

The last four issues carried a set of articles written by Dr. Manoj Ghoda from Ahmedabad. He has a lot of interesting cases that we would like to publish in future issues, with his permission. We thank him in his efforts to increase the awareness and treatments of IEMs.

In this issue we will address a debate in India on the use of Dried Blood Spot (DBS) versus Urine for screening. We present the information we had collected from our discussions with screening experts from around the world. Our goal is to provide you data so that you can make an informed decision for the benefit of your patients.

Dried Blood Spot Vs. Urine: Which One?

Introduction

Recently, there has been some debate within the medical community in India regarding the use of Urine instead of Dried Blood Spot (DBS) for screening. An argument that has been put forth in support of urine is that it can do many more tests than blood and it is confirmatory. Other than in India, there really is no debate on this subject and DBS is the accepted sample for newborn screening (NBS). The information presented here is compiled from multiple peer reviewed publications and discussions with NBS experts (Dr. D. Chace, Dr. K. Pass, Dr. B. Therrell and Dr. M. Rashed) from around the world.

Newborn Screening with Dried Blood Spot (DBS)

1. All comprehensive NBS programs in the world are based on DBS, the only accepted standard for these programs. There are over a million babies screened every year from DBS.
2. The use of DBS and the related technologies (e.g. ELISA assays and Tandem Mass Spectrometry) are supported by hundreds of peer reviewed scientific papers. This large body of evidence has allowed the development of customized algorithms incorporating cut off values for various critical analytes (allowing for age, prematurity, birth weight) that can rapidly analyze the data generated from a dried blood spot specimen. The sensitivity and specificity are close to 100% for TMS methodology and > 90% for enzyme assay or enzyme immunoassay based screening tests.
3. CDC's quality control program for newborn screening, NSQAP (Newborn Screening Quality Assurance Program), is based on DBS. They provide Quality Control (QC) material and Proficiency Testing

(PT) specimens on a quarterly basis. Nearly every newborn screening program and laboratory in the world (over 75 in 58 countries), including NeoGen Labs, participates in this quality assurance program. The CDC NSQAP does not have a similar program for newborn screening based on urine.

4. An attempt to prepare a consensus NBS panel of disorders based on DBS finally reached fruition in 2006 after many scientific discussions and debates. The American College of Medical Genetics (ACMG) published a 'Core' and 'Secondary' classification of metabolic disorders in 2006 which is being used as the basis for preparing screening panels by NBS labs all over the world. The disorders to be screened for were picked based on criteria described in the paper, **"Newborn Screening: Toward a Uniform Screening Panel and System – Executive Summary"**, *Michael S. Watson, Marie Y. Mann, Michele A. Lloyd-Puryear, Piero Rinaldo, R. Rodney Howell and American College of Medical Genetics Newborn Screening Expert Group. Pediatrics 2006;117;S296-S307.* Selection criteria were divided into 3 main categories that covered aspects of the condition, that is, (1) clinical characteristics (e.g. incidence, burden of disease if not treated, and phenotype in the newborn); (2) analytical characteristics of the screening test (eg, availability and features of the platform); and (3) diagnosis, treatment, and management of the condition in acute and chronic forms (this criterion includes the availability of health professionals experienced in diagnosis, treatment, and management). More detail on the criteria is available in the referenced paper. These ACMG guidelines have been used as the basis for preparing screening panels by NBS labs all over the world. There are a total of 54 disorders (including hearing) in these panels and NeoGen Labs tests for 44 of these. The disorders we do not test for are Hearing and Hemoglobinopathies.

5. **Make no mistake.** There is a very significant use for a urine specimen in the diagnosis of metabolic disorders. Urine must be used for confirmatory testing when,
 - a. the index of suspicion based on clinical history or symptoms of a particular metabolic disorder is high, or
 - b. the dried blood specimen screening results are positive.



NBS News 8 2010

The standard of care protocol for newborns is to use DBS for screening, and based on the screening results, do a confirmatory test using a urine specimen. For older children who may have clinical symptoms of a disorder, the protocol is to perform a screen, correlate clinically if the screen is positive, followed by a confirmatory test using a urine specimen. The only rational reason to use urine as a specimen to diagnose (not screen) metabolic disorders is as a confirmatory specimen and that too only when the screening results and clinical history details are known.

Summary

Both the DBS and Urine specimen have a role to play in NBS. In the NBS paradigm that is followed worldwide, they complement each other. DBS is for screening while urine is for confirmatory testing. Today, the first step in newborn screening is built around DBS. If you need additional information on the ACMG Panels, please let me know.

Conferences

The **7th Asia Pacific Regional Meeting** of the International Society for Neonatal Screening will be held in Kuta, Bali, Indonesia from Oct 3rd to 5th, 2010. More information can be found at, <http://www.7thisns-aprm.com/>

The **4th International Congress on Sickle Cell Disease** will be held in Raipur, Chattisgarh, India from Nov 22nd to 27th, 2010. The theme of the conference is "Management and Prevention of Sickle Cell Disease in Developing Societies". More information can be found at <http://www.4sccongress.co.in>. You may not be able to get to this website from BSNL Broadband (We have faced the problem in Bangalore).

Moving On ..

