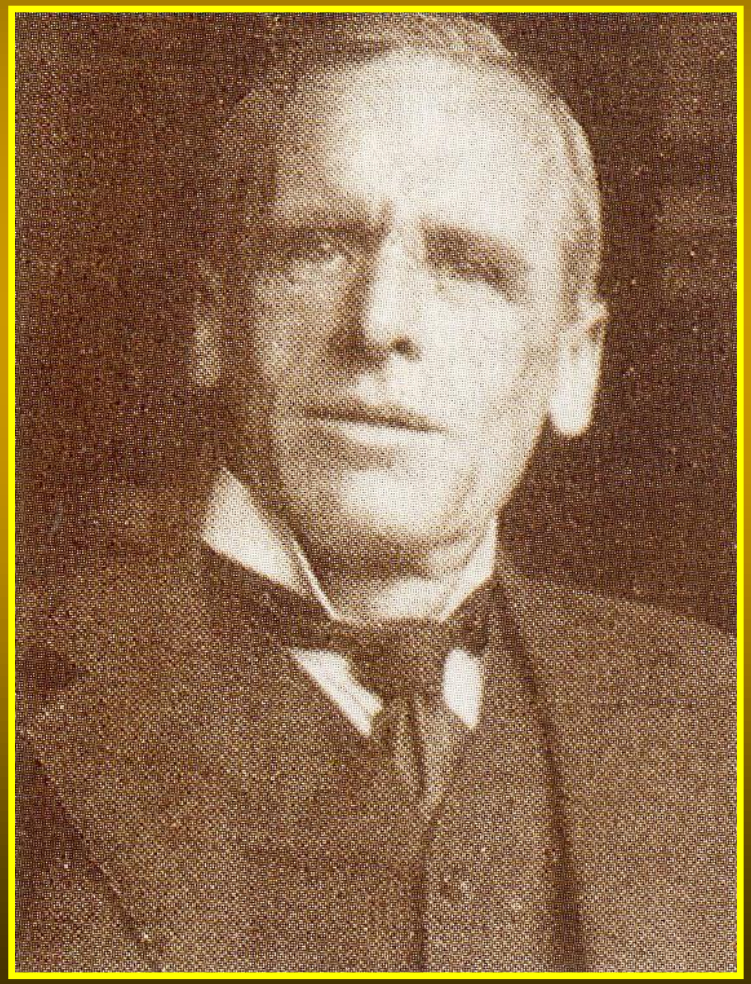
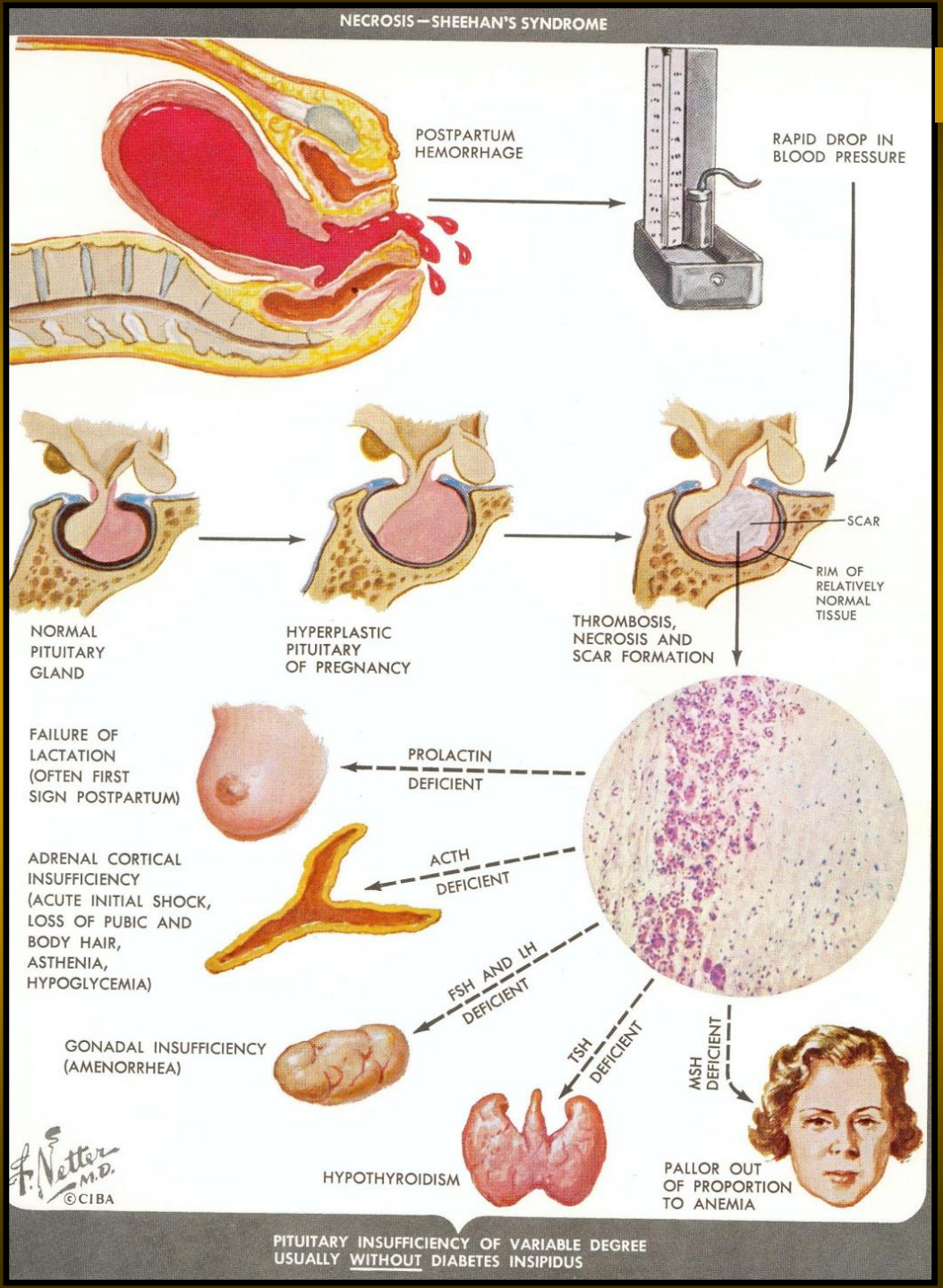
LECTURE ENDOCRINE GLANDS



Ernest Henry Starling

1866-1927

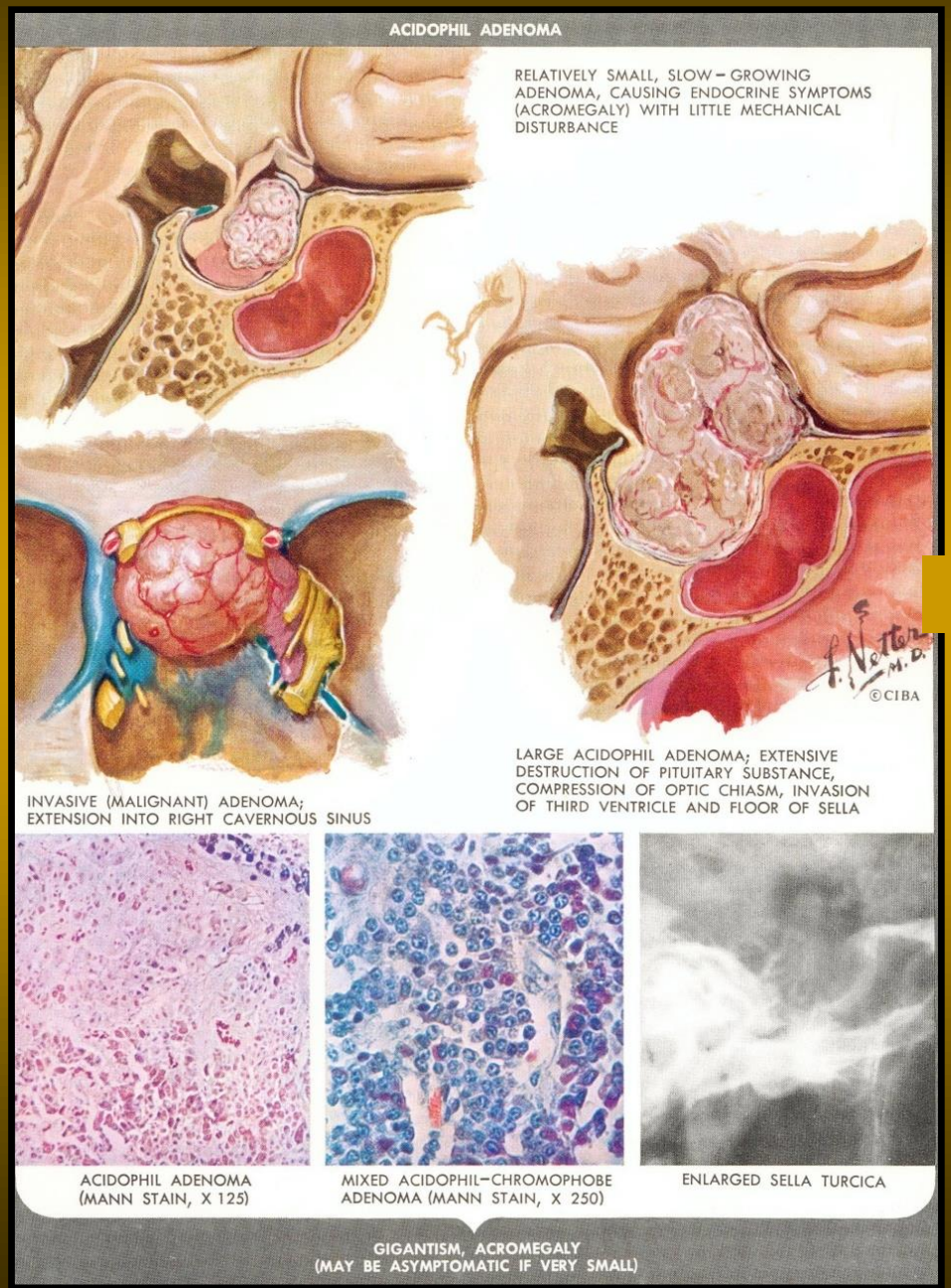


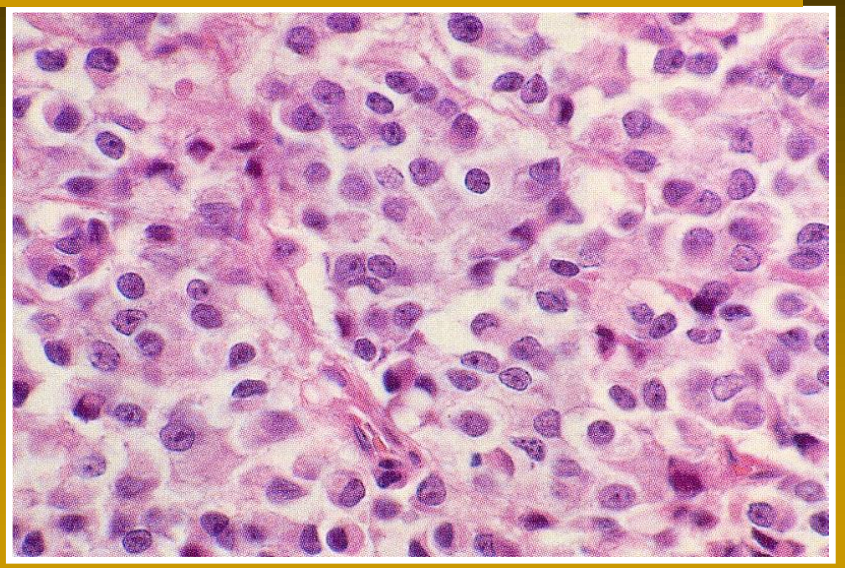
PATHOLOGY OF HYPOPHYSIS

ACUTE POST DELIVERY HYPOPHYSEAL INSUFFICIENCY- SHEEHAN SYNDROME

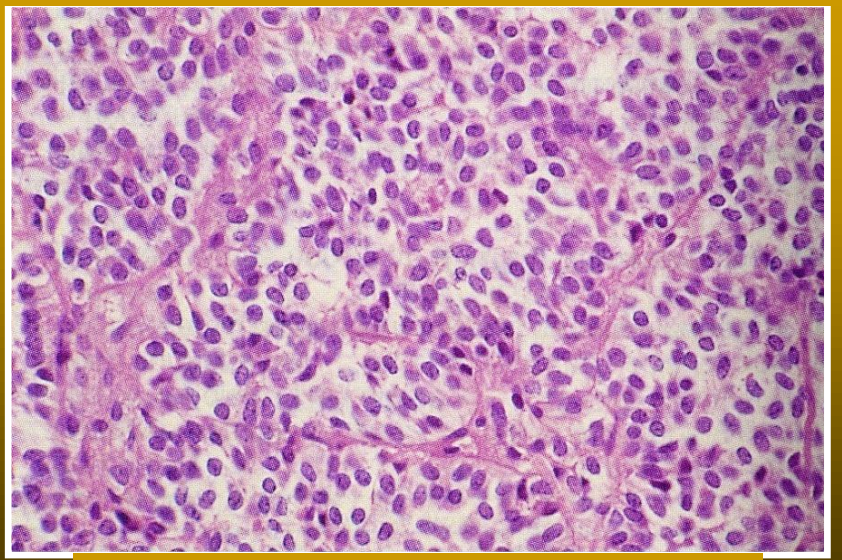
…MAINLY FOLLOWING ANTERIOR LOBE INFARCT (NECROSIS)

