ERNDIM Qualitative Blood Spot Acylcarnitine Scheme

Annual Report 2007

Two circulations (9 & 10) were sent out during 2007. Circulation 9 was sent out on 13th Apr 2007 with a return date of 25th May 2007. Circulation 10 was dispatched on 20th November 2007 with a return date of 15th December 2007. Samples were sent to 74 laboratories for both circulations. 60 returns (81%) were received for circulation 9 (54 of these by the due date) and 60 (81%) for circulation 10 (54 by the due date). Two of those returning late did so for both circulations, in one case due to a clear problem with postal delivery.

There were 14/74 laboratories, on each circulation, who failed to make a return. 8 laboratories did not respond to 1 circulation but reported on the other, and 11 laboratories provided no return for either circulation. One of these informed us by email following the first circulation that they were not ready to participate, but the other 10 gave no reason for non-response.

No formal questionnaire on methodology was sent out in 2007. The majority of laboratories are providing results that are consistent with butylation of the samples and full scan acquisitions. There was again a slight increase in the proportion of laboratories using underivatised samples. Reporting of quantitative results for the diagnostically informative metabolites is almost universal. However, there is still significant variability in both the concentrations reported and laboratory normal ranges.

Respondents were asked to report as they would to a physician at a non-specialist hospital, and to send a scan and/or table of quantitative results. The majority of laboratories provided a suggested/differential diagnosis. Most suggested some form of appropriate follow-up to confirm a putative diagnosis. A summary of the samples sent and number of respondents suggesting the appropriate diagnosis is given in the table below.

Sample	Enzyme/transporter defect	Diagnostic Acylcarnitine	Respondents
9a	Very long chain acyl CoA dehydrogenase deficiency (VLCADD)	C14:1	57/59
9b	Normal (heterozygote for LCHAD)		60/60
9c	malonyl CoA decarboxylase deficiency	Malonyl carnitine	49/60
10a	3-methylcrotonyl CoA carboxylase deficiency (3-MCC)	C5OH	50/59
10b	Normal (sib of MCADD)	C8	60/60
10c	Medium chain acyl CoA dehydrogenase deficiency (MCADD)	C8, C6, C10:1	60/60

The results were, on the whole, very encouraging. There continues to be an issue with the detection of malonyl carnitine, which is not part of the panel for some laboratories. The other disorder which gave rise to variation in interpretation was the sample from a patient with 3-methylcrotonyl CoA carboxylase deficiency. However all participants detected the key acylcarnitine and all but one of those who did not suggest the diagnosis suggested follow-up tests which would have led to it.

Once again, we are extremely grateful to the centres who have provided informative material for circulation. If any participants can provide samples in the future it would enormously facilitate the provision of this scheme, providing, as it does. genuine clinically derived samples for assay and interpretation, The current requirement, there are now 87 participants, is for 5ml of anticoagulated whole blood or 90-100 50µl blood spots on Schleicher & Schuell 903 paper, accompanied by a short clinical history and confirmation that informed consent/local ethical approval for use of the sample had been obtained.

In 2007 we intended to introduce a scoring system, equivalent to the qualitative urine organic acid scheme. On review, this proved significantly more difficult than expected. We have decided to provide an electronic pro-forma (we will distribute this by email when circulation 11 is despatched) similar to that used in some other ERNDIM schemes and that will, subsequently, be adapted for entry of results via the website. We will be asking participants to report as they have before as well as completing the pro-forma.

We have noted the criticisms of the scheme, particularly the delay in sending back reports. This resulted from an effort to minimise costs; results only being sent with the next set of samples. The intention, at this stage, is to establish e-mail contact with each centre by sending the electronic result sheet pro-forma that, once completed, should be returned to us by e-mail. This should ease adoption of electronic reporting on the ERNDIM web-site. The reports will be scored on a 5 point basis similar to the DPT schemes. Individual laboratory results and the usual distribution report will then be sent, as soon as they are ready, to laboratories by e-mail and will not be delayed until the next distribution. On this basis it is also possible to pre-determine the distribution dates for 2008. Circulation 11 will be despatched during the week starting April 14th and circulation 12 during the week starting July 14th.

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