State of Illinois
Illinois Department of Public Health

Newborn Screening Practitioner's Manual

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ILLINOIS DEPARTMENT OF PUBLIC HEALTH
IDPH
PROTECTING HEALTH, IMPROVING LIVES

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Introduction

Newborn screening is a public health activity aimed at early identification of newborns affected with certain genetic and/or metabolic conditions. Early diagnosis and treatment of these conditions has been shown in many cases to reduce morbidity, premature death and other developmental disabilities. Newborn screening is recognized as one of the most successful recent public health accomplishments, and was the first population-based genetic screening program to become an integral component of public health practice.

While newborn screening disorders are individually rare, collectively the incidence of these disorders is around one in 500 births. In Illinois, each year around 350-400 newborns are diagnosed with a condition identified by newborn screening. Newborn screening affects all health care practitioners who work with children and their families. During their practice of medicine, most pediatric and family medicine health professionals will receive a notice that a child in their care has a serious abnormal newborn screen, or has been diagnosed with a newborn screening disorder.

Health care practitioners are vital links within an effective newborn screening system, a system that includes hospitals, the state newborn screening laboratory and follow-up program, parents, health care providers, medical specialists and community service agencies. Health care providers serve as the front line in assuring all newborns receive adequate screenings and, when necessary, appropriate follow-up services within a medical home.

The Illinois Department of Public Health (Department) Newborn Screening Program developed this manual for health care professionals as a reference guide to newborn screening in Illinois. This resource provides protocols for specimen collection, laboratory testing, follow-up services, and the Department's reporting of both normal and abnormal screening results. Information about the disorders included in the current newborn screening test panel also are provided. This manual is intended to provide background information and general guidance on issues related to newborn screening, but does not replace the case specific medical advice available through consult with pediatric medical specialists, including those who may be contacted at the medical centers that can be obtained by contacting the Department's Newborn Screening Follow-up Program at 217-785-8101.

Overview

The Newborn Metabolic Screening Act (410 ILCS 240/) mandates newborn screening for all newborns born in Illinois. This act authorizes the Department to promulgate administrative rules for newborn screening (Title 77: Public Health, Chapter 1: Department of Public Health; Subchapter i: Maternal Child Health; Part 661 Newborn Metabolic Screening and Treatment Code). The Newborn Metabolic Screening Act and the newborn screening administrative rules may be viewed at the Department's website, www.idph.state.il.us.

All Illinois newborn newborns are mandated to have a blood sample collected on the special filter paper specimen cards supplied by the Department. The only valid exception is parental refusal based on religious beliefs and practices; in which case, a written refusal must be signed by the parents and documented in the newborn's medical record.

Newborn screening blood spot specimens should be collected as soon as possible after the first 24 hours of life. If the newborn is to be discharged from the birth center prior to 24 hours of age, the specimen should be collected before discharge. After drying, the specimen cards should be sent by courier to the Department's Newborn Screening Laboratory in Chicago for testing. When testing is completed, a report of all test results is issued by the Department's Newborn Screening Laboratory to the specimen submitter, usually the birthing facility. Birthing facilities are expected to place the original screening report in the newborn's medical record and to relay a copy of the results to the newborn's primary care provider.

In addition to this laboratory report, abnormal, unsatisfactory and invalid test results are reported by the Department's Newborn Screening Follow-up Program to the physician of record, the physician whose name appears on the specimen card. In some cases, hospitals may authorize reporting of results to a specified hospital contact person. The physician of record or the birthing hospital newborn screening contact person is expected to inform the parent or guardian. If the newborn has a new primary care provider, the new physician should follow up on any abnormal test results and facilitate any recommended follow-up activities. Necessary follow-up may include evaluation of the newborn's medical condition and collection of a repeat newborn screening specimen or referral to a pediatric medical specialist for diagnostic testing. If the mother cannot be contacted, the assistance of the birth hospital and/or the local public health department may be needed to help locate the family. The Department's Newborn Screening Program should be informed of any difficulties in locating the family. Every effort should be made to assure each newborn who has an abnormal newborn screen receives the appropriate follow-up services in a timely manner.

For newborns with any abnormal results requiring immediate referral to a pediatric medical specialist, a list of Department designated specialists, information about the suspected disorder and the actual test results will be provided to the physician of record or the hospital newborn screening contact. The American College of Medical Geneticists (ACMG), www.acmg.net, provides detailed action plans for follow-up of suspected newborn screening disorders. The University of Illinois at Chicago, Division of Specialized Care for Children (DSCC), www.uic.edu/hsc/dscc, provides additional information about these conditions and the importance of medical homes for children with special health care needs.

In addition to these resources, the Maternal and Child Health Bureau of the Health Resources and Services Administration provided grant funding to create the Region 4 Genetics Collaborative, which includes Illinois, Indiana, Kentucky, Michigan, Minnesota, Ohio and Wisconsin. The goals of this multi-state collaborative include efforts to address inequities in genetics' resources and to improve the quality of genetics' services, including newborn screening throughout the region. The Region 4 Genetics Collaborative website, www.region4genetics.org, provides information about newborn screening, medical homes, specialty care resources and genetic counseling services available within this seven-state region.

Illinois Newborn Screening Disorder List

Amino Acid Disorders
- Homocystinuria (HCU)/Hypermethioninemia - 2002
- Maple syrup urine disease (MSUD) - 2002
- Phenylketonuria (PKU)/Hyperphenylalaninemia - 1965
- Tyrosinemia (TYR) - 2002
- 5-Oxoprolinuria (5OXP) - 2002

Biotinidase deficiency (BIO) – 1986

Critical Congenital Heart Disease (CCHD) - 2013

Cystic fibrosis (CF) - 2008

Endocrine Disorders
- Congenital adrenal hyperplasia (CAH) - 1987
- Congenital hypothyroidism (HYP) - 1979

Fatty Acid Oxidation Disorders - 2002
- Carnitine/acylcarnitine translocase deficiency (CACT)
- Carnitine palmitoyl transferase deficiency, type 2 (CPT2)
- Carnitine palmitoyl transferase deficiency, type 1A (CPT1A)
- Carnitine uptake defect (CUD)
- Glutaric aciduria, type 2 (GA2)/Multiple acyl-CoA dehydrogenase deficiency (MADD)
- Isobutyryl-CoA dehydrogenase deficiency (IBCD)
- Medium chain acyl-CoA dehydrogenase deficiency (MCADD)
- Medium/Short chain L-3-hydroxyacyl-CoA dehydrogenase deficiency (M/SCHADD)
- Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHADD)
- Short chain acyl-CoA dehydrogenase deficiency (SCADD)
- Trifunctional protein deficiency (TFP)
- Very long chain acyl-CoA dehydrogenase deficiency (VLCADD)

Galactosemia (GALT) - 1984

Hearing Loss - 2002

Hemoglobinopathies
- Sickle cell disease, trait conditions and other hemoglobinopathies (SC) - 1989
- Alpha thalassemia - 2008
- Beta thalassemia major - 1989

Lysosomal storage diseases (LSD) - 2015
- Pompe
- Fabry
- Gaucher
- Krabbe – *This disorder is not currently on the Illinois newborn screening panel.*
- Niemann-Pick
- MPS I (Hurler's Syndrome)
- MPS II (Hunter's Syndrome) – *This disorder is not currently on the Illinois newborn screening panel.*

Organic Acid Disorders - 2002
- 2-methylbutyryl-CoA dehydrogenase deficiency (2MBCD)
- 3-methylcrotonyl-CoA carboxylase deficiency (3MCC)
- 3-hydroxy-3-methylglutaryl-CoA lyase deficiency (HMG)
- 3-methylglutaconic aciduria (3MGA)
- Beta-ketothiolase deficiency (BKT)
- Glutaric aciduria, type 1 (GA1)
- Isovaleric acidemia (IVA)
- Malonic aciduria (MA)
- Methylmalonic acidemia (MMA)
- Multiple carboxylase deficiency (MCD)
- Propionic acidemia (PA)

Severe Combined Immune Deficiency - 2014

Urea Cycle Disorders - 2002
- Argininemia (ARG)
- Argininosuccinic aciduria (ASA)
- Citrullinemia (CIT)

Important Contact Information

Newborn Screening Follow-up Program
Illinois Department of Public Health
Genetics/Newborn Screening Program
535 W. Jefferson St., Second Floor
Springfield, IL 62761
Phone 217-785-8101
FAX 217-557-5396

Newborn Screening Laboratory
Illinois Department of Public Health
Division of Laboratories
2121 W. Taylor St.*
Chicago, IL 60612
Phone 312-793-4752
FAX 312-793-1054

Accounting Services
Illinois Department of Public Health
Account Services Billing Manager
535 W. Jefferson St., Fourth Floor
Springfield, IL 62761
Phone 217-524-5780

Websites
Illinois Department of Public Health Genetics/Newborn Screening Program
www.idph.state.il.us/HealthWellness/newborn_screening/index.htm

Illinois Department of Public Health Newborn Screening Laboratory
http://www.idph.state.il.us/about/laboratories/manual/Manual_of_Services_OHP_LABS.pdf#page=53

***Note: Newborn Screening Shipping Labels**
Special courier service shipping labels are available to birthing facilities. To order labels and newborn screening specimen collection forms, contact the IDPH Laboratory in Springfield at 217-524-6222. To establish this courier service, contact the Department's Newborn Screening Follow-up Program at 217-785-8101.

Other submitters of newborn screening specimens are encouraged to utilize a courier service for prompt delivery of these dried blood samples, and shipping labels should be addressed to the IDPH Newborn Screening Laboratory listed above.

Practitioner's Newborn Screening Responsibilities

Specimen Collection

- Attending physician at birth or in the immediate newborn period has primary responsibility for collection of a specimen for newborn screening. The physician's responsibility may be delegated to the hospital administrator or the administrator's designee.

- If the birth is attended by a licensed nurse midwife, the midwife has primary responsibility for collection of a specimen for newborn screening.

- Parents should be informed a blood specimen will be collected from their newborn and printed information about newborn screening and how parents can access screening results should be provided.

    - *Newborn Screening Guide for Parents: Newborn's First Steps in Life* document is available through the Department's Genetics/Newborn Screening Program. An electronic file of this document may be downloaded from the Department's website, www.idph.state.il.us, and reprinted for distribution.
    - Documentation that a newborn screening specimen was collected and a copy of the screening results should be placed in the newborn's medical record.
    - Parents should be informed that accurate contact information (emergency contact, current address and valid phone number) is vital should their newborn's newborn screening test be abnormal and additional testing or referral of the newborn to a specialist become necessary.

- Physician or health care provider caring for the newborn during the first month of life is responsible for newborn screening if:

    - Birth occurs outside of a hospital or medical facility.
    - Birth occurs without a physician or licensed midwife in attendance.

- The American Academy of Pediatrics, August 2000 supplement to *Pediatrics*, "Serving the Family from Birth to the Medical Home," suggests the role of the medical home health care professional include establishment of office protocol to retrieve the results of newborn screening for newborns admitted to the practice when scheduling the first appointment. When screening results cannot be documented, a newborn screening specimen should be collected from the newborn and submitted for testing.

- The Department encourages primary care practitioners to provide medical homes, and to facilitate follow-up services for newborns with abnormal newborn screening results.

    - The federal Maternal and Child Health Bureau of the Health Resources and Services Administration (HRSA) funded Region 4 Genetics Collaborative website, www.region4genetics.org, provides information about newborn screening, medical homes, pediatric specialty care resources and genetic counseling services available within this seven-state region.

- Primary care providers have an obligation to verify newborn screening results and should not assume lack of notification indicates the newborn's screen was normal.

  - Reports may be sent to the wrong health care provider.
  - Specimens may be lost in transit to the Department laboratory.
  - Hospitals may fail to collect a newborn screening specimen prior to hospital discharge or transfer.

- If there is no physician caring for the newborn, the parents are responsible for obtaining newborn screening for their newborn. Contact the IDPH Newborn Screening Follow-up Program at 217-785-8101 for specimen collection cards and instructions.

Newborn Screening Fee

- A fee will be charged for each specimen submitted to the Department Newborn Screening Laboratory for testing. This fee provides funding for testing, follow-up services for newborns with abnormal results and provision of certain medically necessary dietary treatment formulas.

- The Department bills hospitals, health care agencies and any specimen submitter on a monthly basis for newborn screening specimens submitted during that month.

Repeat Specimens, Diagnostic Testing and Referrals

- Physician of record or hospital designee is responsible for informing parents and/or newborn's primary care/medical home provider of abnormal or unsatisfactory test results. If repeat screening is necessary, the physician of record is responsible for obtaining and submitting a repeat specimen and/or informing the newborn's primary care provider of the need for additional testing.

- If referral of the newborn to a pediatric medical specialist is necessary, the physician of record or hospital designee is responsible for assisting the newborn's family and facilitating the referral. The Department recommends the physician's office contact the medical specialist and provide the screening results to assure the referral is completed, and the screening results are accurately reported.

- Physicians and hospital staff should not refer to the newborn metabolic screen as the "PKU test." Use of this outdated terminology has resulted in confusion about newborn screening results among primary care providers, medical specialists and parents.

Refusal of Newborn Screening

- Parents may refuse newborn screening only on the basis of religious beliefs and practices.

