ENDOCRINE PHYSIOLOGY

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Key to terms used

ADH	Antidiuretic Hormone	T_3	Tri-iodothyronine
GH	Growth Hormone	T_4	Thyroxine
GHRH	GH Releasing Hormone	GHRIH	GH Releasing Inhibiting Hormone
LH	Luteinising Hormone	DDAVP	Desmopressin
TSH	Thyroid Stimulating Hormone	FSH	Follicular Stimulating Hormone
ACTH	Adrenocorticotrophic Hormone	CRH	Corticotrophic Releasing Hormone

INTRODUCTION

The endocrine system acts through chemical messengers, hormones, to coordinate many bodily functions. It maintains the internal environment (homeostasis), controls the storage and utilisation of energy substrates, regulates growth and reproduction and, perhaps of greatest importance to anaesthetists, controls the body's responses to external stimuli, particularly stress.

This paper will concentrate on basic physiology of the principle endocrine glands, the pituitary, thyroid, and adrenal glands. Other endocrine glands include the pancreas, which has been dealt with in a recent paper on diabetes [*Clinical Management of Diabetes Mellitus during Anaesthesia and Surgery, Update in Anaesthesia 2000; 11: 65-73*], the hypothalamus, parathyroids and gonads. In addition, the liver, kidney, lungs, gastrointestinal tract, pineal gland and thymus produce many other hormone-like substances.

THE PITUITARY GLAND.

Anatomy

The pituitary gland lies within a dural covering in a depression of the skull base (sella turcica). On each side lies the cavernous sinus containing the carotid arteries and the III, IV and VI cranial nerves. The pituitary gland is attached to the hypothalmus in the floor of the third ventricle by the pituitary stalk (infundibulum), which passes though an aperture in the fold of dura mater forming the roof of the sella turcica (diaphragma sellae).

The pituitary gland is made up of 2 parts: **The posterior lobe** (neurohypohysis) is the expanded inferior end of the infundibulum, and is developed embryologically from the brain. The infundibulum contains axons of neurones from the supraoptic and paraventricular nuclei of the hypothalamus which terminate on the surface of capillaries in the posterior lobe onto which they secrete the two posterior pituitary hormones, antidiuretic hormone (ADH) and oxytocin.

The anterior lobe (adenohypophysis) is much larger then the posterior lobe, and itself consists of 3 parts which partly surround the posterior lobe and the infundibulum (figure 1). The distal part forms most of the anterior lobe. The intermediate part, a thin sheet of non-functional glandular tissue and a narrow cleft separates the anterior lobe from the posterior lobe. The infundibular part of the anterior lobe is a narrow upward projection which partially encircles the infundibulum.

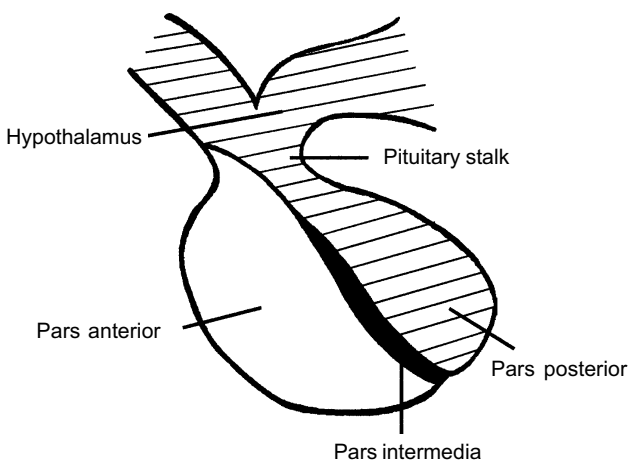

Figure 1. The pituitary gland

The blood supply to the pituitary gland is by twigs from the internal carotid and anterior cerebral arteries. The anterior lobe also receives venous blood from the hypothalamus via the **hypothalamo-hypophyseal portal system** of veins (figure 2), which transmits releasing factors to the pituitary from the lower tip of the hypothalamus. The veins of the pituitary drain into the cavernous sinuses.

