ENDOCRINE SYSTEM DISORDERS

The primary function of the two major organ systems, the nervous system and the endocrine system, is intercellular communication.

The endocrine system releases hormones that induce a more generalized (yet slower and more prolonged comparative with the nervous system) response as they reach target cells in widely separated organs or tissues.

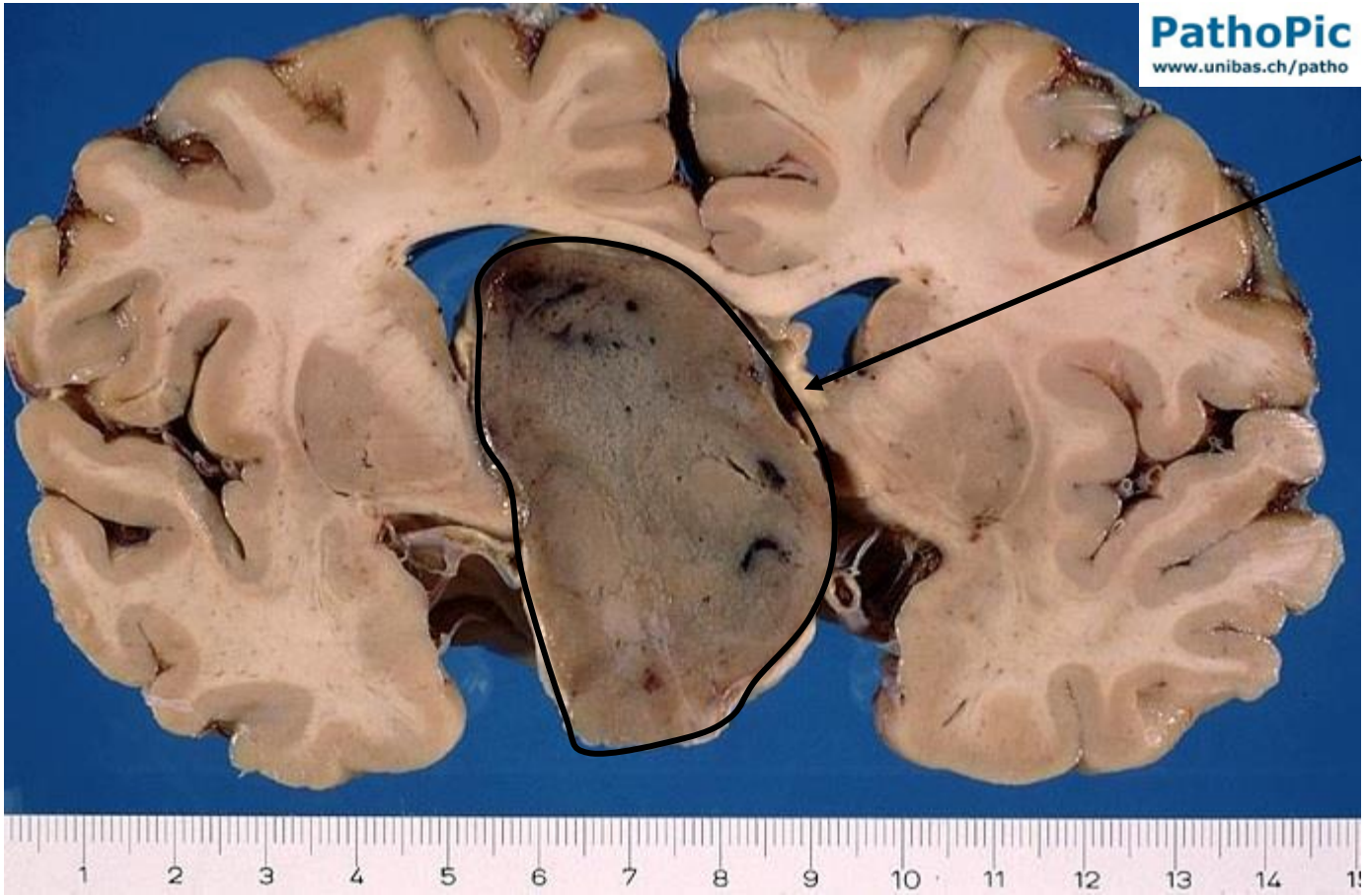
PITUITARY ADENOMAS

- are benign neoplasms of the anterior lobe of the pituitary gland and are often associated with the excess secretion of pituitary hormones and evidence of corresponding endocrine hyperfunction.
- more frequent in men between the ages of 20 and 50 years

Pituitary adenomas have been classically subdivided according to the tinctorial properties of their cells as:

- ➔ **acidophilic adenomas**
  associated with the overproduction of growth hormone
- ➔ **basophil adenomas**
  associated with the excess secretion of ACTH
- ➔ **cromophobe adenomas**
  no endocrine hyperfunction

Nowadays, when immunohistochemical methods are widely applied, pituitary adenomas are classified according to the hormone(s) elaborated by the neoplastic cells (lactotroph, somatotrope, corticotrope, gonadotrope, thyrotrope and, respectively, nonfunctional adenomas).

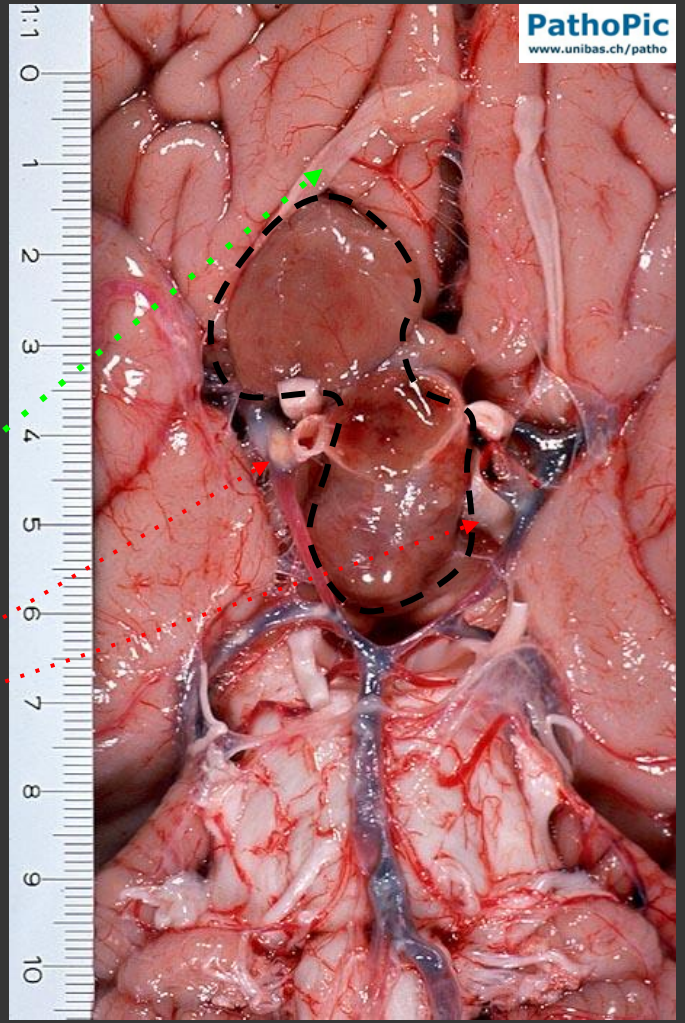


Expansively growing light brown, sharply delimited tumor originating from the pituitary gland.

Pituitary adenomas range from small lesions, **microadenomas** (**less than 10 mm in diameter**), that do not enlarge the gland to expansive tumors that erode sella turcica and impinge on adjacent cranial structures, **macroadenomas (>10mm in diameter)**.

https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=003653

The mass effects of pituitary macroadenomas include impingement on the optic chiasm, often with bitemporal hemianopsia and loss of central vision, oculomotor palsies when the tumour invades the cavernous sinuses, and severe headaches.



View of the brain base with delicate vessels. On both sides of the **optic chiasma**, there is a light brown tumour, which pushes the brain tissue and the **olfactory nerve** to the side.

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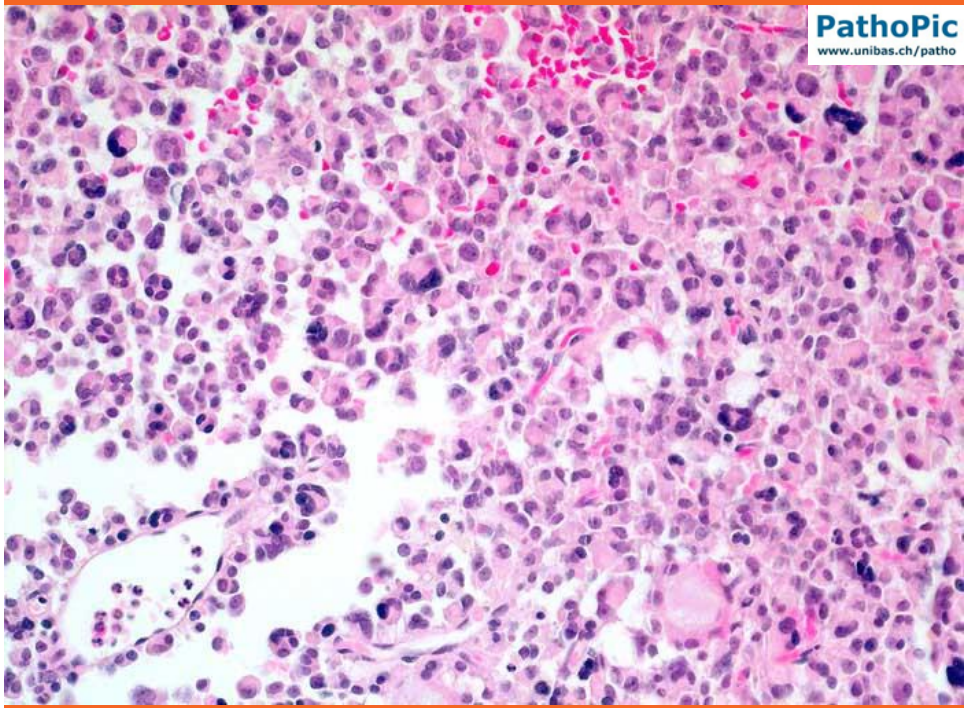
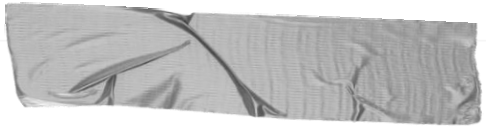
Microscopically, all adenomas have a fairly uniform appearance. The more or less uniform polygonal cells are arranged in sheets, cords, or nests, having only delicate, vascularized stroma. Small or large foci of ischemic necrosis may be present, and psammoma bodies may be found, accompanied by haemorrhage.



THYROID GLAND PATHOLOGY

NONTOXIC GOITER

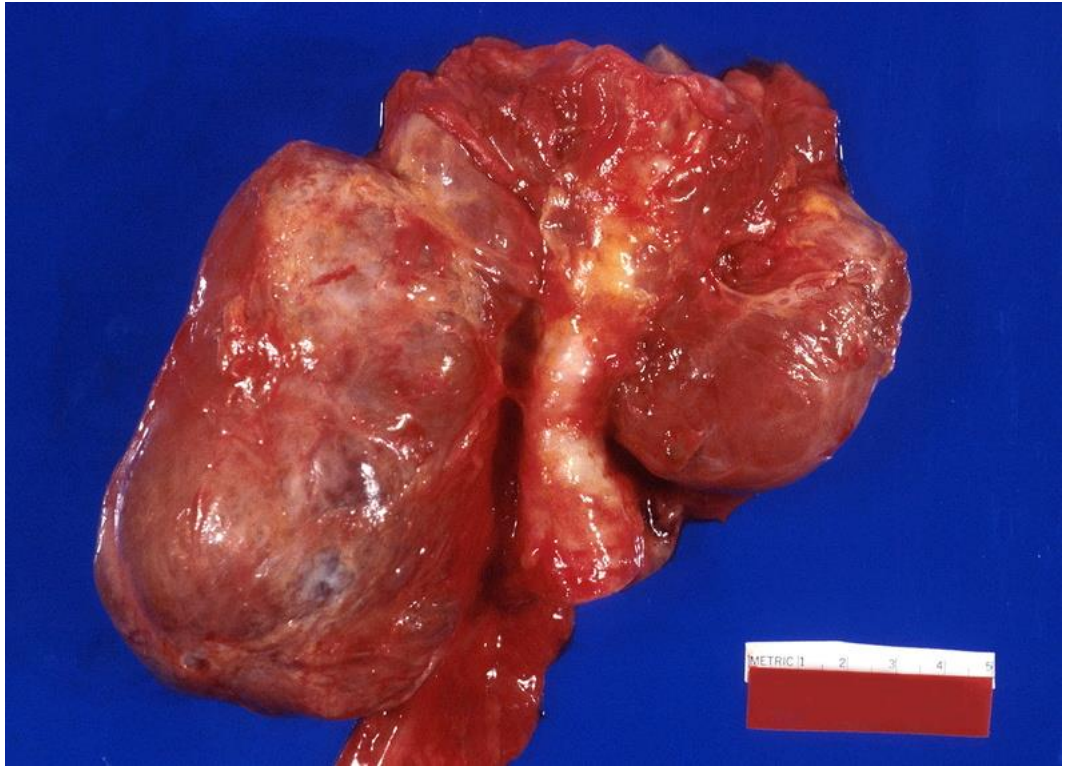
- diffuse nontoxic (simple) colloid goitre
- specifies a form of goitre that diffusely involves the entire gland
- without producing nodularity
- not associated usually with either hyperfunction or hypofunction
- presents enlarged uneven follicles filled with colloid



Two stages can be identified in the evolution of the diffuse nontoxic goitre:

- the **hyperplastic stage** and **colloid involution.**
- **In the stage of hyperplasia,** the gland presents a mild enlargement. It is diffusely involved, markedly hyperemic and rarely exceeds 100 to 150 g.

Histologically, the gland consists mainly of small closely packed acini lined by columnar epithelium and containing a small amount of poorly stained colloid. **The duration of the hyperplastic stage is extremely variable.** With an increased mass of cells, the euthyroid state is reached and **follicular cell growth ceases and is followed by colloid accumulation.**



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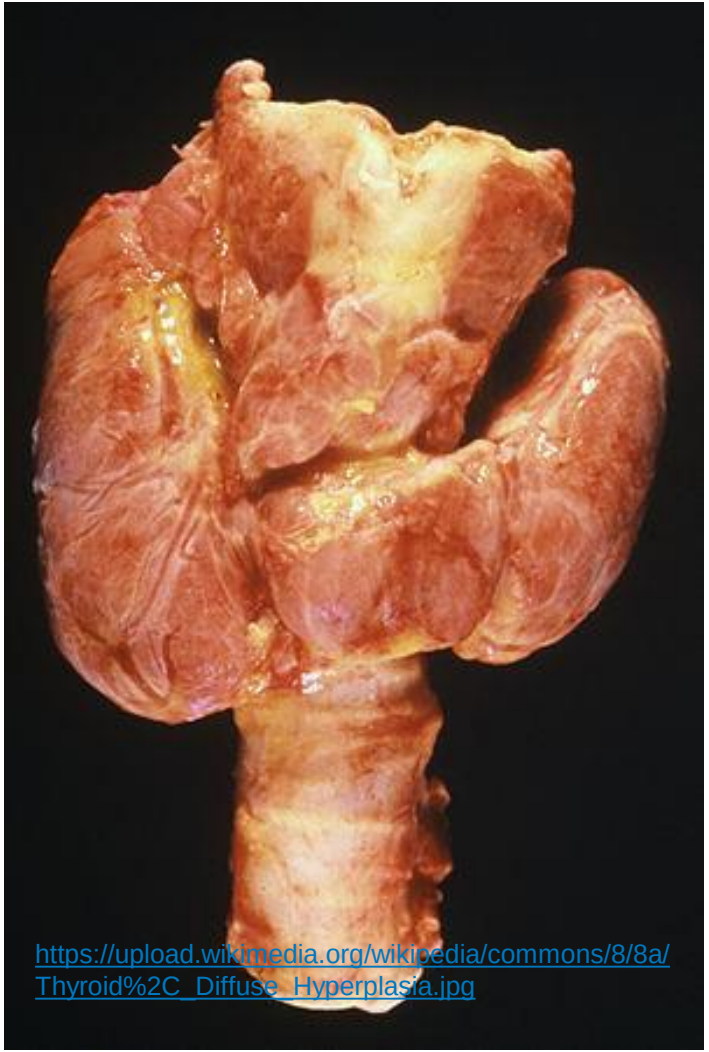
Colloid involution stage of **non-toxic goiter:** the thyroid becomes markedly enlarged (500 g or more), translucent and brown due to the large amount of stored colloid.

