Physiology of the pituitary, thyroid, parathyroid and adrenal glands

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Abstract

Endocrinology is the study of hormones, endocrine glands and related diseases. Understanding basic hormonal physiology is essential for surgeons to manage patients with endocrine disorders. In this article we present the fundamental physiological mechanisms related to pituitary, thyroid, parathyroid and adrenal hormonal production, secretion and action. Moreover the methods used in the investigation for hormonal disturbances associated with these glands, resulting in excess or deficient secretion, are introduced.

Keywords Adrenal; endocrinology; parathyroid; physiology; pituitary; thyroid

Hormones are chemical messengers with specific target organs and actions. If the site of action is distant to the place of secretion, they are known to act as 'endocrine'. 'Paracrine' is if they act on adjacent sites. Meanwhile, when they act on the same cell that secreted the hormones, it is called 'autocrine'.

Hormones can be divided in to five main types according to the chemical composition and this governs the basic physiological characteristics of the hormone (Table 1).

The fifth type of hormone is eicosanoids, such as prostaglandins. They are derived from arachidonic acid. They mainly act locally in paracrine or autocrine fashion.

The pituitary

The anatomy and embryology

The pituitary gland is divided into anterior and posterior portions (Figure 1), with distinct embryology, anatomy, and function. The anterior pituitary (adenohypophysis) arises from Rathke's pouch from the oral cavity, and the posterior pituitary (neurohypophysis) arises from neural ectoderm at the floor of the forebrain. Rathke's pouch differentiates into three parts — the pars distalis, pars intermedia and pars tuberalis which together form the anterior pituitary.

The anterior pituitary lacks a major direct arterial blood supply, but is bathed in a dense capillary network of pituitary portal blood. This makes the anterior pituitary more liable to infarction in hypotension, e.g. Sheehan's syndrome. This portal system has a high concentration of hypothalamic peptides which control secretion of hormones from the anterior pituitary. The portal venous system drains to the petrosal sinuses and then to the internal jugular veins.

These can be accessed in petrosal sinus sampling used for localization of functional pituitary tumours.

The posterior pituitary has direct arterial supply from the inferior hypophyseal artery. Direct relationship with the systemic circulation makes the posterior pituitary more prone to systemic tumour metastasis when compared to the anterior pituitary. Because of this, in pituitary metastasis, diabetes Insipidus (DI) is more common than anterior pituitary hormone deficiencies.

The anterior pituitary contains different groups of cells that produce specific hormones (Table 2).[1] The posterior pituitary contains nerve terminals originating in the nuclei of hypothalamus.

Anterior pituitary hormones

Growth Hormone (GH): GH is synthesized in somatotroph cells of the anterior pituitary. It is a 191 amino acid single-chain polypeptide and has a half-life of about 14 minutes. GH is secreted in a pulsatile manner with about ten pulses a day. Between the pulses, GH levels can be undetectable in a normal person. Table 3 illustrates factors that govern GH secretion.

GH acts by binding to a specific cell membrane receptor. This results in activation of JAK and STAT proteins by dimerization and phosphorylation. Finally, the STAT proteins translocate to the nucleus leading to transcription of specific genes (Figure 2).

GH has direct action and indirect actions via insulin-like growth factor- I (IGF-1). Direct effects of GH include production of IGF-1 in the liver, lipolysis and decreased glucose utilization in the tissues. Indirect effects include growth of cartilage, bone and synthesis of muscle protein. The action on growth plate is also primarily mediated via IGF-1. Insulin-like growth factor binding protein-3 (IGFBP-3) binds IGF-I increasing its half-life. In children, IGFBP-3 is used as a marker for GH deficiency.

GH status can be assessed by GH levels, IGF-1 levels or IGFBP levels. As random levels of GH are misleading, dynamic tests are performed using factors that stimulate or inhibit GH secretion. Stimulatory tests for GH deficiency could be done by stimulation with insulin, glucagon and arginine, and inhibitory tests for GH excess can be done with oral glucose tolerance test (OGTT). There are many factors leading to discrepancies between GH level and IGF-1 levels. In addition, interpretation of IGF-1 level should be done with care as it is significantly affected by the biochemical assay method used for lab analysis.

Insulin regulates the expression of the GH receptor (GHR) in the liver causing increase in IGF-I, whereas oestrogen has been shown to inhibit Janus kinase/signal transducer leading to low IGF-I levels.

