

- **Subject:** Newborn screening  
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**Date:** Wed, 24 May 2006 21:05:14 -0400 (EDT)  
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Clem,

This province is finally catching up with most US states and several Canadian provinces by setting up an expanded newborn screening program. As have many others we have been screening for PKU and congenital hypothyroidism for many years, but now there is a program to increase the number of diseases subject to screening up to 25+.

The scheme will be based on the analysis of blood spots collected in the first days of life, with results being reported as positive or negative, by *disease*, not *metabolic marker*. Thus, the report will look like:

Newborn screen for

Phenylketonuria	negative
Congenital hypothyroidism	negative
Maple syrup urine disease	negative
etc	

In the case of positive findings, the patient is referred to one of several follow-up clinics for confirmatory tests. Generally these confirmatory tests will be looking at specific metabolic markers, and the results will be reported as such.

So, for a patient with a positive screening test for medium chain acyl CoA dehydrogenase deficiency (also known as MCAD deficiency), the follow-up tests will be a series of acyl carnitine measurements, and one might expect to see a report like this:

Caproyl carnitine (C6 carnitine)	v nmol/L
Octanoyl carnitine (C8 carnitine)	w nmol/L
Decanoyl carnitine (C10 carnitine)	x nmol/L

Decenoyl carnitine (C10:1 carnitine) y nmol/L

Comment: pattern compatible with MCAD

The results from the follow-up program will be easily handled within the conventional LOINC rules, but the results from the screening program present an interesting challenge: specifically, the reporting of the test result in terms of a disease rather than a metabolic marker. And of course this has important implications on the order side as well as the result side.

To the best of my recollection, there are no other examples of this type of entry in LOINC, but I would be glad if you would identify one or more. If LOINC has not traveled this path before, I would like to propose that it begin to do so now.

For example, I suggest that we add to the LOINC database entries such as:

Component	Property	Time	System	Scale	
PHENYLKETONURIA	FIND	PT	BLD.DOT	ORD	
CONGENITAL HYPOTHYROIDISM	FIND	PT	BLD.DOT	ORD	
MAPLE SYRUP URINE DISEASE	FIND	PT	BLD.DOT	ORD	
ETC					

I appreciate that these are not Components in the usual LOINC sense, and for Property I have inserted FIND in the absence of a better choice, but possibly PRID would be more logical. In any case, perhaps this is enough to generate some discussion. At a very pragmatic level, such codes could be very useful.

For your records, I will attach to this note three files:

1. ON\_NB screening – a list of tests to be included in the screening program
2. metabolic marker – a list of some of the metabolic markers for confirmatory testing
3. NB codes – a list of diseases and codes

The ordering and reporting of results for genetic metabolic diseases has long been a source of difficulty, exacerbated by the polysyllabic names for the diseases and the tests, and the difficulty for the non-specialist clinician to link tests and diseases. As a consequence, at least some labs use an ordering system based on

the name of the disease, leaving to the lab the choice of test to be performed.

I look forward to your comments and suggestions.

Gil

<b>ON_NB screening.pdf</b>	<b>Content-Description:</b> 2570792186-ON_NB screening.pdf <b>Content-Type:</b> application/pdf <b>Content-Encoding:</b> base64
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<b>metabolic marker.pdf</b>	<b>Content-Description:</b> 1113198733-metabolic marker.pdf <b>Content-Type:</b> application/pdf <b>Content-Encoding:</b> base64
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<b>NB codes.pdf</b>	<b>Content-Description:</b> 138929549-NB codes.pdf <b>Content-Type:</b> application/pdf <b>Content-Encoding:</b> base64
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Heath Card Number: **9999 999 999 AA**  
 D.O.B.: **YYYY/MM/DD**  
 Mother's Name:

Date Sample Received: **YYYY/MM/DD**  
 Date of Report: **YYYY/MM/DD**  
 Infant's Health Care Provider:

**LAST NAME, GIVEN NAMES**

<b>Test</b>	<b>Screening Result</b>
<b>Amino Acidemias:</b>	
Phenylketonuria and Variants / Bioppterin Defects	<b>Negative</b>
Maple Syrup Urine Disease	*
Homocystinuria (Hypermethioninemas)	*
Citrullinemas/Argininosuccinic Aciduria	*
Tyrosinemas	*
Amino Acidopathies, other	*
<b>Organic Acidemias:</b>	
Propionic / Methylmalonic Acidemias	*
Isovaleric Acidemia / 2 Methylbutyric Acidemia	*
Glutaric Acidemia Type I	*
3 Methylcrotonic / Hydroxymethylglutaric / Methylglutaconic /	*
2-Methyl,3-Hydroxybutyric acidemias, or B Ketothiolase Deficiency	*
Organic Acidemias, other	*
<b>Fatty Acid Oxidation Defects:</b>	
Medium Chain Acyl Dehydrogenase Deficiency/ Glutaric Acidemia Type 2	<b>Negative</b>
Very Long Chain Acyl Dehydrogenase Deficiency	*
Long Chain Hydroxy Acyl Dehydrogenase / Trifunctional Protein Deficiencies	*
Carnitine Uptake Defect / CPT1 Deficiency	*
Fatty acid oxidation disorders, other	*
<b>Galactosemia</b>	
	*
<b>Biotinidase Deficiency</b>	
	*
<b>Endocrine Disorders:</b>	
Congenital Hypothyroidism	<b>Positive</b>
Congenital Adrenal Hyperplasia	*
<b>Hemoglobinopathies:</b>	
Hb SS, Hb S/C, Hb S/bThal	*
Hemoglobinopathies, other	*

1. Screen **negative** means that this infant is at decreased risk for the disorder(s).
2. Screen **positive** means that this infant is at increased risk for the disorder(s). It does not mean that a disease is present, but further testing is indicated. If a test is positive and you and/or your patient have not already been contacted please call the NBS laboratory at (613)-738-3222.
3. \* indicates that the laboratory is not yet testing for the disorder(s).

**Table 8.3** Inherited metabolic disorders detectable in the newborn period by tandem MSMS testing of blood spots

Disorder	Primary metabolic indicator
<i>Amino acidopathies</i>	
Phenylketonuria (PKU)	Phe
Maple syrup urine disease (MSUD)	Leu/Ile, Val
Homocystinuria (cystathionine $\beta$ -synthase deficiency)	Met
Hypermethioninemia	Met
Citullinemia	Cit
Argininosuccinic aciduria	Cit
Hepatorenal tyrosinemia (tyrosinemia, type I)	Tyr
<i>Fatty acid oxidation defects</i>	
Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency	C8, C10, C10:1, C6
Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency	C14:1, C14, C16
Short-chain acyl-CoA dehydrogenase (SCAD) deficiency	C4
Multiple acyl-CoA dehydrogenase deficiency (GA II)	C4, C5, C8:1, C8, C12, C14, C16, C5DC
Carnitine palmitoyl transferase (CPT) deficiency	C16, C18:1, C18
Carnitine-acylcarnitine translocase (CACT) deficiency	C16, C18:1, C18
Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency	C16OH, C18:1OH, C18OH
Trifunctional protein deficiency	C16OH, C18:1OH, C18OH
<i>Organic acidopathies</i>	
Glutaric aciduria, type I	C5DC
Propionic acidemia	C3
Methylmalonic acidemia	C3
Isovaleric acidemia	C5
3-Hydroxy-3-methylglutaryl-CoA lyase deficiency	C5OH
3-Methylcrotonyl-CoA carboxylase deficiency	C5OH

*Abbreviations:* Phe, phenylalanine; Tyr, tyrosine; Leu, leucine; Ile, isoleucine; Val, valine; Cit, citrulline; Met, methionine. The abbreviations for fatty acid oxidation products and organic acid intermediates, such as C5, C16OH, C18:1, etc., refer to carnitine esters of aliphatic, monocarboxylic acids with chain length indicated by the number adjacent to C, and the number of double bonds indicated by the number after the colon. For example, C18:1, refers to an aliphatic, monocarboxylic acid with 18 carbon atoms and a single double bond. C5DC refers to a 5-carbon, aliphatic, dicarboxylic acid.

