



education

Tennessee Newborn Screening Program

Guide for Practitioners

**State of Tennessee Department of Health
Family Health and Wellness**

710 James Robertson Parkway • Nashville, TN 37243

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A program administered by Tennessee Department of Health with the assistance of hospitals, primary care providers, cardiologists, pulmonologists, endocrinologists, audiologists, genetic and sickle cell centers from across the state.



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TENNESSEE
DEPARTMENT OF
HEALTH



I. TENNESSEE CODE ANNOTATED TITLE 68, HEALTH, SAFETY, AND ENVIRONMENTAL PROTECTION, CHAPTER 5 PREVENTION OF DISEASES EXCERPTS

Part 4 Newborn Testing – Metabolic Defects

68-5-401 Testing required -- Public policy.

(a)(1) The general assembly declares that, as a matter of public policy of this state and in the interest of public health, every newborn infant shall be tested for phenylketonuria, hypothyroidism, galactosemia and other metabolic/genetic defects that would result in intellectual disability or physical dysfunction as determined by the department, through rules and regulations duly promulgated in accordance with the Uniform Administrative Procedures Act, compiled in title 4, chapter 5, and that the people of this state shall be extensively informed as to the nature and effects of such defects.

Part 9 Early Detection of Hearing Loss

68-5-903 Newborn infant.

Every newborn infant shall be screened for hearing loss in order to prevent the consequences of unidentified hearing loss, unless the parent or parents of the child object on the grounds that the test would conflict with the parent or parents' religious tenets or practices.

68-5-904 Child born in hospital or other specified facilities.

- a) A child born in a hospital or other birthing facility shall be screened for hearing loss prior to discharge from that facility. The attending health care professional shall refer a child born in a setting other than a hospital or other "birthing" facility to the department of health or an appropriate hearing screening provider as listed in the latest edition of the directory of hearing screening providers in Tennessee for hearing screening. A child born on an emergency basis in a hospital that does not otherwise provide obstetrical or maternity services and that does not provide infant hearing screening tests prior to discharge of an infant from the hospital, shall refer a child born in that facility to the Department of Health or an appropriate hearing screening provider as listed in the latest edition of the directory of hearing screening providers in Tennessee for hearing screening. The hearing screening test shall be provided in accordance with current hearing screening standards established by a nationally recognized organization such as the Joint Committee on Infant Hearing Screening of the American Academy of Pediatrics. All screening providers or entities shall report their screening results to the Department of Health.
- b) Any medical or audiologic provider performing follow-up tests shall report the results of the tests to the Department of Health.

68-5-905 Report and referrals.

The results of all hearing screenings performed pursuant to this part shall be reported to the Department of Health. The department of health shall refer any child who does not pass the hearing screening test to the Tennessee Early Intervention System (TEIS) of the Department of Education for follow-up. Children who have been identified with hearing loss or high risk conditions that place them at high risk for hearing loss as identified by standards established by a nationally recognized organization such as the Joint Committee on Infant Hearing Screening of the American Academy of Pediatrics shall be referred to the TEIS.

II. TENNESSEE RULES AND REGULATIONS - EXCERPTS

1200-15-1-.01 TESTS.

The Department of Health will designate the prescribed effective screening tests and examinations which will be performed on newborns in accordance with Rule 1200-15-01-.02 for the detection of hearing loss, critical congenital heart disease and metabolic/genetic disorders as designated by the Department of Health.

- (1) Exemptions for religious beliefs. Nothing in this part shall be construed to require the testing of or medical treatment

for the minor child of any person who shall file with the Department of Health a signed, written statement that such tests or medical treatment conflict with such person's religious tenets and practices, affirmed under penalties of perjury pursuant to T.C.A. § 68-5-403. The newborn screening refusal form provided by the State should be completed, filed with the Department and retained in the medical record for the period of time defined by the hospital or provider policy.

- (2) Failure to have a child tested for the detection of hearing loss and metabolic/genetic disorders as designated by the Department of Health is a Class C misdemeanor pursuant to T.C.A. § 68-5-404.

1200-15-1-.02 PERSONS AND/OR INSTITUTIONS RESPONSIBLE FOR TESTS FOR NEWBORN INFANTS. The following persons or institutions shall be responsible for hearing testing, critical congenital heart disease screening and blood specimen collection for metabolic/genetic disorders as designated by the Department of Health. Specimens and results shall be submitted in a manner as directed by the Department of Health; procedures are located on the Department's web page.