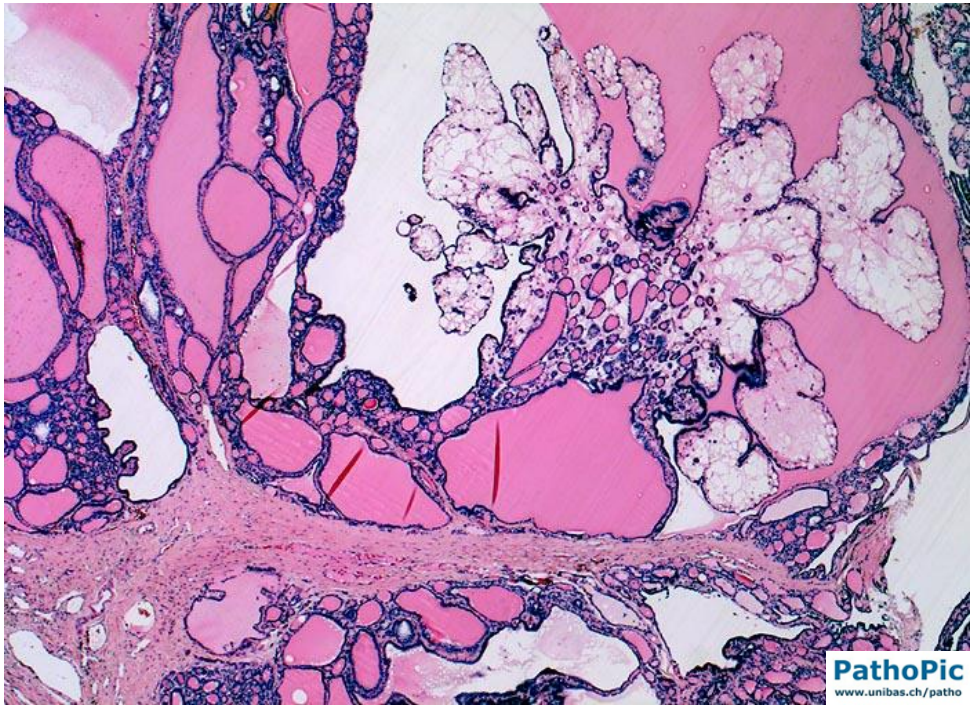


https://upload.wikimedia.org/wikipedia/commons/8/8a/Thyroid%2C_Diffuse_Hyperplasia.jpg

There are usually no symptoms, but pressure symptoms develop if the enlarged thyroid is retrosternal:

- stridor, by compressing the trachea,
- hoarseness, due to the pressure on the recurrent laryngeal nerve,
- dysphagia, due to the pressure on the oesophagus.

At this stage, follicles enlarge as they become filled with dense colloid, and the epithelium undergoes progressive flattening. For unknown reasons, the accumulation of colloid is not uniform throughout the gland and some follicles are hugely distended, whereas others remain small.
During the early stages of endemic goitre, administration of iodine brings about regression but later is without effect. An important aspect of the diffuse goitre is that it may become transformed into a nodular goitre.



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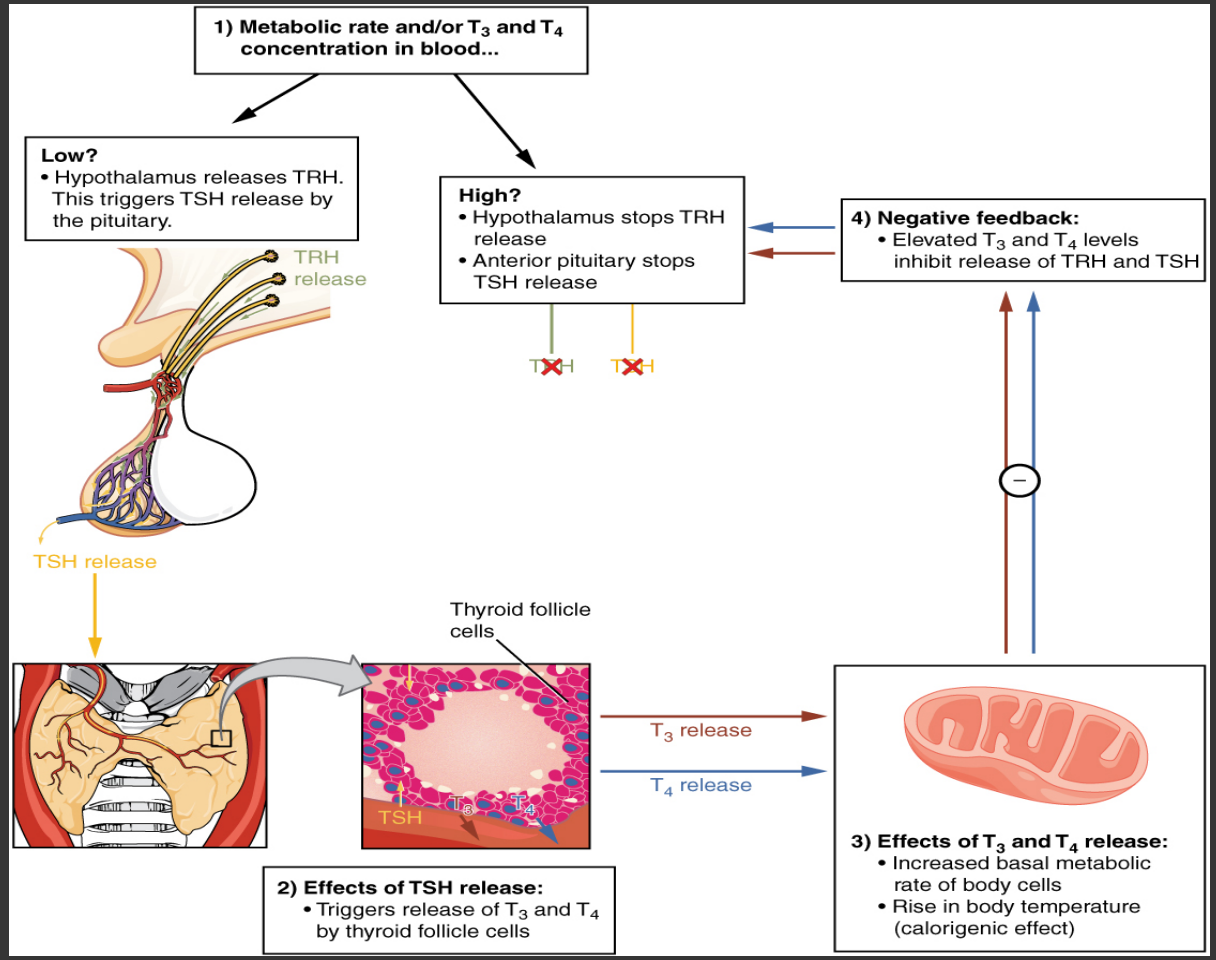

HYPERTHYROIDISM

- clinical consequences of an excessive amount of circulating thyroid hormones, inducing a hypermetabolic state of the target tissues.
- Prolonged hypersecretion of thyroid hormone can result from (1) an excess of production of TSH (rare), (2) the presence of an abnormal thyroid stimulator (Graves' disease), and (3) intrinsic disease of the thyroid gland (toxic multinodular goitre or a functioning adenoma).

Graves' disease, also known as **Basedow disease** in continental Europe, is an **autoimmune disorder** characterized by **diffuse goitre with hyperthyroidism**, and **infiltrative ophthalmopathy (exophthalmos)**, and, **infrequent, infiltrative dermopathy.**

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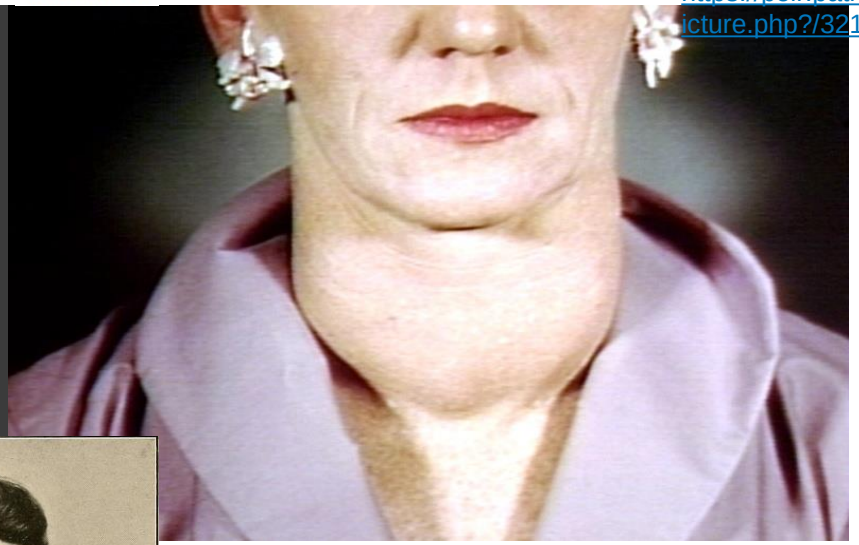
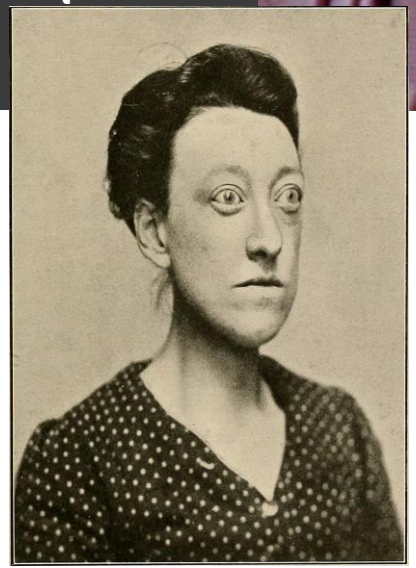




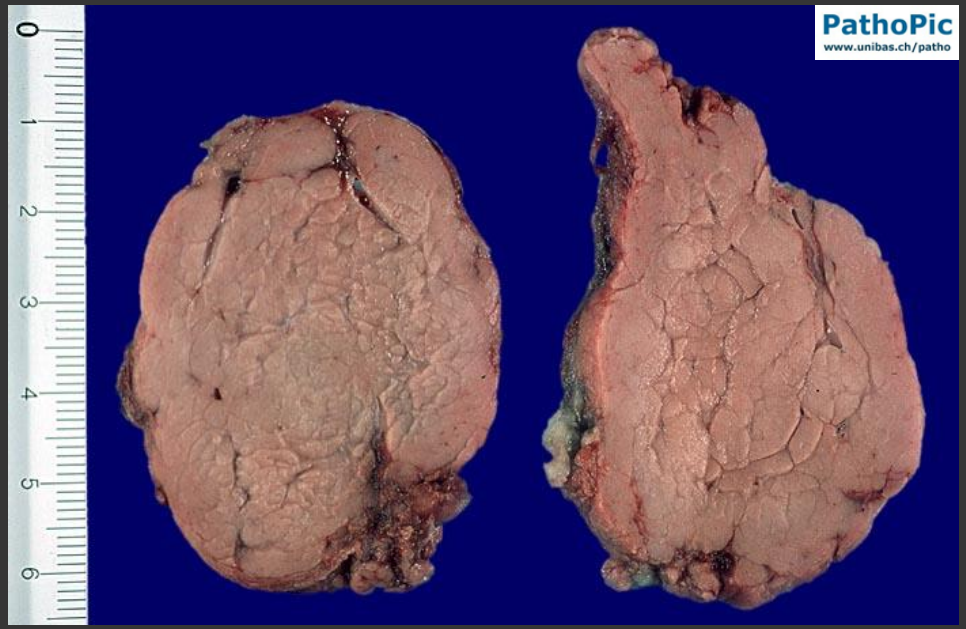
https://www.flickr.com/photos/internetarchivebookimages/

The photograph was taken ~ 1917

Typically, patients have a warm, moist, flushed skin, a *wide-eyed stare*, and general hyperdynamic circulatory state (tachycardia, palpitations, widened pulse pressure, peripheral vasodilatation).

https://www.telegraph.co.uk/books/what-to-read/the-mad-world-of-marty-feldman/

The thyroid in Graves' disease is symmetrically, but not markedly enlarged, usually weighing 35 to 40 g. The capsule is intact and not adherent. The cut surface loses the normal tan translucence consecutive to the decreased amount of stored colloid, the parenchyma has a firm, dark red, meaty appearance closely resembling normal muscle.



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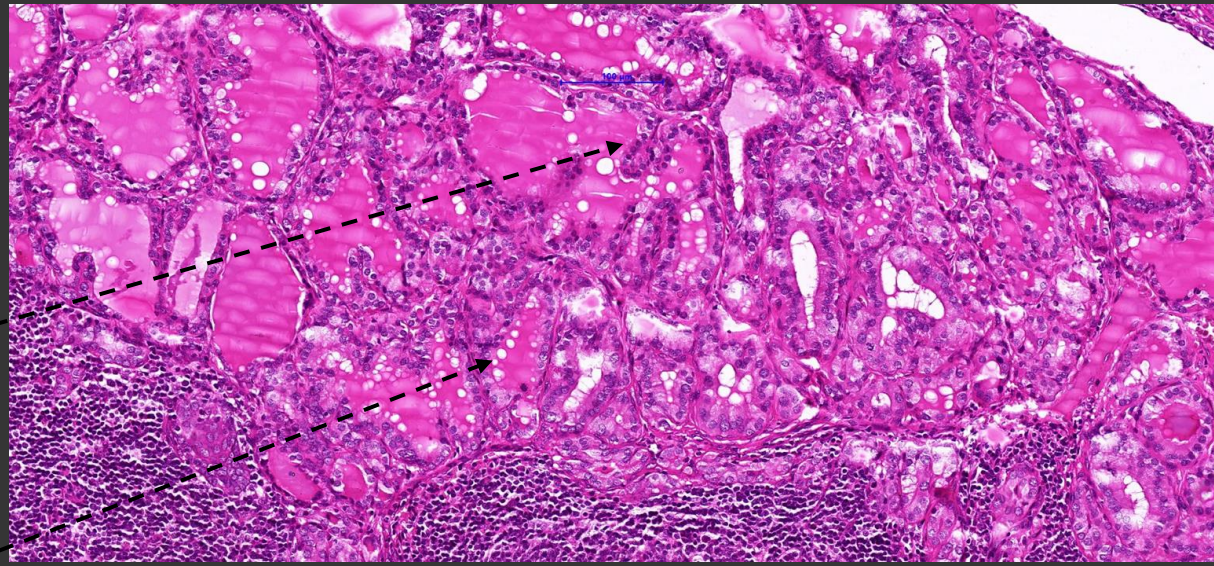
Microscopically, the thyroid is diffusely hyperplastic and highly vascular. The dominant feature - "too many cells" - is imparted by an increased number of closely packed acini of various sizes, an increase in height of the lining epithelium to form tall columnar cells and an increase in the number of follicular cells, **causing them to pile up in pseudopapillary buds** – without fibrovascular cores. The colloid is markedly diminished and has pale pink, watery appearance, showing **small void vacuoles at the contact surface with the epithelial cells - "moth-eaten" aspect.**



H&E slide from own histology slide library.

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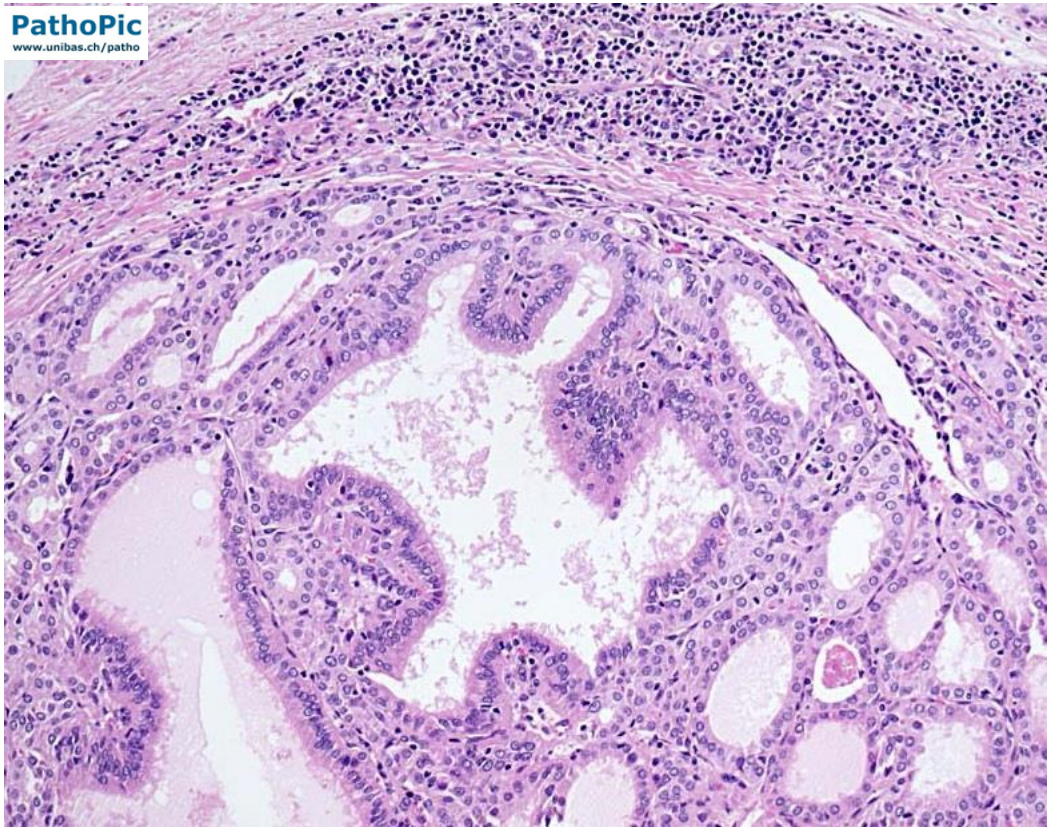

