SISTEM ENDOKRIN

Dr. DIAN YULIARTHA. L

Pembagian sistem endokrine

1. Sistem endokrine klasik
   - Hipofisis
   - Thyroid
   - Adrenal
   - Parathyroid
   - Pulau langerhans pankreas
   - Testis dan ovarium
2. Sistem endokrine diffuse
   - Terdiri dari sel-sel yang tersebar atau dalam kelompok kecil dalam jaringan lain (parakrin)

Penyakit pada sistem endokrine :

1. Fungsi → terlalu banyak/sedikit sekresi hormon
2. Organ → pembesaran akibat hiperplasia atau tumor

- Beberapa penyakit endokrine → familial
- Sindroma MEN (multiple endokrine neoplasia)
  - MEN 1
  - MEN 2

HIPOFISIS

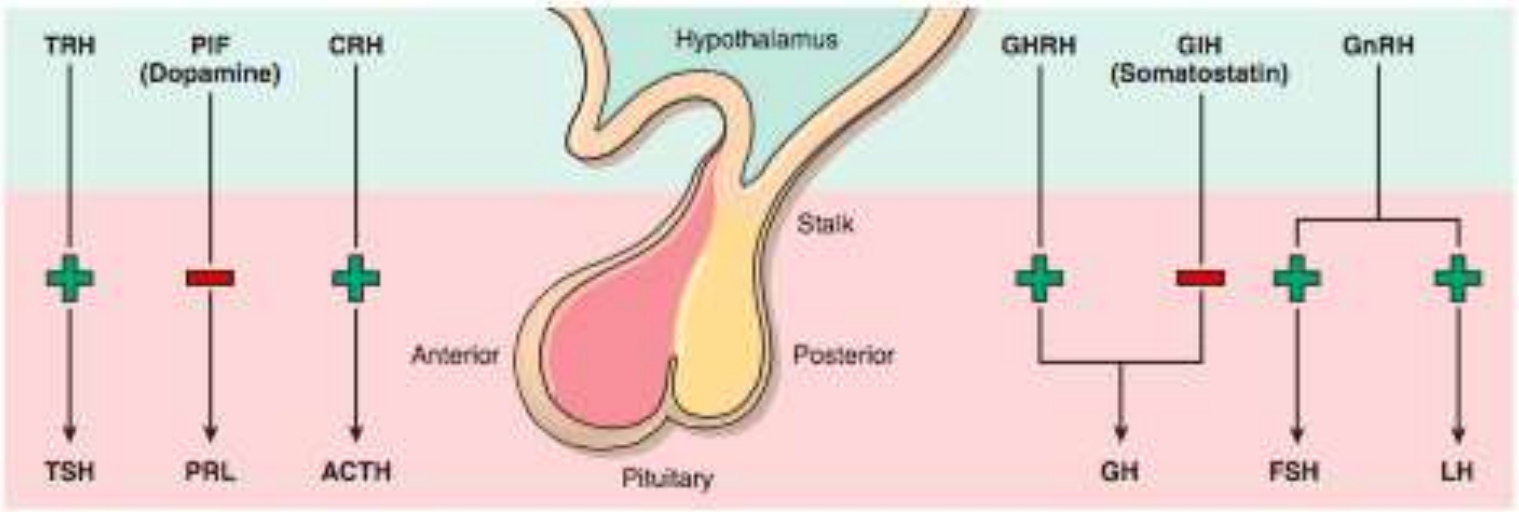


Fig. 20.2 The hypothalamic/pituitary axis. The hypothalamus regulates the secretion of hormones from the adenohypophysis (anterior pituitary gland) by releasing stimulatory (corticotropin-releasing hormone, CRH; growth hormone–releasing hormone, GHRH; gonadotropin-releasing hormone, GnRH; thyrotropin-releasing hormone (TRH) and inhibitory factors (growth hormone inhibitory hormone, GIH or somatostatin; prolactin inhibitory factor, PIF or dopamine). These in turn modulate the release of six hormones from the anterior pituitary: adrenocorticotropic hormone (ACTH or corticotropin); follicle-stimulating hormone (FSH); growth hormone (GH, or somatotropin); luteinizing hormone (LH); prolactin (PRL); and thyroid-stimulating hormone (TSH, or thyrotropin).

Hiperpituitary:

- Akromegali
- Cushing disease
- Hiperpprolaktinemia
- Jarang → hipersekresi hormon lain

Hipopituitary :

- Tekanan pada tumor hipofisis
- Komplikasi iatrogenic setelah operasi/radiasi
- Sindrom sheehan → nekrosis hipofisis sekunder akibat perdarahan post partum

ADENOMA PITUITARY

- Penyebab tersering hiperpituitary
- Klinis : sekresi hormon
- Ukuran :
  - Mikroadenoma < 10mm
  - Makroadenoma >= 10 mm
- sifat : invasive, letak fossa hipofisis

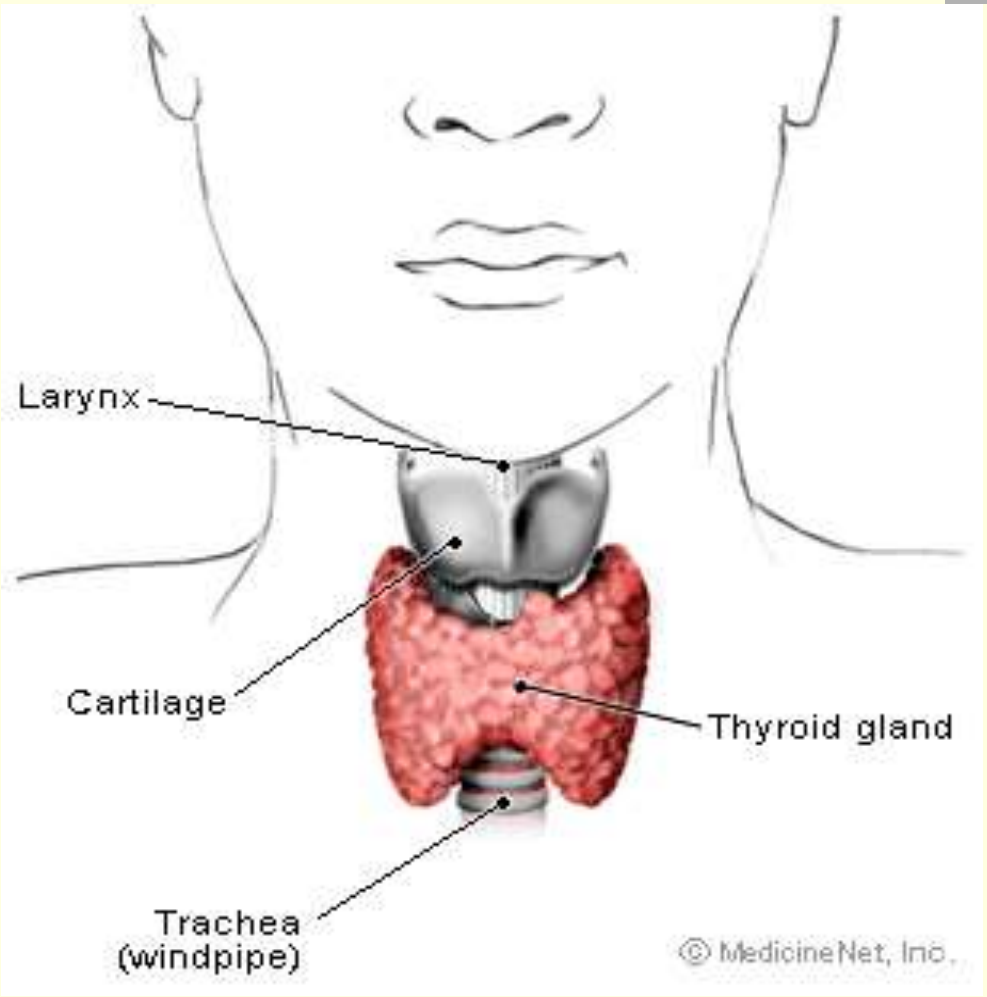
Table 20.1 Classification of Pituitary Adenomas

Pituitary Cell Type	Hormone	Adenoma Subtypes	Associated Syndrome*
Lactotroph	Prolactin	Lactotroph adenoma Silent lactotroph adenoma	Galactorrhea and amenorrhea (in females) Sexual dysfunction, infertility
Somatotroph	GH	Densely granulated somatotroph adenoma Sparsely granulated somatotroph adenoma Silent somatotroph adenoma	Gigantism (children) Acromegaly (adults)
Mammosomatotroph	Prolactin, GH	Mammosomatotroph adenomas	Combined features of GH and prolactin excess
Corticotroph	ACTH and other POMC-derived peptides	Densely granulated corticotroph adenoma Sparsely granulated corticotroph adenoma Silent corticotroph adenoma	Cushing syndrome Nelson syndrome
Thyrotroph	TSH	Thyrotroph adenomas Silent thyrotroph adenomas	Hyperthyroidism
Gonadotroph	FSH, LH	Gonadotroph adenomas Silent gonadotroph adenomas ("null cell," oncocytic adenomas)	Hypogonadism, mass effects, and hypopituitarism

ACTH, Adrenocorticotrophic hormone; FSH, follicle-stimulating hormone; GH, growth hormone; LH, luceinizing hormone; POMC, pro-opiomelanocortin; TSH, thyroid-stimulating hormone.

*Note that nonfunctional (silent) adenomas in each category express the corresponding hormone(s) within the neoplastic cells, as determined by special immunohistochemical staining on tissues. However, these adenomas do not produce the associated clinical syndrome, and typically present with mass effects accompanied by hypopituitarism due to destruction of normal pituitary parenchyma. These features are particularly common with gonadotroph adenomas. Partially adapted from Asa SL, Essat S. The pathogenesis of pituitary tumors. Annu Rev Pathol 4:97, 2009.

THYROID


Larynx
Cartilage
Thyroid gland
Trachea
(windpipe)
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SINTESIS HORMON THYROID

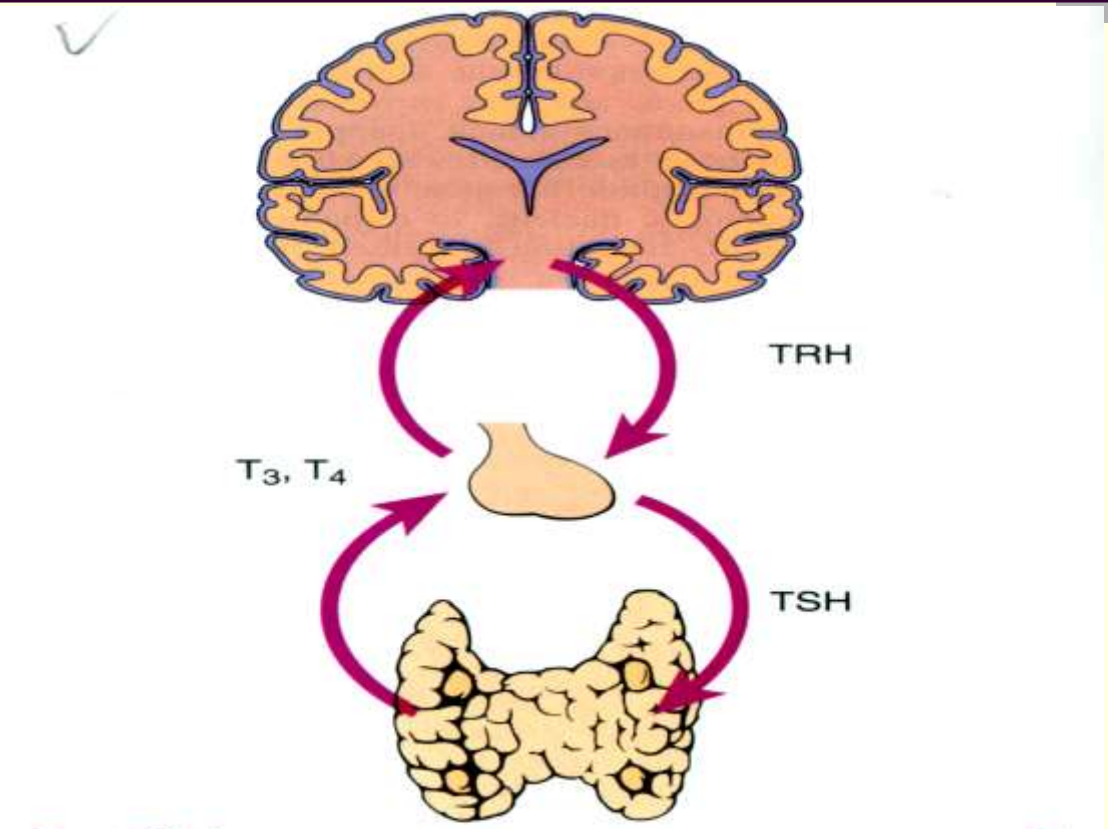


Figure 26–6

Diagram of relationship between the hypothalamus, anterior pituitary, and a peripheral endocrine gland, exemplified here by the thyroid gland. Secretion of thyroid hormones (T_3 and T_4) is controlled by trophic factors secreted by both the hypothalamus and the anterior pituitary. Decreased levels of T_3 and T_4 stimulate the release of thyrotropin-releasing hormone (TRH) from the hypothalamus and thyroid-stimulating hormone (TSH) from the anterior pituitary, causing T_3 and T_4 levels to rise. Elevated T_3 and T_4 levels, in turn, suppress the secretion of both TRH and TSH. This relationship is termed a *negative-feedback loop*. (Modified from Dr. Ronald A. DeLellis, New England Medical Center, Boston.)