- (1) Every chief administrative officer of a hospital and the attending physician in each instance shall:
- a) Submit a satisfactory specimen of blood to the State Public Health Laboratory, Department of Health. This sample shall be collected between twenty-four and forty-eight (24-48) hours of age and mailed within twenty-four (24) hours of collection. In some cases it may be necessary to collect a specimen prior to twenty-four (24) hours of age if the infant is going to be discharged, transferred or transfused.
 - 1. Recollect a specimen of blood if the infant was initially screened before twenty-four (24) hours of age. This repeat sample shall be collected between twenty-four and seventy-two (24-72) hours of age and mailed within twenty-four (24) hours of collection. If the infant has been discharged, instruct every parent, guardian, or custodian to bring the infant back to the hospital or to a physician or the nearest local health department to be re-screened.
 - b) Perform a physiologic hearing screen. The result of the hearing screen is to be reported to the Department of Health and should be done before hospital discharge or prior to one (1) month of age.
 - c) Perform pulse oximetry tests on all newborns to screen for critical congenital heart disease between twenty-four and forty-eight (24-48) hours of age. The recommended protocol for screening is available online at the Department of Health's web page.
- (2) Any health care provider(s) of delivery services in a non-hospital setting shall:
- a) Submit a satisfactory specimen of blood to the State Public Health Laboratory, Department of Health. This sample shall be collected between twenty-four and forty-eight (24-48) hours of age and mailed within twenty-four (24) hours of collection. In some cases it may be necessary to collect a specimen prior to twenty-four (24) hours of age if the infant is going to be discharged, transferred or transfused.
 - 1. Recollect a specimen of blood if the infant was initially screened before twenty-four (24) hours of age. This repeat sample shall be collected between twenty-four and seventy-two (24-72) hours of age and mailed within twenty-four (24) hours of collection. If the infant has been discharged, instruct every parent, guardian, or custodian to bring the infant back to the hospital or to a physician or the nearest local health department to be re-screened.
 - b) Instruct the parent, guardian or custodian to obtain a physiologic hearing screen prior to one (1) month of age. A referral may be made to the State Department of Health to assist in locating a hearing provider.
 - c) Perform pulse oximetry tests on all newborns to screen for critical congenital heart disease between twenty-four and forty-eight (24-48) hours of age. The recommended protocol for screening is available online at the Department of Health's web page.

(3) Any health care provider(s) of delivery services in a non-hospital setting shall:

- a) Between twenty-four to forty-eight (24-48) hours of age present said infant to a primary care provider or local health department for blood specimen collection.
- b) Obtain a physiologic hearing screen prior to one (1) month of age. A referral may be made to the State Department of Health to assist in locating a hearing provider.
- c) Between twenty-four and forty-eight (24-48) hours of age present said infant to a primary care provider to perform pulse oximetry tests to screen for critical congenital heart disease. The recommended protocol for screening is available online at the Department of Health's web page.

1200-15-1-.03 NEWBORN SCREENING PAMPHLET PROVIDED TO PARENTS.

The chief administrative officer of each birthing facility shall order the distribution of a pamphlet to every parent, guardian or custodian of an infant screened. The pamphlet, distributed by the Department of Health, educates and prepares the family for newborn testing on their infant. If an infant's blood specimen was collected earlier than twenty-four (24) hours after birth and the patient is discharged home, the birthing facility must review the information on the back of the pamphlet with the family prior to discharge; the information requires the family to present the infant to the hospital, physician or health department within 24-72 hours for a repeat blood specimen. The pamphlet will have a perforated page that may be signed by the parent and placed in the medical record as documentation that the pamphlet was provided.

1200-15-1-.04 MEDICAL PROVIDERS AND LOCAL HEALTH DEPARTMENTS MUST ASSIST THE DEPARTMENT OF HEALTH.

(1) The primary care provider's responsibility is to:

- a) Ensure that all newborn screening tests were conducted and provide necessary follow up, if needed, as instructed by the Newborn Screening Program.
- b) Recollect a blood specimen before two (2) weeks of age, as instructed by the program or tertiary center staff, or send the infant to the local Health Department for recollection.
- c) Assist the Department of Health in contacting families, submitting follow up information, making appropriate referrals and/or notifying the Department immediately if they are not the provider. The Newborn Screening Program outlines the providers' responsibilities in the practitioner guide which is available online at the Department of Health's web page.
- d) Obtain further hearing tests prior to three (3) months of age if the infant did not pass the hearing screen. A referral may be made to the State Department of Health to assist in locating a hearing provider.
- e) Submit the critical congenital heart disease follow-up form on infants who did not pass the pulse oximetry screen.

(2) Audiologist shall submit the hearing follow-up form on infants referred to them for further testing through the newborn screening process.

(3) Cardiologists shall submit the critical congenital heart disease follow-up form on infants referred to them through the newborn screening process.

III. HOSPITAL RESPONSIBILITY

A. Completion of the Newborn Screening Form

- Collection forms are available from the local Health Department or the State Lab 615-262-6391.
- It is important to fill out all information on the Newborn Screening collection form completely and accurately. Some results are based on age, weight and/or feed status of the infant at the time of collection.
- **Adoption Cases:** If a specimen needs to be repeated, a letter will be sent using the information listed on the

form. Do not put birth mothers information on the form; list either adoptive parents, adoption agency or lawyer. Also write ADOPTION CASE on the collection form.

