



We received excellent feedback from several Doctors. Many of them wanted us to discuss cases. We have several on file and will do so in future newsletters.

Doctor's QUESTION: Can you provide reference ranges and cut off values with the reports?

ANSWER: In the biochemical panel which comprises CH, CAH, CF, GALT and G6PD we can do so, if needed. Here, reference ranges and cut offs are self explanatory.

When it comes to the 45 metabolic disorders we analyze with Tandem Mass Spectrometry (MS/MS) it gets more complicated. The primary reason is that we analyze over 80 parameters for the disorders we screen for. The proprietary technology used at NeoGen Labs relies on multi-analyte analysis for identifying metabolic disorders.

An example of how the technology works, say for Maple Syrup Urine Disease (MSUD) screening analysis, is shown below.

A. Re-Analysis Criteria for MSUD screening

(When do we repeat a screen?)

- Leucine > 300 μ M or
- Leu > 275 and Val > 275 or
- Leu > 250 and Leu/Ala > 1.5
- Leu > 225, Leu/Ala > 1.5, Leu/Phe > 5 or
- Leu > 200, Val > 275, Leu/Ala > 1.5, Leu/Phe > 5

If any one of the above criteria is met, we process another dried blood spot and perform a repeat screen.

B. Notification criteria for MSUD screening

(What do we tell the Doctor/Hospital/Parent?)

Mean results

- Leu > 300
- Leu > 275 and Val > 275
- Leu > 250 and Leu/Ala >
- Leu > 225, Leu/Ala > 1.5, Leu/Phe > 5
- Leu > 200, Val > 275, Leu/Ala > 1.5, Leu/Phe > 5

Report Content: Send repeat sample

Mean results

- Leu > 400
- Leu > 350 and Val > 300
- Leu > 350 and Leu/Ala > 1.5
- Leu > 325, Leu/Ala > 1.5, Leu/Phe > 6
- Leu > 300, Val > 250, Leu/Ala > 1.5, Leu/Phe > 5

Report Content: Send repeat sample immediately

Mean results

- Leu > 500
- Leu > 425 and Val > 300
- Leu > 425 and Leu/Ala > 1.5
- Leu > 425, Leu/Ala > 1.5, Leu/Phe > 6
- Leu > 400, Val > 275, Leu/Ala > 1.5, Leu/Phe > 5

Report Content: Presumptive Positive

Note: Values have been changed to protect proprietary data

As is now obvious, it is impractical to give such detailed results and multiple ranges for over 80 analytes and ratios. In addition, specialized training and certification is required for interpretation of MS/MS results pertaining to metabolic disorders.

Within Normal Limits - What Does it Mean?

The proprietary list of **i)** (multi) analytes, **ii)** (multiple) ratios and **iii)** (graded) cut off values have been determined by analysis of several million samples and has clinical utility across all ethnicities. As in the MSUD screening example showcased, every single one of the 80 analytes and ratios measured by MS/MS is evaluated by proprietary software algorithms to determine if the analyte concentration is either 'normal' or 'abnormal'.

Thus, a 'Within Normal Limits or WNL' result for the Acylcarnitine or Amino Acid Panel of metabolic disorders is a simple, direct way to signify that every analyte and/or ratio associated with the list of treatable metabolic disorders, has been evaluated in a thorough and rigorous fashion by best-in-the-world-class technology and by a trained expert in MS/MS interpretation, and found to be normal.

I strongly encourage a Doctor with doubts or questions to call Dr. Cariappa (0 99006 55112) to discuss some or all aspects of the report. He will be happy to share specific data, cut offs and normal ranges if there is a suspicion of a certain metabolic disorder or class of disorders.

March 2008 Statistics

- 1 Case of MMA/PA (1:100,000)
- 1 Case of CF (1:31,000)

Screening Panels

We offer 3 panels to reflect demand:

First Step (All 50 IEMs for Rs. 3975)

First Step MS/MS (45 IEMs, includes Fatty Acid Oxidation Disorders, Amino Acid Disorders, and Organic Acid Disorder panels for Rs. 3250)

First Step Bio (5 IEMs which include CH, CAH, G6PD, GALT and Cystic Fibrosis for Rs.1250).

As always, we look for your feedback on how this newsletter can be improved. Let us know specific topics you would like us to cover.

Thomas Mookken

T: 0 99006 55115 E: mookken@neogenlabs.com

Lingarajapuram, Bangalore 560 084, KARNATAKA

T: 080 2580 5600, E: info@neogenlabs.com

W: www.neogenlabs.com