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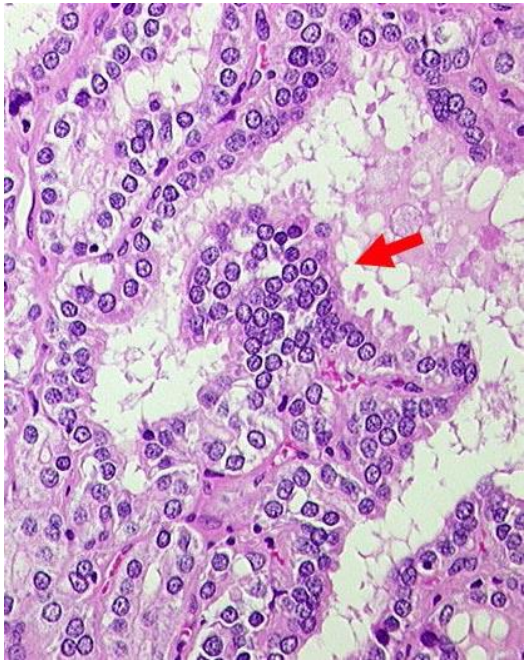
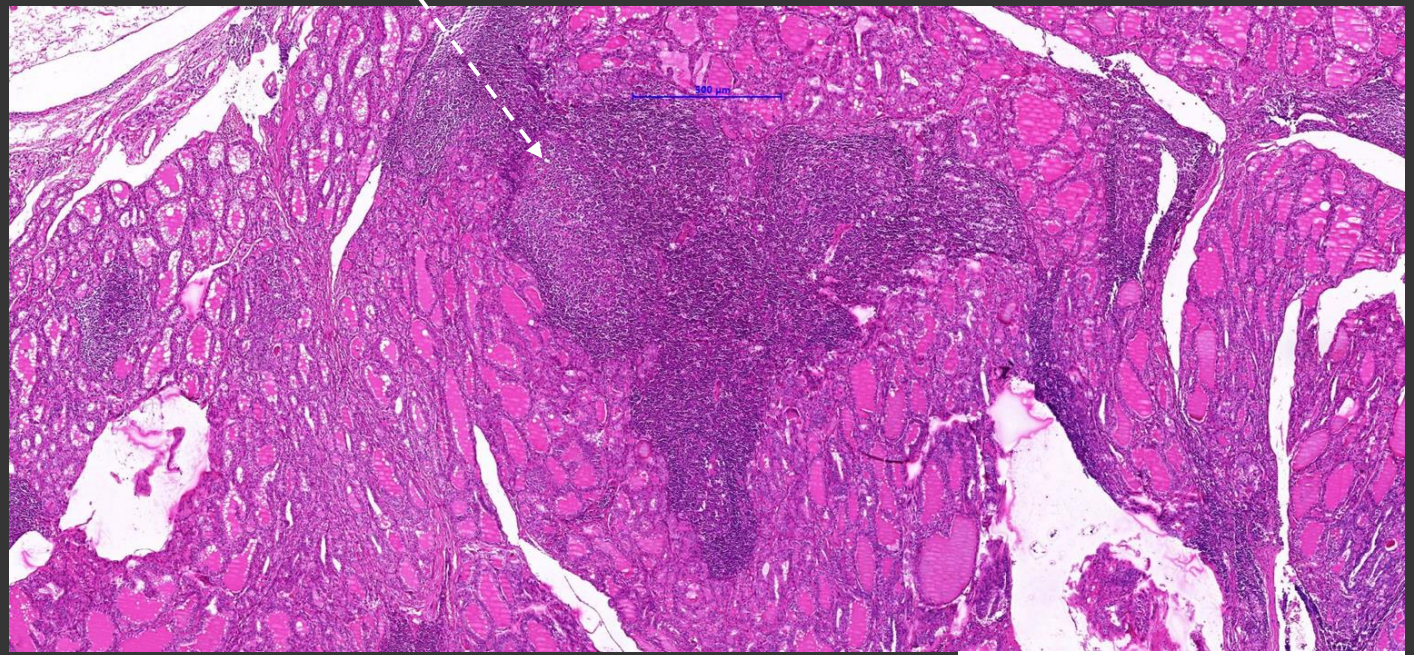


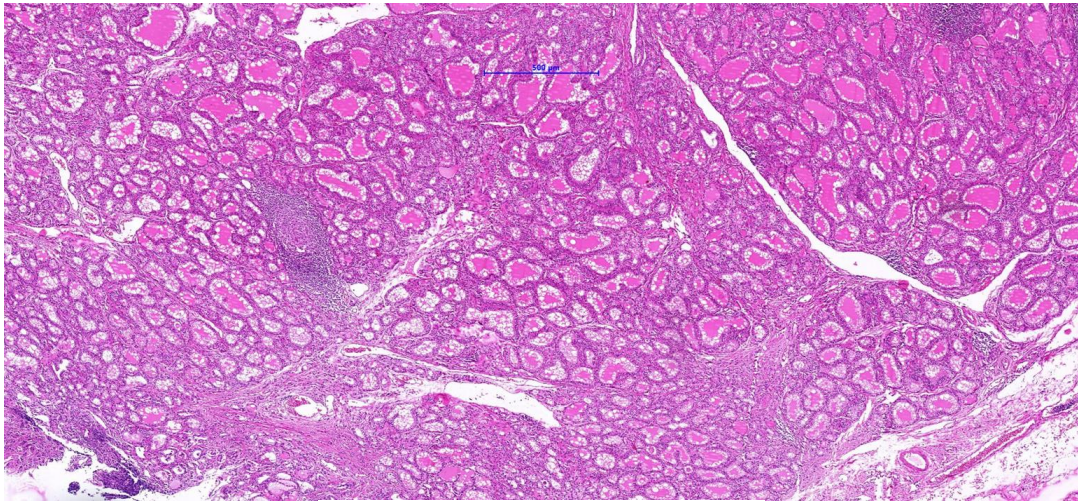
hyperplasia of follicular cells, causing them to pile up in pseudopapillary buds – without fibrovascular cores

Lymphocytes and plasma cells infiltrate the interstitial tissue and may aggregate to form lymphoid aggregates with large germinal centers.



H&E slide from own histology slide library.

The course of Graves' disease is characterized by exacerbations and remissions. Treatment of the disorder includes the use of antithyroid medication, destruction of thyroid tissue with radioactive iodine or, less commonly performed today, surgical ablation of the gland. Unfortunately, despite successful relief of hyperthyroidism, exophtalmos often persists and may even worsen.



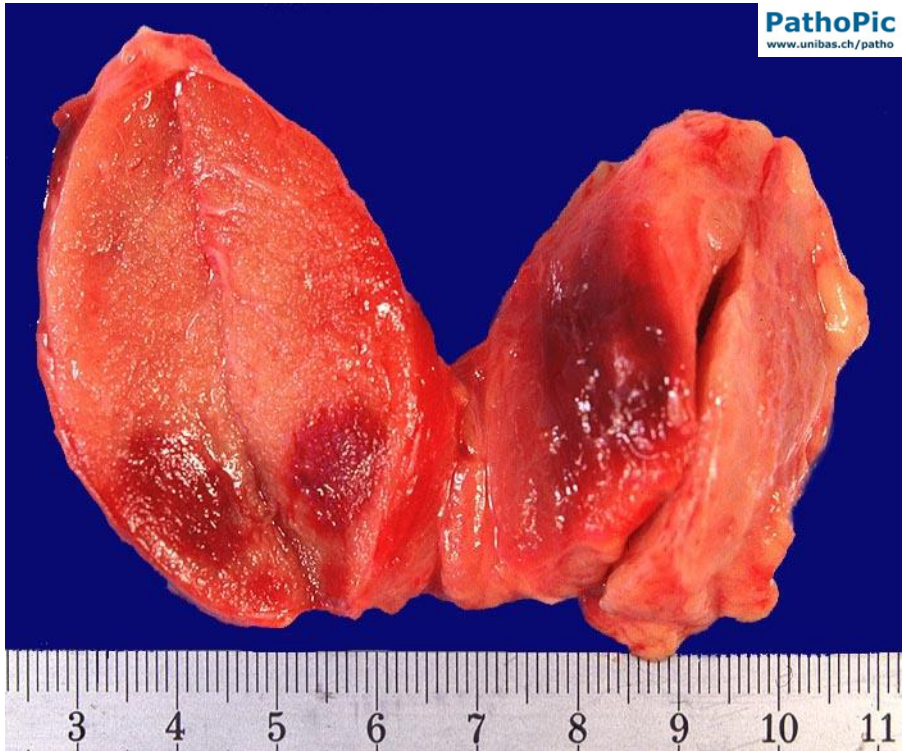
H&E slide from own histology slide library.

THYROIDITIS

is a term that encompasses a heterogeneous group of inflammatory disorders of the thyroid gland, including those that are caused by infectious agents and autoimmune mechanisms.

The acute suppurative or infectious thyroiditis is produced by microbial (Staphylococcus, Streptococcus, Salmonella etc.) and fungal hematogenous seeding of the thyroid. The inflammatory involvement causes painful enlargement of the gland, but almost always the condition is self-limited or controllable with appropriate therapy.

A blurred hemorrhagic septic focus can be seen in both thyroid lobes. parenchymal incision surface visible on the right.



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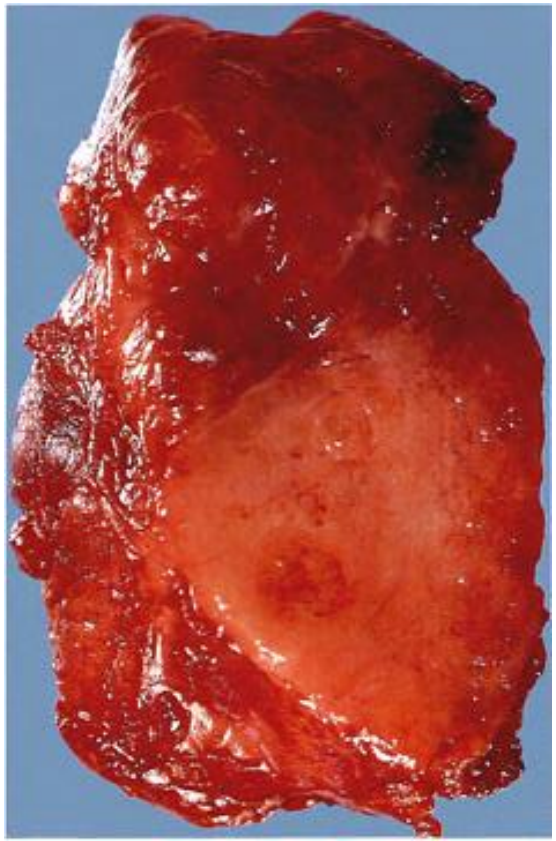
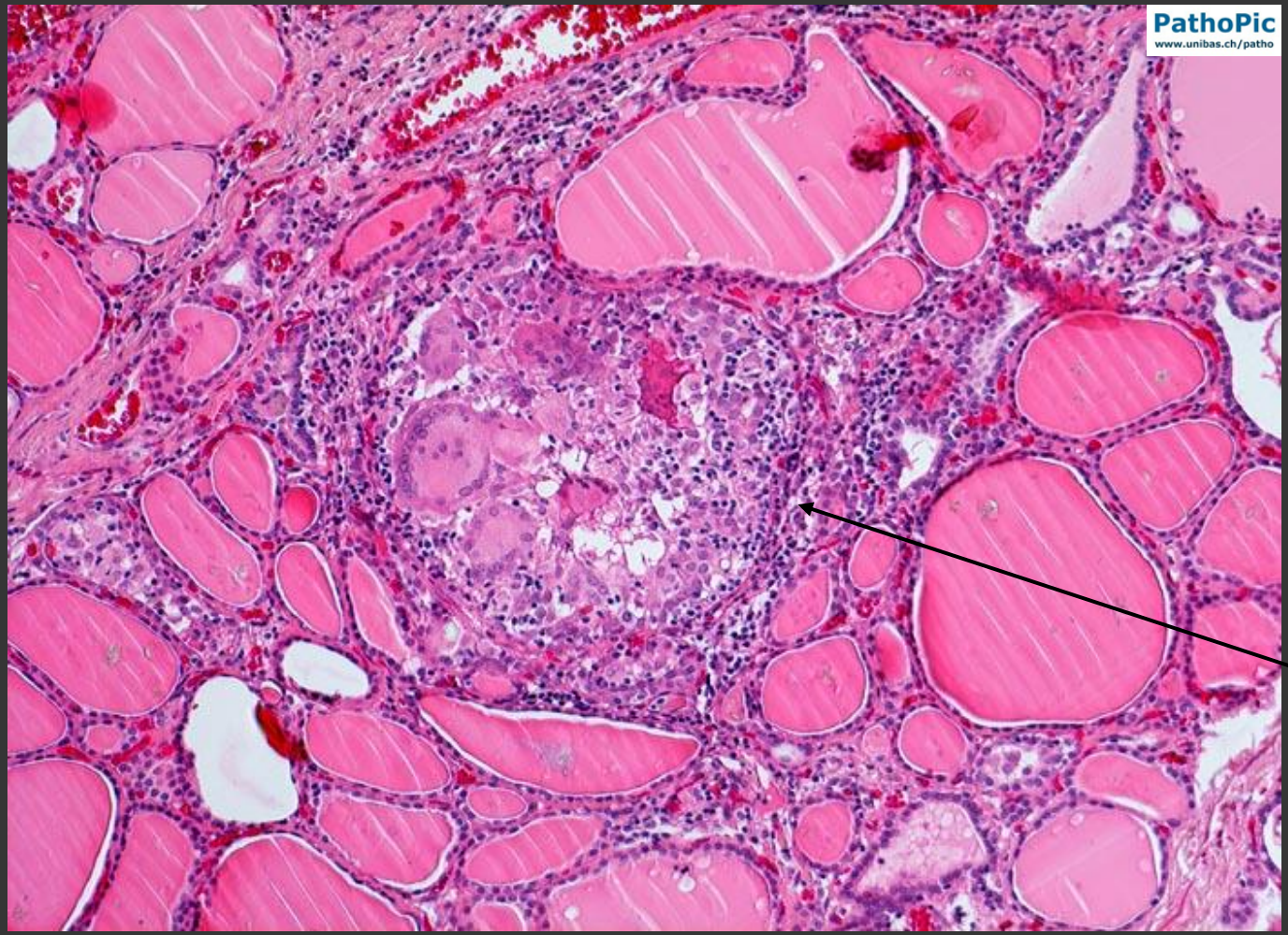


Subacute (De Quervain's) thyroiditis

is an infrequent, self-limited viral infection of the thyroid characterized by granulomatous inflammation, occurring after upper respiratory tract infections (i.e. influenza virus, adenovirus, echovirus, coxsackievirus, mumps virus).

The thyroid gland is enlarged and the cut surface is firm and pale .



Microscopic examination reveals, initially, an acute inflammatory reaction with scattered disrupted follicles replaced by neutrophils forming microabscesses. This is followed by the appearance of a patchy infiltrate of lymphocytes, plasma cells, and macrophages throughout the thyroid. Destruction of follicles allows the release of colloid, which elicits a conspicuous granulomatous reaction. Numerous giant multinucleated cells of the foreign body type, often containing colloid, are present.

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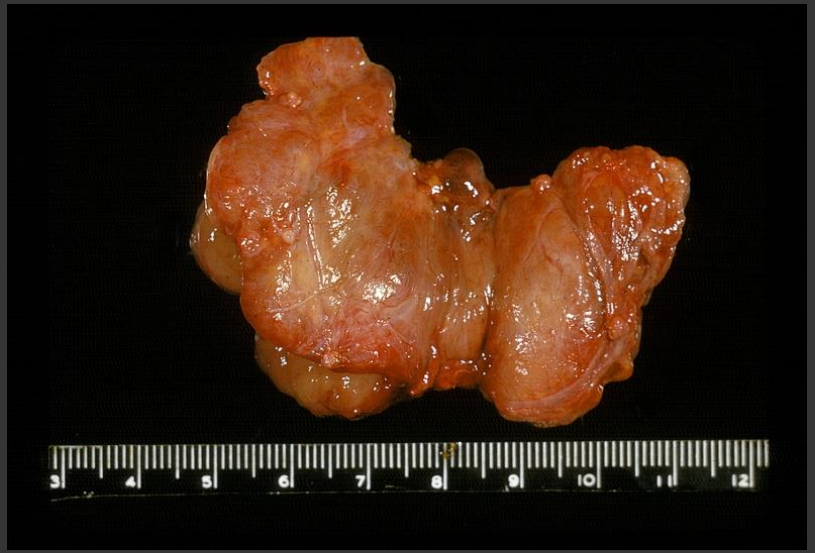
Hashimoto thyroiditis, also termed **lymphocytic thyroiditis**, is an **autoimmune disease** characterized by the presence of **circulating antibodies to thyroid antigens.**



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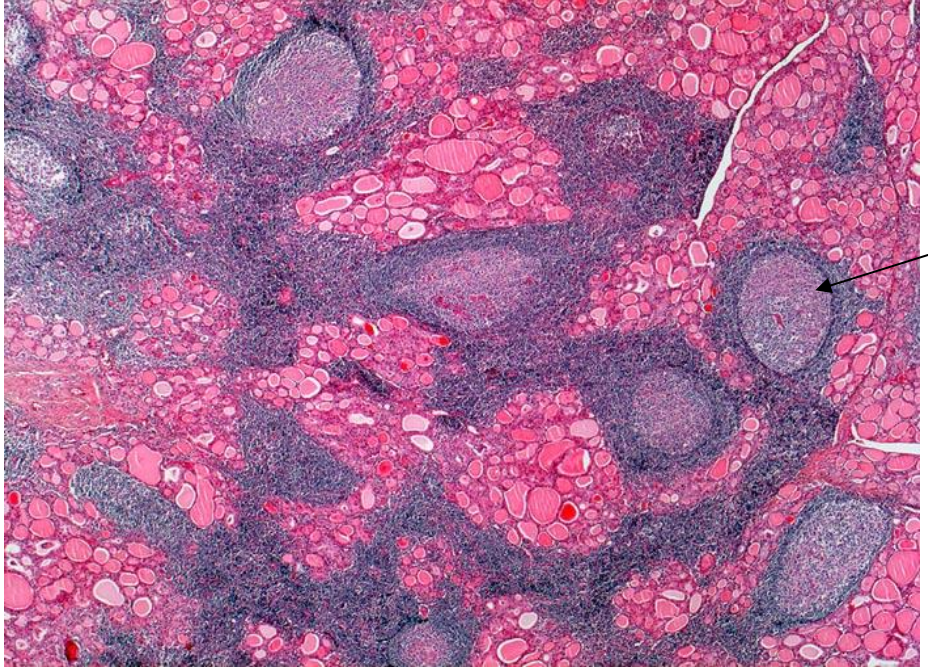
Hashimoto thyroiditis on gross examination, the gland is diffusely enlarged, firm, and slightly lobular, weighing 60 to 200 g. The cut surface is pale tan and fleshy and exhibits a vaguely nodular pattern.



