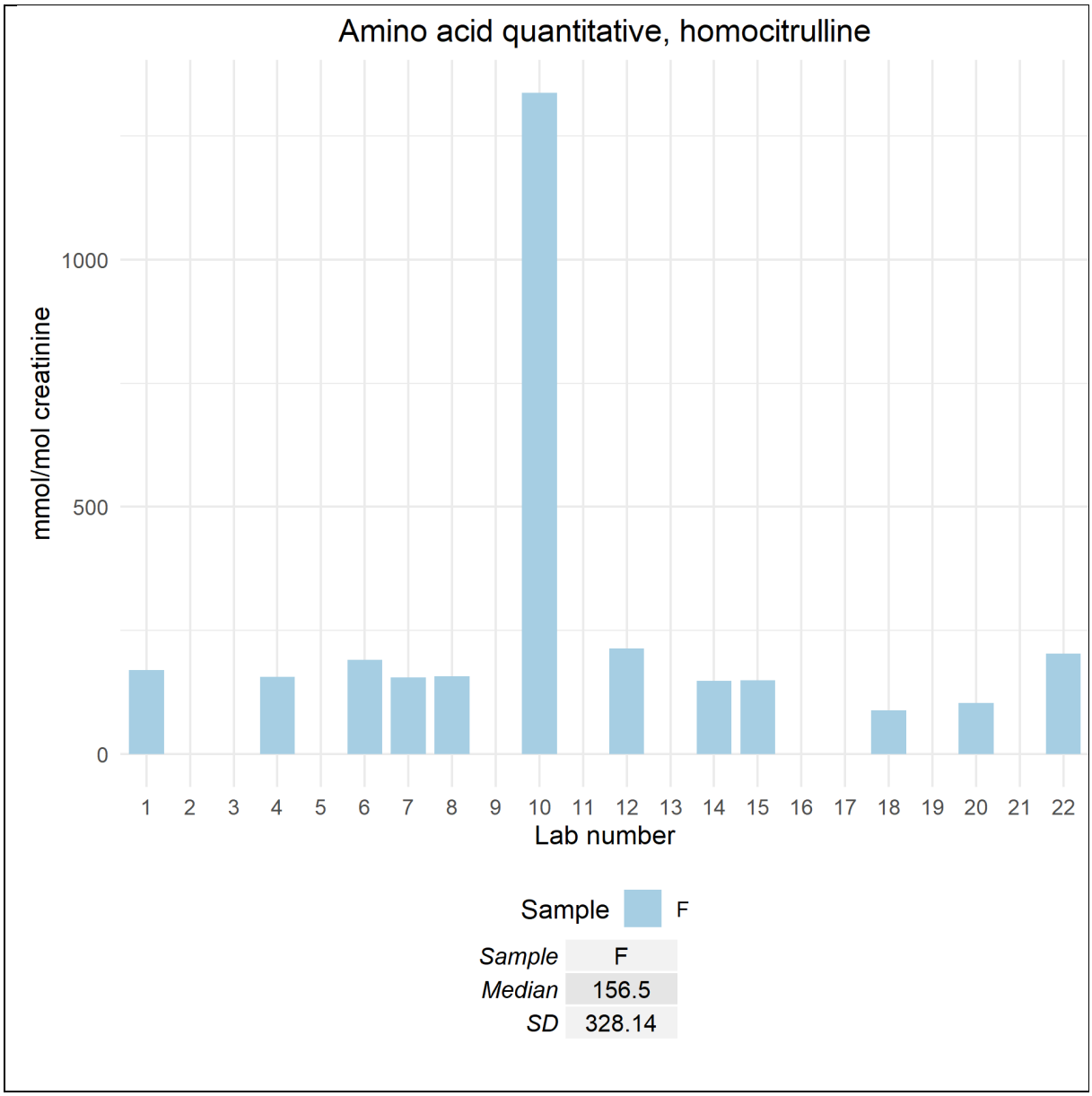
**Patient details**

The patient was discharged from birth clinic on day 3 of life despite tiredness and poor feeding. The patient deteriorated at home and was brought back to the hospital on day 6. On admission, he was lethargic and treatment was started immediately. Discharged home on therapy on day 20. The urine sample was obtained while in hospital. The diagnosis was confirmed by mutation analysis.




