

	ERNDIM Diagnostic Proficiency Testing Centre Central Europe Nijmegen / Amsterdam	
	Prof. dr. J.L. Willems University Medical Centre Nijmegen SKML, Section Metabolic Diseases P.O. Box 9101 NL – 6500 HB Nijmegen e-mail: jl.willems@akc.umcn.nl	Dr. M. Duran Academic Medical Center Amsterdam Lab. Genetic Metabolic Diseases P.O. Box 22700 NL – 1100 DE Amsterdam e-mail : m.duran@amc.nl

ANNUAL REPORT 2007

1 Introduction

The Quality Assurance Program (QAP) for Diagnostic Proficiency Testing (DPT) of Inherited Metabolic Diseases is organised by ERNDIM. As in the previous year, the 2007 DPT scheme was run by five DPT centres located in: Sheffield, UK; Prague, CZ; Nijmegen/Amsterdam, NL; Lyon, FR and Basel, CH. Each centre continues to serve its maximum number of participants, approximately 20.

It turns out to be increasingly difficult to obtain sufficient amounts of genuine patient samples, not in the least as a result of tightening privacy regulations. ERNDIM has taken the initiative to appoint a sample archivist who is to assure a continuing supply of samples. It is considered worthwhile to approach patient/parent societies in this respect.

In 2007 ERNDIM has decided to make website reporting of DPT-schemes operational. The Swiss QA-organization, located in Geneva, will act as the central point dealing with both the shipping of samples and the maintenance of the electronic reporting system. A pilot will probably run in the second half of 2008.

The Nijmegen/Amsterdam DPT-scheme runs in conjunction with SKML.

The SKML (previously called SKZL) is a Dutch QAP-organisation collecting samples of urine from patients with metabolic diseases (participants are obliged to deliver these samples). Twice a year SKML distributes these samples to the participants of the DPT scheme, evaluates all results, prepares a report and make the reports available to the participants. Once a year a meeting of the participants is organised to discuss the results, to bring faulty results into focus and to discuss recommendations for improvement. This meeting is chaired by the Scientific Advisor of the DPT scheme, currently dr. M. Duran, Academic Medical Center Amsterdam. The 2007 participants meeting was held in Hamburg at SSIEM-symposium on 4th September. Unfortunately, not all participants were able to attend this meeting. Those who were present enjoyed the discussion and regarded it as a tool for improving the performance of their labs.

2 Participants

In 2007 Nijmegen/Amsterdam DPT-scheme had 19 participants from Belgium, Germany and The Netherlands.

Country	Number of participants
Belgium	3
Germany	5
The Netherlands	11

3 Logistics of the scheme

Two sets of three urine samples were sent to the participants, the first batch on 8th January and the second batch on 11th June. Results were expected back three weeks (21 days) later. Not all labs met the deadline; returns were received up to 6 days late. It has to be realized that late submissions will be impossible once the web-system is in operation. Many of the participants made a plea for a longer period allowed for reporting.

Sample M was the pan-European sample, collected and distributed by the Sheffield DPT-centre. A summary of the diagnostic findings in this sample can be found in "meetings and reports" of the ERNDIM-website.

The DPT-discussion in Hamburg on 4th September 2007 was attended by representatives from nine participating laboratories, a slight decrease in comparison to the attendance in the previous year.

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 Reports and scores

Nineteen samples were sent out in each circulation. For 2007.1 a total of 18 returns were received, that of 2007.2 reached the maximum of 19 returns.

The summary of the diagnoses is listed below:

Sample	Diagnosis	Correct diagnosis made/ number of reports
G	Aspartylglucosaminuria	14/18
H	Alpha-mannosidosis	14/18
J	Xanthinuria	16/18
K	No diagnosis	15/19
L	Beta-ketothiolase deficiency	19/19
M	Hperlysinemia	13/19

The total number of reports is this year amounted III; of these 81 (74%) were correct diagnoses. The individual performances of the laboratories are listed in the table below. Two labs reached the maximum score of 30 points and two labs failed to reach the minimum level of 15 points.

Lab no	Patient G	Patient H	Patient J	Patient K	Patient L	Patient M	Total
1	5	5	5	5	5	5	30
2	5	5	5	5	5	3	28
3	5	5	5	5	5	5	30
4	5	5	5	5	4	3	27
5	5	5	5	5	5	0	25
6	5	5	5	5	5	3	28
7	5	5	5	4	5	4	28
8	5	5	5	4	5	5	29
9	5	5	5	5	5	4	29
10	5	5	5	4	5	5	29
11	5	5	5	5	3	1	24
12	1	0	5	4	5	4	19
13	5	5	5	5	5	1	26
14	5	2	5	5	4	4	25
15	3	1	0	0	5	0	9
16	0	5	5	4	5	3	22
17	0	0	0	5	5	0	10
18	2	2	5	5	5	3	22
19	5	5	0	5	5	4	24

6 Minutes of the meeting for participants of the Diagnostic Proficiency Test (DPT) Centre of Metabolic Diseases for Central Europe (Nijmegen-Amsterdam) held during the SSIEM Symposium in Hamburg on September 4th 2007.