  If parents refuse newborn screening of their newborn, parent education about the benefits of newborn screening should be provided, and the newborn's primary care provider should be informed about the refusal. A written objection statement is to be signed by the parents and placed in the newborn's medical record.

Newborns Born Outside State of Mother's Residence

- Any newborn born in Illinois will have an Illinois newborn screening specimen submitted regardless of the mother's state of residence.

- Illinois residents whose newborns are born in other states may obtain newborn screening through the Department's Newborn Screening Laboratory. The physician should obtain the

Department's filter paper specimen forms or order the screening test through an Illinois birthing facility. If an initial screening was performed in another state, a second newborn screening specimen may be submitted to the Department. Specimens should be collected and submitted as soon as possible after 24 hours of age. Newborn screening of newborns older than 6 months of age is not recommended as the Department's values are based on normal analytes, distributions and controls for newborns. If you have questions about screening an older newborn, contact the Newborn Screening Follow-up Program at 217-785-8101

- Newborns born in Illinois whose mothers reside in another state must have a specimen sent to the Department's Newborn Screening Laboratory.

Collection of Newborn Screening Specimens

Filter Paper Collection Form

- Only Department filter paper specimen collection forms are accepted by the Department's Newborn Screening Laboratory. The U.S. Food and Drug Administration now requires printed expiration dates on specimen cards, and health care providers are advised to check the card prior to specimen collection.

- Newborn screening filter paper specimen collection forms may be requested by contacting the Department's Division of Laboratories Springfield office, 217-524-6222, or by faxing a request with appropriate contact information to 217-558-3476.

- Filter paper specimen cards should be stored in a cool, dry location out of direct sunlight. Cards should be stored in their original wrappings and stacked in a manner that avoids compressing the paper. When properly stored, specimen cards have a shelf life of approximately two years. Each card has a printed expiration date and once expired, the specimen cannot be considered valid. When expired cards are received, although testing is performed, the Department must issue a report requesting submission of a new sample for a valid screening.

- Birth history and identifying information requested on specimen collection forms should be complete, legible and written in black ink only. Accurate personal health information is necessary for valid and reliable test results.

- Current personal contact information is needed for identifying the newborn and contacting the parents, should abnormalities be detected in the blood sample.

Timing of Specimen Collection

- Newborn screening specimen collection from healthy newborns should occur as soon as possible after 24 hours of age, preferably within the first 24-48 hours of life. Specimens should <u>not</u> be collected prior to 24 hours of age, except in special circumstances.

- Special circumstances

    - Early discharge: If the newborn is to be discharged at less than 24 hours of age, collect specimen prior to discharge. The attending physician, or designee, shall collect a second blood specimen for testing between 48-72 hours of age. Inform parents the newborn must be rescreened during the second day of life.
    - Transfers: If the newborn requires transfer to another facility, if at all possible, a specimen should be collected prior to transfer, regardless of newborn's age. If a specimen cannot be collected prior to transfer due to the medical instability of the neonate, the transferring facility is responsible for informing the admitting facility of the need for specimen collection prior to transfusion and/or within first 24-48 hours of life.
    - Newborns born outside of hospital/medical facilities: These newborns should have a specimen collected at 24-48 hours.

- If a specimen is collected prior to 24 hours of age, repeat specimen collection is

necessary as soon as possible during the second day of life.

- Preterm, Low Birth Weight, and Sick Newborns: Any newborn admitted to the neonatal intensive care unit (NICU), special care newborn unit (SCBU), newborn's who are younger than 34 weeks' gestation and/or < 2,000 grams

    - Newborns admitted to a NICU or SCBU should have a blood specimen collected regardless of age, medical condition or feeding status upon admission.
    - A second specimen shall be collected between 48-72 hours of age.
    - A third specimen shall be collected at 28 days of age or prior to discharge from the NICU or SCBU, whichever situation precedes.
    - The "NICU" check box on the specimen card should be marked on specimens from all newborns admitted to a NICU or SCBU.
    - The "Retest" check box should be marked for all repeat specimens.

- Special feedings: Newborns requiring soy formula, hyperalimentation or total parenteral nutrition (TPN), and those not yet receiving milk (galactose) feedings at the time of specimen collection require documentation of feeding type or status on the specimen card.
    - The feeding type check box should be clearly marked for "Breast," "Soy," "TPN," "Carnitine," "NPO" (nothing by mouth) or "Other." This information is important to newborn screening laboratory staff and the newborn's physician should an abnormality be detected.
    - Soy formula or lack of milk feeding **may affect** screening for galactosemia.
    - Hyperalimentation and TPN **may affect** tandem mass spectrometry screening for some amino acid, fatty acid oxidation and organic acid disorders.

        - If screening results suggest TPN effects, another specimen is requested when the newborn has been off TPN for 48 hours or on day 28 of life if the newborn was admitted to NICU or SCBU.

- Antibiotics: When newborns are receiving antibiotics at the time of specimen collection, the "Antibiotic" check box on the specimen collection card should be marked, as the presence of antibiotics and some other medication metabolites (valproic and benzoic acids) may be detected by tandem mass spectrometry. In these cases, a repeat sample will be requested.

- Transfusions: If at all possible, collect an initial specimen prior to transfusion regardless of the newborn's age. If this is not possible and the newborn was transfused prior to specimen collection, indicate the last transfusion date prior to the specimen collection on the filter paper collection form.

    - Transfusions **may affect** screening for classical galactosemia, biotinidase deficiency, hemoglobinopathies and lysosomal storage disorders.
    - If the newborn's **initial specimen** was collected post-transfusion, a second specimen should be collected 48-72 hours post-transfusion, and a third specimen is required 120 days after the final transfusion.
    - If the newborn has multiple blood transfusions after birth, a newborn screening specimen should be collected at 48-72 hours of age regardless of timing of last blood transfusion.

Tips for Specimen Collection

- Electronic copies of the newborn screening specimen collection posters "Neonatal Screening: Blood Specimen Collection and Handling Procedure" and "Simple Spot Check" are available for download and printing through the Department's Genetics/Newborn Screening Program, or for purchase through the Clinical Laboratory Standards Institute (CLSI) at http://www.clsi.org/edu/education-resources/companion-products/

- A copy of the Clinical Laboratory Standards Institute (CLSI) document, "Blood Collection on Filter Paper for Neonatal Screening Programs; Approved Standard" (NBS01-A6) can be purchased at http://shopping.netsuite.com/s.nl/c.1253739/it.A/id.1659/.f?sc=7&category=8514.

- Heel stick is the preferred mode of collection for newborn screening whenever possible.

    - After the heel has been punctured, wipe away the first drop of blood with a sterile gauge pad or cotton ball and allow a large drop of blood to form.
    - Touch the filter paper gently against the large blood drop and allow a sufficient quantity of blood to soak through and completely fill preprinted circle on the filter paper.
    - Do <u>not</u> press the filter paper against the puncture site on the heel.
    - Blood should be applied only to one side of the filter paper.
    - Excessive squeezing of the puncture site may cause hemolysis of the specimen or result in an admixture of tissue fluids with the specimen adversely affecting the test result.
    - Do not apply layers of successive blood drops to already partially dried blood spots. This causes nonuniform analyte concentrations and invalidates the specimens.

- Collection of specimens in capillary tubes is not the method of choice but can be used as a mode of collection.

    - Specimens can be obtained by applying blood collected in sterile heparinized capillary tubes to the collection device.
    - Use a fresh capillary tube for each circle to be filled on the screening card.
    - Immediately apply blood in the tube to the center of a single, preprinted circle on the filter paper, completely filling the circle.
    - The capillary tube should not come in contact with the filter paper.
    - Apply blood to only one side of the filter paper.
    - Do not apply layers of successive blood drops to already partially dried blood spots. This causes non-uniform analyte concentrations and invalidates the specimens.

- If a heel stick is not possible, umbilical catheters may be used to obtain blood for newborn screening, provided the line is cleared of IV fluids, heparin, antibiotics and other extraneous substances.

- Blood should not be drawn from an extremity into which IV fluids are being or have been infused.

- Although not the method of choice, blood collected from a venous needle puncture and its application directly onto the preprinted circles of the filter paper is possible. Proper procedure of venous collection:

    - After blood is drawn, remove the needle from the syringe and apply the blood to the center of each preprinted circle on the filter paper, completely filling each circle.
    - The syringe should not come in contact with the filter paper.
    - Apply blood to only one side of the filter paper.
    - Do not apply layers of successive blood drops to already partially dried blood spots. This causes non-uniform analyte concentrations and invalidates the specimen.

- The routine practice of venous collection is discouraged for the following reasons:

    - Test results may be affected by blood from different vessel sources.
    - Veins might be needed for IV fluids.
    - Venous sampling is more invasive than a heel stick puncture.

Collection of Repeat Specimens

- Repeat screening is requested by the Department when results of the original specimen were borderline abnormal, the specimen was declared unsatisfactory for testing, or the specimen was declared invalid due to delayed submission or incomplete information on the specimen card.

- Routine repeat screening also is required for all newborns admitted to the NICU or SCBU. See Section “Preterm, Low Birth Weight, and Sick Newborns.” Submitters should mark the “Retest” box on the specimen card.

- Submitters should provide adequate information to allow matching of any retest specimens to the newborn’s original newborn screening record. All known names of the newborn (beginning with the birth name), the mother’s full name, date of birth and the newborn’s medical record number will greatly assist Newborn Screening Program staff in matching the specimens.

Handling and Submission of Newborn Screening Specimens

Submitting Specimens

- It is recommended that newborn screening specimen collection forms be air dried for a minimum of three to four hours and submitted to the Department laboratory for testing **within 24 hours of collection** using a courier service.

- Newborn screening disorders are serious and can be life threatening, therefore early detection and treatment is vital. Failure to submit specimens promptly may unnecessarily delay detection and treatment of affected newborns. Batching of specimens from multiple collection days is **unacceptable**.

- Illinois birthing facilities may utilize the Department supported courier service for pickup of newborn screening specimens and shipment to the Department's Chicago laboratory.

Timeliness

- Specimens should be submitted to the Department's Division of Laboratories on a daily basis, during regular business days Monday through Friday. Saturday courier service pickup of specimens for next business day delivery also is available to birthing facilities, but must be requested in advance and arranged directly with the courier service.

- Tracking courier service delivery of specimens to the Department's Chicago laboratory is the **responsibility of birthing facilities**. It is recommended that birthing facilities keep a log of their courier tracking numbers, along with the newborn screening specimen medical record numbers. Contact the Newborn Screening Program at 217-785-8101 for more information about tracking deliveries and reporting courier service problems.

- Reports on the timeliness of specimen delivery for each hospital submitting specimens to the Department are available through the Department's Newborn Screening Program's website at http://www.idph.state.il.us/HealthWellness/newborn_screening/index.htm.

Reporting of Screening Results

Normal Results

- Laboratory results are sent to the submitting facility or submitting agent when testing is completed. Auto faxing and HL7 messaging of results also are available to facilities.

Abnormal Results

- Newborn screening is not diagnostic. Abnormal screening results are designated by Department laboratory staff as "presumptive positive" results or "suspect borderline" results.

- **Presumptive positive results** indicate a high probability the newborn may have a disorder. The Department's Newborn Screening Program staff will recommend newborns with presumptive positive screening be referred to medical specialists for consultation and/or diagnostic testing.

    - These results will be reported by telephone to the submitting physician or the submitting facility contact person, followed by a letter reporting the abnormal results and recommendations (sent by fax and mail).
    - A complete laboratory report (mailer) of all results will be sent to the submitting facility or submitting agent by the Department's Chicago laboratory for every specimen received.

- **Suspect borderline results** indicate the screening is slightly abnormal and the newborn needs a medical evaluation and a repeat newborn screen. If the newborn has any symptoms of a disorder, referral to a medical specialist for diagnostic testing is indicated.

    - These results will be reported by letter indicating abnormal results and recommendations to the submitting physician or facility contact person.
    - A complete laboratory report (mailer) of all results also will be sent to the submitting facility or submitting agent for each specimen received.

Unsatisfactory Specimens

- Unsatisfactory specimen reports indicate the test results may be invalid due to improper collection, handling, submission or other factors as determined by the Department's Division of Laboratories. Specimens must be of good quality to assure reliable, valid newborn screening; unsatisfactory specimens require collection and submission of a new sample to assure every newborn receives a valid newborn screening.

    - These results are reported by letter indicating the unsatisfactory nature of the specimen and the need for immediate repeat specimen collection to the submitting physician or submitting facility contact person.

    - The number of unsatisfactory specimen results also is included in the Department's submission timelines report posted on the Department's Newborn Screening website at http://www.idph.state.il.us/HealthWellness/newborn_screening/index.htm.

Referrals to Pediatric Medical Specialists and Other Agencies

Pediatric Medical Specialists

- A list of Department designated pediatric medical specialists is included with each presumptive positive result (those indicating need for referral to a medical specialist).

- Newborns with family history of a disorder or those who appear symptomatic, require consultation with a pediatric medical specialist regardless of newborn screening results or Department recommendations suggested on the report.

Services for Newborns with Sickle Cell Disease and Other Hemoglobin Disorders

- Family education, genetic counseling and diagnostic services are available to families of newborns with sickle cell disease, other hemoglobinopathies and those heterozygote for a hemoglobin disorder trait (carrier).

