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The Iowa PERINATAL Letter

Newborn Screening Myths and Information

Bloodspot screening has changed remarkably since the 1960s. Up until 1998, additions to the panel were generally one disorder at a time. Keeping up with changes were not difficult and there was plenty of preparation time available for training and education. With the introduction of tandem mass spectrometry, multiple disorders were added in a short time frame. In 2000 Iowa was screening for five disorders, by 2003 the newborn screening panel had expanded to more than 40 disorders. Needless to say, keeping up with timing and other requirements has become increasingly complicated. Hopefully this will provide you with some insight and guidance for appropriate newborn screening and possible complications.

Myth 1: No tests are accurate if done before 24 hours of age.

An initial screen for babies admitted to the NICU or special care nurseries upon admission is preferred timing, even if only a few hours/minutes old. This way, at

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Newborn Screening Myth-Information

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least one screen is assured to be done prior to any blood transfusions that may be needed. All the enzyme disorders are accurate, as is screening for hemoglobinopathies. So, if normal at admission, you can feel confident that biotinidase, galactosemia and hemoglobinopathy testing is normal. Congenital adrenal hyperplasia and congenital hypothyroidism are not accurate because of collection prior to physiological hormone surge, and cutoffs are set for 24-72 hours of age, based on birth weight. Cystic fibrosis testing may be falsely elevated in the first 24-48 hours of age, especially in premature and sick infants.[1] Tandem mass spectrometry for the other disorders is probably not accurate since we are probably seeing mostly affects of placental clearance and not the baby's physiology.

Myth 2: Baby must be eating prior to NBS collection.

This is a frequently cited reason for waiting to screen babies later in life, about 72 hours of age or later. The concern being that PKU or other disorders may be missed because of lack of protein intake. With the older modes of testing, testing was limited to milligrams per deciliter of serum. With newer technologies utilizing tandem mass spectrometry, sensitivities are improved to micromoles per liter of serum. So, sensitivity is much better and elevations of amino acids start at the time of birth, so 24 hours is plenty of time to see elevations.[2] Some conditions like the fatty acid oxidation defects may be easier to detect when the infant is a bit underfed as most are in the first 24-48 hours of life.

Myth 3: More blood is better when applying it to the card.

The CDC has standardized the amount of blood that is in a punch from a blood spot and the calculations are based on this amount of blood.[3] When blood is layered, the amount of serum in a punch is more than what our calculations are based upon.

Myth 4: Baby looks fine so therefore it is unaffected.

The goal of newborn screening is to detect disorders prior to illness or complications. Many of the disorders will not have signs or symptoms until after a week of life or later. Some disorders will present with sudden onset of vomiting, hypoglycemia or electrolyte disorders, but will not be occur until later in life. Other disorders may have a subtle onset with initial symptoms being missing developmental milestones or hypotonia. The point of this is that babies will be normal when testing is done and we should not rely on symptoms to determine the need for newborn screening.[4] By the time symptoms appear, some damage has already occurred.

Myth 5: There are no family histories of disease; therefore, there is no need to screen for it since the disorders are so rare.

The majority of disorders covered by newborn screening are inherited in an autosomal recessive manner. The incidence of disease is then based on how often people are carriers for the disorder or if there is a history of consanguinity. In the absence of consanguinity, unless there is an increased frequency in the population, there generally will not be a family history of the newborn-screened disorders. However, if there is a high frequency of the gene mutation in the populations, such as sickle cell in those with African descent, then there is more likely to be a family history. Needless to say, family history or lack thereof is not a good reason to not screen an infant.[5]

Myth 6: Antibiotics interfere with newborn screening results.

This was a previous complication with bacterial inhibition assays since the reading was dependent upon growth of bacteria on an agar plate, so antibiotics could kill the bacteria and give a false negative reading. Then the next generation flurometric assays cross-reacted with antibiotics causing false positive results.[6] However, this is not a problem inherent to tandem mass spectrometry.

Myth 7: If transfused prior to screening, none of the tests are accurate for 120 days.

Transfusion with red blood cells will give false normal results for galactosemia, hemoglobinopathy and biotinidase enzyme assays. Transfusion of fresh frozen plasma or other plasma products will give false normal results for biotinidase enzyme assay. Otherwise, in the absence of complete or partial exchange transfusion, the tandem mass spectrometry tests, cystic fibrosis test, and endocrinopathies will be accurate if collected appropriately in the correct time frame.[7]

Myth 8: For sick and premature infants, once you have a normal thyroid or CAH screen, then you know they are not affected.

False-negative results may be observed in preterm infants whose mothers were treated with steroids (to mature fetal lungs) and in neonates receiving dexamethasone for management of unrelated problems.[8] The hypothalamic-pituitary axis is immature in premature infants and thus thyroid levels may appear normal initially but require rechecks periodically to insure that infants will not eventually need thyroid replacement.[9]

Myth 9: It doesn't make a difference if the baby is screened at 24 hours or 72 hours since Iowa Administrative Rules say screening can be done up to five days of age.