Present:

Amsterdam: Duran (chairman)(AMC), Wamelink (VUMC)

Brussel: Martens and Gerlo

Groningen: Reijngoud

Leiden: Onkenhout

Maastricht: Dorland, Bierau, Spaapen and Keularts

Nijmegen: Kluijtmans and Ruitenbeek

Rotterdam: Huijtmans (minutes) and Ruijter

Tilburg: van den Berg and Jakobs

Utrecht : Prinsen and de Sain

Welcome

The chairman welcomes the participants. Next year it will be the last time for Ries Duran to chair this meeting. A candidate for this position is asked. The candidate will also be Scientific Adviser of ERNDIM and contact person for SKML

Minutes of the meeting in Prague, October 5th, 2006

It is confirmed that the period for analysing and reporting will be 4 weeks from the moment that website-reporting is possible.

The minutes were accepted, with thanks to the secretary Wim Ruitenbeek.

Information from Executive Board, Trust Board, and Scientific Advisory Board

1. Accreditation of ERNDIM will be started. Fowler will present a proposition and a time-table
2. A pilot for website-reporting is now ongoing in two DPT centers. It will start in all centers in 2009
3. ERNDIM looks for a Patient Sample Archivist, who will be active in collecting patient samples for 3-6 years. Please contact Jim Bonham
4. ERNDIM will be involved in the training for Clinical Chemist (hereditary metabolic diseases) and Clinical biochemical geneticist. In England exists a good structure for this (see www.metbio.net). From the Netherlands Ron Wevers has been asked to participate.
5. Next year Brian Fowler will step down as chairman. Also Malcolm Heron from SSIEM will retire next year. The SSIEM office will go to a professional organization. For ERNDIM this may become more expensive once it decides to follow SSIEM in this respect.

Patient samples

Patient G : aspartylglucosaminuria (14 out of 18 were correct)

6/18 reported a normal amino acid chromatogram. The type of amino acid analyzer may be important : probably Jeol does not separate aspartylglucosamine from the urea peak.

Spraying the oligosaccharide plate with ninhydrin gives additional information. This is also true for the sialyloligosaccharides. Total sialic acid is not increased.

Patient H : α -mannosidosis (14 out of 18 correct)

The urine was 1 :3 diluted with water and was a combination of samples from two sisters. Two labs reported the creatinine, recalculated from the dilution. The message is that with mental retardation and hearing loss, α -mannosidosis should always be excluded. Two labs found a normal oligosaccharide pattern.

Patient J : xanthinuria (16 out of 18 correct)

7/18 labs did not report uric acid. There is a good correlation between tandem-MS and HPLC uric acid measurements. The correlation with the clinical chemistry lab is not good. Advice : measure uric acid in all urines.

Only two labs reported normal sulphocysteine. Other labs did look after that but did not report it. One lab found xanthine in the organic acid analysis: this is peculiar.

The diagnosis xanthine dehydrogenase deficiency should be specified: Sulfurase deficiency (see Mol. Genet Metab 91 : 23 (2007)). The enzyme assay can be done in liver and intestine. Jorgen knows of an assay in erythrocytes and will report this.

The allopurinol test can differentiate between xanthinuria type I and II.

Allopurinol treatment reduces the formation of xanthine through inhibition by oxypurinol.

However, the latter is not formed in xanthinuria type II

Patient K : no diagnosis (15 out of 19 correct)

10/19 reported increased β -AIB. In two labs this resulted in the subtraction of 1 point which has been corrected. It is generally agreed that only metabolites which are essential for the diagnosis should be mentioned.

Only 8/19 reported creatine : this should be measured with this clinical picture. If you do not measure it yourself, ask another laboratory.

Patient L : β -ketothiolase deficiency (19 out of 19 correct)

Because 2-methyl-3-oxo-butyric acid was not present, you should also think of SCHMAD deficiency. However this is artificial because due to the heat inactivation of the sample, 2-methyl-3-oxo-butyric acid has disappeared.

The acylcarnitine pattern in the urine can give additional information by showing C5:1-carnitine and OH-C5-carnitine.

Some labs measured MPS : this is not indicated by this clinical picture. An isoleucine challenge test is not necessary. Measuring acylcarnitines in blood (9/19) can be important to monitor carnitine deficiency.

Patient M :

Will be discussed in the general workshop.

Wim Ruitenbeek states that on his Jeol analyser saccharopine and cystine are poorly but definitely separated.

Questions

Is there a form for sending samples to SKML? Yes, available from scheme organizer.

Should participation to this meeting be obligatory? That will be difficult. But Ries Duran will contact the absent laboratories and stress the importance of participation.

Next meeting

Tuesday 2nd September 2008 in Lisboa