- **Death of a Newborn:** If a screen was collected and a newborn has died, notify the newborn screening follow-up program by fax. Include the child's name, birth date, mother's name and the date of death. Follow up will close the case so mother will not receive letters requesting a repeat specimen if needed. Fax # (615) 532-8555
- **Hearing Screening:** It is the responsibility of the hospital to record the results of the hearing screening on the blood spot form or the "Hearing Only" form.
- **CCHD Screening:** It is the responsibility of the hospital to record the results of the CCHD screening on the blood spot form.
- **Refusal of Test by Parent:** The parent should sign the refusal form designated by the State Newborn Screening program. Retain a copy in the medical record and send a copy with a completed blood spot form with no blood.

B. Obtain a Satisfactory Specimen

- A satisfactory specimen is: Drops of whole blood applied evenly and allowed to soak through the filter paper and can be seen clearly with no white showing through on either side. Preferably these spots should be large enough to punch at least 9 - 1/8 inch discs with no white areas.
- Recommended techniques are available upon request. All Tennessee birthing hospitals/facilities and health departments were provided with a newborn screening video, "Let's Do it Right the First Time." The video demonstrates collection procedures and reviews the diseases screened for by the State of Tennessee.
- An unsatisfactory specimen of a newborn with one of the disorders can cause a possible delay in diagnosis and treatment. A specimen can be considered unsatisfactory for several reasons, including quantity insufficient, blood did not soak completely through filter paper; specimen was contaminated or arrived in a plastic bag. A complete list of descriptions for unsatisfactory specimens is available upon request.
- Reports are mailed to each birthing hospital on a monthly basis. These reports alert hospitals to the number of unsatisfactory specimens collected at the hospital. Monitor these reports and take steps to decrease the number of unsatisfactory specimens submitted.

C. Transfused Newborns

- **Always collect a newborn screening before any transfusion** even if the infant is < 24 hours old, the hemoglobin and biotinidase enzyme results will be accurate and will not need to be repeated if the results are normal.
- **All tests except Hgb (see next bullet for hgb):** Collect a filter paper **4 days** after the last transfusion if baby did not have a normal newborn screen on lactose feed or if the 1st specimen was collected at < 24 hours of age.
- **Hgb (hemoglobin): 3 months** after the last transfusion collect a filter paper, if a filter paper was not collected prior to transfusion identifying normal hemoglobin. Send to the State Laboratory.
- If an infant has symptoms such as vomiting, diarrhea, dehydration and/or jaundice the test should be repeated immediately and the Genetic Center should be contacted.

D. Parent Education and Pamphlets

- As required Rules and Regulations by (Refer to Section II **TENNESSEE RULES AND REGULATIONS** Chapter 1200-15-1-.03). The chief administrative officer of each birthing facility shall order the distribution of a pamphlet to every parent, guardian or custodian of an infant screened. The pamphlet, distributed by the Department of Health, educates and prepares the family for newborn testing on their infant. Order forms are available: <http://health.state.tn.us/MCH/NBS.shtml>

- Hearing educational materials (posters, brochures and DVD's) for hospitals, primary care providers and parents. Materials can be ordered using a form located on the department's website: <http://health.state.tn.us/MCH/NBH.shtml>
- Newborn Screening Prenatal Fact sheets are available to obstetricians and hospitals for prenatal classes and can be ordered using a form located on the department's website: <http://health.state.tn.us/MCH/NBS.shtml>

E. Quality Assurance

- Set up a system ensuring every infant born in your facility has a screen collected.
- Set up a system ensuring results from the state laboratory are received on all NBS specimens your facility submits.
- Teach new personnel the proper methods of specimen collection and review with existing personnel on a regular basis.
- Review quarterly unsatisfactory specimen reports and take steps to lower the rate by identifying areas of weakness in your internal procedures.

IV. NEWBORN SCREENING STATE LABORATORY AND FOLLOW-UP SECTION RESPONSIBILITIES

The Laboratory performs tests on all specimens, reports the results to both the provider and to the hospital of collection listed on the NBS form. Presumptive positives for diseases are immediately reported to the follow-up program. The follow up staff contacts providers and tertiary centers about the abnormal results, and follows up to ensure the patient has confirmatory testing, diagnosis and treatment when necessary. Follow up also informs the parent and provider by letter of the need for a repeat specimen due to either abnormal values, unsatisfactory specimen, transfusion, specimen collected at <24 hrs of age or possible hemoglobin trait.

