

Panhypopituitarism

CAUSES OF HYPOPITUITARISM

To determine a specific cause for the hypopituitarism, a head MRI (with intravenous administration of contrast dye) must be performed. A CAT scan does not provide the same degree of resolution. Causes of congenital (from birth) hypopituitarism that can be detected by MRI include a transected or interrupted hypothalamic-pituitary stalk and various “midline defect syndromes” (groupings of medical problems involving structures in the middle of the brain, such as septo-optic dysplasia, in which there may be absence of the midline brain structure known as the septum pellucidum and underdevelopment of the optic nerves associated with variable degrees of reduced vision). Causes of acquired hypopituitarism that can be detected by MRI include tumors in the hypothalamic-pituitary region, the most common one of which in childhood is a craniopharyngioma. If there are no associated radiological abnormalities, the hypopituitarism is said to have an idiopathic basis.

EXTENT OF HYPOPITUITARISM

To characterize the extent of the hypopituitarism, appropriate testing for all clinically relevant pituitary hormones needs to be undertaken. GH is the most commonly affected pituitary hormone in childhood hypopituitarism. Thus, the initial clue to the diagnosis of hypopituitarism is almost always short stature and slow growth, testing for which then confirms the diagnosis of GH deficiency and begins the process of investigation for other hormonal deficiencies.

Deficiency of TSH causes central hypothyroidism (thyroid hormone deficiency). Unlike children whose hypothyroidism is due to thyroid gland damage, those with hypopituitarism typically have somewhat higher thyroid hormone levels and, thus, may have little or no symptoms, but sometimes present, like those patients with primary thyroid disease, with short stature and slow height velocity, relative weight excess, constipation, dry skin, and fatigue. A low total and/or free thyroxine (T_4) level with a normal or low TSH level confirms the diagnosis of central hypothyroidism.

Younger children with deficiencies of the gonadotropins (luteinizing hormone = LH and follicle-stimulating hormone = FSH) show no abnormalities as, prior to puberty, these levels are normally very low. In contrast, older, adolescent-aged children with deficiencies of the gonadotropins present with failure to start or continue with puberty (breast development and menstrual periods in girls and enlargement of the penis and testicles in boys). During this age period, low levels of LH and FSH, along with a pelvic ultrasound in females that shows prepubertal-sized ovaries and uterus, may be diagnostic.

Loss of ACTH causes adrenal insufficiency (cortisol deficiency). This is the most likely hormone, if deficient, to place a child in a life-threatening situation. While there would likely be no symptoms under normal circumstances, except maybe mild fatigue, lack of ACTH and cortisol in the setting of infection, fever, surgery, etc., may cause vomiting, dehydration, shock, and even death. It is, therefore, imperative to have this hormonal system evaluated. Testing usually requires some sort of stimulation, such as with insulin, metyrapone, or low-dose ACTH.

ADH (also known as vasopressin) from the posterior or rear portion of the pituitary gland, if deficient, causes central or neurogenic diabetes insipidus (DI). Infants and toddlers manifest diabetes insipidus with excessively wet diapers. If unrecognized and, hence, untreated, in this age group, dehydration with elevated salt (sodium) concentrations in the blood ensues, as young children cannot report and easily satisfy heightened thirst. Older children with DI typically present with excessive day- and night-time urination, new onset of bed-wetting, and increased thirst. DI most often occurs unintentionally as a result of surgical treatment of a hypothalamic-pituitary tumor. In some cases, DI is temporary due to surgical swelling, but it will be permanent if surgical sacrifice close to the hypothalamus was required for complete cure of a brain tumor in the vicinity.

TREATMENT AND FOLLOW-UP OF PANHYPOPITUITARISM

If an underlying cause for the child's hypopituitarism is found on the head MRI, directed therapy should be undertaken. For example, if a tumor is found, referral to a pediatric neurosurgeon is the first step. Similarly, if hydrocephalus (increased fluid build-up in the brain) is noted, the neurosurgeon needs to place a shunt to drain the extra fluid. In most cases, however, the treatment, while life-saving, does not reverse the hypopituitarism.

The management of childhood hypopituitarism is best supervised by a pediatric endocrinologist. The treatment of GH deficiency consists of replacement of GH by daily injection with a needle or pen system. A long-acting, once- or twice-monthly formulation has recently been approved by the FDA. Other delivery systems, such as intranasal administration, are being developed. The adequacy of treatment is generally determined by quarterly height measurements (using special measuring equipment known as a stadiometer) in the endocrinologist's office.

Treatment of central hypothyroidism entails once-daily oral administration of oral levo-thyroxine (brand name or generic). The adequacy of treatment can generally be determined by annual measurements of total or free T4 (not TSH).

For older children, with proven deficiencies of gonadotropins, sex steroid replacement is required. In females, this consists of estrogen (oral or patch) and progesterone (oral) and, in boys, testosterone either as a long-acting shot in younger or older boys or as a patch or gel in older boys. The adequacy of treatment is best determined by clinical response and, in the case of testosterone replacement in males, by periodic blood testosterone measurements.

For treatment of adrenal insufficiency, oral hydrocortisone is given either two or three times daily and affected (older) child must wear Medic-Alert identification. The adequacy of treatment is best determined by general health as there are no specific

blood tests for this purpose. To prevent an adrenal crisis secondary to unanticipated stress or illness, these doses should be doubled or tripled. Lastly, there should also be an injectable form of hydrocortisone available in the home. Children with DI should be treated with either oral (pills) or intranasal DDAVP (either as a metered-pulse spray or as a solution given by rhinal tube into the nose). The adequacy of treatment is best determined on clinical grounds (i.e., frequency of urination); occasionally measurements of serum sodium can be helpful, especially in younger children.

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The MAGIC Foundation is a national nonprofit organization created to provide support services for the families of children afflicted with a wide variety of chronic and/or critical disorders, syndromes and diseases that affect a child's growth. Some of the diagnoses are quite common while others are very rare.

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