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Acylcarnitines in dried blood spots

Centre: Germany

Final Report 2021

prepared by
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Note: This annual report is intended for participants of the ERNDIM Acylcarnitines in dried blood spots (ACDB) Heidelberg 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 performance of your laboratory, unless ERNDIM is required to disclose performance data by a relevant government agency. For details, please see the terms and conditions in the EQA Schemes Catalogue and Participant Guide and the ERNDIM Privacy Policy on www.erndim.org.

1. Introduction

The ERNDIM Acylcarnitine in dried blood spots scheme offers dried blood spots obtained from confirmed patients with confirmed diagnoses to enable laboratories to gain or maintain experience to identify organoacidopathies and fatty acid β-oxidation defects. The scheme is organised by Dr. Claus-Dieter Langhans and Dr. Joachim Janda (Metabolic Centre Heidelberg) in conjunction with CSCQ (sub-contractor on behalf of ERNDIM), both appointed by and according to procedures laid down the ERNDIM Board. CSCQ dispatches the EQA samples to the scheme participants and provides a website for on-line submission of results and access to scheme reports.

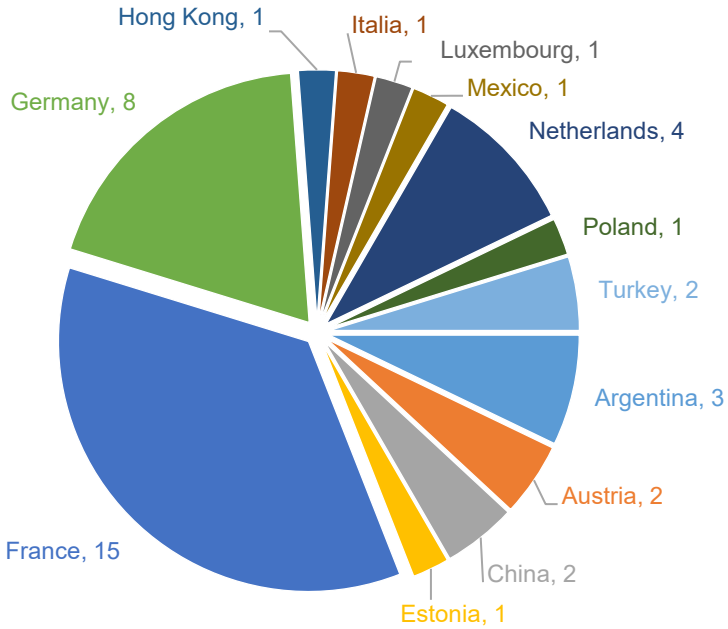
As in previous years, samples were sent out to cover the spectrum of what is typically observed in the metabolic laboratory. A mix of clearly diagnostic profiles and some more challenging profiles were

[1] If this report is not Version 1 for this scheme year, go to APPENDIX 1 for details of the changes made since the last version of this document.

provided. As in previous years normal profiles were also sent out. The requirement to interpret a normal profile, as such, is as important as correctly identifying abnormal profiles. Correctly identifying a profile as normal can avoid unnecessary further investigation and distress to the patient and family.

2. Geographical distribution of participants

In 2021, 42 laboratories from many different countries participated in the ACDB Heidelberg scheme. As in the year before, there was no educational participant in 2021. Educational participants take part in all aspects of the scheme and receive interim reports with scores, but performance is not indicated on the ERNDIM certificate of performance.
Participants and new applicants will be distributed between the Heidelberg, London and Rome acylcarnitine in dried blood spots schemes which are run separately. The three organising laboratories each participate in the other's scheme by rotation.



Geographical distribution and corresponding number of labs participating in the 2021 ACDB-DH scheme.

3. Design and logistics of the scheme including sample information

As usual, the samples used in 2021 were authentic human blood spot samples, 5 from affected patients and one from a healthy individual.
All samples selected by the Scientific Advisor are prepared from 30-50µl of lithium heparin anticoagulated whole blood on Whatman (Schleicher & Schuell) 903™ paper. All samples are obtained following local ethical and consent guidelines.
The scheme has been designed and planned by Claus-Dieter Langhans and Joachim Janda as Scientific Advisors and coordinated by CSCQ as scheme organiser (sub-contractor on behalf of ERNDIM), both appointed by and according to procedures laid down by the ERNDIM Board.
CSCQ dispatched the ACDB EQA samples to the scheme participants and provides a website for on-line submission of results and access to scheme reports. Existing QLOU, ACDB, 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

Participants are also encouraged to make use of the option to upload labelled copies of scans and/or chromatograms on the CSCQ website together with their analytical and interpretative results.