    - The Department, through grants to pediatric hematology centers, provides diagnostic and treatment services for newborns and children identified with sickling hemoglobin disorders or traits.
    - Additional services for newborns, children and adults with thalassemia disorders are available through Chicago's Ann & Robert H. Lurie Children's Hospital Comprehensive Hemoglobinopathies Program, Division of Hematology, Oncology and Stem Cell Transplant. Call 312-227-4817 for more information about these services.
    - In addition, the Department has joined with the Sickle Cell Disease Association of Illinois (SCDAI) to provide educational services to families of individuals with various types of sickle cell disease or trait. Call 773-526-5016 or visit the SCDAI website at www.scdai.com to learn more about its services.

University of Illinois at Chicago, Division of Specialized Care for Children (DSCC)

- DSCC provides payment for the initial diagnostic services for newborns with certain abnormal metabolic newborn screening results provided these services are coordinated by specialists jointly approved by the Department and DSCC. The specific disorders for which these services are available are determined by DSCC.

    - DSCC provides these services in conjunction with other third-party payers and remains the payer of last resort.
    - DSCC covers the ongoing medical care for newborns and children diagnosed with certain metabolic disorders, and in those cases in which the family meets certain eligibility requirements.
    - DSCC may be able to provide families with transportation services for medical evaluation.
    - DSCC provides care coordination services through a medical home approach for children with special health care needs.

Local Public Health Departments

- The Department works in cooperation with local public health departments to provide follow-up services to the families of newborns with abnormal newborn screening test

results and newborns diagnosed with newborn screening disorders. In some cases, the assistance of a local public health nurse may be requested in order to locate and to help the family obtain necessary follow-up services.

- The Department's Newborn Screening Program staff and/or the newborn's pediatrician may have difficulty locating the families of newborns with abnormal test results, or parents may not understand the importance of seeking additional medical care.
- Following the diagnosis of a disorder identified through newborn screening, the pediatric medical specialist may recommend community support services for the families of children with these serious disorders.
- As families relocate or change medical care providers, the medical specialist may lose contact with the parents of children diagnosed with a disorder identified through newborn screening. The assistance of a local health department public health nurse may be requested to locate these families and to assure continuity of long-term care for the children.
- A list of local public health department contacts may be requested by calling 217-785-8101.

Newborn Screening Disorders

Amino Acid/Urea Cycle Disorders

Amino Acid disorders are inherited as autosomal recessive defects of amino acid metabolism. Each amino acid disorder is associated with a specific enzyme defect. Affected newborns cannot properly metabolize certain amino acids, resulting in elevated levels of the amino acid or metabolites in body fluids. Accumulation of some amino acids or metabolites may become neurotoxic, causing damage to organs and resulting in developmental delays, mental retardation or death. Clinical findings may include poor feeding, vomiting, lethargy or irritability, seizures, coma, respiratory distress and liver damage.

Urea cycle disorders involve metabolic defects in the breakdown of proteins and the conversion of ammonia and bicarbonate to urea for elimination of waste nitrogen. The resulting accumulation of ammonia in blood and tissues is neurotoxic and requires immediate detection and medical intervention. Urea cycle disorders may result in severe hyperammonemia. Newborns with this condition require prompt medical intervention that may include hemodialysis.

See the Department's website for newborn screening fact sheets with additional information about urea cycle disorders (http://www.idph.state.il.us/HealthWellness/newborn_screening/index.htm) and visit the American College of Medical Genetics website to review the ACMG "ACT" sheets.

In Illinois, newborn screening includes screening for the following amino acid disorders:

- 5-oxoprolinuria
- Homocystinuria
- Maple syrup urine disease (MSUD)
- Phenylalanine hydroxylase deficiency [also see section on Phenylketonuria (PKU)]
    - Tyrosinemia type 1, and possibly types 2 and 3. Newborn screening may not detect all cases of tyrosinemia as tyrosine levels may not increase to detectable levels until after the fifth day of life.
- Urea cycle disorders: Citrullinemia, Argininosuccinic aciduria and Argininemia

Incidence

- **5-oxoprolinuria** - extremely rare, actual incidence unknown
- **Homocystinuria** - 1 in 200,000 births
- **MSUD** - 1 in 200,000 births
- **Phenylalanine hydroxylase deficiency, including Phenylketonuria (PKU)** – 1 in 10,000 births
- **Tyrosinemia** - 1 in 500,000 births (1 in 12,500 births among French Canadian populations)
- **Urea Cycle Disorders** - 1 in 200,000 to 300,000 births

Analytes Measured in Screening

Measurement of specific analytes by tandem mass spectrometry (MS/MS) are reported in micro-Moles/Liter (uM/L).

Analytes Measured in Screening	Possible Disorder
5-oxoproline	5-oxorolinuria (5Oxp)
Arginine	Argininemia
Citrulline	Citrullinemia or Argininosuccinic aciduria
(Iso)leucine and Valine	Maple syrup urine disease (MSUD)
Methionine	Homocystinuria
Tyrosine	Tyrosinemia

Additional abnormal amino acid levels may be reported if secondary analytes are detected by tandem mass spectrometry; if so, referral to a pediatric metabolic specialist is recommended. These abnormalities may include:

- Elevated Glycine – indicative of non-ketotic hyperglycinemia
- Elevated Ornithine and elevated Citrulline – indicative of hyperammonemia/ ornithinemia/citrullinemia (HHH)
- Low Citrulline – indicative of ornithine transcarbamylase deficiency
- Low Citrulline/elevated Glutamine –indicative of carbamoylphosphate synthetase deficiency

Reporting Ranges with Respective Follow-up Referrals and Testing

Reporting Ranges	Follow-up Referrals and Testing
Presumptive Positive	Immediate referral to pediatric metabolic disease specialist for diagnostic testing.
Suspect Borderline	Medical evaluation and repeat newborn screening specimen within one to two days; mark “Retest” box on specimen card. If retest remains abnormal, refer to pediatric metabolic disease specialist.
Suspect Amino Acid Abnormal due to TPN (reported by fax and letter)	If newborn is still in NICU or on TPN, repeat newborn screen 48 hours after TPN is discontinued, at day 28 of life or prior to discharge, whichever comes first. If newborn has been discharged from hospital or was not on TPN at time of specimen collection, repeat newborn screen within one to two days. If retest remains abnormal, refer to metabolic specialist.

Additional Information	Follow-up Referrals and Testing
Feeding Effect	Hyperalimentation and TPN may affect results. Unless otherwise instructed, repeat specimens are best collected 48 hours after TPN is discontinued.
Transfusion Effect	Specimen collection prior to transfusion is always recommended. If newborn’s initial specimen was collected post-transfusion, a second specimen should be collected 48-72 hours post-transfusion, and a third specimen is required 120 days after the final transfusion.
Timing Effect	If specimen is collected less than 24 hours of age, submit second sample at 48-72 hours of life.
Specialist	Disease specialist that meets qualification listed in administrative code for newborn metabolic screening and treatment.

Additional Information	Follow-up Referrals and Testing
Treatment	Treatment is disorder specific and may include specialized prescription medical formula, special diet limited in specific proteins and, in some cases, supplements and medications. The Department provides prescription metabolic treatment formula without charge to Illinois residents who are under comprehensive medical management by a metabolic disease specialist designated by the Department/DSCC. Patients must remain under the care of a Department metabolic disease specialist in order to receive formula provided by the state.

All presumptive positive and suspect borderline results are reported by phone, letter, and fax to physician of record or hospital contact, unless otherwise specified.

For questions about the most current laboratory reporting values for these disorders, contact the Department's Division of Laboratories at 312-793-4752.

Biotinidase Deficiency

Biotinidase deficiency is an autosomal recessive disorder of biotin recycling that leads to multiple carboxylase deficiency. Individuals with biotinidase deficiency cannot recycle biotin (vitamin B) and cannot process dietary protein-bound biotin. Early detection and treatment is essential to prevent permanent neurological damage, seizures, hypotonia, respiratory problem, hearing loss and visual problems.

See the Department's website, www.idph.state.il.us/HealthWellness/newborn_screening/index.htm, for newborn screening fact sheets with additional information about this disorder and visit the American College of Medical Genetics website to review the ACMG "ACT" sheets.

Incidence

- 1 in 180,000 births

Analyte Measured in Screening

Biotinidase enzyme activity is determined by colorimetric analysis.

Reporting Ranges with Respective Follow-up Referrals and Testing

Reporting Ranges	Follow-up Referrals and Testing
Biotinidase activity absent	Medical evaluation and repeat newborn screening specimen within one to two days; mark "Retest" box on specimen card. If retest sample does not have detectable biotinidase activity, referral to pediatric metabolic disease specialist for diagnostic testing.

Additional Information	Follow-up Referrals and Testing
Feeding Effect	None
Transfusion Effect	Transfusions may have long-term effects due to biotinidase activity of transfused red blood cells and may result in false negative screens for biotinidase deficiency. Specimen collection prior to transfusion is always recommended. If newborn's initial specimen was collected post-transfusion, a second specimen should be collected 48-72 hours post-transfusion, and a third specimen is required 120 days after the final transfusion.
Timing Effect	If specimen is collected less than 24 hours of age, submit second sample at 48 hours of life.
Specialist	Disease specialist that meets qualification listed in administrative code for newborn metabolic screening and treatment.
Treatment	Daily prescription dosage of biotin supplement.

All abnormal results are reported by phone, letter and fax to physician of record or hospital contact. Improper collection and care of specimens may cause biotinidase enzyme degradation. Exposure of

specimens to excessive heat and/or delayed submission may result in false positive screening results. For questions about the most current laboratory reporting values for these disorders, contact the Department's Division of Laboratories at 312-793-4752.

Congenital Adrenal Hyperplasia

Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder of steroid hormone synthesis. Ninety percent of individuals with CAH cannot produce adequate amounts of the enzyme 21-hydroxylase, which is necessary for synthesis of cortisol. In Illinois, newborn screening includes testing for CAH due to 21-hydroxylase deficiency. In 50-75 percent of 21-hydroxylase deficiency cases, in addition to cortisol deficiency, the newborn cannot synthesize adequate amounts of aldosterone, resulting in salt-wasting CAH. In utero, the developing fetus with CAH is exposed to excessive levels of androgen, and female newborns may have varying degrees of virilization of external genitalia. Male newborns usually appear normal at birth. Both males and females are susceptible to acute adrenal insufficiency. Newborns with salt-wasting CAH are susceptible to electrolyte imbalance and dehydration. Early detection and treatment of CAH is essential to prevent adrenal crisis, dehydration and sudden death in the first few weeks of life.

See the Department's website, www.idph.state.il.us/HealthWellness/newborn_screening/index.htm, for newborn screening fact sheets with additional information about this disorder and visit the American College of Medical Genetics website to review the ACMG "ACT" sheets.

Incidence

- 1 in 20,000 births

Analyte Measured in Screening

17-Hydroxyprogesterone (17-OHP) level is measured by fluorometric assay, reported in nanograms per milliliter (ng/mL). Reference laboratories may use different units of measurement.

Due to the effects of prematurity and physiological stress on 17-OHP levels, a tiered system of reporting abnormal results has been developed based on birth weight and/or gestational age of newborns.

- **Pre-term** is defined as gestational age less than or equal to 36 weeks.
- **Low birth weight** is defined as birth weight less than 2,000 grams.
- **Very low birth weight** is defined as less than or equal to 1,500 grams.

Reporting Ranges with Respective Follow-up Referrals and Testing

Reporting Ranges	Follow-up Referrals and Testing
Presumptive Positive: Full-term newborn ≥ 55 ng/mL	Immediate referral to pediatric endocrinologist and serum electrolytes and 17-OHP.
Presumptive Positive: Pre-Term newborn/low birth weight ≥ 80 ng/mL	Referral/consultation with pediatric endocrinologist, evaluation of risk for CAH, serum electrolytes and 17-OHP or repeat newborn screen. If retest remains abnormal, refer to pediatric endocrinologist.
Suspect Borderline: Full-term newborn 30-54 ng/mL	Medical evaluation and repeat newborn screen within one to two days, unless newborn was admitted to NICU and will be tested at a later date. If retest remains abnormal, refer to pediatric endocrinologist.
Suspect Borderline: Pre-term newborn/low birth weight 55-79 ng/mL	Medical evaluation and repeat newborn screen within one to two days, unless newborn was admitted to NICU and will be tested at a later date. If retest remains abnormal, refer to pediatric endocrinologist.

Additional Information	Follow-up Referrals and Testing
Feeding Effect	None
Transfusion Effect	Specimen collection prior to transfusion is always recommended. If newborn's initial specimen was collected post-transfusion, a second specimen should be collected 48-72 hours post-transfusion, and a third specimen is required 120 days after the final transfusion.
Timing Effect	If specimen is collected less than 24 hours of age, submit second sample at 48-72 hours of life.
Specialist	Disease specialist that meets qualification listed in administrative code for newborn metabolic screening and treatment.
Treatment: Simple virilizing CAH	Daily cortisol replacement therapy.
Treatment: Salt-wasting CAH	Daily cortisol and aldosterone replacement therapy, dietary salt supplements.

All presumptive positive results are reported by phone, letter and fax to the physician of record or hospital contact, with suspect borderline results reported by letter only.

Laboratory reporting cut-off values are procedure dependent and are subject to periodic revision. For questions about the most current laboratory cut-off values for this disorder, contact the Department's Division of Laboratories at 312-793-4752.