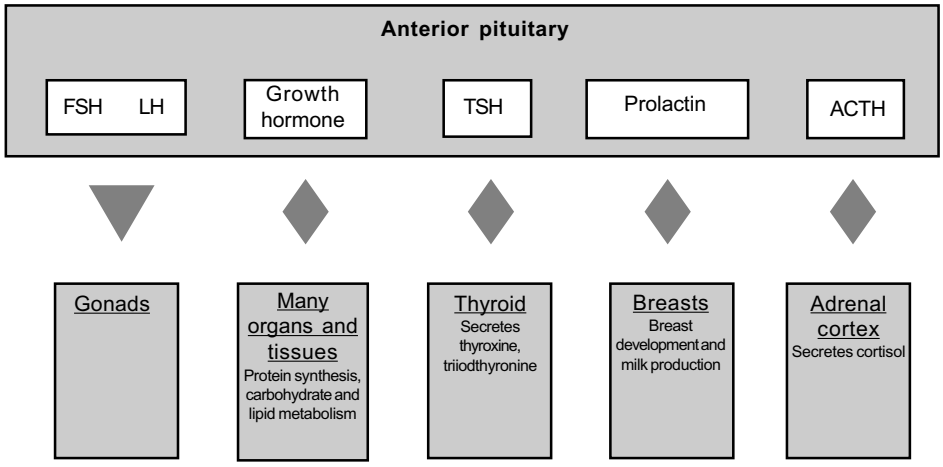

Figure 3. The widespread effects of the pituitary gland

Human anterior pituitary cells have traditionally been classified according to their staining characteristics into chromophobes, acidophils or basophils. With more modern techniques of immunochemistry and electron microscopy, it is now possible to distinguish 5 cell types: somatotropes, which secrete growth hormone (GH); lactotropes, which secrete prolactin; thyrotropes, which secrete thyroid stimulating hormone (TSH); gonadotropes, which secrete luteinizing hormone (LH) and follicle-stimulating hormone (FSH); and corticotropes, which secrete adreno-corticotropic hormone (ACTH). They control a wide range of functions (figure 3). There are also functionally inert cells within the gland known as null cells.

Control of pituitary secretion by the hypothalamus

Almost all hormone secretion by the pituitary is controlled by either hormonal or nervous signals from the hypothalamus. The hypothalamus receives signals from almost all possible sources in the nervous system, and is itself under **negative feedback** control (figure 4) from the hormones regulated by the pituitary gland. This means that when there is a low level of hormone in the blood supplying the hypothalamus, it produces the appropriate releasing hormone or factor which stimulates the release of the hormone by the pituitary and this in turn stimulates the target gland to produce and release its hormone. As a result, the blood level of that hormone rises and inhibits the secretion of releasing hormone or factor by the hypothalamus.

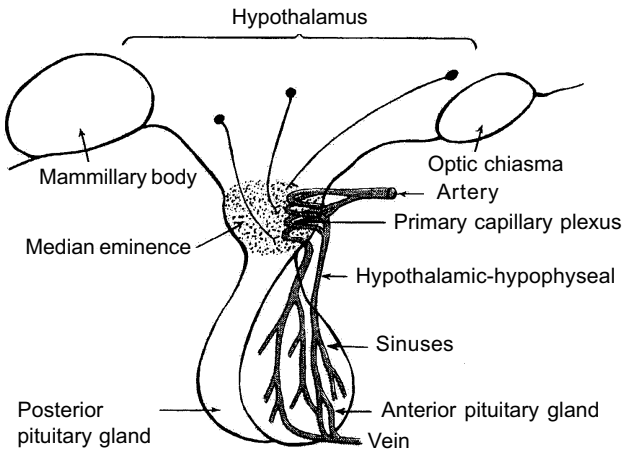

Figure 2. The hypothalamic-hypophyseal portal system

Secretion from the posterior pituitary is controlled by nerve fibres arising in the hypothalamus which pass along nerve axons and terminate on blood vessels in that part of the gland.

Secretion from the anterior pituitary is controlled by hormones called **hypothalamic releasing** and **hypothalamic inhibitory hormones** (or factors) carried from the hypothalamus to that part of the gland by the hypothalamo-hypophyseal portal system. These hormones act on the glandular cells of the anterior pituitary to regulate their secretion.

Hormones of the anterior pituitary gland

Growth Hormone

Effects

1. Promotes the growth of bone, cartilage and soft tissue via the effects of insulin-like growth factor, IGF-1, (formerly known as somatomedin C) whose production is increased in the liver, kidney and other tissues in response to GH. If excess GH levels are present before fusion of the epiphyses occurs, **gigantism** occurs. After the epiphyses are closed, linear bone growth is no longer possible and excess GH leads to **acromegaly**.

There are a number of problems which are described briefly in Box 1.

- Increases the rate of protein synthesis in all cells of the body,
- Fat mobilisation by release of fatty acids from adipose tissue.
- Decreases the rate of glucose utilisation throughout the body due to diminished uptake of glucose by cells (i.e. it is counter-regulatory to insulin).
- Increased hepatic glucose output.

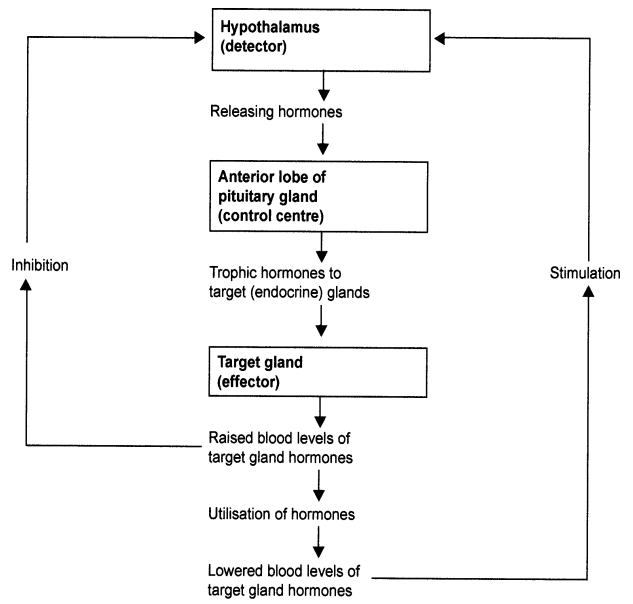

Figure 4. Negative feedback regulation of secretion of hormones by the anterior lobe of the pituitary gland

- Stimulates erythropoiesis.
- Na^+ and K^+ excretion are reduced, while Ca^{++} absorption from the intestine is increased.