4. Schedule of the scheme

Time schedule in the 2021 ERNDIM ACDB Heidelberg scheme.

	1st Submission Round	2nd Submission Round
Sample ID's:	ACDB-DH-2021-A ACDB-DH-2021-B ACDB-DH-2021-C	ACDB-DH-2021-D ACDB-DH-2021-E ACDB-DH-2021-F
Shipment of samples	February 9th, 2021	
Start of analysis (clinical data available)	March 8th, 2021	June 7th, 2021
Reminder for result submission	March 22th, 2021	June 21st, 2021
Results submission deadline:	March 29th, 2021	June 28th, 2021
Interim reports available on CSCQ website	September 1st, 2021	September 17th, 2021

Samples included in the 2021 ERNDIM ACDB Heidelberg scheme.

Survey	Sample no.	Diagnosis
21-03-ACH	ACDB-DH-2021-A	Propionic acidaemia
	ACDB-DH-2021-B	Multiple Acyl-CoA dehydrogenase (MAD) deficiency
	ACDB-DH-2021-C	Methylmalonic aciduria
21-06-ACH	ACDB-DH-2021-D	Isovaleric aciduria
	ACDB-DH-2021-E	Normal
	ACDB-DH-2021-F	Propionic acidaemia

The scheme format was kept identical to those of previous years. Samples were shipped by regular mail. Details regarding stability of samples are provided in the sample package. Interim reports were generated by the evaluation program developed by CSCQ.

Origin of patients: All blood samples have been provided by the scheme organizers or specified participants.

Patient A:	Propionic acidaemia (PA)	*(Common sample for the ACDB schemes)*
Patient B:	Multiple Acyl-CoA Dehydrogenase (MAD) deficiency	
Patient C:	Methylmalonic acidaemia (MMA)	
Patient D:	Isovaleric acidaemia (IVA)	
Patient E:	normal	
Patient F:	Propionic acidaemia (PA)	

To be able to continue this scheme we need a steady supply of new patient samples. Several laboratories have donated samples to the ACDB scheme in the past, for which they are gratefully acknowledged. If you have one or more samples available and are willing to donate these to the scheme, please contact us at admin@erndim.org.
Laboratories which donate samples that are used in the scheme are eligible for a 20% discount on their participation in the ACDB scheme in the following year.

5. Results

Returned results in the 2021 ERNDIM ACDB Heidelberg scheme.

	Survey 1	Survey 2
Receipt of results	39	39
Non-submitters	3	3

6. Web site reporting

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

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.

Diagnosis

- Don't enter the diagnosis 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 on treatment will not be 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

A scoring system was developed in 2012 and approved by the ERNDIM Scientific Advisory Board (SAB). Similar to other qualitative (proficiency testing) ERNDIM schemes, the maximum score for a sample is 4 points.
Qualitative results and diagnostic proficiency of the 2021 samples were scored using the criteria given below. These criteria have been set by the Scientific Advisor and approved by the SAB of ERNDIM. The final decision on scoring of the scheme has been made by the SAB during its autumn meeting (November 25th, 2021).

General criteria used to score results

Item	Description of scoring criteria	Score
Quantitative results	Correct classification of quantitative results (i.e. normal or increased) according to reference values	1
	Incorrect classification of quantitative results	0
Qualitative results	Correct results according to criteria set for the sample	1
	Incorrect: minimally required results not reported	0
Diagnostic proficiency	Correct according to criteria set for the sample	2
	Partially correct	1
	Unsatisfactory or misleading	0
	Maximum total score	**4**

Starting with the 2014 schemes, the concept of 'critical error' has been introduced to the assessment of the qualitative schemes. Labs failing to make a correct diagnosis of a sample considered eligible for this

category will be deemed not to have reached a satisfactory performance even if their total points for the year is sufficient according to the requirement set by the SAB.
The classification of samples to be judged for critical error was undertaken at the SAB meeting held on November 12th, 2021.

Score for satisfactory performance

For satisfactory performance, at least 17 points out of a maximum of 24 points (71%) are required.
For the Annual Certificate of Participation covering all ERNDIM programmes, the term "participation" for this scheme (ACDB) is defined as meaning that at least two returns are required during the year. If this requirement is not met, the certificate of participation will state "non-submitter" instead of "satisfactory" or "unsatisfactory".
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. Details of how to appeal poor performance are included in the Performance Support Letter sent to poor performing laboratories.

