Policy #006
Center for Congenital and Inherited Disorders

Newborn Screening for Newborns < 30 Weeks Gestational Age or Birth Weight < 1500 grams

I. Overview

The Iowa Department of Public Health (IDPH) is authorized pursuant to Iowa Code 136A and Iowa Administrative Code (IAC) 641IAC 4.3 to establish a newborn screening program, and directs that all newborns born in the state of Iowa be tested for specific congenital and inherited disorders as determined by the Center for Congenital and Inherited Disorders (CCID) at the Iowa Department of Public Health and approved by the State Board of Health. Comprehensive newborn screening services including laboratory, follow-up, consultative, and educational services are provided through the Iowa Newborn Screening Program (INSP), a program of the IDPH.

INSP is a program under the CCID pursuant to Iowa Code chapter 136A and Iowa Administrative code 614 IAC 4.3. The CCID provides administrative oversight to the INSP for the Iowa Department of Public Health. The State Hygienic Laboratory (SHL) at The University of Iowa (UI) is the designated central screening laboratory pursuant to IC chapter 136A and 641 IAC 4.2. SHL tests Iowa newborns as set forth in 641 IAC 4.3 (5) and is the custodian of the residual specimens collected for newborn screening in Iowa on behalf of the INSP. Staff within the UI Departments of Internal Medicine, Pathology, and Pediatrics serve as consultants for the INSP pursuant to 641 IAC 4.3 and provide program coordination, consultation, follow up, and education activities. IDPH and the UI maintain a 28E agreement to ensure the provision of comprehensive newborn screening services for congenital and inherited disorders in the state of Iowa through the INSP.

The goal of newborn screening (NBS) is to detect infants at increased risk for having a particular condition. Because screening is, by definition, not diagnostic, more testing is needed after an out-of-range result. Additionally, screening may provide false-positive and/or false-negative results. Iowa's Newborn Screening Program (INSP) works to reduce these as much as possible.

The population targeted by this guideline are those newborns who are < 30 completed weeks' gestation or with a birth weight < 1500 grams. This population is more likely to receive a transfusion, which is the primary confounder for producing false positive results when the baby has been transfused prior to collection of the NBS specimen. Additionally, this population is at higher risk for a false negative screen result for congenital hypothyroidism. Therefore, serial screening, with the collection of two to three specimens, is proposed for newborns who are < 30 completed weeks' gestation or with a birth weight <1500 grams as the most efficient and effective model.
This policy considers these principles:

- Efficient utilization of the newborn's limited blood resources
- Sufficient specimen collection, but no more than necessary and only when required, in order to minimize the stress for these medically fragile babies
- Avoidance of missed screens
- Timely specimen collection to identify time-critical conditions so treatment can begin as soon as possible

II. Definitions

dried blood spot (DBS) – blood collected from a heel stick or other appropriate modality and air dried on an approved collection device.

false-negative result – "in-range" result in an affected newborn; a test result which indicates that an individual is unaffected when he or she is actually affected.

false-positive result – "out-of-range" result in an unaffected newborn; NOTE: A test result which indicates that an individual is affected when he or she is actually unaffected.

gestational age – the length of the pregnancy at birth (measured from the first day of the last menstrual period), in completed weeks.

in-range result – screening result that is within the expected range of normal/negative testing results established for a particular analyte and particular population.

neonatal intensive care unit (NICU) – hospital facility or unit staffed and equipped with capabilities of supporting infants born < 30 weeks' gestation and weighing < 1500 g and all critically ill newborns.

neonatologist – a pediatrician with specialized training and certification in the care of neonates that require intensive care.

newborn dried blood spot (DBS) screening – process of collecting blood onto an approved collection device, testing defined analytes by approved laboratory methods, and reporting results as appropriate.

out-of-range result – screening result that is outside the expected range of normal/negative testing results established for a particular analyte and a particular population.

transfusion – the transfer of whole blood or blood products from one individual to another, as well as the administration of IVIG (intravenous immunoglobulin)

Sections A, B, and C below are the routine collection practices currently in place in each of the described situations. Section D **ADDS** a serum thyroid function test for infants <1500 grams Birth Weight OR < 30 weeks gestational age. It is highly recommended that all Iowa NICUs follow this as the official screening protocol for these infants, although neonatologists have responsibility for management of the NICU infant's care. Clinical judgement should prevail.

