Newborn Screening Facts

As a public health program, the goal of newborn screening is early identification of children at increased risk for selected metabolic or generic diseases so that medical management can be promptly initiated to avert metabolic crises and prevent irreversible neurological and developmental sequelae. Early identification of these conditions is crucial, as timely intervention may lead to a significant reduction of morbidity, mortality ad associated disabilities in affected infants.

Table 1. Recommended Newborn Screening Tests

Name	Abbreviation	Incidence	Description Without Treatment	With Treatment
Hemoglobinopathies Associated with Hb/S allele				
Sickle Cell Anemia	Hb SS	>1 in 5,000; 1 in 400 African American	Inherited anemia that can cause pain, damage to vital organs, stroke and sometimes death.	Beginning in infancy; vigilant medical care, all regular childhood vaccinations and begin treatment with penicillin to reduce the risk of infections, such as pneumonia and meningitis. Treatment may include intermittent pain medications and blood infusions depending on symptoms.
HB S/Beta-Thalessemia 3	Hb S/BTH	>1 in 50,000	A form of sickle cell anemia, the child inherits one sickle cell gene and beta thalessemia gene, another inherited anemia. Symptoms are often milder than Hb SS, but severity varies.	Routine treatment with penicillin may not be universally recommended.
HB S/C Disease	Hb S/C	>1 in 25,000	Another form of sickle cell anemia, the child inherits one sick cell gene and one gene from another hemoglobin variant called HbC. This form is often milder than Hb SS	Routine treatment with penicillin may not be universally recommended.
Amino Acidurias				
Phenylketonuria	PKU	>1 in 25,000	Individuals cannot process phenylalanine, which can accumulate and cause severe mental retardation if not detected and treated soon after birth.	Adherence to a low-phenylaline diet, at least throughout childhood and adolescence, for females during pregnancy.
Maple Syrup Urine Disease	MSUD	<1 in 100,000	MSUD has a wide spectrum of presentations, from mild to severe, although it can be lethal if untreated.	A special, low-protein diet, sometimes supplemented by thiamin, continued indefinitely.

			Babies with MSUD appear normal at birth then quickly deteriorate neurologically, and the urine smells of maple syrup.	
Homocystinuria	HCY	<1 in 100,000	Individuals lack an enzyme to convert homocysteine to cystathionine, which is needed for brain development. Without treatment HCY leads to mental retardation, eye problems, skeletal abnormalities and stroke.	A special diet, vitamins B6 or B12, and betaine.
Citrullinemia	CIT	<1 in 100,000	Untreated individuals with CIT have a buildup of citrulline and ultimately ammonia during the newborn period or infancy that can result in seizures, coma, brain damage and death.	Normal development is possible with early detection and treatment of a low-protein diet, medications to prevent ammonia buildup and nutritional supplements.
Argininosuccinic Academia	ASA	<1 in 100,000	Symptoms commonly begin in the first few days of life (sometimes later in infancy or childhood) with a buildup of arginonosuccinic acid and ultimately ammonia, resulting in brain swelling, coma and sometimes death. Early treatment can be lifesaving, but all individuals with ASA have episodes of ammonia buildup and most have some degree of brain damage.	A low-protein diet, avoiding fasting, medications to prevent ammonia buildup, nutritional supplements and sometimes liver transplant.
Tyrosinemia Type 1	TYR1	<1 in 100,000	The absence of an enzyme causes buildup in the liver of succinylacetone, a byproduct of tyrosine. Without treatment, symptoms begin in the first weeks or months of life and progress to liver or kidney failure, nerve damage and death.	Drug treatment, sometimes with a low-protein diet, can prevent liver and kidney damage in most patients. Hepatic transplant may be considered.
Fatty Oxidation Disorders				
Medium-Chain Acyl-CoA Dehydrogenase Deficiency	MCAD	>1 in 25,000	Infants seem well, then suddenly develop seizures caused by low blood sugar, liver failure, coma and death.	Treatment consists of avoidance of fasting and the addition of nutritional supplements.
Very Long-Chain Acyl-CoA	VLCAD	>1 in 75,000	Symptoms can present at any age from the newborn period to adulthood, but tend to be	Treatment includes a high-carbohydrate/low-fat diet, nutritional