V. WEEKEND AND HOLIDAY CALLS

When the result of a specimen is abnormal, the lab repeats the test in singleton. Anytime a critical result is identified on Friday and needs to be repeated, the lab personnel will complete the testing that day or on the following day. Results will be called to follow up, who will contact the provider listed on the newborn screening form and the on call personnel with the appropriate tertiary center. On any holidays greater than 3 days, lab personnel will come in to perform testing, specimens will not go longer than 3 days without being tested.

VI. PRIMARY CARE PROVIDER RESPONSIBILITIES FOR FOLLOW-UP

When the laboratory receives specimens, they are separated according to the age of the infant and the quality of the specimen then assigned a Tennessee Department of Health Number (TDH#) before tests are performed.

- A. Specimens Within Normal Limits (WNL)** - Reports of normal specimens are mailed within 5-7 working days from receipt of specimen to provider and hospital of collection listed on the newborn screening form. No follow-up is needed, although providers are responsible for making sure their patient has had a newborn screen, reviewed and interpreted results with respect to blood transfusion and diet status. The provider is also responsible for informing parent/guardian of the results.
- B. Unsatisfactory Specimens:** Medical technologists closely examine each specimen for quality and quantity before performing tests. There are several reasons a specimen might be marked unsatisfactory, some of the more common are: quantity not sufficient, the blood spots did not uniformly soak through the filter paper, the specimen was too old by the time it arrived in the state lab or the baby was <24 hours of age when collected. When a specimen is identified as unsatisfactory, the lab notifies the provider and hospital of collection by mail the next working day. Follow up staff also notifies the provider and parents by mail, and requests a repeat specimen to be obtained. It is the responsibility of the parents and provider once notified to obtain a repeat specimen. Specimens are mailed to the state laboratory; a second unsatisfactory specimen at this point can cause a costly delay in diagnosis and treatment. A description of unsatisfactory specimens is available upon request.

C. Process for Presumptive Positive for Disease: The laboratory reports a presumptive positive result to follow up as soon as it has been determined, generally within 24-48 hours after the specimen is received. Follow up staff notifies the provider listed on the newborn screening form by telephone and fax to initiate confirmatory testing, follow-up, and treatment of the patient. Follow up also notifies the appropriate Endocrinologist, Genetic, Pulmonology or Sickle Cell Center. Results will be mailed to provider and hospital of collection when other tests are completed, within 5-7 days from receipt of specimen. Remember, this is a screening program and further testing will need to be performed prior to diagnosis and treatment.

D. Unable to locate: When follow up and/or the physician are unable to contact or locate an infant for repeat testing due to unsatisfactory or abnormal results, the local health department should be contacted to assist.

E. Keep in mind, this is a SCREEN, not a diagnostic test: The newborn screening (NBS) test can be affected by baby's age, medical or treatment status at the time of specimen collection; the quality and quantity of the specimen or other variables and may not detect all affected babies. The possibility of false negative or false positive results must always be considered when screening newborns for metabolic disorders. Regardless of NBS results, diagnostic evaluation should be performed on an infant presenting with clinical symptoms.

F. Hearing Screening

- Infants that did not receive a hearing screening before hospital discharge should have a hearing screening before one month of age.
- Infants that did not pass one or both ears (or were unable to be tested due a malformation of the ear) should be referred for a second screening or referred directly to hearing provider for diagnostic audiologic evaluation.
- Infants identified with a Risk Indicator for hearing loss should receive periodic hearing assessment as recommended by the Joint Committee on Infant Hearing (JCIH).
 - ▶ Always inform the family if the baby has a risk indicator.
 - ▶ Any risk indicator - First audiologist assessment between 6-9 months of age.
 - ▶ Higher risk Indicator – Continue to receive audiologic assessments every 6 months until the age of 3 years.
 - ▶ Lower risk indicators – Continue to receive annual audiologic assessments until age 3 years.
 - ▶ A “Chart of Risk Indicators” is sent to providers with referral follow-up letters. It is available at the MCH website <http://health.tn.gov/MCH/NBS.shtml>
- Report all hearing screening and follow-up tests (passes and not passes) to the Newborn Hearing Program. Fax 615-532-8555

G. Critical Congenital Heart Disease (CCHD) Screening

- Perform screen at 24-48 hours of age or shortly before discharge if <24 hours old.
- Screen foot only (either foot) and document date and time in area for initial screen:
 - ▶ If 97 - 100%: Mark PASSED on form. No further testing needed.
 - ▶ If <90%: Mark FAILED on form.
 - ▶ If <90-96%: Add the screening of Right Hand
- If both RH and Foot need to be screened, note it on the collection form:

1. Mark **PASSED** if:

- ▶ $\geq 95\%$ in either extremity with a $\leq 3\%$ difference between the right hand and foot.