**Analytical performance**

The increase of ornithine (median 1339 mmol/mol creat) AND homocitrulline (median 156 mmol/mol creat) was scored one point (19/22 labs). The increase of orotic acid (median 18 mmol/mol creat) was scored one point (16/22 labs).




| | | | |
|---|---|---|---|
| Creatinine (mmol/L): | n 22 | median 0.65 | range 0.57 – 0.77 |
| pH: | n 12 | median 7.5 | range 7.0 – 8.0 |

Organic acids (mmol/mol Creat.)

| | | | |
|---|---|---|---|
| Orotic acid | n 6 | median 16.5 | range 9-22 |

Orotic acid specific (mmol/mol Creat.)

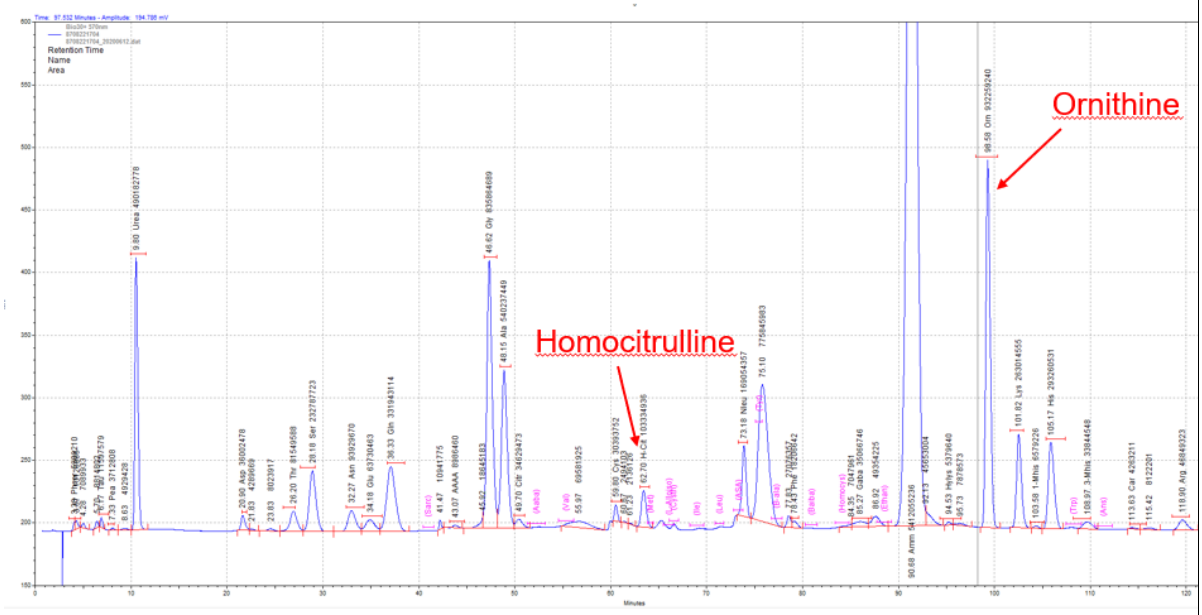
| | | | |
|---|---|---|---|
| Orotic acid | n 5 | median 19.4 | range 14-23 |

**Diagnosis / Interpretative proficiency**
The correct diagnosis (HHH syndrome) was scored with 2 points (18/22 labs). Other urea cycle defect as first or other possible diagnosis was scored one point (4 labs).

