June 19, 2008

Newborn Screening Set to Expand

Beginning July 1, 2008, newborn screening in Arkansas will undergo a major expansion. In addition to the traditional screening for congenital hypothyroidism, galactosemia, and hemoglobinopathies, infants born here will now be screened for cystic fibrosis, congenital adrenal hyperplasia, biotinidase deficiency, and 20 metabolic disorders detectable through tandem mass spectrometry (MS/MS). Screening for PKU will now be conducted using MS/MS technology.

Screening for all of these disorders has been recommended by the American College of Medical Genetics and other groups. Arkansas is one of the last states to implement expanded newborn screening.

Collection of filter paper specimens will remain essentially unchanged, although the collection form (HL-11) has been modified somewhat. The amount of blood that needs to be collected will remain the same. The newborn screening fee has been increased to $89.25 to cover costs of the expansion.

The Department of Health has partnered with Arkansas Children’s Hospital (ACH), the University of Arkansas for Medical Sciences (UAMS), the March of Dimes, and other groups in order to make the transition to expanded screening as smooth as possible. Primary care physicians will continue to be notified of abnormal results as in the past, with recommendations for follow-up as always. Because parts of the screens for cystic fibrosis and congenital adrenal hyperplasia will be performed by the ACH laboratory, the PCP may at times be contacted by the newborn screening coordinator at ACH regarding abnormal results and suggested follow-up. The Department of Health, ACH, and UAMS have established protocols that ensure close communication among all involved parties.

Confirmatory testing for “presumed positive” results will be available through the ACH laboratory and certain commercial laboratories. In addition, contact information for relevant subspecialists at ACH will be provided on the interpretive materials that will accompany positive screening result reports.

The “new” disorders:

Cystic fibrosis (CF) is familiar to most clinicians. Early identification of affected infants through newborn screening has been found to improve nutritional and pulmonary outcomes, and to reduce hospitalizations and even mortality. Screening will consist of an initial immunotrypsin (IRT) level performed at ADH, which if elevated will be followed by DNA mutation analysis at ACH. Infants with either one or two CF mutations will need further evaluation by a pediatric pulmonologist and usually a sweat test, which will be arranged through the ACH newborn screening coordinator.

Congenital adrenal hyperplasia (CAH) is caused in most cases by a deficiency of the 21-hydroxylase enzyme complex. Affected female infants are typically highly virilized, sometimes to the point of ambiguous genitalia, and thus are usually detected clinically at birth. Male infants, however, usually
display no obvious clinical abnormalities at birth. Whether male or female, about two-thirds of 21-hydroxylase-deficient patients are “salt-wasters” due to inadequate mineralocorticoid (e.g. aldosterone) production. Salt-wasting infants are at risk of presenting in the first 1-2 weeks of life with poor feeding, vomiting, weight loss and dehydration which can progress rapidly to shock and death if not treated appropriately. Lab findings for ill salt-wasters would include a low serum sodium (often <120) and high potassium (often >7.0). Aggressive re-hydration and institution of cortisone and mineralocorticoid supplements are life-sustaining interventions for such affected infants.

Screening for CAH will consist of an initial 17-hydroxyprogesterone (17-OHP) level, which if elevated will be followed by a more in-depth steroid panel (using the same initial filter paper specimen) at ACH. Normally the PCP will be notified by the ACH coordinator only after results from the steroid panel are found to be positive. However, in some cases the ADH newborn screening nurse may contact the PCP to report extremely high initial 17-OHP values that warrant at least clinical assessment of the infant even before steroid panel results are available.

**Biotinidase deficiency** causes seizures, developmental delay, hypotonia, ataxia, hearing loss, and severe seborrheic dermatitis. These problems can be prevented with oral biotin supplementation. Screening consists of qualitative enzyme assay; positive results require quantitative assay.

Disorders detectable by MS/MS include **amino acid disorders, organic acidemias, and fatty acid oxidation defects.** The most common amino acid disorder is PKU. Others to be screened for include maple syrup urine disease, homocystinuria, tyrosinemia type 1, argininosuccinic aciduria, and citrullinemia. Nine organic acidemias will be screened for, all of which are relatively rare. These include glutaric acidemia type 1, 3-hydroxy-3-methylglutaric acidemia, 3-methylcrotonyl-CoA carboxylase deficiency, beta-ketothiolase deficiency, multiple carboxylase deficiency, propionic acidemia, methylmalonic acidemia-mutase deficiency, methylmalonic acidemia-cobal A,B defect, and isovaleric acidemia. The organic acidemias tend to present early in life with poor feeding, vomiting, lethargy, which may progress to coma and death if not recognized and treated appropriately. Early consultation with a metabolic geneticist is necessary when presumed positive screening results are obtained for any of the above conditions.

Fatty acid oxidation defects to be screened for include medium chain acyl-CoA dehydrogenase (MCAD) deficiency, very long chain acyl-CoA dehydrogenase deficiency, long chain hydroxyacyl-CoA dehydrogenase deficiency, trifunctional protein deficiency, and carnitine uptake defect. Of these, MCAD is the most common, with an incidence similar to that of PKU. Infants with these defects tend to manifest symptoms (vomiting, lethargy, hypoglycemia) in the context of fasting or acute infectious illness, due to their inability to oxidize fats for “fuel” when glucose reserves are exhausted. Symptom onset, while variable, may be as early as the first weeks of life. Heart, skeletal muscle, and liver may also be affected in these conditions. Avoidance of fasting, often coupled with carnitine and other dietary supplements, have proven effective in many cases.

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