NEBRASKA

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DEPT. OF HEALTH AND HUMAN SERVICES

Congenital Adrenal Hyperplasia Information

Congenital Adrenal Hyperplasia or CAH, is a group of autosomal recessive genetic conditions. The Nebraska Newborn Screening Program screens for the most common form of CAH which is due to 21-hydroxylase deficiency. In its severest form, CAH is a life threatening disorder affecting 1:15,000 newborn infants worldwide. It is caused by a defect in the gene coding for the enzyme steroid 21-hydroxylase, important to cortisol and aldosterone production and without which adrenal insufficiency results. There are generally three classes of CAH. These are CAH salt-wasting or salt-losing, CAH simple virililizing, and non-classical CAH. Patients with CAH have insufficient cortisol and aldosterone, and overproduction of the androgens.

Clinical Features:

TEST RESULTS	LIKELY CAUSES	ACTIONS TO TAKE WHEN POSITIVE RESULT FOUND
"Critical" Elevated 17-OHP	CAH salt-wasting CAH simple virilizer CAH non-classical False Positive Prematurity	Term babies: emergency protocol (see ACT sheet), NICU babies monitor electrolytes and await extracted 17-OHP results

"Inconclusive" Elevated 17OHP, and elevated extracted 17-OHP	CAH salt-wasting CAH simple virilizer CAH non-classical False Positive	Collect and test repeat dried blood spot filter paper specimen
	Prematurity	

Girls may have ambiguous genitalia. Symptoms of adrenal insufficiency include: emesis, excessive weight loss relative to birth weight, diaphoresis, hyperventilation, pallor, dry mucosa and lethargy. A salt-wasting crises can develop rapidly, and emergency medical management is indicated. Non-classical or simple virilizing patients are at less risk of neonatal adrenal crisis, but have other complications associated with the hormonal imbalance, such as precocious puberty, advanced bone age, and short stature for which monitoring and treatment by a pediatric endocrinologist is recommended.

Laboratory Tests:

The laboratory uses a radio-immunoassay to look for elevated levels of 17-alpha hydroxyprogesterone(17-OHP). Cut-offs for normal reference ranges are birth weight adjusted as premature infants typically present with higher levels than term babies of 17-OHP. Two sets of cut-offs are used: one for "Critical" or alert levels, with corresponding urgent followup action recommendations, and the other for "inconclusive" elevations that are not normal, but not as immediately concerning. For this latter group, repeat dried blood spot filter paper testing is recommended. For both the critical and inconclusive results, a second tier test using an organic extraction step to assay 17-OHP is done in an attempt to reduce the false positive rate especially associated with prematurity. **17-hydroxyprogesterone activity in Premature Infants**

It is not uncommon for 17 hydroxyprogesterone to be elevated in premature infants. Therefore birth weight adjusted cut-offs for normal reference ranges are used to reduce the false positive rate associated with testing 17-OHP in this group. Furthermore the newborn screening laboratory reflexes to a second tier test for those with elevated 17OHPs. The second tier test is an organic extracted assay designed to remove several of the interferences commonly associated with specimens from premature babies.

Confirmation and Treatment:

Critical or Alert level findings suggest the patient should have a clinical evaluation immediately. Specimens should be collected and tested include electrolytes done immediately, and a steroid profile as recommended by a pediatric endocrinologist. **These specimens need to be collected first before administering any treatment/ medications to avoid masking the disorder on confirmatory tests.** If the newborn presents signs of adrenal crisis, IV glucose/saline and hydrocortisone should be administered upon consultation with a pediatric endocrinologist. Referral to pediatric endocrinology is recommended for all patients confirmed with CAH.

Screening Practice Considerations:

Detection of CAH does not depend on nutritional factors. A blood transfusion may alter

the values; therefore **THE NEWBORN SCREENING SPECIMEN SHOULD ALWAYS BE COLLECTED PRIOR TO A BLOOD TRANSFUSION.**