Note: While neonates in the NICU with abnormal CAH screens need additional testing to rule out CAH, the neonatologist may use discretion monitoring in these cases. Administrative rules for newborn screening require newborns admitted to a NICU or SCBU should have a newborn screening specimen collected regardless of age, medical condition or feeding status on admission. A second specimen shall be collected between 48-72 hours of age. A third specimen shall be collected at 28 days of age or prior to discharge from the NICU or SCBU, whichever situation precedes.

Comments

Factors, such as specimen collection prior to 24 hours of age, prematurity, low birth weight and illness, may cause elevation of 17-OHP levels. However, follow-up screening and/or diagnostic testing are necessary to rule out this life-threatening disorder.

Newborns with symptoms of vomiting, dehydration, weight loss, poor feeding, electrolyte imbalance and/or lethargy, require immediate medical attention, emergency care and referral to a pediatric endocrinologist.

Treatment with glucocorticoids (cortisone, dexamethasone) may cause false negative results.

Congenital Hypothyroidism

Congenital hypothyroidism results from an inability of the thyroid gland to produce adequate amounts of the hormone, thyroxine, that is essential for healthy growth and development. Congenital hypothyroidism is usually due to a failure of the thyroid gland to develop properly in utero. Less frequently, the disorder can result from an autosomal recessive defect in thyroid hormone synthesis. Primary congenital hypothyroidism usually requires lifetime treatment. Occasionally, cases of transient hypothyroidism occur as a result of maternal anti-thyroid medications or temporary thyroid suppression in the newborn due to exposure to iodine, prematurity or other causes. If left untreated, congenital hypothyroidism can cause sluggishness, slow growth and learning delays. Consultation with a pediatric endocrinologist is usually recommended in these cases.

See the Department's website, www.idph.state.il.us/HealthWellness/newborn_screening/index.htm, for newborn screening fact sheets with additional information about this disorder and visit the American College of Medical Genetics website to review the ACMG "ACT" sheets.

Incidence

- 1 in 2,000 births

Analytes Measured in Screening

Thyroid stimulating hormone (TSH) and thyroxine (T4). Specimens in the top 3.0 percent of the initial TSH run are repeated in duplicate and a T4 test is run in duplicate. The average of the duplicate values for TSH and T4 are used to report results.

Reporting Ranges with Respective Follow-up Referrals and Testing

Reporting Ranges	Follow-up Referrals and Testing
Presumptive Positive: [TSH] ≥ 54.0 uIU/mL serum and/or [T4] < 5.0 ug/dL serum TSH and free T4	Immediate referral to pediatric endocrinologist and serum TSH and free T4.
Suspect Borderline: Specimens that have a [T4] level ≥ 5.0 ug/dL and < 8.0 ug/dL and [TSH] < 54.0 uIU/mL. Specimens with a repeat TSH value in the top 0.5 percent for the specimens received for an accession day and [TSH] < 54.0 uIU/mL. Specimens not in the top 0.5 percent, but have a TSH level ≥ 36.0 uIU/mL and < 54.0 uIU/mL.	Medical evaluation and repeat newborn screen within one to two days; mark "Retest" on specimen card. If retest remains abnormal, refer to pediatric endocrinologist.

Additional Information	Follow-up Referrals and Testing
Feeding Effect	None
Transfusion Effect	Specimen collection prior to transfusion is always recommended. If newborn's initial specimen was collected post-transfusion, a second specimen should be collected 48-72 hours post-transfusion, and a third specimen is required 120 days after the final transfusion.
Timing Effect	If specimen is collected less than 24 hours of age, submit second sample at 48-72 hours of life. TSH increases dramatically in first few hours after birth and gradually returns to normal levels in about 72 hours. This normal TSH elevation will be detected if the specimen is collected before the newborn is 24 hours of age. In pre-term newborns, production of TSH may be delayed in the first few days of life.
Specialist	Disease specialist that meets qualification listed in administrative code for newborn metabolic screening and treatment.
Treatment	Daily thyroid supplement.

All presumptive positive results are reported by phone, letter and fax to the physician of record or hospital contact, with suspect borderline results reported by letter only. Laboratory reporting cut-off values are procedure dependent and are subject to periodic revision.

For questions about the most current laboratory cut-off values for this disorder, contact the Department's Division of Laboratories at 312-793-4752.

Comments

Regardless of newborn screening results:

- Very low birth weight newborns and newborns with cardiac defects, congenital craniofacial anomalies and Down syndrome may be at increased risk of late onset hypothyroidism, and consult with pediatric endocrinology and/or diagnostic testing is advisable regardless of newborn screening results.

- Although newborn screening can detect congenital hypothyroidism with a high degree of accuracy, other forms of hypothyroidism may develop within the first few weeks of life. Therefore, the physician must remain alert to clinical symptoms in older newborns despite normal newborn screening results. Repeat the screening or refer to a pediatric endocrinologist if any suspicions exist about possible hypothyroidism, regardless of newborn screening results.

- Family history of thyroid disorders may indicate the need for diagnostic testing or pediatric endocrinology consult regardless of newborn screening results.

Critical Congenital Heart Disease

Critical congenital heart disease (CCHD) is a term that refers to a group of life-threatening structural cardiac defects that are present at birth. These abnormalities result from malformation of one or more parts of the heart during the early stages of embryonic development. CCHD prevents the heart from pumping blood effectively or reduces the amount of oxygenated blood. As a result, organs and tissues throughout the body do not receive enough oxygen, which can lead to organ damage and life-threatening complications. CCHDs account for nearly 30 percent of infant deaths due to birth defects and, out of these, 3 percent of infants die in the first year of life. The seven heart defects included in CCHD screening are hypoplastic left heart syndrome, pulmonary atresia (with intact septum), tetralogy of Fallot, total anomalous pulmonary venous return, transposition of the great arteries, tricuspid atresia and truncus arteriosus.

CCHD can be detected using pulse oximetry screening. Newborns with cardiac defects can appear healthy at birth, but can deteriorate rapidly or die. These newborns are at risk of having serious complications within the first few days or weeks of life and often require emergency care and surgery.

Incidence

- 18 per 10,000 births per year

Analyte Measured in Screening

Blood saturation levels are measured using pulse oximetry.

Preductal and Postductal

- Preductal – relating to the part of the aorta proximal to the aortic opening of the ductus arteriosus. Pulse oximeter should be used on the right hand.
- Postductal – relating to that part of the aorta distal to the aortic opening of the ductus arteriosus. Pulse oximeter should be used on either foot.

Reporting Ranges with Respective Follow-up and Referrals

Refer to the CCHD pulse oximetry screening algorithm chart on page 30.

Reporting Ranges	Follow-up Referrals and Testing
Positive	If a positive screening is identified, the newborn should be evaluated by a physician and receive an echocardiogram prior to hospital discharge in accordance with the national guidelines.

Additional Information	Follow-up Referrals and Testing
Feeding Effect	None
Transfusion Effect	None
Timing Effect	Newborns should receive a pulse oximetry screening after 24 hours of age or before discharge from the hospital. This includes newborn in the NICU who are stable and preparing for discharge. The only newborns who shall be excluded are those with a prenatal diagnosis of a cardiac defect or newborns who have already had a complete postnatal echocardiogram performed.
Specialist	Pediatric cardiologist.
Treatment	Treatment is defect specific. Most heart defects can be corrected or improved with surgery, procedures and/or medications.

Procedure Regarding Pulse Oximetry Screening

A. Identify newborn readiness for pulse oximetry screening

1. 24 hours of age or greater (can be done < 24 hours of age, if the newborn is being discharged)
2. Vital signs within normal limits
3. On room-air

B. Preparation for screening

1. Provide parent(s) with educational material related to pulse oximetry screening and CCHD.
2. A quiet environment is ideal. Testing may be done in the nursery or patient room. Parent(s) may be present.
3. It is preferred that the newborn is awake, alert, but quiet during the test. Calm the newborn, if possible.
4. Do not test on an actively crying newborn or on a cold stressed newborn.
5. Bright lights and bilirubin lights should be turned off prior to screening.

C. Application of pulse oximeter probe

1. Pulse oximeter screenings should be both a preductal and postductal reading.
2. Do not apply pulse oximeter probe to the same extremity with a blood pressure cuff.
3. Assure the limb is clean and dry.
4. Apply the pulse oximeter probe to the newborn's right hand (preductal) and either foot (postductal).
5. Assure there are no gaps between the sensor and the newborn's skin. Sides of the probe should be directly opposite each other.
6. Screening may be done simultaneously on both extremities or in direct sequence.
7. Apply the probe first to the newborn and then connect to the oximeter to facilitate a more reliable and quick reading.

Recommendations

Contact newborn's primary care provider if the newborn fails the pulse oximetry screening. A newborn with oxygen saturation < 90 percent requires immediate clinical assessment. Evaluate for infections and/or pulmonary causes for low oxygen saturations. Arrange for an echocardiogram, if no other cause for low oxygen saturation is found. Refer to pediatric cardiologist for clinical management of newborn.

If an echocardiogram cannot be performed at the hospital where the positive screen is identified, the newborn may need to be transferred to the nearest facility with echocardiogram capabilities.

The echocardiogram should be performed by a sonographer and read by a pediatric cardiologist. If a pediatric cardiologist is not available, the hospital should work through their perinatal network to utilize telemedicine or identify an appropriate cardiologist to read the echocardiogram.

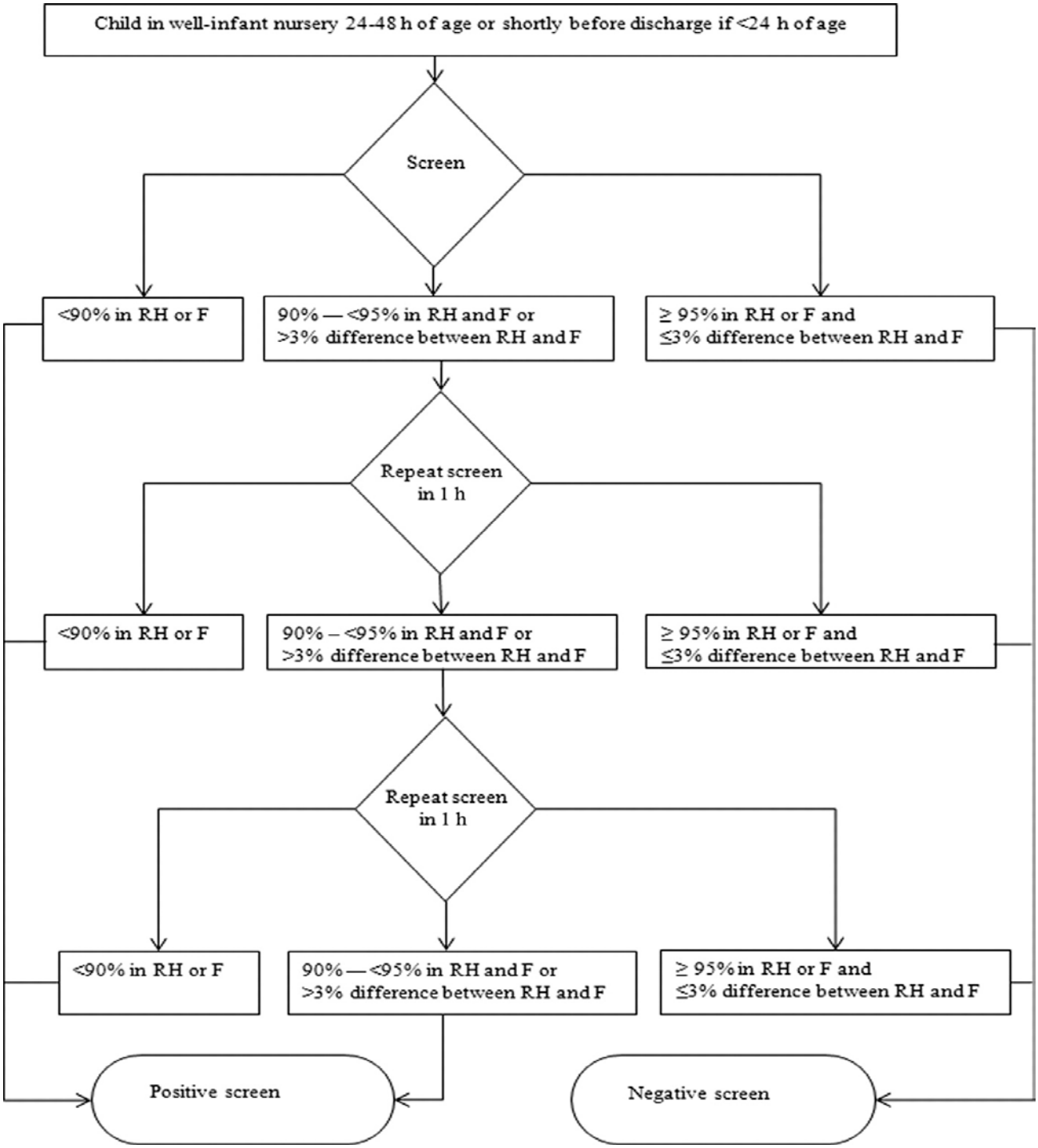
Comments

Newborns should receive a pulse oximetry screening after 24 hours of age or before discharge from the hospital. This includes NICU newborns who are stable and preparing for discharge.