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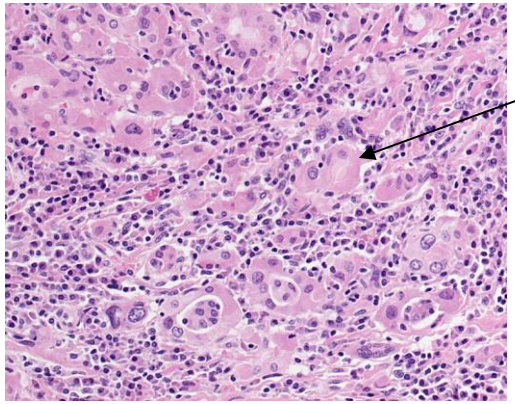
Hashimoto thyroiditis microscopically: the thyroid displays:

1. a conspicuous infiltrate of lymphocytes, plasma cells, macrophages, which, focally, is arranged in lymphoid follicles, often with germinal centres.

2. destruction and atrophy of the thyroid follicles, which are replaced by the inflammatory infiltrate and interstitial fibrosis. Isolated follicles contain a small amount of deeply stained colloid.

3. oxyphilic metaplasia of the follicular epithelial cells – **Hürthle** or **Askanazy cells** or **oncocyte;**. these are thought to represent a degenerated state of the follicular epithelium.

PathoPic
www.unibas.ch/patho



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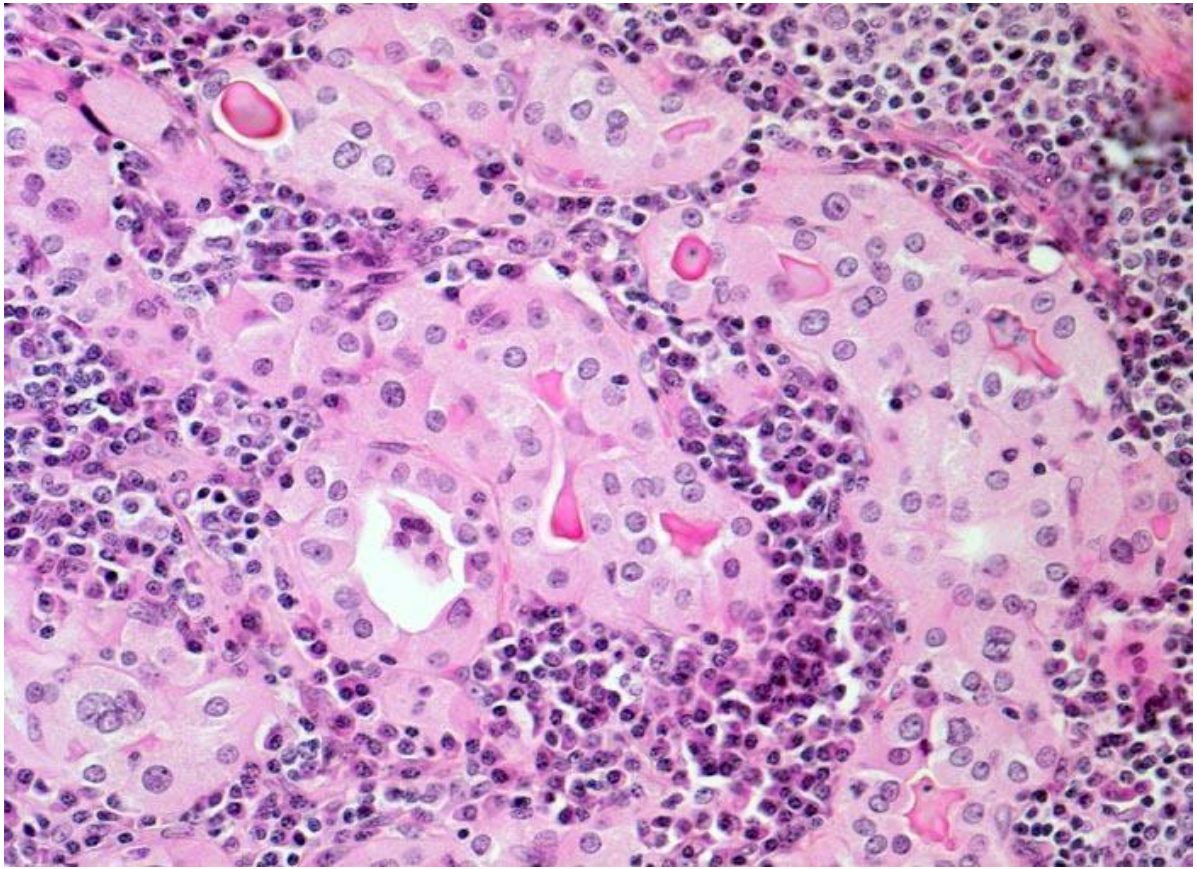
Hashimoto thyroiditis

- **oxyphilic metaplasia of the follicular epithelial cells = Hürthle cells** with an abundant, brightly eosinophilic granular cytoplasm



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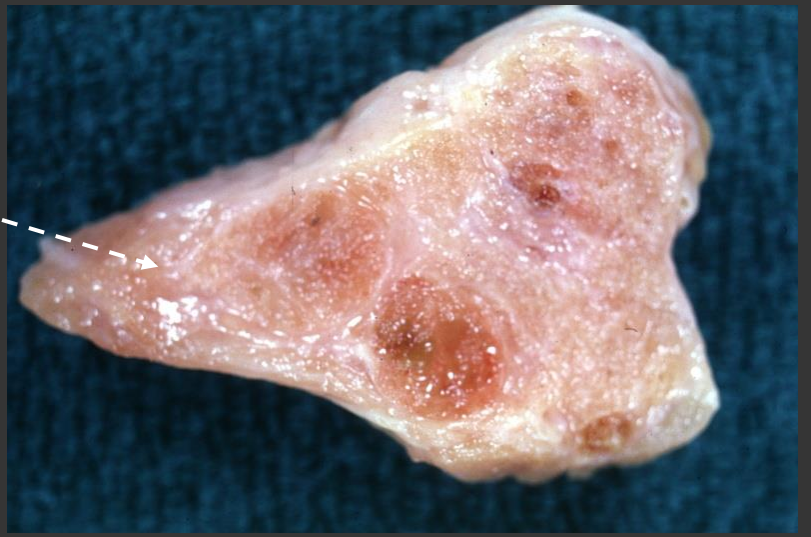
Riedel thyroiditis is a rare disease, of unknown cause, characterized by **glandular atrophy**, **hypothyroidism**, and r**eplacement of the thyroid by fibrous tissue**, with **adhesion to surrounding structures**. The term “thyroiditis” is something of a misnomer since the disease also involves extrathyroidal soft tissue of the neck and is often associated with progressive fibrosis in other locations, including the retroperitoneum, mediastinum, and orbit.



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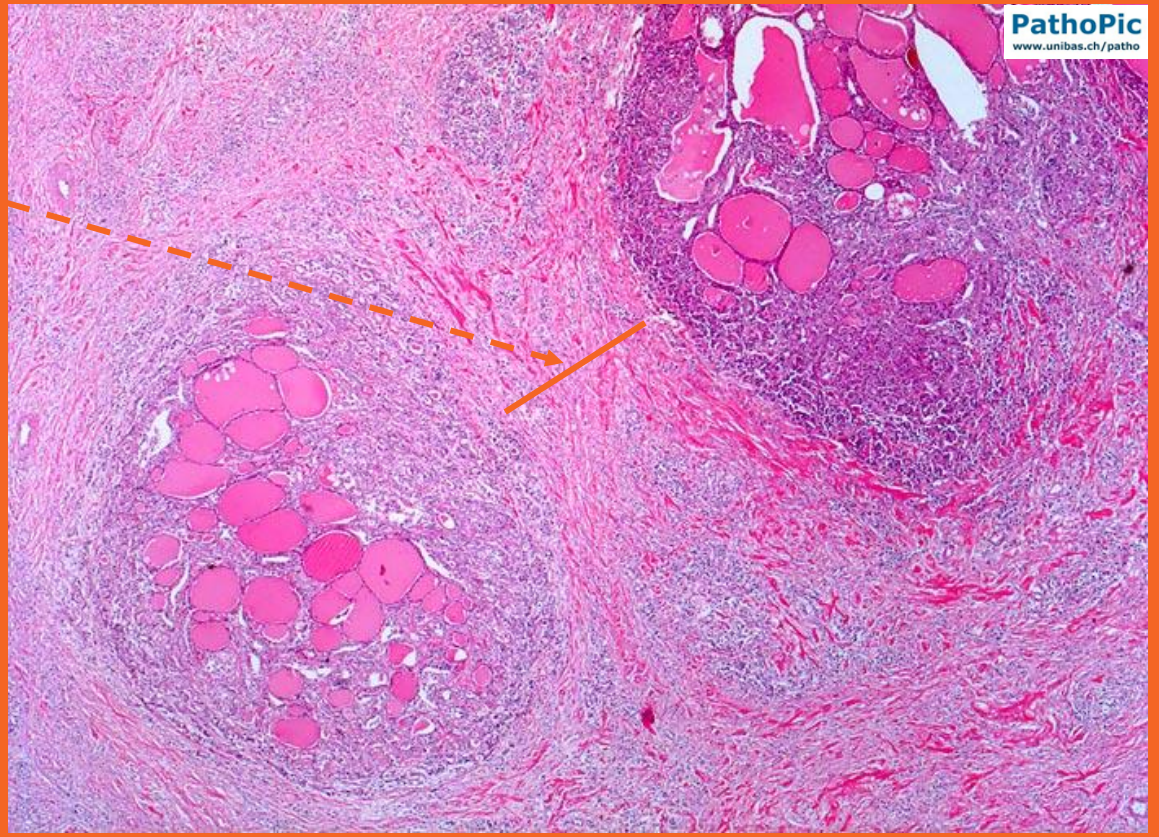
Microscopic examination reveals admixed areas of dense, **hyalinized fibrous tissue** and a chronic inflammatory infiltrate replacing the parenchyma with other areas where thyroid follicles are normally preserved.



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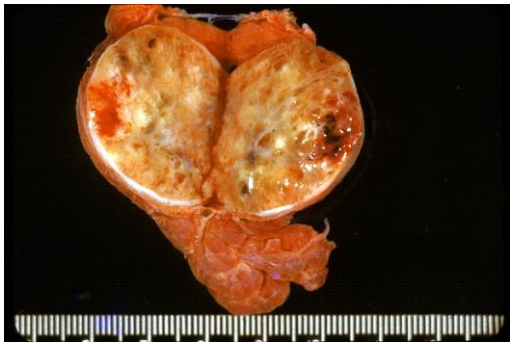
THYROID ADENOMAS are by definition benign neoplasms. With rare exceptions, they all are derived from the follicular epithelium and so might all be called follicular adenomas.

On gross examination, the follicular adenoma is a solitary, circumscribed nodule, 1 to 3 cm in diameter, which protrudes from the surface of the thyroid. The cut surface of the tumour is soft and paler than surrounding parenchyma. Haemorrhage, fibrosis, and cystic change are common.



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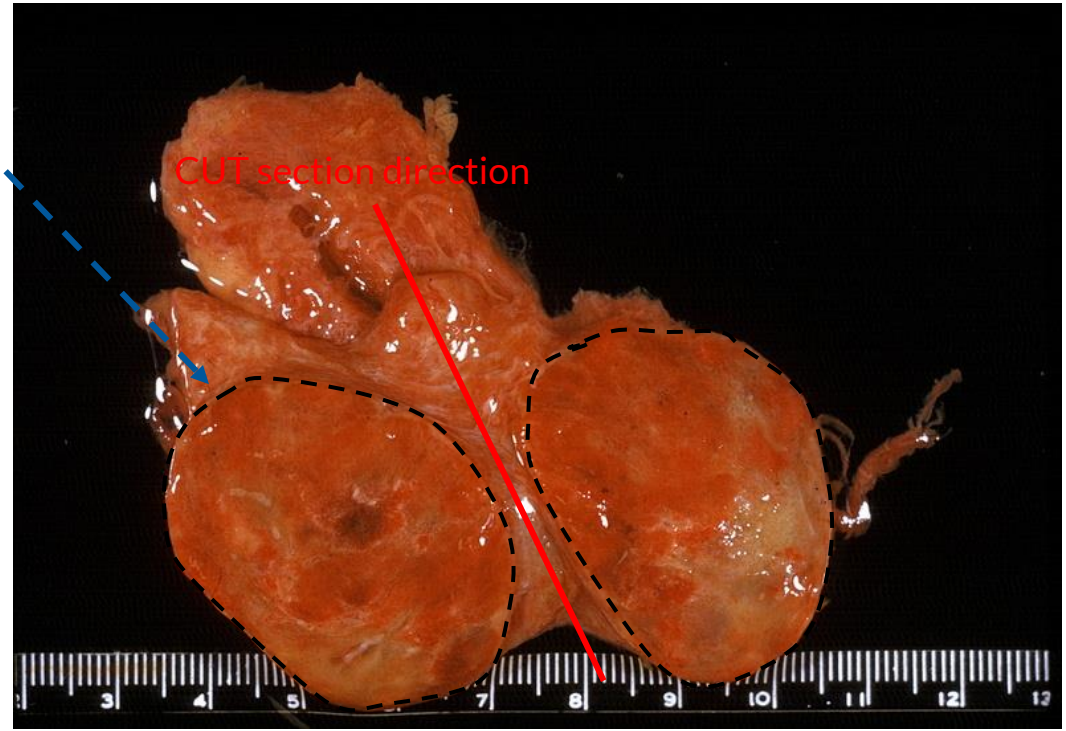

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Microscopically, a variety of patterns can be identified that recapitulate stages in the embryogenesis of the normal thyroid, and so they have been divided into several subtypes:

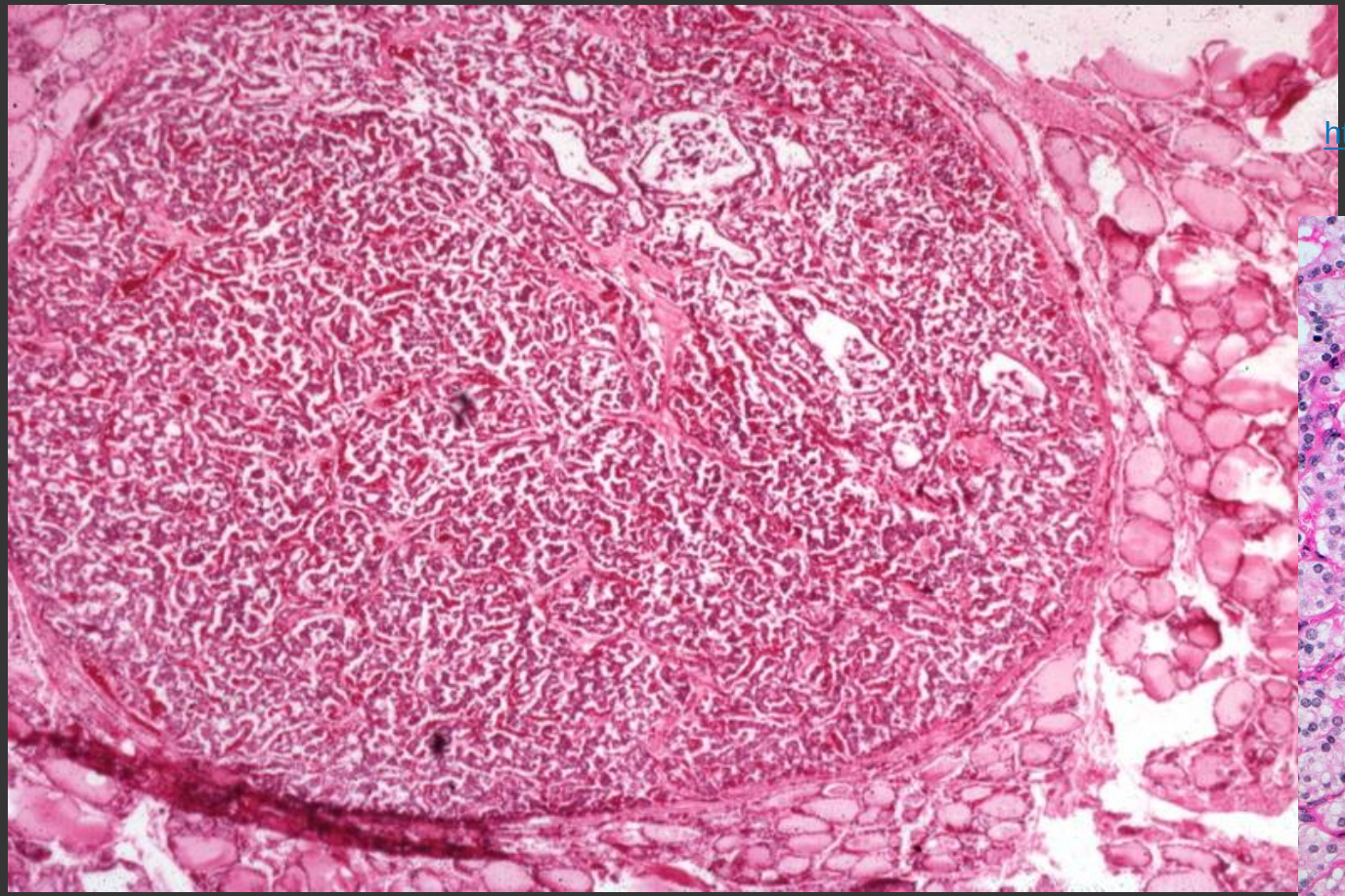
embryonal: a trabecular pattern in which poorly formed follicles contain little or no colloid

fetal: cells tend to be arranged in micro follicles containing little colloid

simple: mature follicles with a normal amount of colloid

colloid: large follicles containing abundant colloid

microfollicular and **macrofollicular** patterns



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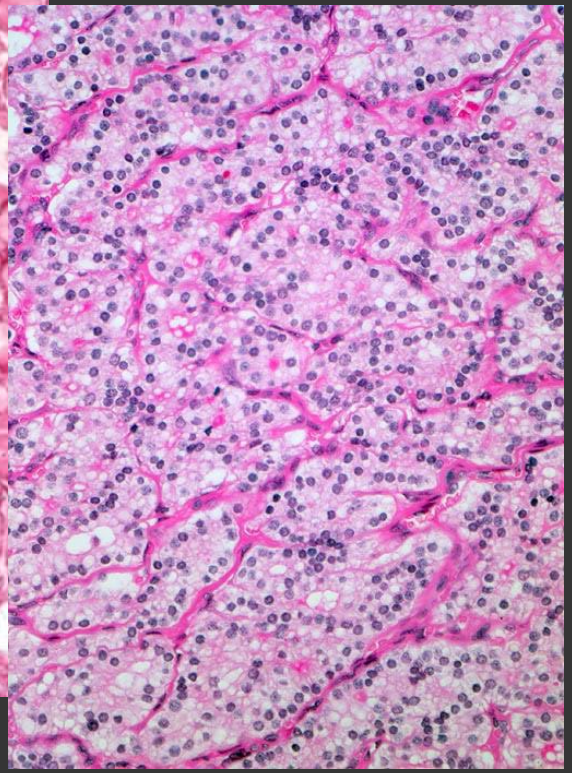


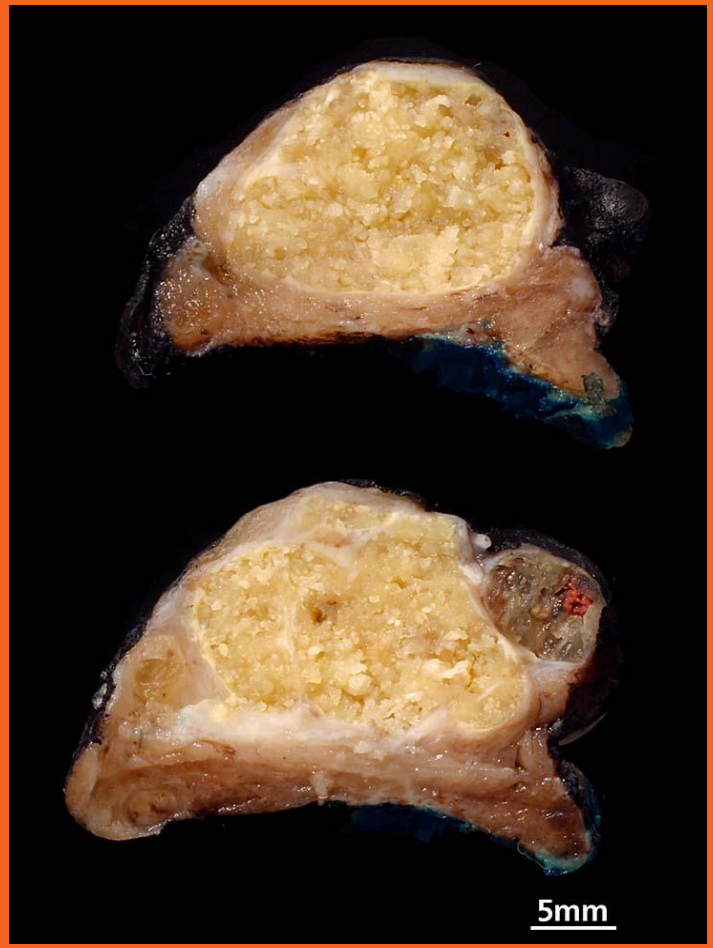
THYROID CANCERS, almost all carcinomas, are uncommon, representing less than 1% of all cancer deaths. The morphologic variants of thyroid carcinoma with their frequencies are as follows:

papillary carcinoma – 75 to 85%

follicular carcinoma – 10 to 20%

medullary thyroid carcinoma – 5%

anaplastic carcinoma – rare.



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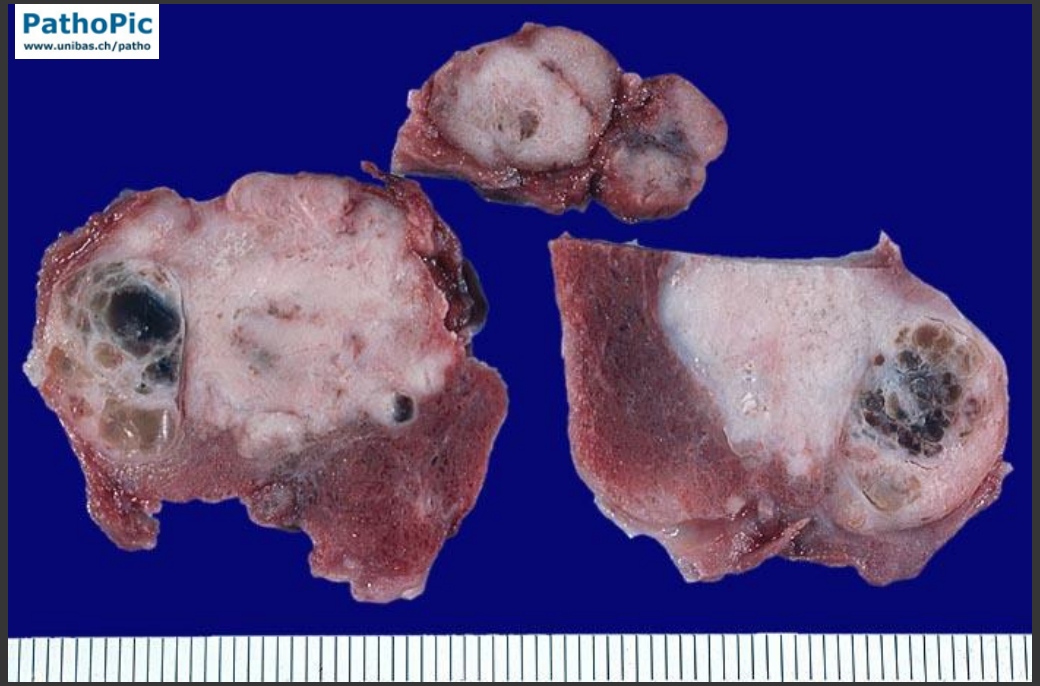
Papillary carcinoma is the **predominant form of thyroid cancer**. It often appears as **multifocal tumoral nodules**, and **regional lymph node metastases are present at the time of diagnosis in 50% of cases. On cross-section, these lesions are grey-white and firm and sometimes have foci of calcification or areas of cystic change.**



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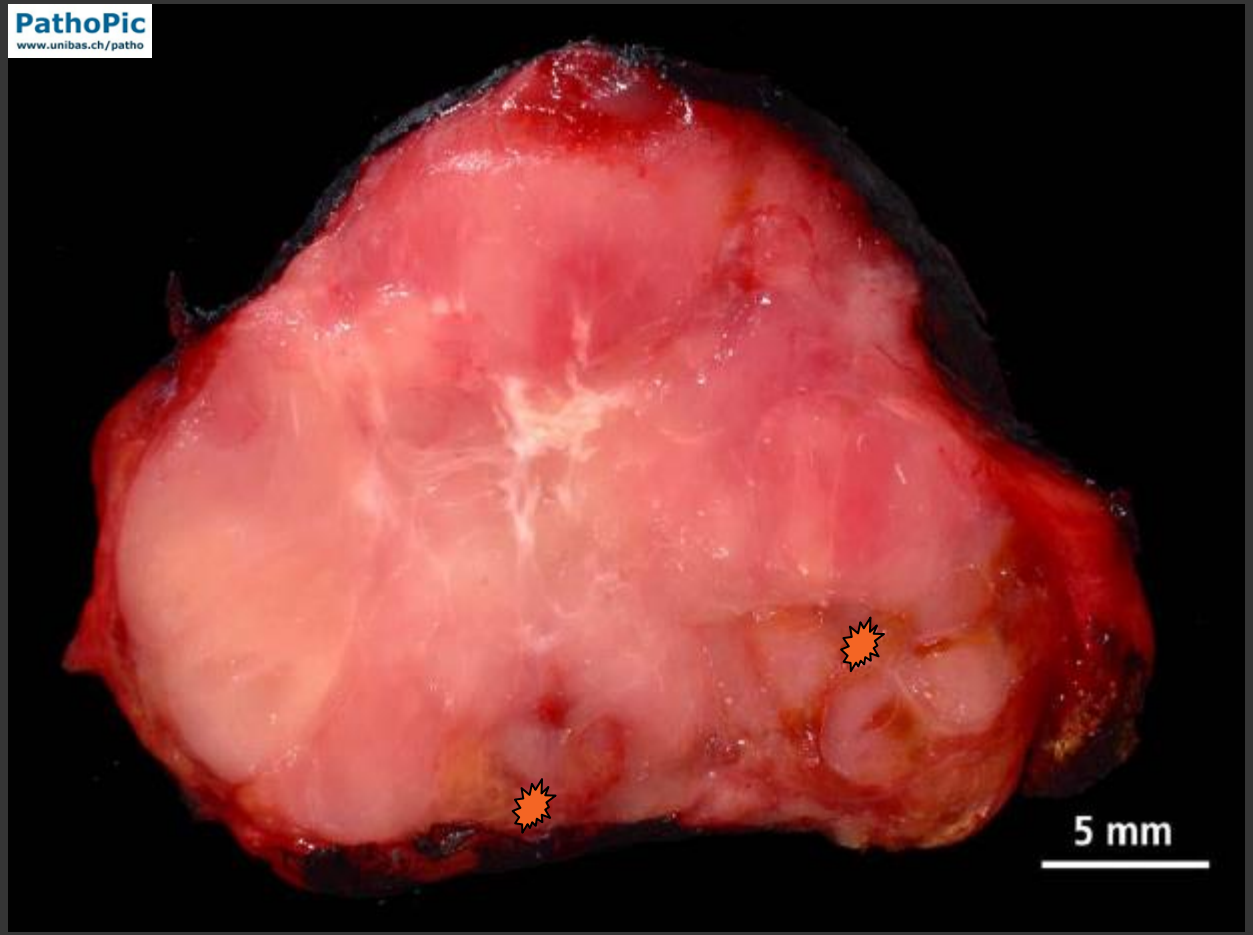


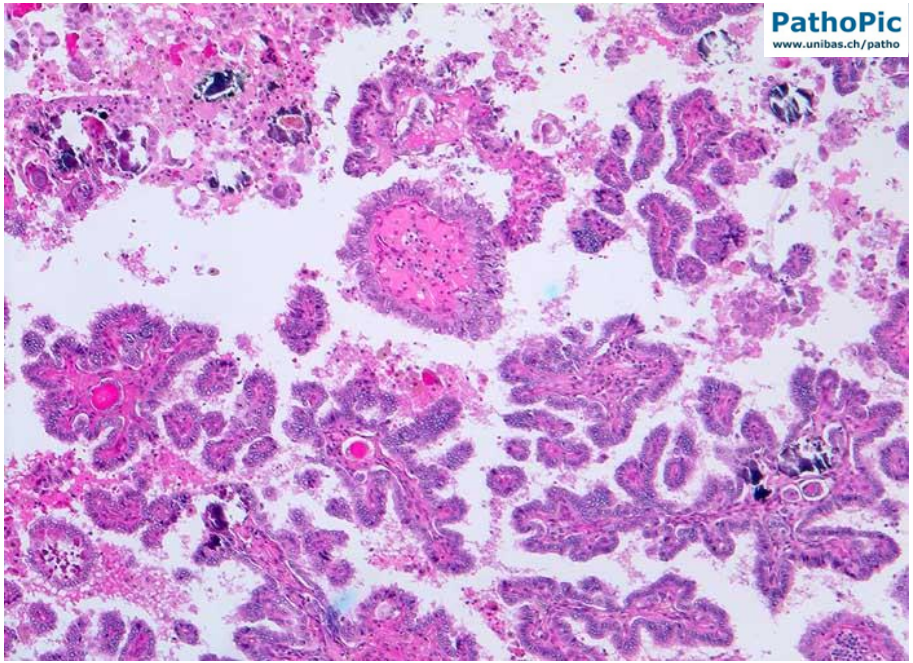
Thyroid papillary carcinoma is rarely encapsulated but instead infiltrates surrounding thyroid parenchyma and sometimes the perithyroid soft tissue.

Grey lobulated tumor with central scar. Infiltration of the perithyreoidal fat*

http://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=008631

Histologically, this cancer type ranges from predominantly papillary (about a third) to follicular appearance (another third) to equal parts of papillary and follicular architecture (the last third). At least 2/3 of cases reveal some branching papillae having a fibrovascular stalk covered by a single to multiple layers of cuboidal crowded epithelial cells. Despite the considerable architectural and cellular variations, the characteristic hallmarks of papillary carcinoma can be found in all

- hypochromic "empty" nuclei – "orphan Annie eyes",
- nuclear grooves,
- eosinophilic intranuclear inclusions representing invaginations of cytoplasm,
- psammoma bodies - calcific lamellations, usually in the cores of papillae.