2. Mark **FAILED** if:

- ▶ <90% in either the RH or the foot at anytime. Babies should have IMMEDIATE CLINICAL ASSESSMENT.
 - ▶ <95% in both the RH and the foot or a >3% difference between RH and foot on three measurements each separated by one hour.
- Referred to Cardiology: Only mark “yes” if the baby was referred after clinical assessment.

VII. NEWBORN SCREENING VIDEOS

1. Metabolic/Genetic Blood Spot Screening-

“Let’s Do it Right the First Time” is a self instructional CD-ROM for practitioners. This course was designed for as a multidimensional tool which includes information about the disorders, techniques needed to properly collect blood specimens that are acceptable for the laboratory screening process, hearing screening information and the newborn screening follow up programs duties. For ordering information visit the website <http://health.tn.gov/MCH/NBS.shtml>

2. Newborn Hearing Screening

“Newborn Hearing Screening Training Curriculum – Competency-Based Training for Hearing Screeners”. Available at www.infanthearing.org (National Center for Hearing Assessment and Management)

VIII. NEWBORN SCREENING PROGRAM SECURE REMOTE VIEWER (SRV)

The Newborn Screening Program now has screening results available for healthcare providers to view and print via the web. SRV is a web based application which will allow you to view digital copies of the patient result reports. This will take the place of the current Voice Response System (VRS) that providers call to get results using their physician license number. Healthcare providers must be registered with the Department of Health in order to gain access to the SRV.

If you would like access to the system please fill out the SRV Access Form (<http://health.state.tn.us/MCH/NBS/PDFs/PH3909.pdf>) and FAX it to (615) 532- 8555. An email address is required. Once this form is received, you will be notified via email of your Username and Password. The email will not include the link to the SRV website for security purposes. Please log into the State of Tennessee Newborn Screening Program Results Website (<https://tnicms.neometrics.com/toolbar/login.aspx>) to access the SRV once you receive your Username and Password.

IX. List of Newborn Screening Specialty Providers

A. Genetic/Metabolic Centers

University of Tennessee
Department of Medical Genetics
Knoxville (865) 305-9030
(800) 325-3894

University of Tennessee
Division of Medical Genetics
Memphis (901) 448-6595

Vanderbilt University Medical Center
Division of Medical Genetics
Nashville (615) 322-7601

B. Satellite Genetic Centers

East Tennessee State University
Medical Genetics Center
Johnson City (423) 439-8714

T. C. Thompson Children's Hospital
Division of Medical Genetics
Chattanooga (423) 778-6112

C. Hearing Providers

Call (888)-202-1357
(615)-532-8555
<http://health.tn.gov/MCH/NBS.shtml>

D. Hematology (Sickle Cell) Centers

T.C. Thompson Children's Hospital
Pediatric Hematology
Chattanooga (423) 778-7289

Meharry Sickle Cell Center
Meharry Medical College
Nashville (615) 327-6763
<http://www.mmc.edu/research/centers/sicklecell/index.html>

University of Tennessee
Department of Medical Genetics
Knoxville (865) 305-9030
(800) 325-3894

St. Jude Children's Research Hospital
St. Jude Hematology
Memphis (901) 595-5691
<http://www.stjude.org/sicklecell>

E. Cystic Fibrosis Centers

T.C. Thompson Children's Hospital
Pediatric Pulmonology
Chattanooga (423) 778-2001

University of Tennessee at
Le Bonheur Children's Medical Ctr.
Pulmonary Medicine
Memphis (901) 287-5222

Vanderbilt University Medical Center
Division of Pediatric Pulmonary,
Allergy and Immunology
Nashville (615) 343-7617

East Tennessee Children's Hospital
Pediatric Pulmonology
Knoxville (865) 637-8481
(865) 541-8698

F. Pediatric Endocrinologists

T.C. Thompson Children's Hospital
Pediatric Endocrinology
Chattanooga (423) 778-6405

East Tennessee State University
Pediatric Endocrinology
Johnson City (423) 439-7320

U.T Medical Group
Department of Pediatrics
Division of Endocrinology
Memphis (901) 284-6399

The Endocrine Clinic
Memphis (901) 763-3636

Jackson Pediatric Center Endocrinology
Jackson (731) 664-9928

East Tennessee Children's Hospital
Department of Pediatric Endocrinology
Knoxville (865) 971-7400

Monroe Carell Jr. Children's Hospital
Vanderbilt Department of Pediatric
Endocrinology and Diabetes
Nashville (615) 322-7427

G. Cardiac Providers

LeBonheur Children's Hospital
50 N. Dunlap Street Lobby Level
Memphis, (901) 866-8817

Pediatric Cardiology, PC
805 Estate Place #1
Memphis, (901) 287-4150

Dr. Dane Douglas
6401 Poplar Avenue #402
Memphis, (901) 682-7774

Children's Hearts
1919 Charlotte Ave Suite 230
Nashville, (615) 321-8549

Vanderbilt Pediatric Heart Institute
2200 Children's Way
Nashville, (615) 322-7447

