ERNDIM Qualitative Blood Spot Acylcarnitine Scheme

Annual Report 2008

Two circulations (11 & 12) were sent out during 2008. Circulation 11 was sent out in April 2008 with a return date of 16th May 2008. Circulation 12 was dispatched in December 2008 with a return date of 16th January 2009. Samples were sent to 87 laboratories for both circulations. 57 returns (66%) were received for circulation 11 (51 of these by the due date) and 61 (71%) for circulation 12 (57 by the due date).

There were 28 laboratories who failed to make a return on circulation 11 and 24 on circulation 12, 17 laboratories provided no return for either circulation. 2 laboratories withdrew from the scheme during 2008.

Most laboratories reported quantitative results for diagnostically informative metabolites. Variability in the concentrations reported and laboratory normal ranges, differs considerably, for example C8 (octanoyl) carnitine concentrations and ranges were very consistent between laboratories, whereas quoted ranges for C3 (propionyl) carnitine varied more widely.

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
11a	multiple acyl CoA dehydrogenase deficiency (MADD, GA-II)	C5, C8, C10	35/57
11b	Carnitine palmitoyl transferase 1 deficiency (CPT1)	Free carnitine, C16	54/57
11c	Chronic renal failure		
12a	Medium chain acyl CoA dehydrogenase deficiency (MCADD)	C8, C6, C10:1	61/61
12b	Methylmalonyl-CoA epimerase deficiency	C3	30/61
12c	Long chain hydroxyacyl CoA dehydrogenase deficiency (LCHADD)	C16:1OH, C16OH, C18:1OH, C18OH	55/61

The samples which proved difficult to interpret were samples 11a, 11c and 12b. Sample 11a was from a patient with multiple acyl CoA dehydrogenase deficiency and a number of laboratories interpreted the increase of C8 carnitine as indicative of Medium chain acyl

CoA dehydrogenase deficiency, despite the increases in C5 and C10, and the relative lack of C10:1. Sample 11c was from a patient with chronic renal failure. The range of interpretation of the slight increase of C5DC illustrates the difficulty posed by samples of this type. Sample 12b was from a patient with methylmalonyl-CoA epimerase deficiency and many centres interpreted the slight increase in propionyl carnitine concentration as a normal pattern. This may result from the use of neonatal normal ranges in an older patient.

This year we trialled a scoring system analogous to that used for the qualitative organic acid scheme. Participants will be circulated with their notional scores, for information only, by traditional mail.

Once again, we are extremely grateful to the centres that have provided informative material for circulation. If any participants can provide samples in the future it would enormously facilitate this scheme, providing, as it does, genuine clinically derived samples for assay and interpretation. 4ml of anticoagulated whole blood or 60-70 30-50µl blood spots on Whatman (Schleicher & Schuell) 903 paper would provide sufficient material for one circulation from one centre (see below). Samples for use in the scheme should be accompanied by a short clinical history and confirmation that informed consent/local ethical approval (as required) for use of the sample had been obtained.

The number of participants, there are now 93, has grown to the point that the sample requirements are difficult to fulfil for a single circulation, and as happened last year, delays in scoring may occur. It is proposed to split the scheme from 2010. The centre in Heidelberg (Dr Claus-Dieter Langhans) have agreed to take on approximately half of the workload. Participants will be allocated to a centre, either ourselves or Dr Langhans, when they register for the 2010 acylcarnitine scheme.

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