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Managing panhypopituitarism in adults

By Fay Mitchell-Brown, PhD, RN, CCRN, and Rose Stephens-DiLeo, SN

LR, 56, WAS ADMITTED to a rural acute care hospital with a diagnosis of pneumonia. As a child of 6, he'd undergone surgery and radiation therapy to treat a malignant anterior pituitary gland tumor. This resulted in a deficiency of all anterior pituitary gland hormones. Called panhypopituitarism, this disorder includes deficiencies in growth hormone, thyroid-stimulating hormone, and adrenocorticotropic hormone.

Both authors cared for LR during this admission. Using his case as an example, the authors will discuss the pathophysiology of panhypopituitarism, significant diagnostic studies, and treatment related to this disorder. Identifying details have been changed to maintain patient confidentiality.

Two components

The pituitary gland has two components, the anterior pituitary (adenohypophysis) and posterior pituitary (neurohypophysis).[1,2] (See *Pituitary anatomy and physiology.*) The anterior pituitary receives signals from the hypothalamus that either stimulate or inhibit secretion of pituitary hormones. These hormones are then secreted directly into the systemic circulation to act on target organs. The level of pituitary hormones in the blood influences the release of pituitary hormones through a negative feedback mechanism (see *Hypothalamic-pituitary control of hormone levels*). The pituitary gland has been called the master gland because its hormones control the

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functions of many target glands and cells.

The anterior pituitary gland contains five cell types:[2]

- thyrotrophs, which produce thyrotropin, or thyroid-stimulating hormone (TSH)
- corticotrophs, which produce corticotropin, or adrenocorticotropic hormone (ACTH)
- gonadotrophs, which produce the gonadotropins, follicle-stimulating hormone (FSH), and luteinizing hormone (LH)
- somatotrophs, which produce somatotropin, or growth hormone (GH)
- lactotrophs, which produce prolactin.

The posterior pituitary doesn't synthesize hormones. Antidiuretic hormone (ADH) and oxytocin are synthesized in the cell bodies of neurons in the hypothalamus that have axons that travel to the posterior pituitary, where these hormones are stored and released (see *Major actions of select hormones*).[1,2]

Decreased hormonal secretion

Hypopituitarism refers to decreased secretion of one, a few (isolated or partial hypopituitarism), or all the anterior pituitary hormones, which is known as panhypopituitarism.[1,2] A rare disorder, panhypopituitarism affects fewer than 200,000 patients in the United States according to the National Institutes of Health.[3]

Panhypopituitarism can result from diseases of the hypothalamus or pituitary gland:[4,5]

- Diseases of the hypothalamus include traumatic brain injury, stroke, tuberculous meningitis, and benign tumors that arise in the hypothalamus, such as craniopharyngiomas, and malignant tumors that metastasize to the hypothalamus, such as lung and breast cancers.
- Diseases of the pituitary gland include infections, infarction, pituitary adenomas, pituitary surgery (such as pituitary adenoma excision), and radiation therapy of pituitary adenoma.

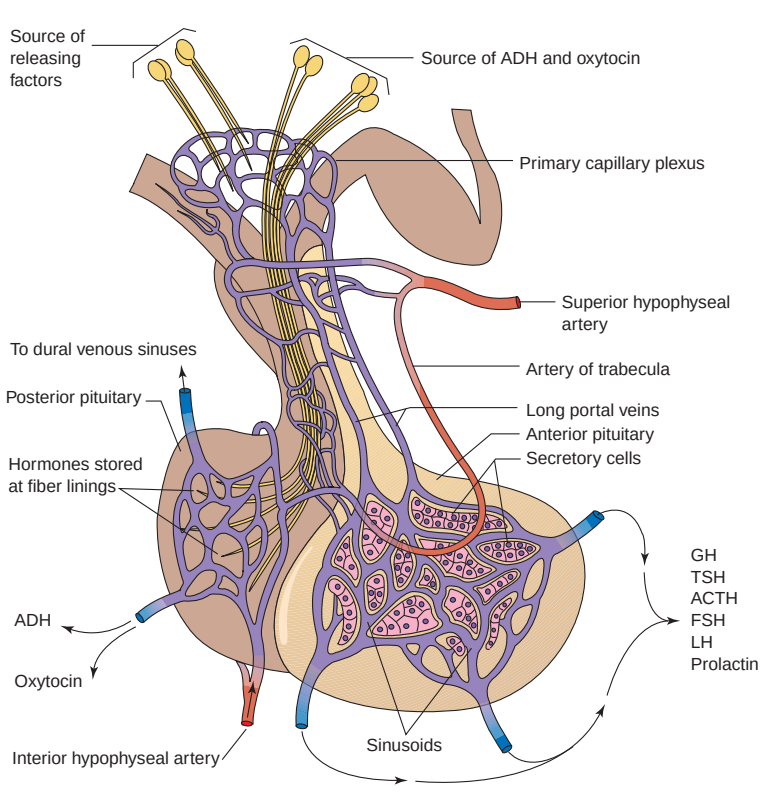
The excision of a pituitary tumor and radiation therapy placed LR at risk for panhypopituitarism due to damage of the pituitary gland and resulting deficiency of anterior pituitary hormones. Although the hypothalamus may still attempt to control the level of pituitary hormones by releasing and inhibiting hormones, the anterior pituitary can't respond appropriately. This means that blood levels of anterior pituitary hormones—FSH, LH, ACTH, TSH, GH, and prolactin—become deficient. Similarly, damage to the posterior pituitary gland inhibits the release of oxytocin and ADH.[1]