III. Procedure

A. Routine Initial Screen at 24 Hours of Age, Unless Transfusion is Planned

1. The first screen should be collected at 24 hours of age from birth, regardless of medical condition or feeding status.
2. A specimen collected routinely at 24 hours of age increases the chances that a screening specimen will be drawn on every infant, because there is a uniform protocol for the timing of specimen collection, regardless of the newborn's medical status.
3. If a transfusion is planned, the initial screening specimen should be collected prior to the transfusion treatment. This is critical to ensure timely screening of the baby. If the baby receives a transfusion prior to initial specimen collection there is a risk for significant delay in obtaining valid results.

B. Screening of Newborns with a Planned Transfusion – Initial and Repeat Screening

1. A pre-transfusion specimen, even if the baby is less than 24 hours old, is essential for detection of galactosemia, sickle cell disease, cystic fibrosis, and biotinidase deficiency. For those babies that were less than 24 hours old, there will need to be a second specimen collected after the baby is 24 hours old This will allow for valid screening of those conditions where the test assay is unaffected by transfusion status.
2. If the infant receives a blood transfusion before the first specimen is collected, collect the first specimen at the routine timing of 24 hours of age.
3. Another screening specimen will need to be collected 56 days (8 weeks) after the last transfusion given to validate all results, ensuring the baby's blood is tested and not the donor blood. Results from a transfused specimen may not be valid and may represent a false result.

C. Second Screen at 24 Hours of Age, if Previous Early Collection

1. A repeat blood specimen should be drawn at 24 hours of life for infants who were less than 24 hours of age at initial specimen collection.
2. This specimen provides reliable screening for congenital adrenal hyperplasia (CAH), most amino acidopathies (AA), organic acid (OA) disorders, urea cycle disorders (UCD), and fatty acid oxidation (FAO) disorders early enough to diagnose and treat time-critical disorders effectively.
3. It may detect newborns at risk for congenital hypothyroidism (CH), but should not be considered reliable for preterm or low birth weight babies.

D. Infants < 1500 Grams Birth Weight OR < 30 Completed Weeks Gestational Age

1. A serum specimen should be drawn at discharge or at day of life 30, whichever comes first.
2. Thyroid function may take up to a month to mature to expected newborn levels in preterm newborns. A serum thyroid function test collected at the 30th day of life or discharge should provide a reasonable measure of the baby's thyroid status, and also allow detection of preterm infants with CH and thyroid stimulating hormone (TSH) rise.
3. TSH should be tested within each hospital's clinical laboratory. Serum TSH results must be faxed to the newborn screening program at 319-384-5116 upon completion. These results will be reviewed and further recommendations provided on whether treatment, further testing, and/or a referral to a pediatric endocrinologist is necessary.
4. If the serum TSH is missed before discharge it is recommended that the test be completed as an outpatient as soon as possible.

IV. References

1. Clinical and Laboratory Standards Institute (CLSI). *Newborn Screening for Preterm, Low Birth Weight and Sick Newborns, 1st ed.* CLSI Guideline NBS03-A. Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500 Wayne, Pennsylvania 19087 USA. 2009.
2. Franco RS. The measurement and importance of red cell survival. Am J Hematol. 2009;84:109–114.
3. Kaluarachchi DC, Colaizy TT, Pesce LM, Tansey M, Klein JM. Congenital hypothyroidism with delayed thyroid-stimulating hormone elevation in premature infants born at less than 30 weeks gestation. J Perinatology. 2017;37:277-282.

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