Dehydrogenase Deficiency			more severe in infants. Left untreated, infants develop heart and liver failure and can die during the first year of life.	supplements and the avoidance of fasting and prolonged exercise.
Long-Chain 3-OH Acyl-CoA Dehydrogenase Deficiency	LCHAD	>1 in 75,000	Symptoms resulting in heart, lung, or liver failure and death can present soon after birth, or in other cases low muscle tone, developmental delay, heart, lung or liver failure may develop later in infancy or childhood, often following an illness. Early treatment can prevent death but some children still develop symptoms.	Treatment includes a high carbohydrate/low-fat diet, nutritional supplements and avoidance of fasting. Women pregnant with fetus with LCHAD are at an increased risk of developing acute fatty liver of pregnancy and other complications.
Trifunctional Protein Deficiency	TFP	<1 in 100,000	A seemingly well infant can die of what appears to be sudden infant death syndrome or develop low muscle tone, seizures, heart failure and coma, often following illness.	Treatment includes a strict avoidance of fasting, a low-fat diet and nutritional supplements.
Carnitine Uptake Defect	CUD	<1 in 100,000	In this condition, cells are unable to bring in carnitine (necessary to transfer fatty acids across mitochondrial membranes) from the blood. Symptoms include episodes of hypoglycemia and sudden unexpected death in infancy. Older children may present with progressive heart failure.	Early diagnosis and treatment with carnitine permits normal development.
Organic Acidurias				
Isovaleric Academia	IVA	<1 in 100,000	Individuals with IVA cannot process leucine, which can cause coma, permanent neurological damage and death in the newborn period. Later onset cases can develop in infancy or childhood following an infectious illness.	Early treatment of a low-protein diet and nutritional supplements can result in normal development.
Glutaric Academia Type 1	GAI	>1 in 75,000	GAI is characterized by normal development up to 18 months until a trigger, such as a viral illness, leads to brain damage, seizures, low muscle tone, cerebral palsy-like symptoms and death within the first decade of life. Some babies with GAI are born with an enlarged heart.	Treatment of dietary protein restriction and L-carnitine supplement along with the prompt treatment of illness and fever can prevent brain damage.

Hydroxymethyl-Glutaric Aciduria or HMG-CoA Lyase Deficiency or 3-OH D-CH3 Glutaric Aciduria	HMG	<1 in 100,000	An inability to process leucine results in low blood sugar and the accumulation of several organic acids, especially after illness or fasting, can result in brain damage, mental retardation, coma and death without treatment.	Avoiding fasting and a diet low in leucine and fat and high in carbohydrates can lead to normal development.
Multiple Carboxylase Deficiency	MCD	<1 in 100,000	A lack of enzymes required to activate several biotin-dependent enzymes results in a buildup of lactic and other organic acids. Symptoms usually begin before age 15 months and may include skin rashes, hair loss, brain damage, coma and death without treatment.	Biotin can result in normal growth and development.
Methylmalonic Academia due to Mutase Deficiency	MUT	>1 in 75,000	Severity of symptoms vary greatly, but a processing defect of four essential amino acids and other substances results in illness in the first week of life and can results in death during the first month of life.	Treatment with a special metabolic formula/low protein diet and medication minimize, but cannot prevent central nervous system dysfunction.
3-Methyl-crotonyo-CoA Carboxylase Deficiency	3MCC	>1 in 75,000	The inability to process leucine can lead to brain damage, seizures, liver failure and death in infancy or no symptoms at all into adulthood. Symptoms often develop after childhood illness.	Treatment with a low-protein diet; in some cases nutritional supplements may be helpful.
Methylmalonic Academia cblA and cblB forms	Cbl A, B	<1 in 100,000	A defect of vitamin metabolism can lead to a buildup of organic acids in the blood and result in brain damage, seizures, paralysis, coma and death. Symptoms can begin in the first week of life, though most affected individuals remain symptom- free.	Treatment of vitamin B12 injections and a special metabolic formula/low-protein diet can often prevent serious problems.
Propionic Academia	PROP	>1 in 75,000	This defect in the processing of four amino acids leads to brain damage, coma and death in the newborn period without treatment.	Treatment includes a low-protein diet and nutritional supplements. Even with treatment some children experience developmental delays, seizures, abnormal muscle tone, frequent infections and heart problems.
Beta-Ketothiolase	BKT	<1 in	Episodes of organic buildup often triggered	With prompt intravenous treatment to keep

