NeoGen Labs

Dried Blood Spot Vs. Urine

Introduction

Recently, there have been some debates within the medical community in India regarding the use of Urine instead of Dried Blood Spot (DBS) for screening. One of the arguments that have 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 recommendations 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.

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.

   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 scientifically proven 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 both 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.

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