8. Proficiency of the 2021 surveys

ERNDIM provides a single certificate for all its schemes with details of participation and performance.

In 2021, 38 participants submitted 2 reports. From the 40 ordinary (non-educational) participants, 38 (91%) achieved satisfactory performance (score ≥ *71%*, no critical error). Four participants did not attain satisfactory performance, including two due to incomplete submission of results (i.e. no report or only one survey report submitted instead of two).

Overall proficiencies of the 2021 surveys.

Sample ID	Patient diagnosis	Proficiency (%)
ACDB-DH-2021-A	Common sample: Propionic acidaemia (PA)	99
ACDB-DH-2021-B	Multiple Acyl-CoA dehydrogenase (MAD) deficiency	(educational)
ACDB-DH-2021-C	Methylmalonic acidaemia (MMA)	96
ACDB-DH-2021-D	Isovaleric acidaemia (IVA)	100
ACDB-DH-2021-E	normal	97
ACDB-DH-2021-F	Propionic acidaemia (PA)	96

For the 2021 surveys, no Performance Support letters were required to be sent due to the overall very good performance of participants.

9. Results of samples and evaluation of reporting

9.1. Patient A

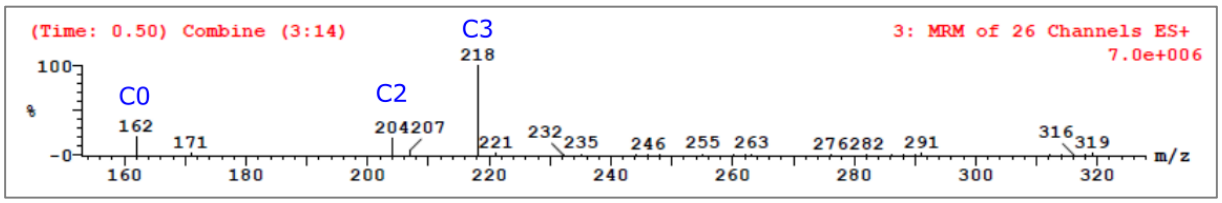
Propionic acidaemia (PA)

Patient details provided to participants

Patient admitted for vomit, asthenia, cardiac insufficiency and acidosis. In treatment with carnitine

Analytical performance

The acylcarnitine profile is characterized by an elevated propionylcarnitine (C3), leading to correspondingly elevated C3/C2 and C3/C0 ratios. Elevated C0 is due to carnitine supplementation.



Example MS/MS spectrum obtained with an AC-Kit for non-derivatized detection.

The key parameters C3 and C3/C2 were reported as increased by thirty-nine (100%) and seventeen participants (44%), respectively. In addition, sixteen laboratories (41%) reported methylmalonyl-/ succinylcarnitine (C4DC), mostly as normal (14 of 39).

Diagnosis / Interpretative proficiency

Thirty-six participants (92%) gave diagnosed propionic acidaemia as their first diagnosis, while two laboratories (5%) preferred methylmalonic acidaemia (mut 0 type) and mentioned propionic acidaemia as an alternative.

Recommendations

Most participants focused primarily on confirmatory analysis and the differentiation between PA and MMA.
The analysis of organic acids in urine (37/39) and mutation analysis (34/39) were mentioned most often. About one third of the participants pointed out the measurement of enzyme activities (15/39), as well as the determination of amino acids (13/39) and homocysteine (12/39) in plasma.

Scoring

While the analytical performance of all laboratories was very good at 100%, the diagnostic performance was slightly lower at 95%.

Overall impression

The overall performance of all laboratories was excellent at 97%.