Following treatment of acromegaly, IGF-1 levels take longer to drop compared to GH level due to its long half-life.[2]

Obesity is associated with reduced GH levels but despite that, the IGF-1 levels remain normal. It has been hypothesized that this is due to up regulation of GH receptors in the liver.[3]

Insulin, IGF-1 and IGF-2 have similar structures. Thus, at high levels, cross reaction between receptors can occur. In severe insulin resistance, extremely high levels of insulin can act on IGF-1

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Basic characteristics of hormones

	Amines	Peptides	Steroids	Iodothyronines
Transport in plasma	Soluble	Soluble	Insoluble — need transport proteins	Insoluble — need transport proteins
Half-life	Short	Short	Long — due to protein binding	Long — due to protein binding
Hormone receptor	Cell surface cannot diffuse through membrane	Cell surface cannot diffuse through membrane	Intracellular as lipid soluble	Intracellular as lipid soluble
Examples	Adrenaline Noradrenalin Dopamine	Anterior pituitary Hormones PTH Angiotensin-II	Vitamin D Gonadal steroids corticosteroids (cortisol)	Levothyroxine Liothyronine

Table 1

Structure of the pituitary

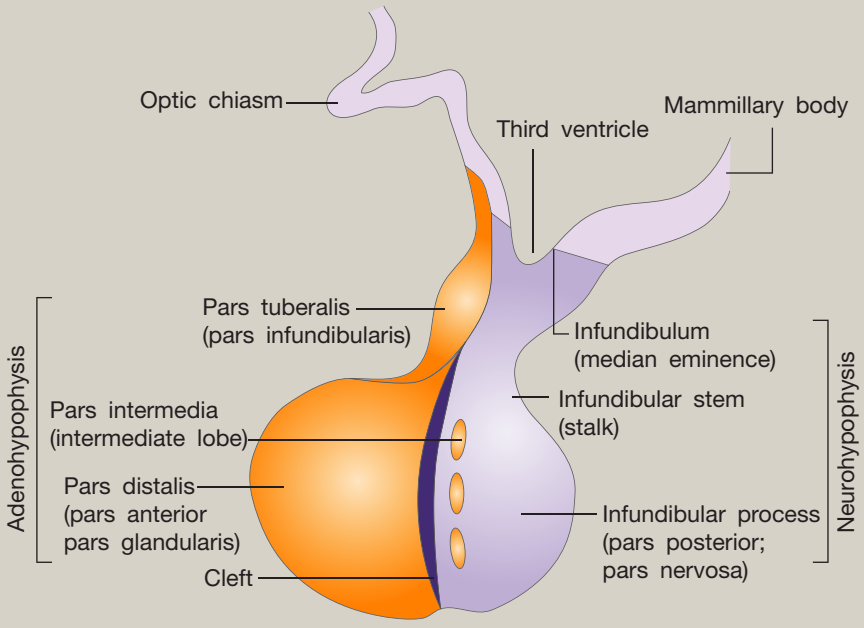

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Figure 1

receptors leading to phenotypical features of acromegaly, pseudo acromegaly. The affinity of IGF-1 to insulin receptors is low thus, hypoglycaemia is not seen with high IGF-1. Conversely, IGF-2 can act on insulin receptors causing hypoglycaemia. IGF-2 is secreted by various neoplasms (e.g. sarcomas).

Prolactin (PRL) is a peptide hormone and half life is about 30–60 minutes.[1] It is secreted by lactotrophs (L) of the anterior pituitary gland under control of the hypothalamus. PRL secretion has diurnal variation with a peak level in the late-night/early morning hours. Dopamine is the main regulator, but a number of physiological and pathological conditions can affect the serum prolactin level. Physiological factors include pregnancy, intercourse, nipple stimulation and stress. Drugs such as neuroleptics, anti-depressants, dopamine receptor antagonists, opiates, some antihypertensives, OCP and H2 receptor blockers can raise prolactin level. Other pathologies that can affect serum prolactin include prolactin secreting pituitary tumours, hypothalamic pathology, cranial irradiation, hypothyroidism, chronic renal and liver disease, burns and trauma.

PRL acts on a cell membrane receptor activating the JAK/STAT pathway. Its main action is to promote lactation. High levels of PRL dampens down GnRH pulses causing suppression of gonadotropins and sex hormones leading to menstrual irregularities, loss of libido, erectile dysfunction and secondary osteoporosis. PRL testing is done by random sampling. Dynamic studies are usually not required.

Adrenocorticotrophic hormone (ACTH) is derived from a larger amino acid precursor, pro-opiomelanocortin (POMC), released

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