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Nijmegen / Amsterdam

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1 Introduction

The Diagnostic Proficiency Test (DPT) scheme for inborn errors of metabolism is run by ERNDIM as before from five DPT-centres spread throughout Europe. The Nijmegen/Amsterdam scheme serves the region of The Netherlands, Belgium and the Northwestern part of Germany. This year's participation amounted to 20 laboratories again, which is considered to be the optimum size of a scheme.
Last year a decision was made by ERNDIM to develop website reporting for the DPT-scheme. The Swiss CSQC organisation has encountered serious difficulties in setting up the program and is obliged to postpone the test phase until 2009. It is hoped that formal website reporting can start in 2010. In accordance with this, the status of DPT-centres will slightly change in a way that they will act only as scientific advisors.

As before the Nijmegen / Amsterdam scheme runs in conjunction with SKML, The Dutch QA-organization for medical laboratories.
The urine samples were shipped in January and June, thereby enabling a constructive discussion of results in September. This meeting is a closed meeting for participants and chaired by the Scientific Advisor, currently M. Duran, Academic Medical Center Amsterdam. His task will be taken over by G. Ruijter, Erasmus Medical Center Rotterdam following the completion of the 2009 series of DPT-tests.
The annual meeting in Lisbon was this time attended not only by the Dutch, Belgian, and Luxembourg participants, but also by representatives of two novel participants. Unfortunately, as in previous years none of the German participants was present at the meeting.

2 Participants

The 2008 scheme had 20 participants with the following allocation:

Country	Number of participants
Luxembourg	1
Belgium	3
Germany	5
The Netherlands	11

3 Logistics of the scheme

As in previous years, the samples were dispatched to the participating labs in January and in June. Shipment was carried out by regular mail, a system which may turn out to give rise to a potential delay. This may limit the available time for analysis of the labs. Sample F was the pan-European sample, distributed by the colleagues of the Prague scheme. Its results were discussed at the Lisbon ERNDIM-workshop and can be viewed in the workshop summaries on the website.

The Annual DPT-meeting was attended by representatives of 12 participating labs.

4 Scoring of results

Following lengthy discussions in the Scientific Advisory Board, a scoring system was agreed upon in 2002.

For each individual sample a score can be achieved for:		
		Score
Analytical performance:	Correct results of the appropriate tests	2
	Partially correct or non-standard methods	1
	Unsatisfactory or misleading	0
Interpretative performance:	Good (diagnosis was established)	2
	Helpful but incomplete	1
	Misleading / wrong diagnosis	0
Recommendations: (for further investigations)	Helpful	1
	Unsatisfactory or misleading	0
	Total score	5

Poor performers are those participants who score less than 15 points out of the maximum 30 in a given year. These poor performers will receive a so-called warning letter from the Scientific Advisor.
At the request of several participants, individual scoring results will be sent to each individual participant.

5 Results of individual samples.

In 2008 the following results were observed for 20 participants.

Sample	**Diagnosis**	**Nº reports**	**Nº correct diagn.**	**Nº partial correct diagn.**
A	Mucopolysaccharidosis IIIB	19	6	2
B	Maple syrup urine disease	19	19	
C	Hyperoxaluria Type I	19	14	1
D	G_{M2}-gangliosidosis	17	9	
E	None	17	13	
F	Mucopolysaccharidosis III	17	9	5

The total number of reports was 108 out of 120 which were expected based on the number of participants. Of these 70 submissions, (65%) had a correct diagnosis. For comparison: the percentage of correct diagnoses was 74 in 2007. It can be observed that the two MPS samples in the 2008 series scored particularly low which may have contributed to the slightly less successful series of DPT analyses this year. In order to exemplify the potential pitfalls of the MPS-test, the results of all submissions concerning patient A were tabulated.

Lab.no	MPS	MPS ref	Electrof	
1	5.9	1.5-3.8	HS	
2	7.8			No diagnosis
3	11		HS	
4	12		np	
5	6.9	normal		No diagnosis
6	11			No diagnosis
7	7	normal		
8	3.8	normal		
9	9	1-8	np	
10	11		HS (other lab)	
11	6 (↑)		HS	
12	np			No diagnosis
13	13.2	<5.2	HS	
14	9.9 (↑)			No diagnosis
16	4.96	3.3 +/- 0.9		No diagnosis
17	4.3	normal		No diagnosis
18	np			No diagnosis
19	7.4	2.4-3.8	DS	
20	np			No diagnosis

This example clearly shows the difficulties in interpreting quantitative MPS-values in adult patients and further strengthens the need to compose in-house reference values.

All scores of the 2008 scheme are summarized in the next Table, showing that 4 out of 20 labs did not meet the criteria of adequate performance.

