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ERNDIM
Diagnostic proficiency testing
2002
Southern Europe

ANNUAL REPORT 2002

In 2002, 17 labs participated to the Proficiency Testing Scheme Southern Europe.
Organizing Center : Dr Christine Vianey-Saban, Service de Biochimie Pédiatrique, Hôpital Debrousse, Lyon, in collaboration with Pr Claude Bachmann, CHUV.

Geographical distribution of participants

Country	Number of participants
France	5
Italy	5
Portugal	2
Spain	4
Switzerland	1
TOTAL	**17**

Logistic of the scheme

- 2 surveys 2002-1 : patient P1 and P2
  2002-2 : patient P3 and P4

- Origin of patients
  - Patient P1 and P2 were diagnosed in Service de Biochimie Pédiatrique, Hôpital Debrousse, Lyon
  - Patient P3 was a common sample from Nijmegen sent to all centres
  - Patient P4 was from Service de Biochimie, Hôpital Pasteur, Nice

- Mailing : samples were sent by rapid mail (EMS Chronopost) at room temperature. We had repeated problems with customs for Switzerland

Timetable of the schemes

- February 11th : shipment of samples of Survey 1 by rapid mail and of the form by e-mail
- March 22nd : deadline for results submission (Survey 1)
- July 8th : shipment of samples of Survey 2 by rapid mail and of the form by e-mail
- July 10th : report of Survey 1 by e-mail
- August 15th : deadline for results submission (Survey 2)
- August 26th : report of Survey 2 by e-mail

How good is our mailing service ?

	Survey 1	Survey 2
+ 24 hours	5	12
+ 48 hours	4	2
+ 72 hours	2	
+ 4 days		1
+ 16 days	1	
Not indicated	5	2

How long can a patient wait for a result ?

	Survey 1	Survey 2
	(6 weeks)	(6 weeks)
Receipt of results :		
Before deadline	10 / 17	13 / 17
+ 2 days		1 / 17
+ 4 days	1 / 17	
+ 6 days	1 / 17	
+ 11days	1 / 17	
No answer	**4** / 17 (24 %)	**3** / 17 (18 %)

Scoring of results

The International Scientific Advisory Board of ERNDIM decided to establish a scoring system. Three criteria are evaluated :

A	Analytical performance	Correct results of the appropriate tests	2
		Partially correct or non-standard methods	1
		Unsatisfactory of misleading	0
I	Interpretation of results	Good, diagnosis is established	2
		Helpful but incomplete	1
		Misleading / wrong diagnosis	0
R	Recommendations for further investigations	Complete	1
		Unsatisfactory of misleading	0

Since most of the laboratories in Southern Europe don't give therapeutic advices to the attending clinician, this criterium was not evaluated.
The **total score** is calculated as the sum of these 3 criteria. The maximum that can be achieved is 5 for one sample.
No answer to one survey has been scored as 0 for the 2 samples.

Scores of participants

Survey 2002-1

Lab number	Patient P1 LCHAD deficiency				Patient P2 Sulphite oxidase deficiency			
	A	I	R	Total	A	I	R	Total
1	2	1	1	**4**	2	2	1	**5**
2	2	2	1	**5**	2	2	1	**5**
3	2	2	1	**5**	0	0	0	**0**
4	2	2	1	**5**	0	0	0	**0**
5	2	2	1	**5**	2	2	1	**5**
6	0	0	0	**0**	0	0	0	**0**
7	0	0	0	**0**	0	0	0	**0**
8	2	2	1	**5**	2	2	1	**5**
9	0	0	0	**0**	0	0	0	**0**
10	2	2	1	**5**	2	2	1	**5**
11	2	2	1	**5**	2	2	1	**5**
12	2	2	1	**5**	0	0	0	**0**
13	1	2	1	**4**	0	0	0	**0**
14	0	0	0	**0**	0	0	0	**0**
15	2	1	1	**4**	2	2	1	**5**
16	2	2	1	**5**	2	2	1	**5**
17	2	2	1	**5**	0	0	0	**0**