Regulation

GH release from the anterior pituitary is under the control of the hypothalamus which secretes both a releasing hormone (growth hormone releasing hormone - GHRH) and an inhibitory hormone (growth hormone release-inhibiting hormone - GHRIH, or somatostatin) into the hypothalamo-hypophyseal portal system. GH and IGF-1 produce negative feedback effects on the hypothalamus and pituitary.

The stimuli that increase GH secretion fall into 3 general categories:

- Hypoglycaemia and fasting
- Increased amounts of certain amino acids in the plasma
- Stressful stimuli

Secretion of GH is reduced in response to increased concentrations of glucose, free fatty acids or cortisol in the plasma, and is also reduced during rapid eye movement sleep.

Prolactin

Effects

Prolactin stimulates secretion of milk and has a direct effect on the breast immediately after parturition. Together with oestrogen and progesterone, prolactin initiates and maintains lactation.

Regulation

Secretion is tonically inhibited by the release of dopamine from the hypothalamus into the hypothalamo-hypophyseal portal system. Prolactin secretion can be intermittently increased by release of prolactin releasing hormone from the hypothalamus, such as when the baby suckles the breast.

Thyroid Stimulating Hormone

Effects

Increases all the known activities of the thyroid glandular cells with increased production and secretion of thyroxine (T_4) and triiodothyronine (T_3) by the thyroid gland. Persistently elevated levels of TSH leads to hypertrophy of the thyroid with increased vascularity.

Regulation

TSH is produced and released from the anterior pituitary in response to thyrotropin releasing hormone released from the hypothalamus and carried to the pituitary via the hypothalamo-hypophyseal portal system. The hypothalamus can also inhibit TSH secretion via the effects of released somatostatin, in the same way that GH inhibition occurs. Free T_3 and free T_4 in the plasma exert a negative feedback effect on the hypothalamus and the pituitary to regulate the circulating levels of these hormones.

Box 1. Outline of anaesthetic problems associated with pituitary surgery for acromegaly

PROBLEM	MANAGEMENT
Overgrowth of the mandible, pharyngeal and laryngeal structures which may lead to difficult airway maintenance and intubation, and sleep apnoea with its complications	Careful pre-operative assessment. Consider tracheostomy under local anaesthesia or fibreoptic intubation
Cardiomyopathy with cardiac enlargement leading to congestive cardiac failure.	Cardiovascular assessment including ECG and chest X-ray. Medical management of hypertension prior to surgery.
Impaired glucose tolerance	Regular assessment of blood glucose. May require peri-operative insulin therapy

Follicle stimulating hormone and Luteinizing hormone

Effects

In men, FSH stimulates spermatogenesis by the Sertoli cells in the testis. In females, FSH causes early maturation of ovarian follicles.

In men, LH causes testosterone secretion by the Leydig cells in the testis. In females, LH is responsible for the final maturation of ovarian follicles and oestrogen secretion from them.

Regulation

In males and females, LH and FSH production by the anterior pituitary is regulated by release of gonadotropin releasing hormone from the hypothalamus, which is carried to the pituitary in the hypothalamo-hypophyseal portal system. Feedback effects of testosterone, oestrogen and inhibin (produced in the testes and ovaries in response to FSH stimulation) on the hypothalamus and anterior pituitary regulates the levels of circulating LH and FSH.

Adrenocorticotropic hormone (ACTH)

ACTH is formed in the anterior pituitary by enzymatic cleavage of the prohormone pro-opiomelanocortin (POMC). This polypeptide is hydrolysed in the corticotropes to produce ACTH and β-lipotrophin (β-LPH). Some of the β-LPH is split to produce β-endorphin. The anterior pituitary secretes all 3 hormones - ACTH, β-LPH and β-endorphin. The physiologic role of β-LPH is unknown, β-endorphin is an endogenous opioid peptide.

Effects

ACTH stimulates the production of cortisol (hydrocortisone) and androgens from the zona fasiculata and zona reticularis of the adrenal cortex. ACTH also acts on the cells in the zona glomerulosa to enable them to produce aldosterone in response to increased potassium ion concentration, elevated angiotensin levels or reduced total body sodium.

Regulation

ACTH is secreted from the anterior pituitary in response to the production of corticotropin releasing hormone (CRH) from the hypothalamus, which is carried to the pituitary along the hypothalamo-hypophyseal portal system (figure 5). Excitation of the hypothalamus by any type of stress causes release of CRH, leading to secretion of ACTH from the anterior pituitary and subsequent release of cortisol from the adrenal cortex. There is direct feedback of the cortisol on the hypothalamus and anterior pituitary gland to stabilise the concentration of cortisol in the plasma.

Hormones of the posterior pituitary gland

Antidiuretic hormone (ADH) is formed primarily in the supraoptic nuclei of the hypothalamus, while **oxytocin** is formed primarily in the paraventricular nuclei. Both hormones are transported from the hypothalamus to the posterior pituitary along axons in the infundibulum. Under resting conditions, large quantities of both hormones accumulate in the endings of the nerve fibres in the posterior pituitary. Excitatory nerve impulses in these fibres from their relevant nuclei cause release of the hormones with their subsequent absorption into adjacent capillaries.