HYPERTHYROIDISM

- Oleh karena produksi T3 dan T4 yang meningkat

Table 20.2 Causes of Thyrotoxicosis

Associated With Hyperthyroidism
Primary
Diffuse toxic hyperplasia (Graves disease)
Hyperfunctioning ("toxic") multinodular goiter
Hyperfunctioning ("toxic") adenoma
Iodine-induced hyperthyroidism
Secondary
TSH-secreting pituitary adenoma (rare)*
Not Associated With Hyperthyroidism
Granulomatous (de Quervain) thyroiditis (painful)
Subacute lymphocytic thyroiditis (painless)
Struma ovarii (ovarian teratoma with thyroid)
Factitious thyrotoxicosis (exogenous thyroxine intake)

TSH, Thyroid-stimulating hormone.
*Associated with increased TSH; all other causes of thyrotoxicosis associated with decreased TSH.

HYPOTHYROIDSM

- Kegagalan / kekurangan produksi hormon thyroid

Table 20.3 Causes of Hypothyroidism

Primary
Postablative
Surgery, radioiodine therapy, or external irradiation
Autoimmune hypothyroidism
Hashimoto thyroiditis*
Iodine deficiency*
Drugs (lithium, iodides, p-aminosalicylic acid)*
Congenital biosynthetic defect (dyshormonogenetic goiter) (rare)*
Genetic defects in thyroid development (rare)
Thyroid hormone resistance syndrome (rare)
Secondary (Central)
Pituitary failure (rare)
Hypothalamic failure (rare)

*Associated with enlargement of thyroid ("goitrous hypothyroidism"). Hashimoto thyroiditis and postablative hypothyroidism account for the majority of cases of hypothyroidism in developed countries.

Cretinism

- Hypothyroid saat kehamilan ⇨ retardasi mental dan intelektual
- Etiologi :
  - Agenesis thyroid
  - Defisiensi iodium berat saat hamil
  - Goitrogen
  - Defisiensi enzim resesif autosomal (kretisme sporadik)

- Gejala kx :
  - Somnolen
  - Suara parau / serak
  - Hidung pesek
  - Lidah menonjol
  - Fontanella dan epiphyse terlambat menutup

MYXEDEMA

- Hypothyroid saat anak atau dewasa muda

- Etiologi :
  - Tyhroiditis Hashimoto
  - Kegagalan hipofisis
  - Hipotirodisme latrogenik
  - Goitrogenik

- Gejala awal :
  - Letargi, intoleransi dingin, peningkatan BB, konstipasi
  - Kerontokan rambut di seluruh tubuh
  - Myxedema madness
- Lanjut :
  - Anemia, efusi pleura, efusi perikardial

⇨ Terjadi penumpukan mukopolisakarida

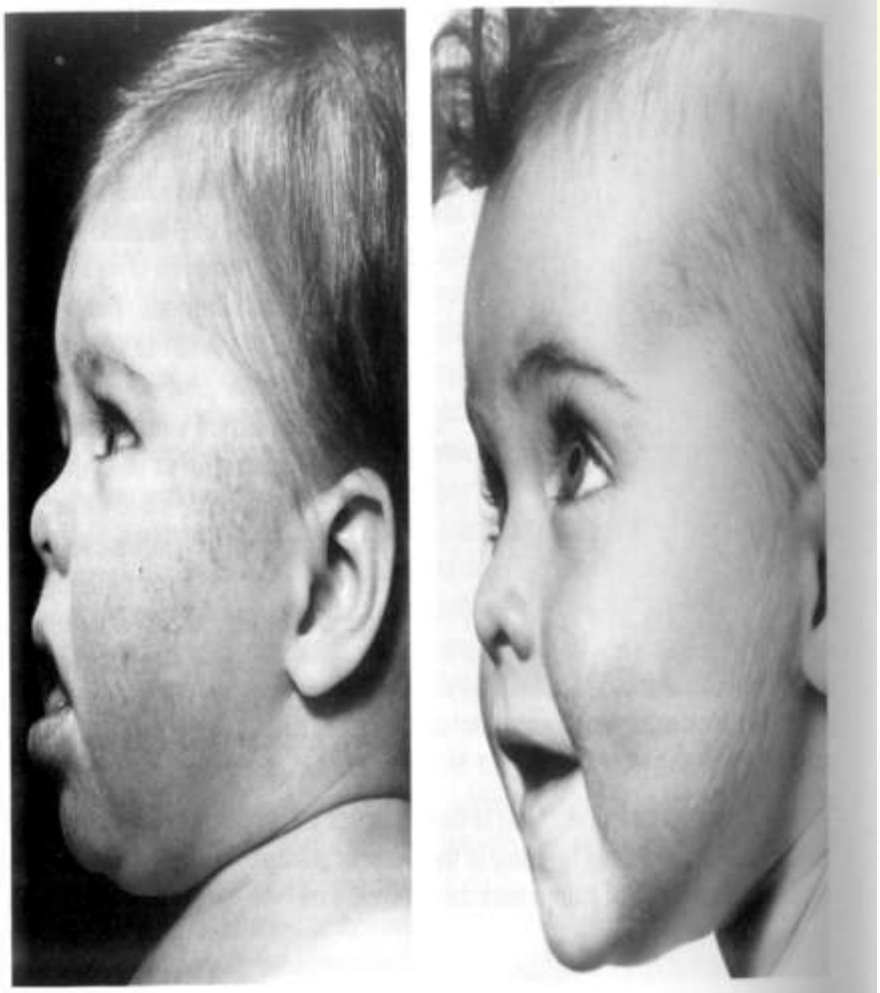
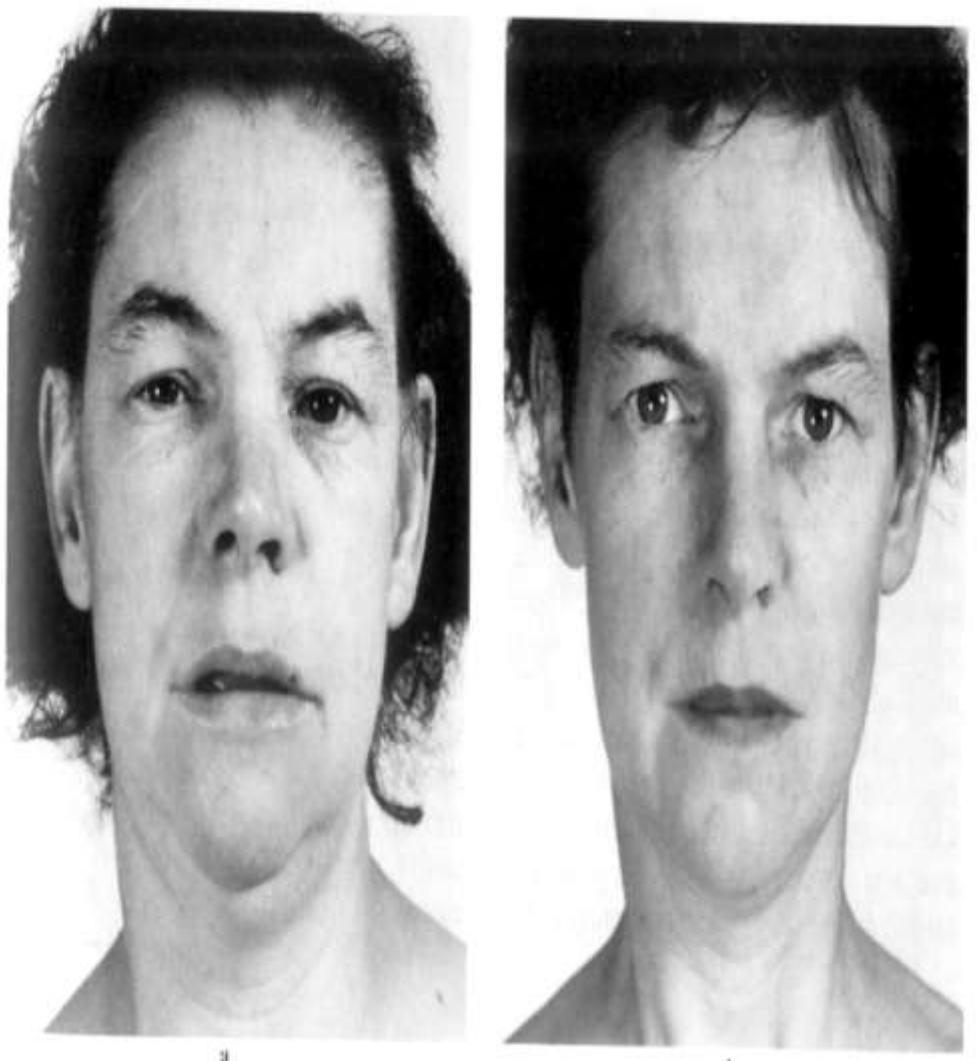


Fig. 24.11 A cretin aged 17 months (**a**), showing the enlarged, protruding tongue, coarse dry skin and dull expression. (**b**), showing the effects of thyroxine treatment for two months. (Prof. J. H. Hutchison.)



a b

Fig. 24.6 Myxoedema, (**a**): before treatment, (**b**): the effects of administration of thyroxine.

	HYPERTHYROID	HYPOTHYROID
LABORATORIUM Indeks T3 & T4 bebas	↑	↓
MEKANISME FISIOLOGIK Metabolisme selular dan sintesis protein Potensiasi efek β adrenergik Antagonisme insulin	↑	↓
EFEK KLINIS BMR	↑	↓
Struma	Biasanya ada	Dapat ada
BB	↓	↑
Aktivitas	Hiperaktif, insomnia	Letargik, somnolen
Refleks	Cepat	Lambat
Kardiovaskular	Takikardi, aritmia	Bradikardi
Gastrointestinal	Diare ringan	Konstipasi
Rambut	Halus	Kasar, mudah patah, rontok
Miksedema	Batas tegas, pretibia	Menyeluruh, wajah & extremitas
Toleransi suhu	Intoleransi panas	Intoleransi dingin
Lain-Lain	eksoftalmus	Retardasi mental dan pertumbuhan

AUTOIMMUN THYROID DISEASE

- Berhubungan dengan antibodi terhadap antigen thyroid
- Gambaran klinis bervariasi tergantung antibodi yang diproduksi
- Wanita lebih sering dibanding pria

GRAVE'S DISEASE

- Karakteristik
  1. Tirotoksikosis → akibat pembesaran diffuse dan hipertiroid
  2. Ophtamolpathy → 40%
  3. Dermopathy
- Wanita > pria = 7 : 1
- Usia 20-40 th
- Didapatkan adanya Human leucocyte antigen (HLA-DR3)

- Multiple antibodi pada grave's disease :
  - TSI (thyroid stimulating imunoglobulin) → berikatan dengan TSH receptor, sehingga meningkatkan sekresi hormon thyroid
  - TGSI (thyroid growth stimulating imunoglobulin) → secara langsung menghambat TSH receptor
  - TSH binding inhibitor imunoglobulin → mecegah TSH berikatan dengan receptor

morphology

- Makros :
  - Diffuse hypertrofi dan hyperplasia
  - Kapsul (+)
  - Konsistensi padat kenyal
- Mikros :
  - Hiperplasia sel folikel : tall, columner yang tersusun padat → pseudo papilary
  - Adanya sekresi koloid yang berlebih → rand vacuole/scalloped

