# ENDOCRINE PHYSIOLOGY 2

Thyroid physiology The thyroid is the largest endocrine gland in the human body, weighing about 20–30 g. The normally developed thyroid is a bilobed structure lying next to the thyroid cartilage, in a position anterior and lateral to the junction between the larynx and the trachea. The two lobes are joined at the midline by an isthmus which encircles about 75% of the diameter of the junction betweeen the larynx and upper trachea. A feedback loop between hypothalamus, pituitary, and thyroid regulates the secretion of thyroid hormone. The hypothalamus generates thyrotropin-releasing hormone (TRH), which in turn stimulates the production and release of thyrotropin or thyroid stimulating hormone (TSH) from thyrotropic cells in the anterior pituitary gland. TSH stimulates thyroid hormonal output, which feeds back on both hypothalamus and pituitary to complete the circle. The secretory products of the thyroid gland are thyroxine (T4), triiodothyronine (T3) and calcitonin. T4 is produced only by the thyroid gland, and its daily production ranges between 80 and 100 μg. In contrast, 20% of T3 is derived directly from thyroid secretion and 80% from peripheral T4 conversion. The daily T3 production is 30–40 μg. Reverse T3 (rT3) is a thyroid hormone identified only in humans and differs from normal T3 by the location of iodine on the molecule. Free thyroid hormones are added to the circulating pool by the thyroid. It is the free thyroid hormones in the plasma that are physiologically active and feed back to inhibit TSH secretion. Thyroid hormone is important for growth and development, the regulation of intermediary metabolism, and has effects on the cardiovascular system.
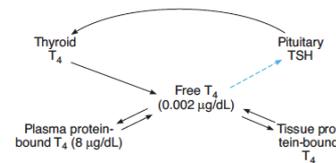
Hypothyroidism leads to a slowing of metabolic processes Cardiovascular effects of hypothyroidism include impaired cardiac contractility with decreased cardiac output, increased peripheral vascular resistance, decreased systolic blood pressure, increased diastolic blood pressure, and bradycardia. Pericardial effusion occurs in up to 50% of individuals, and cases of torsades de pointes have been reported. Pulmonary function is characterized by shallow and slow breathing, and impairment of both hypoxic and hypercapneic ventilatory drive. L-thyroxine replacement, even in the absence of obesity, may improve respiratory function. Hypothyroid patients have slowed drug metabolism and are very sensitive to sedatives or anesthetic agents that can precipitate respiratory failure. The use of tranquilizers, narcotics, and hypnotics should be avoided, or reduced to a minimum.

Hyperthyroidism The clinical syndrome of a hypermetabolic state which results from the increased plasma concentration of thyroid hormones is usually named thyrotoxicosis. Cardiac signs include high-output cardiac failure and congestive heart failure with peripheral edema. Arrhythmias include ventricular tachycardia, increased sleeping pulse rate, or atrial fibrillation, atrial flutter, paroxysmal supraventricular tachycardia, and premature ventricular beats. There may be thyroid swelling and exophthalmos. Sometimes a goiter may cause tracheal compression. Clinically overt myopathy is infrequent. The most frequent anesthetic problems in the perioperative period are caused by the adrenergic and metabolic abnormalities of hyperthyroidism. Adrenergic effects place hyperthyroid patients at great risk during surgery. Increased numbers of β-adrenergic receptors in the heart of hyperthyroid animals have been reported, but the most important effect is the direct inotropic and chronotropic actions of T3 and T4 on cardiac muscle. Cardiac hypertrophy is common, and atrial fibrillation occurs in 10–15% of hyperthyroid patients. A basal increase in cardiac output in hyperthyroidism significantly limits cardiac reserve during surgery. Cardiovascular symptoms of anesthesiologic interest include resting tachycardia, wide pulse pressure, exercise intolerance, and dyspnea on exertion. Decreased peripheral resistance, decreased cardiac filling times, increased blood volume, and fluid retention are also of interest. Increased basal oxygen consumption, cardiac arrhythmias, mild anemia, and vitamin B6 deficiency secondary to increased coenzyme requirements may contribute to cardiac decompensation. Signs and symptoms of congestive heart failure are common in young and old individuals with thyrotoxicosis. Clinical signs of thyrotoxic crisis are fever with a temperature of 41°C (or even higher), mental disorientation, anorexia, extreme anxiety and restlessness, agitation, tremor, and tachycardia. Hypotension with congestive heart failure and signs of acute abdomen can develop. The diagnosis is made clinically. Treatment is both specific and supportive. Antithyroid drugs such as carbimazole 60–120 mg or propylthiouracil 600– 1200 mg should be given orally or by nasogastric tube. This usually starts to act within 1 hour of administration. Potassium or sodium iodide acts immediately to inhibit further release of thyroid hormone, but it should not be given until 1 hour after the antithyroid drug. The use of β-adrenoceptor antagonists includes oral propranolol 20–80 mg 6-hourly or IV 1–5 mg 6- hourly.

