



Newborn Screening Newsletter



Dr. David Nickels and Staff

17-OHP Screening

By Dr. David Nickels, Endocrinologist

Newborn screening for congenital adrenal hyperplasia (CAH) in the state of Tennessee started in late 2000. Through the end of 2005, a total of 30 cases of CAH have been identified by the newborn screening system. Many of these infants would not have been diagnosed in a timely manner previously, and in these infants, early diagnosis by newborn screening has prevented severe adrenal crisis with its' resulting potential severe morbidity and mortality. Early diagnosis by newborn screening also helps to prevent incorrect gender assignment which can occur in severely virilized females who can sometimes be incorrectly assigned male gender by mistake.

Newborn screening for CAH is performed by measuring 17-OH progesterone (17OHP) on filter paper samples. In CAH due to 21 hydroxylase deficiency, which is the most common cause, the level of 17OHP is usually

quite elevated due to the inability to convert 17OHP to 11-deoxycortisol, and then to cortisol. Infants affected with classic CAH usually will have 17OHP levels over 90 ng/ml (9,000 ng/dl) measured by RIA, while normal infants have levels about 10-fold lower.

While CAH screening has clear-cut benefits for those infants diagnosed early, there are potential pitfalls to CAH screening also. A small percentage of infants affected with CAH can have normal initial screening (falsely normal screening test). This can occur for several reasons, including early discharge from the hospital, infant's mother being treated with certain steroid medications before delivery, lab error/specimen collection problem, or the presence of one of the other less common forms of CAH which does not result in severely elevated 17OHP levels. Even though these false negatives are not common (probably 5-10% of all cases of CAH), we all should keep this in mind when examining infants who have symptoms that could be consistent with CAH in the first weeks or months of life, even if their newborn screen was normal. (Continued on P.2)

Tertiary Centers

Newborn Screening Follow-up and Laboratory are considered fortunate to have accessibility to regional tertiary centers. All presumed positives are forwarded to the regional tertiary center that provides treatment for babies according to the baby's home county. For critical values, the tertiary centers are called and recommendations are received prior to calling those caring for the baby. Did you know that there is a genetic, endocrine and sickle cell center assigned for every county in Tennessee? When positives are called and additional information is needed, the tertiary

center listed can be a helpful resource. There will be times when a tertiary center will desire to see the baby and provide treatment. We appreciate them and consider them our community helpers!

17-OHP SCREENING con't

A potentially larger problem with CAH screening in newborns is the vexing issue of false positives, which are much more common than false negative screening tests. In the state of Tennessee, as well as other states, only about 1 out of every 30-50 abnormal CAH screening tests in newborns actually turns out to truly have CAH, meaning that the positive predictive value of an initial abnormal screening test is only 2-3%. The high rate of false positive screening tests occurs for several reasons. Most false positives are associated with prematurity. It is known that premature infants, especially below 32 weeks, often have elevated 17OHP values. False positives can also be seen in stressed or ill newborns of any gestational age. In addition, the assay procedure used for 17OHP testing on filter paper samples inherently seems to have more variability than some of the other newborn screens. Of course, any positive newborn screen, even in an ill premature infant, requires follow-up testing to rule-out the presence of CAH. Repeat screening samples are required as the infant grows, and sometimes additional testing sent to a reference lab along with ongoing monitoring of electrolytes are also required. The toll of false positive tests leads to increased cost of screening, and also can cause increased parental stress and anxiety while follow-up tests are pending. In addition, delays in diagnosis can lead to either unnecessary corticosteroid treatment or to delayed start of treatment.

The Tennessee newborn screening office is taking steps to reduce the number of false positive tests by making changes to the type of assay used to measure 17OHP. The new assay should be ready to go by late 2006, and it is hoped that the improved accuracy with the new assay will reduce the number of false positive reports. Also, by continuing to fine-tune the cut-offs for abnormal values based on birth weight

and gestational age, the number of false positives can continue to be reduced. Other steps are also being investigated, including the use of certain second-tier assays which could be done when the initial 17OHP is elevated, which may also assist with reducing the number of false positive sample reports.

Currently, 46 of the 50 states in the U.S. are screening for CAH. We in Tennessee should be proud of the fact that we were one of the earlier states to start CAH screening, and no doubt there have been lives saved in our state due to this screening program. The efforts of all caregivers in Tennessee in promptly responding to abnormal CAH screen reports, following the detailed instructions received on the screening test report, and consultation with your local pediatric endocrinologists when necessary will help to ensure that the infants entrusted to our care are diagnosed in a timely manner and that no infant with classic CAH will be missed.

State Laboratory Director

Please join us in welcoming Dr. David L. Smalley, Ph.D., M.S.S., BCLD, MT (ASCP) as the new Public Health Laboratory Director!

Remaining 2006 State Holidays

As listed below, there are several holidays remaining in 2006 when the Newborn Screening Office will be closed. When the office is closed, reports may still be obtained through the Voice Response System. If your physicians have not been registered to access the voice response system, please notify the office.

November 11, 2006 Veteran's Day

November 23, 2006 Thanksgiving Day (any additional Thanksgiving holidays TBD)

December 25, 2006 Christmas Day (any additional Christmas holidays TBD)

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