Deficiency		100,000	by childhood illness; can progress to coma, brain damage and death. These serious consequences are most often seen in infants.	blood sugar levels up and blood acid levels down during illness, children can develop normally. Parents must be alert to early signs of illness. Additional treatments may include avoidance of protein-rich diets and long-term treatment with bicarbonate.
Other Conditions				
Congenital Hypothyroidism	CH	>1 in 5,000	A deficiency of thyroid hormone severely retards growth and brain development.	If detected soon after birth, treatment with oral doses of thyroid hormone can result in normal development.
Biotinidase Deficiency	Biot	>1 in 75,000	The deficiency of biotinidase, the enzyme that recycles the vitamin biotin, may cause frequent infections, alopecia, skin rash, uncoordinated movement, hearing loss, seizures and mental retardation. Left untreated, the deficiency can lead to coma and death.	If detected soon after birth, oral doses of biotin can prevent illness.
Congenital Adrenal Hyperplasia	CAH	>1 in 25,000	CAH includes a set of conditions resulting from defects in the synthesis of hormones produced by the adrenal gland. In female infants, CAH can result in masculinization of the genitals (ambiguous genetalia). Severe forms of CAH cause life-threatening salt loss from the body.	Treatment includes salt and hormone replacement.
Hearing Loss	HEAR	>1 in 5,000; up to 3-4 in 1,000 newborns	Without early testing, hearing loss is usually not diagnosed until ages 3 to 4 years; children often have delayed speech and language development.	Early diagnosis allows hearing aids by age 6 months and helps prevent speech and language problems.
Cystic Fibrosis	CF	>1 in 5,000	Abnormalities in the CF protein result in lung and digestive problems, often beginning in early infancy. Recurrent pneumonia and failure to thrive are common and death occurs at an average of 30-35 years.	Early diagnosis and treatment may improve the growth of babies and children with CF. Treatment varies depending on severity, but may include a high-calorie diet supplemented with vitamins and medications to improve digestion; respiratory therapy to help clear mucus from lungs, and medications to improve breathing

				and prevent lung infections.
Classical Galactosemia	GALT	>1 in 50,000	A missing enzyme prevents the conversion of galactose (sugar from the breakdown of lactose in milk) to glucose, another simple sugar. Galactose then accumulates and damages vital organs, leading to blindness, severe mental retardation, infection and death.	Milk and dairy products must e eliminated from the diet for life. Though treatment dramatically improves symptoms, there continues to be a chance of development delays.

Overview of Screening Protocol

Specimens are samples of blood collected from infants by saturating marked areas of a filter paper card with blood obtained by stick of the heel. Many factors determine the acceptability and quality of a specimen: the timing of collection, the completeness and accuracy of patient and specimen information, adequacy of the blood specimen information, adequacy of the blood specimen and its subsequent handling. Problems with any of these may render a specimen invalid.