Survey 2002-2

Lab number	Patient P3 Biotinidase deficiency				Patient P4 Mucopolysaccharidosis type I			
	A	I	R	Total	A	I	R	Total
1	2	2	1	**5**	1	2	1	**4**
2	1	2	1	**4**	2	2	1	**5**
3	2	0	0	**2**	2	2	1	**5**
4	2	2	1	**5**	2	2	1	**5**
5	2	2	0	**4**	2	2	1	**5**
6	0	0	0	**0**	0	0	0	**0**
7	1	1	1	**3**	1	1	0	**2**
8	1	0	0	**1**	1	1	0	**2**
9	0	1	0	**1**	0	1	0	**1**
10	0	0	0	**0**	2	2	1	**5**
11	2	2	1	**5**	2	1	1	**4**
12	0	0	0	**0**	0	0	0	**0**
13	0	0	0	**0**	0	0	0	**0**
14	2	2	1	**5**	2	2	1	**5**
15	2	2	1	**5**	1	2	1	**4**
16	2	2	1	**5**	2	2	1	**5**
17	0	0	0	**0**	2	1	1	**4**

Total scores

Lab number	Survey 2002-1	Survey 2002-2	Cumulative score	Cumulative score (%)
1	9	9	**18**	90 %
2	10	9	**19**	95 %
3	5	7	**12**	60 %
4	5	10	**15**	75 %
5	10	9	**19**	95 %
6	0	0	**0**	0 %
7	0	5	**5**	25 %
8	10	3	**13**	65 %
9	0	2	**2**	10 %
10	10	5	**15**	75 %
11	10	9	**19**	95 %
12	5	0	**5**	25 %
13	4	0	**4**	20 %
14	0	10	**10**	50 %
15	9	9	**18**	90 %
16	10	10	**20**	100 %
17	5	4	**9**	45 %

Summary of scores

We excluded from this table, the labs who did not send results. The percentages given are the scores obtained from labs who sent a report.

Sample	Diagnosis	Analytical (%)	Interpretation (%)	Recommen-dations (%)	Total (%)
Patient P1	LCHAD	96	92	100	**95**
Patient P2	SO def.	62	62	62	**62**
Patient P3	Biotinidase	68	64	57	**64**
Patient P4	MPS I	79	82	79	**80**

Meeting of participants

40th SSIEM meeting Dublin, September 3rd 2002, 9:30 – 11:30

Participants

Representatives from 9 labs were present :

Drs Sylvie Stastna (Czech Republic), Soumeya Bekri, Mirande Candito, Christine Vianey-Saban (France), Ubaldo Caruso, Silvia Junghini, Elisabetta Pasquini, Cristiano Rizzo, Maria Cristina Schiaffino (Italy), Maria Luis Cardoso, Isable Tavares de Almeida, Laura Vilarinho (Portugal), Begoña Merinero, Antonia Ribes, Pedro Ruiz-Sold (Spain), Claude Bachmann (Switzerland)

Decisions of the International Scientific Advisory Board for next year

The participants were informed of the decisions that the Advisory Board of ERNDIM took for 2003, during his meeting of September 2nd 2002 :