HYPERACTIVITY OF THE ANTERIOR LOBE - ADENOMAS



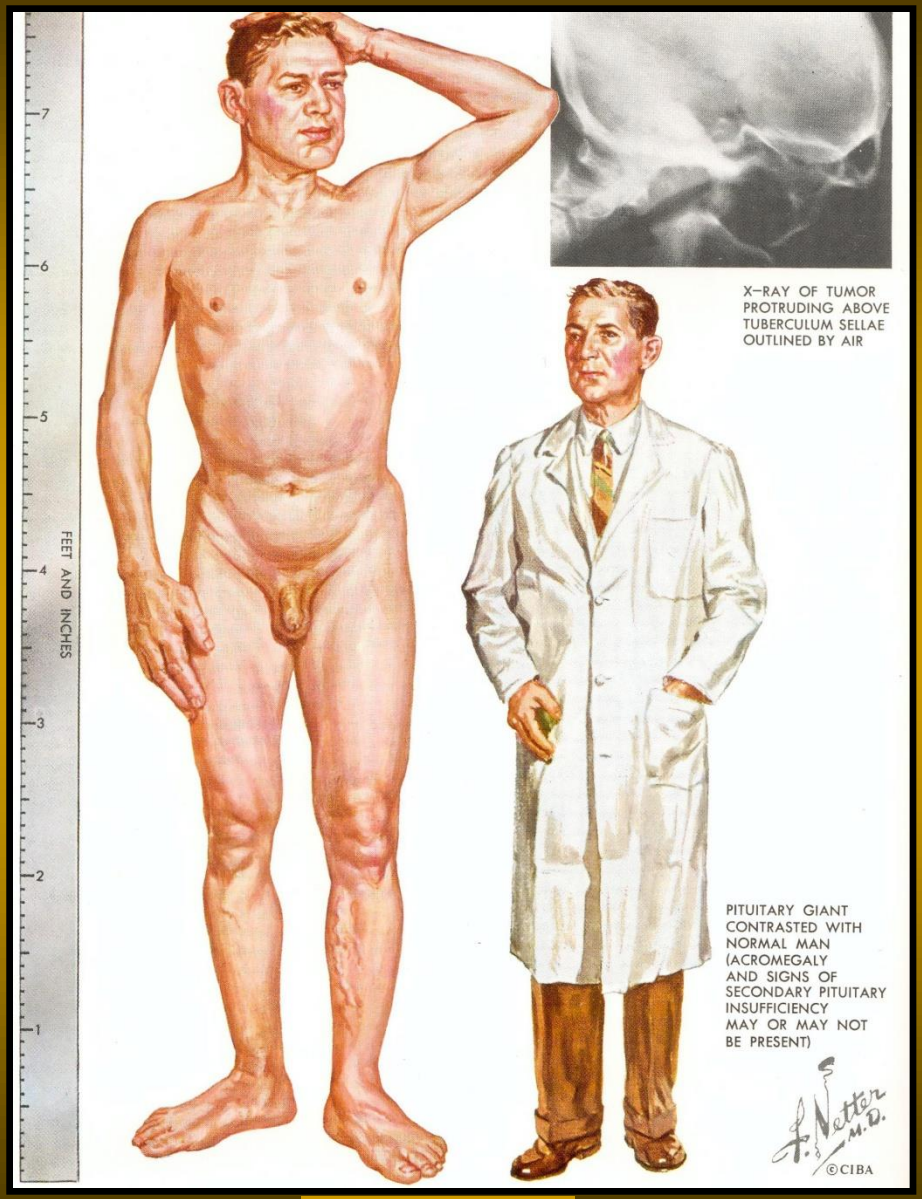


EOSINOPHILIC (ACIDOPHIL) ADENOMA

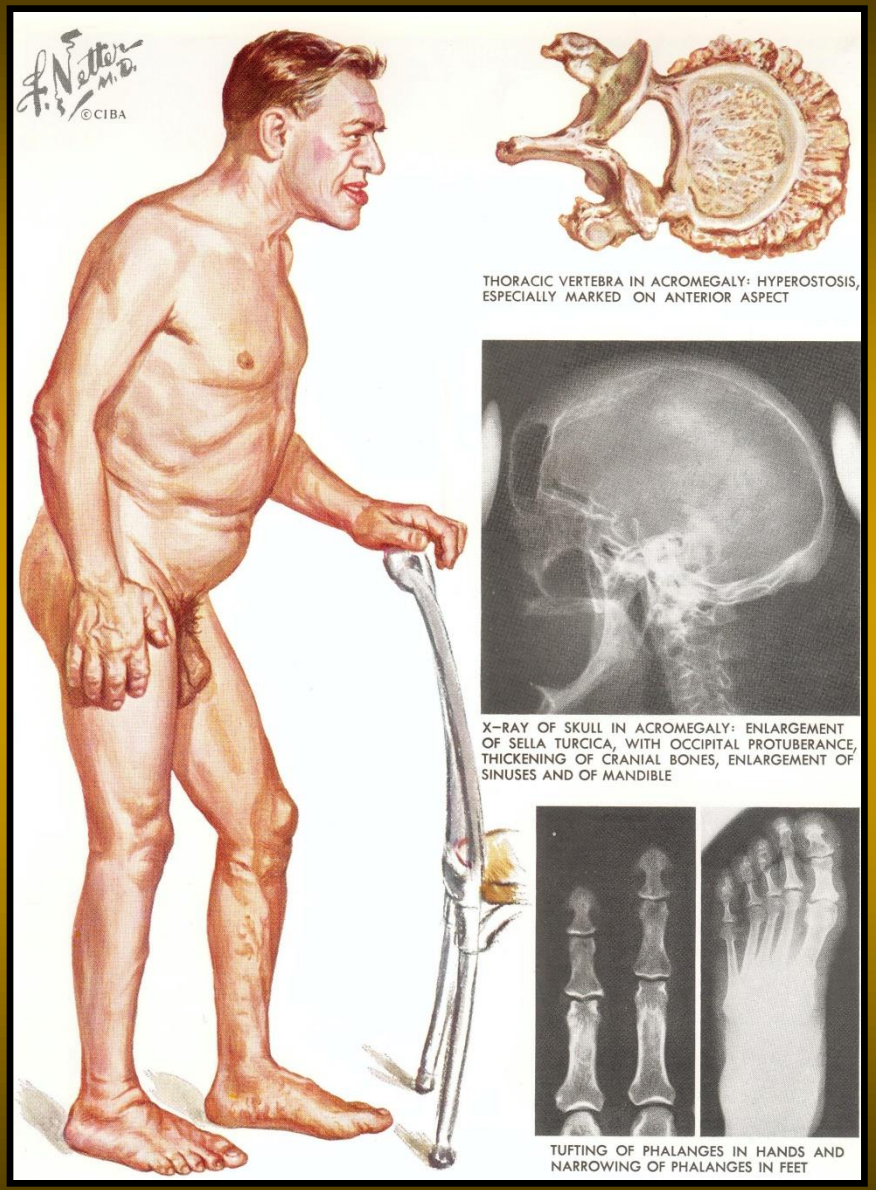


CHROMOPHOBE ADENOMA

PATHOLOGY OF HYPOPHYSIS

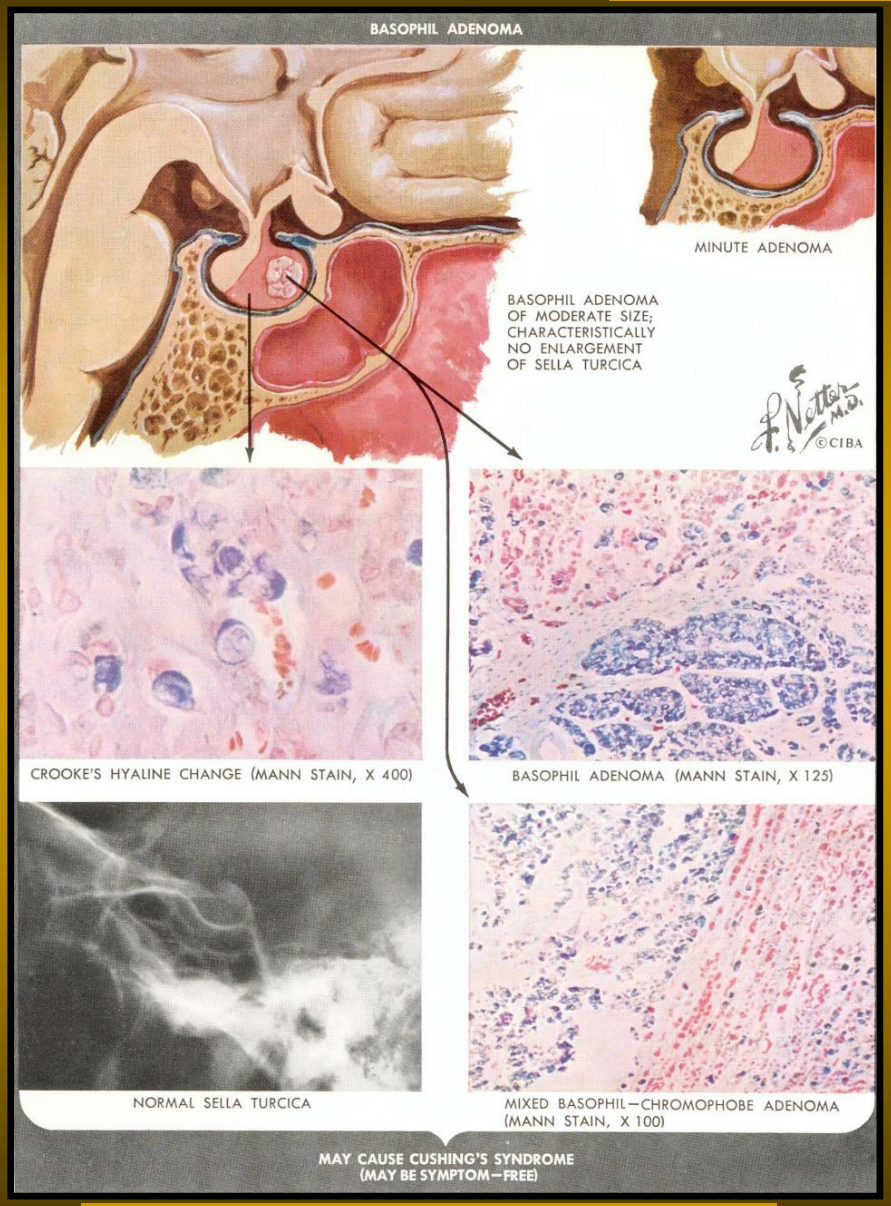


GIANTISM

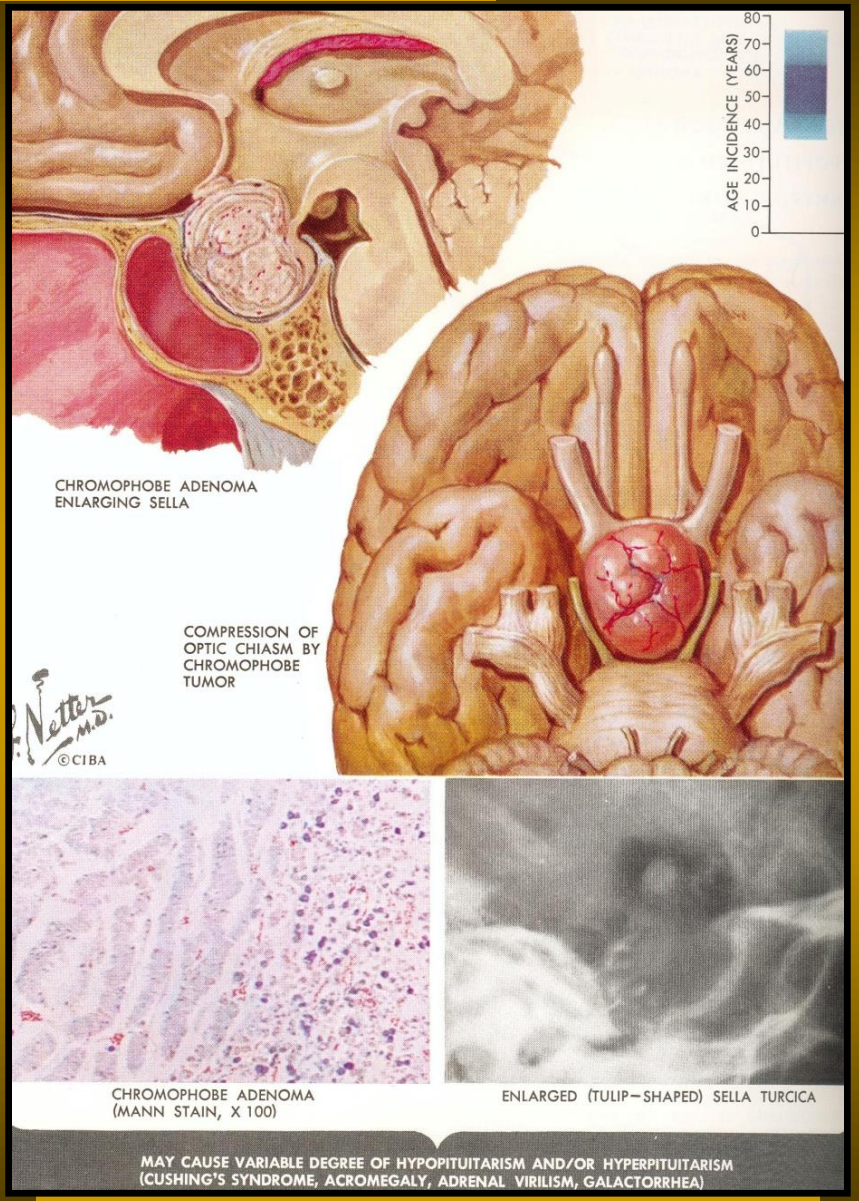


ACROMEGALY

PATHOLOGY OF HYPOPHYSIS

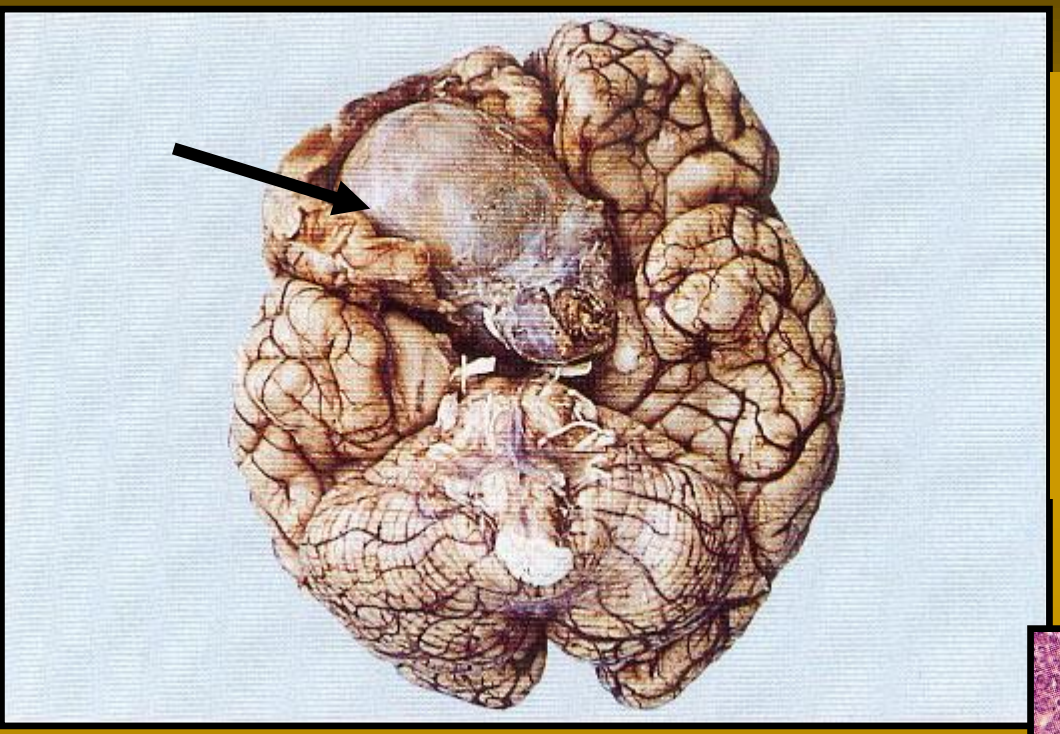


BASOPHIL ADENOMA



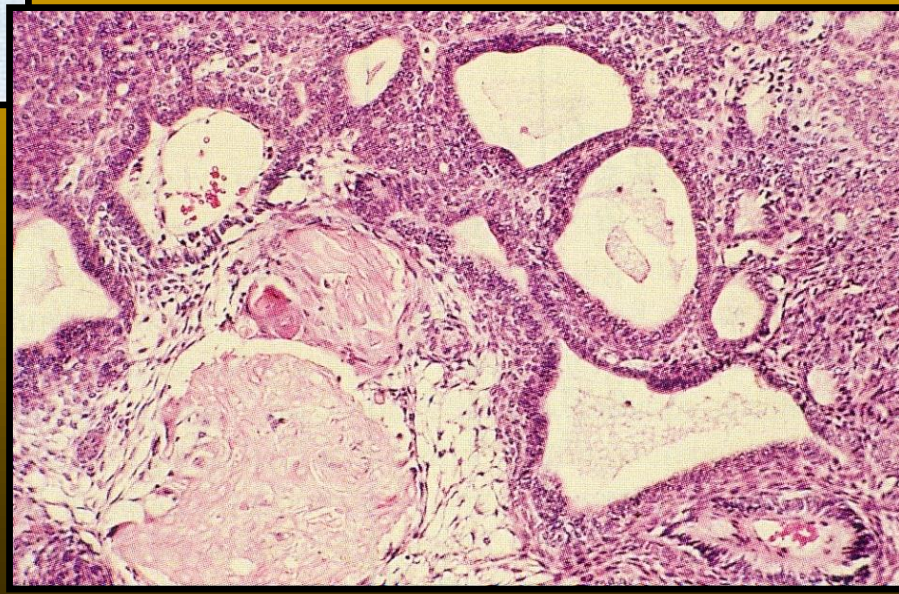
CHROMOPHOBE ADENOMA

CRANIOPHARYNGEOMA



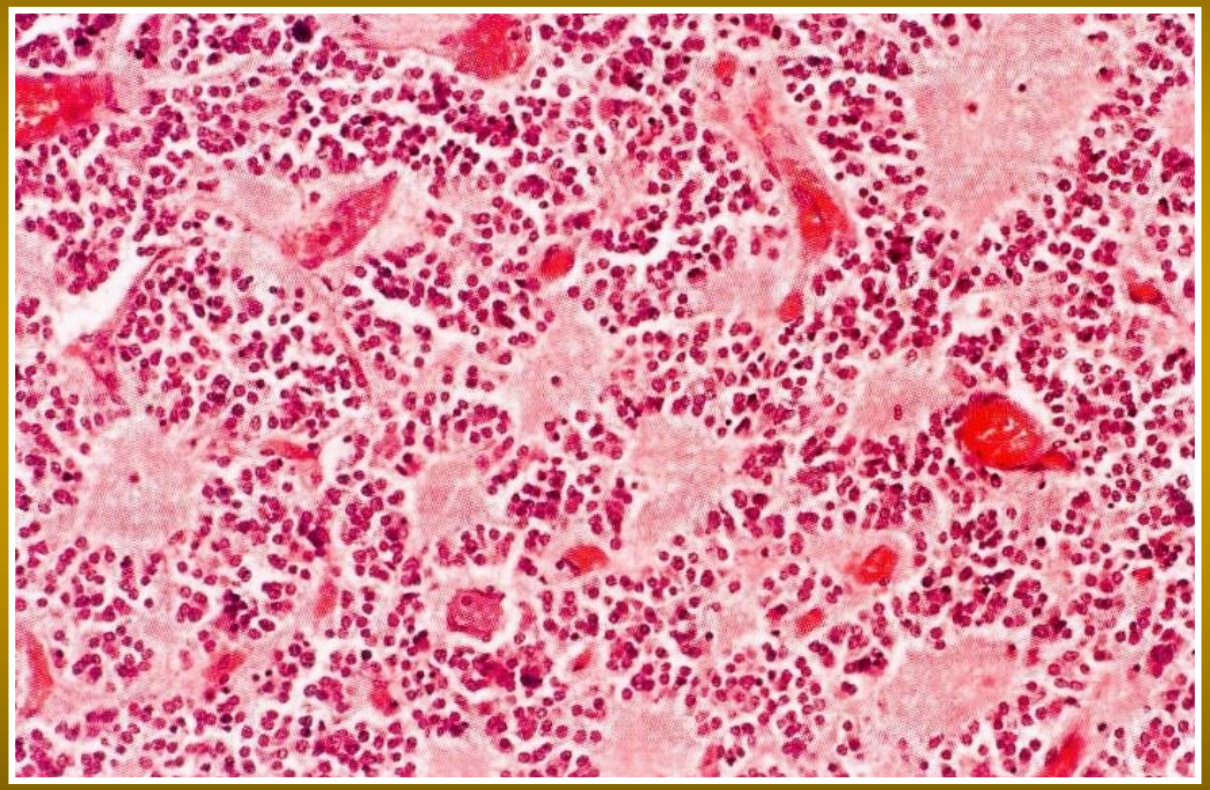
TUMOR DERIVED FROM THE RATHKE POUCH (ANTERIOR PART OF HYPOPHYSIS DEVELOPS FROM THIS POUCH)

IT HAS A FORM OF CYST BOUND WITH SELLA AND WITH BASE OF BRAIN



PATHOLOGY OF PINEAL BODY

**PATHOLOGIC LESIONS OF P.B. ARE VERY RARE.
MAINLY – TUMORS. TUMORS MAY CAUSE OCCLUSION OF SYLVIAN AQUEDUCT AND → HYDROCEPHALUS**

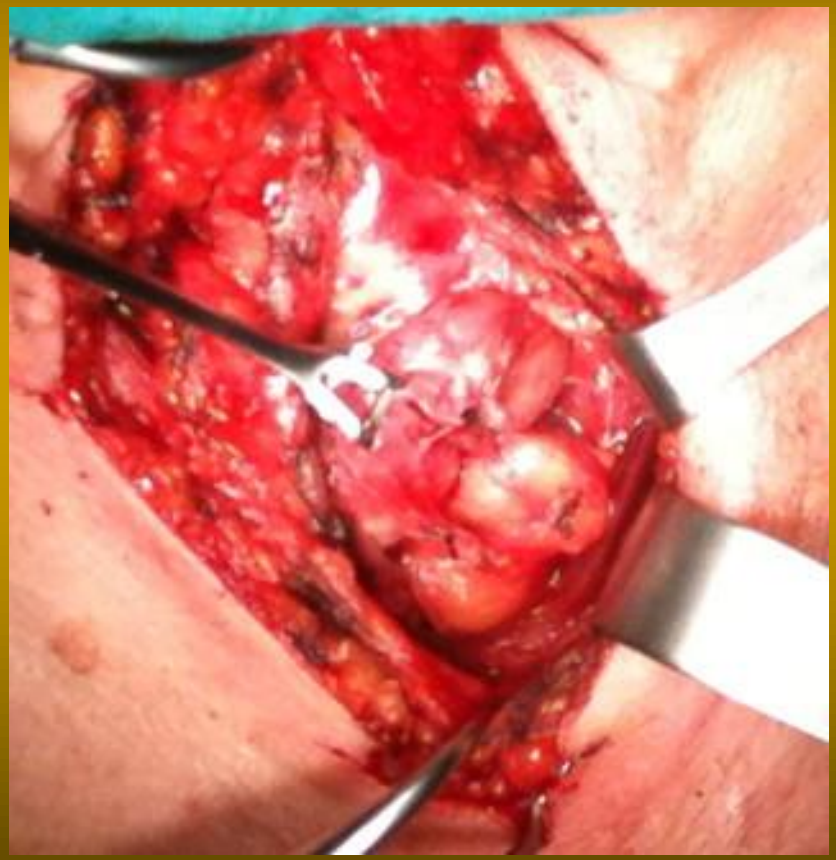


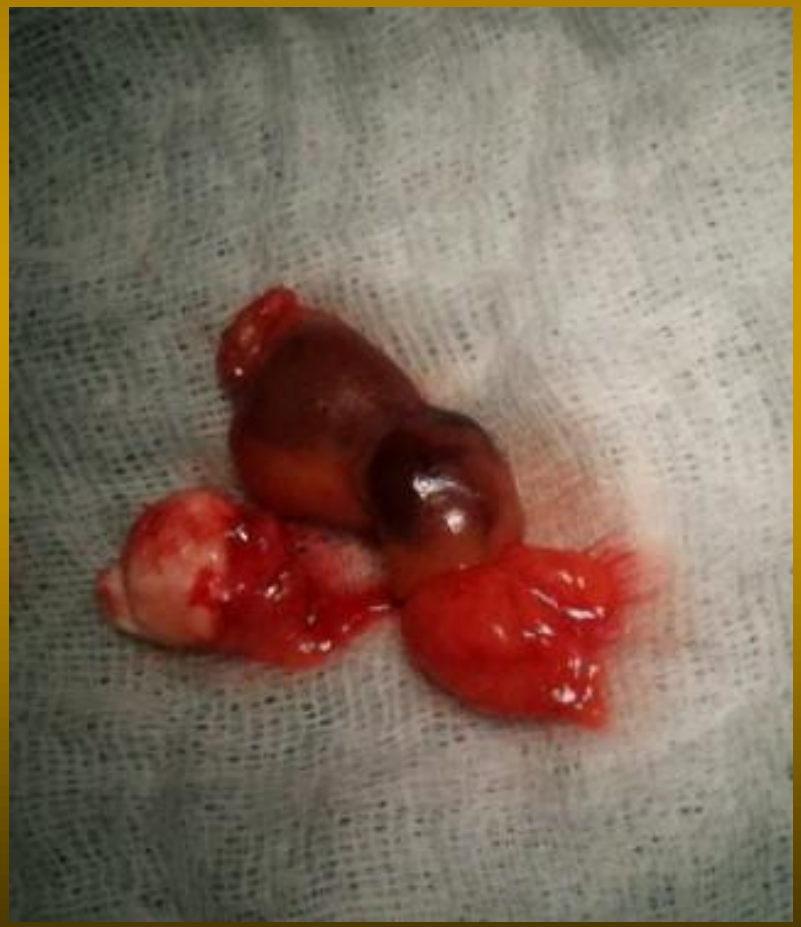
PINEALOMA

Parathyroid gland

- **ADENOMA:** Usually monoclonal but hyperplastic glands may also be monoclonal
- Difficult to diagnose - best criterion is lack of hypercalcemia for 5 years after excision
- Remaining glands usually normal in size or shrunken due to feedback inhibition from elevated serum calcium (presence of microscopically normal second gland strongly suggests that parathyroid lesion is an adenoma); 10% of patients show minimal hyperplasia in remaining glands

Parathyroid gland adenoma





Parathyroid gland