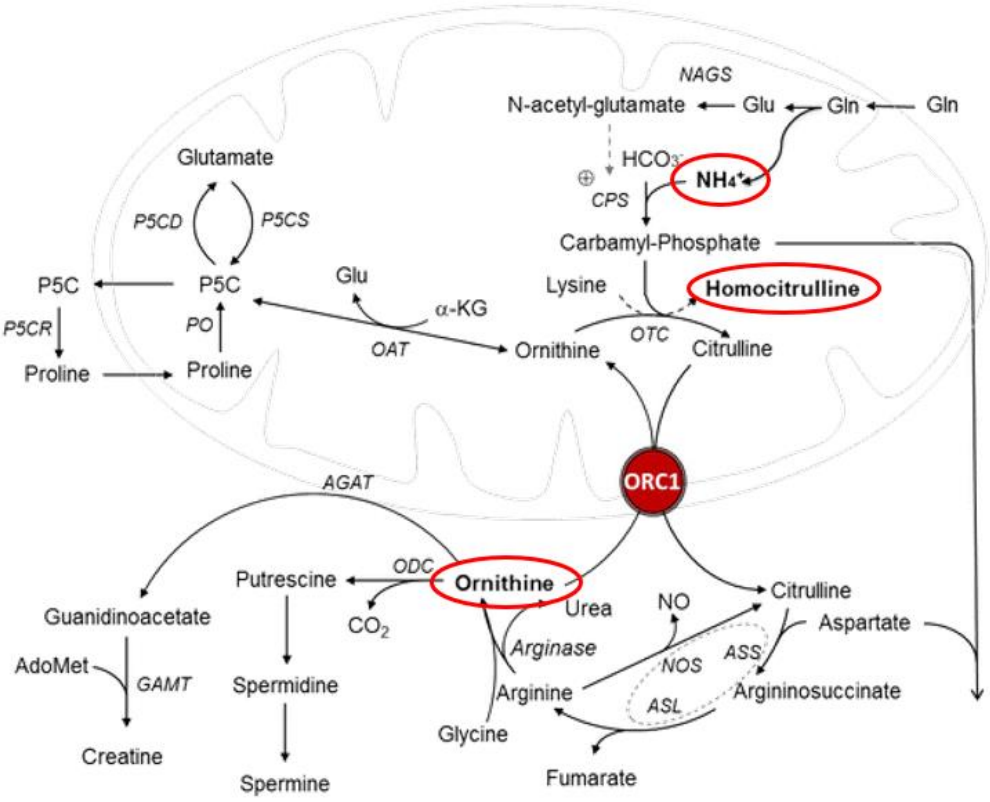
**Recommendations**
Appropriate: plasma ammonia (17 labs), plasma amino acids (19 labs), mutation analysis of the SLC25A15 gene (20 labs), orotic acid in urine (6 labs).
Other: liver transaminases (3 labs), acylcarnitines in DBS (2 labs), coagulation (2 labs), urinary organic acids (1 lab), LDH (1 lab), ferritin (1 lab), alpha-fetoprotein (1 lab), neuroimaging (1 lab), EEG (1 lab).

**Overall impression**
Some labs did not report for homocitrulline and/or orotic acid, which lead to a proficiency for analytical findings of 77%. Good proficiency of 91% for interpretation.

# HHH Syndrome in urinary amino acids




# HHH Syndrome



## 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 PKU | | | Patient B α-Mannosidosis | | | Patient C No IEM | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 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 | 0 | 2 | 10 |
| **3** | 2 | 2 | 4 | 2 | 2 | 4 | 1 | 0 | 1 | 9 |
| **4** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 1 | 3 | 11 |
| **5** | 2 | 2 | 4 | 2 | 2 | 4 | 1 | 1 | 2 | 10 |
| **6** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **7** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **8** | 2 | 2 | 4 | 0 | 1 | 1 | 2 | 1 | 3 | 8 |
| **9** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 1 | 3 | 11 |
| **10** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 1 | 3 | 11 |
| **11** | 1 | 2 | 3 | 2 | 2 | 4 | 1 | 2 | 3 | 10 |
| **12** | 2 | 2 | 4 | 0 | 0 | 0 | 2 | 1 | 3 | 7 |
| **13** | 2 | 2 | 4 | 1 | 1 | 2 | 2 | 1 | 3 | 9 |
| **14** | 2 | 2 | 4 | 0 | 1 | 1 | 2 | 1 | 3 | 8 |
| **15** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 1 | 3 | 11 |
| **16** | 2 | 2 | 4 | 2 | 2 | 4 | 1 | 1 | 2 | 10 |
| **17** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 0 | 2 | 10 |
| **18** | 2 | 2 | 4 | 0 | 1 | 1 | 2 | 2 | 4 | 9 |
| **19** | 2 | 2 | 4 | 0 | 1 | 1 | 2 | 2 | 4 | 9 |
| **20** | 2 | 2 | 4 | 0 | 0 | 0 | 2 | 1 | 3 | 7 |
| **21** | 2 | 2 | 4 | 2 | 2 | 4 | 1 | 1 | 2 | 10 |
| **22** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |