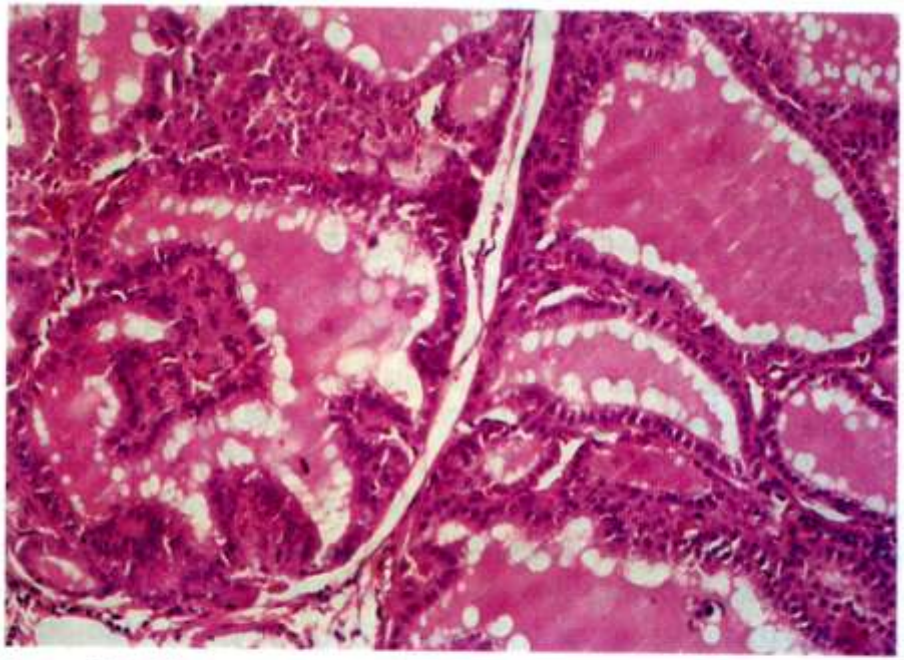
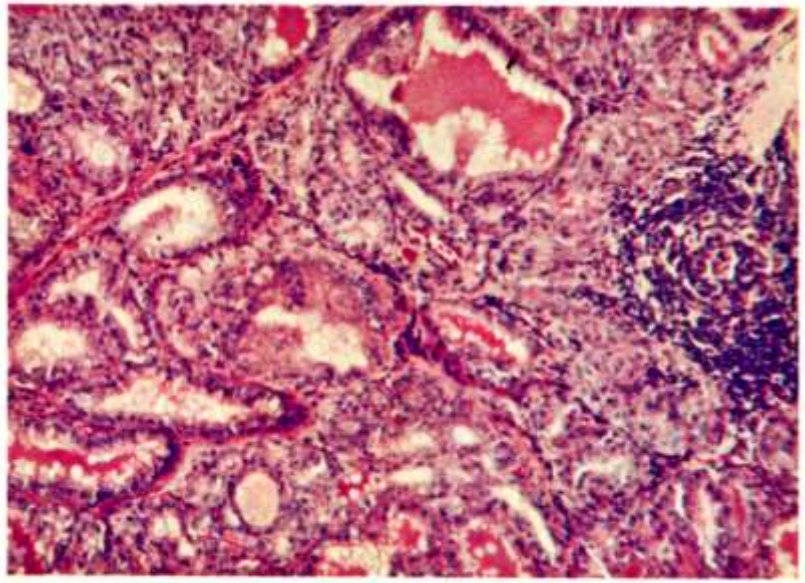
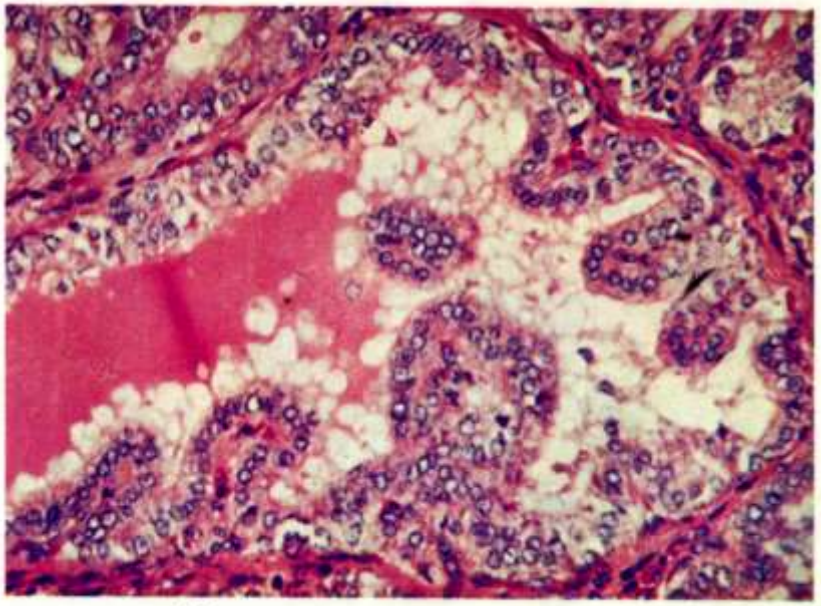


Figure 26–10

Photomicrograph of a diffusely hyperplastic gland in a case of Graves disease. The follicles are lined by tall, columnar epithelium. The crowded, enlarged epithelial cells project into the lumens of the follicles. These cells actively resorb the colloid in the centers of the follicles; resulting in the scalloped appearance of the edges of the colloid.



8.5 Primary thyrotoxicosis



8.6 Primary thyrotoxicosis

HASHIMOTO THYROIDITIS

- Disebut juga = Chronic limfocytic thyroiditis
- Wanita : Pria = 10 : 1 / 20 : 1
- 30 – 50 tahun
- Pembesaran diffuse (asymetric / lobulated)
- Kapsul intact + padat kenyal

Etiologi :

- TGI >> TSI <
- Antibogi TGI dan TSI

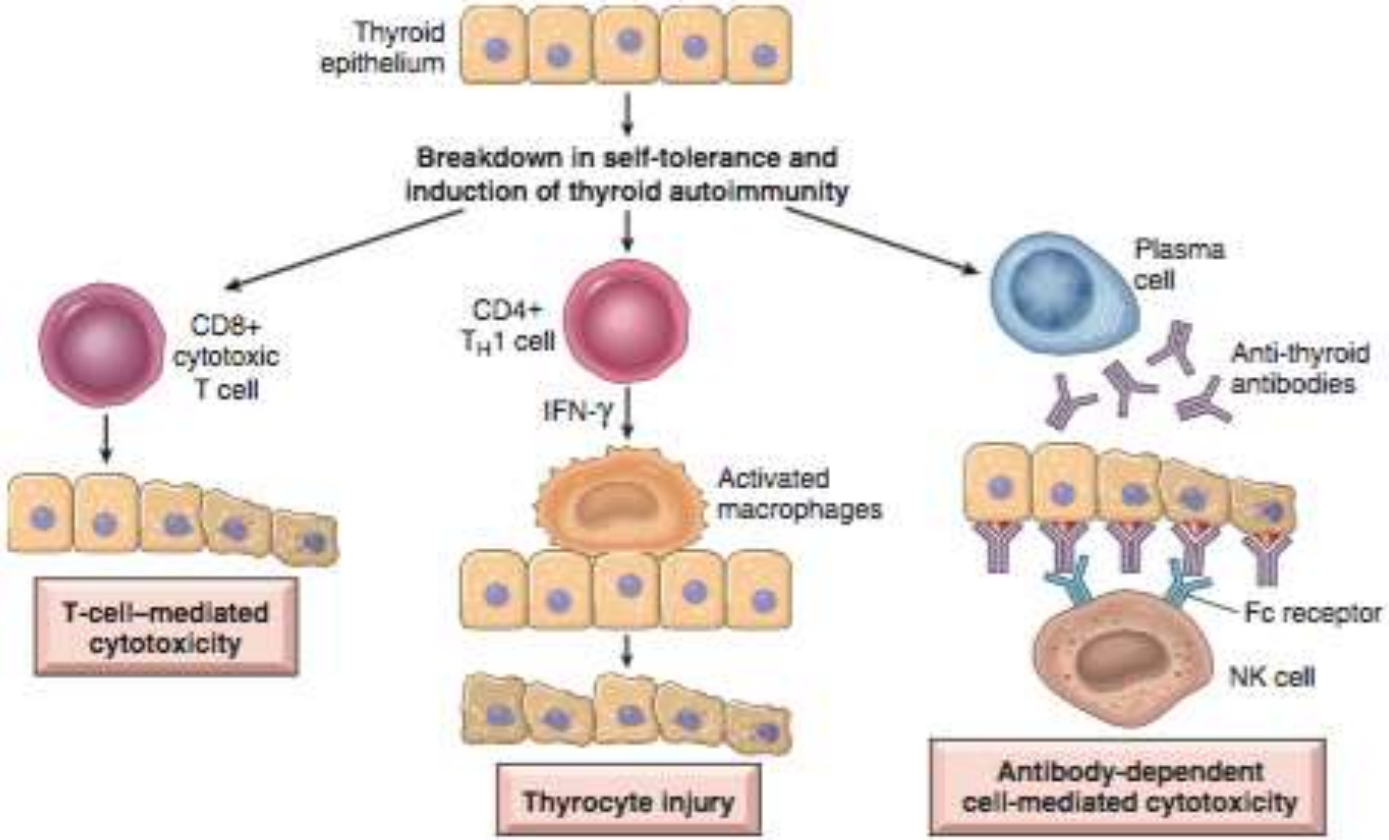
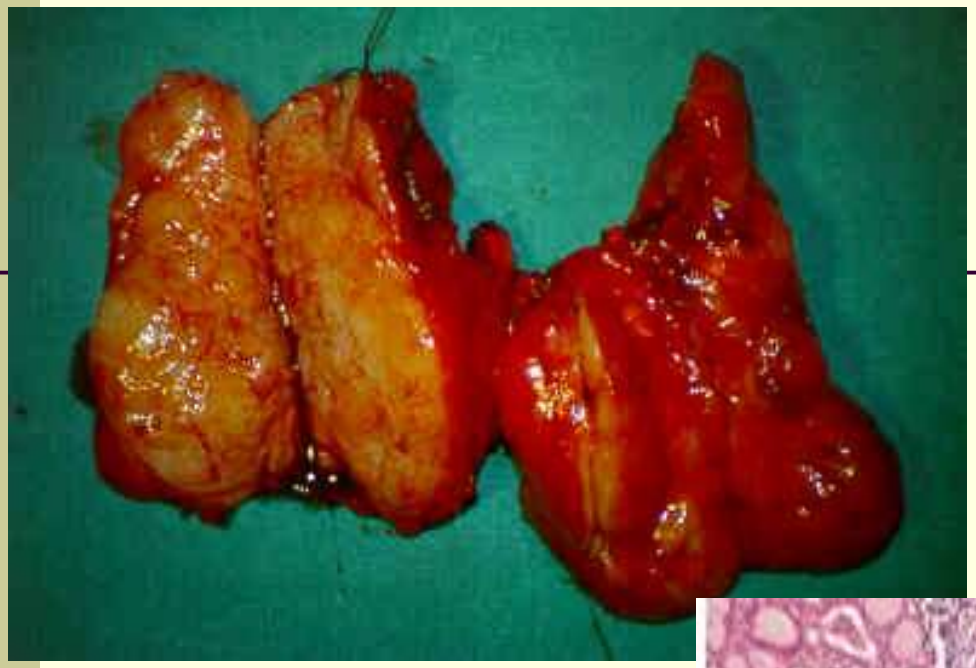


Fig. 20.8 Pathogenesis of Hashimoto thyroiditis. Breakdown of immune tolerance to thyroid autoantigens results in progressive autoimmune destruction of thyrocytes by infiltrating cytotoxic T cells, locally released cytokines, or antibody-dependent cytotoxicity.



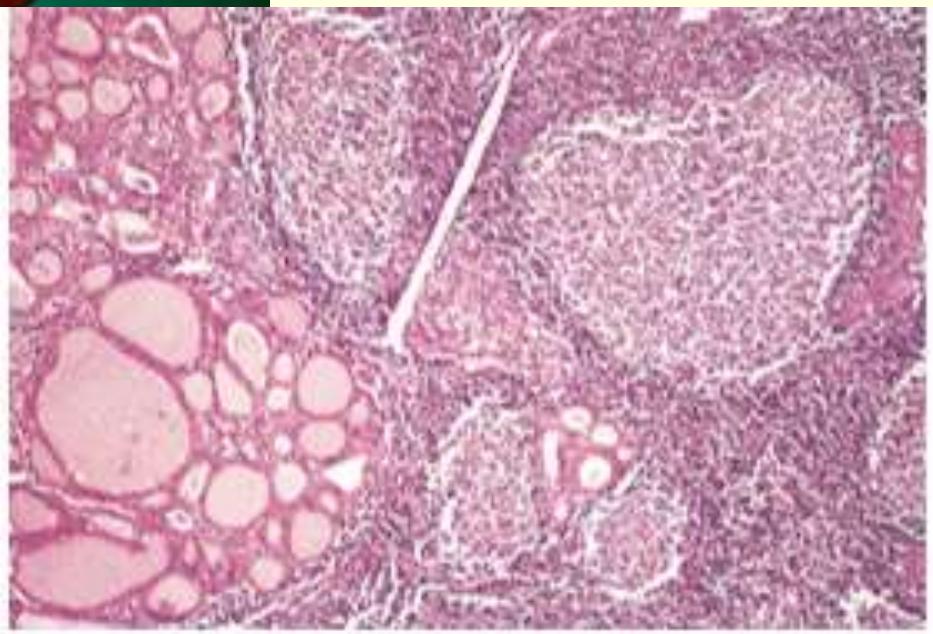
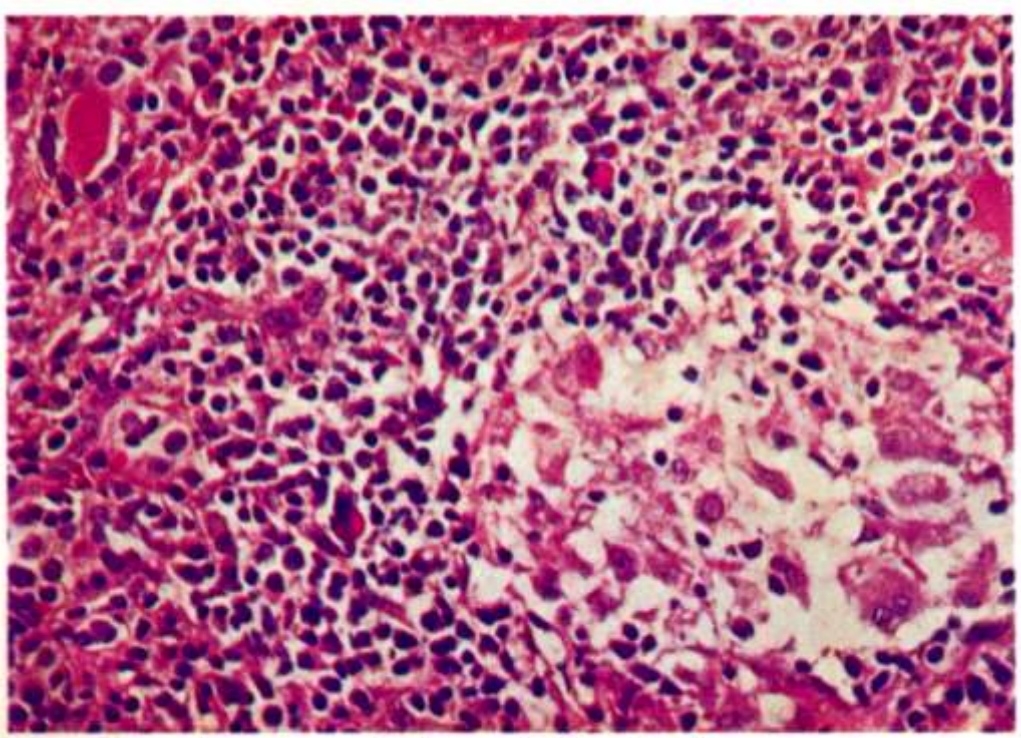