9.2. Patient B

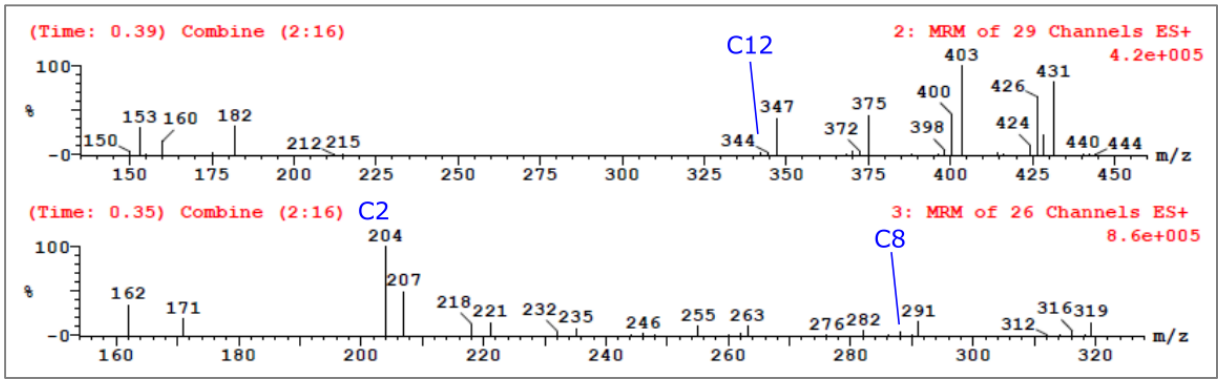
Multiple Acyl-CoA dehydrogenase (MAD) deficiency

Patient details provided to participants

66-year-old female, myopathy after longer walking, head drooping, elevated aminotransferases

Analytical performance

In the acylcarnitine profile, only a slight increase in octanoylcarnitine (C8) is found. However, the elevated ratios C8/C2 and C8/C12, together with the clinical details provided, may give an indication of the diagnosis.



Example MS/MS spectrum obtained with an AC-Kit for non-derivatized detection.

Elevated C8/C2 was reported by 6 participants (15%) and elevated C8/C12 by three (8%). The combination of elevated C8 and C10 was mentioned most frequently (six labs / 15%). Twenty participants (51%) did not report any noticeably elevated metabolites or ratios in this sample.

Taken together, the analytical performance was 45%.

Diagnosis / Interpretative proficiency

MAD deficiency was mentioned as primary or alternative diagnosis by only eight laboratories (21 %). Twenty-five participants (64%) found the sample to be normal or found no evidence of fatty acid oxidation disorders. Even if MAD deficiency and diagnoses suggestive of mitochondriopathies are considered as correct diagnoses, the interpretative proficiency was 32%.

Recommendations

Many participants recommended analysis of organic acids (44%) and / or repetition of acylcarnitine profile (31%).

Scoring

This was not an easy sample and caused problems for many participants as relevant metabolites showed little or no increase.

During its November 2021 meeting, the SAB of ERNDIM has decided to consider this sample as educational.

9.3. Patient C

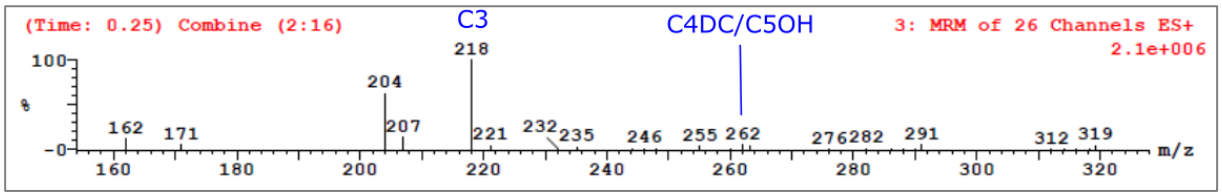
Methylmalonic acidaemia (MMA) due to methylmalonyl-CoA-mutase deficiency, mut(0) type

Patient details provided to participants

8-month-old girl with failure to thrive and feeding intolerance

Analytical performance

The acylcarnitine profile shows clearly elevated propionylcarnitine (C3) and C3/C2 ratio together with slightly elevated methylmalonylcarnitine (C4-DC).



Example MS/MS spectrum obtained with an AC-Kit for non-derivatized detection.

Thirty-eight (97%) of the reporting labs detected elevated amounts of C3-carnitine and thirty-four (87%) reported abnormal concentrations of C4DC or (C4DC+C5OH). The C3/C2 ratio was reported as elevated or even grossly elevated by seventeen (44%) participants. The overall analytical proficiency was 96%.

Diagnosis / Interpretative proficiency

Methylmalonic acidaemia was diagnosed by thirty participants (77%). Including participants who reported MMA or PA as an alternative diagnosis, the interpretative proficiency was 96%.

Recommendations

95% of participants suggested further investigations focusing on confirmation of the reported diagnosis, mostly by determination of organic acids in urine (37/39). Of the thirty laboratories with an initial diagnosis of methylmalonic acidaemia, most referred to mutation analysis directly (23/30).