Timing of Specimen

- The American Academy of Pediatrics recommends that the specimen not be collected until the newborn is at least 24 hours old.
- Analysis of screening results suggests that a specimen taken on the second day of life is usable for testing, with a slightly increased risk of not detecting an abnormal condition.
- Discharging an infant without collecting a specimen, with intent to collect it later, greatly increases the risk of missing an infant with one of the screened conditions.

Specimen Handling

Contamination of the filter paper (e.g., by skin oils, latex and powder) or the areas within the circle of the filter paper (e.g., by feeding formulas, antiseptic solutions, water, lotions, powder, etc.) should be voided since test results can be affected or invalidated, respectively. The perfect specimen:

- Has all information legibly and accurately recorded on the blood collection form required by your state.
- Is collected from an infant between 24-48 hours of age.
- Is dried for at least four hours away from direct heat and sunlight.

What abnormal results mean:
Talking points regarding a positive test, not-normal screening result or screen-positive infants.

An abnormal result does not mean that the baby has the indicated illness. Overall, most babies who have an abnormal screening result turn out not to have the illness. However, an abnormal result does mean that the child should have additional testing to confirm or rule out the condition.

A positive test results means:

- The test result was out of the normal range.
- The baby should have additional testing to confirm or rule out the condition.
- The newborn screening test may be repeated or another type of test may be requested.

A positive test results **does not mean**:

- That the baby has the indicated condition (most babies who have a positive test result turn out *not* to have the condition).
- The initial screening provides only preliminary information that must be followed up with more specific diagnostic testing.
- That it is a false positive because the baby appears to be in good health. The screening process is successful when affected babies are identified before onset of symptoms.

Resources for Newborn Screening Information

The full breadth of information surrounding the components of newborn screening (NBS) cannot be sufficiently presented in a pocket guide format. Below is a list of selected online resources where additional information can be obtained. Icons adjacent to the URL indicate whether available information and resources are written for health professionals (P) or for consumers and patients (C).

American Academy of Pediatrics:
Committee of Genetics, Newborn Screening Introduction and Fact Sheets:
http://www.aappolicy.aappublications.org/cgi/reprint/pediatrics; 118/3/1304.pdf (P)

- Introduction

http://www.aapolicy.aappublications.org/cgi/reprint/pediatrics; 118/3/e934.pdf (P)

- Fact sheets to assist pediatricians in understanding the individual tests, their characteristics and their strengths and weaknesses.

March of Dimes:
www.marchofdomes.com/professionals/24279.asp (P)

- What caregivers need to know, an online course by Region 4 Genetics Collaborative

- Clinical issues and considerations
- What providers can do
- Resources for families

www.marchofdimes.com/nbs/ (C)

- Fact sheets for patients
  - *What You Need to Know*
  - *What You Can Do*
  - *Caring for Your Baby: Testing the Newborn for Metabolic Birth Defects*
- Link to video *A Parents Guide to Newborn Screening* (English and Spanish)

National Coordinating Center for Genetics and Newborn Screening Regional Collaborative Groups:
www.nccrcg.org (P) (C)

- Links to seven regional collaborative groups
- Project descriptions and resources for patients

National Newborn Screening and Genetics Resource Center (NNSGRC):
http://genes-r-us.uthscsa.edu/ (P) (C)

- Information about your state's NBS program
- Information about disorders that your state currently screens for
- Calendar of events; U.S. state map with NBS and genetics program links

http://genes-r-us.uthscsa.edu/state_contacts.pdf (P) (C)

- State NBS program contacts

Save Babies Through Screening Foundation:
www.savebabies.org/index.php (C)

- Screening FAQs
- Disease descriptions with support group information and references
- Resource library (items can be ordered from the website)
- How to advocate for and promote screening
- List of awareness projects

U.S. National Library of Medicine and the National Institutes of Health, Medline Plus:
www.nlm.nih.gov/medlineplus/newbornscreening.html (C)

- Latest NBS news, overviews, tutorials, links to information about specific conditions from Genetics Home Reference
- Find related issues, genetics research articles, glossary, directories and organization links