Clinical manifestations

Signs and symptoms of anterior pituitary deficiencies can range from mild to severe, depending on how many hormones are affected and whether the disorder develops rapidly or slowly.[1,6]

- ACTH deficiency. The presentation of ACTH deficiency reflects the resulting cortisol deficiency. When cortisol release is inhibited by lack of stimulation from ACTH, gluconeogenesis is decreased and the inflammatory response becomes exaggerated. Inhibition of gluco-

Pituitary anatomy and physiology[11]



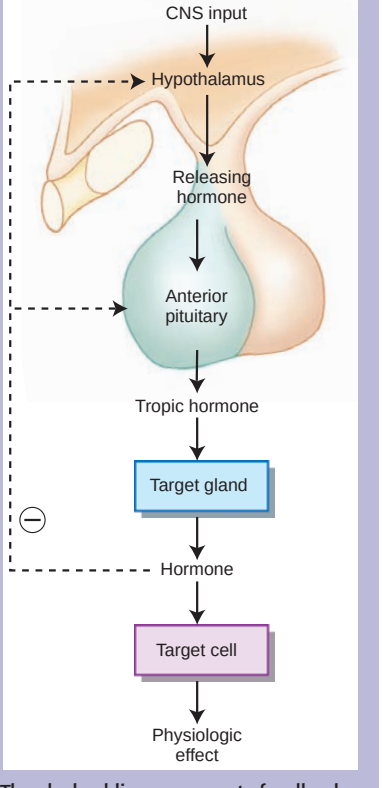
The hypothalamic releasing or inhibiting hormones are transported to the anterior pituitary through the portal vessels. Antidiuretic hormone (ADH) and oxytocin are produced by nerve cells in the supraoptic and paraventricular nuclei of the hypothalamus and transported through the nerve axon to the posterior pituitary, where they're released into the circulation.

neogenesis results in hypoglycemia. Signs and symptoms of hypoglycemia include palpitations, nervousness, shakiness, anxiety, diaphoresis, hunger, pallor, and visual disturbances. However, LR didn't exhibit any signs or symptoms of hypoglycemia.

An exaggerated inflammatory response related to a cortisol deficiency can also increase vulnerability to infection.[1] LR's pneumonia was probably related to a cortisol deficiency.

Because ACTH is necessary to maintain peripheral vascular tone, a severe deficiency can lead to death from vascular collapse. Postural hypotension and tachycardia are possible signs of a less severe ACTH deficiency.[6]

Hypothalamic-pituitary control of hormone levels[12]



The dashed line represents feedback control.

The level of pituitary hormones in the blood influences the release of pituitary hormones through a negative feedback mechanism.

- TSH deficiency. Signs and symptoms include fatigue, cold intolerance, anorexia, constipation, facial puffiness, dry skin, bradycardia, delayed relaxation phase of the deep tendon reflexes, and anemia, although some patients with TSH deficiency have few or no symptoms.[6]
- GH deficiency. Signs and symptoms in adults may include an increase in fat body mass in relation to lean body mass, dyslipidemia, increased inflammatory markers, and increased biochemical markers of endothelial dysfunction. GH deficiency has been associated with decreased quality of life and increased mortality.[6]
- Gonadotropin deficiency. Deficient secretion of FSH and LH results in hypogonadotropic hypogonadism (secondary hypogonadism) in both women and men.

In men, this results in testicular hypofunction, infertility, and decreased testosterone secretion, leading to decreased energy and libido. Women may experience menstrual irregularities and changes in secondary sex characteristics such as decreased breast size.[1,6]
- Prolactin deficiency. The inability to lactate after childbirth is the only known clinical manifestation of prolactin deficiency.[6]

At the time the authors cared for LR, a diagnosis of panhypopituitarism had been made. His history indicated that he'd experienced several chronic physiologic consequences, including adrenal insufficiency, hypothyroidism, developmental delay, hydrocephalus, dyslipidemia, mild hyponatremia, chronic anxiety, seizure disorder, depression, and chronic fatigue.