Scoring

Both analytical and diagnostic proficiency were 96%, resulting the same score for the overall proficiency here.

Overall impression

This sample was not very challenging for the participants.

9.4. Patient D

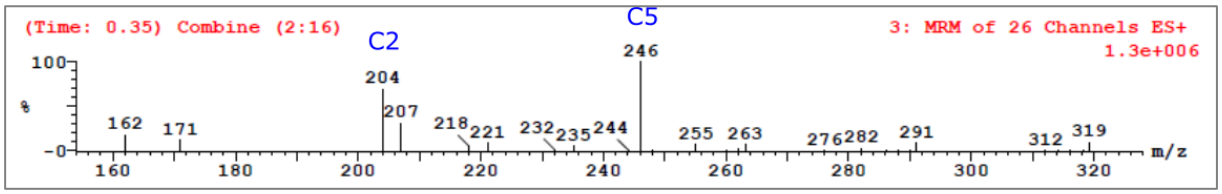
Isovaleric acidaemia (IVA)

Patient details provided to participants

5 year-old girl with recurrent episodes of ketoacidosis

Analytical performance

For isovaleric acidaemia, the key acylcarnitine-metabolites are C5 and the C5/C2 ratio, which are clearly elevated in this sample.



Example MS/MS spectrum obtained with an AC-Kit for non-derivatized detection.

All active participants (39, 100%) identified elevated C5-carnitine.
Nine laboratories (23%) reported an increased ratio of C5/C2.

Diagnosis / Interpretative proficiency

Isovaleric acidaemia was diagnosed by all participants (100%).

Recommendations

For confirmation of isovaleric acidaemia the majority of the labs recommended the analysis of organic acids in urine (38/39) and mutation analysis (36/39).
Fourteen participants (36%) advised on determination of enzyme activities of isovaleryl-CoA-dehydrogenase (14/39).
Amino acid analysis in plasma (5/39), determination of carnitine status (4/39) and measurement of acyl glycines in urine (4/39) were also suggested.
A few laboratories pointed out that elevated C5 requires a differential diagnosis of isovaleric acidaemia from short/branched-chain acyl-CoA dehydrogenase (SBCAD) deficiency and administration of pivaloyl containing drugs, either by chromatographic separation of the C5 isomers in a second-tier test or via analysis of organic acids and arylglycines in urine by looking for the corresponding glycine derivatives.

Scoring

As expected, analytical and diagnostic performance of all laboratories was very good at 100%.

Overall impression

This sample was straightforward and not very challenging for the participants as shown by the excellent results.

9.5. Patient E

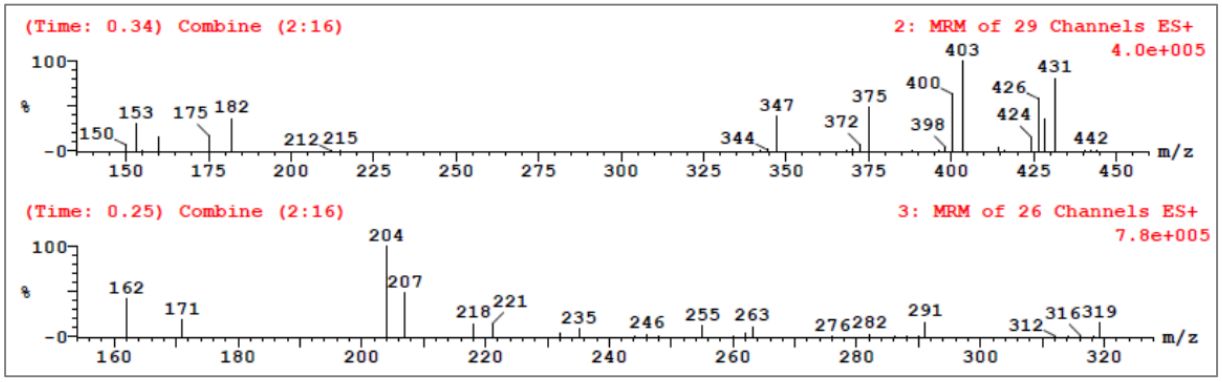
Normal control sample

Patient details provided to participants

55-year-old man with chronic myopathy

Analytical performance

This sample of a healthy adult shows a normal profile of acylcarnitines.



Example MS/MS spectrum obtained with an AC-Kit for non-derivatized detection.

Thirty participants (77%) reported a normal acylcarnitine profile. Nine laboratories (23%) found several acylcarnitines elevated, of which C3 and C4DC were mentioned most frequently.

