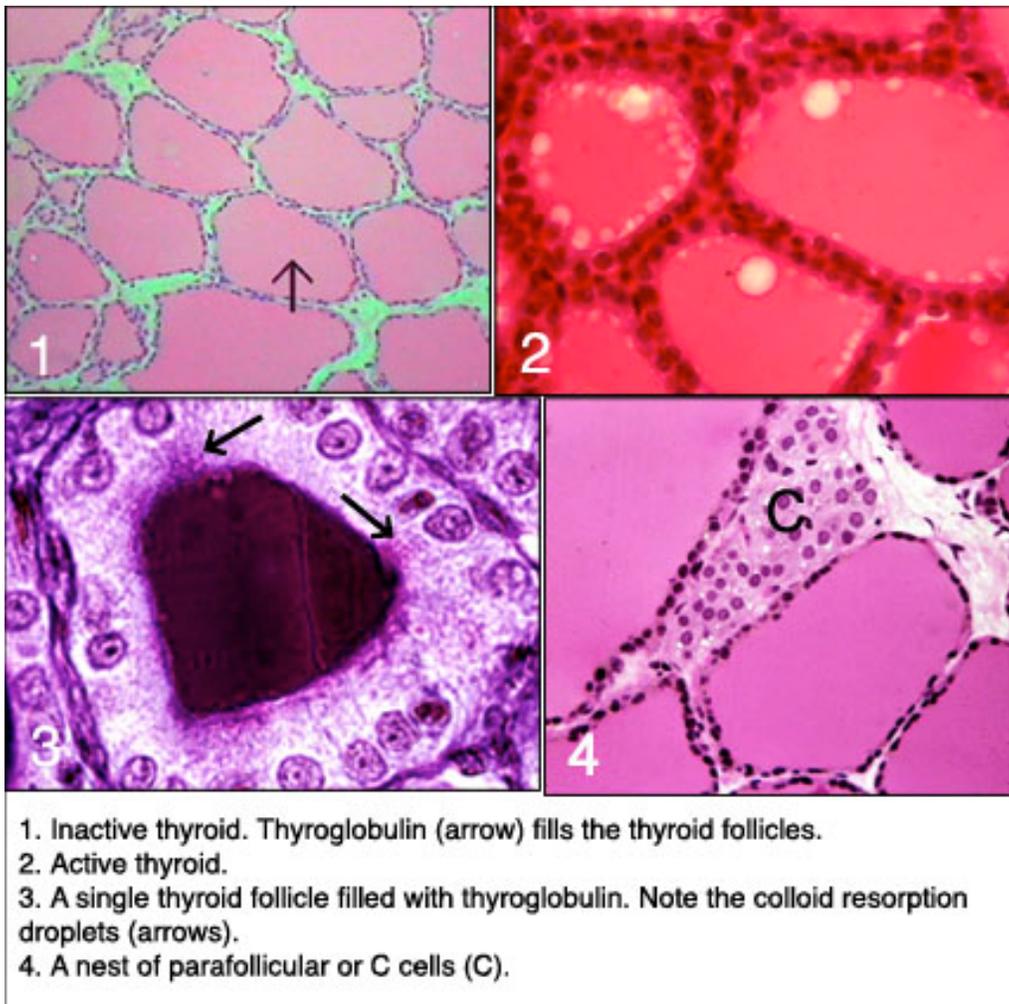


Thyroid



1. Inactive thyroid. Thyroglobulin (arrow) fills the thyroid follicles.
2. Active thyroid.
3. A single thyroid follicle filled with thyroglobulin. Note the colloid resorption droplets (arrows).
4. A nest of parafollicular or C cells (C).

The thyroid gland normally weighs between 20 and 30 g, being slightly heavier in men, and is located in the anterior region of the neck, below the cricoid cartilage. It consists of two lateral lobes and an isthmus that forms a narrow bridge across the trachea between the two lobes. A small pyramidal lobe extends cranially in about 15% of the population.

The parenchyma of the thyroid gland is enclosed in a connective tissue capsule and organized into hollow spherical structures, the follicles, which vary considerably in diameter and contain a gelatinous material called colloid. The walls of the follicles consist of a simple epithelium that rests on a thin basal lamina, about 50 nm thick. A delicate reticular network that contains a vast capillary plexus, numerous nerve fibers, and blindly ending lymphatic vessels supports each follicle. The follicular epithelium consists mainly of *principal (follicular) cells*, which usually are squamous to cuboidal in shape; depending on the functional status of the thyroid, the cells may become columnar. The nuclei are spherical, contain one or more nucleoli, and have a central position. The lateral cell membranes are united at the apex by junctional complexes, and the luminal surfaces bear short microvilli. The basal plasmalemma is smooth, with no infoldings. Mitochondria are evenly distributed throughout the cytoplasm and vary in number according to the activity of the cell. Active cells take on a cuboidal shape and show many profiles of granular endoplasmic reticulum. Inactive cells are squamous, and granular endoplasmic reticulum is sparse. Golgi complexes usually have a supranuclear location in

active cells, and the apical cytoplasm contains numerous small vesicles, lysosomes, and multivesicular bodies. Colloid resorption droplets also are found in the apical cytoplasm. Follicular cells contain thyroid-stimulating hormone (TSH) receptors.