The only newborns excluded should be those newborns with a prenatal diagnosis of a cardiac defect or newborns who have already had a complete postnatal echocardiogram performed.

ILLINOIS DEPARTMENT OF PUBLIC HEALTH
PULSE OXIMETRY SCREENING ALGORITHM

IDPH recommends screening for all newborns, including newborns in the neonatal intensive care unit (NICU) who are stable and preparing for discharge.



The proposed pulse-oximetry monitoring protocol based on results from the right hand (RH) and either foot (F).

Cystic Fibrosis

Cystic fibrosis (CF) is an autosomal recessive disorder that results in production of a defective form of cystic fibrosis transmembrane conductance regulator (CFTR) protein. CFTR protein is an important chloride channel within epithelial cells of multiple organs, and regulates movement of salt and water into and out of the cells. In individuals with CF, the cells lining passageways of the lungs, pancreas and other organs produce thick, sticky mucus. Clinical signs and disease progression vary among affected individuals, but may include progressive lung disease, pancreatic insufficiency, male infertility and elevated sweat chloride levels. Early detection and diagnosis with adequate nutritional support and aggressive therapies to reduce risks of respiratory exacerbations have been shown to improve clinical outcomes.

See the Department website, www.idph.state.il.us/HealthWellness/newborn_screening/index.htm, for newborn screening fact sheets with additional information about this disorder and visit the American College of Medical Genetics website to review the ACMG "ACT" sheet.

Incidence

- **Cystic fibrosis -** in 1 in 3,200 Caucasian births, but also occurs in all races and ethnic groups.

Analyte Measured in Screening

Measurement of immunoreactive trypsinogen (IRT) level by fluorometric assay reported as nanograms per milliliter (ng/mL). If the IRT is in the top 4 percentile for the day, DNA mutation analysis for a panel of CFTR mutations also is performed.

Reporting Ranges with Respective Follow-up Referrals and Testing

Reporting Ranges	Follow-up Referrals and Testing
Presumptive Positive: IRT in top 4 percentile for the day, two CFTR mutations IRT in top 4 percentile for the day, one CFTR mutation IRT ≥ 170 ng/mL	Immediate referral to CF specialist. All newborns with abnormal CF newborn screening results should be referred to a CF specialist for confirmatory pilocarpine iontophoresis sweat testing and genetic counseling services. Sweat testing for newborns should only be performed under the direction of a CF specialist at laboratories in compliance with Clinical Laboratory Standards Institute (CLSI) guidelines.

Additional Information	Follow-up Referrals and Testing
Feeding Effect	None
Transfusion Effect	Specimen collection prior to transfusion is always recommended. If newborn's initial specimen was collected post-transfusion, a second specimen should be collected 48-72 hours post-transfusion, and a third specimen is required 120 days after the final transfusion.
Timing Effect	If specimen is collected less than 24 hours of age, submit second sample at 48-72 hours of life.
Treatment	Dietary and vitamin supplements, respiratory therapies and frequent visits for evaluation and support are usually provided.

Additional Information	Follow-up Referrals and Testing
Specialist	Disease specialist that meets qualification listed in administrative code for newborn metabolic screening and treatment.

All presumptive positive results are reported by phone, letter, and fax to physician of record or hospital contact. Laboratory reporting cut-off values are procedure dependent and are subject to periodic revision.

For questions about the most current laboratory cut-off values for this disorder, contact the Department's Division of Laboratories at 312-793-4752.

Comments

Meconium ileus has been clinically associated with the diagnosis of cystic fibrosis in newborns. Any newborn with this condition should have diagnostic evaluation through a CF specialist, regardless of the newborn screening results. In some cases, normal IRT levels causing false negative newborn screening results for CF have been reported in newborns with meconium ileus

If there is a family history of cystic fibrosis or reason to be suspect, the laboratory may be contacted to ensure DNA testing is performed on the newborn screening sample.

More than 1,000 mutations have been identified in the CF gene, and this screening includes only a fraction of them.

Fatty Acid Oxidation Disorders

Fatty acid oxidation (FAO) disorders are autosomal recessive inherited metabolic conditions. Each FAO disorder is associated with a specific enzyme defect in the fatty acid metabolic pathway, and affects utilization of dietary and stored fats. These disorders lead to an accumulation of fatty acids in the body, or an inability to break down dietary or stored fats, with a decrease in cell energy metabolism. Many of the FAO disorders cause a significant risk of death during the first clinical episode. In most cases, the first episode arises following illness or fasting, and occurs in infancy or early childhood. FAO disorders can cause recurrent episodes of hypoglycemia. Clinical findings may include lethargy, hypotonia, failure to thrive, persistent vomiting and hepatomegaly, rhabdomyolysis and Reye syndrome-like episodes. Significant disability may result from prolonged episodes of hypoglycemia.

See the Department's website, www.idph.state.il.us/HealthWellness/newborn_screening/index.htm, for newborn screening fact sheets with additional information about these disorders and visit the American College of Medical Genetics website to review the ACMG "ACT" sheets.

In Illinois, newborn screening includes testing for a panel of acylcarnitines. Following is a list of the FAO disorders that may be detected:

- Carnitine/acylcarnitine translocase deficiency (CACT)
- Carnitine palmitoyl transferase deficiency type 1 (CPT 1 or CPT 1A)
- Carnitine palmitoyl transferase deficiency type 2 (CPT 2)
- Carnitine uptake defect (CUD)
- Glutaric aciduria type 2 (GA 2)/Multiple acyl-CoA dehydrogenase deficiency (MADD)
- Isobutyryl-CoA dehydrogenase deficiency (IBCD)*. IBCD is categorized as an organic acid disorder in most reference materials.
- Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)
- Medium chain acyl-CoA dehydrogenase deficiency (MCADD)
- Medium/Short chain L-3-hydroxyacyl-CoA dehydrogenase deficiency (M/SCHAD)
- Short chain acyl-CoA dehydrogenase deficiency (SCADD)
- Trifunctional protein deficiency (TFP)
- Very long chain acyl-CoA dehydrogenase deficiency (VLCAD)

Incidence

- **LCHAD –** 1 in 400,000 births
- **MCADD –** 1 in 18,000 births
- **SCADD –** 1 in 20,000 births
- **VLCAD –** 1 in 100,000 births
- **Other Disorders –** 1 in 500,000 births

Analytes Measured in Screening

Specific acylcarnitines measured by tandem mass spectrometry (MS/MS), reported as micro-Moles per Liter (μM/L).

For substituted carnitines, a notation of (Cx) is used where (x) denotes the number of carbons in the fatty acid radical.

Free carnitine is designated as (C0), acetyl carnitine as (C2), and propanoyl carnitine as (C3).

Hydroxylation is designated by (-OH), dicarboxylic acid is designated by (-DC) and unsaturation is designated by (:1).

A particular acylcarnitine pattern, or group of abnormal acylcarnitines may be detected by MS/MS screening; while not diagnostic, these patterns may be suggestive of a certain type of fatty acid oxidation disorder.

Analytes Measured in Screening	Possible Disorder
Acylcarnitine 3-hydroxy-butyryl carnitine (C4-OH) is the primary analyte	M/SCHAD
Butanoyl carnitine (C4) is the primary analyte	SCADD/IBCD
Free carnitine (decreased level) is the primary analyte (C0 and C0/C16+C18 ratio decreased)	CUD
Free carnitine (elevated level) is the primary analyte (C0 and C0/C16+C18 ratio elevated)	CPT1/CPT1A
Multiple acylcarnitines (C4, C5, C8, C12, C14, C16 and C5-DC)	GA2/MADD
Multiple long chain acylcarnitines Hexadecanoyl carnitine (C16) or Octadecenoyl carnitine (C18:1) is the primary analyte (C16, C18:1 and C18:2)	CPT II/CACT
Multiple long chain acylcarnitines Hydroxy-hexadecanoyl carnitine (C16:OH) is the primary analyte (C16-OH, C16:10H, C18:1-OH)	LCHAD/TFPD
Multiple long chain acylcarnitines Tetradecenoyl carnitine (C14:1) is the primary analyte (C:14:1, C14 and C16)	VLCAD
Multiple medium chain acylcarnitines Octanoylcarnitine (C8) is the primary analyte (C8, C10, C10:1 and C6)	MCADD

Reporting Ranges with Respective Follow-up Referrals and Testing

Reporting Ranges	Follow-up Referrals and Testing
Presumptive Positive	Immediate referral to pediatric metabolic disease specialist.
Suspect Borderline	Medical evaluation and repeat newborn screen within one to two days; mark “Retest” on specimen card. If retest remains abnormal, refer to pediatric metabolic disease specialist.
Suspect Acylcarnitine Abnormal due to TPN (reported by fax and letter)	If newborn is still in NICU or on TPN, repeat newborn screen 48 hours after TPN is stopped, at day 28 of life or prior to discharge, whichever comes first. If newborn has been discharged from hospital or was not on TPN at time of specimen collection, repeat newborn screen within one to two days. If retest remains abnormal, refer to metabolic specialist.

Additional Information	Follow-up Referrals and Testing
Feeding Effect	Hyperalimentation, TPN and certain medications may affect results. Unless otherwise instructed, repeat specimens are best collected 48 hours after TPN is discontinued.
Transfusion Effect	Specimen collection prior to transfusion is always recommended. If newborn's initial specimen was collected post-transfusion, a second specimen should be collected 48-72 hours post-transfusion, and a third specimen is required 120 days after the final transfusion..
Timing Effect	If specimen is collected less than 24 hours of age, submit second sample at 48-72 hours of life. If repeat screening is requested, collect and submit new specimen within one to two days. If a repeat specimen cannot be collected quickly, you may need to refer the patient to a metabolic specialist. Acylcarnitine levels tend to normalize quickly in newborns once the newborn begins to feed well; specimen collection as soon as possible after 24 hours of age is optimal and repeat specimens must be collected quickly to avoid false negative results for FAO disorders.
Specialist	Disease specialist that meets qualification listed in administrative code for newborn metabolic screening and treatment.
Treatment	Treatment is disorder specific and usually includes frequent feeding and avoidance of fasting, high carbohydrate, low-fat diet and, in some cases, specialized medical formula, or supplements and medications. Special precautions, such as glucose monitoring, and, in some cases, intravenous therapy may be required during intercurrent illnesses. If indicated, the Department provides special, medically necessary formula without charge to Illinois residents who are under comprehensive medical management provided by a metabolic disease specialist designated by the Department.

All presumptive positive and suspect borderline results are reported by phone, letter, and fax to physician of record or hospital contact unless otherwise specified.

For questions about the most current laboratory reporting values for these disorders, contact the Department's Division of Laboratories at 312-793-4752.

Galactosemia

An autosomal recessive disorder of galactose metabolism, galactosemia is due to insufficient enzyme activity, usually of galactose-1-phosphate uridyl transferase (GALT) or, in some cases, deficiency of galactokinase or uridine diphosphate galactose-4-epimerase. In Illinois, newborn screening for galactosemia is designed to detect classical galactosemia due to GALT enzyme deficiency. Some variant forms of galactosemia, such as Duarte variant, epimerase deficiency (GALE) and kinase deficiency (GALK) also may be identified. These enzymes are necessary to convert galactose to glucose for energy and cellular growth. The main dietary source of galactose is lactose, the principle carbohydrate found in all forms of milk. Early detection and treatment of classical galactosemia is essential to prevent severe liver disease and complications, including bleeding, overwhelming sepsis and death in the early neonatal period.

See the Department's website, www.idph.state.il.us/HealthWellness/newborn_screening/index.htm, for newborn screening fact sheets with additional information about these disorders and visit the American College of Medical Genetics website to review the ACMG "ACT" sheets.

Incidence

- **Classical Galactosemia -** 1 in 75,000 births

Analyte Measured in Screening

Total galactose (free galactose and galactose-1-phosphate) and GALT enzyme activity are determined by fluorometric assay.

Improper specimen collection or inappropriate shipping and handling, including exposure of the specimen to excessive heat, humidity and/or delayed submission, may cause GALT enzyme degradation.

Reporting Ranges with Respective Follow-up Referrals and Testing

Reporting Ranges	Follow-up Referrals and Testing
Presumptive Positive: Total galactose > 6.5mg/dL with no or low GALT activity Total galactose ≥ 19.5mg/dL with normal GALT activity	Immediate referral to pediatric metabolic disease specialist for diagnostic testing and change feeding to soy formula; encourage breastfeeding mothers to temporarily avoid nursing and use a breast pump to maintain a milk supply until a pediatric metabolic disease specialist advises otherwise.
Suspect Borderline: Total galactose ≥ 6.5mg/dL with reduced or absent GALT activity Normal total galactose with reduced GALT activity	Medical evaluation and repeat newborn screen within one to two days; mark "Retest" box and indicate the newborn's feeding type on the specimen card. If retest sample remains abnormal, referral to pediatric metabolic disease specialist.

Additional Information	Follow-up Referrals and Testing
Feeding Effect	Screening may be affected. Mark specimen collection form to indicate type of feeding.
Transfusion Effect	Screening may be affected. Transfusions may have long-term effects due to GALT enzyme activity of transfused red blood cells and may result in false negative screening for classical galactosemia. Specimen collection prior to transfusion is always recommended. If newborn's initial specimen was collected post-transfusion, a second specimen should be collected 48-72 hours post-transfusion, and a third specimen is required 120 days after the final transfusion.
Timing Effect	If specimen is collected less than 24 hours of age, submit second sample at 48-72 hours of life.
Specialist	Disease specialist that meets qualification listed in administrative code for newborn metabolic screening and treatment.
Treatment	Soy or galactose-free formula and lactose free diet. Variant forms of galactosemia may or may not require dietary restrictions.