Diagnosis / Interpretative proficiency

Thirty-seven participants (95%) stated that the acylcarnitine profile has no abnormalities.
Some participants reported diagnoses, such as methylmalonic acidaemia, carnitine-palmitoyl-transferase II deficiency (CPT 2) or “exclusion of fatty acid oxidation defects” (reported by one participant each.

Recommendations

Due to the clinical description and a normal acylcarnitine profile, the focus of the proposed investigations was on the clarification of a possible fatty acid oxidative disorder and mitochondriopathies.

For this purpose, organic acid analysis (13/39), repetition of the acylcarnitine analysis after 14h fasting or under metabolic stress (8/39), determination of acylcarnitines in plasma (4/39) or amino acid analysis in plasma (4/39) were most frequently suggested.

Scoring

Almost all participants found this acylcarnitine profile to be normal.

Overall impression

In this sample, recognizing a normal sample was not a major difficulty.

Despite the good performance, it must again be pointed out that the comment fields should not be used for reporting normal controls. Instead, a key metabolite "normal profile" should be created and entered into the result field.

9.6. Patient F

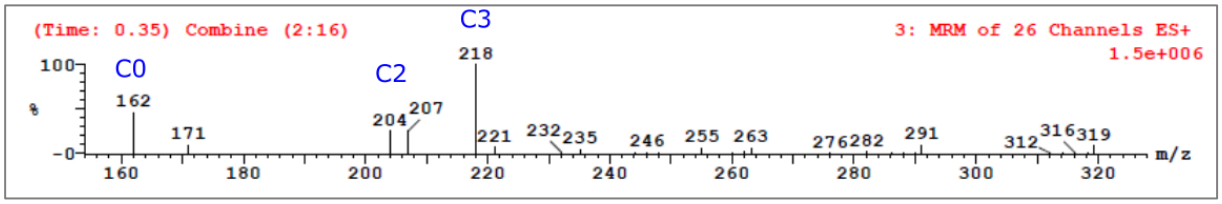
Propionic acidaemia (PA)

Patient details provided to participants

4-year-old male with recurrent hyperammonaemic episodes

Analytical performance

The acylcarnitine profile shows increased C3-carnitine and C3/C2 ratio. C4DC is within the normal range.



Example MS/MS spectrum obtained with an AC-Kit for non-derivatized detection.

Thirty-eight participants (97%) detected elevated amounts of C3-carnitine. Seventeen labs (44%) reported C3/C2 ratio. Sixteen of them (41%) found an increased ratio, one a normal ratio.
Methylmalonyl-carnitine, either as C4DC or as (C4DC+C5OH), was found to be normal or low by twenty-one laboratories (54%). Only one participant found this metabolite to be elevated.
Twenty-nine respondents (74%) reported free carnitine as elevated and two as normal (5%).

Diagnosis / Interpretative proficiency

Thirty-eight participants (97%) detected elevated amounts of C3-carnitine. Seventeen labs (44%) reported C3/C2 ratio. Sixteen of them (41%) found an increased ratio, one a normal ratio.
Methylmalonyl-carnitine, either as C4DC or as (C4DC+C5OH), was found to be normal or low by twenty-one laboratories (54%). Only one participant found this metabolite to be elevated.
Twenty-nine respondents (74%) reported free carnitine as elevated and two as normal (5%).

Recommendations

All participants (100%) suggested further investigations, focusing on differentiation of propionic acidaemia/ methylmalonic acidaemia (determination of organic acids in urine; 38/39) or direct confirmation of the suspected diagnosis via molecular genetic testing (29/39).

Scoring

The differential diagnosis propionic acidaemia / methylmalonic acidaemia was correctly recognized by almost all participants (38/39), resulting in an overall proficiency of 96%.

Overall impression

Almost all participants produced correct analytical results and gave correct diagnoses, resulting in excellent combined proficiency.

10. Scores of participants

All data transfer, the submission of data as well as the request and viewing of reports proceed via the ACDB-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.