Antidiuretic hormone

Effects

ADH promotes water retention by the kidneys by causing increased permeability of the collecting ducts to water, and its subsequent reabsorption from the tubular fluid *(Physiology of the Kidney, Update in Anaesthesia 1998; No 9:24-28)*

Regulation

ADH is secreted in response to increased plasma osmolality, decreased extracellular fluid volume, pain and other stressed states, and in response to certain drugs including morphine and barbiturates. ADH secretion is inhibited by alcohol.

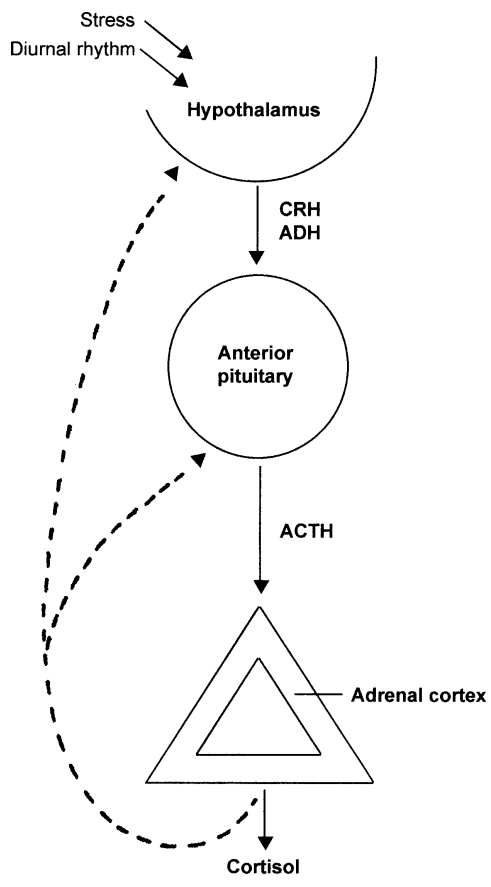

Figure 5. Control of glucocorticoid function

Oxytocin

Effects

- Contraction of the pregnant uterus.
- Contraction of the myoepithelial cells in the lactating breast, causing ejection of milk out of the alveoli into the milk ducts and thence out of the nipple.

Regulation

Oxytocin secretion is increased during labour. Descent of the fetus down the birth canal initiates impulses in the afferent nerves that are relayed to the hypothalamus, causing release of oxytocin, which enhances labour. During suckling, touch receptors in the nipple of the breast transmit signals that terminate in the hypothalamus resulting in release of oxytocin to eject milk.

THE THYROID GLAND.

Embryology

The thyroid develops from the floor of the pharynx between the first and second pharyngeal pouches. It grows caudally as a tubular duct which eventually divides to form the isthmus and lobes. The thyroglossal duct extends from the foramen caecum, in the floor of the mouth, to the hyoid bone. The pyramidal lobe of the thyroid develops from the distal part of the duct. Aberrant thyroid tissue, eg a lingual thyroid, may develop from persistent remnants of the thyroglossal duct.

Anatomy

Although the term *thyroid* is derived from the Greek word meaning shield, the gland is most commonly described as 'butterfly' shaped. The thyroid gland lies in the neck related to the anterior and lateral parts of the larynx and trachea. Anteriorly, its surface is convex; posteriorly, it is concave. It is composed of two lobes joined by an isthmus (figure 6). The isthmus lies across the trachea anteriorly just below the level of the cricoid cartilage. The lateral lobes extend along either side of the larynx as roughly conical projections reaching the level of the middle of the thyroid cartilage. Their upper extremities are known as the upper poles of the gland. Similarly, the lower extremities of the lateral lobes are known as the lower poles. The gland is brownish- red due to a rich blood supply.

Histology

Each lobe is composed of spherical follicles surrounded by capillaries. The follicles comprise a single layer of epithelial cells forming a cavity that contains colloid where the thyroid hormones are stores as thyroglobulin. C-cells, which secrete calcitonin, are found outside the follicles.

Synthesis and transport of thyroid hormones

Dietary iodide is concentrated by the thyroid gland and is oxidised, in the follicle cells, to iodine. The iodine is linked to tyrosine molecules in thyroglobulin, a large protein synthesised by the follicular cells into the cavity (figure 7). Iodinated tyrosine is coupled to form tri-iodothyronine (T_3) and thyroxine (T_4) which are then released into the circulation. Anti-thyroid drugs block

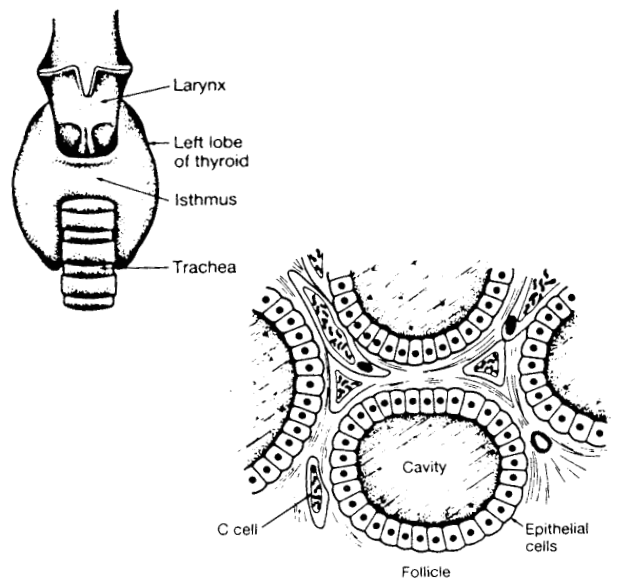

Figure 6. The thyroid gland

the synthesis of T_3 and T_4 by interfering with various steps of this process, for example, carbimazole blocks oxidation of iodide and iodination of tyrosine. All the steps in the synthesis of thyroid hormones are stimulated by thyroid stimulating hormone (TSH) secreted from the anterior pituitary gland.