Life-threatening complication

Adrenal crisis (acute cortisol insufficiency) is a life-threatening complication of panhypopituitarism. Signs and symptoms of adrenal crisis include fever, weakness, confusion, hypotension, tachycardia, vomiting, diarrhea, abdominal pain, hyponatremia, hyperkalemia, and hypoglycemia. Hypotension can lead to shock.[1] Because adrenal crisis is life-threatening, it must be identified and treated promptly. If hypothyroidism occurs concurrently with adrenal crisis, glucocorticoid replacement should be provided before thyroid hormone replacement because of the increased metabolic demand for cortisol.[7]

Diagnostic studies

Diagnostic tests for panhypopituitarism include magnetic resonance imaging (MRI) and computed tomography (CT). Brain MRI is considered the radiologic study of choice for identifying a pituitary tumor; however, head CT with or without a contrast medium can also reveal tumors.[1]

Hormonal studies should be performed in pairs of target gland and their respective stimulatory pituitary hormone for proper interpretation, as follows:[8]

- ACTH stimulation test (or morning cortisol and ACTH)
- TSH and thyroxine
- FSH, LH, and either estradiol (if amenorrheic) or morning testosterone (as appropriate for sex)
- prolactin
- GH provocative test.

Because LR had previously been diagnosed with panhypopituitarism, no further diagnostic testing was required for his endocrine disorder. He was transferred to the ICU for treatment of pneumonia, which required a higher level of care. After responding well to treatment, LR was transferred to the stepdown unit.

Management of panhypopituitarism

Medications play an important role in the treatment of panhypopituitarism; patients require lifetime hormone replacement therapy unless the underlying etiology can be reversed. These patients may be generally asymptomatic, but they require increased doses of glucocorticoids before and/or during any stressful event, emotional or physical. Physical stressors include fever, influenza, tooth extraction, and rigorous activity, with infection being the most common stressor.[1] Patients should be taught the signs and symptoms of infection as well as those of hormone deficiencies, and told to notify the healthcare provider about potential problems as soon as possible so that medications can be adjusted.

LR's medications during this hospitalization included the following:

- levothyroxine, a synthetic thyroxine (T4) hormone that exerts the same physiologic effect as endogenous T4, maintaining normal T4 levels when a deficiency is present.[9]
- I.V. hydrocortisone, an anti-inflammatory glucocorticoid used to treat secondary adrenal insufficiency caused by panhypopituitarism.[10]
- I.V. vancomycin and micafungin to treat pneumonia.

Nursing implications

Patient education is an important part of nursing care for patients with panhypopituitarism. Nurses need to teach patients about the pituitary gland and the crucial role pituitary hormones play in homeostasis. Emphasize the need for lifelong hormone replacement therapy,

Major actions of select hormones[13]

Source	Hormone	Major actions
Hypothalamus	Corticotropin-releasing hormone (CRH), thyrotropin-releasing hormone (TRH), growth hormone–releasing hormone (GHRH), gonadotropin-releasing hormone (GnRH)	control release of pituitary hormones
	Somatostatin	inhibits growth hormone (GH) and thyroid-stimulating hormone (TSH)
Anterior pituitary	GH	stimulates growth of bone and muscle, promotes protein synthesis and fat metabolism, decreases carbohydrate metabolism
	Adrenocorticotropic hormone (ACTH)	stimulates synthesis and secretion of adrenal cortical hormones
	TSH	stimulates synthesis and secretion of thyroid hormone
	Follicle-stimulating hormone (FSH)	*Female:* stimulates growth of ovarian follicle, ovulation *Male:* stimulates sperm production
	Luteinizing hormone (LH)	*Female:* stimulates development of corpus luteum, release of oocyte, production of estrogen and progesterone *Male:* stimulates secretion of testosterone, development of interstitial tissue of testes
	Prolactin	prepares female breast for breastfeeding
Posterior pituitary	Antidiuretic hormone (ADH)	increases water reabsorption by kidney
	Oxytocin	stimulates contraction of pregnant uterus, milk ejection from breasts after childbirth.

increased glucocorticoid replacement preceding and/or during stressful events, and prompt medical attention as appropriate. Tell them that regular follow-up visits with a healthcare provider are essential to ensure adequate hormone replacement and to prevent excessive hormone replacement. Encourage all patients to wear a medical-alert tag.[1]

Patients need to understand that panhypopituitarism is a chronic disorder that can increase their risk for infection, hospitalization, and death. Treatment that focuses on replacing the deficient hormones reduces these risks.

LR's discharge instructions included education about the importance of taking prescribed medications as directed to help balance hormone levels. His nurses emphasized the need to follow up with his healthcare provider as directed to ensure proper responses to medications.

By understanding the functions of pituitary hormones and the pathophysiology of panhypopituitarism, nurses can prepare themselves to give patients like LR the best possible care. ■

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