Newborn Screening

Samples, Panels, Technologies
(Practical information you can use)

Newborn Screening

- Screens infants shortly after birth for a list of disorders that are treatable, but difficult or impossible to detect clinically.
- Whole blood samples are collected from the infant's heel on specially designed filter paper, and then tested for a panel of disorders.
- The disorders tested can vary from region to region, based on funding and the prevalence of a condition in the population.

Newborn Screening Panel

- **Tandem Mass Spectrometry Tests (45 Disorders)**
  - Dried Blood Spot
  - 1 Test 45+ Conditions
  - Highly Accurate
- **Biochemical Tests (6 Disorders)**
  - Dried Blood Spot
  - 1 Test 1 Condition
  - Focus on CH, CAH, G6PD, GALT, Cystic Fibrosis, Biotinidase

Samples

- Dried Blood Spot (DBS)
- Urine
- Cord Blood
- Venous Blood

Dried Blood Spot (DBS)

- Easy to Collect
  - Heel Prick
- Easy to Store
- Easy to Transport
- Use with ELISA, TMS and HPLC Systems and supported by hundreds of peer reviewed papers
- **Preferred sample for Newborn Screening**

Urine

- Collection is more complicated than DBS
- Contamination Issues
  - Contact with fecal matter
- Cannot screen for
  - Fatty Acid Oxidation disorders, G6PD deficiency, Biotinindase Deficiency, Congenital Hypothyroidism (requires blood)
- NBS Programs worldwide are standardized on DBS
  - Limited research programs based on urine but none adopted for routine screening
- CDC's Newborn Screening Quality Assurance Program (NSQAP) is standardized on DBS
- Can be used for confirmation of disorders screened with DBS

Cord Blood

- Limited to a few disorders
  - CH, G6PD Deficiency, Hemoglobinopathies
- Timing of the collection is important because some metabolite and hormone levels vary markedly in the neonatal period both in normal and affected babies*.
- Maternal contamination is a problem in cord blood
- If additional disorders are to be screened, a second collection will be required
  - Most efficient to collect a sample between 24 to 72 hours of birth, before discharge

***Wilcken B, Wiley V, Newborn Screening, Pathology 2008;40:104-15**

Venous Blood

- Not as easy as Heel Prick to collect
- If a central line already exists, venous blood can be used
  - Do not apply blood to filter paper with a needle smaller than 21 gauge as hemolysed samples are not acceptable
  - Samples collected while the patient is on intravenous fluid or nasogastric feeding (Rhys Tube) are acceptable.

Intravenous Feed (IV)

- If the infant is on intravenous feeding and sample is collected, results for the Galactosemia screen will be affected (could lead to false negative results)
- If IV feed is discontinued, wait 2 days (on regular feed) before collecting the sample

Transfusion

- Rejection of samples if collected less than 72 hours after blood transfusion (if the patient has been transfused with whole blood, wait 96 hours before collection of sample)

Type of Transfusion	Disorders	DBS Sample
Small Volume	FAOD, AAD, OAD, CH	72 Hours+
	G6PD/TGAL/BIOT/SCD	4 Months+
Exchange Transfusion/ Large Volume	FAOD/AAD/OAD CH/CAH/CF	96 Hours+
	G6PD/TGAL/BIOT/SCD	4 Months+
Packed RBC's (pRBC's)	FAOD, AAD, OAD, CH	72 Hours+
	G6PD/TGAL/BIOT/SCD	4 Months+
Platelets	CH	72 Hours+
Fresh Frozen Plasma (FFP)	CH	72 Hours+

Technologies

- ELISA & Enzyme Assay
- FEIA
- Tandem Mass Spectrometry
- HPLC

TMS Interpretation

- Measurement of Multiple Analytes
- Semi Quantitative
  - Use of Standards to Measure Values
- Complex Interpretation
- False Positives < 1%, False Negatives ~ 0% (?)

Interpretation @ NeoGen Labs

- Based on a Database of 4 Million+ Babies
- Proprietary Analyte Ratios
- Aligned with the PerkinElmer Genetics Lab in the US

Confirmatory Testing Technologies

Performed only when there is a
Positive Screening Result or High Index of Suspicion

- HPLC for Amino Acid Disorders
  - Urine or Plasma Specimen
- GC/MS for Fatty Acid Oxidation or Organic Acid Disorders
  - Urine Specimen
- DNA Analysis for Select Disorders
  - Dried Blood Spot