All presumptive positive and suspect borderline results are reported by phone, letter, and fax to physician of record or hospital contact. The Department laboratory cut-off values are procedure dependent and are subject to periodic revision.

For questions about the most current laboratory cut-off values for this disorder, contact the Department's Division of Laboratories at 312-793-4752.

Hearing Loss

Hearing loss is the most frequently occurring birth defect in the United States and occurs when any part of the ear does not function properly. This includes dysfunctions in the outer ear, middle ear, inner ear, auditory nerve and auditory system. The auditory system is fully developed by 25 weeks gestation, but after birth, requires outside stimulation to be able to process stimuli. Hearing loss may be due to genetic inheritance, including syndrome associated hearing loss, physical anomaly of the ear, infection and other causes.

The goal of the Illinois Early Hearing Detection and Intervention (EHDI) / Newborn Hearing Screening Program is for all Illinois newborns to have:

- Screening completed no later than **1** month of age,
- Diagnosis completed no later than **3** months of age,
- Intervention initiated no later than **6** months of age,
- Parent support after identification.

The EDHI program is a collaboration among the Illinois Department of Public Health, the University of Illinois at Chicago - Division of Specialized Care for Children and the Department of Human Services Early Intervention Program.

Causes

- **Genetic hearing loss**: There are over 400 known genetic causes related to hearing loss. One gene, Connexin 26 (CX26), is estimated to be responsible for half of all the recessive cases of hearing loss. Of the 50 percent of genetic forms of hearing loss, an estimated seventy percent are due to recessive inheritance. Approximately fifteen percent are inherited in a dominant manner, and fifteen percent include other forms of inheritance. Genetic hearing loss can be syndromic or non-syndromic. Some of the syndromes associated with a hearing loss include Waardenburg Syndrome, Branchio-oto-Renal Syndrome, Neurofibromatosis Type II, Stickler Syndrome, Treacher-Collins Syndrome, Usher Syndrome, Alport Syndrome, Jervell and Lange-Nielson Syndrome and Pendred Syndrome.

- **Non-genetic hearing loss:** Non-genetic hearing loss of the newborn may be caused by illness or trauma in utero or during the birth process. In about fifty percent of hearing loss cases, a non-genetic cause can be identified. Older newborns and young children may also develop non-genetic hearing loss due to illness or trauma.

- **Viral infections:** Certain viral infections, such as toxoplasmosis, syphilis, rubella, cytomegalovirus and herpes simplex, are known to be associated with hearing loss. These infections carry the highest risk for hearing loss if the mother has the illness during pregnancy or passes the infection to her newborn during the birth process.

- **Low birth weight:** Low birth weight has also been identified as a risk factor for hearing loss. Specialists have identified newborns with a birth weight less than 1,500 grams to have an increased likelihood of hearing loss.

- **Hyperbilirubinemia:** Hyperbilirubinemia that is severe enough to require a blood transfusion can also result in hearing loss. This is related to the potential damage that high levels of bilirubin can cause to a newborn’s auditory nerves.

- **Ototoxic medications:** Ototoxic medications that are prescribed to treat serious infections or birth complications may result in hearing loss. The most common otoxic medications are aminoglycosides, which includes gentamycin, tobramycin, kanamycin and streptomycin.

- **Prolonged Ventilation:** Prolonged mechanical ventilation of the newborn for duration of five days or longer due to persistent pulmonary hypertension also increases the risk for hearing loss.

- **Meningitis:** Bacterial meningitis has a high risk of causing hearing loss and/or problems with equilibrium. Because meningitis is an infection of the lining of the brain and spinal cord, the sensory organs of hearing and balance are especially sensitive to this infection.

Physiological Measures

- **Automated Auditory Brainstem Response**: With automated auditory brainstem response (AABR) screening, a fixed intensity stimulus is placed on the newborn's ears. Electrodes are positioned on the newborn's head to detect responses to the sounds presented. AABR measures how the auditory nerve responds to sounds at one level. When the newborn hears at the presented level, a response from the brainstem is recorded. If the newborn cannot hear, no response is recorded.

- **Otoacoustic Emissions:** With otoacoustic emissions (OAE) screening, a small probe is placed in the newborn's ear canal which delivers a low-volume stimulus into the ear. The cochlea responds by producing an otoacoustic emission, sometimes described as an “echo,” that travels back through the middle ear to the ear canal and is analyzed by the screening unit. If a newborn hears normally, an echo is reflected back into the ear canal and is measured by the microphone. When there is a hearing loss, no echo can be measured on the OAE screening test.

These two screening tests can be used separately or together. In some hospitals, newborns are first screened using OAE testing. Newborns that refer on the first OAE test can be given a second screening using the AABR. The screening methodology that should be used in the NICU population of newborns is AABR.

Incidence

- 2-3 in 1,000 births have unilateral or bilateral hearing loss that is sensorineural, mixed or permanent conductive in nature.

Reporting Ranges with Respective Follow-Up and Referrals

Reporting Ranges	Follow-up Referrals and Testing
Refer	All newborns who refer on the inpatient hearing screening should receive an outpatient hearing screening within two weeks of hospital discharge. If the newborn refers on the outpatient hearing screening, he/she should be referred immediately to an audiologist for diagnostic testing.

Additional Information	Follow-up Referrals and Testing
Specialist	Pediatric audiologist or pediatric otolaryngologist
Treatment	Treatment depends on the type and severity of hearing loss as well as the parent's choice for communication options. Most children with a hearing loss may have social, emotional, educational, language and communication development equivalent to their hearing peers if diagnosis is no later than 3 months of age and intervention is initiated no later than 6 months of age.

Procedure Regarding Inpatient Hearing Screening

A. Identify newborn readiness for hearing screening

1. Typical screening time is between 6 and 24 hours of life.

2. While testing may be completed when the newborn is awake, a sleeping newborn may be easier to screen.

3. The newborn must be free of any craniofacial anomalies or malformations of the ear. If these are present, the newborn should be referred directly to an audiologist for testing.

B. Preparation for screening

1. Provide parent(s) with the *Information for Parents* brochure (43.00 brochure found at www.illinoissoundbeginnings.org) that contains hearing screening information required to be given to parents in accordance with the Illinois Newborn Hearing Screening Program's administrative code.

2. Screening may be done in the nursery or patient room. Parent(s) may be present.

3. All ambient room noise should be reduced prior to screening; all non-essential hospital equipment should be turned off during screening.

4. Do not test an actively crying newborn.

5. Examine the newborn's ear for any pits or tags and determine if the ear canal is open and free of debris.

C. Screening techniques

1. Automated Auditory Brainstem Response - AABR screens for hearing loss from the outer ear to the level of the lower brainstem. Testing is conducted by introducing sound into the ear through a probe or through earphones placed on or in the newborn's ears. The sound travels through the outer, middle and inner ear along the neural pathway to the brain. The response from the newborn's nerve is picked up from electrodes that have been placed on the newborn. This response is recorded and analyzed by the computer. Most AABR equipment is automated and gives a "Pass" or "Refer" response. No interpretation is needed by the screener.

a. Clean and prepare the skin.

b. Place the electrodes on the appropriate sites. Refer to the screening manual regarding proper electrode placement sites for your equipment.

c. After the electrodes are in place and connected, place ear covers on each ear or insert probe in each ear.

d. Place the cable above the newborn's head to make sure the probe insert stays in place if the newborn is active. Verify the cables are connected to the cable box per the manufacturer's requirements.

e. Initiate the AABR screening.

2. Otoacoustic Emissions - When the probe is placed in the ear canal, sound enters the ear causing the eardrum to vibrate. This vibration causes the ossicles to move, which then pushes in on the inner ear and stimulates the outer hair cells in the cochlea. When the cochlea is functioning it responds by producing an otoacoustic emission, which is sometimes described as an echo that travels back through the middle ear to the ear canal. This emission is then picked up by the probe, analyzed, and displayed on the computer screen as a "Pass" or "Refer."

a. Position the newborn. Newborns are typically placed supine so the screener can see the ear canal. Gently turn newborn's head so the ear being tested is facing up. Make sure the newborn is swaddled and comfortable.

b. The screener should stand behind the newborn that is on his/her side with their nose pointing forward so the screener can see the ear canal clearly. The screener should move to the other side of the newborn to test the opposite ear. Do not reach across a newborn to screen.

c. Prepare the ear for screening. Gently massage or pull back on the ear to make sure the ear canal is open.

d. Choose the appropriate size probe tip. Probe tips come in various shapes and sizes. It is important that the probe tip fits snugly to help reduce background noise. When selecting a probe tip, choose a size that is slightly larger than the opening of the ear canal to make sure it is a secure fit.

e. Place the probe and cable. With one hand, gently pull back on the outer ear so you can see the ear canal. With the other hand, lay the probe on the ear aiming it toward the ear canal then gently push it forward; the push pull motion will place the probe while also sealing off the canal. After you have placed the probe, position the cable above the newborn's head so the cable cannot easily be pulled out of the canal if the newborn moves. If the probe is properly fitted, it should stay in place.

f. Prepare to conduct the screening. If the newborn is restless, hold the probe lightly in place only until he/she quiets down. Do not hold the probe in place during the screening because it may cause noise interference during the test. After the screening has been completed on the first ear, check the probe tip to make sure it is clear of debris, and repeat steps 5 and 6 on the opposite ear.

g. When the screening is complete, discard the probe tip. The same probe tip can be used to screen both ears on the same newborn during the same screening attempt. A new probe tip must be used for subsequent screenings on the same newborn or on a different newborn.

D. After screening and before hospital discharge

1. Document the hearing screening results according to hospital protocol. All screening results must be reported to the Illinois Department of Public Health Early Hearing Detection and Intervention Program through the data and tracking system, without delay.
2. Complete the "crib card" and use suggested scripted messages to relay hearing screening results directly to the parent(s) after the screening, and not only at time of discharge.
3. At the time of relaying results to the parent verify the name of the Medical Home/ Primary Care Physician (PCP) who will be caring the newborn after discharge.

4. For newborns that "Refer" on the newborn hearing screening, provide the *Next Steps* brochure (43.01 brochure found at llinoissoundbeginnings.org) to the parent.
5. Whenever possible, schedule the newborn with a "Refer" on newborn hearing screening for an outpatient follow-up appointment prior to hospital discharge.

Comments

Every newborn who receives a birth certificate should be entered into the Illinois Newborn Hearing Screening Program's data system.

Hospital "Refer" rates for newborn hearing screening should be between one and four percent.

Newborns should receive up to two inpatient screenings if the newborn refers on the initial screening. If the newborn passes the initial screening, a second screening does not have to be completed.

Newborns who "Refer" should receive an outpatient hearing screening.

Newborns that do not pass both inpatient and outpatient newborn hearing screenings should be seen by a pediatric audiologist who has equipment and training to assess hearing thresholds. For assistance locating an audiologist, visit EHDIPALS.ORG or call the Division of Specialized Care for Children 800-322-3722.

Brochures and other materials related to the Early Hearing Detection and Intervention Program in Illinois may be found at www.illinoissoundbeginnings.org. The brochure order form is available for download on the website. Brochures 43.00 and 43.01 are provided free of charge and are double-sided in both English and Spanish. Brochures in Polish, French and Arabic can be printed on demand from the website.

All hospital screeners should complete the Newborn Hearing Screening Training Curriculum. Information can be found at www.infanthearing.org/nhstc/index.html or contact the EHDI Program Coordinator at 217-782-4733.

Hemoglobin Sickling Disorders; Alpha and Beta Thalassemias (FS, FSC, FSa, FNA, Bart's)

This group of autosomal recessive hemoglobin disorders is characterized by production of abnormal forms of hemoglobin and no adult, or normal hemoglobin. In sickling diseases, this abnormal hemoglobin may be less stable and can cause red blood cells to sickle after repeated deoxygentaion. Sickled cells can block blood vessels causing pain, stroke and other complications. The severity of the disorder varies greatly, but newborns with sickle cell disease, sickle hemoglobin C disease, sickle beta thalassemia and beta thalassemia major are susceptible to anemia, life-threatening infections and other complications. Prophylactic penicillin by 2 months of age and adequate immunizations have been shown to greatly reduce morbidity and mortality associated with sickling hemoglobinopathies. Newborns and children diagnosed with alpha thalassemia or beta thalassemia major may experience severe anemia requiring blood transfusions and ongoing medical care best provided by a pediatric hematologistor in consultation with a thalassemia specialist at the Comprehensive Hemoglobinopathies Program at Ann & Robert H. Lurie Children's Hospital of Chicago.

See the Department website, www.idph.state.il.us/HealthWellness/newborn_screening/index.htm, for newborn screening fact sheets with additional information about these disorders and visit the American College of Medical Genetics website to review the ACMG "ACT" sheet.