T_4 is transported in the blood bound to plasma proteins, mainly T_4-binding globulin and albumin. T_3 is less firmly bound to plasma proteins than T_4. Thyroid hormones are broken down in the liver and skeletal muscle and while much of the iodide is recycled some is lost in the urine and faeces. There is a need, therefore, for daily replacement of iodide in the diet. The half-life of T_4 is 7 days and the half life of T_3 is 1 day.

Control of thyroid hormone secretion

There are two main factors controlling secretion of thyroid hormones. The first is autoregulation of the thyroid which adjusts for the range of iodide in the diet. The other is the secretion of TSH by the anterior pituitary. Other compounds may play a regulatory role such as neurotransmitters, prostaglandins and

Box 2. Hormonal problems occurring during pituitary surgery

1. Continue pre-operative hormone replacement therapy into the operative and post-operative period. Additional intravenous hydrocortisone (100mg IV) should be given at induction. Post-operative assessment by endocrinologist to determine duration of steroid replacement and need for thyroxine replacement. If medical hormonal assessment is unavailable, some authorities recommend the following regimen:-
   - 50mg hydrocortisone 12 hourly for 24 hours
   - 25mg hydrocortisone 12 hourly for 24 hours
   - 20mg hydrocortisone am 10 mg hydrocortisone pm
2. Post operative diabetes insipidus due to reduced production of ADH from the posterior pituitary following surgery
3. Careful assessment of post-operative fluid balance. Administration of DDAVP may be required. Patients are very sensitive, use 0.04 mcg IV in the acute phase, usual dose 0.1mcg as required

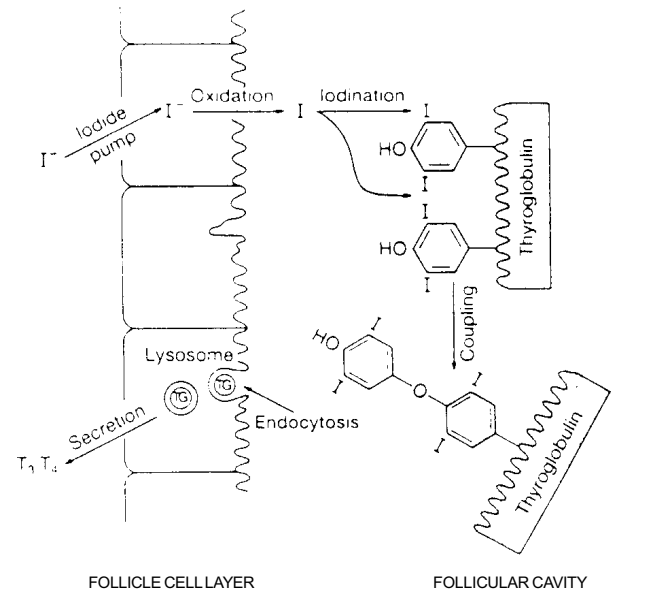

Figure 7. Synthesis of thyroid hormones (T_3, T_4) and their storage in association with thyroglobulin secretion

growth factors but their physiological relevance remains to be demonstrated.

Iodide supply is monitored through its effects on the plasma level of thyroid hormone and in the thyroid itself, where it depresses the response of the thyroid cells to TSH. Large doses of iodine inhibit the release of thryoglobulin bound hormones and thereby reduce the vascularity of the gland. For this reason, iodine was given to hyperthyroid patients before surgery.

Thyroid hormone plasma levels and action are monitored by the supraoptic nuclei in the hypothalamus and by cells of the anterior lobe of the pituitary. Thyrotrophin-releasing hormone (TRH) is transported from the hypothalamus to the pituitary via the hypophyseal portal vessels and stimulates the secretion of TSH. Rising levels of T_3 and T_4 reduce the secretion of TRH and TSH - negative feedback mechanism (figure 8)

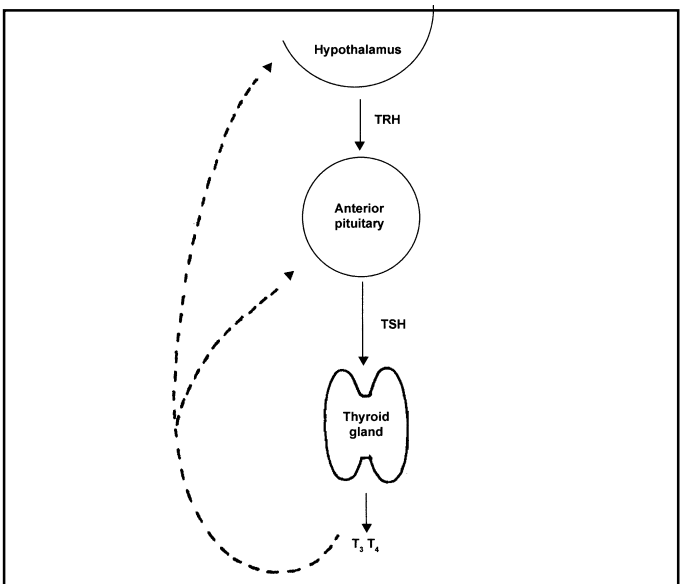

Figure 8. Control of thyroid secretion

Actions of thyroid hormones

Thyroid hormones exert their effects by binding to specific receptors, in the nuclei of cells in target tissues. They are involved in metabolism, thermogenesis, growth, development and myelination in childhood.