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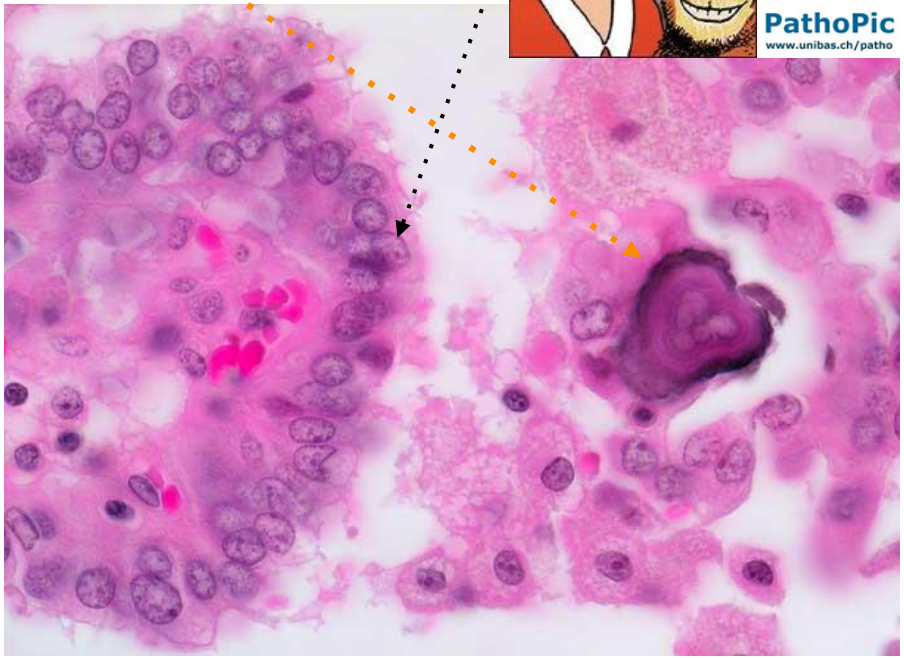

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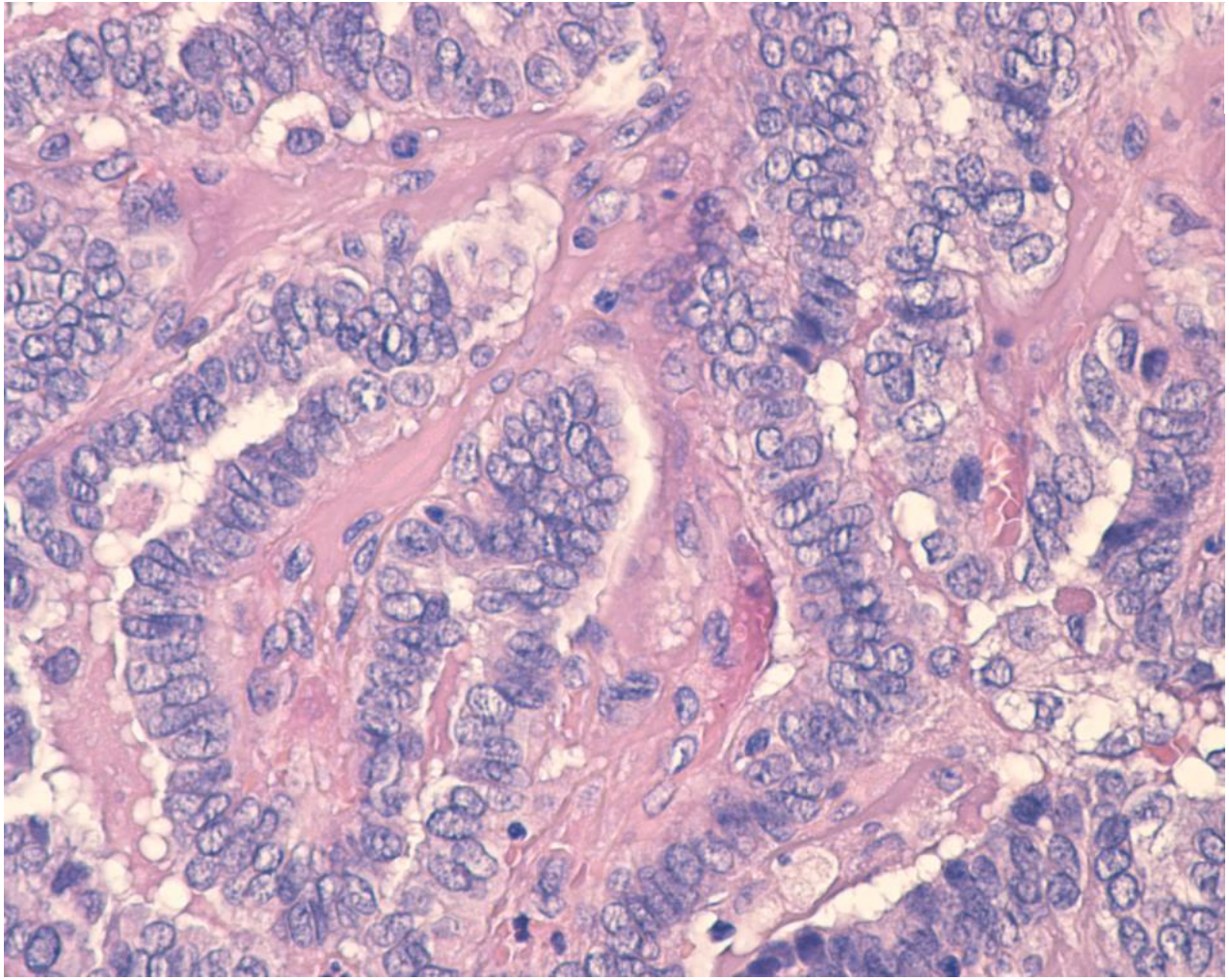
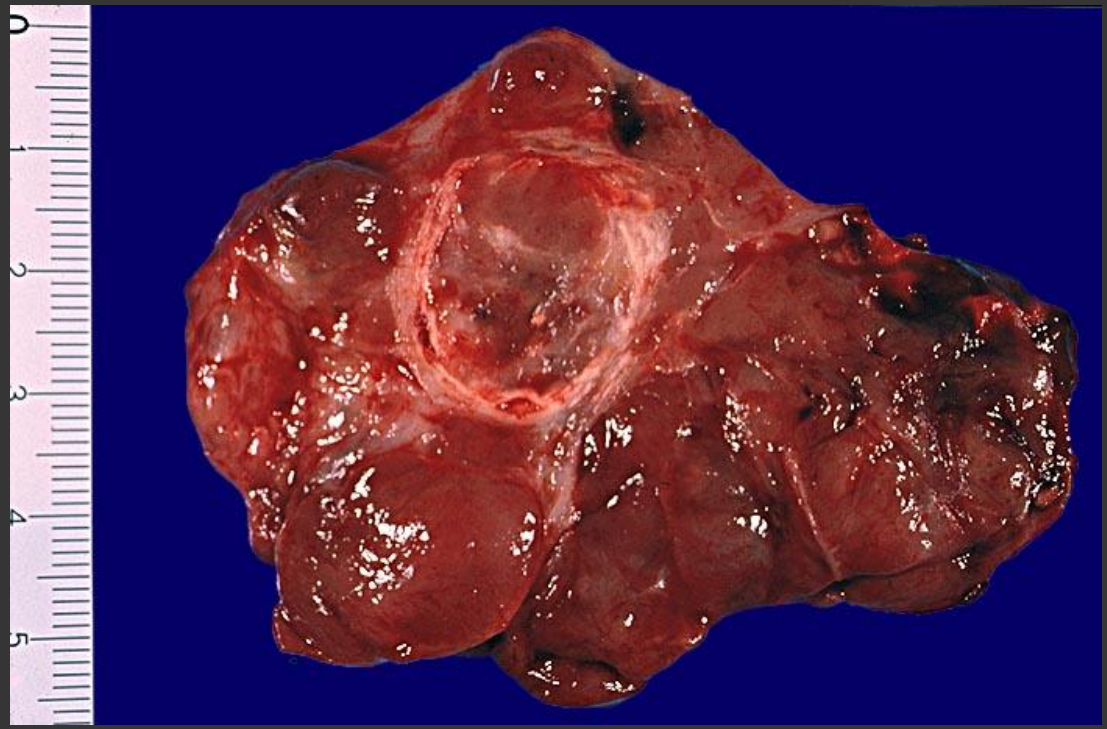


H&E slide from own histology slide library.

Follicular carcinoma of the thyroid is defined as a malignant neoplasm that is purely follicular and does not contain any papillary or other elements. Typically, they are encapsulated tumours, grey to pink coloured and present foci of fibrosis and calcification.



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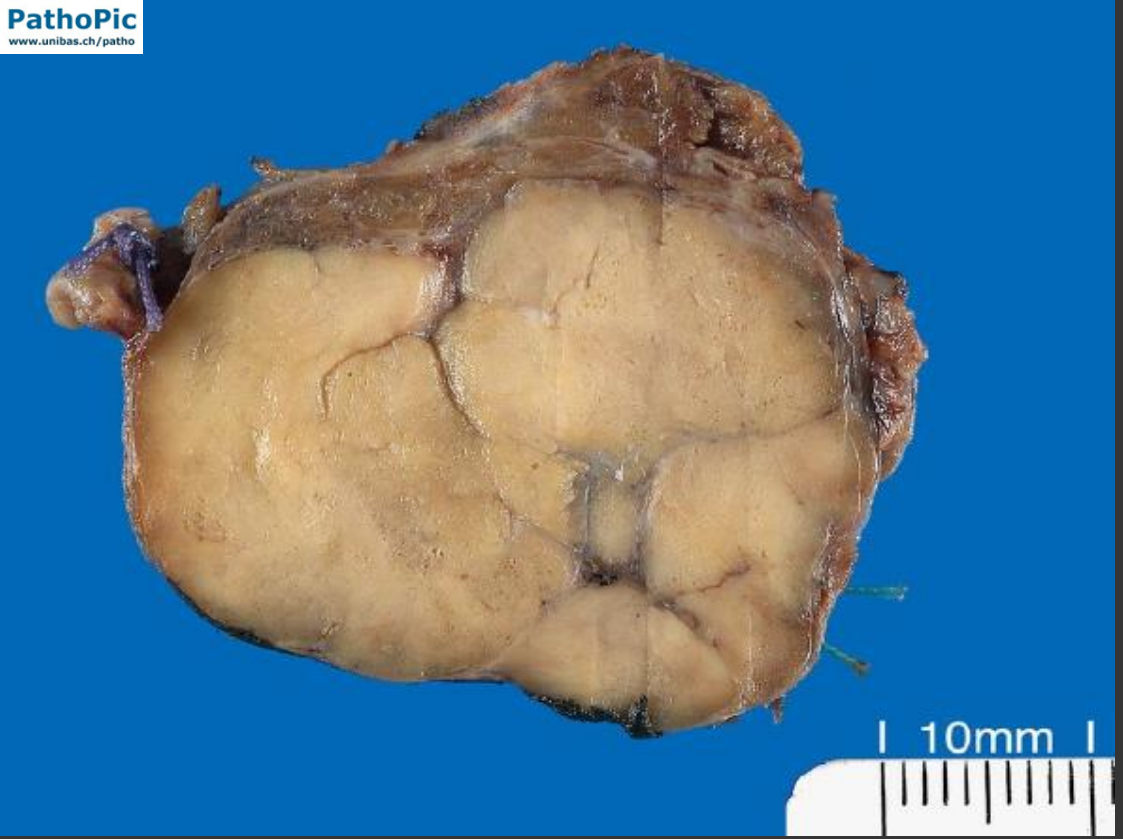

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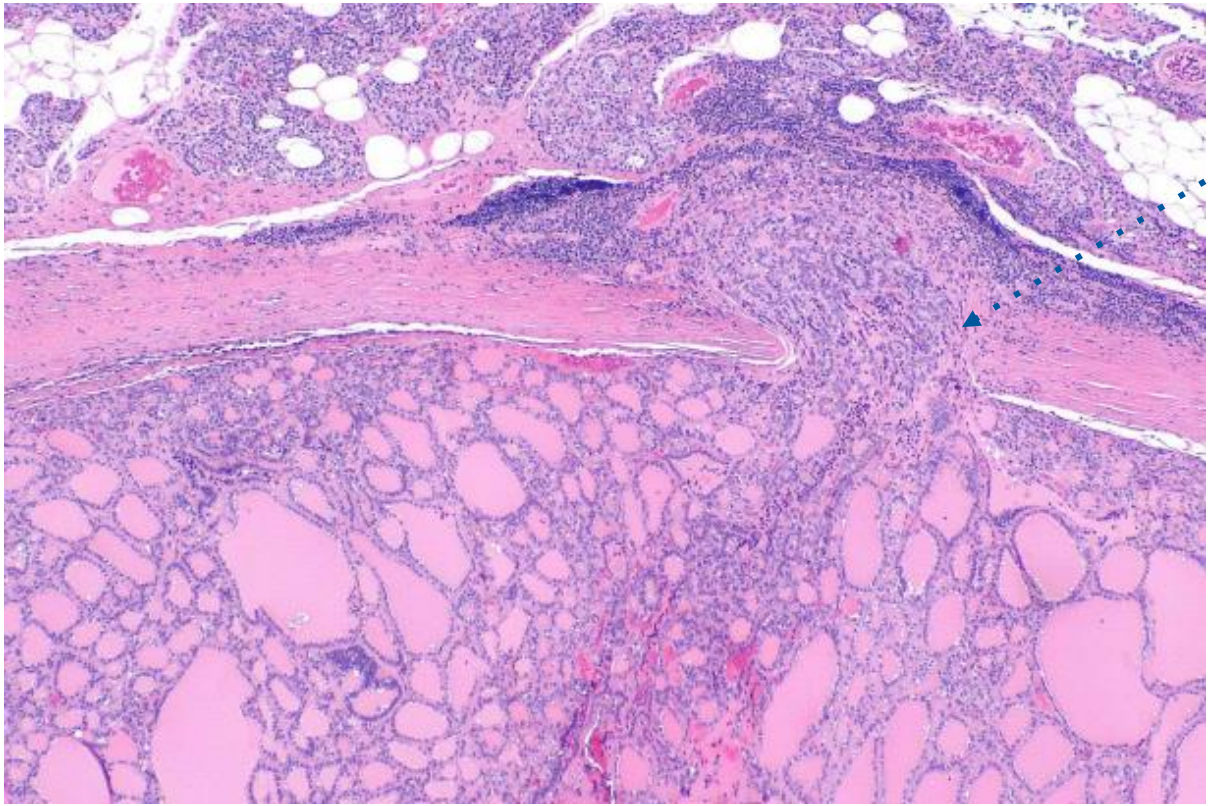
Microscopically, follicular carcinoma present a microfollicular architecture with relatively uniform, orderly, cuboidal cells lining colloid-filled follicles, which is sometimes exceedingly difficult to differentiate from follicular adenoma. **What clears up the diagnosis is the presence of microscopic invasion into the capsule and blood vessels carcinomatous emboli.**



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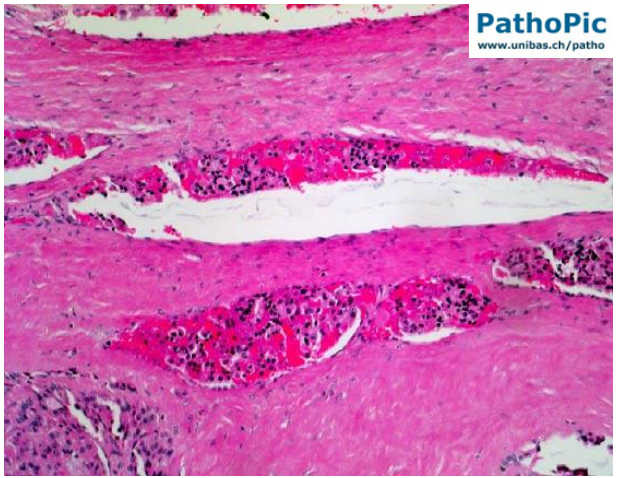

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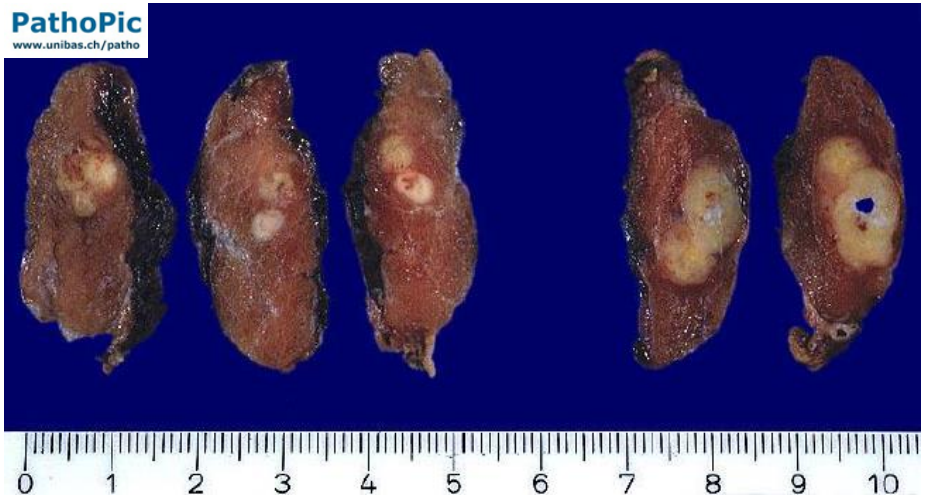
Blood vessels with tumor emboli, thyroid follicular carcinoma.