Reporting Classifications are as follows:

F-Bart's – Fetal and Bart's hemoglobin- probable alpha thalassemia/hemoglobin H disease
FNA – Fetal and no adult hemoglobin - probable beta thalassemia major
FS – Fetal and sickle hemoglobins - probable homozygous sickle cell disease
FSa – Fetal, sickle and beta thalassemia hemoglobin - probable sickle/beta thalassemia
FSC – Fetal and hemoglobin C - probable sickle/ hemoglobin C disease
6U – Fetal and anomalous unidentified hemoglobin

Incidence

- **Sickle cell disease** - 1in 1 in 375 African Americans.
- **Sickling hemoglobinopathies** - occur in all races and ethnic groups.
    - Hemoglobin C is more common among individuals with West African heritage.
    - Hemoglobin E is more common among individuals with Mediterranean, African or Southeast Asian heritage.
    - Hemoglobin S is more common among individuals with West African, Middle Eastern, Mediterranean or Central Indian heritage.
    - Thalassemias are more common among individuals with Mediterranean, African or Southeast Asian heritage, but do occur worldwide.

Analyte Measured in Screening

Identification of types of hemoglobin present in the screening sample is performed by high performance liquid chromatography (HPLC). This screening is not quantitative.

Reporting Ranges with Respective Follow-up Referrals and Testing

Reporting Ranges	Follow-up Referrals and Testing
Presumptive Positive	Immediate referral to pediatric hematologist for diagnostic testing.

Additional Information	Follow-up Referrals and Testing
Feeding Effect	None
Transfusion Effect	Screening may be affected by transfusions. Specimen collection prior to transfusion is always recommended. If newborn's initial specimen was collected post-transfusion, a second specimen should be collected 48-72 hours post-transfusion, and a third specimen is required 120 days after the final transfusion.. Donor red blood cells may mask hemoglobin disorders due to presence of transfused adult hemoglobin. Specimens from transfused newborns with disease conditions may have false negative results or results that falsely indicate carrier (trait) status.
Timing Effect	If specimen is collected less than 24 hours of age, submit second sample at 48-72 hours of life. Usually no effect in first two weeks of newborn period, although older newborns will have a gradual decrease in fetal hemoglobin. Bart's hemoglobin levels decline rapidly during the neonatal period, and newborns with positive screens for possible alpha thalasemia/hemoglobin H disease require immediate diagnostic testing, not a repeat newborn screen.
Specialist	Disease specialist that meets qualification listed in administrative code for newborn metabolic screening and treatment. Referral to the Comprehensive Hemoglobinopathies Program at Ann & Robert H. Lurie Children's Hospital of Chicago is recommended for abnormal screens indicative of possible alpha thalassemia/hemoglobin H disease and require immediate molecular diagnostic testing. Hemoglobin electrophoresis cannot diagnose alpha thalassemia.
Treatment	Prophylactic penicillin is recommended for children with sickling disorders from ages 2 months to 5 years. In addition to all regular childhood immunizations, pneumococcal conjugate vaccine also is recommended to help prevent pneumococcal infections. While prophylactic penicillin is **not** usually indicated for treatment of thalassemias, these disorders are associated with severe anemia usually requiring medical management by a pediatric hematologist. Services also are available through the Comprehensive Hemoglobinopathies Program.

All presumptive positive results are reported by letter, phone and fax to physician of record or hospital contact unless otherwise specified.
Confirmatory diagnostic testing along with genetic counseling and education are necessary. Referral to pediatric hematologist for testing and genetic counseling services is recommended.

Comments

Family education, genetic counseling and diagnostic services are available to families of newborns with sickling hemoglobin disorders. The Department, through grants to university-based medical clinics, provides diagnostic and treatment services for newborns and children identified with hemoglobin disorders or traits. In addition, family counseling and educational services regarding sickling disorders are offered through the Sickle Cell Disease Association of Illinois (see page 17).

Hemoglobin Traits

Hemoglobin traits are autosomal recessive disorders of hemoglobin production that usually do not require treatment. Individuals with these conditions produce adequate amounts of functional hemoglobin and usually do not have complications associated with the conditions.

See the Department's website, www.idph.state.il.us/HealthWellness/newborn_screening/index.htm, for newborn screening fact sheets with additional information about these disorders and visit the American College of Medical Genetics website to review the ACMG "ACT" sheets.

Incidence

- **Sickle cell trait** - 1 in 100 African Americans.
- **Hemoglobinopathies -** occur in all races and ethnic groups.

Analyte Measured in Screening

Identification of types of hemoglobin present in the sample is performed by high performance liquid chromatography (HPLC). This screening is not quantitative.

Reporting Ranges with Respective Follow-up Referrals and Testing

Reporting Ranges	Follow-up Referrals and Testing
FAC – Fetal, adult hemoglobin C: probable hemoglobin C carrier status	Confirmatory diagnostic testing, family and genetic counseling services are highly recommended.
FAD – Fetal, adult hemoglobin D: Probable hemoglobin D carrier status	Confirmatory diagnostic testing, family and genetic counseling services are highly recommended.
FAE – Fetal, adult and E hemoglobins: Probable E hemoglobin carrier status	Confirmatory diagnostic testing, family and genetic counseling services are highly recommended.
FAS – Fetal, adult and sickle hemoglobin: Probable sickle cell carrier status	Confirmatory diagnostic testing, family and genetic counseling services are highly recommended.

Additional Information	Follow-up Referrals and Testing
Feeding Effect	None
Transfusion Effect	Screening may be affected by transfusions. Specimen collection prior to transfusion is always recommended. If newborn's initial specimen was collected post-transfusion, a second specimen should be collected 48-72 hours post-transfusion, and a third specimen is required 120 days after the final transfusion.
Timing Effect	If specimen is collected less than 24 hours of age, submit second sample at 48-72 hours of life. Usually no effect in first two weeks of newborn period, although older newborns will have a gradual decrease in fetal hemoglobin.
Specialist	Disease specialist that meets qualification listed in administrative code for newborn metabolic screening and treatment.
Treatment	Carrier status (hemoglobin traits) usually are considered benign with no treatment necessary.

All abnormal results are reported by letter to physician of record or hospital contact.

Comments

Family education, genetic counseling and diagnostic services are available to families of newborns with sickling hemoglobin disorders or traits. The Department, through grants to university-based medical clinics, provides diagnostic and treatment services for newborns and children identified with hemoglobin disorders or traits. The Sickle Cell Disease Association of Illinois also will provide educational services to families of individuals with sickle cell diseases or carrier status.

Collegiate Sports Participation

The National Collegiate Athletic Association (NCAA) requires all athletes at Division I and II schools to be tested for sickle cell trait before competing or to sign a written release declining the test as their method for reducing the incidence of training-related deaths. In Illinois, newborn screening has included testing for sickle cell trait since 1989; however, the Department may not have newborn screening records readily available for all children born in Illinois during 1989. When available, a copy of newborn screening test results, which includes testing for sickle cell trait, will be provided by the Department to individuals 18 years of age and older, to parents of children under age 18 and to college athletic trainers, upon submission of the proper, notarized consent form and payment of a $25 processing fee.

Newborn screening results also may be obtained from the hospital of birth, a physician can order a hemoglobin electrophoresis test as part of the sports physical or the athlete can discuss other means of obtaining this test with the college athletic department staff.

For further information about the collegiate athletic requirement for documentation of sickle cell trait testing, visit the NCAA website at http://www.ncaa.org/health-and-safety/medical-conditions/sickle-cell-trait.

Hemoglobinopathies-Other Types and Low Fetal Hemoglobin

Other hemoglobin diseases are autosomal recessive disorders of hemoglobin production that usually do not require treatment. Individuals with these conditions produce adequate amounts of functional hemoglobin and usually do not have complications associated with the conditions.

See the Department's website, www.idph.state.il.us/HealthWellness/newborn_screening/index.htm, for newborn screening fact sheets with additional information about these disorders and visit the American College of Medical Genetics website to review the ACMG "ACT" sheets.

Low fetal hemoglobin usually indicates the newborn was older at the time of specimen collection or, in newborns, that the newborn was transfused. If the newborn was transfused prior to collection of the initial newborn screening specimen, another specimen is required three months after the last transfusion, when the effects of donor red blood cells have dissipated.

Incidence

- **Hemoglobinopathies** - Occur in all races and ethnic groups.
    - Hemoglobin C is more common among individuals with West African heritage.
    - Hemoglobin E is more common among individuals with Mediterranean, African or Southeast Asian heritage.
    - Hemoglobin S is more common among individuals with West African, Middle Eastern, Mediterranean, or Central Indian heritage.
    - Thalassemias are more common among individuals with Mediterranean, African or Southeast Asian heritage, but do occur worldwide.

Analyte Measured

Identification of types of hemoglobin present in the sample is performed by high performance liquid chromatography (HPLC). This screening is not quantitative.

Reporting Ranges with Respective Follow-up Referrals and Testing

Confirmatory diagnostic testing, family education and genetic counseling services highly recommended.

Screening results for diseases not usually requiring treatment

- FD – Fetal and D hemoglobin – Hemoglobin D disease (DD)
- FE – Fetal and E hemoglobin – Hemoglobin E disease (EE)
- FX – Fetal and anomalous, unidentified hemoglobin – unidentified hemoglobin disorder

Other Hemoglobin Results

- LFA – Low fetal and elevated adult hemoglobin – probable transfusion or older newborn

Reporting Ranges	Follow-up Referrals and Testing
Presumptive Positive	Immediate referral to pediatric hematologist.

Additional Information	Follow-up Referrals and Testing
Feeding Effect	None
Transfusion Effect	Screening may be affected by transfusions. Specimen collection prior to transfusion is always recommended. If newborn's initial specimen was collected post-transfusion, a second specimen should be collected 48-72 hours post-transfusion, and a third specimen is required 120 days after the final transfusion.
Timing Effect	Usually no effect in first two weeks of newborn period, although older newborns will have a gradual decrease in fetal hemoglobin.
Specialist	Disease specialist that meets qualification listed in administrative code for newborn metabolic screening and treatment.
Treatment	Carrier status (hemoglobin traits) usually are considered benign with no treatment necessary.

All abnormal results are reported by letter to physician of record or hospital contact.

Note: Hemoglobin E and Hemoglobin D disease should be verified by further diagnostic testing. Referral to the Comprehensive Hemoglobinopathies Program at Ann & Robert H. Lurie Children's Hospital of Chicago for diagnostic testing is recommended for newborns with results indicating possible thalassemia disorders.

Comments

Family education, genetic counseling and diagnostic services are available to families of newborns with sickling hemoglobin disorders or traits. The Department, through grants to university-based medical clinics, provides diagnostic and treatment services for newborns and children identified with hemoglobin disorders or traits. In addition, family counseling and educational services regarding sickling disorders are offered through the Sickle Cell Disease Association of Illinois (see page 17).

Lysosomal Storage Disorders

Lysosomal storage disorders are inherited metabolic conditions caused by deficiency of a specific enzyme related to the metabolism of lipids or glycogen. Of the lysosomal storage disorders included in the Illinois newborn screening panel, each disorder causes an accumulation of metabolites, primarily sphingolipids, or in the case of Pompe disease, harmful amounts of glycogen, in the lysosomes of cells. Over time, these accumulated lipids or glycogen deposits cause permanent cellular and tissue damage. Lysosomal storage disorders affect different organ systems, including the brain and nervous system, liver, renal system, heart, skeletal muscles, lungs, spleen and bone marrow. Treatment options vary among the disorders and are disease specific, but may include enzyme replacement therapy or stem cell transplantation.

See the Department's website, www.idph.state.il.us/HealthWellness/newborn_screening/index.htm, for newborn screening fact sheets with additional information about this disorder and visit the American College of Medical Genetics website to review the ACMG "ACT" sheets.

In Illinois, newborn screening includes testing for enzyme activity levels of specific lysososmal storage disorders. Following is a list of the lysosomal storage disorders that may be detected:

Fabry Disease
Gaucher Disease
Krabbe Disease
MPS I (Mucopolysaccharidosis Type I)/Hurler Syndrome
MPS II (Mucopolysaccharidosis Type II)/Hunter Syndrome
Niemann-Pick Disease
Pompe Disease

Incidence

- These are rare disorders and the actual incidence is unknown. Cumulatively, the incidence of all lysosomal storage diseases is approximated at 1 in 40,000 births.

Analytes Measured in Screening

Enzyme activity quantified by tandem mass spectrometry (MS/MS), in micro-Moles per Liter per hour (μM/L/hour).

Screening for Krabbe also includes DNA sequencing of the GALC (Galactocerebrosidase) gene when there is low enzyme activity. Improper specimen collection or inappropriate shipping and handling, including exposure of the specimen to excessive heat, humidity and/or delayed submission may cause enzyme degradation.

Analytes Measured in Screening	Possible Disorder
Acid beta-glucocerebrosidase (ABG)	Gaucher Disease
Acid sphingomyelinase (ASM)	Niemann-Pick Disease
Alpha-galactosidase (GAA)	Fabry Disease
Alpha-glucosidase (GAA)	Pompe Disease
Alpha-L-iduronidase (IDUA)	MPS I/Hurler Syndrome
Galactocerebrosidase (GALC)	Krabbe Disease
Iduronate-2-sulphatase (ID2A)	MPS II/Hunter Syndrome

Reporting Ranges with Respective Follow-up Referrals and Testing

Reporting Ranges	Follow-up Referrals and Testing
Presumptive Positive	Immediate referral to pediatric metabolic specialist for evaluation and diagnostic testing.
Suspect Borderline	Medical evaluation and repeat newborn screening specimen within one to two days; mark "Retest" on specimen card. If retest remains abnormal, refer to pediatric metabolic disease specialist.