**Detailed scores – Round 2**

| Lab n° | Patient D SSADH deficiency | | | Patient E SCAD deficiency | | | Patient F HHH Syndrom | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | A | I | Total | A | I | Total | A | I | Total | Total |
| **1** | 2 | 2 | 4 | 2 | 2 | 4 | 1 | 2 | 3 | 11 |
| **2** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **3** | 2 | 2 | 4 | 2 | 2 | 4 | 0 | 1 | 1 | 9 |
| **4** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **5** | 2 | 2 | 4 | 1 | 2 | 3 | 2 | 2 | 4 | 11 |
| **6** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **7** | 2 | 2 | 4 | 2 | 2 | 4 | 1 | 2 | 3 | 11 |
| **8** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **9** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **10** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **11** | 2 | 2 | 4 | 1 | 2 | 3 | 2 | 2 | 4 | 11 |
| **12** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **13** | 2 | 2 | 4 | 2 | 2 | 4 | 0 | 1 | 1 | 9 |
| **14** | 2 | 2 | 4 | 2 | 2 | 4 | 1 | 2 | 3 | 11 |
| **15** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **16** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **17** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |
| **18** | 2 | 2 | 4 | 1 | 2 | 3 | 2 | 2 | 4 | 11 |
| **19** | 2 | 2 | 4 | 2 | 2 | 4 | 1 | 1 | 2 | 10 |
| **20** | 2 | 2 | 4 | 2 | 2 | 4 | 1 | 2 | 3 | 11 |
| **21** | 2 | 1 | 3 | 1 | 2 | 3 | 1 | 1 | 2 | 8 |
| **22** | 2 | 2 | 4 | 2 | 2 | 4 | 2 | 2 | 4 | 12 |

## Total scores

| Lab n° | A | B | C | D | E | F | Cumulative score | Cumulative score ( % ) | Critical error |
|---|---|---|---|---|---|---|---|---|---|
| **1** | 4 | 4 | 4 | 4 | 4 | 3 | 23 | 96 | |
| **2** | 4 | 4 | 2 | 4 | 4 | 4 | 22 | 92 | |
| **3** | 4 | 4 | 1 | 4 | 4 | 1 | 18 | 75 | |
| **4** | 4 | 4 | 3 | 4 | 4 | 4 | 23 | 96 | |
| **5** | 4 | 4 | 2 | 4 | 3 | 4 | 21 | 88 | |
| **6** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |
| **7** | 4 | 4 | 4 | 4 | 4 | 3 | 23 | 96 | |
| **8** | 4 | 1 | 3 | 4 | 4 | 4 | 20 | 83 | |
| **9** | 4 | 4 | 3 | 4 | 4 | 4 | 23 | 96 | |
| **10** | 4 | 4 | 3 | 4 | 4 | 4 | 23 | 96 | |
| **11** | 3 | 4 | 3 | 4 | 3 | 4 | 21 | 88 | |
| **12** | 4 | 0 | 3 | 4 | 4 | 4 | 19 | 79 | |
| **13** | 4 | 2 | 3 | 4 | 4 | 1 | 18 | 75 | |
| **14** | 4 | 1 | 3 | 4 | 4 | 3 | 19 | 79 | |
| **15** | 4 | 4 | 3 | 4 | 4 | 4 | 23 | 96 | |
| **16** | 4 | 4 | 2 | 4 | 4 | 4 | 22 | 92 | |
| **17** | 4 | 4 | 2 | 4 | 4 | 4 | 22 | 92 | |
| **18** | 4 | 1 | 4 | 4 | 3 | 4 | 20 | 83 | |
| **19** | 4 | 1 | 4 | 4 | 4 | 2 | 19 | 79 | |
| **20** | 4 | 0 | 3 | 4 | 4 | 3 | 18 | 75 | |
| **21** | 4 | 4 | 2 | 3 | 3 | 2 | 18 | 75 | |
| **22** | 4 | 4 | 4 | 4 | 4 | 4 | 24 | 100 | |

