REGULATORY PEPTIDES IN THE THYROID GLAND

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BACKGROUND

The mammalian thyroid gland harbours two different endocrine cell types: follicular and parafollicular (C) cells. The follicle cells are of entodermal origin and develop from the thyroglossus duct in the floor of the pharyngeal cavity(1,2). The C cells are thought to derive from the neuroectoderm(3). The C cell precursors migrate to form the ultimobranchial bodies which persist as separate organs throughout life in submammalian vertebrates(4,5). In mammals the ultimobranchial bodies fuse with the thyroid anlage during the fetal development (6-8). The follicle cells synthesize and secrete triiodothyronine (T₃) and tetraiodothyronine or thyroxine (T₄), which control energy metabolism and are necessary for normal growth(9). The C cells synthesize, store and secrete calcitonin (CT), which is thought to be involved in the regulation of serum Ca by suppressing bone resorption(10,11).

The thyroid gland receives its blood supply from the carotid artery via the thyroid arteries which divide into smaller branches before penetrating the upper and lower poles of the gland(12). Within the thyroid, the blood vessels ramify in the connective tissue between the follicles(12-15). Capillaries form a dense network around each follicle(16). The follicles are the most conspicuous feature of the thyroid gland and form the major portion of the parenchyma. A thin basement membrane surrounds each follicle, which is composed of a single
layer of epithelial cells (follicle cells) enclosing the follicle lumen. The C cells are generally larger than the follicle cells and occur scattered in the follicle wall or in small clusters in the interfollicle space(17). They are located predominantly in the central and dorsolateral parts of the thyroid lobes(18). As a rule the C cells do not reach the follicle lumen(17).

The activity of the follicle cells is controlled by the thyroid stimulating hormone (TSH) from the pituitary gland(19-21). Although TSH is thought to be the principal regulator of thyroid function, an involvement of the autonomic nervous system has been suggested(22,23). Such an involvement is likely in view of the rich supply of noradrenaline (NA)–storing and acetylcholinesterase (AChE)–positive nerve fibres in the thyroid gland(24,25). The adrenergic innervation of the thyroid has been examined by histofluorescence techniques in several species (26,27). Adrenergic nerve fibres occur both around blood vessels and follicles. The fibres derive from the superior cervical and stellate ganglia and seem to enter the thyroid gland via the blood vessels(24,27-32). As studied by electron microscopy adrenergic nerve terminals are sometimes in close apposition to follicle cells(24). Exogenous catecholamines and electrical stimulation of sympathetic branches to the thyroid gland cause colloid droplet formation and thyroid hormone secretion in mice (24). Interestingly, catecholamines inhibit TSH–induced secretion of thyroid hormones(24,33,34). The sympathetic nerves are thought to interact with TSH in the regulation of thyroid hormone secretion(24). In addition, catecholamine–induced vasoconstriction reduces the thyroid blood flow and indirectly the capacity of the thyroid gland to release its hormones(30). There is also evidence that the sympathetic nervous system may play a role in the control of thyroid growth(35).

In the parasympathetic nervous system the classical postganglionic neurotransmitter is acetylcholine(36). Acetylcholinesterase (AChE)–positive nerve fibres are present in the thyroid gland(25,37). It is generally assumed that these fibres represent cholinergic, presumably postganglionic parasympathetic fibres. However, AChE may occur also in adrenergic and sensory neurones(38-40). Whatever the nature of the AChE–positive fibres, their distribution around blood vessels and follicles suggests a role in the regulation of local blood flow and thyroid hormone secretion(25,41-44).

Until fairly recently our knowledge of the morpho-