Pediatric Cardiology, Winchester Pediatrics
155 Hospital Road Suite E
Winchester, (931) 962-0672

Tri-City Pediatric Cardiology
2312 Knob Creek Road Suite 208
Johnson City, (423) 610-1099

ETSU Pediatric Cardiology
325 N. State of Franklin Road
Johnson City, (423) 439-7320

East Tennessee Pediatric Cardiology
2001 Highland Avenue Suite B
Knoxville, (865) 971-6897

Knoxville Pediatric Cardiology
2100 Clinch Avenue
Knoxville, (865) 522-0420

TC Thompson Children's Hospital Cardiology
910 Blackford Street
Chattanooga, (423) 778-6180

X. Metabolic/Genetic Disorders

Disorder Incidence Genetics	Defect	Clinical Symptoms (untreated)	Screening Method	Goals of Screening	Pitfalls of Screening/Comments
Amino Acid Disorders Screening Began:2004	Defect in amino acid metabolism caused by a specific defect in the biosynthesis of one of the enzymes.	Hypotonia, hypothermia, poor feeding, persistent vomiting, developmental delays, damaged to vital organs, seizures or coma. The effect of the disorder will depend on the age at which symptoms occur.	Elevated metabolites using MS/MS related to specific disorder.	Identify all infants with elevated metabolite levels. Assess need for diet and cofactor therapy and begin immediately.	Inadequate oral/IV protein/amino acid intake can delay rise in amino acid levels. Infant receiving hyperalimentation may have mildly elevated levels.
Biotinidase Deficiency Incidence: 1/61,000 Screening Began:2003	Decrease in biotinidase activity which is needed to free biotin from protein which is required for carboxylases to function properly. When carboxylase is unable to perform their normal functions, altering fat, carbohydrate and protein metabolism, harmful byproducts collect in the body.	Hypotonia, seizures, coma, tachypnea, stridor, alopecia, conjunctivitis and dermatitis.	Biotinidase Enzyme Activity.	Identify all infants with deficient biotinidase activity.	Severity of symptoms and age of onset can vary. False negative test results may occur with the use of sulfonamides, repeat filter paper 5 days after sulfonamides discontinued.
Congenital Adrenal Hyperplasia (CAH) Incidence: 1/19,000 Screening Began:2000	Enzyme defect in cortisol and aldosterone synthesis. Leads to high ACTH, over secretion of adrenal androgens, and virilization of genitalia. Death from circulatory collapse and salt loss (salt wasting form).	Virilized female genitalia, males not apparent. Vomiting, circulatory collapse, hyponatremia, and hyperkalemia as early as 5 days of life.	Elevated 17 α -hydroxyprogesterone (17-OHP)	Identify all infants with the salt wasting form, 21 hydroxylase deficiency and treat within first week of life. Correct sex assignment in affected females.	Early sample inconclusive due to placental 17-OHP. Screening only identifies 21-Hydroxylase form (90% of cases).
Congenital Hypothyroidism (CH) Incidence: 1/3,000 Screening Began:1980	Insufficient production of thyroxine due to absent, dysfunctional or ectopic thyroid gland (Primary CH) or to defective TSH secretion by the pituitary (Secondary CH).	Most newborns show none. Jaundice, constipation, coarse facies/ tongue, delayed skeletal maturity, posterior fontanelle, bradycardia, hypothermia.	Elevated TSH When pituitary is normal indicates absent or hypofunctioning thyroid gland.	To identify all infants with primary CH and initiate therapy by day 14 of life.	Early samples inconclusive due to TSH surge at birth TSH screen only identifies Primary CH Some (VLBW) infants with CH display delayed TSH rise
Critical Congenital Heart Disease (CCHD) Incidence: 11/10,000 Screening Began: 2013	Structural heart defects that result in low levels of oxygen in the blood (hypoxia) in the newborn period. Primary target of screening: 1. Hypoplastic left heart syndrome (HLHS) 2. Tricuspid atresia 3. Pulmonary atresia 4. Tetralogy of Fallot (TOF) 5. Total anomalous pulmonary venous return (TAPVR) 6. Transposition of the great arteries (TGA) 7. Truncus arteriosus	Defect in amino acid metabolism caused by a specific defect in the biosynthesis of one of the enzymes.	Decreased oxygen saturation on pulse oximeter.	Early identification can potentially improve the prognosis and decrease the mortality and morbidity of affected infants. Infants may need medical and/or surgical intervention . There may be some cardiac conditions that are not identified by the screen.	The CCHD screen is a point of care testing. Point-of care testing refers to those tests administered outside of a laboratory but close to the site of direct delivery of medical care for a patient. Intervention will take place at the hospitals and birthing facilities if the infant fails the pulse oximetry test.