- **Atypical adenoma**
- Has some features of malignancy (broad fibrous bands crossing the tumor, trabecular growth, pseudocapsular invasion [clusters of parathyroid cells trapped within the capsule in 50%]) but no vascular invasion, no metastases, rarely increased mitotic activity (Hum Pathol 2003;34:54)
- Unpredictable clinical behavior

Parathyroid gland Hypoparathyroidism - Causes

- **Condition of parathyroid hormone (PTH) deficiency (eMedicine: Hypoparathyroidism)**
- DiGeorge syndrome: complete or partial absence of third and fourth pharyngeal pouches, causing thymic aplasia and T cell deficiency, conotruncal cardiac defects; -22 by FISH
- Familial: syndrome of chronic mucocutaneous candidiasis, then hypoparathyroidism, then primary adrenal insufficiency
- Idiopathic atrophy: antibodies directed against calcium sensing receptor in parathyroid gland
- Radiation
- Surgery (including thyroidectomy)

Hypoparathyroidism - Symptoms

- Cataracts
- Circumoral numbness or paresthesias of distal extremities
- Dental abnormalities during early development: dental hypoplasia, failure of eruption, defective enamel and root formation, abraded carious teeth
- Laryngospasm
- Prolonged QT interval
- Seizures; Tetany / neuromuscular irritability

Parathyroid gland

- Neoplasms:
- World Health Organization (WHO) classification
- Tumours of the parathyroid glands
- Parathyroid carcinoma
- Parathyroid adenoma
- Secondary, mesenchymal and other tumours