Many of you may have interacted with Nihal George, Sr. Business Development manager. He was our first employee and was with us from Feb 2007 when we started our lab. He was a crucial team member and managed all our business development activities. He trained himself on the heel stick and often stepped in during situations where we did not have access to a technician.

Nihal left us in mid July to pursue an MBA in the UK. We wish him the best and thank him for his contributions to NeoGen and our customers.

Ravindra Ghadiyar (+91 99006 55117) will take over Nihal's role at NeoGen.

NeoGen Lab Visits

If you are visiting Bangalore, we would like to host you at our lab. We feel it is very important to share with you the processes and the interpretation we use to deliver an accurate result. We can arrange transportation, if needed. Please give us a few days notice.

IMPORTANT: Feedback Request

Once in a while we are faced with a situation where our report does not agree with your suspicions or differ from that of another lab's. Please call us immediately to discuss. We take these issues very seriously and will research it. We will share additional test data with you, and, if necessary, we will rerun the test on the same sample or request a fresh sample.

We are constantly improving our services and your feedback will help us in this effort. Please do not keep silent. We value your feedback.

Logistics, Kits, Reports, Etc.

Please send e-mail to info@neogenlabs.com in case you need kits, looking for reports or any general question. You can expect a reply or call within 24 hours (except for holidays) to address your request.

Please call me if you feel your concerns are not addressed to your satisfaction.

Newsletter Subscription

If you wish to be removed from the newsletter distribution list, please send a note to newsletter@neogenlabs.com with the subject line, REMOVE. We will do so immediately.

Thomas Mookken, CEO

E: mookken@neogenlabs.com

T: +91 99006 55115

www.neogenlabs.com

First Step Newborn Screening Panel

ACYLCARNITINE PROFILE (MS)

Fatty Acid Oxidation Disorders

- Carnitine / Acylcarnitine Translocase Deficiency
- Carnitine Palmitoyl Transferase Deficiency Type I
- 3-Hydroxy Long Chain Acyl-CoA Dehydrogenase Deficiency
- 2,4-Dienoyl-CoA Reductase Deficiency¹
- Medium Chain Acyl-CoA Dehydrogenase Deficiency
- Multiple Acyl-CoA Dehydrogenase Deficiency
- Neonatal Carnitine Palmitoyl Transferase Deficiency Type II
- Short-chain Acyl-CoA Dehydrogenase Deficiency
- Short chain Hydroxy Acyl-CoA Dehydrogenase Deficiency
- Trifunctional Protein Deficiency
- Very Long Chain Acyl-CoA Dehydrogenase Deficiency

Organic Acid Disorders

- 3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency
- Glutaric Acidemia Type I
- Isobutyryl-CoA Dehydrogenase Deficiency
- Isovaleric Acidemia
- 2-Methylbutyryl-CoA Dehydrogenase Deficiency
- 3-Methylcrotonyl-CoA Carboxylase Deficiency
- 3-Methylglutaconyl-CoA Hydratase Deficiency
- Methylmalonic Acidemias
- Methylmalonic Acidemias
 - Methylmalonyl-CoA Mutase Deficiency
 - Some Adenosylcobalamin Synthesis Defects
 - Maternal Vitamin B12 Deficiency
- Mitochondrial Acetoacetyl-CoA Thiolase Deficiency
- Propionic Acidemia
- Multiple CoA Carboxylase Deficiency
- Malonic Aciduria

AMINO ACID PROFILE (MS)

Amino Acid Disorders

- Argininemia
- Argininosuccinic Aciduria
- 5-Oxoprolinuria
- Carbamoylphosphate Synthetase Deficiency
- Citrullinemia
- Homocystinuria
- Hypermethioninemia
- Hyperammonemia, Hyperornithinemia, Homocitrullinuria Syndrome
- Hyperornithinemia with Gyral Atrophy
- Maple syrup disease
- Phenylketonuria
 - Classical/Hyperphenylalaninemia
 - Biotpterin Cofactor Deficiencies
- Tyrosinemia
 - Transient Neonatal Tyrosinemia
 - Tyrosinemia Type I
 - Tyrosinemia Type II
 - Tyrosinemia Type III

OTHER (MS)

- Hyeralimentation
- Liver Disease
- Medium Chain Triglyceride Oil Administration
- Presence of EDTA Anticoagulants in blood specimen
- Treatment with Benzoate, Pyvalic Acid, or Valproic Acid
- Carnitine Uptake Deficiency

BIOCHEMICAL ANALYSIS (BIO)

- Galactosemia (GALT)
- Congenital Hypothyroidism (CH)
- Congenital Adrenal Hyperplasia (CAH)
- G6PD
- Cystic Fibrosis
- Biotinidase (BIOT)

Screening Panels

MS - Mass Spectrometry Panel (45 Disorders)

(45 IEMs; includes Fatty Acid Oxidation Disorders, Amino Acid Disorders, and Organic Acid Disorder panels)

BIO - Biochemical Panel (6 Disorders)

CH, CAH, G6PD, GALT, CF, BIOT

- **First Step PLUS** MS/Bio6 Rs. 4,250/-
- **First Step** MS/Bio4 Rs. 3,975/-
- **First Step MS** MS Rs. 3,250/-
- **First Step Bio6** BIO Rs. 2,000/-
- **First Step Bio4** CH/CAH/GALT/G6PD Rs. 1,500/-