Oxidative metabolism, basal metabolic rate and therefore heat production is stimulated by T_3 and T_4. They are essential for normal growth in childhood and neonatal deficiency results in severe mental retardation (cretinism). Classical symptoms and signs of hypothyroidism include cold intolerance, lethargy, obesity, hoarseness, bradycardia and a low metabolic rate. Overproduction of thyroid hormones results in hyperthyroidism which is characterised by heat intolerance, loss of weight, hyperexcitability, tachycardia and exophthalmos. An enlarged thyroid gland, or goitre, may be associated with hyperthyroidism (Graves' disease) and retrosternal extension of the goitre may cause tracheal compression.

ADRENAL PHYSIOLOGY

The adrenal glands are complex multi-functional organs whose secretions are required for maintenance of life. Failure of the adrenal glands leads to derangement in electrolyte and carbohydrate metabolism resulting in circulatory collapse, hypoglycaemic coma and death.

Each adrenal gland is situated on the superior aspect of each kidney and consists of two endocrine organs (figure 9). The inner adrenal medulla is mainly concerned with the secretion of the catecholamines epinephrine (adrenaline), norepinephrine (noradrenaline), and dopamine in response to nerve impulses that pass along the preganglionic sympathetic nerves. The outer cortex secretes the steroid hormones, the glucocorticoids, mineral-ocorticoids and the sex hormones.

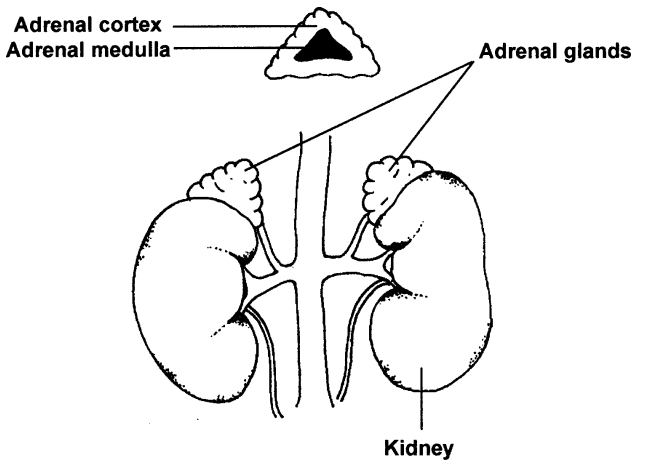

Figure 9. The adrenal glands

The adrenal cortex and medulla have separate embryological origins. The medullary portion is derived from the chromaffin ectodermal cells of the neural crest, which split off early from the sympathetic ganglion cells, while cells of the adrenal cortex are derived principally from coelomic mesothelium.

The adrenal glands are very vascular, the arterial blood supply coming from branches of the renal and phrenic arteries and the aorta. The medulla receives blood from the cortex rich in corticosteroids, which regulate the synthesis of the enzymes that converts norepinephrine to epinephrine. Venous drainage is mainly via the large adrenal vein into either the renal vein or inferior vena cava.

Adrenal Medulla

The adrenal medulla is a modified sympathetic ganglion made up of densely innervated granule containing cells and constitutes about 30% of the mass of the adrenal gland. Approximately 90% of cells are epinephrine secreting cells while the other 10% are mainly the norepinephrine secreting cells. It is still unclear as to which type of cells secrete dopamine. Small collections of chromaffin cells are also located outside the medulla, usually adjacent to the chain of sympathetic ganglia.

Synthesis

The pathways for the biosynthesis of dopamine, norepinephrine and epinephrine are shown in figure 10. They are stored in membrane-bound granules and their secretion is initiated by the release of acetylcholine from sympathetic nerve fibres that travel in the splanchnic nerves. Catecholamines have an extremely short half-life in the plasma of less than 2 minutes. Clearance from the blood involves uptake by both neuronal and nonneuronal tissues where they are either recycled or degraded by either monoamine oxidase or catechol-O-methyltransferase. About 50% of the secreted catecholamines appear in the urine as free or conjugated metanephrines and normetanephrines and about 35% as vanillymandelic acid (VMA).