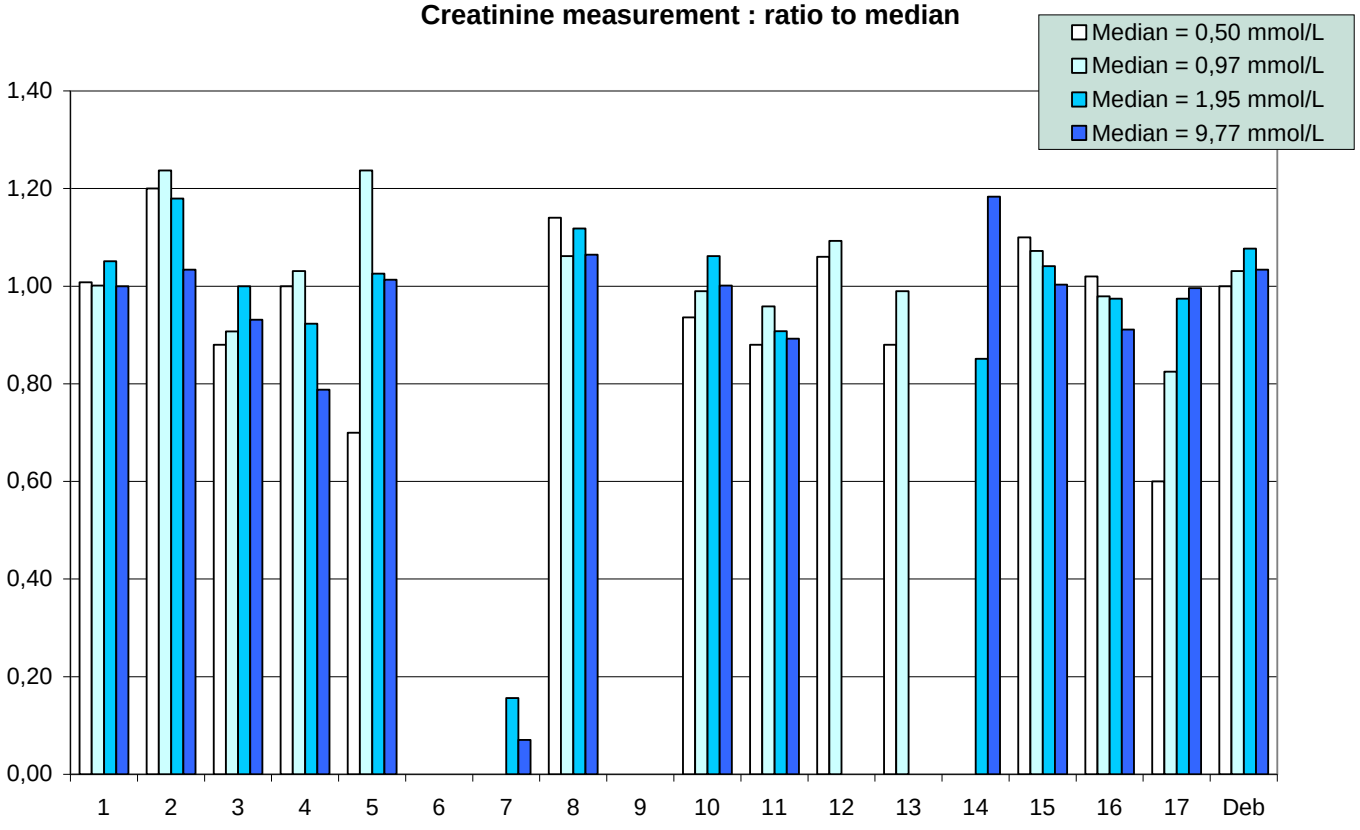
- 2 surveys of 3 samples will be sent
- these 6 samples can include urine from patients not affected with an inborn error of metabolism
- the delay to send the results will be 3 weeks, instead of 6 weeks
- every year, each participant must provide to the scheme organizer at least 300 ml of urine from a patient affected with an established inborn error of metabolism or a "normal" urine, together with a short clinical report. Each urine sample must be collected from a single patient. Please don't send a pool of urines. 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 44 tubes), add stoppers and freeze. Send the aliquots on dry ice by rapid mail or express transport to: Christine Vianey-Saban, Service de Biochimie Pédiatrique, Bâtiment D, Hôpital Debrousse, 29 Rue Sœur Bouvier, 69322 Lyon cedex 05, France. Please send me an e-mail on the day you send the samples.

Discussion of results

- **Creatinine measurement**

There is an important improvement of the accuracy in creatinine measurement, compared to previous years, as illustrated on the figure. One lab had obviously a calculating error.