Fig. 20.9 Hashimoto thyroiditis. The thyroid parenchyma contains a dense lymphocytic infiltrate with germinal centers. Residual thyroid follicles lined by deeply eosinophilic Hürthle cells also are seen.

DeQuervain's Thyroiditis

- Disebut juga = sub acute granulomatous thyroiditis
- Wanita : Pria = 3-6 : 1
- 30 – 50 tahun
- Etiologi → diduga akibat virus
- **Gx klinis** :
  - Didahului infeksi upper respiratory
  - Nyeri pada leher menjalar ke rahang dan telinga, sakit saat menelan
  - Self-pertuating → spontaneus remits

- **Gross** : pembesaran **+/-** 3x, kadang asimetri / focal, perlekatan ringan, irisan padat, putih kekuningan.
- **Mikros** : awal tampak sekumpulan folikel rusak dan terbentuk microabscess – macrophage + giant cell



8.13 Granulomatous (subacute) thyroiditis

Subacute Lymphocytic Thyroiditis

- Silent/painless thyroiditis
- Post partum thyroiditis
- Autoimun → circulating antithyroid antibody
- Middle aged women
- Fase awal →
- Thyrotoxicosis →
- euthyroid

dalam beberapa bulan

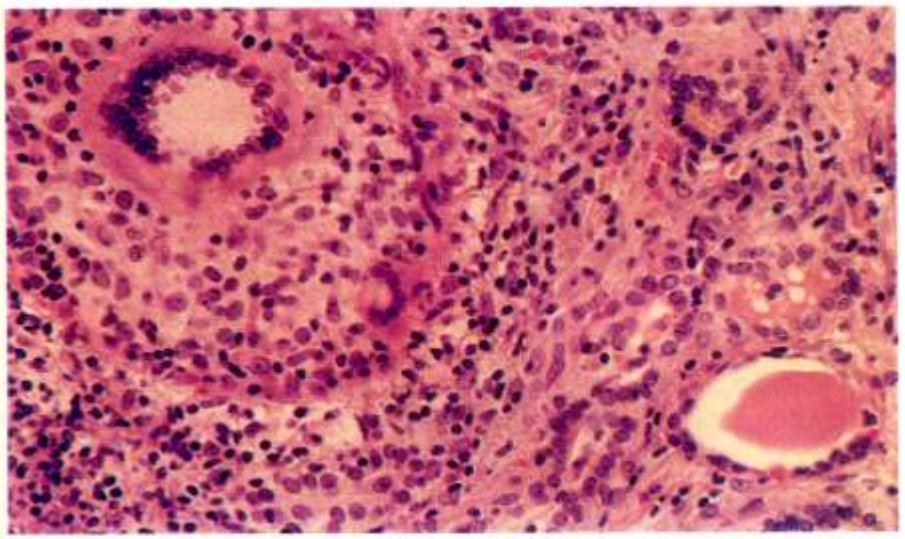


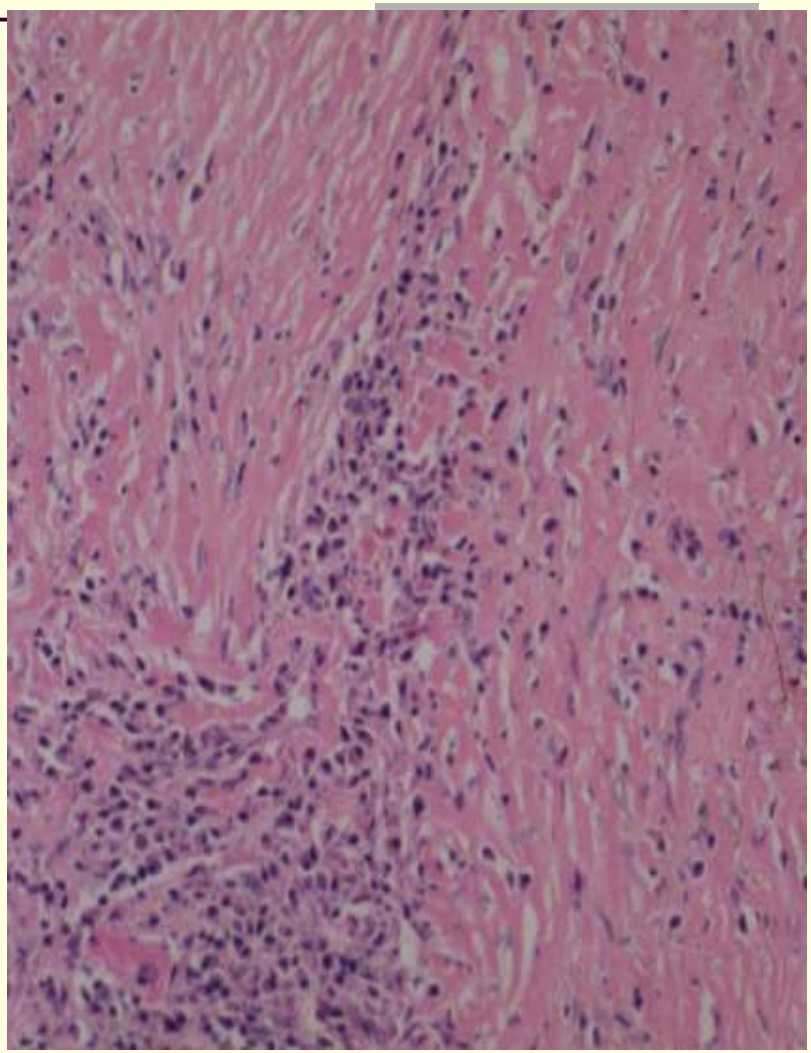
Figure 26–9

Subacute thyroiditis. The thyroid parenchyma contains a chronic inflammatory infiltrate with a multinucleate giant cell *(above left)* and a colloid follicle *(bottom right)*.

Riedel thyroiditis

- **Khas** : pembentukan jaringan fibrous yang luas.
- Wanita : pria = 3 : 1
- **Usia** : dekade IV-VII
- Sering dianggap ganas
- Sering dianggap end stage dari Hashimoto's (fibrosing)

- Gx : terjadi penekanan
- Gross : mengecil / contracted, padat keras / woody hard, asimetri, nodular, abu-abu.
- Mikros : parenchym atropi, jaringan fibrous collagen, infiltrasi sel lymphocyt



Struma yang berhubungan dengan kelainan fungsi

Agar bentuk dan fungsi normal :

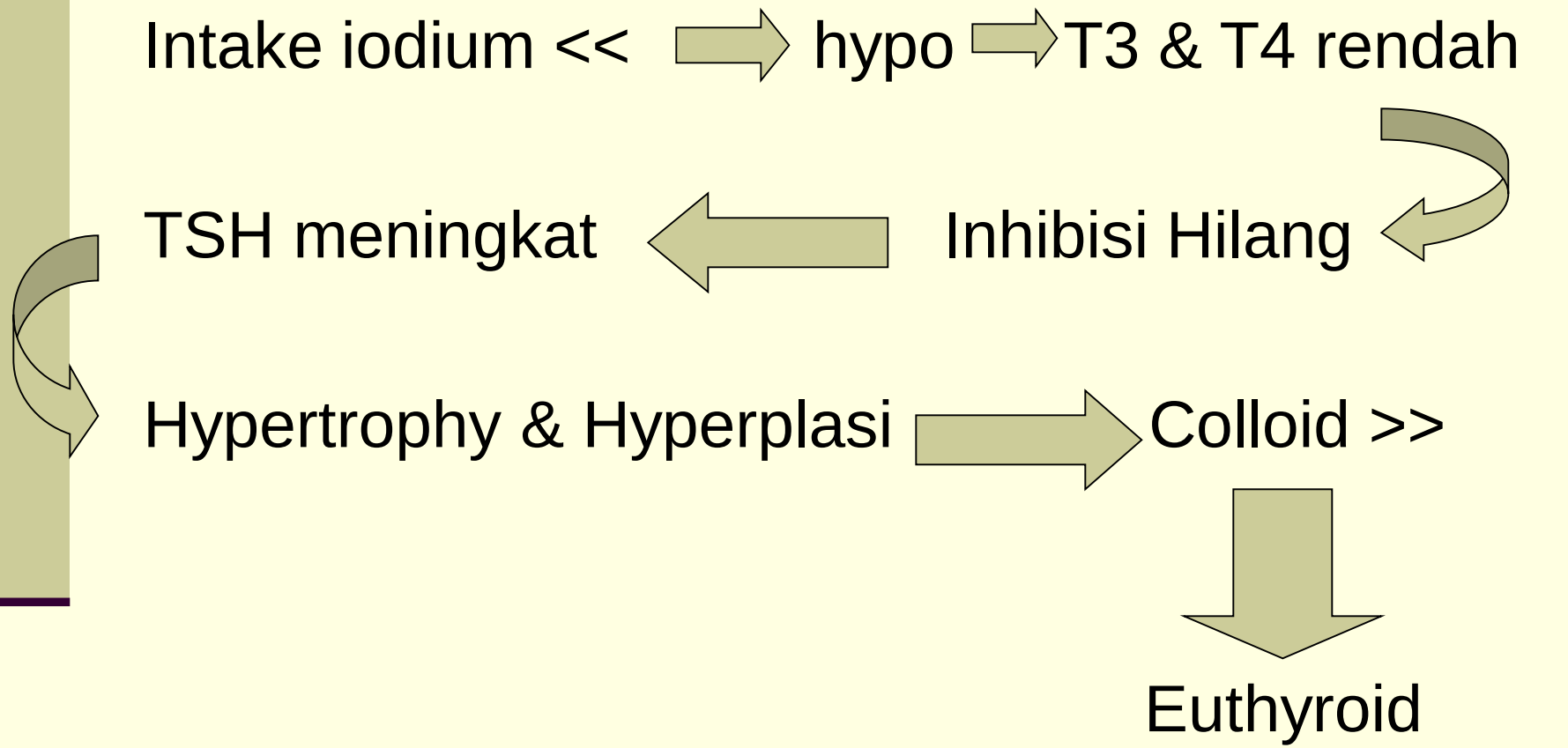
- intake yodium
- hormon / TSH
- metabolisme
- TBG

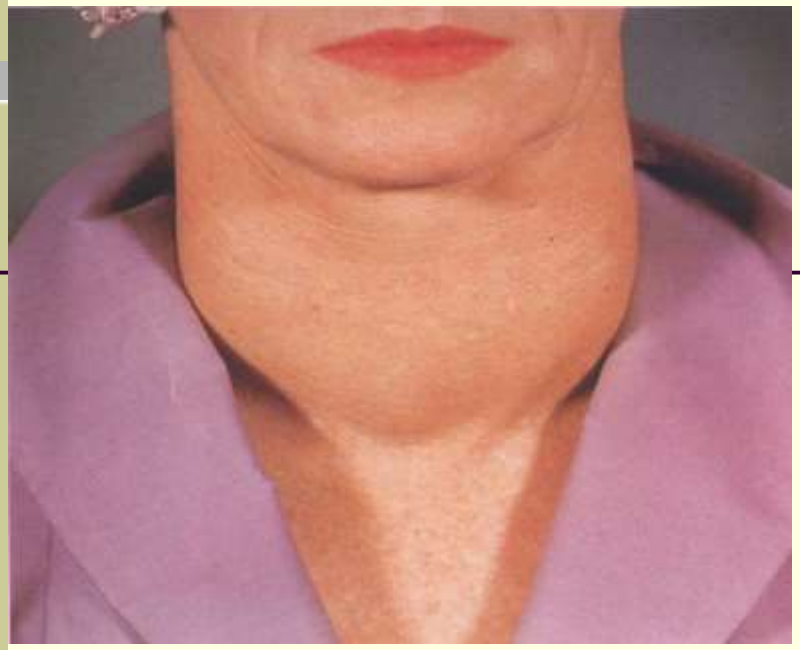
Estrogen ~> TBG meningkat ~> hormon thyroid terikat ~> kadar hormon menurun ~> TSH meningkat ~> gangguan.

