

Hello!

*This is the first in a series of monthly newsletters with the purpose of increasing awareness of **Newborn Screening (NBS)** for Inborn Errors of Metabolism (IEM), in India. Subsequent newsletters will present information on i) the different IEMs, ii) screening and diagnostic technology, iii) patient and clinician resources for treatment therapies, iv) answers to FAQ's about NBS, and other related topics. I hope you will find the contents useful.*

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## History of NBS

### 'One test-one disease' Screening

NBS is the process of testing newborn infants for treatable genetic, endocrinologic, metabolic and hematologic diseases. Dr. Robert Guthrie is given much of the credit for pioneering the earliest screening for phenylketonuria, more commonly referred to as PKU, in the early 1960's. He used blood samples collected on filter paper obtained by pricking a newborn baby's heel ("Heel Stick") on the second day of life to get a few drops of blood which were analyzed. This test was commonly referred to as "The Guthrie Test". Other 'one test-one disease' screening tests were added in the 1970 - 1980's (eg. Congenital Hypothyroidism ,CH).

### 'One test-multiple diseases' Screening

The development of Tandem Mass Spectroscopy (MS/MS) and its application for NBS by Edwin Naylor and others, in the early 1990's, led to a large expansion in the number of congenital metabolic diseases that could potentially be detected based on abnormal blood levels of amino acids, organic acids and acyl-carnitines. Today, MS/MS can routinely screen for over 42 IEM conditions from a single dried blood spot collected on a

filter paper. It is a very efficient and economical method of making available NBS to every baby born.

There are 9 other tests, recommended by the American College of Medical Genetics (ACMG), that cannot be done (for the moment) by MS/MS and continue to rely on earlier 'one test-one disease' biochemical analysis.

### India versus the US with respect to NBS

In India, many labs use biochemical analysis for NBS. The rarity of each individual disease, coupled with the high costs for each individual test, result in only a few high risk babies being screened for a few select conditions. In the US however, NBS is mandated by law and all babies are screened for IEMs between 24 and 72 hours after they are born. This is in large part due to parental advocacy groups and the implementation of MS/MS technology. The cost savings associated with early detection and treatment of affected babies has justified universal NBS in the US.

### Major Benefit of NBS

The major benefit of NBS is that detection of an IEM is possible before clinical symptoms manifest themselves. This allows for treatment of the afflicted baby to start immediately, and in most cases, allows the baby to develop normally and lead a healthy life. Quite often the treatments are very economical and require a dietary restriction or a vitamin/hormone/dietary supplement. With current MS/MS technology coupled with expert interpretation, the false positive rate for the screening process is < 1%, provided the sample collection and delivery is done properly.

If an IEM in an afflicted baby goes undetected after birth (as in unscreened babies) and clinical symptoms of disease appear, it is usually too late to initiate preventative treatment, leading to death or permanent mental illness and disability. It follows that ideally, it would be advisable to screen every baby, as the vast majority of babies born

with an IEM are cases where the parents exhibited no symptoms (they were carriers).

## IEM Conditions detected by MS/MS

The following 20 IEMs are a subset (recommended for testing by the ACMG) of the 42+ conditions that are detected by MS/MS from a single dried blood spot collected on a filter paper.



### Organic Acid (OA) Conditions

1. IVA Isovaleric Acidemia
2. GAI Glutaric Acidemia Type I
3. HMG 3-Hydroxy 3-Methylglutaric Acidemia,
4. MCD Multiple Carboxylase Deficiency
5. MUT Methylmalonic Acidemia (Mutase Deficiency)
6. 3MCC 3-Methylcrotonyl-CoAcarboxylase Deficiency
7. Cbl A, B Methylmalonic Acidemia
8. PROP Propionic Acidemia
9. BKT Beta-Ketothiolase Deficiency



### Fatty Acid Oxidation (FAO) Conditions

1. MCAD Medium-Chain Acyl-CoA Dehydrogenase Deficiency
2. VLCAD Very Long-Chain Acyl CoA Dehydrogenase Deficiency
3. LCHAD Long Chain L-3-OH Acyl-CoA Dehydrogenase Deficiency
4. TFP Trifunctional Protein Deficiency
5. CUD Carnitine Uptake Defect



### Amino Acid (AA) Conditions

1. PKU Phenylketonuria
2. MSUD Maple syrup disease
3. HCY Homocystinuria
4. CIT Citrullinemia
5. ASA Argininosuccinic Acidemia
6. TYR I Tyrosinemia Type I.

## Information Links

### Save Babies Through Screening Foundation

[www.savebabies.org](http://www.savebabies.org)

### American College of Medical Genetics

[www.acmg.net](http://www.acmg.net)

### Pediatrix Screening

[www.pediatrixscreening.com](http://www.pediatrixscreening.com)

### NeoGen Labs

[www.neogenlabs.com](http://www.neogenlabs.com)



NeoGen Labs will offer NBS services for detecting IEMs in India beginning in July 2007 using MS/MS and Biochemical Analysis. NeoGen Labs has an exclusive technology licensing agreement with Pediatrix Screening, Bridgeville, Pennsylvania, USA, the company that pioneered the use of MS/MS in NBS. Since 1994, Pediatrix has screened over 2 million babies of all ethnicities and continues to screen over 200,000 babies every year with very high sensitivity and specificity.

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