- **Patient P1 : LCHAD deficiency, homozygous for the G1528C mutation of the ~-subunit of the mitochondrial trifunctional protein (MTP)**

13 reports - The urine sample was collected when the patient, a 10 month-old girl, was acutely ill. She died in the course of this episode. All labs identified the increased excretion of dicarboxylic and 3-hydroxydicarboxylic acids. Quantification, when performed, was correct, except one lab who had a systematic error and another who had an error on sebacic quantification. The interpretation of results was good, even if some labs were somewhat too "shy".

- **Patient P2 : Isolated sulphite oxidase (SO) deficiency**

13 reports - The clinical presentation of this patient was somewhat misleading, because this patient was asymptomatic until 4 months of age. Five labs could not identify sulphocystein some of which used a HPLC method. One lab informed us that he reinvestigated the urine sample after he got the report and successfully identified sulphocystein using HPLC. Quantification of taurine and sulphocystein, when performed, was satisfying. Two labs got positive results for the measurement of thiosulfate. Two labs did not find any increase of xanthine, another had a normal uric acid level and they concluded to an isolated SO deficiency. Conversely, one lab found a decreased uric acid level.

- **Patient P3 : Biotinidase deficiency**

14 reports - The urine sample from this 5 year-old boy has been sent to all labs in Europe participating to the DPT scheme. In Southern Europe, all labs except 2 reported an increased excretion of 3-hydroxyisovaleric acid (3OHIVA). Quantification of 3OHIVA, when performed was acceptable, except for one lab. The interlaboratory variance could still be improved. Half of participants identified a slight increase of either methylcitrate, 3-methylcrotonylglycine or tiglylglycine. Nine labs concluded correctly to a possible multiple carboxylase deficency (biotinidase ou holocarboxylase synthetase deficiency).

- **Patient P4 : Mucopolysaccharidosis type I (Hurler syndrome) : ~-iduronidase deficiency**

14 reports - All labs performed quantification (DMB test or other methods) and/or identification of GAGs. Among the 11 labs who performed quantification, all except 1, found abnormal high result. The 12 labs who performed identification, detected an increase of dermatane sulfate and 10 of them also an increase of heparane sulfate. But two labs furthermore reported an increase of chondroitine sulfate and one reported trace amounts of keratane sulfate. Identification of abnormal fractions should have been performed by all participants and this explains the non conclusive reports : mucopolysaccharidosis. Correct identification is essential to orient the diagnosis and then the measurement of the enzyme activities for confirmation.

Meeting in 2003

There is no SSIEM meeting next year but the International Congress of Inborn Errors of Metabolism (ICIEM) will take place in Brisbane (Australia) September 2 – 6.

Can you please inform the scheme organizers if it will be possible for you to attend the Brisbane meeting. If less than 50 % of the labs participating to the DPT scheme can go to Brisbane, the meeting will take place in Madrid. This meeting is scheduled on Friday 7th November from 12.30 to 14.30 during the meeting of the Spanish Society for the Study of Inborn Errors of Metabolism.

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ANNEX 1

PROFICIENCY TESTING – SOUTHERN EUROPE
URINE SAMPLES ALREADY SENT

• **1998 : 1**	**A**	**OCT**	
	B	**Propionic**	
• **1999 : 1**	**C**	**MPS I ou II**	
	E	**Cystinuria**	SKZL
• **1999 : 2**	**D**	**CblC**	
	F	**HMG-CoA lyase**	
• **2000 : 1**	**G**	**Iminodipeptiduria**	SKZL
	H	**Glutathion synthetase**	
• **2001 : 1**	**P1**	**Mevalonate kinase**	
	P2	**L-2-OH glutaric**	
• **2001 : 2**	**P3**	**Methylmalonic**	SKZL
	P4	**MPS IIIA San Fillippo**	
• **2002 : 1**	**P1**	**LCHAD**	
	P2	**Sulphite oxidase**	
• **2002 : 2**	**P3**	**Biotinidase**	SKZL
	P4	**MPS I**	