- **THYROID GLAND**

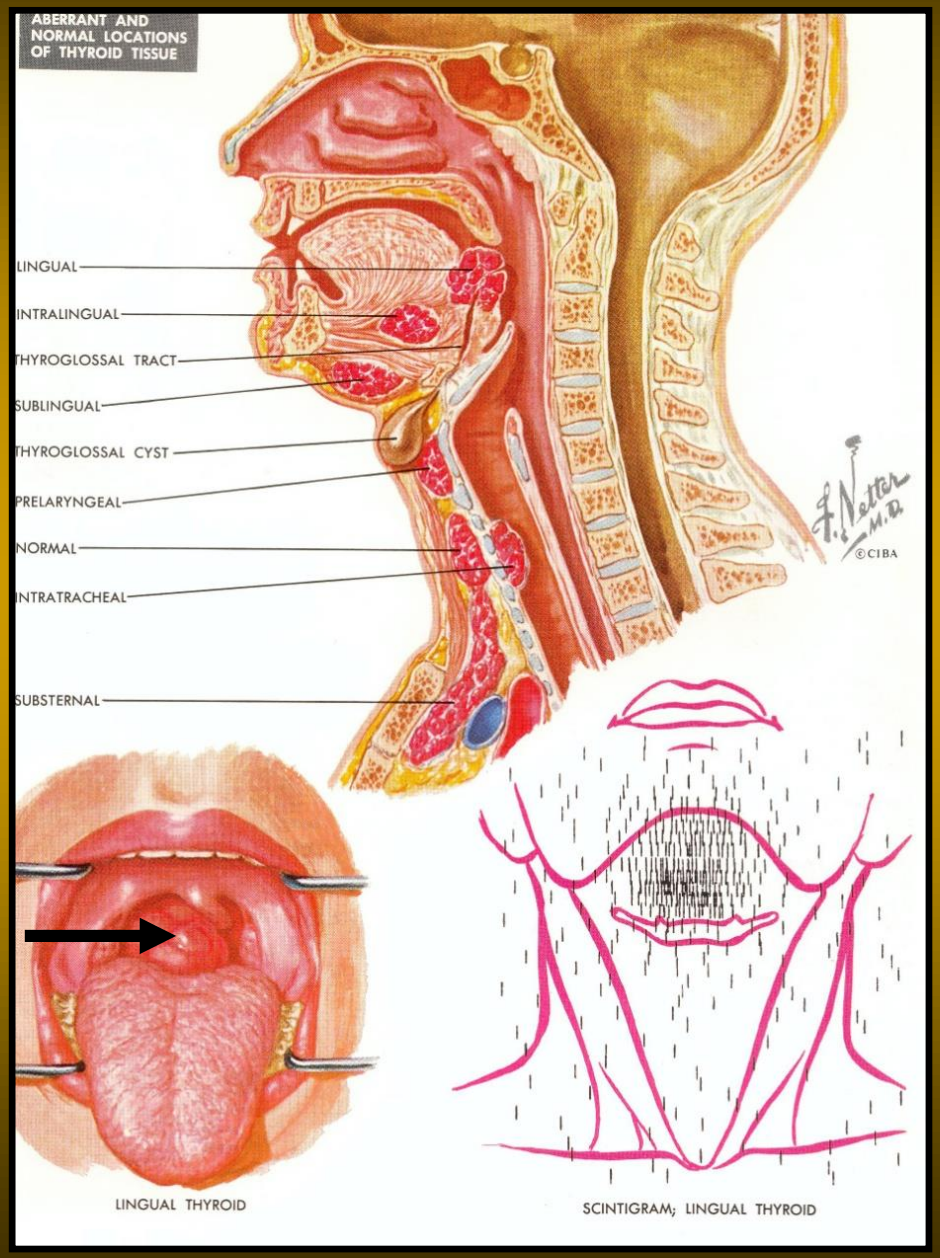
- Bethesda systems for cytology:
- Assessment of adequacy is the first step in the evaluation of a thyroid fine needle aspiration (FNA) sample (Clark: Thyroid Cytopathology, 1st Edition, 2005)
- Rapid, low magnification review of all cytologic slides by pathologist or cytotechnologist
- Rapid on site evaluation helps assess adequacy after sampling; if smear is inadequate, the thyroid nodule can be reaspirated immediately

Factors influencing adequacy (Ali: The Bethesda System for Reporting Thyroid Cytopathology, 2nd Edition, 2018):

Nature of the nodule (location, size, cystic component)
Skills of operator and reader
Technical setup (gauge size, ultrasound guidance, etc.)
Criteria of adequacy
FNA smear should contain ≥ 6 groups of well visualized follicular cells (≥ 10 cells/group), preferably on a single slide
Exceptions (a minimum number of follicular cells is not required)

Solid nodules with cytologic atypia, which qualify into categories III - VI
Solid nodules with inflammation are considered benign (Diagn Cytopathol 2008;36:407, Diagn Cytopathol 2008;36:161)
Only numerous inflammatory cells
Lymphocytic thyroiditis, thyroid abscess or granulomatous thyroiditis
Nodules with abundant colloid are placed in the benign category even in the absence of follicular epithelium

PATHOLOGY OF THYROID GLAND

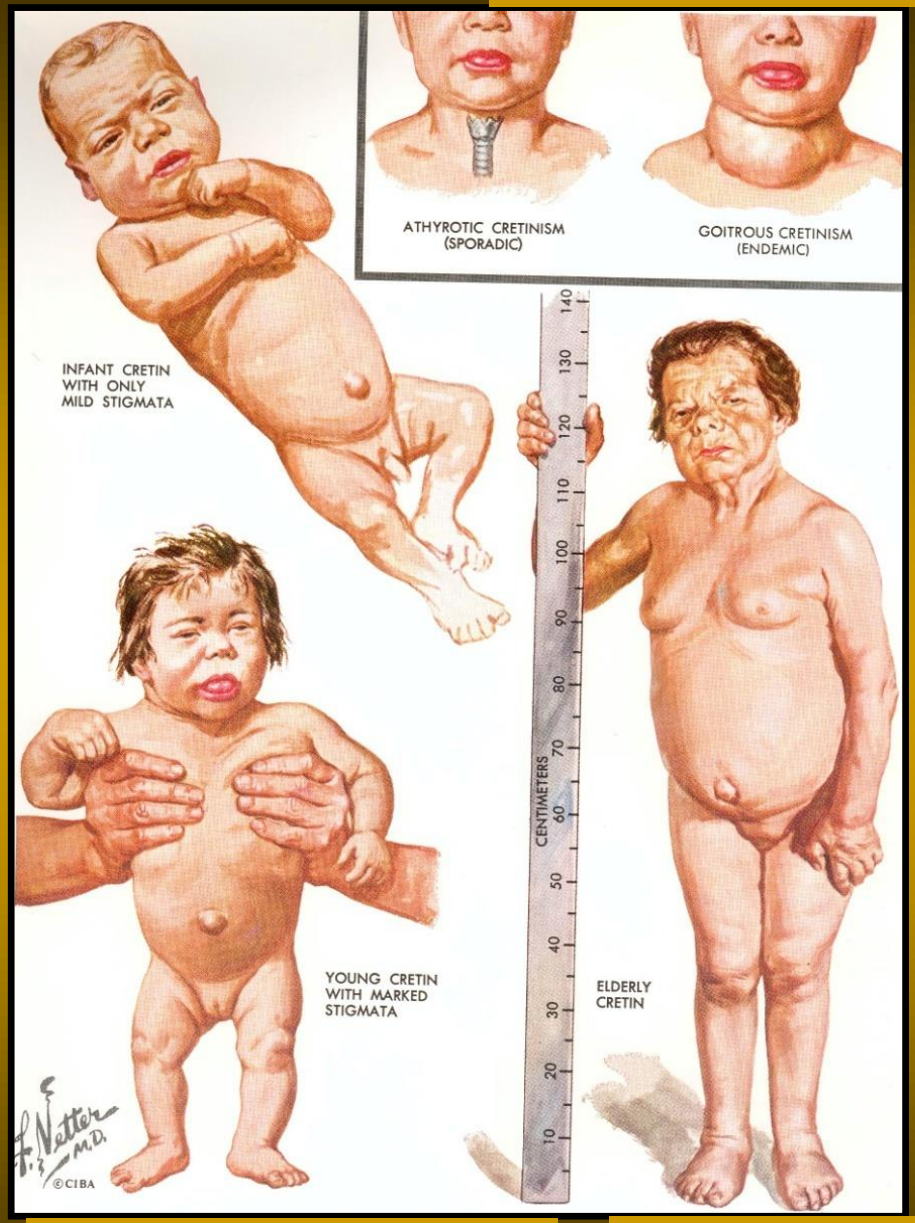


Developmental abnormality characterized by the presence of thyroid tissue in any location other than its normal anatomic position.

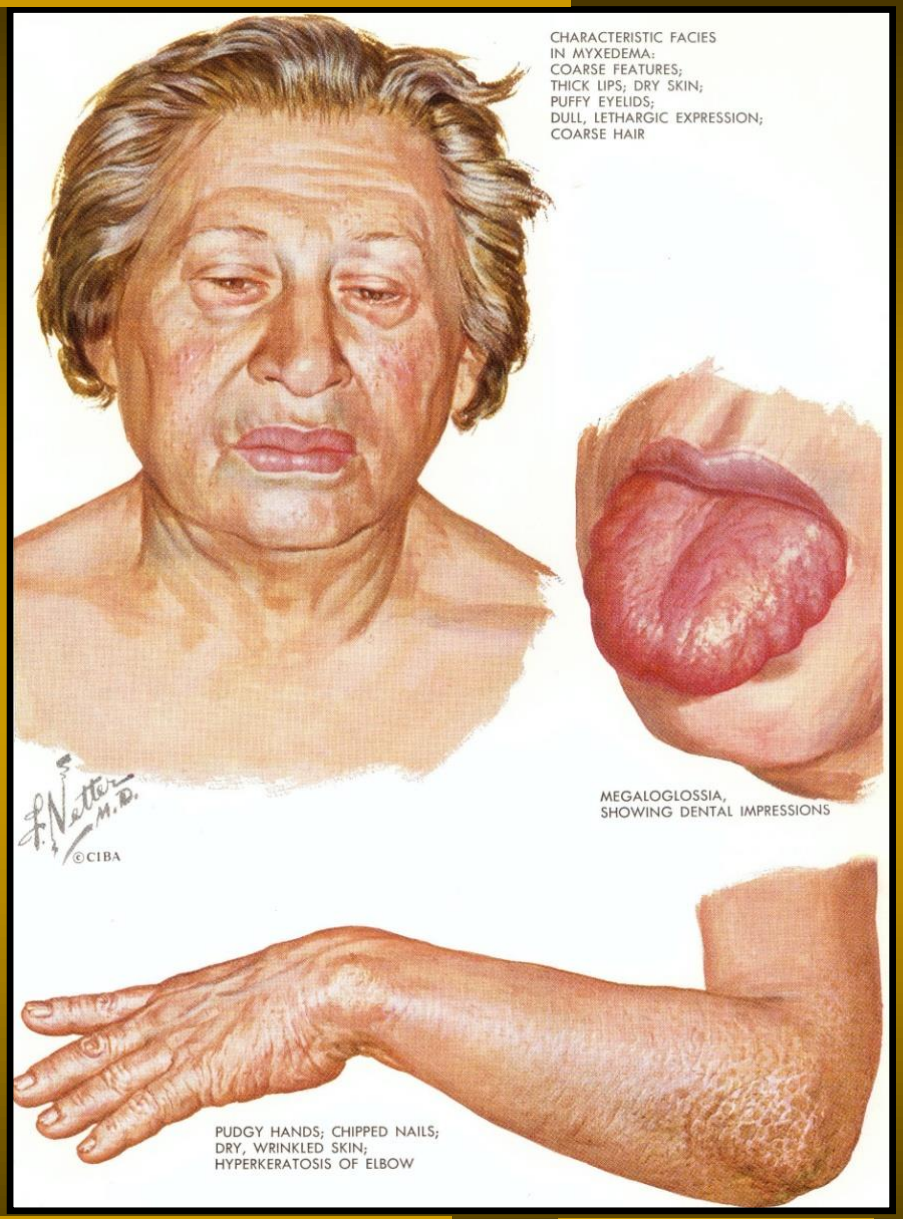
First well documented case was reported by Hickman in 1869