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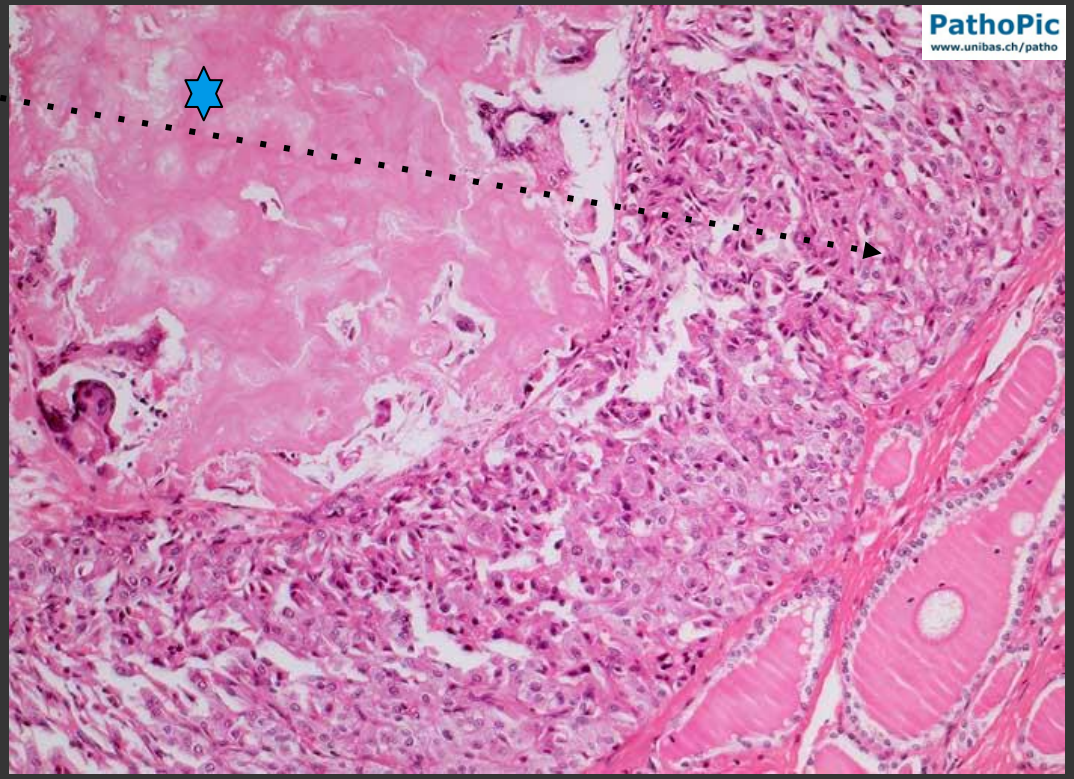
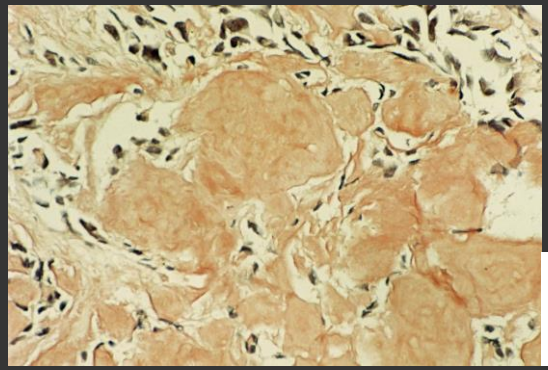
Medullary carcinoma of the thyroid is a tumor derived from the parafollicular or C cells of the thyroid, which are distinguished by their secretion of calcitonin. **On gross examination, medullary carcinoma tends to arise in the superior portion of the thyroid as a single or multiple nodular lesions.** The tumour tissue is **firm, whitish-grey, and infiltrative.** Frequently, there is spotty calcification and minimal to extensive fibrosis.

Histologically, the tumor **cells are usually polygonal or spindled** and disposed in cellular nests separated by a scant to abundant fibrovascular stroma. In about half of the cases, the stroma contains broad bands / large masses of **amyloid deposition.**





H&E slide from own histology slide library.

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Thyroid medullary carcinoma: polygonal cells disposed in cellular nests separated by abundant fibrovascular stroma.

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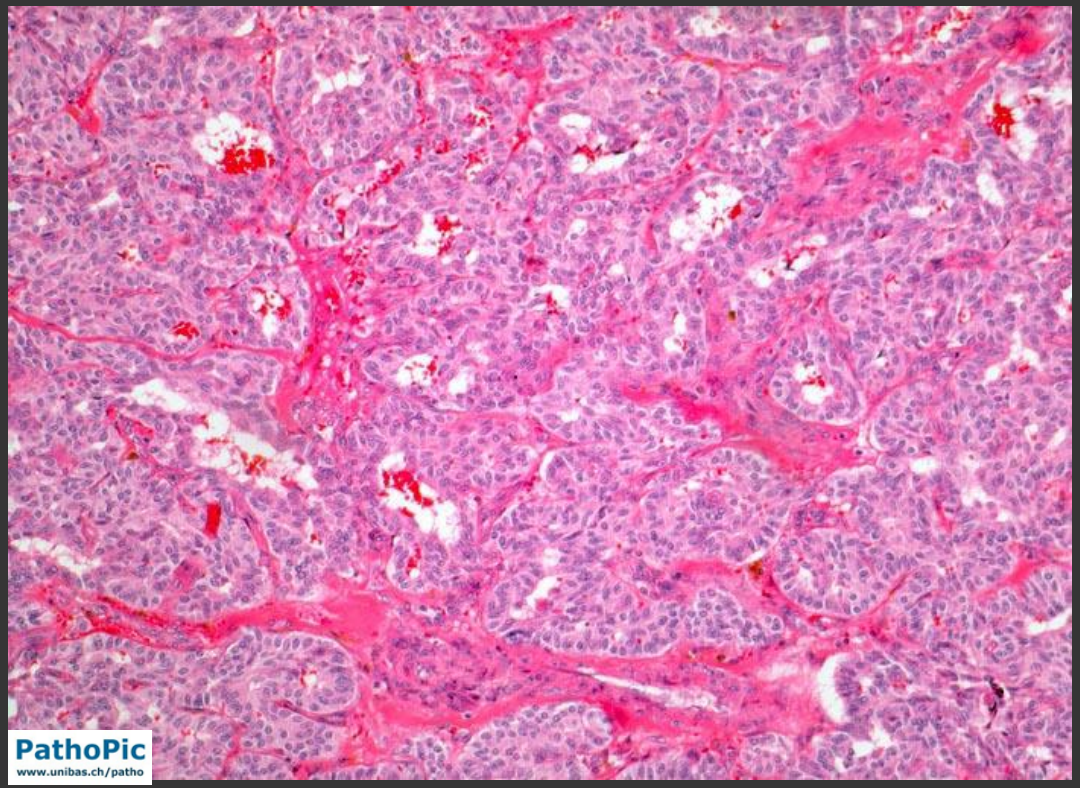
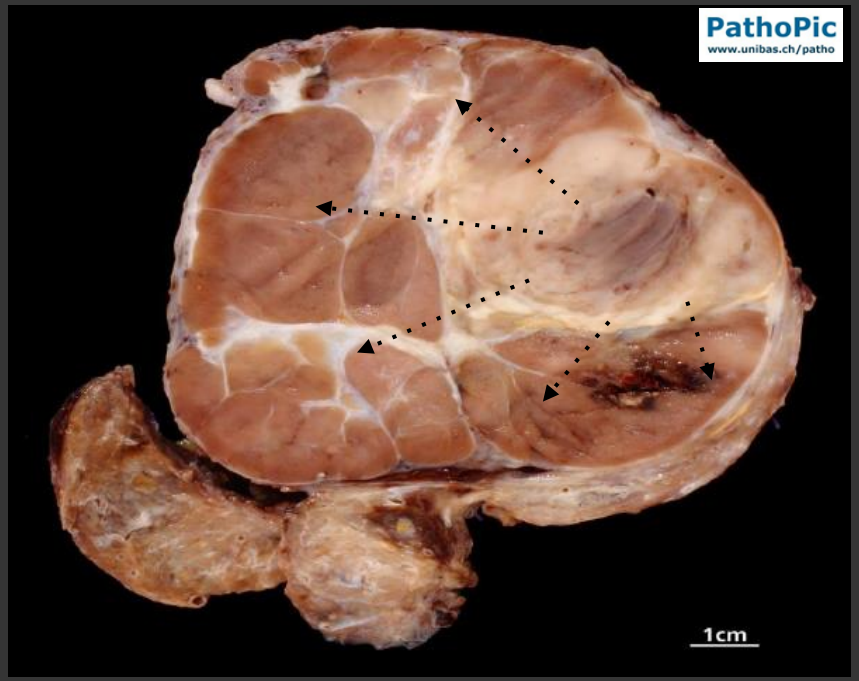


Anaplastic (undifferentiated) carcinoma is highly aggressive thyroid cancer, which is usually rapidly fatal. It presents as large masses in the gland, which are poorly circumscribed and frequently extend into the soft tissue of the neck. The cut surface is hard and greyish white.



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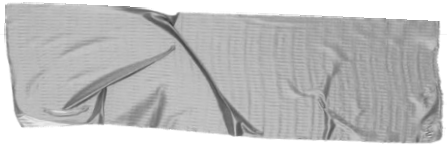
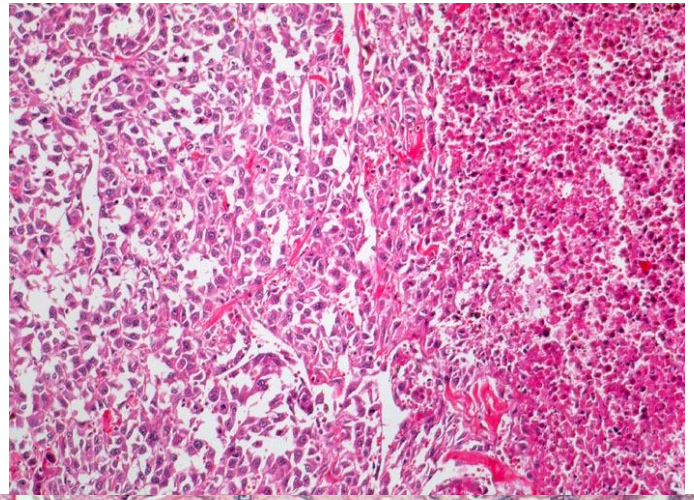


There are three histologic patterns: (1) spindle cells “sarcoma-like” proliferation, (2) giant cells lesion, and (3) small cell carcinoma. The tumor tends to invade and occlude the vessels, producing foci of infarction within the tumor.

3



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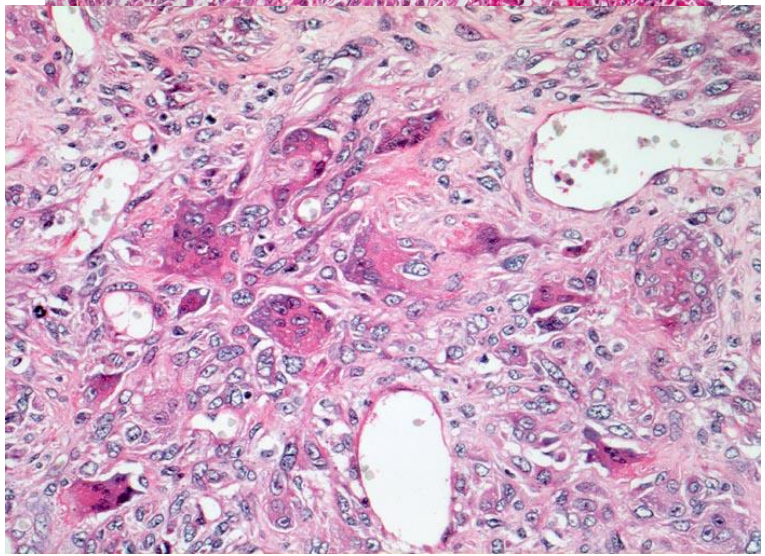

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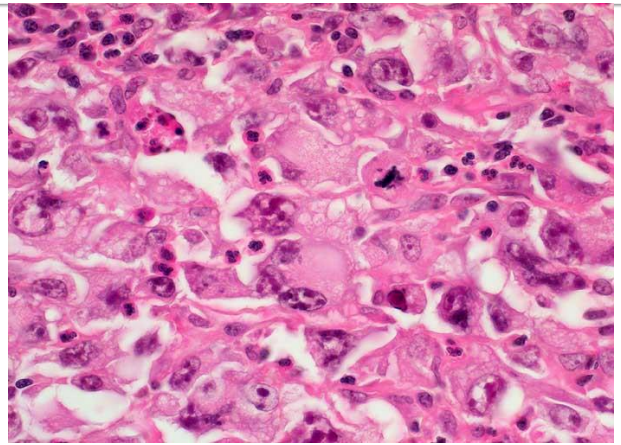

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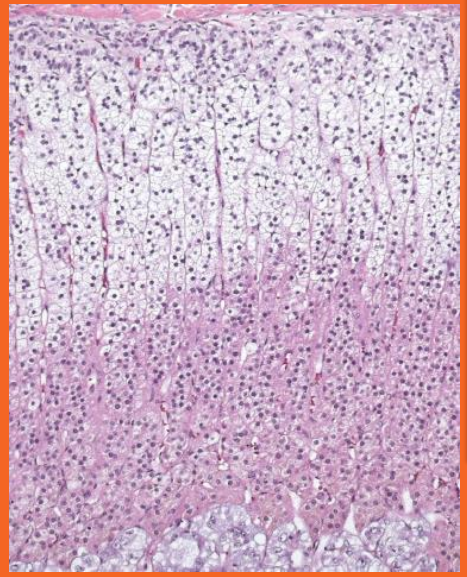
ADRENAL GLAND PATHOLOGY

ADRENAL CORTEX TUMORS. The proliferative lesions of the adrenal cortex range from diffuse hyperplasia to nodular hyperplasia to benign and malignant tumors, and they may be or not associated with steroidogenesis.

Histologically normal adrenal gland



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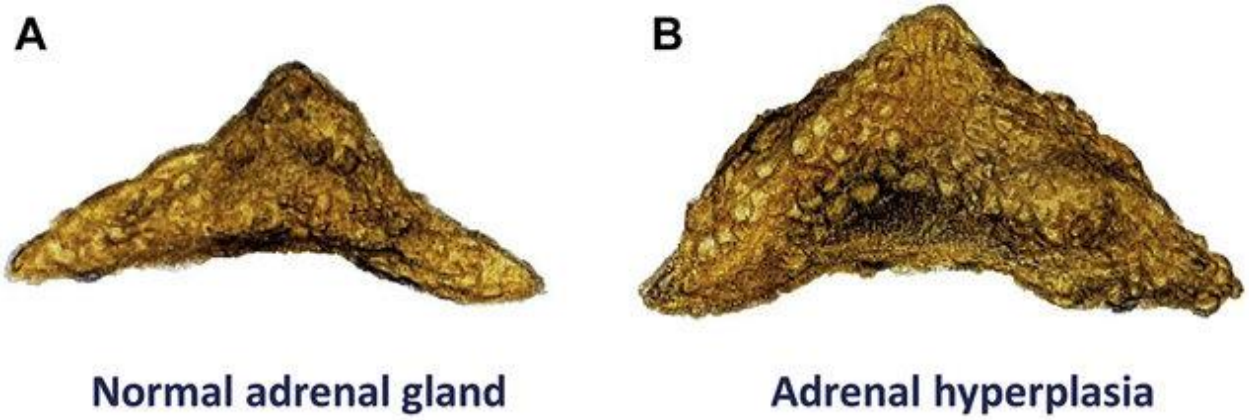
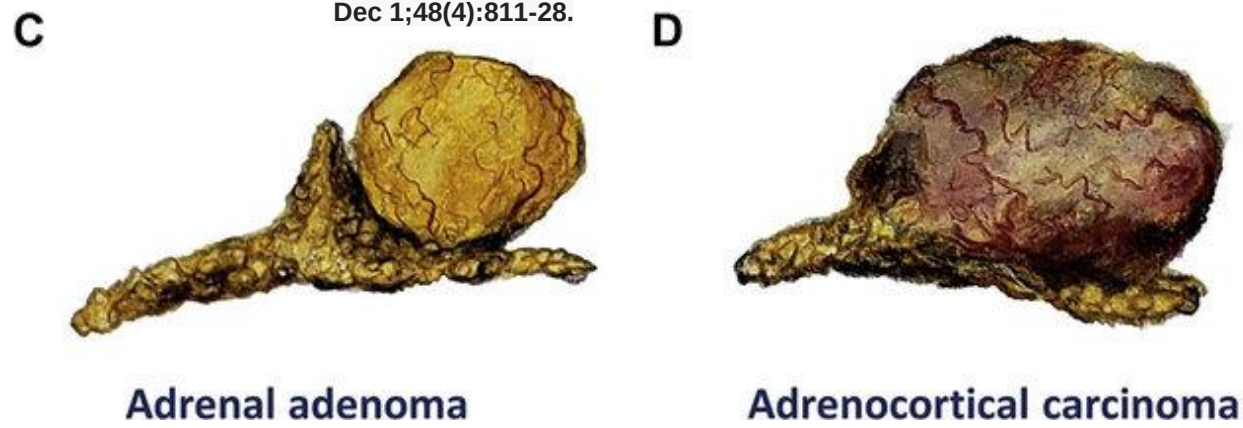
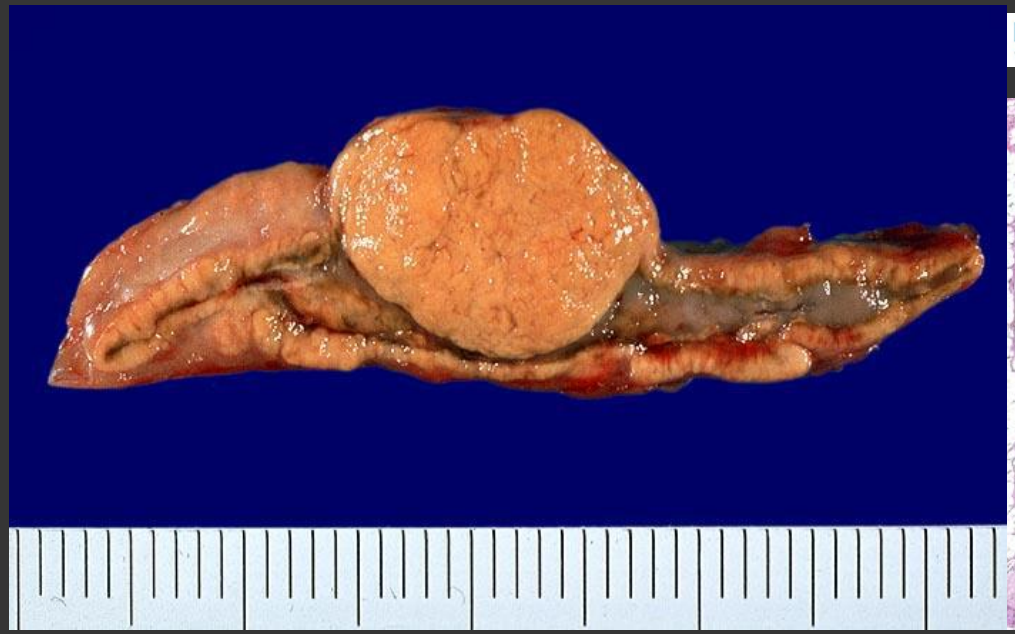
https://www.researchgate.net/publication/336927543_Resistant_Hypertension_A_Clinical_Perspective



Hannah-Shmouni F, Gubbi S, Spence JD, Stratakis CA, Koch CA. Resistant Hypertension: A Clinical Perspective. Endocrinology and Metabolism Clinics. 2019 Dec 1;48(4):811-28.



