

HORMONE AND ENZYME DISORDERS

Primary Congenital Hypothyroidism (CH)

Primary congenital hypothyroidism (CH) occurs when the thyroid gland fails to produce thyroxine (T4), a hormone necessary for proper central nervous system development. Deficiency of thyroid hormone in an infant usually results in mental retardation and poor growth. The most common causes are total or partial failure of the gland to develop (aplasia or hypoplasia) or development of the gland in an abnormal place (ectopic gland).

Inheritance:	Most cases of primary CH not genetic
Estimated Incidence:	1:4000
Abnormal Screen Result:	Elevated TSH
Method of Notification:	All results where the TSH is ≥ 40 μ IU/mL called to provider of record. Lower elevations of TSH are mailed to provider of record.
Next Steps if Abnormal:	Repeat as soon as possible on filter paper. Consider serum thyroid function tests and referral to pediatric endocrinologist if TSH is ≥ 40 μ IU in first specimen. If TSH is still abnormal on repeat filter paper testing, refer to pediatric endocrinologist for further evaluation.
Neonatal Presentation:	None
Treatment:	Thyroxine replacement medication

Special Considerations

***Other forms of hypothyroidism*—Newborn screening will not identify other forms of hypothyroidism such as transient hypothyroidism, central hypothyroidism and/or TBG deficiency. Physicians must remain alert to clinical signs of other forms of hypothyroidism in infants despite normal TSH screening results.**

Specimen Collection in the First 24 Hours of Life—Interpretation of TSH result is more difficult if the specimen is collected within the first 24 hours of life. This is due in part to the physiologic surge in TSH shortly after birth.

Formula type—Infants diagnosed with primary congenital hypothyroidism should not be routinely fed soy based infant formula. It is thought that soy binds with thyroxine replacement medication and slows its absorption.

Later Developing Primary Congenital Hypothyroidism—The vast majority of infants with primary congenital hypothyroidism are detected on the first specimen even if it is collected within the first 24 hours of life. However, in a few cases primary congenital hypothyroidism develops in the weeks after the initial screening test would have been collected. **Physicians must remain alert to clinical signs of primary congenital hypothyroidism in older infants despite normal initial screening results.**

Congenital Adrenal Hyperplasia (CAH)

Congenital adrenal hyperplasia (CAH) is an enzyme defect which affects the functioning of the adrenal cortex. A metabolic block produces varying degrees of insufficiency of corticosteroids (cortisone and aldosterone) and an excess of male sex hormones. Females have ambiguous or male-like genitalia and will undergo increasing masculinization if untreated. Infants with the salt-losing form of the disorder can develop an acute crisis with failure to thrive, dehydration and shock in the first month of life. Untreated males may present with precocious puberty at 3 to 5 years of age, and untreated females may be virilized. Androgenic compounds also cause accelerated early growth with premature fusion of the epiphyses and ultimate short stature.

Inheritance:	Autosomal recessive
Estimated Incidence:	1:16,000
Abnormal Screen Result:	Elevated 17-OH progesterone
Method of Notification:	All results where the 17-OH progesterone is ≥ 48 ng/mL in infants with birth weights ≥ 2500 g are called to provider of record. All results where the 17-OH progesterone is ≥ 130 ng/mL in infants with birth weights < 2500 g are called to the provider of record. Any other abnormal 17-OH progesterone results are mailed to provider of record.
Next Steps if Abnormal:	Potential medical emergency. See infant as soon as possible to ascertain health status. Consult pediatric endocrinologist for further instructions. Repeat 17-OH progesterone as soon as possible on filter paper. Initiate treatment and diagnostic evaluation as recommended by specialist.
Neonatal Presentation:	Females may have ambiguous genitalia.
Treatment:	Replacement of the deficient hormones. If the infant does not have the salt-losing form of CAH, only glucocorticoid (cortisone) is required. For infants with the salt-losing form of CAH, mineralocorticoid (aldosterone) is required in addition to cortisone. Increased dosages of medications are usually required in times of stress, trauma, illness or surgery.

Special Considerations

Specimen Collection in the First 24 Hours of Life—Interpretation of 17-OH progesterone result is more difficult if the specimen is collected within the first 24 hours of life. This is due in part to the physiologic surge in 17-OH progesterone shortly after birth.

Premature/Sick Infants—A large percentage (relative to the overall birth population) of infants with abnormal 17-OH progesterone results are premature and/or sick infants. This is a physiologic response to the stress of prematurity and illness.

Biotinidase Deficiency

Biotinidase is a key enzyme in the biotin cycle. Biotinidase releases biotin from dietary proteins and recycles biotin. Free biotin is necessary for activation of four carboxylase enzymes. Carboxylases are important enzymes in the metabolism of amino acids, in gluconeogenesis, and in the synthesis of fatty acids. Infants who have untreated biotinidase deficiency may develop hypotonia, seizures, developmental delay, ataxia, breathing problems, hair loss and hearing loss. Screening may also identify infants with partial biotinidase deficiency.

Inheritance:	Autosomal recessive
Estimated Inheritance:	1:60,000
Abnormal Screen Result:	Deficient Biotinidase
Method of Notification:	All abnormal test results are called to provider of record.
Next Steps if Abnormal:	Repeat biotinidase as soon as possible on filter paper. See infant as soon as possible to ascertain health status. If biotinidase is still deficient on repeat testing, consult pediatric metabolic specialist for further instructions. Initiate treatment and diagnostic evaluation as recommended by specialist.
Neonatal Presentation:	Usually none. However, some affected infants has presented as early as one week of age.
Treatment:	Daily biotin supplements for life.

Special Considerations

Transfusion—Transfusion of red blood cells prior to drawing the newborn screening specimen may affect the biotinidase result. Repeat screening for biotinidase should be done 120 days after the last transfusion. If the date of the last transfusion is unknown, put the date of hospital discharge on the collection form next to “Transfused” .