ECTOPIA, ECTOPY

PATHOLOGY OF THYROID GLAND

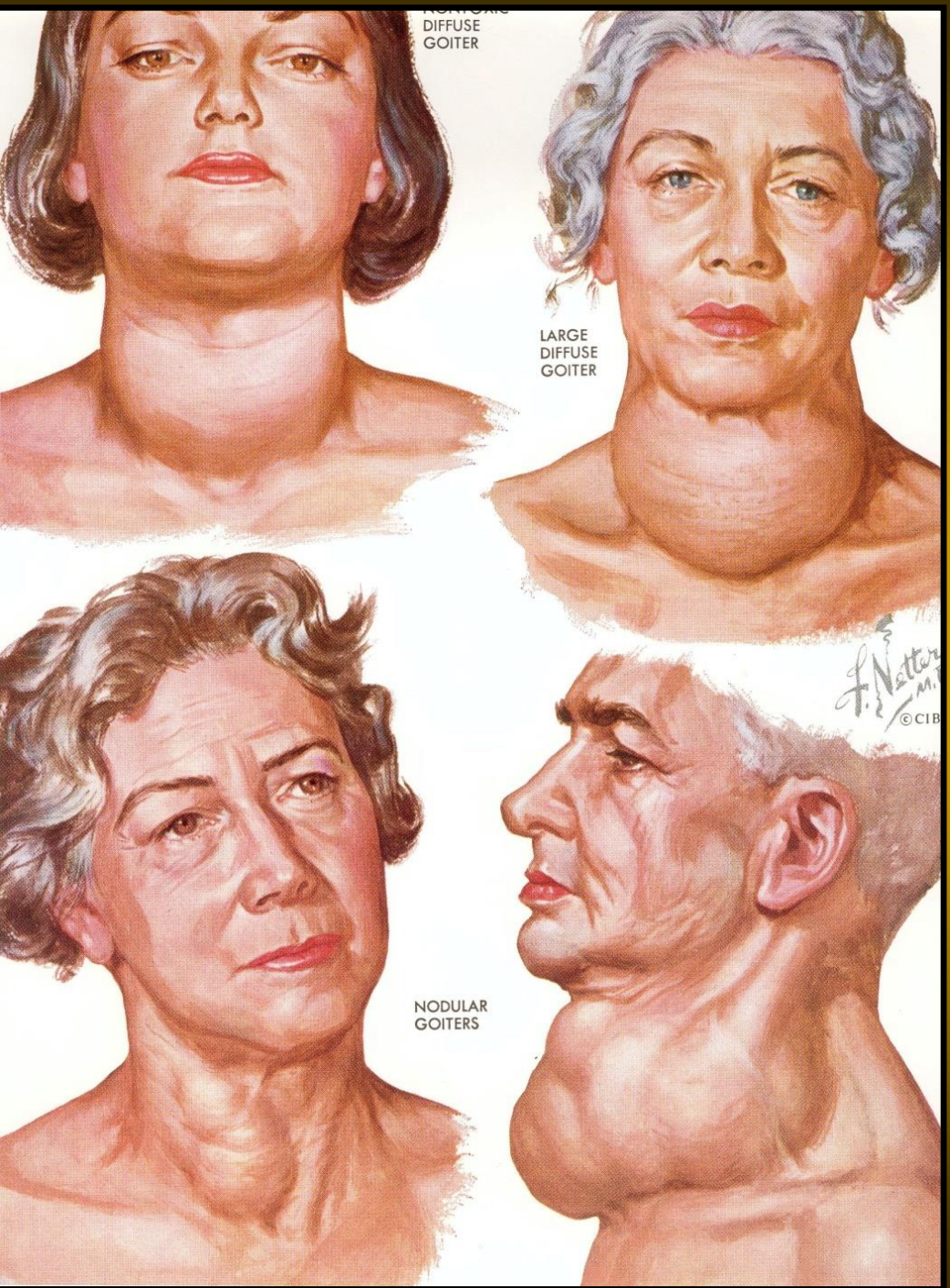


THYROID CRETINISM



THYROID GLAND HYPOACTIVITY

MYXEDEMA



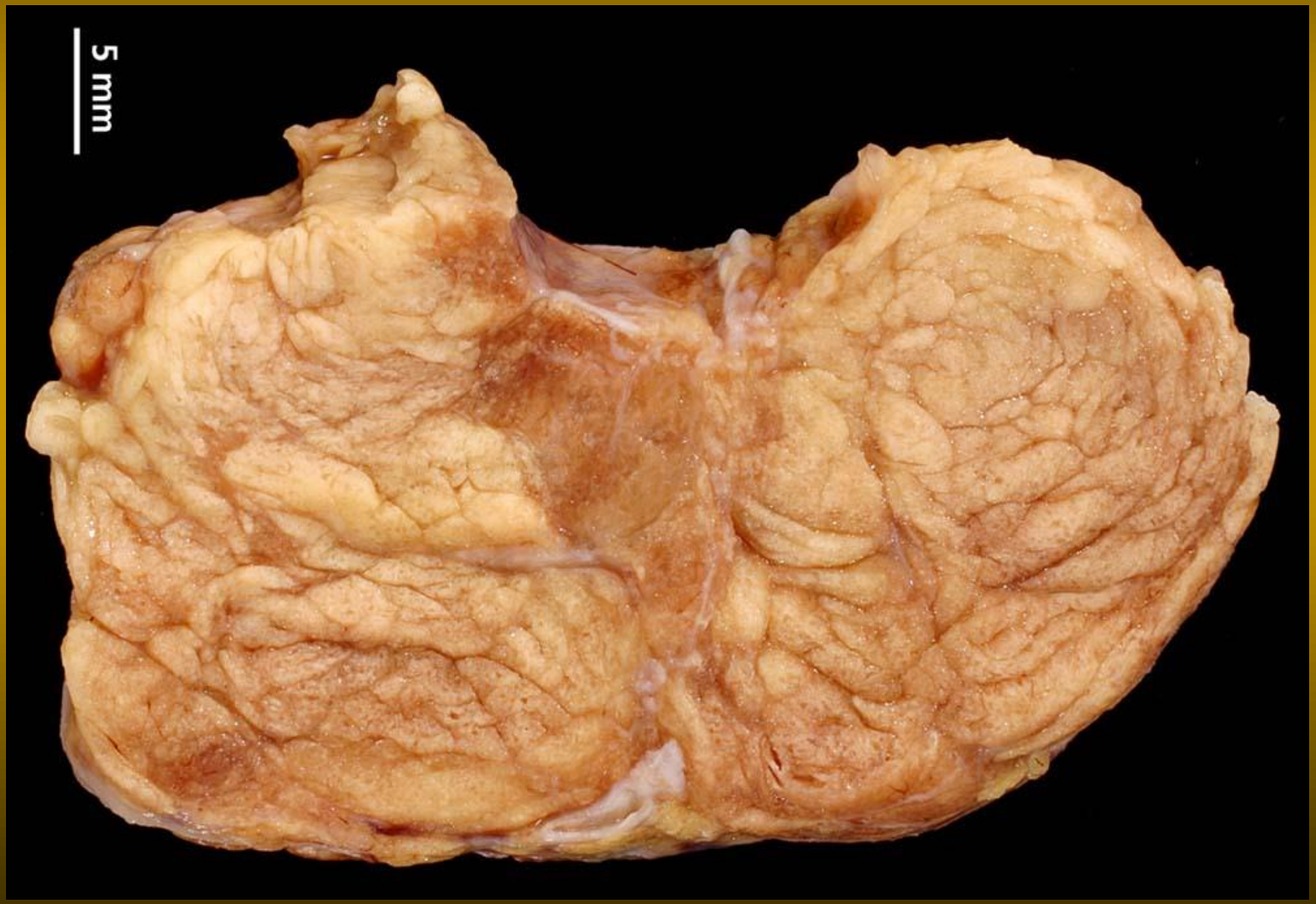
DIFFUSE AND NODULAR GOITRE

GOITRE = ENLARGEMENT OF THYROID GLAND AS A DIFFUSE OR NODULAR TYPE. IT DOES NOT DETERMINE ITS PATHOGENESIS (RETROGRADE LESION, INFLAMMATION, HYPERTROPHY, TUMORS)

AMYLOID GOITRE

- **First reported in 1855 (Rokitansky: A Manual Of Pathological Anatomy; Vol: I, 2008)**
- **Defined as a diffuse clinically apparent enlargement of the thyroid gland due to widespread amyloid deposits (von Eisenberg: Ueber einen Fall von Amyloid-Kropf, 1904)**
- **Rare entity**
- **Diagnosis often made at autopsy**

AMYLOID GOITRE

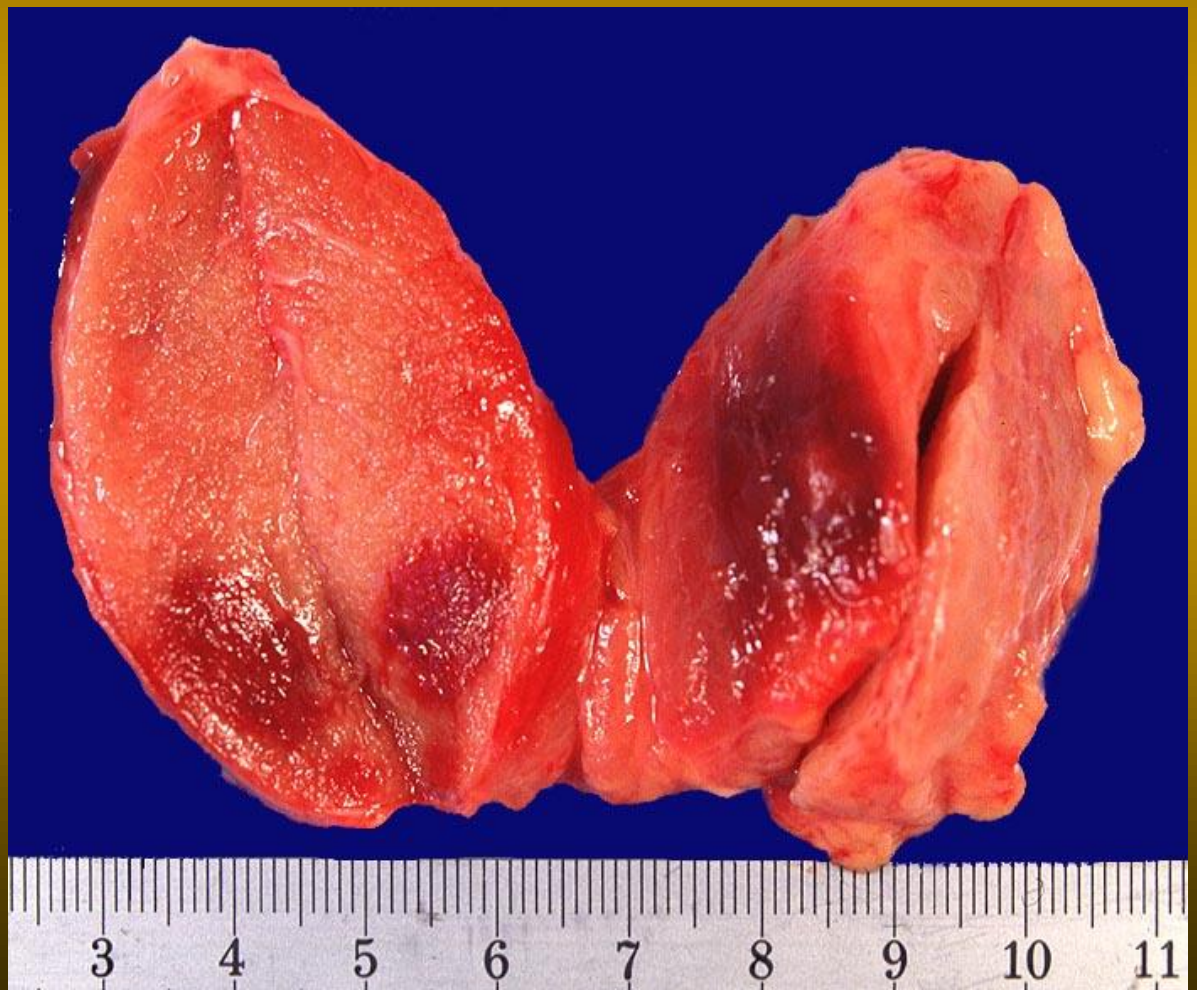


Infectious thyroiditis

- **Also called acute thyroiditis**
- Via blood or direct seeding from upper respiratory infections, causes sudden onset of pain and glandular enlargement
- Risk factors: malnourished infant, debilitated elderly, immunosuppression, trauma
- Often Streptococcus haemolyticus, Streptococcus pneumoniae, Staphylococcus aureus; gram negative bacteria associated with trauma; also Pneumocystis jiroveci in HIV+ patients with low CD4 counts

Aspergillus sepsis: septic lesions

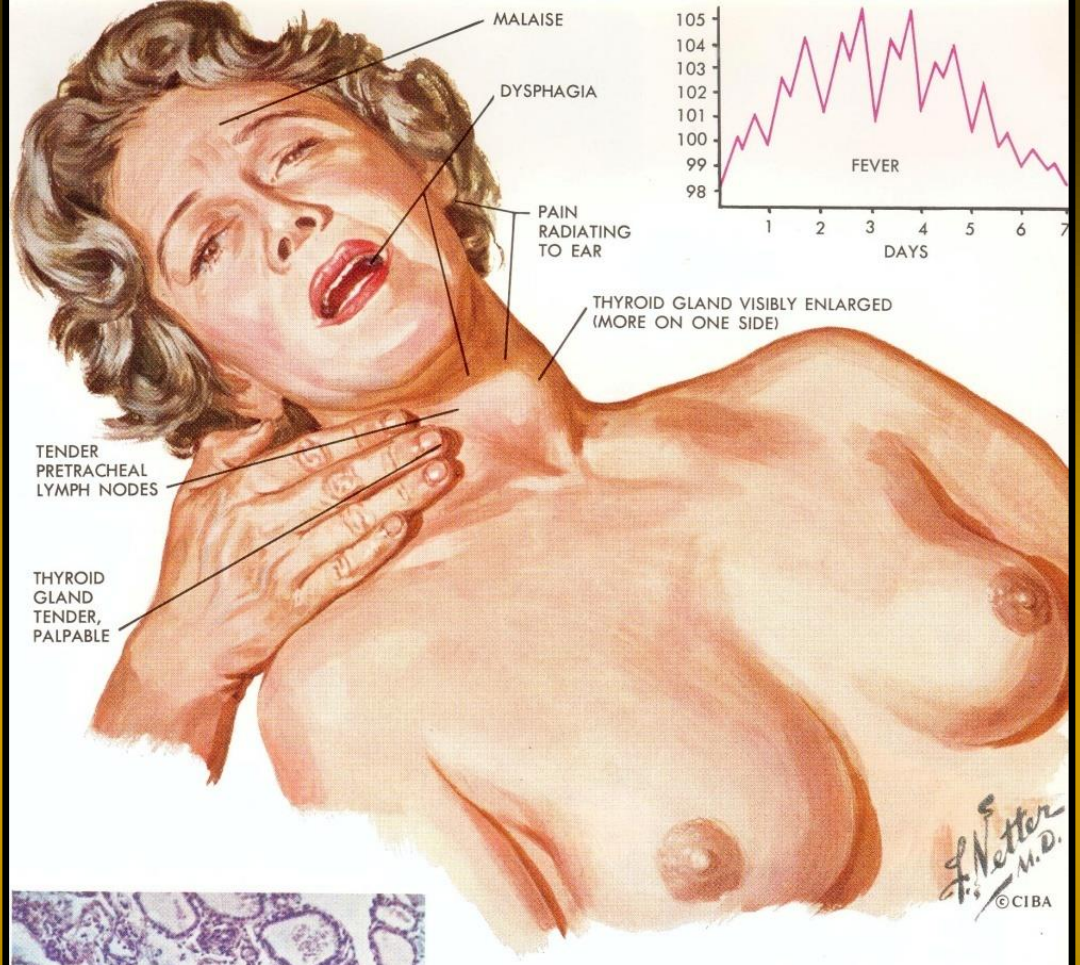
In each of the two thyroid lobes, one blurred hemorrhagic septic focus is identifiable.