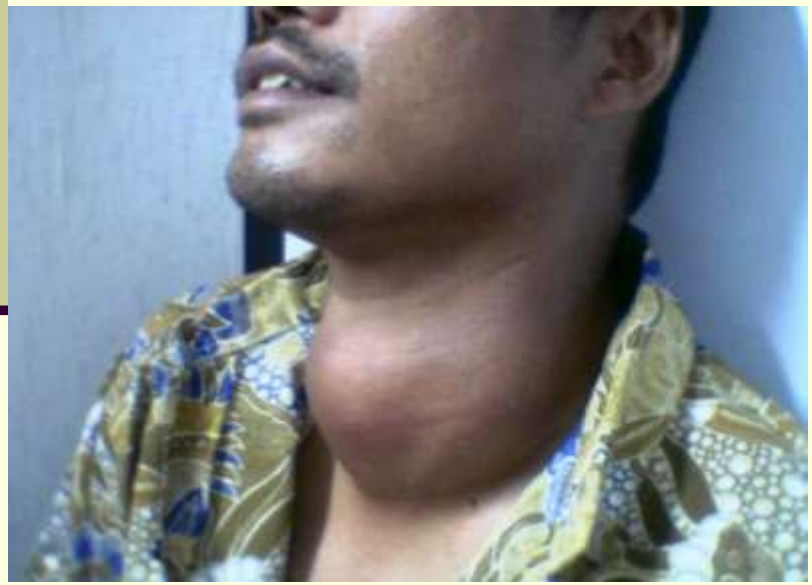
Colloid goiter / Simple goiter

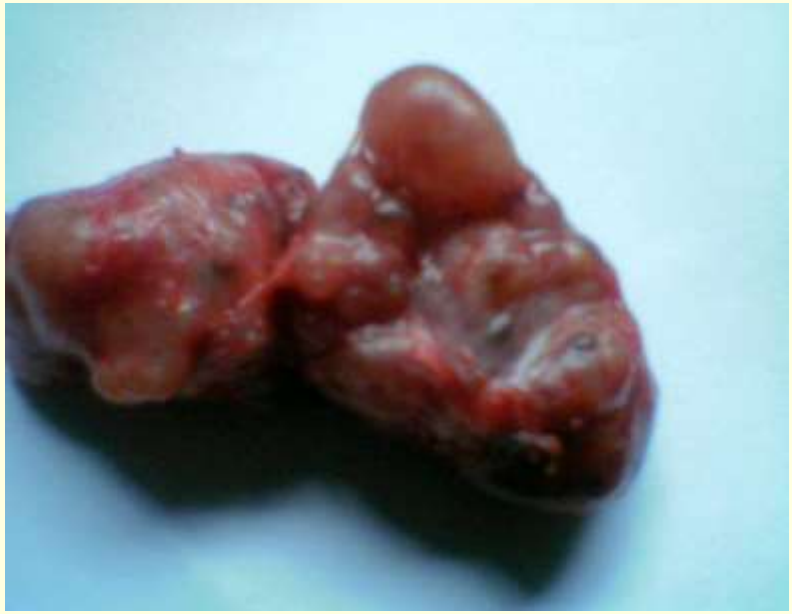
- Diffuse
- Euthyroid
- Endemik : defisiensi iodium (pegunungan)
  goitrogenik
- Wanita : Pria = 8 : 1
- Pubertas / Dewasa Muda

Prinsip :


Intake iodium <<
hypo
T3 & T4 rendah
Inhibisi Hilang
TSH meningkat
Hypertrophy & Hyperplasi
Colloid >>
Euthyroid







Multinodular Goiter

- Adenomatous Goiter
- Hampir semua Simple menjadi multinodular
- Morfologi :- Nodular
  - irregular scarring
  - perdarahan / hemosiderin
  - focal calcifikasi
  - mikrocystis

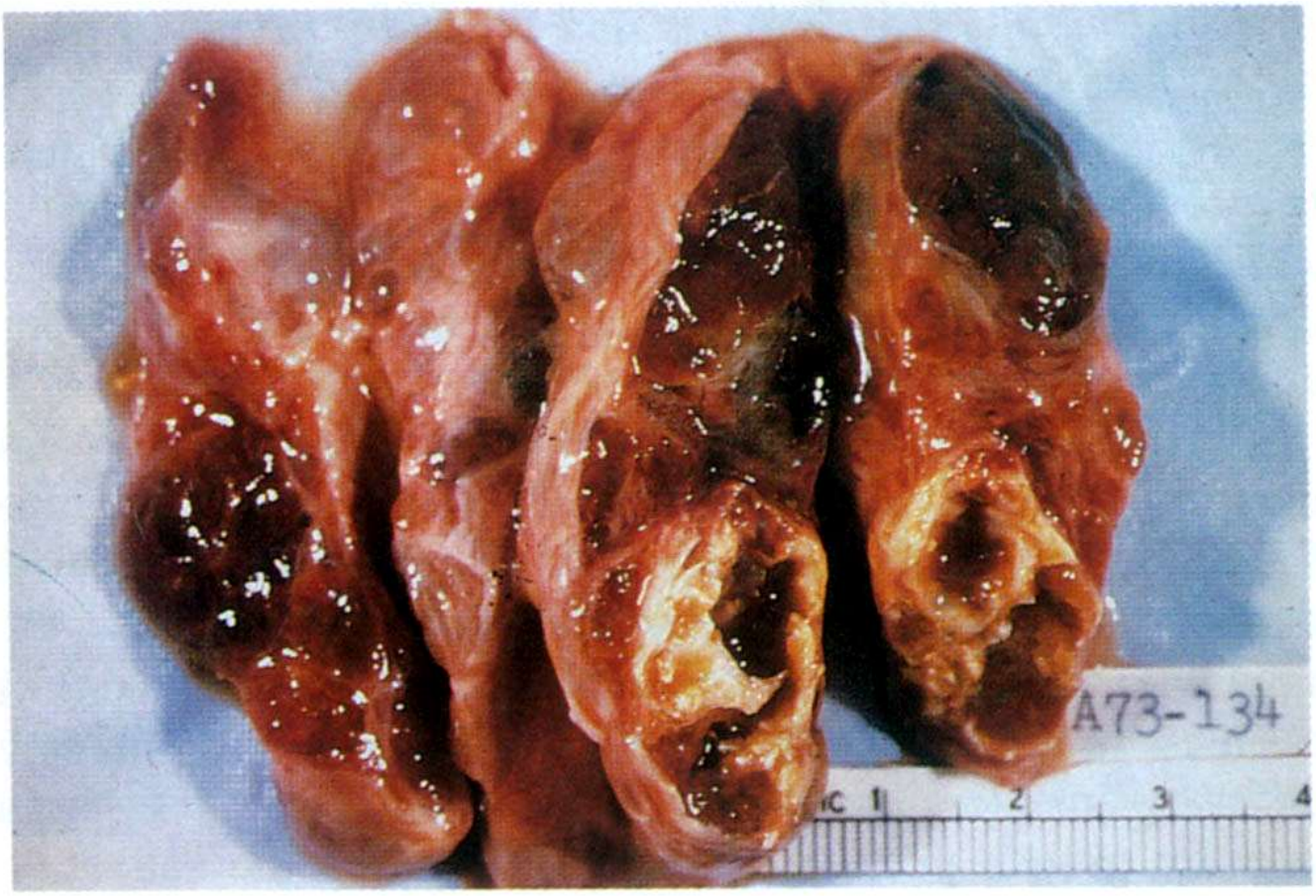


Figure 26–11

Gross photograph of nodular goiter. The gland is coarsely nodular and contains areas of fibrosis and cystic change.

NEOPLASMA

- Nodul soliter
- Nodul pada usia muda
- Nodul pada pria
- Pernah radiasi
- Cold nodul

ADENOMA

- Kapsule +, arsitektur luar & dalam berbeda, kompresi pada kapsul, tidak multinodule
  - Adenoma Follicular : embrional, fetal, simple, colloid.
  - Adenoma papilary
  - Adenoma Hurthle cell
- **Prinsip Adenoma** :- pembesaran lambat
  - ukuran mencapai plateau
  - membesar mendadak
  - jarang hyperfungsi
- Tumor jinak yang lain : dermoid cyst. Lipoma, hemangioma, teratoma

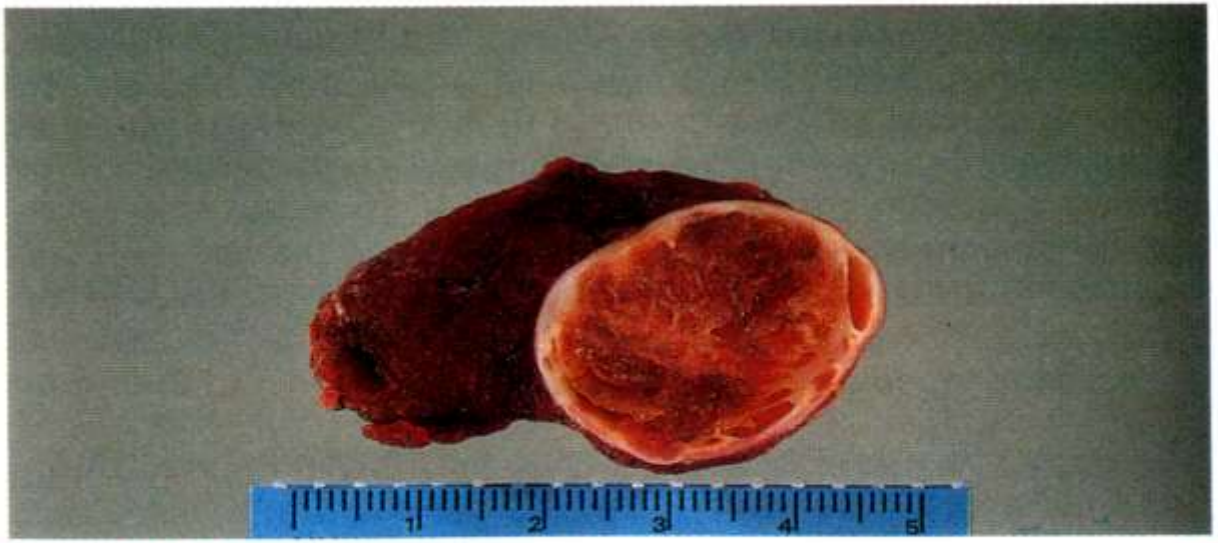
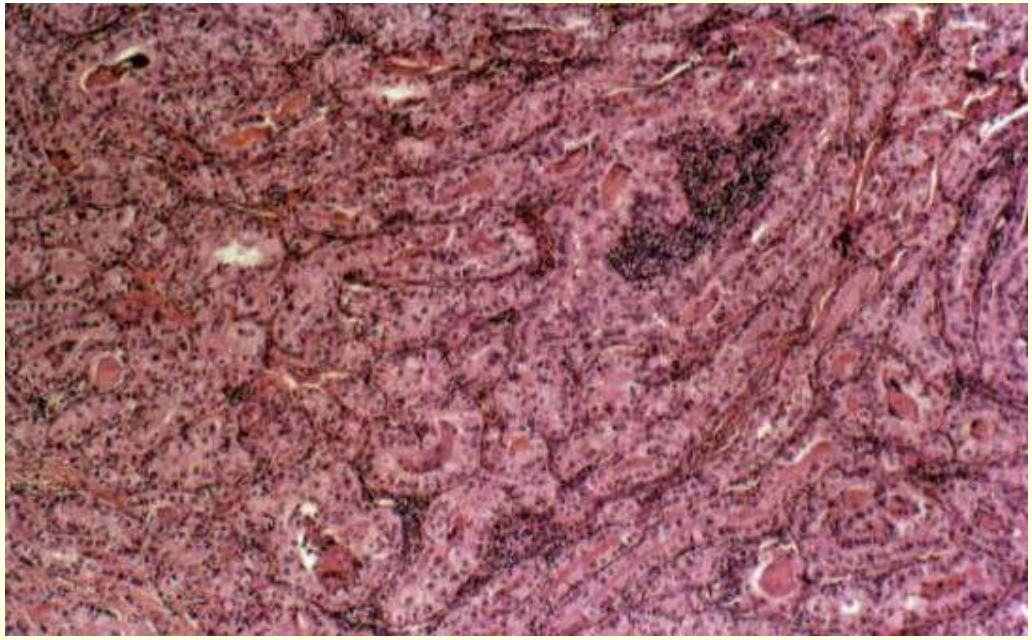


Figure 26–12

Follicular adenoma of the thyroid. A solitary, well-circumscribed nodule is seen.