The functional adenoma is an encapsulated, firm, yellow mass, measuring about 4 cm in diameter, associated with the atrophy of the adjacent cortex. **Microscopically**, it is composed of mixtures of lipid-rich and lipid-poor cortical cells with little variation in cell and nuclear size.



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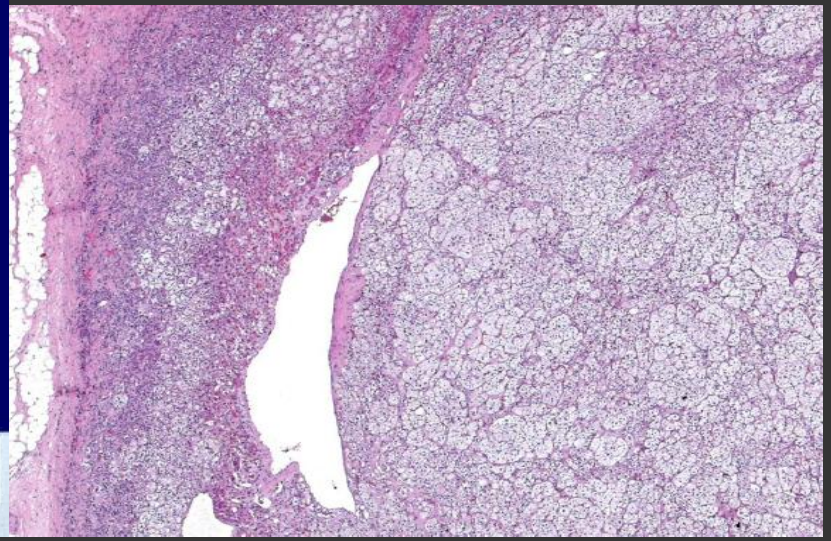

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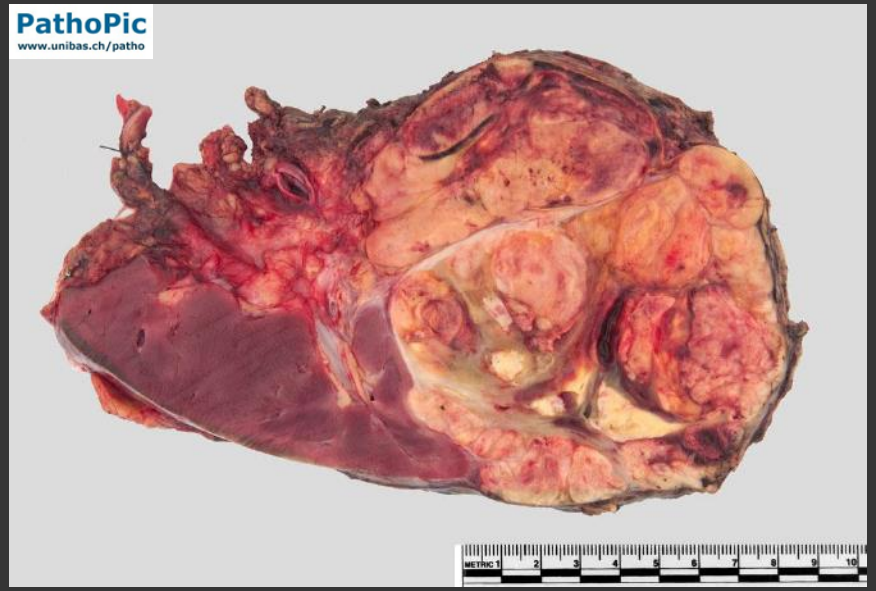
Adrenal carcinoma, commonly (80% of cases) functional, tends to be large, soft, unencapsulated mass, frequently exceeding 200 to 300 g in weight. The cut surface has a variegated pink, brown, or yellow color, often with necrosis, hemorrhage, and cystic change. The contralateral adrenal cortex is atrophic.



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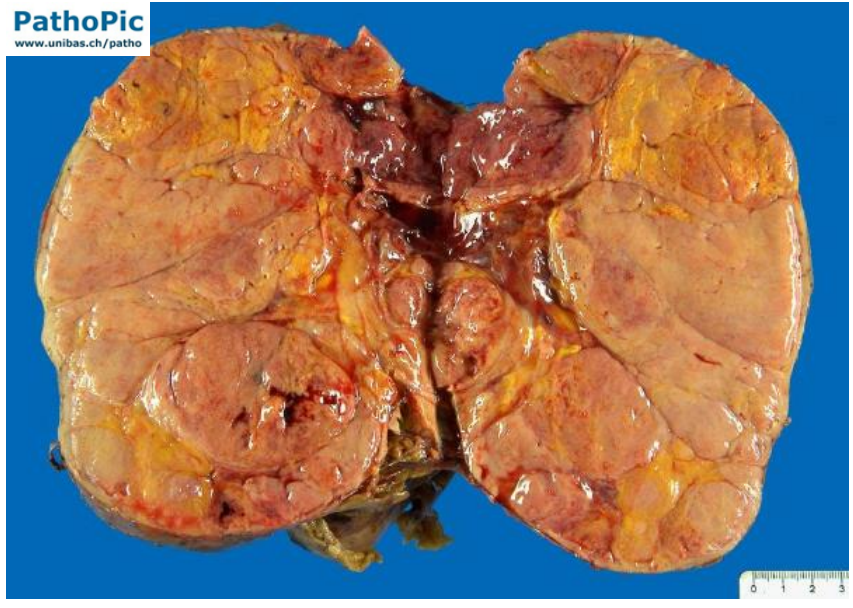
Nonfunctional **adrenal carcinoma** is a highly malignant and large tumor, when discovered, exceeding 20 cm in diameter and 1 kg in weight. **Microscopically**, both clear and compact cells are present with varying degrees of nuclear pleomorphism, abnormal mitotic figures and, sometimes, vascular invasion.
Cellular morphology ranges from mild degrees of atypia to wildly anaplastic neoplasm composed of monstrous giant cells.



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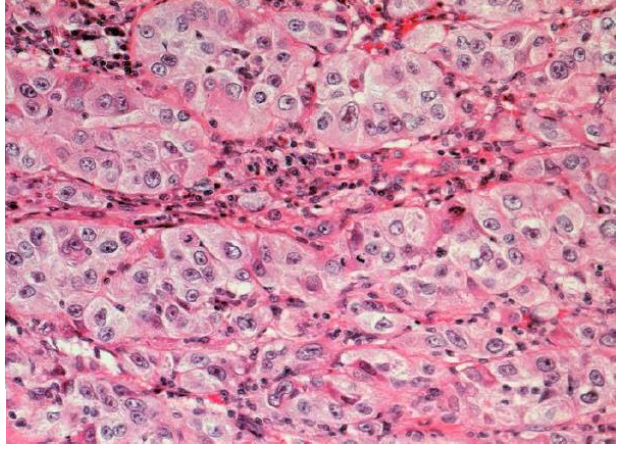

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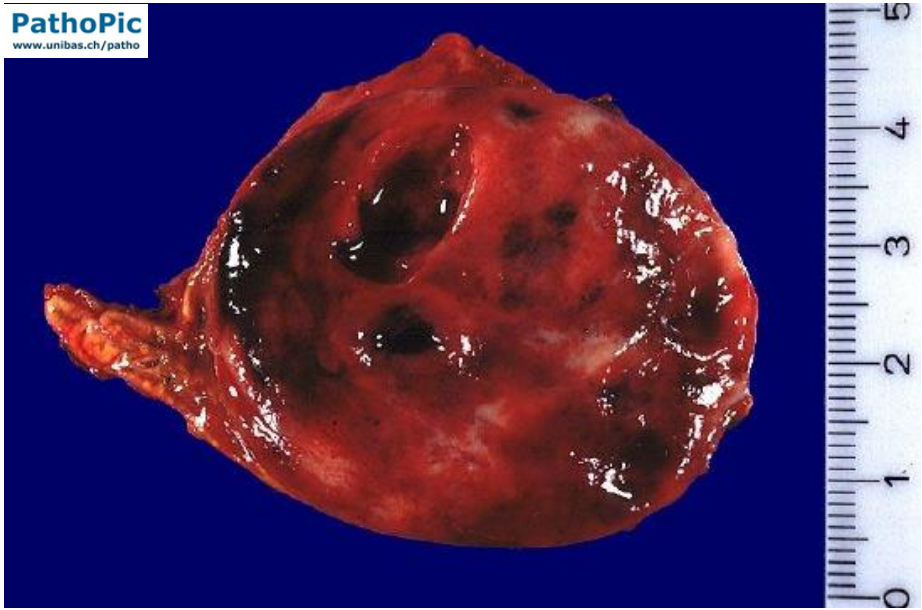

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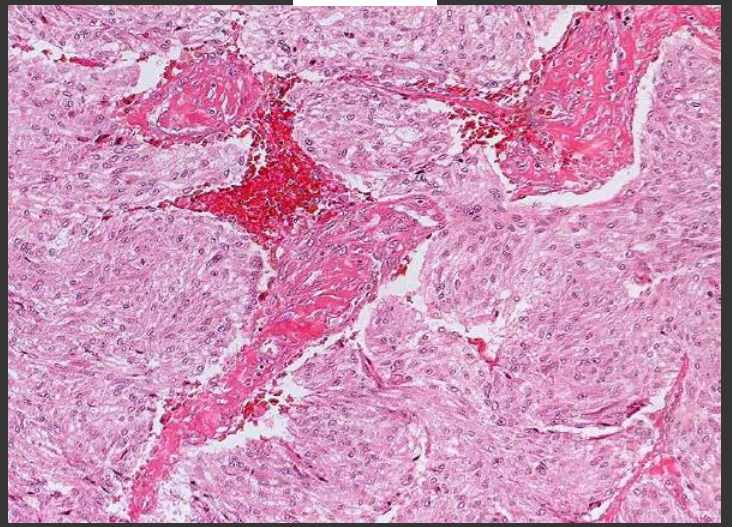
PHEOCHROMOCYTOMA refers to a rare tumor of **chromaffin cells of the adrenal medulla** that secretes catecholamines. **Such tumor also originates in extra-adrenal sites, in which case it is termed paraganglioma.**

Pheochromocytoma tends to be encapsulated, spongy, reddish mass, with prominent central scars, hemorrhage, and cystic degeneration.

On the light microscope, the cells are arranged either in large trabeculae, punctuated by thin-walled sinusoids, or in small alveoli (“zellballen”) enclosed within a fibrovascular stroma derived from the tumor capsule. Cellular and nuclear pleomorphism is often present and may include multinucleated giant and bizarre cells. Mitotic figures are rare. Because malignant and benign pheochromocytomas may have an identical histologic appearance, the only absolute criterion of malignancy is metastasis to the related lymph nodes, liver, lungs and bones.



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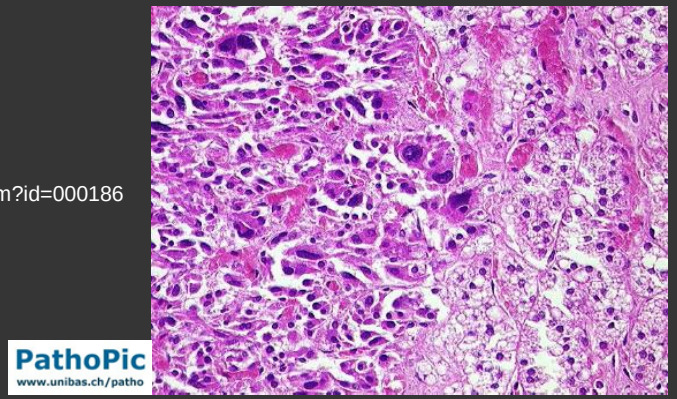

NEUROBLASTOMA, a malignant tumor of neural crest origin, composed of neoplastic neuroblasts, may arise in the adrenal medulla or sympathetic ganglia. It is one of the most important malignant tumors of childhood, accounting for up to 10% of all childhood cancers and 15% of cancer deaths among children. The peak incidence is in the first 3 years of life.

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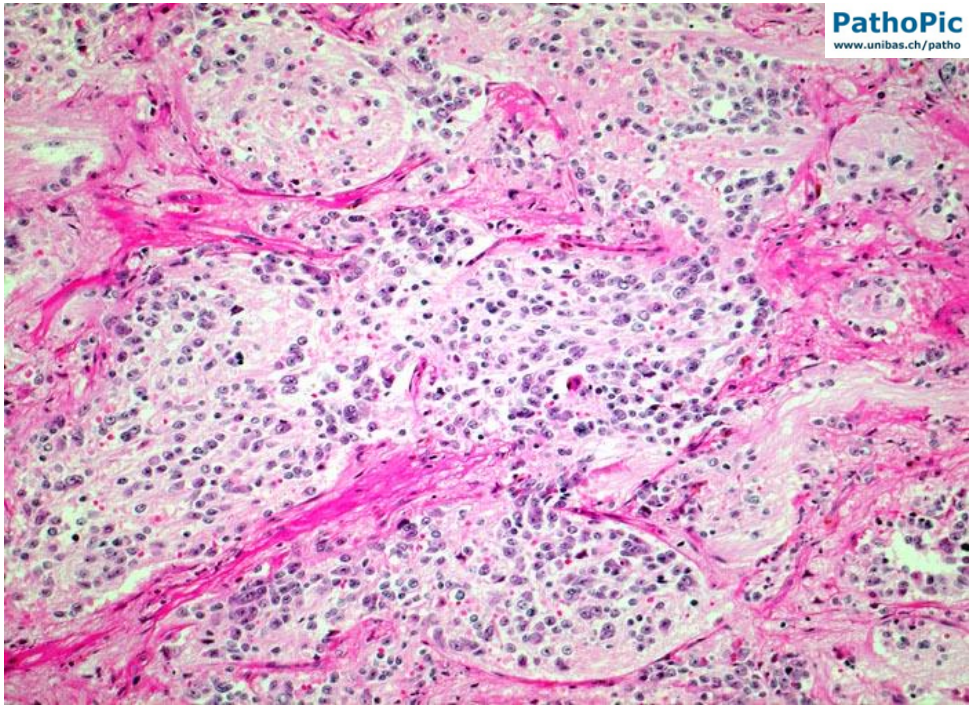
Neuroblastomas range in size from minute, barely discernable nodules to tumors readily palpable through the abdominal wall. The cut surface is soft and friable, with a variegated maroon color. Areas of necrosis, hemorrhage, calcification, and cystic change are frequently found. In the case of small neuroblastomas, a yellow rim of compressed adrenal cortex may be noted.

Microscopically, the tumor is composed of dense sheets of small, round to fusiform cells with hyperchromatic nuclei and scanty cytoplasm. Mitoses are frequent. Characteristic Homer Wright rosettes are defined by a rim of dark tumor cells in a circumferential arrangement around a central pale fibrillar core. Neuroblastomas readily infiltrate the surrounding structures and metastazise to regional lymph nodes, the liver, lungs, bones .



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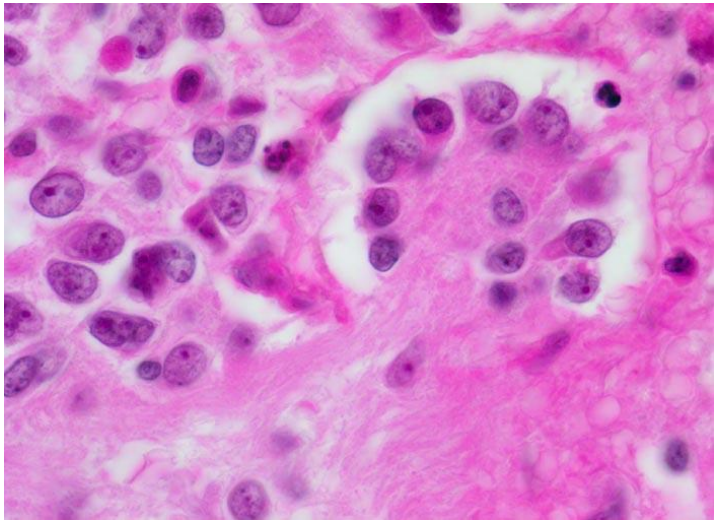
Neuroblasts with cytoplasmic processes polarized toward a central point to form a Homer Wright rosette.



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