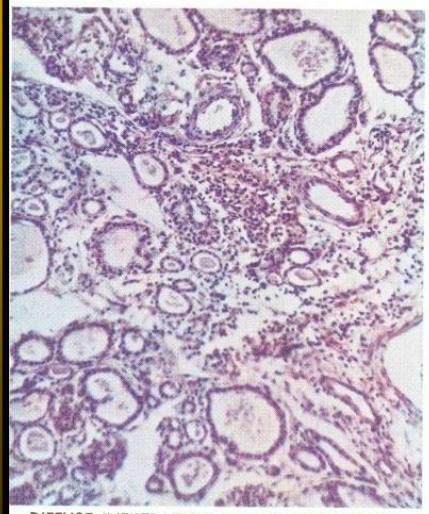


THYROIDITIS

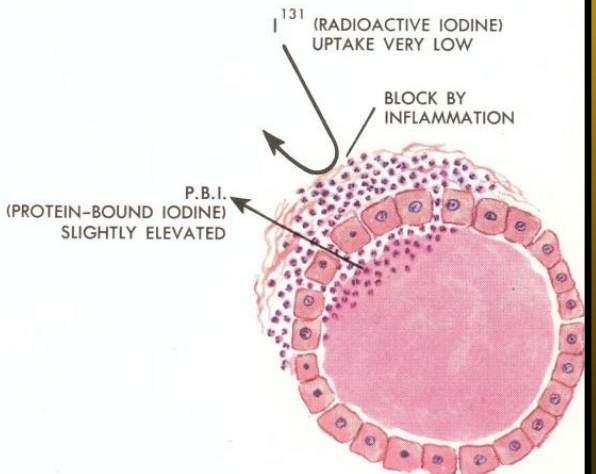
ACUTE THYROIDITIS

PATHOGENS – MAINLY BACTERIA, LESS FREQUENT VIRUSES

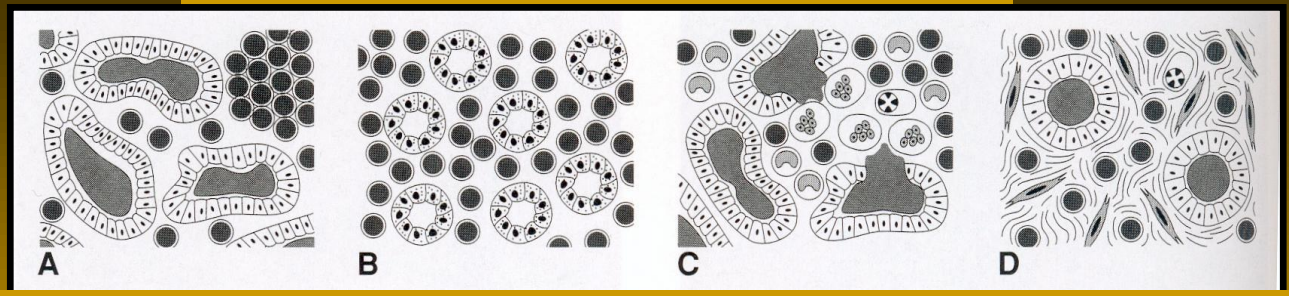




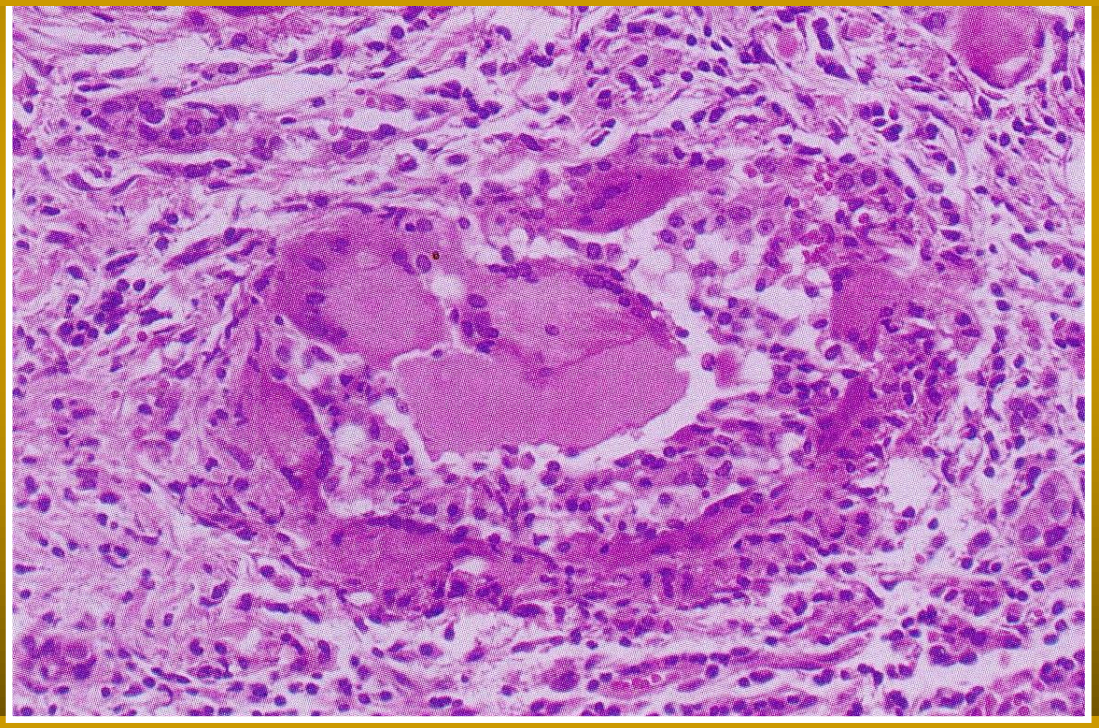
DIFFUSE INFILTRATION OF THYROID STROMA



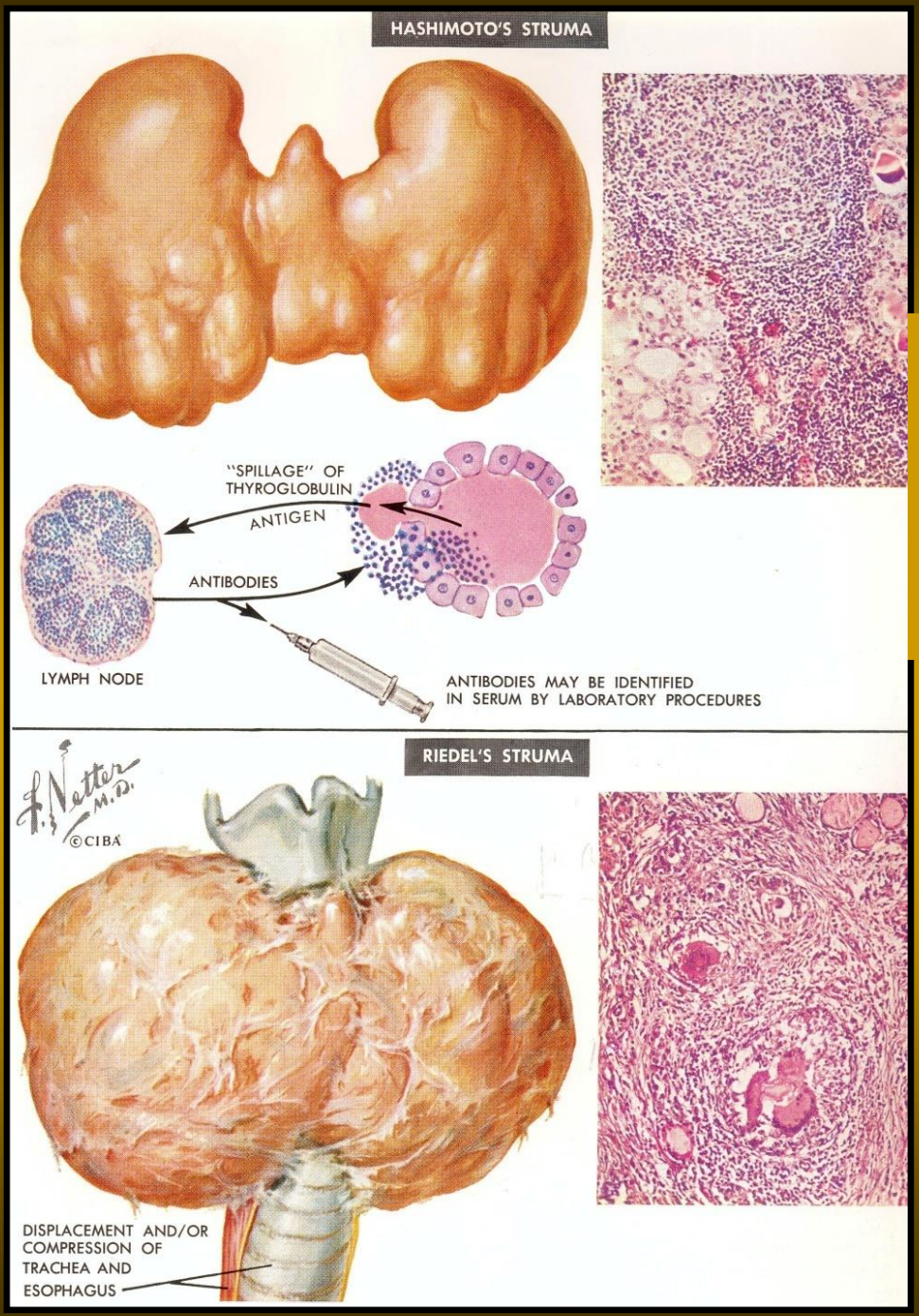
CHRONIC THYROIDITIS



A. GRAVES (BASEDOW) GOITRE, B. HASHIMOTO THYROIDITIS, C. THYROIDITIS de QUERVAIN, D. LIGNEOUS THYROIDITIS (RIEDEL GOITRE)



SUBACUTE GRANULOMATOUS THYROIDITIS (DE QUERVAIN) ETIOLOGY-PROBABLY VIRAL. FEVER AND THYROID GLAND PAINS. HISTOLOGICALLY – GIANT CELL GRANULOMA

