CONGENITAL ADRENAL HYPERPLASIA (CAH)

Congenital adrenal hyperplasia (CAH) consists of a group of disorders arising from specific defects in the enzymes of the adrenal cortex required for the biosynthesis of adrenal corticosteroids. The most common form results from 21-hydroxylase deficiency, which accounts for more than 90% of all recognized cases. This form can be detected by neonatal screening and is the condition addressed in this fact sheet. The defect results in increased androgen production, which is responsible for the ambiguous genitalia observed in affected female infants and for the physical signs of androgen excess that will later develop in untreated/inadequately treated males and female infants. In the most severely affected female newborn, the fetal adrenal androgens may masculinize the external genitalia to the extent that an incorrect male sex assignment is made. In approximately 75% of affected newborn boys, a life threatening “salt-losing syndrome”, may be the only clinical finding leading to the correct diagnosis. Treatment prevents acute adrenal insufficiency by replacing the deficient steroid hormones, prevents the long-term consequences of excess virilization, advanced bone maturation leading to precocious puberty, and adult short stature by suppressing the excess adrenal androgens. Screening in Connecticut was instituted in October of 1997.

GENETIC BASIS
- Autosomal recessive condition - Recurrence risk is 25%
- 90% of cases caused by 21-hydroxylase deficiency
- Prenatal and genetic testing may be determined through HLA typing and DNA analysis.

CT PREVALENCE  1:32,930

CLINICAL FEATURES OF UNTREATED DISEASE
Severity
- Physical disabilities: masculinization of female genitalia, accelerated early growth, short stature, adrenocortical insufficiency, hyperpigmentation
- Developmental disabilities: infrequent, but may occur from salt-losing crisis and shock
- Mortality: newborn adrenal crisis can cause death; 9% mortality

Symptomatic diagnosis
A symptomatic diagnosis at birth is easier for females born with ambiguous genitalia. Males usually do not show initial outward signs of CAH making symptomatic diagnosis difficult. Of major concern are those newborns who also have a defect in their ability to synthesize aldosterone and may die in the newborn period from shock caused by salt wasting.

Variants
Children with less severe CAH disorders may not present until later in childhood with physical signs of androgen access such as rapid growth, associated with accelerated skeletal maturation, and early onset of pubic hair.

CLINICAL OUTCOME WITH SCREENING AND TREATMENT
Early diagnosis and treatment is directed at preventing life threatening salt wasting crisis in infants with the most severe disorder and lead to correct sex identification. It also allows the early institution of treatment to replace the deficient hormones and suppress the elevated androgens.

INTERVENTIONS
Consultation at one of the Endocrinology Regional Treatment Centers at Connecticut Children’s Medical Center or Yale is recommended. Treatment with glucocorticosteroids serves the dual purpose of replacing cortisol and suppressing excessive corticotropin production. Patients with loss of salt and elevated plasma renin activity should receive mineralocorticoid therapy and may need supplemental salt intake in addition to hydrocortisone. The dose of glucocorticosteroids should be appropriately increased for stress or illness.

1/19/2005
SCREENING FOR CAH

Laboratory tests
- Test for level of enzymatic activity of 17-hydroxyprogesterone (17-OHP) in 21-hydroxylase deficiency on filter paper blood specimen utilizing fluorometric immunoassay.

ABNORMAL TEST RESULTS

<table>
<thead>
<tr>
<th>Birth Weight &lt; 1700 grams</th>
<th>Birth Weight &gt; 1700 grams</th>
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</thead>
<tbody>
<tr>
<td>Presumptive positive &gt; 150 ng/ml</td>
<td>Presumptive positive &gt; 100 ng/ml</td>
</tr>
<tr>
<td>Borderline 130 – 150 ng/ml</td>
<td>Borderline 65 – 100 ng/ml</td>
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- The primary care provider is notified by the DPH, Genetic NBS Tracking Unit nurse consultant of all presumptive positive results.
- A referral is made by the DPH, Genetic NBS Tracking Unit nurse consultant to one of the Endocrinology Regional Treatment Centers at CCMC or Yale.
- The primary care provider will be advised by the DPH, Genetic NBS Tracking Unit nurse consultant to contact the Endocrinology Regional Treatment Center to make a prompt referral and arrange for confirmation testing and evaluation.
- DPH, Genetic NBS Tracking Unit nurse consultants notify the primary care provider’s office of borderline results and the need to obtain a second specimen.

The information provided is offered for general informational and educational purposes only. It is not offered as and does not constitute medical advice. In no way are any of the materials presented meant to be a substitute for professional medical care or attention by a qualified practitioner, nor should they be construed as such. Contact your physician if there are any concerns or questions.