Prior to tandem mass spectrometry, the disorders screened on the heelstick panel all had a window of asymptomatic time from three to five days and treatment could be started at a week without significant problems. Now, with the addition of fatty acid oxidation defects, urea cycle disorders and organic acidurias, onset of symptoms can be faster with more signficant complications, as early as in the first 72 hours of life.[10] Thus, screening at 24 hours of age will allow for detection hopefully before metabolic decompensation, and allowing for early treratment with good outcomes. In Iowa with the use of the courier system and same day delivery, we can have results back to physicians within 24 hours, which will allow us to detect and start treatment much earlier.[11]

Myth 10: Thyroid screening on newborn screening is sensitive for all forms of congenital hypothyroidism.

In Iowa we only screen for TSH on the bloodspot. Thus, while the test is more specific for the majority of congenital forms of hypthyroidism, with fewer false positive results, some rare forms of hypothalamic-pituitary hypothyroidism may be missed.[12]

Myth 11: The newborn screen blood spot is only valid if done from a heelstick.

There are some differences in serum levels for the analytes on newborn screen if collected from heelstick vs. venous/arterial line, but the differences are unlikely to cause false negatives or false positive results. Heelstick is preferred, but sick and premature infants often have mutliple other factors and allowances can be made. If the line is cleared appropriately with 2-2.5mL of blood prior to collection, it should be a valid specimen. For further clarification, please see citation #3. However, umbilical cord blood is NEVER appropriate for the newborn screening bloodspot.

Myth 12: Infant has condition incompatible with life; therefore, no need to perform newborn screening.

The Iowa Administrative Rules specify that all infants born must have a newborn screen. The rules also specify that even infants with a condition incompatible with life need a newborn screen. The reason for this is more for future pregnancies and recurrence risk. In particular, a fetus with nonimmune hydrops may have a particularly severe hemoglobinopathy that would not be detected otherwise. Other instances are congenital malformations that may be completely unrelated, such as anencephaly but also has classic galactosemia. In this case, while the recurrence for the anencephaly is about 2 percent, the recurrence risk for galactosemia is 25 percent. So, getting a screen is important; however, timing may be a bit more problematic, but it should still be collected as close to 24 hours as possible. The specimen could even be from cardiac blood specimen.

Conclusion

Hopefully this will clarify some of the myths and misunderstandings about newborn screening. As noted above, there are several issues related to sick and premature infants that make getting an accurate specimen difficult. Currently the Clinical and Laboratory Standards Institute (CLSI) is compiling a recommendation related specifically to these infants. The recommendations will likely include several collection times, depending on specific reasons related to the condition of the infant and medical interventions. These time recommendations will probably be as outlined below:

1. Upon admission to the NICU or special care nursery to avoid complications related to transfusions
2. At 48-72 hours of age for the illnesses that require more rapid intervention
3. At 28 days of age or discharge for late elevations related to CH and CAH as well as some complications related to hyperalimentation

For further direction and information there are many good online resources. Below are two that can be good starting points and that have contact numbers and information for practitioners and the public.

http://www.idph.state.ia.us/genetics/manual_toc.asp

- This is the Iowa Department of Public Health practitioner's manual which will include Iowa specific testing rules.

http://genes-r-us.uthscsa.edu/

-National Newborn Screening and Genetics Resource Center has information on all of the state programs and is the most up-to-date resource currently available.

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Guidelines for Perinatal Services, 8th edition, 2008

The revised Guidelines for Perinatal Services has recently been published and distributed to hospitals. For individual physicians, nurses or nursing units who wish to have a copy, an electronic version can be found on the Iowa Department of Public Health/Statewide Perinatal Care Program website. **http://www.idph.state.ia.us/hpcdp/statewide_perinatal_care.asp**

Though there have been many updates to the 8th edition of the 2008 Guidelines, major additions include:

1. Revised guidelines for the use of Pitocin.
2. Inclusion of approved NICHD/AWHONN/ACOG nomenclature for electronic fetal monitoring.
3. Revised guidelines for HIV testing and treatment during pregnancy.
4. Guidelines for the screening of infants and women for perinatal illicit substance exposure.

Annual Iowa Conference on Perinatal Medicine

The 2008 Annual Iowa Conference on Perinatal Medicine was held April 9-10, 2008 at the West Des Moines Marriott Hotel. The conference was an overwhelming success with the largest number of physician and nurse participants in many years. Themes included *The Current and Future Role of Genetics in Medicine*, *Maternal Depression*, and *Care for the Obese Parturient*. A link to view the 2008 brochure that includes a complete list of conference topics can be found at the Statewide Perinatal Care Program website. **http://www.idph.state.ia.us/hpcdp/statewide_perinatal_care.asp**

Mark your calendars!

The 2009 Annual Iowa Conference on Perinatal Medicine will be held on **April 8-9, 2009 (Wednesday-Thursday)** at the West Des Moines Marriott Hotel. Please mark your calendars and plan to attend this important educational event designed to provide state-of-the-art information on obstetric and newborn care practices.

NOTE:

To be added to The Iowa Perinatal Letter mailing list contact Kathy Brogden via email at katherine-brogden@uiowa.edu or call 319-356-2637.

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