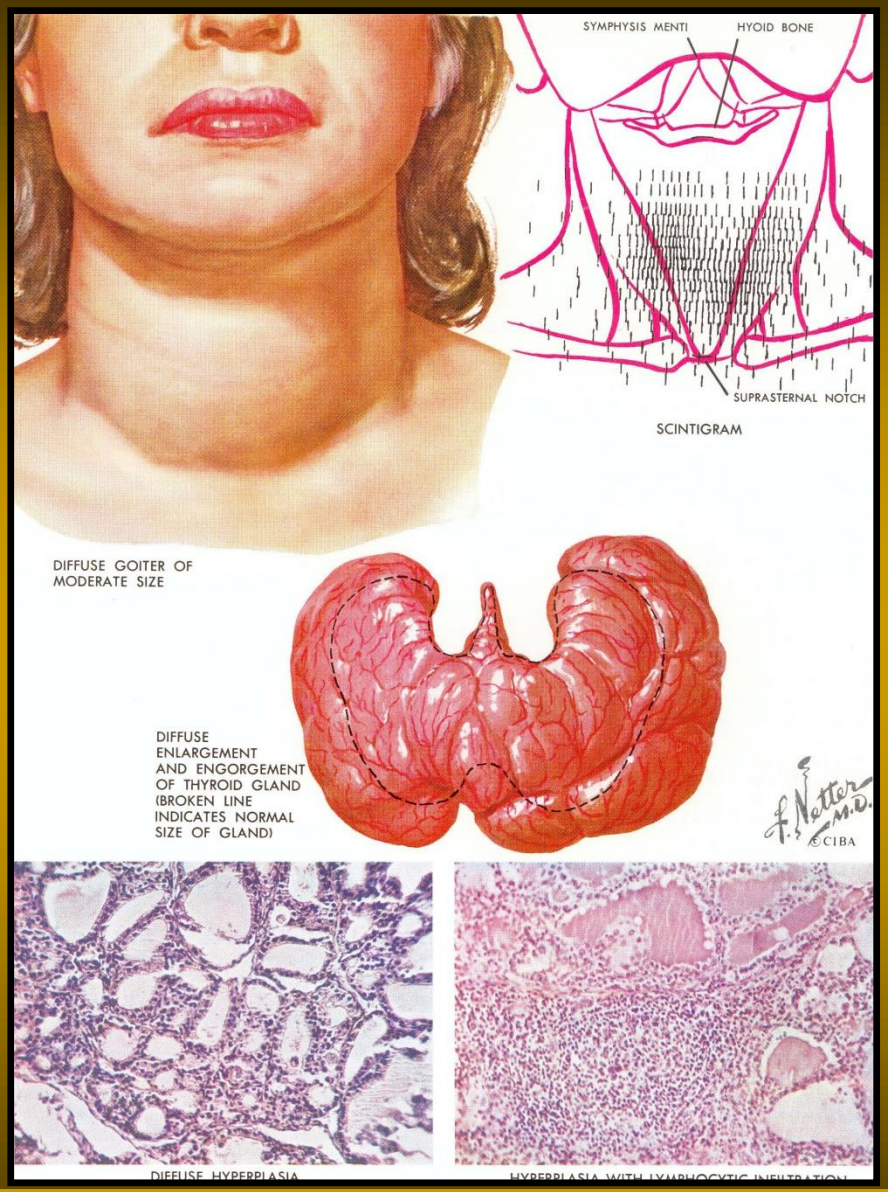


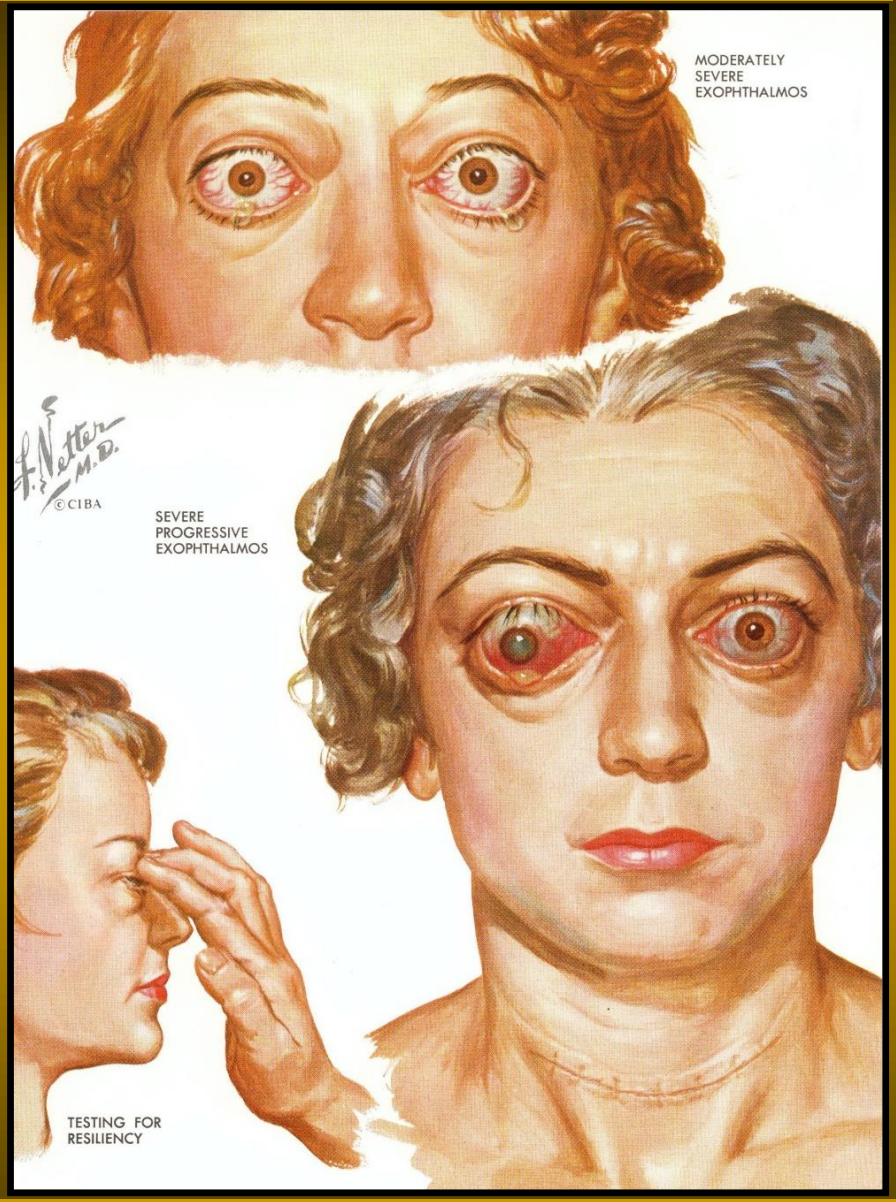
CHRONIC THYROIDITIS

THYROIDITIS HASHIMOTO – *STRUMA LYMPHOMATOSA*. AUTOAGRESSION AGAINST THYROID GLAND CELLS AND SUBSEQUENT FIBROSIS. PREDOMINANCE OF WOMEN 5:1

STRUMA RIEDEL – *THYROIDITIS LIGNOSA* UNKNOWN ETIOLOGY -> FIBROSIS AND HYPOTHYREOSIS; ADHESIONS WITH SURROUNDING TISSUES

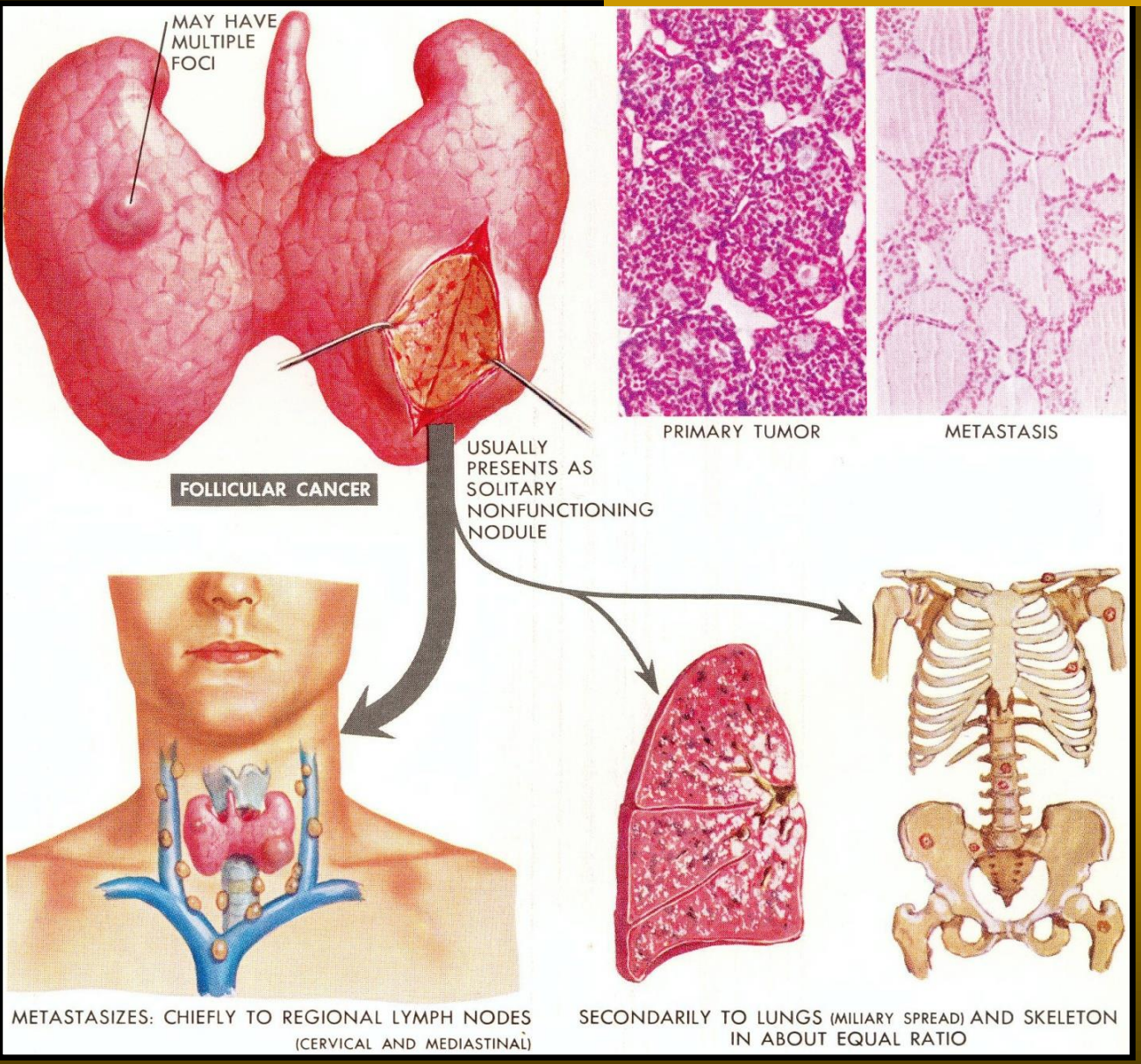
GOITRE WITH HYPERACTIVITY – GRAVES (BASEDOW) GOITRE

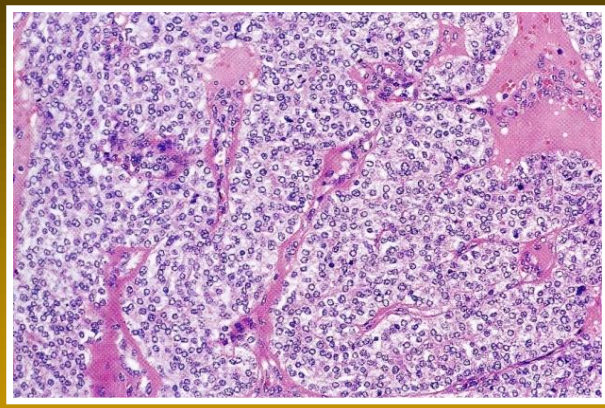




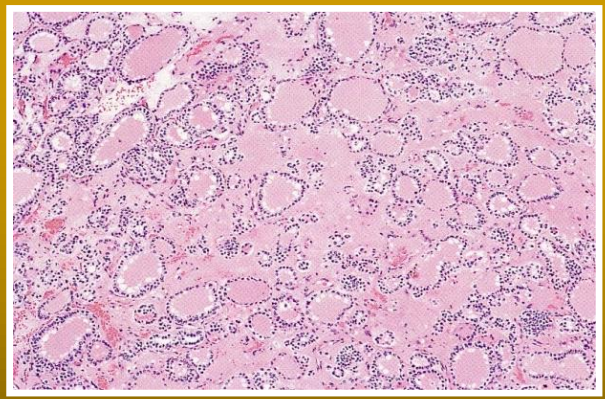
GRAVES (BASEDOW) GOITRE – A STRONG HYPERTHYROIDISM, A DIFFUSE, HYPERTROPHIC GOITRE, ENDOCRINE OPHTHALMOPATHY AND DERMATOPATHY

THYROID GLAND TUMORS





FOLLICULAR CARCINOMA



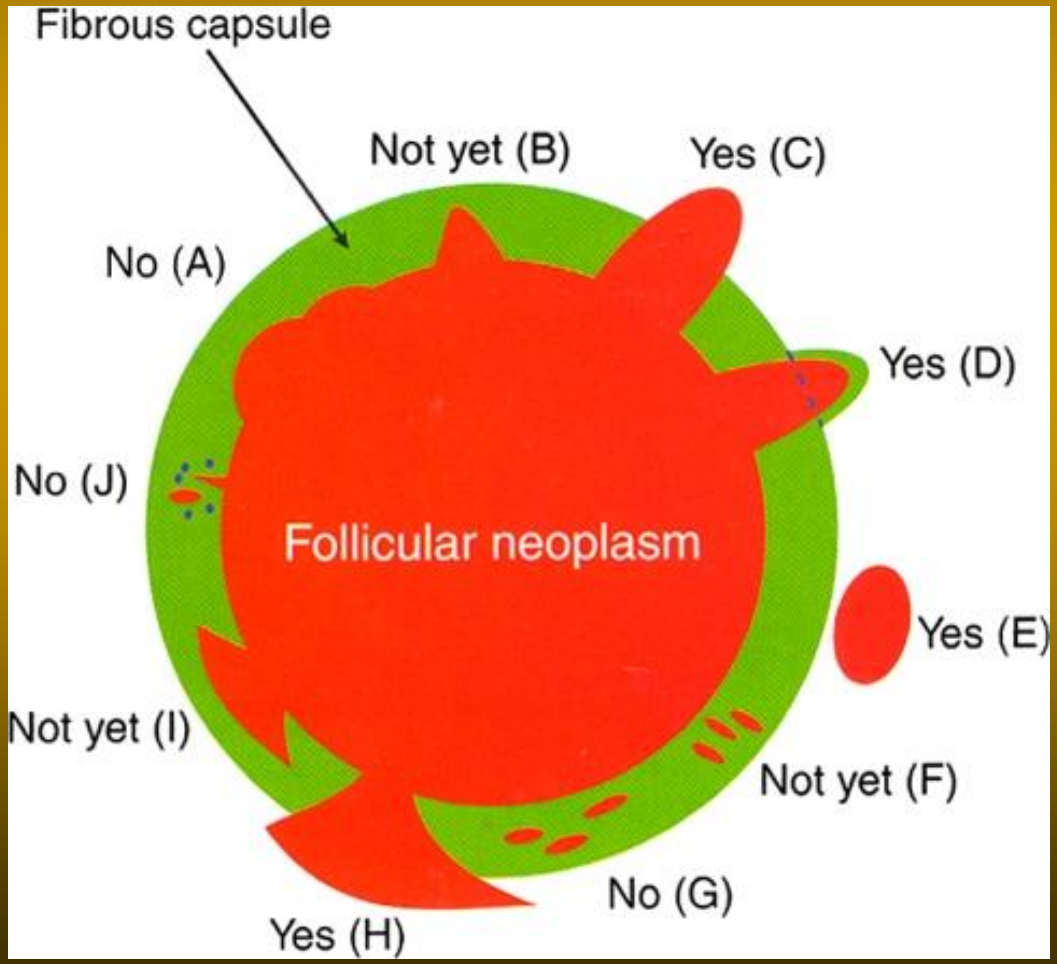
BONE METASTASIS

CARCINOMA FOLLICULARE

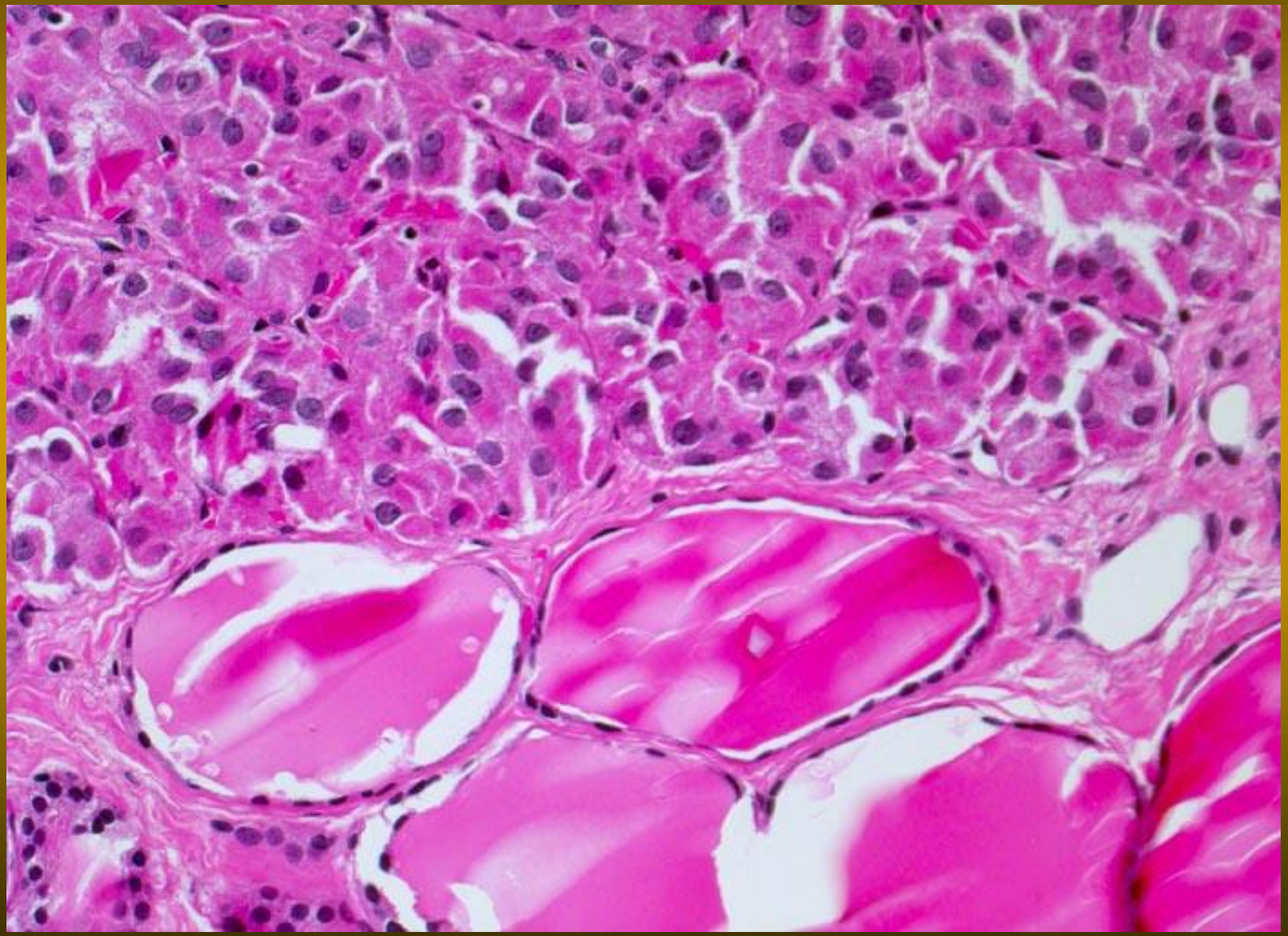
Follicular carcinoma

- **Thyroid carcinoma** with follicular differentiation but no papillary nuclear features (Hürthle cell (oncocytic) carcinoma is discussed separately)
- Comprises 6 - 10% of thyroid carcinomas
- Insufficient dietary iodine is a risk factor
- Usually solitary "cold" nodule on radionuclide scan