Centre ERN/skml	subscribed	submitted results	satisfactory performance	
1	yes	all	yes	28
2	yes	all	yes	22
3	yes	all	yes	25
4	yes	all	yes	23
5	yes	all	yes	20
6	yes	all	yes	26
7	yes	all	yes	24
8	yes	all	yes	23
9	yes	all	yes	23
10	yes	all	yes	28
11	yes	all	yes	26
12	yes	all	yes	21
13	yes	all	yes	29
14	yes	all	yes	16
15	yes	no results	no	0
16	yes	all	yes	16
17	yes	3 of 6	no	5
18	yes	all	no	12
19	yes	all	yes	21
20	yes	3 of 6	no	8

6. Minutes of the Annual meetingfor participants of the ERNDIM Diagnostic Proficiency Test (DPT-Amsterdam/Nijmegen); Lisbon, September 2nd 2008.

Present:
Amsterdam: Duran (chairman, AMC), Blom (VUMC)
Rotterdam: van Diggelen, Huijmans, Schoonderwoerd, Ruijter, Wijgerde,
Nijmegen: Ruitenbeek,
Leiden: Onkenhout,
Utrecht: Prinsen, Verhoeven-Duif,
Almelo: Maatman,
Maastricht: Bakker, Bierau, Keularts, Spaapen (minutes),
Groningen: Reijngoud,
Tilburg: van den Berg, Jakobs,
Luxembourg Hoffmann,
Liege: Boemer,
Bruxelles: Marie, Vincent,
Brugge: Bernard.

Welcome:
The chairman welcomes the participants. As DPT scientific adviser Ries Duran will be replaced by George Ruijter, Dept. of Clinical Genetics, Erasmus MC, Rotterdam. They will take care of the DPT-affairs together in year 2009.
Absence of German participants was noticed. This is a regretful development.
20 Laboratories were participating in 2008.

Minutes of the meeting in Hamburg, September 4th 2007
The minutes were approved, with thanks to the secretary Jan Huijmans.

Information from the Executive Board, Trust Board and Scientific Advisory Board
In 2009:

1. Mick Henderson will replace Brian Fowler as chairman of ERNDIM
2. The participation fees will rise with 2% in 2009
3. Participants are asked for patient's urine samples. When the urine is used in the scheme DPT participation at a discount will be offered.
4. At the end of 2009 Malcolm Heron will retire
5. Because of the need for accreditation of ERNDIM an official office will be established
6. Camilla Reed, Sheffield, is appointed to be sample archivist for ERNDIM quality control samples
7. Jan Huijmans will start a pilot MPS scheme
8. The amounts of urine samples have been too low (< 10 ml) in 2008. To be checked by SKML

Web-site reporting
A new Web-sit reporting system is designed by Swiss CSCQ, Geneva. The option "advice to the referring physician" has not yet been completed.
The pilot Web-site reporting system will be made available for testing in 2009
Colleagues from Utrecht, Rotterdam, Nijmegen, Amsterdam, Groningen and Maastricht will try to report via this system.

DPT 2008 results
Patient A: Mucopolysaccharidosis III {Sanfilippo type B}; (6 out of 19 correct)
This case was experienced as difficult. Huijmans's scan was negative. Clinical presentation was considered to be not really specific of Sanfilippo.

Patient B: MSUD; (19 out of 19 correct)
pH of the urine is high. Origin of 3-HIVA and lactate not clear.

Patient C: Hyperoxaluria type I; (4 out of 19 missed)
Great variation in oxalic acid, possibly due to differences in analytic methods.

Patient D: GM2-gangliosidosis; (10 out of 19 correct)
Difficult interpretation of TLC, diluted urine, sample too small.

Patient E: No metabolic disorder. A few labs suggested the possibility of a disorder such as carnosinase deficiency based on the slightly elevated levels of carnosine and anserine in the urine. It was, however, generally agreed that these substances are derived from the diet.
Two labs reported a modest increase of glyceric acid in their organic acid profile. Glyceric acid is generally present in control urines in concentrations up to 30 mmoles/mole creatinine according to the chapter on organic acids in the Blau-book (Physician's Guide to the Laboratory Diagnosis of Metabolic Diseases)

Patient F: Mucopolysaccharidosis III (Sanfilippo type ?) ; (common sample : 57% correct)
76 out of 79 correctly found increased GAG
53 out of 59 correctly found increased HS

Next meeting
Because in 2009 the ICIEM meeting will take place in San Diego the ERNDIM meeting will be organized in Basel, Switzerland, 22-23 October.

George Ruijter, ErasmusMC Rotterdam
has been found able and willing to act as
Scientific Advisor DPT in the near future