**Performance**

| | Number of labs | % total labs |
|---|---|---|
| **Satisfactory performers (≥ 60 % of adequate responses)** | 22 | 100 |
| **Unsatisfactory performers (< 60 % adequate responses and/or critical error)** | 0 | 0 |
| **Partial and non-submitters** | 0 | 0 |

**Overall Proficiency**

| Sample | Diagnosis | Analytical (%) | Interpretation (%) | Total (%) |
|---|---|---|---|---|
| **DPT-SZ-2020-A** | PKU | 98 | 100 | 99 |
| **DPT-SZ-2020-B** | α-Mannosidosis | 70 | 80 | 75 |
| **DPT-SZ-2020-C** | No IEM | 89 | 59 | 74 |
| **DPT-SZ-2020-D** | SSADH deficiency | 100 | 98 | 99 |
| **DPT-SZ-2020-E** | SCAD deficiency | 91 | 100 | 95 |
| **DPT-SZ-2020-F** | HHH Syndrom | 77 | 91 | 84 |

## 10. Annual meeting of participants

Due to the cancellation of the Annual Symposium of the SSIEM, planned for Freiburg this year, there was no meeting of participants. Instead a web-based seminar was held on September 1st.

**Participants** totalled thirty representing 16 different centers (Bern, Durham, Freiburg, Gothenburg, Heidelberg, Innsbruck, Lausanne, Montreal, Oslo, Perth, Rochester, Sheffield, Sherbrooke, Sydney, Tartu, Vancouver).

We remind you that attending the annual meeting is an important part of the proficiency testing scheme. 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

We advise you to check on this link to the ERNDIM website for latest news.
(https://www.erndim.org/home/news.asp)

- **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!). Annex 1 gives the list of the urine samples we already sent.

  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:

ERNDIM DPT Switzerland
Déborah Mathis
Stoffwechseldiagnostik
Zentrum für Labormedizin
INSELSPITAL, Universitätsspital Bern
3010 Bern
Switzerland
Phone, +41 31 632 2790

Please send us an e-mail on the day you send the samples.
deborah.mathis@insel.ch

## 12. Reminders

We remind you that to participate in the DPT-scheme, you should perform:

- Amino acids
- Organic acids
- Oligosaccharides
- Mucopolysaccharides
- Purine and pyrimidine analysis

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.

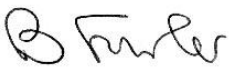
## 13. Tentative schedule and fee in 2021

| | |
|---|---|
| Sample distribution | 9 February 2021 |
| Start of analysis of Survey 2021/1 Website open | March 8 |
| Survey 2021/1 - Results submission | March 29 |
| Survey 2021/1 - Reports | April |
| Start of analysis of Survey 2021/2 | June 7 |
| Survey 2021/2 – Results submission | June 28 |
| Survey 2021/2 - Reports | July |
| Annual meeting of participants | 20/21 October 2021, Rome (to be confirmed) |
| Annual Report 2021 | 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, 2021-02-15
Name and signature of Scientific Advisor
Brian Fowler



**APPENDIX 1. Change log (changes since the last version)**

| Version Number | Published | Amendments |
|---|---|---|
| 1 | 17 February 2021 | 2020 annual report published |
| | | |
| | | |

**END**