X. Metabolic/Genetic Disorders

Disorder Incidence Genetics	Defect	Clinical Symptoms (untreated)	Screening Method	Goals of Screening	Pitfalls of Screening/Comments
<p>Cystic Fibrosis</p> <p>Incidence: 1/3,000 Caucasian 1/6,000 Hispanic 1/10,000 African-American 1/90,000 Asian-American</p> <p>Screening Began:2008</p>	<p>Defect in cystic fibrosis transmembrane conductance regulator (CFTR) gene.</p> <p>CFTR regulates the movement of salt (sodium chloride) and water into and out of cells, when it does not work properly high levels of salt are found in the sweat.</p> <p>This also results in thick, sticky secretions in the respiratory and digestive tracts, as well as in the reproductive system.</p>	<p>Failure to thrive, bulky and greasy stools (steatorrhea), failure of newborn to pass stool, frequent sinopulmonary infections, nasal polyps, clubbing, excessive salt in sweat, dehydration.</p>	<p>Elevated immunoreactive trypsinogen (IRT), a pancreatic enzyme elevated in most CF affected newborns.</p>	<p>Identify all infants with elevated IRT so CF can be diagnosed early and patient referred to an accredited CF center for assessment and management.</p> <p>Aggressive nutritional support and respiratory care can be started before the infant gets sick.</p>	<p>IRT may be elevated in many newborns and slowly decrease to normal with age increasing the number of false positives identified.</p> <p>Delays in specimen transport or if exposed to heat may cause false negative results.</p> <p>Diagnostic evaluation should be performed on all infants with meconium ileus (MI) regardless of NBS results because they may have low initial IRT values.</p>
<p>Fatty Acid Oxidation Disorders</p> <p>Screening Began:2004</p>	<p>Accumulation of fatty acids and a decrease in cell energy metabolism due to an enzyme defect in the fatty acid metabolic pathway (use of dietary and stored fat).</p>	<p>During the first crisis children have presented with metabolic acidosis, persistent vomiting, hypoglycemia, lethargy, apnea, encephalopathy, coma, cardiopulmonary arrest, or sudden unexplained death.</p>	<p>Elevated metabolites using MS/MS related to specific disorder.</p>	<p>Identify all infants with elevated metabolite levels. Assess need for diet and cofactor therapy and begin immediately.</p>	<p>Confirmation may require analysis of urine organic acid, blood Acylcarnitine profile and DNA studies.</p>
<p>Galactosemia</p> <p>Incidence: 1/62,000 (classical) 1/6,000 (variants)</p> <p>Screening Began:1992</p>	<p>Enzyme defect (transferase) Elevation of galactose and galactose metabolites.</p>	<p><u>Classical:</u> Sudden death (E. coli sepsis); jaundice, hepatomegaly, acidemia, cataracts, mental retardation</p> <p><u>Variants:</u> milder</p>	<p>Elevated total Galactose in blood</p> <p>RBC based assay (Enzyme screened in specified situation only; RBC based).</p>	<p>Identify all infants with classical galactosemia, prevent death, and begin diet immediately.</p> <p>Identify all treatable variant forms.</p>	<p>Test not reliable on non-lactose/IV intake, or post RBC transfusion.</p>
<p>Hearing Loss</p> <p>Incidence: 1-3:1000</p> <p>Screening Began:2008</p>	<p>Targeted hearing loss is permanent sensory neural or conductive hearing loss averaging 30-40 dB or more in the frequency important for speech recognition (500-4000 Hz).</p>	<p>Difficulty learning grammar, word order, idiomatic expressions, and other forms of verbal or visual/manual communication. May result in delayed language and speech, low educational attainment, increased behavioral problems, decreased psychosocial well-being and poor adaptive skills.</p>	<p>Automated Auditory Brainstem Response (AABR) or Otoacoustic Emissions (OAE)</p> <ul style="list-style-type: none"> • Screen before discharge. • Home births and other non-hospital births screened prior to one month of age. <p>Either or both methods can be utilized by the hospital.</p> <p>AABR is recommended for NICU infants.</p>	<p>To identify deafness or hard of hearing prior to 3 months of age and implement early intervention services for communication prior to 6 months of age.</p>	<p>The Hearing screen is a point of care testing. Point-of care testing refers to those tests administered outside of a laboratory but close to the site of direct delivery of medical care for a patient. Intervention referrals take place at the hospitals and birthing facilities if the infant fails the hearing test.</p>
<p>Hemoglobinopathy</p> <p>Incidence:1/350 African Americans</p> <p>Screening Began:1988</p>	<p>Abnormal Hb (homozygous SS, doubly heterozygous SC, or heterozygous AS, AC).</p>	<p>Sickle cell disease associated sepsis, pain crises, pneumonia, anemia, gallstones, splenic enlargement etc.</p>	<p>Isoelectirc focusing, with HPLC or cellulose acetateelectrophoresis for confirmation</p>	<p>Identify infants with sickle cell disease for case management; identify infants with trait conditions for genetic counseling.</p>	<p>Abnormal hemoglobins must be confirmed.</p> <p>RBC transfusion affects results; screen before transfusion</p>