The thyroid is a unique endocrine gland in that the secretory product, colloid, is stored extracellularly in the lumen of the follicle. Colloid consists of mucoproteins, proteolytic enzymes, and a glycoprotein called thyroglobulin, the primary storage form of thyroid hormone. Synthesis of thyroglobulin occurs in the principal cells along the same basic intracellular pathway as glycoprotein in cells elsewhere in the body. Amino acids are synthesized into polypeptides in the granular endoplasmic reticulum and then carried in transport vesicles to the Golgi complex, where the carbohydrate moiety is conjugated to the protein. From the Golgi complex, the glycoprotein (noniodinated thyroglobulin) is transported to the apical surface in small vesicles, from which it is discharged by exocytosis into the follicular lumen and stored as part of the colloid.

While thyroglobulin is being synthesized, thyroperoxidase is assembled in the granular endoplasmic reticulum and then passes through the Golgi complex and is released by small vesicles at the apical surface of the cells. Follicular cells have a unique ability to take up iodide from the blood using a Na^+/I^- cotransporter and concentrate it. The iodide subsequently is oxidized to iodine by this intracellular peroxidase and used in the iodination of tyrosine groups in thyroglobulin. Formation of monoiodotyrosine and diiodotyrosine is thought to occur in the follicle, immediately adjacent to the microvillus border of the follicular cells. When one molecule of monoiodotyrosine is linked to one of diiodotyrosine, a molecule of triiodothyronine is formed. Coupling of two molecules of diiodotyrosine results in the formation of tetraiodothyronine (thyroxine). The thyronines make up a small part of the thyroglobulin complex but represent the only constituents with hormonal activity. Thyroglobulin and the thyronines are stored in the lumen of the follicle as colloid until needed.

When follicular cells are stimulated by TSH, droplets of colloid are sequestered from the follicular lumen by endocytosis and the formed colloid resorption droplets enter the apical cytoplasm of the follicular cells. Lysosomes coalesce with the resorption droplets and hydrolyze the contained thyroglobulin, liberating monoiodotyrosine, diiodotyrosine, triiodothyronine, and tetraiodothyronine into the cytoplasmic matrix. The mono- and diiodotyrosines are deiodinated by the enzyme deiodinase, and the iodine is reused by the follicular cell. Thyroxine (tetraiodothyronine) molecules constitute what is known as thyroid hormone and are released with triiodothyronine at the base of the cell into blood and lymphatic capillaries. Thyroxine is transported in the blood plasma complexed to a binding protein called thyroxine-binding globulin. Triiodothyronine, which hormonally is the more potent of the two, but is not as abundant, is not as firmly bound to the binding protein.

Thyroxine binding globulin (TBG) is important in regulating the amount of free hormone that circulates in the blood plasma. Thyroxine and triiodothyronine are released from TBG only in response to metabolic needs, thus preventing rapid fluctuations in the levels of these hormones.

As they are released and elicit their effects, the hormones are replaced by other thyroxine and triiodothyronine molecules from the thyroid. The activity of the thyroid is regulated by a thyroid-stimulating hormone (TSH) secreted by thyrotrophs in the anterior lobe of the pituitary.

Most of the secreted thyroid hormone (90%) is thyroxine but is converted to the more active form, triiodothyronine, by peripheral target tissues. The kidney and liver are important deiodinators of thyroxine and convert it to the functionally more potent triiodothyronine. Triiodothyronine then binds to a nuclear receptor in cells of the target organ the net result of which is an increase in oxygen consumption and metabolic rate. Thyroid hormone has general

effects on the metabolic rate of most tissues, and among its functions are increased carbohydrate metabolism, increased rate of intestinal absorption, increased kidney function, increased heart rate, increased ventilation, normal body growth and development, and increased mental activities.

The thyroid also contains a smaller number of cells variously called *parafollicular*, *light*, or *C cells*, which are present adjacent to the follicular epithelium and in the delicate connective tissue between follicles. The C cells adjacent to the follicular epithelium appear to be sandwiched between the bases of follicular cells and lie immediately adjacent to the basal lamina; parafollicular cells never directly border on the lumen of the follicle. Between follicles, the cells may occur singly or in small groups. In electron micrographs, the parafollicular cells show numerous moderately dense, membrane-bound secretory granules that measure 10 to 50 nm in diameter. The cytoplasm also contains occasional profiles of granular endoplasmic reticulum, scattered mitochondria, and poorly developed Golgi complexes. Parafollicular cells secrete calcitonin (thyrocalcitonin), another polypeptide hormone that regulates blood calcium levels. Calcitonin lowers blood calcium by acting on osteocytes and osteoclasts to suppress resorption of calcium from bone and its release into the blood. Thus, calcitonin has an effect opposite that of parathyroid hormone, serves to control the action of parathyroid hormone, and helps regulate the upper levels of calcium concentration in the blood.

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