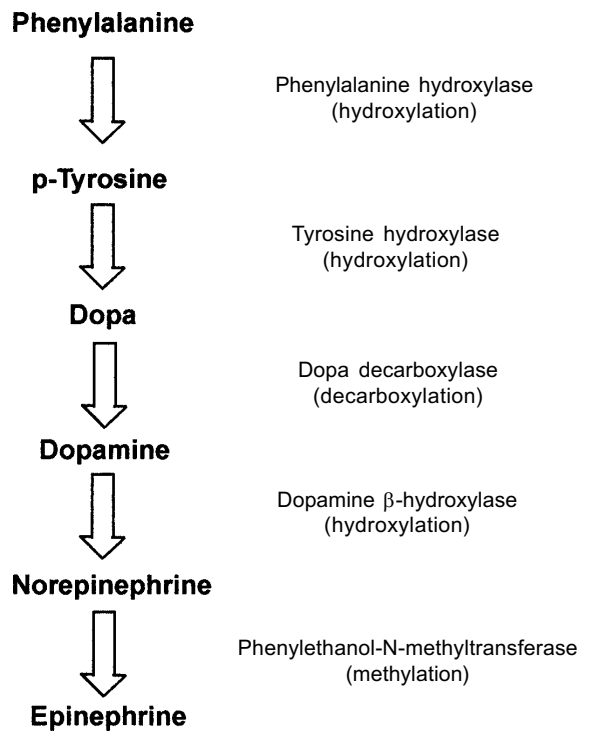

Figure 10. Catecholamine synthesis

Effects

The actions of norepinephrine and epinephrine are numerous and complex and depend on their binding to α (α_1, α_2) and β (β_1, β_2) adrenergic receptors while dopamine also acts at specific dopaminergic receptors (*The Autonomic Nervous System, Update in Anaesthesia 1995; No 5:3-6*). The individual actions at these receptors are beyond the scope of this article. They mimic the effects of noradrenergic nervous discharge, stimulate the nervous system, and exert metabolic effects that include glycogenolysis in the liver and skeletal muscle, mobilisation of free fatty acids, increase plasma lactate and increase the metabolic rate. Norepinephrine causes a marked increase in peripheral vascular resistance as a result of widespread vasoconstriction, while epinephrine causes vasoconstriction in skin and viscera but vasodilatation in skeletal muscle so that total peripheral resistance may decrease. While the direct effect of both is an increase in heart rate, the administration of norepinephrine results in reflex bradycardia due to the marked increase in peripheral resistance and mean arterial pressure. They increase alertness, although in humans epinephrine frequently evokes anxiety and fear.

Control of adrenal medullary secretions

Catecholamine secretion is low in basal states and is further reduced during sleep. Secretion is initiated by sympathetic activity controlled by the hypothalamus and occurs in response to pain, anxiety, excitement, hypovoleamia and hypoglycaemia. With emergency stimulation you get diffuse medullary secretion preparing the person for the fight or flight response.

Disorders of adrenomedullary function

Phaeochromocytomas arise from chromaffin cells in the adrenal medulla and in other paraganglia of the sympathetic nervous system. They are usually benign tumours and the clinical features depend on the activity of the tumour and the relative amounts of epinephrine and norepinephrine secreted. Typical signs and symptoms may include hypertension, hyperglycaemia, headache, palpitations, sweating, pallor and nausea.

Definitive treatment generally involves surgical removal of the tumour.

Adrenal cortex

The adrenal cortex is responsible for the secretion of the glucocorticoids, mineralocorticoids and androgens (sex hormones). Gucocorticoids affect the metabolism of carbohydrates, fats and proteins and are important in mediating the response to fasting and stress. Mineralocorticoids are essential for sodium balance and consequently extracellular fluid balance. Androgens have a minor role in reproductive function when compared to the pituitary hormones, FSH and LH.

Histologically the adrenal cortex is divided into three distinct layers. The outer most layer contains the cells of the zona glomerulosa, the middle layer, the largest layer, contains the cells of the zona fasciculata, while the innermost layer contains the cells of the zona reticularis. All 3 zones secrete corticosterone, while, in contrast, aldosterone biosynthesis occurs in the zona glomerulosa. The enzyme mechanism for forming cortisol (hydrocortisone) and androgens is mainly found in the 2 inner zones.

Synthesis

The hormones produced by the adrenal cortex contain the cyclopentanoperhydrophenantrene nucleus with the glucocorticoids and mineralocorticoids containing 21 carbon atoms and the androgens 19. The precursor of all steroid hormones is cholesterol. ACTH releases cholesterol from lipid droplets in the cytoplasm of the cells. It is converted in the mitochondria to pregnenolone. This is the rate limiting step in the biosynthesis of the steroidal hormones and is again regulated by ACTH. The pregnenolone is then transferred to the smooth endoplasmic reticulum where it undergoes further modification to form the three main classes of steroids. The actions of ACTH are thought to be mediated by cyclic-AMP. While several steroids have been identified, the steroids that are secreted in clinically significant amounts are aldosterone, the glucocorticoids cortisol and corticocosterone, and the androgens dehydro-epiandrosterone and androstenedione. The adrenal glands can also produce small amounts of estrogens.

The corticosteroids in the circulation are mainly bound to plasma proteins such as corticosteroid-binding globulin (transcortin) and albumin. Inactivation of the hormones occurs mainly in the liver where they are conjugated with glucuronic acid or sulphate and excreted in the urine.

Actions of glucocorticoids

Glucocorticoids play a vital role in the control of carbohydrate, fat and protein metabolism. They promote glycogen storage in the liver. During fasting they promote gluconeogenesis in the liver to provide glucose for brain metabolism. They are counter-regulatory to insulin, resulting in elevated blood glucose. Glucocorticoids potentiate the vasoconstrictor effects of catecholamines and decrease the permeability of vascular endothelium essential for maintenance of normal vascular function. Cortisol release increases during stress, and in patients with adrenocortical insufficiency absence of this response can result in hypotension and death. The glucocorticoids also have some mineralocorticoid activity. They have been shown to have anti-inflammatory properties and can suppress the immune response.