MALIGNANT

- well diff : - papilary Ca.
  - follicular Ca
  poorly diff : - medulary Ca.
  - undiff Ca / anaplastik Ca.

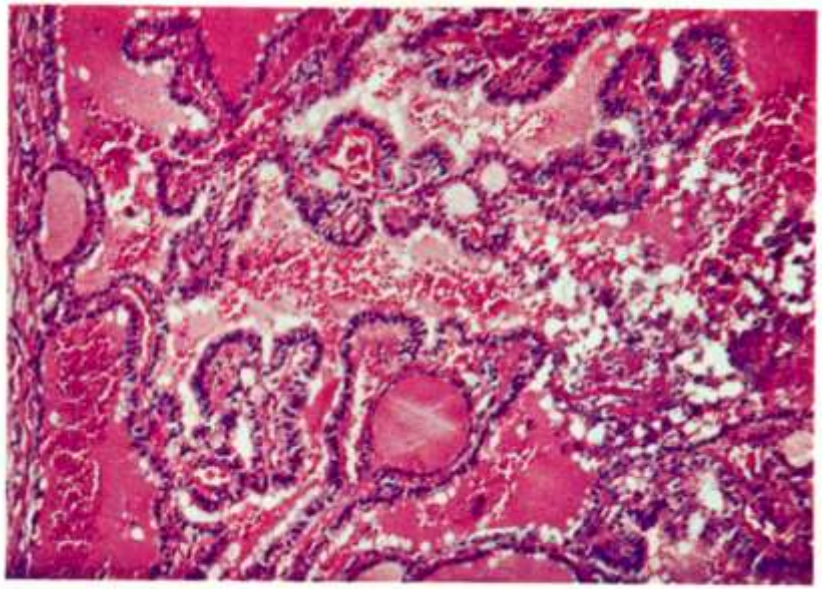
- Stage I : intrathyroid
- Stage II : tidak ada perlekatan
- Stage III : perlekatan lokal
- Stage IV : metastase jauh

Papillary Ca

- Dekade III – IV ; 80 % < 40 tahun
- Wanita : Pria = 2-3 : 1
- 10 ysr SR 98 %

- Karakteristik mikroskopik :

~ papilae dengan fibrovaskuler
~ orphan annie nuclei / ground glass
~ intranuclear inclusions atau adanya groove
~ psammoma bodies



8.20 Primary papillary carcinoma: thyroid

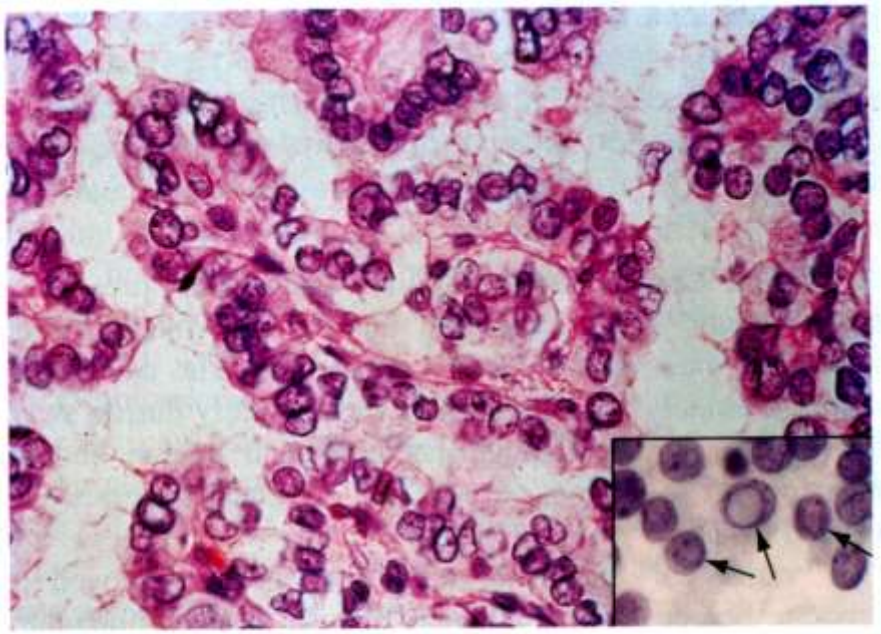
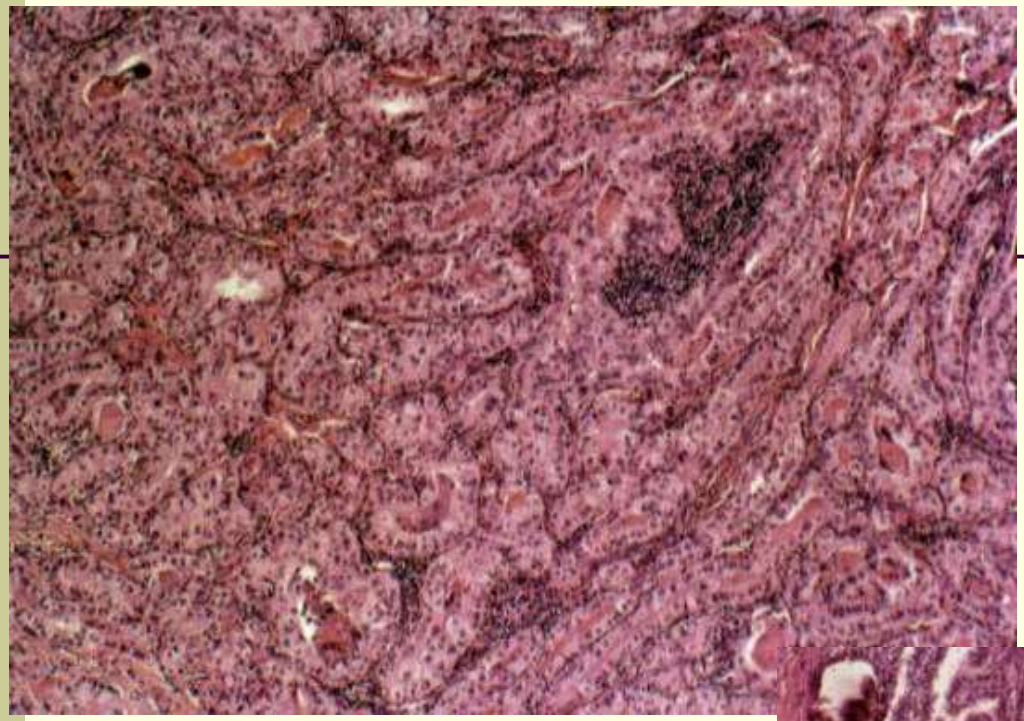
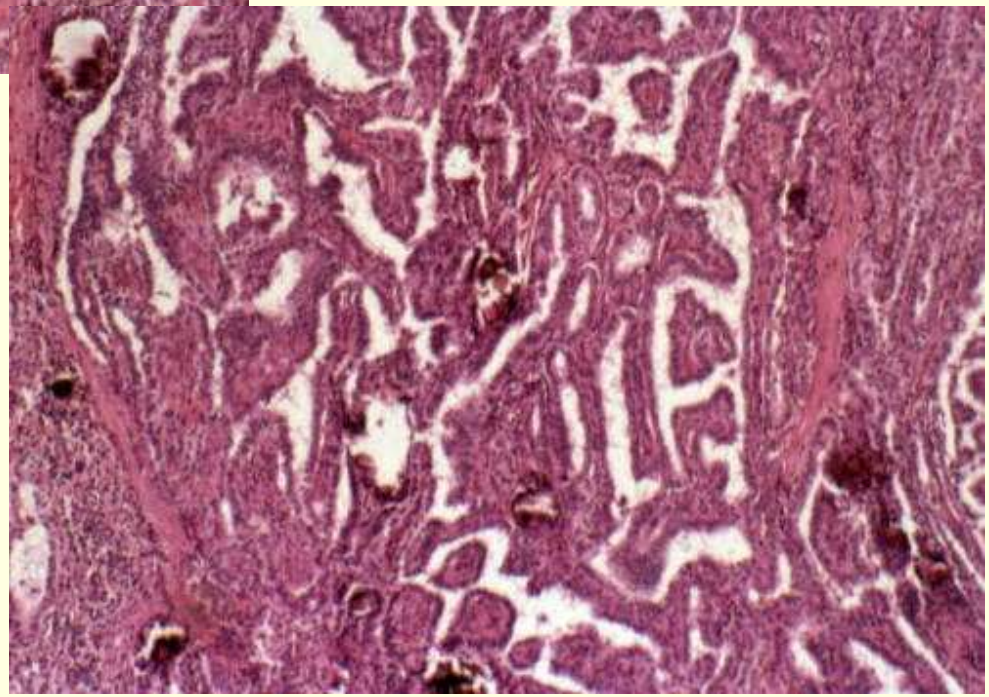


Figure 26–15

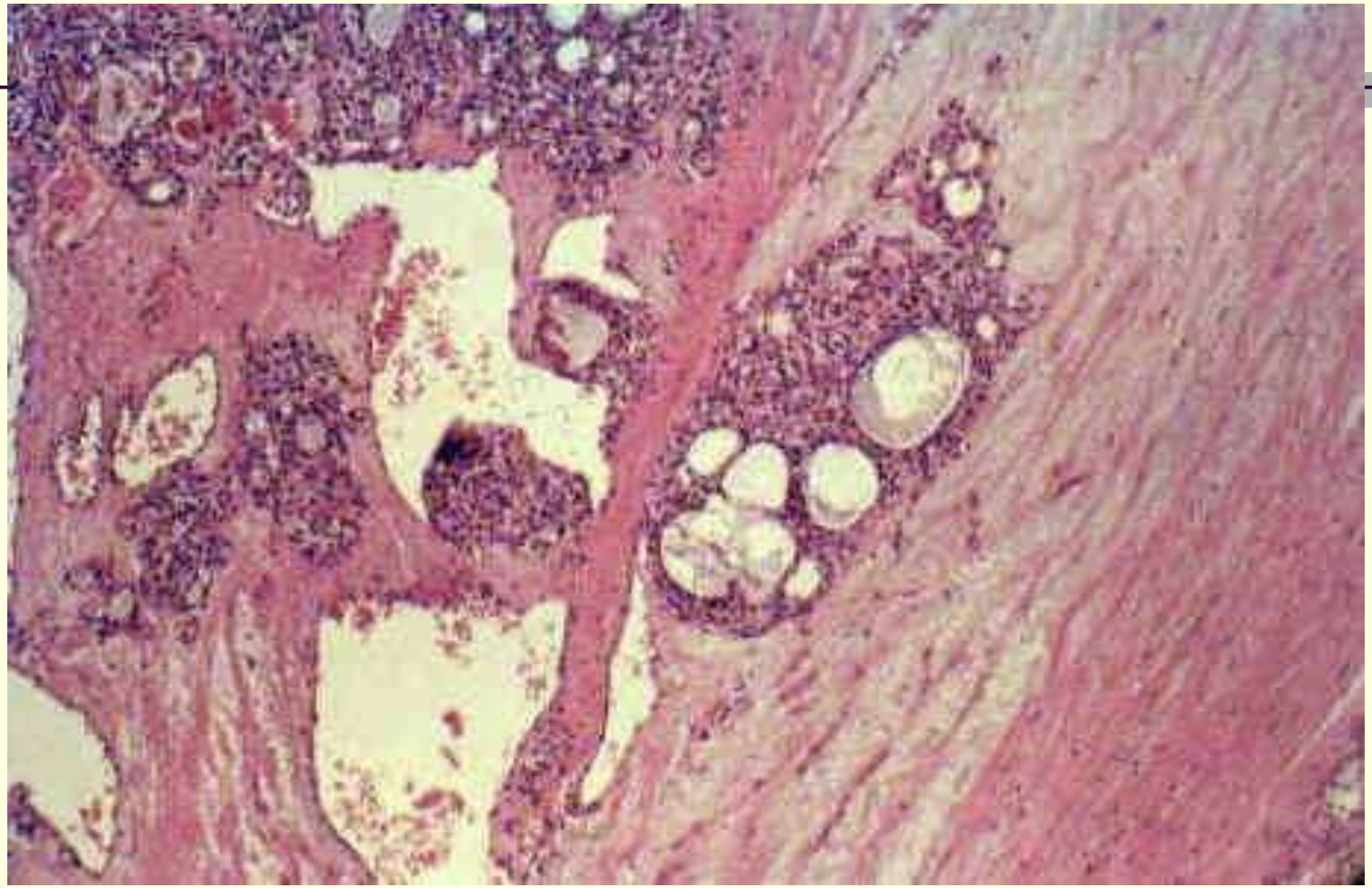
Papillary carcinoma of the thyroid. This particular example contains well-formed papillae lined by cells with characteristic empty-appearing nuclei, sometimes termed *Orphan Annie eye* nuclei. *Inset* shows cells obtained by fine-needle aspiration of a papillary carcinoma. Characteristic intranuclear *inclusions* (*arrows*) are visible in cytologic preparations. (Courtesy of Dr. Edmund Cibas, Brigham & Women's Hospital, Boston.)