X. Metabolic/Genetic Disorders

Disorder Incidence Genetics	Defect	Clinical Symptoms (untreated)	Screening Method	Goals of Screening	Pitfalls of Screening/Comments
Homocystinuria Incidence: 1/340,000 Screening Began:2004	Reduced activity of cystathionine beta synthase, which is required for the conversion of homocysteine to cystathionine and cysteine, needed for proper growth and development. An amino acid disorder.	Mental retardation, seizures, thrombosis and dislocated lens.	Elevated Methionine levels.	Identify all infants with elevated methionine levels. Assess and initiate diet and cofactor treatment immediately.	Inadequate oral/IV protein/amino acid intake can cause methionine to rise slowly.
Maple Syrup Urine Disease (MSUD) Incidence:1/230,000 Screening Began:2004	Enzyme defect or deficiency which is needed for metabolism of leucine, isoleucine and valine, amino acids. Life threatening complications may occur due to accumulation of derivatives of above amino acid. An amino acid disorder.	Maple syrup odor of urine/sweat. Poor feeding, high pitched cry, vomiting, mental retardation hypertonica or hypotonia, convulsions and/or coma.	Elevated Leucine and/or Valine Levels.	Identify all infants with elevated leucine levels. Assess need for diet and cofactor therapy and begin immediately.	Inadequate oral/IV protein/amino acid intake can delay rise in leucine levels. Infant receiving hyperalimentation may have mildly elevated leucine levels.
Medium Chain Acyl-CoA Dehydrogenase (MCAD) Incidence: 1/12,000 Screening Began:2004	Deficiency of the enzyme MCAD, which is necessary for the breakdown of certain fatty acids leading to the accumulation of Acyl-CoA derivatives of fats in the liver and the brain. A fatty acid disorder.	Triggered during periods of fasting. Hypoglycemic, lethargy, vomiting and/or liver malfunction. Viral illnesses that limit food intake may cause symptoms to occur.	Elevated C8 levels	Identify all infants with elevated Octanoylcarnitine levels. Assess need for therapy with low fat diet and carnitine; begin treatment immediately.	Confirmation may require analysis of urine organic acid, Acyl carnitine profile and DNA studies.
Organic Acid Disorders Screening Began:2004	Defect in protein metabolism where an essential enzyme is absent or malfunctioning causing accumulation of organic acids in blood and urine.	Vomiting, metabolic acidosis, ketosis, hyperammonemia, lactic acidosis, hypoglycemia, failure to thrive, hypotonia, global developmental delay, sepsis, hematological disorders and ultimately death. The effect of the disorder will depend on the age at which symptoms occur.	Elevated metabolites using MS/MS related to specific disorder.	Identify all infants with elevated metabolite levels. Assess need for diet and cofactor therapy and begin immediately.	Confirmation may require analysis of urine organic acids, blood Acyl carnitine profiles and enzymatic studies.
Phenylketonuria (PKU) Incidence: 1/15,000 Screening Began:1968	Enzyme defect (phenylalanine hydroxylase);increased phenylalanine/phenylketones An amino acid disorder.	Mental retardation Seizures.	Elevated phenylalanine.	Identify all infants with elevated phenylalanine levels. Assess for therapy before day 14 of life.	Inadequate oral/IV protein or amino acid intake.
Severe Combined Immunodeficiency (SCID) Incidence: 1/50,000 to 1/100,000 Screening Began:2016	Defect in production of T and B lymphocytes (cells) resulting in absent or very low production of T cells. Decreased cellular and humoral immunity. Leading to serious or life threatening bacterial, viral and fungal infections.	Infants usually look normal outwardly. Recurrent severe infections. Chronic diarrhea. Recurrent Fever. Failure to thrive (FTT). Peripheral lymphoid tissue may be absent. Persistent mucocutaneous candidiasis. XRAY may show absence of thymic shadow.	T-cell Receptor Excision Circles (TREC) DNA circles measured by PCR using a dried blood spot to detect low T cell. The absence of TREC (or low numbers of TREC) indicates low T cell production.	Identify all infants with low T cell production to facilitate early SCID diagnosis to decrease the morbidity and mortality of the disease and provide aggressive support and minimize infectious exposures prior to the infant becoming ill.	Premature infants with gestational age <37 weeks present with lower TREC values. Low TREC levels can also be from other immunodeficiencies requiring DNA tests to confirm.



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