Regulation of adrenal cortical function

Secretion of the glucocorticoids is controlled by ACTH produced by the anterior pituitary (figure 5). This is controlled by the hypothalamic secretion of corticotropin-releasing hormone (CRH) into the hypophyseal portal system. The release of cortisol exerts a negative feedback effect on both the anterior pituitary and the hypothalamus. Plasma cortisol levels follow a diurnal pattern, peak levels occurring in the morning just before waking.

Actions of mineralocorticoids

Aldosterone and the other steroids with mineralocorticoid activity (corticocosterone, deoxycorticocosterone) increase the reabsorption of sodium acting mainly on the distal tubules of the kidney, resulting in the retention of sodium in extracellular fluids. Sodium is in effect exchanged for potassium and hydrogen, resulting in a potassium diuresis and an acidic urine. In adrenal insufficiency, sodium is lost in the urine while potassium is retained resulting in raised plasma potassium. Plasma volume may also be reduced resulting in hypotension and circulatory insufficiency. The renin-angiotensin system has a major role in the maintenance of blood volume and electrolyte balance *(Physiology of the Kidney, Update in Anaesthesia 1998; No 9:24-28)*

Regulation of aldosterone secretion

The main factors regulating aldosterone secretion are the renin-angiotensin system, ACTH from the pituitary, and the effects of a rise in plasma potassium or a fall in plasma sodium, which results in a direct stimulatory effect on the adrenal cortex.

Aldosterone is only one of many factors affecting sodium secretion. Other major factors include the glomerular filtration rate, atrial natriuretic peptide (ANP) and changes in tubular reabsorption of sodium independent of aldosterone. It is likely that the primary function of the aldosterone secreting mechanism is in the maintenance of the intravascular volume, although there are several other mechanisms involved.

Disorders of adrenocortical function

Cushing's syndrome is the result of excess corticosteroids, the commonest cause being prolonged treatment with relatively large doses. Apart from the iatrogenic causes this disorder is very rare, other causes being primary tumours of the adrenal gland, adenoma or hyperplasia of the pituitary gland. In addition Cushing's syndrome can be secondary to carcinomas elsewhere, such as oat cell carcinoma of the lung, due to uncontrolled ACTH secretion, the 'ectopic ACTH syndrome'. Conn's syndrome is also very rare, caused by a benign adenoma or hyperplasia of the zona glomerulosa producing excess aldosterone.

Acute adrenal insufficiency can occur after trauma, severe hypotension and sepsis. It may follow surgical removal of the adrenals unless there is adequate replacement therapy. Chronic adrenal insufficiency (Addison's disease) occurs when there is destruction of the adrenal gland, caused by autoimmune disease, secondary tumour infiltration, tuberculosis or amyloidosis.

Excess androgen secretion causes masculinisation (adrenogenital syndrome). This can result from an androgen secreting adrenocortical tumour or due to a congenital enzyme defect affecting cortisol synthesis. In the latter case, the resulting decrease in circulating cortisol stimulates the overproduction of ACTH, which in turn stimulates the adrenals to produce excess androgenic steroids. Females show signs of virilisation while males show precocious puberity. Extreme feminisation in males can occasionally be due to an oestrogen producing tumour of the adrenal gland.

Table 1 summarises the more common disorders of adrenocortical function.

Conclusion

The anaesthetist should, obviously, have a basic understanding of the physiology of the pituitary, thyroid and adrenal when involved with the management of patients with endocrine disease. Furthermore, this knowledge is fundamental to understanding the metabolic changes that occur following the stress of surgery.

Table 1. Disorders of adrenocortical function

Hormone	Syndrome	Symptoms & Signs
Glucocorticoid excess	Cushing's syndrome	Moon facies, truncal obesity, buffalo hump, abdominal striae, muscle weakness & wasting, hypertension, diabetes mellitus, hypokalemia and metabolic alkalosis.
Mineralocorticoid excess	Conn's syndrome	K^+ depletion, Na^+ retention, polyuria and hypokalemic alkalosis, hypertension, tetany & weakness.
Adrenocortical insufficiency *(Adrenocortical atrophy due to autoimmune diseases or diseases of the adrenal gland)*	Addison's disease	Skin pigmentation, Na^+ depletion, decreased plasma volume, weakness, tiredness and weight loss.
Adrenal androgen excess *(Androgen secreting tumour, or congenital)*	Adrenogenital syndrome	*In women*: hirsutism, acne, oligomenorrhea & virilisation.
	Congenital adrenal hyperplasia	*In male*: precocious puberty.

Further Reading

1. Brady JJ, Cragg PA, MacKnight ADC, Mills RG. Lecture notes on Human Physiology. 4th edition, 1999.

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3. Ganong WF. Review of Medical Physiology. 19th edition, 1999.

4. Goodman HM. Basic Medical Endocrinology. 2nd edition, 1994.

5. Guyton AC, Hall JE. Textbook of Medical Physiology. 9th edition, 1996.

6. Smith M Hirsch P. Pituitary disease and anaesthesia. British Journal of Anaesthesia 2000; **85**: 3- 14

7. (A good example of an internet resource is www.thyroidmanager.org)