Follicular Ca

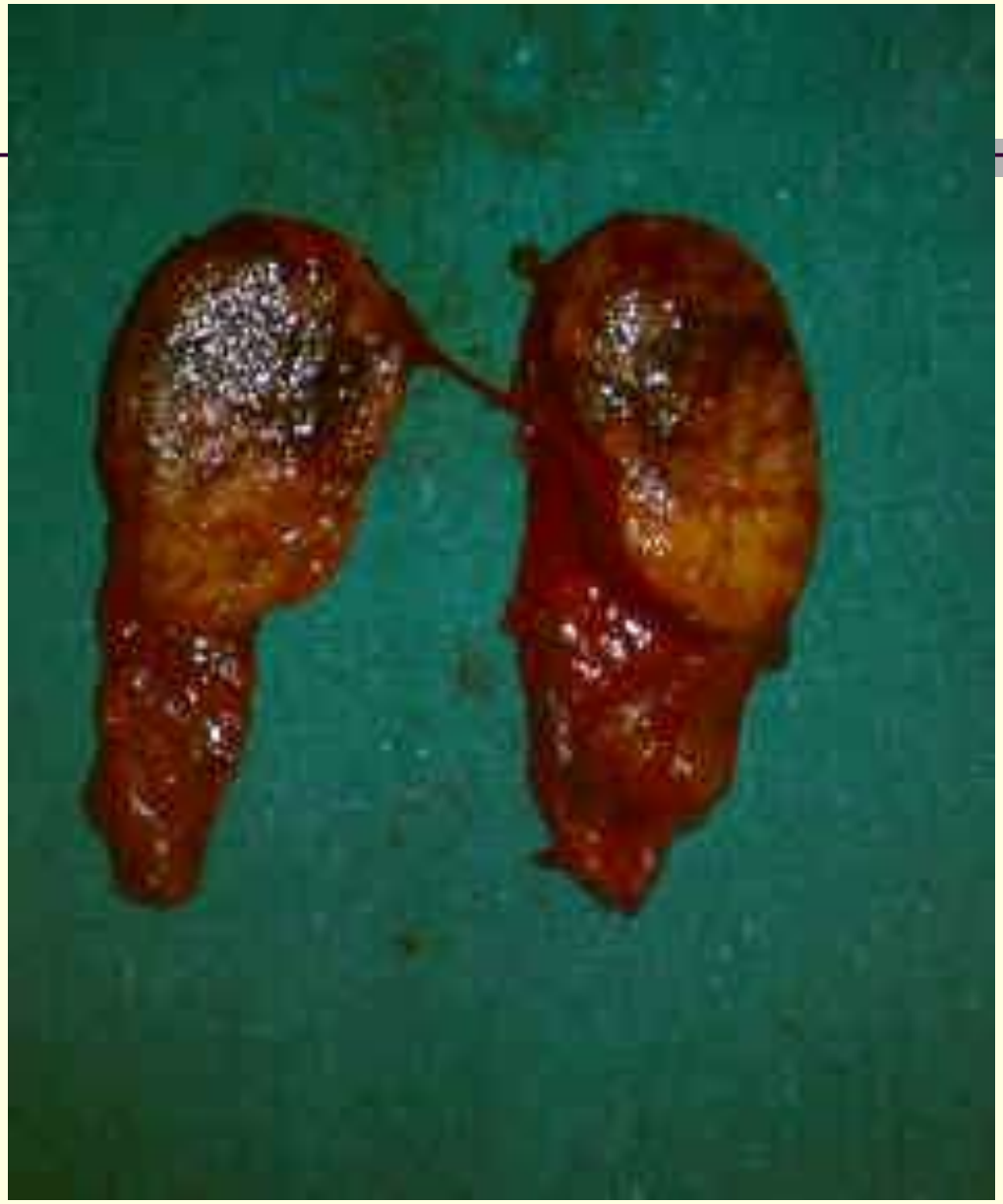
- wanita > pria segala umur
  dekade V & VI
  tumor ini +/- 10-20% kasus > aggressive dbd.
  Papilary Ca; banyak di daerah endemik
- Gross : pembesaran irregular, perlekatan,
  padat, irisan abu-abu putih.
- Mikros : Adeno Ca



Medulary Ca

- 5-10% dekade II, VI-VII
  Apud tumor : ~ timbunan amyloid
  ~ genetik
  ~ polypeptida (VIP, CEA, Somatostatin, serotonin)
  Sipple syndrom : pheochromocytoma + medulary Ca (MEN)
  80-90% sekresi calcitonin
  Gross : padat, keras, putih abu – kuning kecoklatan.
  Perdarahan + nekrosis

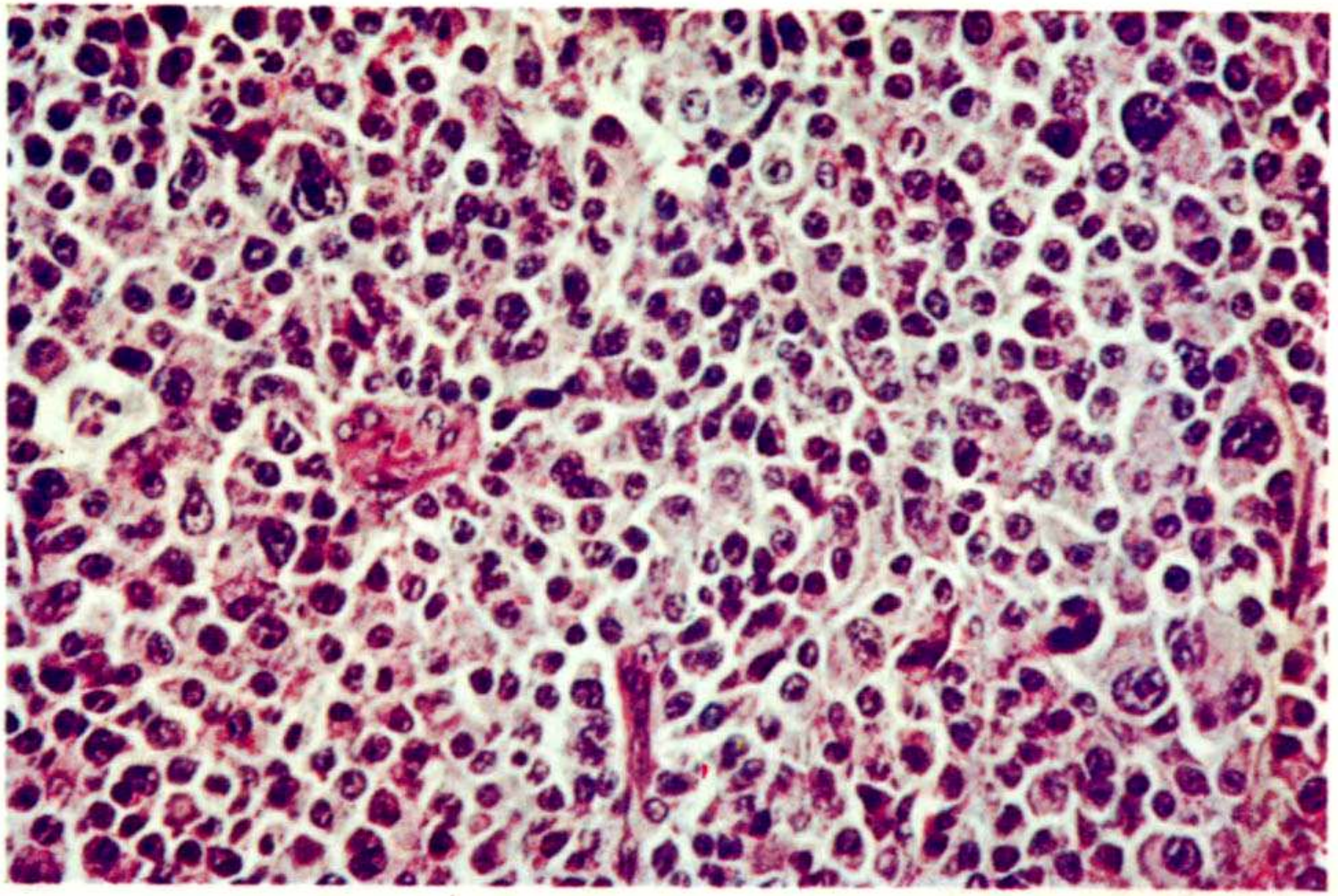
  Mikros : bulat – poligonal, spindle cell, sel ganas diantara jaringan ikat



Anaplastik Ca

- < 5% dekade VII – VIII
  suatu tumor yang agresif,
  mortalitas 100%, kurang dari 1 thn
- Mikroskopik :

1. Large, pleomorphic giant cell
2. Spindle cell + sarcomatus appearance
3. Small anaplastik cells mirip small cell



8.24 Primary undifferentiated carcinoma: thyroid

PARATHYROID

- HYPERPARATHYROID
  - Primary → penyebab penting dr hipercalcemia
  - Etiologi :
    - Adenoma 85-95%
    - Primary hyperplasia 5-15%
    - Parathyroid carcinoma 1%
  - Pathogenesis
    - cyclin D1-rearrangement
    - Mutasi MEN 1
  - Sekunder → serum Ca rendah yang kronis (akibat gagal ginjal)

Morpholgy :

- Adenoma → soliter, single gland, circumscribed
- Hyperplasia → multigladular proses
- Pth carcinoma → mirip adenoma, invasi (+)

Other organs :

- Skeletal → peningkatan osteoclastik dan osteoblastik
- Renal → nephrolitiasis dan nephrocalcinosis