Additional Information	Follow-up Referrals and Testing
Feeding Effect	None
Transfusion Effect	Screening may be affected by transfusions. Specimen collection prior to transfusion is always recommended. If newborn's initial specimen was collected post-transfusion, a second specimen should be collected 48-72 hours post-transfusion, and a third specimen is required 120 days after the final transfusion.
Timing Effect	If specimen is collected at less than 24 hours of age, submit second sample at 48-72 hours of life.
Specialist	Disease specialist that meets qualification listed in administrative code for newborn metabolic screening and treatment.
Treatment:	Treatment is disease specific.
Fabry Disease	Not typically treated during early childhood. Enzyme replacement therapy.
Gaucher Disease	Enzyme replacement therapy.
Krabbe Disease	Some individuals may benefit from stem cell transplant early in life. Positive newborn screens for possible Krabbe disease require immediate referral to pediatric metabolic specialists at children's hospitals with access to a pediatric stem cell transplant center.
MPS I/Hurler Syndrome	Enzyme replacement therapy is available to help relieve symptoms, but it is not a cure. Bone marrow transplant is another treatment for MPS I patients.
MPS II/Hunter Syndrome	Enzyme replacement therapy is available to help ameliorate the somatic features of the disorder, but is not effective in treating symptoms involving the central nervous system.
Niemann-Pick Disease	Bone marrow transplants have been attempted and clinical trials of enzyme replacement therapy are under study.
Pompe Disease	Enzyme replacement therapy.

Presumptive positive and suspect borderline results are reported by letter, phone and fax to physician of record or hospital contact unless otherwise specified.

For questions about the most current laboratory reporting values for these disorders, contact the Department's Division of Laboratories at 312-793-4752.

Organic Acid Disorders

Organic acid disorders are autosomal recessive inherited metabolic conditions. Each organic acid disorder is associated with a specific enzyme deficiency that causes the accumulation of organic acids in blood and urine. The accumulated compounds or their metabolites are toxic and may result in metabolic acidosis, hyperammonemia or ketotic hyperglycinemia. Usually newborns with organic acid disorders appear normal at birth, but may develop vomiting, poor feeding, hypoglycemia, seizures, hypotonia and lethargy progressing to coma. Common features may include ketotic hyperglycinemia, metabolic acidosis and, sometimes, an unusual odor. There is significant risk of death in infancy due to organic acid disorders; early diagnosis and treatment can greatly improve disease outcome. Minimization of ketoacidotic episodes improves prognosis and, during such episodes, aggressive treatment, including administration of glucose, may be warranted.

See the Department's website, www.idph.state.il.us/HealthWellness/newborn_screening/index.htm, for newborn screening fact sheets with additional information about these disorders and visit the American College of Medical Genetics website to review the ACMG "ACT" sheets.

In Illinois, newborn screening includes testing for a panel of acylcarnitines. Following is a list of the organic acid disorders that may be detected:

Betaketothiolase deficiency (BKT)
Glutaric acidemia, type 1 (GA 1)
Isovaleric acidemia (IVA)
Isobutyryl-CoA dehydrogenase deficiency (IBCD); IBCD can also be characterized as a fatty acid oxidation disorder.
Malonic aciduria (MA)
Methylmalonic acidemia (MMA)
Multiple carboxylase deficiency (MCD)
Propionic acidemia (PA)
2-methylbutyryl-CoA dehydrogenase deficiency (2MBCD)
3-hydroxy-3-methylglutaryl-CoA lyase deficiency (3HMG)
3-methylglutaconic aciduria (3MGA)
3-methylcrotonyl CoA carboxylase deficiency (3-MCC)

Incidence

- **GA1 –** 1 in 110,000 births
- **IVA –** 1 in 50,000 births
- **MMA –** 1 in 100,000 births
- **PA, 3HMG, 3MGA, BKT, MCD, MA –** very rare; estimated at 1 in 100,000 to 500,000 births
- **3MCC –** 1 in 50,000 births

Analytes Measured in Screening

Specific acylcarnitines measured by tandem mass spectrometry (MS/MS) in micro-Moles per Liter (µM/L).

For substituted carnitines, a notation of (Cx) is used where (x) denotes the number of carbons in the fatty acid radical. Free carnitine is designated as (C0), acetyl carnitine as (C2), propanoyl carnitine as (C3), etc. Hydroxylation is designated by (-OH), dicarboxylic acid is designated by (-DC), and unsaturation is designated by (:1).

Acylcarnitine Measured in Screening	Possible Disorder
Pentanoyl carnitine (C5) is the primary analyte	IVA/2MBCD
Propanoyl carnitine (C3) is the primary analyte	MMA/PA
3-hydroxy-isovaeryl carnitine (C5-OH) is the primary analyte	3MCC, 3HMG, 3MGA, MCD

Reporting Ranges with Respective Follow-up Referrals and Testing

Reporting Ranges	Follow-up Referrals and Testing
Presumptive Positive	Immediate referral to pediatric metabolic disease specialist.
Suspect Borderline	Medical evaluation and repeat newborn screening specimen within one to two days; mark "Retest" on specimen card. If retest sample remains abnormal, refer to pediatric metabolic disease specialist.
Suspect Acylcarnitine Abnormal due to TPN (reported by fax and letter)	If newborn is still in NICU or on TPN, repeat newborn screen 48 hours after TPN is discontinued, at day 28 of life or prior to discharge, whichever comes first. If newborn has been discharged from hospital or was not on TPN at time of specimen collection, repeat newborn screen within one to two days. If retest remains abnormal, refer to metabolic specialist.

Additional Information	Follow-up Referrals and Testing
Feeding Effect	Hyperalimentation and TPN may affect results. Unless otherwise instructed, repeat specimens are best collected 48 hours after TPN is discontinued.
Transfusion Effect	Specimen collection prior to transfusion is always recommended. If newborn's initial specimen was collected post-transfusion, a second specimen should be collected 48-72 hours post-transfusion, and a third specimen is required 120 days after the final transfusion..
Timing Effect	If specimen is collected less than 24 hours of age, submit second sample at 48-72 hours of life. If repeat specimen is requested, collect and submit new specimen within one to two days.
Specialist	Disease specialist that meets qualification listed in administrative code for newborn metabolic screening and treatment.
Treatment	Treatment is disorder specific and may include low-protein diet and avoidance of fasting and, in some cases, specialized medical formula, or supplements and medications. Special precautions, such as close monitoring, and, in some cases, intravenous therapy may be required during intercurrent illness and introduction of new foods. If indicated, the Department provides special medical formula without charge to Illinois residents who are under comprehensive medical management provided by metabolic disease specialist designated by the Department.

All presumptive positive and suspect borderline results are reported by phone, letter and fax to physician of record or hospital contact unless otherwise specified.

For questions about the most current laboratory reporting values for these disorders, contact the Department's Division of Laboratories at 312-793-4752.

Phenylketonuria

Phenylalanine hydroxylase deficiency, including Phenylketonuria (PKU), is an autosomal recessive disorder of amino acid metabolism resulting in excess levels of phenylalanine in body fluids. Hyperphenylalaninemia is usually due to a deficiency of the phenylalanine hydroxylase enzyme or, in some cases, impaired synthesis or recycling of biopterin cofactor. Elevated levels of phenylalanine can become neurotoxic; early detection and treatment of hyperphenylalaninemia is necessary to prevent severe mental retardation. Phenylalanine is an essential amino acid, and individuals with PKU require careful dietary management and monitoring for life. Women of childbearing age, who are diagnosed with PKU or hyperphenylalaninemia, require strict dietary control prior to conception and throughout pregnancy to reduce their risk of pregnancy complications, including miscarriage, or of having an newborn with birth defects and developmental delays due to high maternal levels of phenylalanine.

See the Department's website, www.idph.state.il.us/HealthWellness/newborn_screening/index.htm, for newborn screening fact sheets with additional information about this disorder and visit the American College of Medical Genetics website to review the ACMG "ACT" sheets.

Incidence

- **Classical PKU –** 1 in 10,000 births

Analytes Measured in Screening

Phenylalanine level and phenylalanine/tyrosine ratio measured by tandem mass spectrometry (MS/MS) in micro-Moles per Liter (μM/L).

Reporting Ranges with Respective Follow-up Referrals and Testing

Reporting Ranges	Follow-up Referrals and Testing
Presumptive Positive: Seriously elevated phenylalanine level and/or elevated phenylalanine/tyrosine ratio	Immediate referral to PKU pediatric metabolic disease specialist.
Suspect Borderline: Slightly elevated phenylalanine level	Medical evaluation and repeat newborn screening specimen within one to two days; mark "Retest" on specimen card. If retest sample remains abnormal, refer to pediatric metabolic disease specialist.
Multiple Abnormal Acylcarnitine Elevation: Acylcarnitine elevations detected, usually associated with TPN effects (reported by letter and fax)	If newborn is still in NICU or on TPN, repeat newborn screen 48 hours after TPN is discontinued, at day 28 of life or prior to discharge, whichever comes first. If newborn has been discharged from hospital or was not on TPN at time of specimen collection, repeat newborn screen within one to two days. If retest remains abnormal, refer to pediatric metabolic disease specialist.

Additional Information	Follow-up Referrals and Testing
Feeding Effect	Laboratory detection of phenylalanine is not necessarily diet dependent. Screening is sensitive to catabolic activity occurring shortly after birth. TPN and hyperalimentation may cause false positive screening results.
Transfusion Effect	Specimen collection prior to transfusion is always recommended. If newborn's initial specimen was collected post-transfusion, a second specimen should be collected 48-72 hours post-transfusion, and a third specimen is required 120 days after the final transfusion.
Timing Effect	If specimen is collected less than 24 hours of age, submit second sample at 48-72 hours of life.
Specialist	Disease specialist that meets qualification listed in administrative code for newborn metabolic screening and treatment.
Treatment	Low phenylalanine diet consisting of specialized medically necessary formula in combination with foods that are low in phenylalanine. This meal plan should be started as soon as possible after birth, ideally within the first 7-10 days of life. The Department provides PKU medically necessary formula without charge to Illinois residents who are under comprehensive medical management provided by a metabolic specialist designated by the Department/DSCC. PKU patients must remain under the care of a Department metabolic disease specialist in order to receive formula provided by the state.

All presumptive positive and suspect borderline results are reported by letter, phone and fax to physician or record or hospital contact unless otherwise specified.

For questions about the most current laboratory reporting values for these disorders, contact the Department's Division of Laboratories at 312-793-4752.

Severe Combined Immune Deficiency

Severe combined immune deficiency (SCID) includes a group of rare inherited disorders in which genetic defects cause improper development of T lymphocytes. These lymphocytes serve as primary defenses in the identification of invading viruses, bacteria and fungi and help facilitate the immune system's response to pathogenic invasion. Individuals with SCID are susceptible to recurrent infections and without treatment may succumb to pneumonia, meningitis or other infection related complications. All forms of SCID are inherited and not acquired as side-effects of infection or immune response suppression therapies.

See the Department's website, www.idph.state.il.us/HealthWellness/newborn_screening/index/htm, for newborn screening fact sheets with additional information about this disorder and visit the American College of Medical Genetics website to review the ACMG "ACT" sheets.

Incidence

- **SCID** - 1 in 50,000 births.
- **All types of immunodeficiency** - 1 in 15,000 births.

Analytes Measured in Screening

Performed by measuring the T-cell receptor excision circles (TRECs) in DNA extracted from T lymphocytes. The absence of TREC's or lower numbers of TRECs may indicate the newborn has SCID or profound T-cell lymphopenia.

Reporting Ranges with Respective Follow-up Referrals and Testing

Reporting Ranges	Follow-up Referrals and Testing
Presumptive Positive (Term Newborn)	Immediate referral to pediatric immunologist for diagnostic flow cytometry.
Presumptive Positive (Pre-Term Newborn)	Medical evaluation and repeat newborn screening specimen within two weeks for premature newborns (<38 weeks gestation); mark "Retest" on specimen card.

Additional Information	Follow-up Referrals and Testing
Feeding Effect	None
Transfusion Effect	Specimen collection prior to transfusion is always recommended. If newborn's initial specimen was collected post-transfusion, a second specimen should be collected 48-72 hours post-transfusion, and a third specimen is required 120 days after the final transfusion.
Timing Effect	If specimen is collected at less than 24 hours of age, submit second sample at 48-72 hours of life.
Specialist	Disease specialist that meets qualification listed in administrative code for newborn metabolic screening and treatment.
Treatment	Hematopoietic stem cell/bone marrow transplant.

All presumptive positive results are reported by letter, phone and fax to physician of record or hospital contact unless otherwise specified.

For questions about the most current laboratory reporting values for these disorders, contact the Department's Division of Laboratories at 312-793-4752.

Resources

American College of Medical Genetics (ACMG): https://www.acmg.net/

Newborns First Test: http://www.newbornsfirsttest.org/

Division of Specialized Care for Children (DSCC): http://dscc.uic.edu/

NewSTEPs: https://www.newsteps.org/

Region 4: https://www.region4genetics.org/

Save Newborns: http://www.savenewborns.org/

Sickle Cell Disease Associate of Illinois (SCDAI): http://www.sicklecelldisease-illinois.org/

References

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