10.1. Detailed scores of 1st circulation

Lab n°	Patient A Propionic acidaemia			Patient B MAD Deficiency			Patient C Methylmalonic aciduria			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	1	3	2	2	4	2	2	4	11
2	2	2	4	2	2	4	2	2	4	12
3	2	2	4	0	0	0	2	2	4	8
4	0	0	0	0	0	0	0	0	0	0
5	2	2	4	2	2	4	2	2	4	12
6	2	2	4	2	1	3	2	2	4	11
7	2	2	4	2	0	2	2	2	4	10
8	2	2	4	2	2	4	2	2	4	12
9	2	2	4	2	1	3	2	2	4	11
10	2	2	4	1	0	1	2	2	4	9
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	2	2	4	12
14	2	2	4	2	0	2	2	2	4	10
15	2	2	4	2	0	2	2	2	4	10
16	2	2	4	0	0	0	2	2	4	8
17	2	2	4	0	0	0	2	2	4	8
18	2	2	4	2	2	4	2	2	4	12
19	2	2	4	0	0	0	2	2	4	8
20	2	2	4	2	1	3	2	2	4	11
21	2	2	4	0	1	1	1	2	3	8
22	2	2	4	0	0	0	2	2	4	8
23	2	2	4	1	0	1	2	2	4	9
24	2	2	4	0	0	0	2	2	4	8
25	2	2	4	1	0	1	2	2	4	9

Lab n°	Patient A Propionic acidaemia			Patient B MAD Deficiency			Patient C Methylmalonic aciduria			
	A	I	Total	A	I	Total	A	I	Total	Total
26	2	2	4	1	1	2	2	2	4	10
27	2	2	4	0	0	0	2	2	4	8
28	2	2	4	0	0	0	2	2	4	8
29	2	2	4	0	0	0	2	2	4	8
30	2	2	4	0	0	0	2	2	4	8
31	2	2	4	0	0	0	1	1	2	6
32	2	2	4	2	2	4	2	2	4	12
33	2	2	4	0	0	0	1	2	3	7
34	2	2	4	0	0	0	2	2	4	8
35	2	2	4	0	0	0	2	2	4	8
36	2	2	4	1	0	1	2	2	4	9
37	2	2	4	0	1	1	2	2	4	9
38	0	0	0	0	0	0	0	0	0	0
39	2	2	4	0	0	0	2	2	4	8
40	0	0	0	0	0	0	0	0	0	0
41	2	2	4	0	0	0	2	0	2	6
42	2	2	4	1	1	2	2	2	4	10

10.2. Detailed scores of 2nd circulation

Lab n°	Patient D Isovaleric aciduria			Patient E Normal			Patient F Propionic acidemia			
	A	I	Total	A	I	Total	A	I	Total	Total
1	2	2	4	2	0	2	2	2	4	10
2	2	2	4	2	2	4	2	2	4	12
3	2	2	4	2	2	4	2	2	4	12
4	0	0	0	0	0	0	0	0	0	0
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	2	2	4	12
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	2	2	4	2	2	4	12
12	2	2	4	2	2	4	2	2	4	12
13	2	2	4	2	2	4	2	2	4	12
14	2	2	4	2	2	4	2	2	4	12
15	2	2	4	2	2	4	0	0	0	8
16	2	2	4	2	2	4	2	2	4	12
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20	2	2	4	2	2	4	2	2	4	12
21	2	2	4	2	2	4	2	2	4	12
22	2	2	4	2	2	4	2	2	4	12
23	2	2	4	2	2	4	2	2	4	12
24	2	2	4	2	2	4	2	2	4	12
25	2	2	4	2	2	4	2	2	4	12
26	2	2	4	2	2	4	2	2	4	12
27	2	2	4	2	2	4	2	1	3	11
28	2	2	4	2	2	4	2	2	4	12
29	2	2	4	2	2	4	2	2	4	12
30	2	2	4	2	2	4	2	2	4	12

Lab n°	Patient D Isovaleric aciduria			Patient E Normal			Patient F Propionic acidemia			
	A	**I**	**Total**	**A**	**I**	**Total**	**A**	**I**	**Total**	**Total**
31	2	2	4	2	1	3	2	2	4	11
32	2	2	4	2	2	4	2	2	4	12
33	0	0	0	0	0	0	0	0	0	0
34	2	2	4	2	2	4	2	2	4	12
35	2	2	4	2	2	4	2	2	4	12
36	2	2	4	2	2	4	2	1	3	11
37	2	2	4	2	2	4	2	2	4	12
38	0	0	0	0	0	0	0	0	0	0
39	2	2	4	2	2	4	2	2	4	12
40	2	2	4	2	2	4	2	2	4	12
41	2	2	4	2	2	4	2	2	4	12
42	2	2	4	2	2	4	2	2	4	12

10.3. Total scores

Sample B was considered as an educational sample. The maximum achievable score is therefore 20 points.