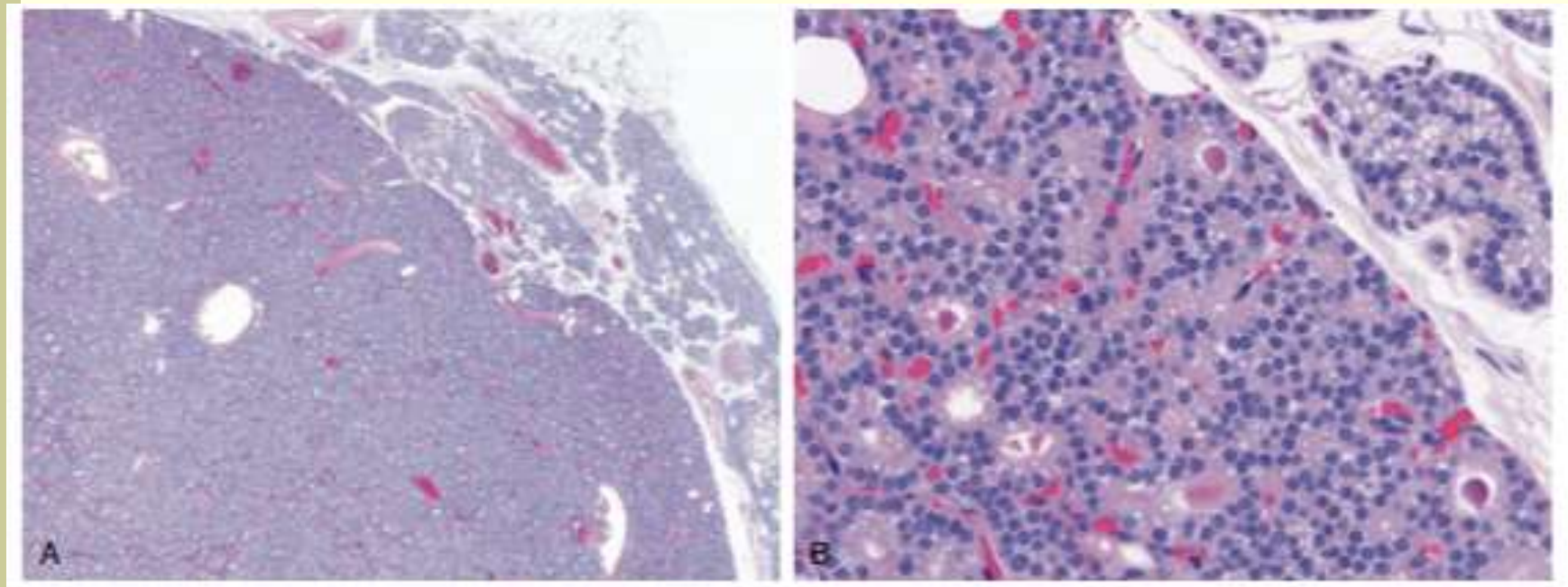
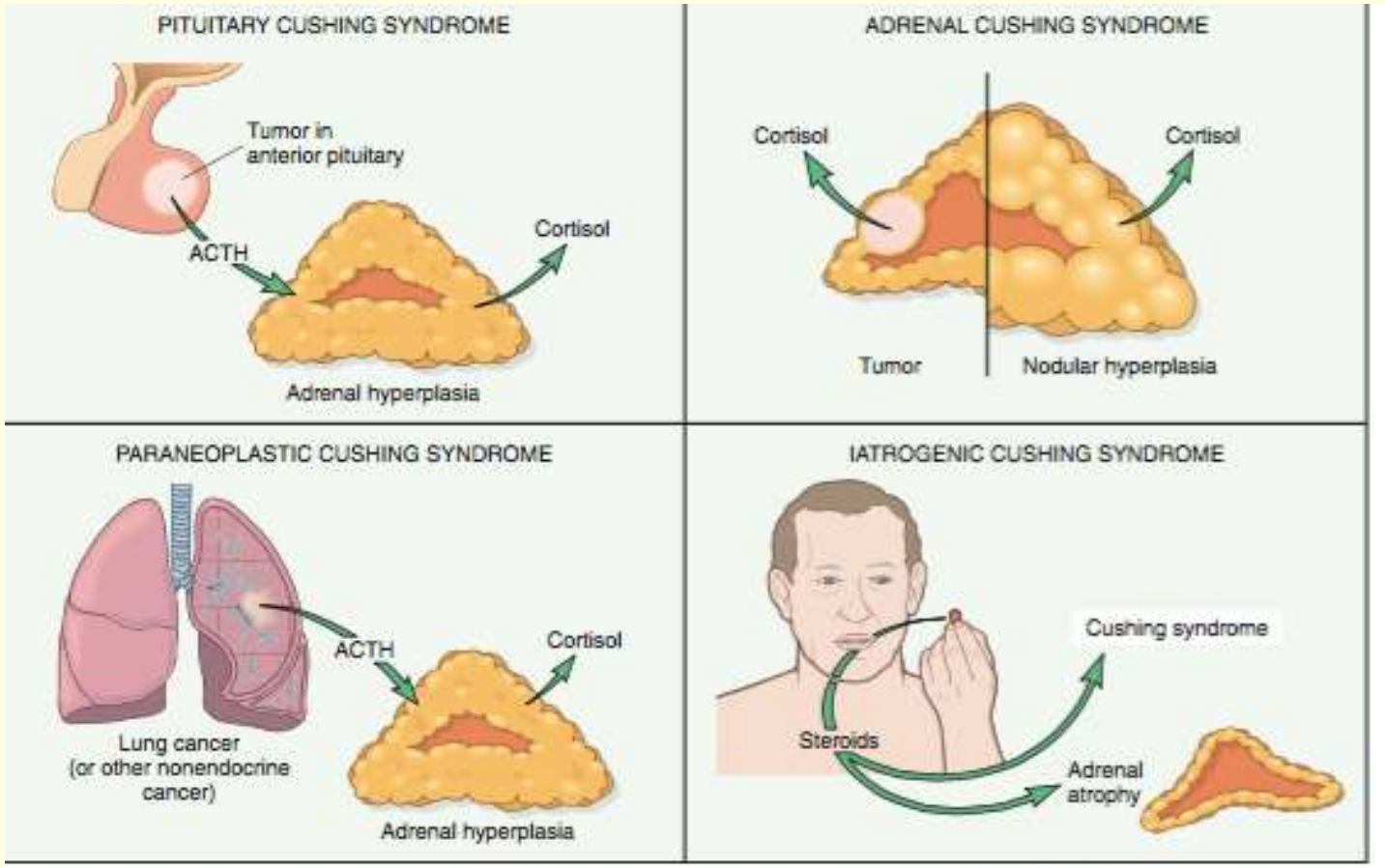


Fig. 20.20 Chief cell parathyroid adenoma. (A) In this low-power view, a solitary hypercellular adenoma is delineated from the residual normocellular gland on the upper right. (B) High-power detail shows minimal variation in nuclear size and occasional follicle formation. *(Courtesy of Dr. Nicole Cibrioni, Department of Pathology, University of Chicago, Chicago, Illinois.)*

ADRENOCORTICAL

- Hyperadrenalism



g. 20.34 Schematic representation of the various forms of Cushing syndrome: The three endogenous forms, as well as the more common exogenous trogenic) form. *ACTH*, Adrenocorticotropic hormone.

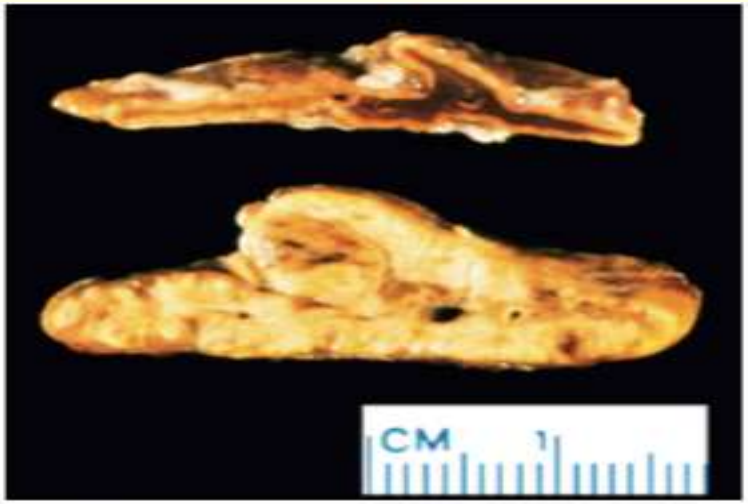


Fig. 20.35 Diffuse hyperplasia of the adrenal gland (bottom) contrasted with a normal adrenal gland (top). In a cross-section, the adrenal cortex is yellow and thickened, and a subtle nodularity is evident. The abnormal gland was from a patient with ACTH-dependent Cushing syndrome, in whom both adrenal glands were diffusely hyperplastic. *ACTH*, Adrenocorticotropic hormone.

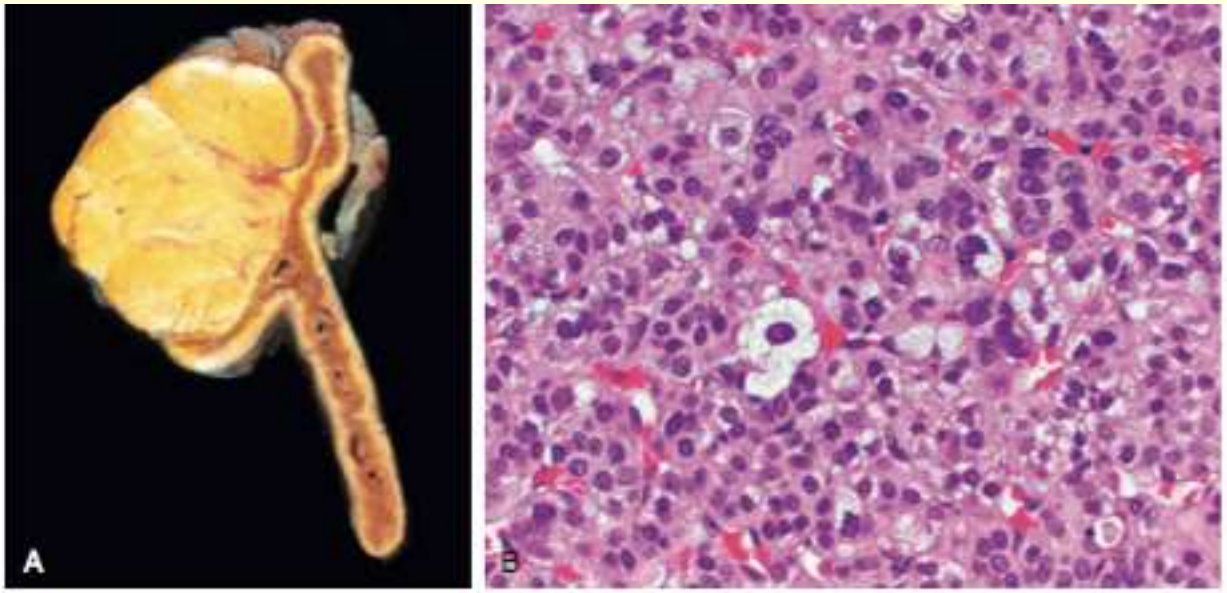


Fig. 20.37 Adrenocortical adenoma. (A) The adenoma is distinguished from nodular hyperplasia by its solitary, circumscribed nature. The functional status of an adrenocortical adenoma cannot be predicted from its gross or microscopic appearance. (B) Histologic features of an adrenal cortical adenoma. The neoplastic cells are vacuolated because of the presence of intracytoplasmic lipid. There is mild nuclear pleomorphism. Mitotic activity and necrosis are not seen.

ADRENAL INSUFFICIENCY (ADDISON)

Table 20.7 Causes of Adrenal Insufficiency

Acute
Waterhouse-Friderichsen syndrome
Sudden withdrawal of long-term corticosteroid therapy
Stress in patients with underlying chronic adrenal insufficiency
Chronic
Autoimmune adrenalitis (60%–70% of cases in developed countries)—includes APS1 (AIRE mutations) and APS2 (polygenic)
Infections Tuberculosis Acquired immunodeficiency syndrome Fungal infections
Hemochromatosis
Sarcoidosis
Systemic amyloidosis
Metastatic disease

APS1, APS2, Autoimmune polyendocrine syndrome types 1 and 2; AIRE, autoimmune regulator gene.

Tumor Adrenal Medulla

- PHAECROMOCYTOMA

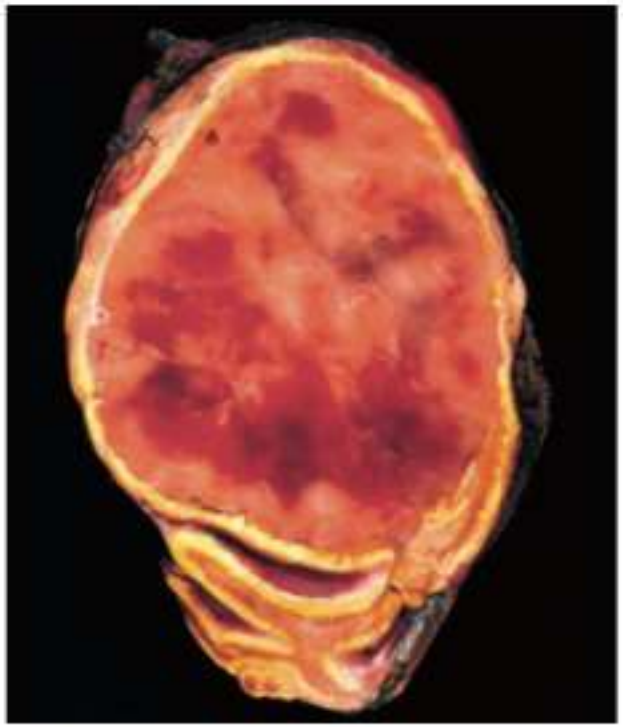


Fig. 20.44 Pheochromocytoma. The tumor is enclosed within an attenuated cortex and demonstrates areas of hemorrhage. The comma-shaped residual adrenal gland is seen *(lower portion)*.

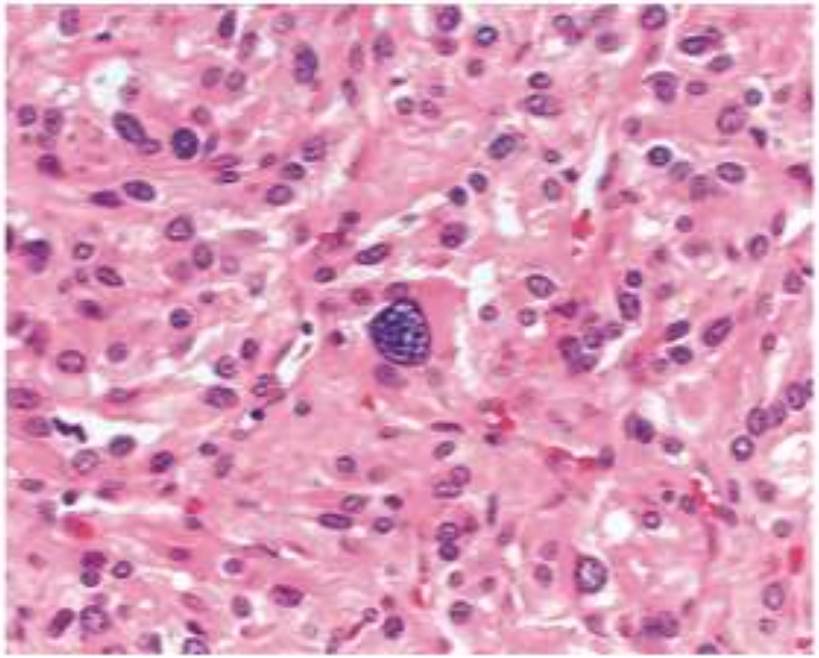


Fig. 20.45 Photomicrograph of pheochromocytoma, demonstrating characteristic nests of cells with abundant cytoplasm. Granules containing catecholamine are not visible in this preparation. It is not uncommon to find bizarre cells (such as the one in the center of this image), even in pheochromocytomas that are benign.