The adrenal glands are situated in the retroperitoneum and are composed of an outer cortex, which comprises 80% of the gland, and an inner medulla. The cortex is composed of an outermost zone, the zona glomerulosa, which is very thin and consists of small cells with numerous elongated mitochondria, the middle zone, the zona fasciculata, with columnar cells, and the innermost zone, the zona reticularis, which contains interconnecting cells. The major hormones of the cortex are the glucocorticoids, cortisol and corticosterone; a mineralcorticoid, aldosterone; and precursors to the sex steroids, androgens and estrogens. All hormones represent chemical modifications of the steroid nucleus (see adjacent). To remember the cortex it is GFR, and things get sweeter on the way in, aldeterone in the glomerulosa, the glucocorticoids in the fasciulata and the sex steroids in the reticularis. As with T3 the steroid hormones act by binding to intracellular receptors. The inner zone of the adrenal gland, or medulla, is derived from neuroectodermal cells of the sympathetic ganglia and is the source of circulating catecholamines, adrenaline and to a lesser extent noradrenaline. The adrenal medulla is activated in association with the rest of the sympathetic nervous system. All circulating adrenaline derives from adrenal medullary secretion, whereas noradrenaline derives from nerve terminal endings. The hormones are synthesized from tyrosine and stored within the chromaffin cells, an energy-requiring process. Their half-life is 1–3 minutes and they are metabolized in the liver and kidney.
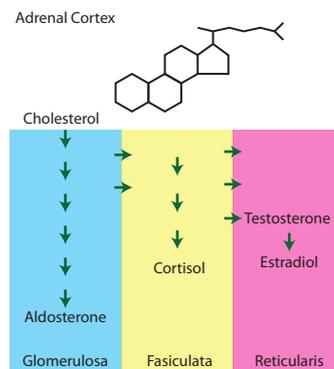
Control of plasma calcium Three hormones are primarily concerned with the regulation of calcium metabolism. 1,25-Dihydroxycholecalciferol is a steroid hormone formed from vitamin D by successive hydroxylations in the liver and kidneys. Its primary action is to increase calcium absorption from the intestine. Parathyroid hormone (PTH) is secreted by the parathyroid glands. Its main action is to mobilize calcium from bone and increase urinary phosphate excretion. Calcitonin, a calcium lowering hormone that in mammals is secreted primarily by cells in the thyroid gland, inhibits bone resorption. Parathyroid glands, through the release of parathyroid hormone (PTH) from the chief cells, are important regulators of serum Ca2+ levels. The primary target tissues for PTH action are bone, kidneys, and intestines. PTH increases extracellular calcium through a direct effect on bone resorption by osteoclasts and through renal Ca2+ resorption, and indirectly enhancing gastrointestinal absorption by activating the enzyme in the kidney (1α-hydroxylase) that converts vitamin D to its active form (calcitriol, or 1,25-dihydroxycholecalciferol). Additionally, parathyroid hormone reduces serum phosphate by increasing renal excretion. Calcitonin, secreted by the thyroid gland, counteracts the effect of PTH on Ca2+ levels. PTH secretion is regulated by the serum Ca2+ concentration, with low levels stimulating PTH secretion and elevated level inhibiting it.

Natriuretic peptides play an important role in the regulation of ECF and blood volume. It is now appreciated that the heart is an important endocrine organ. This peptide family consists of four peptides: atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), C-type natriuretic peptide (CNP), and Dendroaspis natriuretic peptide (DNP). These peptides are structurally similar but genetically distinct peptides that have diverse actions in cardiovascular, renal, and body fluid homeostasis. Atrial natriuretic peptide (ANP), a polypeptide hormone of 28 amino acids, is produced in the cardiac atria and to a lesser extent in the ventricles, and is released in response to increased wall tension. Brain natriuretic peptide (BNP) was discovered in porcine brain and subsequently found to be produced in greater quantity in human heart, primarily by the left ventricle. It is released in response to increased ventricular wall stress. Serum concentration of BNP has recently been clinically used as a biomarker to assist in the diagnosis and prognostic assessment of patients with suspected heart failure. The physiologic actions of natriuretic peptides involve the kidneys, vasculature, heart, sympathetic nervous system, and RAA axis. ANP and BNP exert similar actions in humans. Natriuretic peptides regulate fluid volume homeostasis through their natriuretic and diuretic effects. They dilate the afferent arterioles and constrict the efferent arterioles, leading to increased glomerular filtration while maintaining a constant renal blood flow. They also exert an effect on the collecting ducts to inhibit tubular water transport by antagonizing the action of vasopressin. In the heart, natriuretic peptides reduce intracellular calcium concentration by a protein kinase-mediated pathway and promote relaxation. The hemodynamic effects of therapeutic BNP include a reduction of both preload and afterload and a consequent improvement in cardiac performance. The FDA has recently approved recombinant BNP for the treatment of refractory heart failure. Natriuretic peptides reduce sympathetic tone in the peripheral vasculature. This is accomplished through dampening of barorecep-tors, suppressing the release of catecholamines from autonomic nerve endings and inhibiting sympathetic outflow from the central nervous system. These peptides also reduce the activation threshold of vagal efferents and thereby blunt the extent of tachycardia and vasoconstriction that typically results from a drop in blood pressure.

Christopher Andersen 2012