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score in %	Critical error
1	3	--	4	4	2	4	17	85	
2	4	--	4	4	4	4	20	100	
3	4	--	4	4	4	4	20	100	
4	0	--	0	0	0	0	0	0	
5	4	--	4	4	4	4	20	100	
6	4	--	4	4	4	4	20	100	
7	4	--	4	4	4	4	20	100	
8	4	--	4	4	4	4	20	100	
9	4	--	4	4	4	4	20	100	
10	4	--	4	4	4	4	20	100	
11	4	--	4	4	4	4	20	100	
12	4	--	4	4	4	4	20	100	
13	4	--	4	4	4	4	20	100	
14	4	--	4	4	4	4	20	100	
15	4	--	4	4	4	0	16	80	
16	4	--	4	4	4	4	20	100	
17	4	--	4	4	4	4	20	100	
18	4	--	4	4	4	4	20	100	
19	4	--	4	4	2	4	18	90	
20	4	--	4	4	4	4	20	100	
21	4	--	3	4	4	4	19	95	
22	4	--	4	4	4	4	20	100	
23	4	--	4	4	4	4	20	100	
24	4	--	4	4	4	4	20	100	
25	4	--	4	4	4	4	20	100	
26	4	--	4	4	4	4	20	100	
27	4	--	4	4	4	3	19	95	
28	4	--	4	4	4	4	20	100	
29	4	--	4	4	4	4	20	100	

Lab n°	A	B	C	D	E	F	Cumulative score	Cumulative score in %	Critical error
30	4	--	4	4	4	4	20	100	
31	4	--	2	4	3	4	17	85	
32	4	--	4	4	4	4	20	100	
33	4	--	3	0	0	0	7	35	
34	4	--	4	4	4	4	20	100	
35	4	--	4	4	4	4	20	100	
36	4	--	4	4	4	3	19	95	
37	4	--	4	4	4	4	20	100	
38	0	--	0	0	0	0	0	0	
39	4	--	4	4	4	4	20	100	
40	0	--	0	4	4	4	12	60	
41	4	--	2	4	4	4	18	90	
42	4	--	4	4	4	4	20	100	

10.4. Performance

	Number of labs	% total labs
Satisfactory performers (≥ 71 % of adequate responses)	38	95
Unsatisfactory performers (< 71 % adequate responses and/or critical error)	2	5
Partial and non-submitters	4	10

10.5. Overall Proficiency

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Total (%)
ACDB-DH-2021-A	Propionic acidaemia	93	92	92
ACDB-DH-2021-B	MAD Deficiency*	42	30	36*
ACDB-DH-2021-C	Methylmalonic aciduria	89	89	89
ACDB-DH-2021-D	Isovaleric acidaemia	85	85	85
ACDB-DH-2021-E	Normal	85	79	82
ACDB-DH-2021-F	Propionic acidaemia	83	80	82

* Evaluated as educational sample

11. Tentative schedule in 2022

Sample Dispatch Date	02 February 2022	
Circulation	**2022/1**	**2022/2**
Sample IDs	ACDB-DH-2022-**A** ACDB-DH-2022-**B** ACDB-DH-2022-**C**	ACDB-DH-2022-**D** ACDB-DH-2022-**E** ACDB-DH-2022-**F**
Analysis start and Website submission availability	14 March 2022	06 June 2022
Reminder for result submission	28 March 2022	21 June 2022
Results submission deadline	04 April 2022 (23:59 CET*)	28 June 2022 (23:59 CET*)
Annual Report 2022 available	December 2022	

* CET = Central European Time, UTC +01:00

There will be no changes in the structure and design of the ACDB scheme in 2022.
However, from 2022 onwards, Dr Joachim Janda from the metabolic centre Heidelberg will replace Dr Claus-Dieter Langhans as the new scientific advisor for ACDB Heidelberg.

12. 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 ACDB scheme this certificate will indicate if results were submitted and whether satisfactory performance was achieved in the scheme.

Date of report, 2022-05-24
Name and signature of Scientific Advisor

Dr C. D. Langhans
Scientific Advisor
Laboratory of Metabolic Diseases

Dr J. Janda
Deputy Scientific Advisor
Laboratory of Metabolic Diseases

Prof. Dr. G. F. Hoffmann
Director
Department of General Paediatrics

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

Version Number	Published	Amendments
1	24 May 2022	2021 annual report published

END