*Source:* CDC Morbidity and Mortality Weekly Report, Using tandem mass spectrometry for metabolic disease screening among newborns (2001).

**Table 1: Scores of All Conditions (Sorted in Descending Order of the Sum of the Means Scores)**

Condition	Code	SCORE Sum of the Means	Rank (%ile)
Medium-chain acyl-CoA dehydrogenase deficiency	MCAD	1799	1.00
Congenital hypothyroidism	CH	1718	0.99
Phenylketonuria	PKU	1663	0.98
Neonatal hyperbilirubinemia (Kernicterus)	HPRBIL	1584	0.96
Biotinidase deficiency	BIOT	1566	0.95
Sickle cell anemia (Hb SS disease)	Hb SS	1542	0.94
Congenital adrenal hyperplasia (21-hydroxylase deficiency)	CAH	1533	0.93
Isovaleric acidemia	IVA	1493	0.89
Very long-chain acyl-CoA dehydrogenase deficiency	VLCAD	1493	0.89
Maple syrup disease	MSUD	1493	0.89
Classical galactosemia	GALT	1473	0.88
Hb S/ $\beta$ -thalassemia	Hb S/ $\beta$ Th	1455	0.87
Hb S/C disease	Hb S/C	1453	0.86
Long-chain L-3-OH acyl-CoA dehydrogenase deficiency	LCHAD	1445	0.84
Glutaric acidemia type I	GA I	1435	0.83
3-OH 3-CH <sub>3</sub> glutaric aciduria	HMG	1420	0.82
Trifunctional protein deficiency	TFP	1418	0.81
Multiple carboxylase deficiency	MCD	1386	0.80
Benign hyperphenylalaninemia	H-PHE	1365	0.78
Methylmalonic acidemia (mutase deficiency)	MUT	1358	0.77
Homocystinuria (due to CBS deficiency)	HCY	1357	0.76
3-Methylcrotonyl-CoA carboxylase deficiency	3MCC	1355	0.75
Hearing loss	HEAR	1354	0.73
Methylmalonic acidemia (Cbl A,B)	Cbl A,B	1343	0.72
Propionic acidemia	PROP	1333	0.71
Carnitine uptake defect	CUD	1309	0.69
Galactokinase deficiency	GALK	1286	0.69
Glucose-6-phosphate dehydrogenase deficiency	G6PD	1286	0.67
$\beta$ -Ketothiolase deficiency	BKT	1282	0.66
Citrullinemia	CIT	1266	0.65
Argininosuccinic acidemia	ASA	1263	0.64
Tyrosinemia type I	TYR I	1257	0.63
Short-chain acyl-CoA dehydrogenase deficiency	SCAD	1252	0.61
Tyrosinemia type II	TYR II	1249	0.60
Glutaric acidemia type II	GA2	1224	0.59
Medium/short-chain L-3-OH acyl-CoA dehydrogenase deficiency	M/SCHAD	1223	0.58
Cystic fibrosis	CF	1200	0.57
Variant Hb-pathies (including HB E)	Var Hb	1199	0.55
Human HIV infection	HIV	1193	0.54
Defects of bipterin cofactor biosynthesis	BIOPT (BS)	1174	0.53
Medium-chain ketoacyl-CoA thiolase deficiency	MCKAT	1170	0.52
Carnitine palmitoyltransferase II deficiency	CPT II	1169	0.51
Methylmalonic acidemia (Cbl C,D)	Cbl C,D	1166	0.49