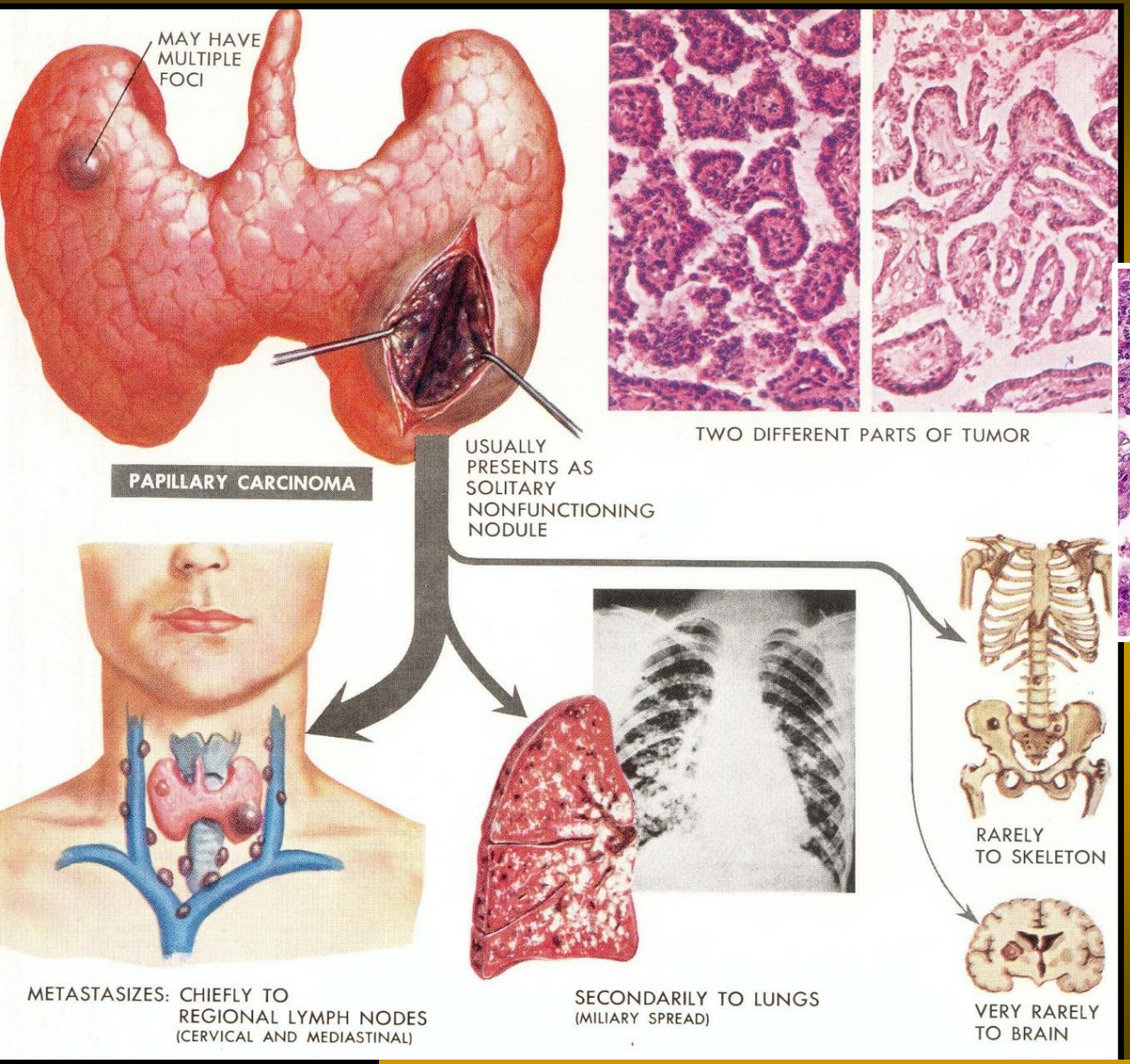
Capsular invasion (CI): Schematic drawing for the interpretation of the presence or absence of CI. The diagram depicts a follicular neoplasm (orange) surrounded by a fibrous capsule (green)

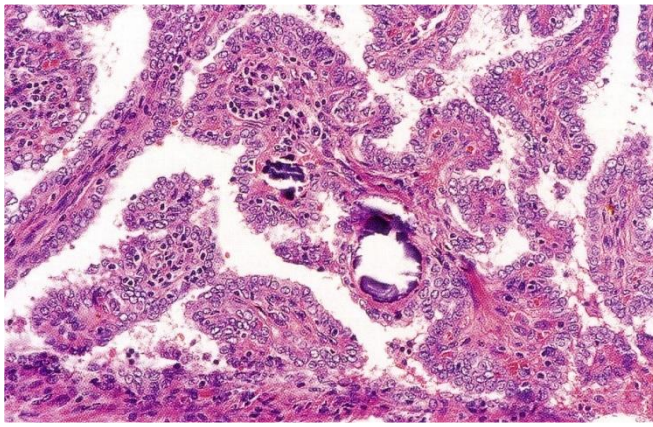


Follicular carcinoma



THYROID GLAND TUMORS





***CARCINOMA PAPILLARE* – PAPILLARY CARCINOMA**

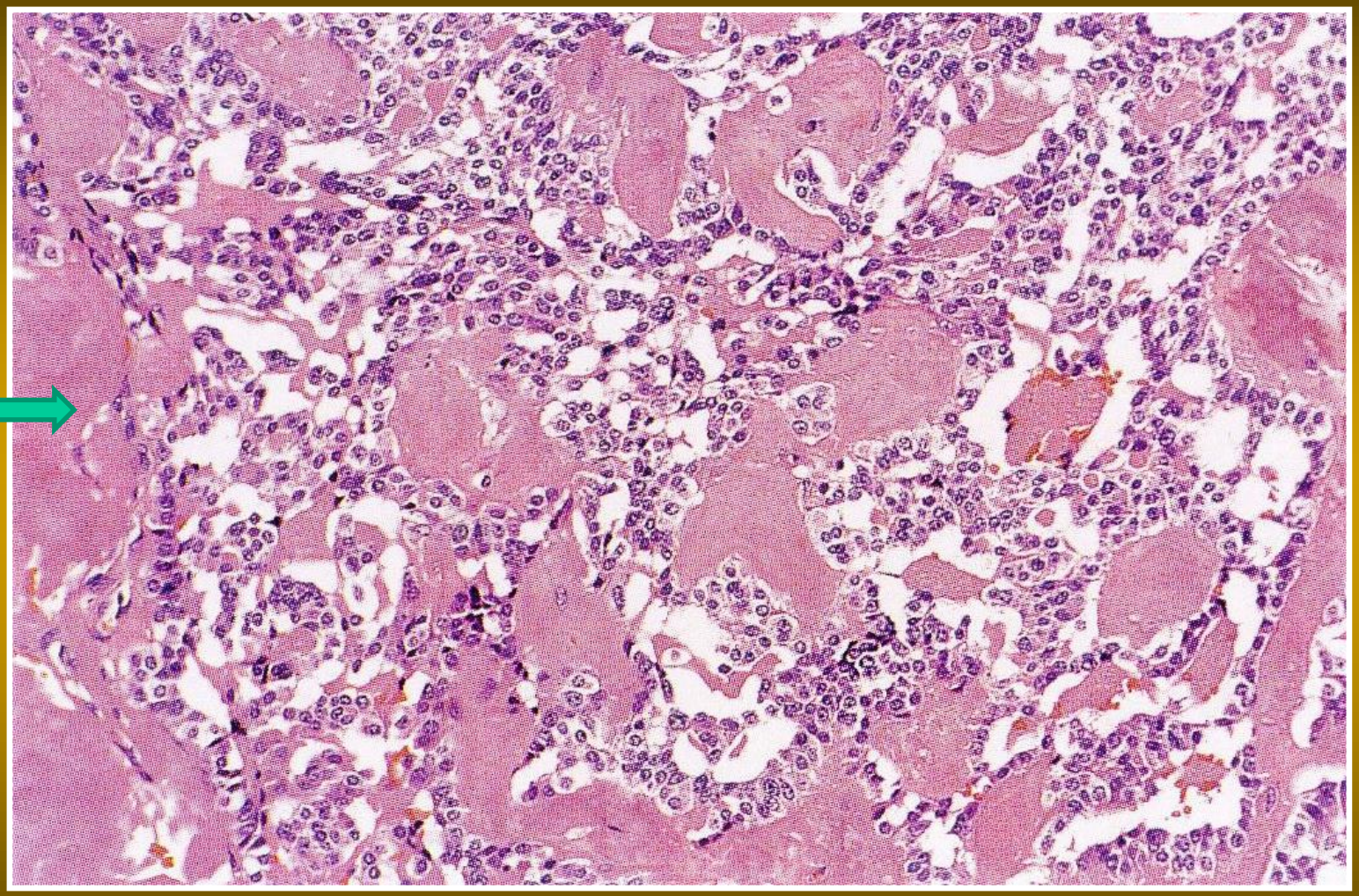
Papillary carcinoma Follicular variant

- **Papillary carcinoma** composed almost completely of follicles, with classic papillary nuclear features
- First described in 1977 (Am J Surg Pathol 1977;1:123)
- Metastases are usually nodal, not distant, with classic papillary features
- Metastatic tumor to tumor lesions may simulate a thyroid primary

Papillary carcinoma Follicular variant

- Wide fibrous bands incompletely divide tumor into lobules
- Follicular architecture but papillary cytology
- Usually infiltrative with fibrous trabeculation, psammoma bodies, strongly eosinophilic colloid with scalloping

THYROID GLAND TUMORS

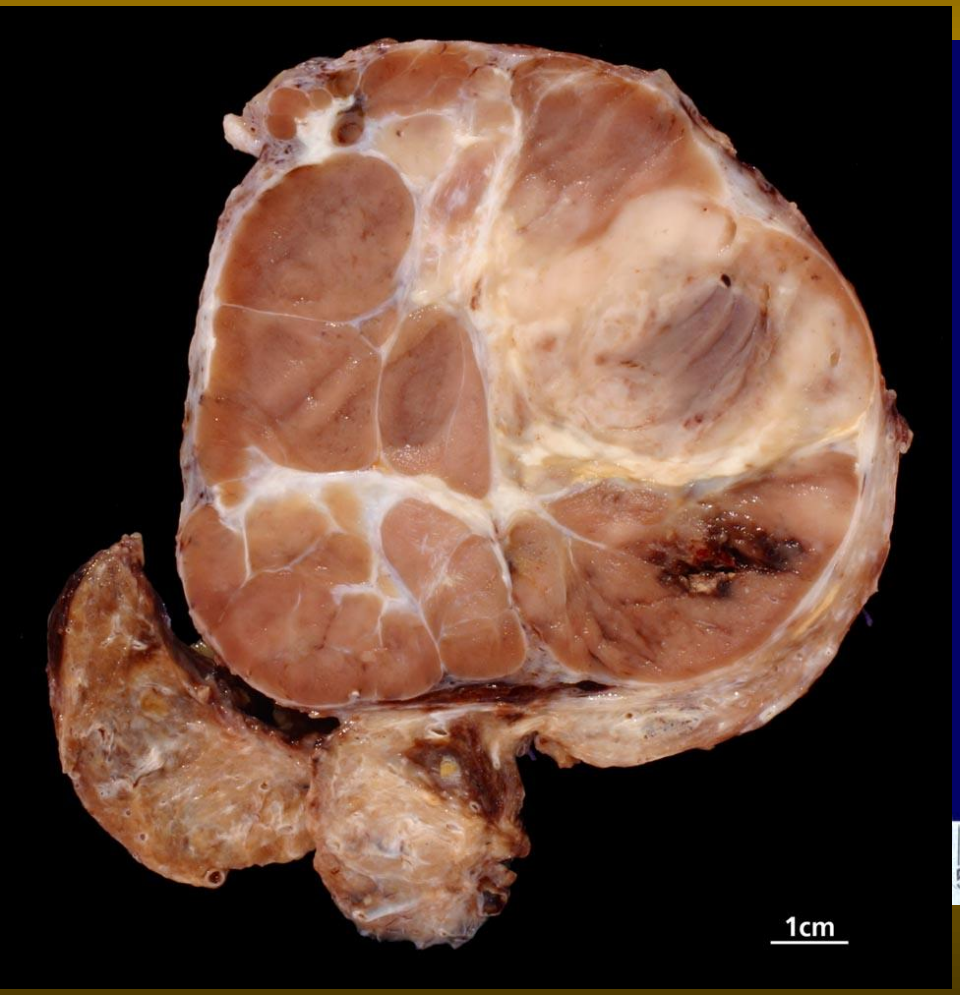


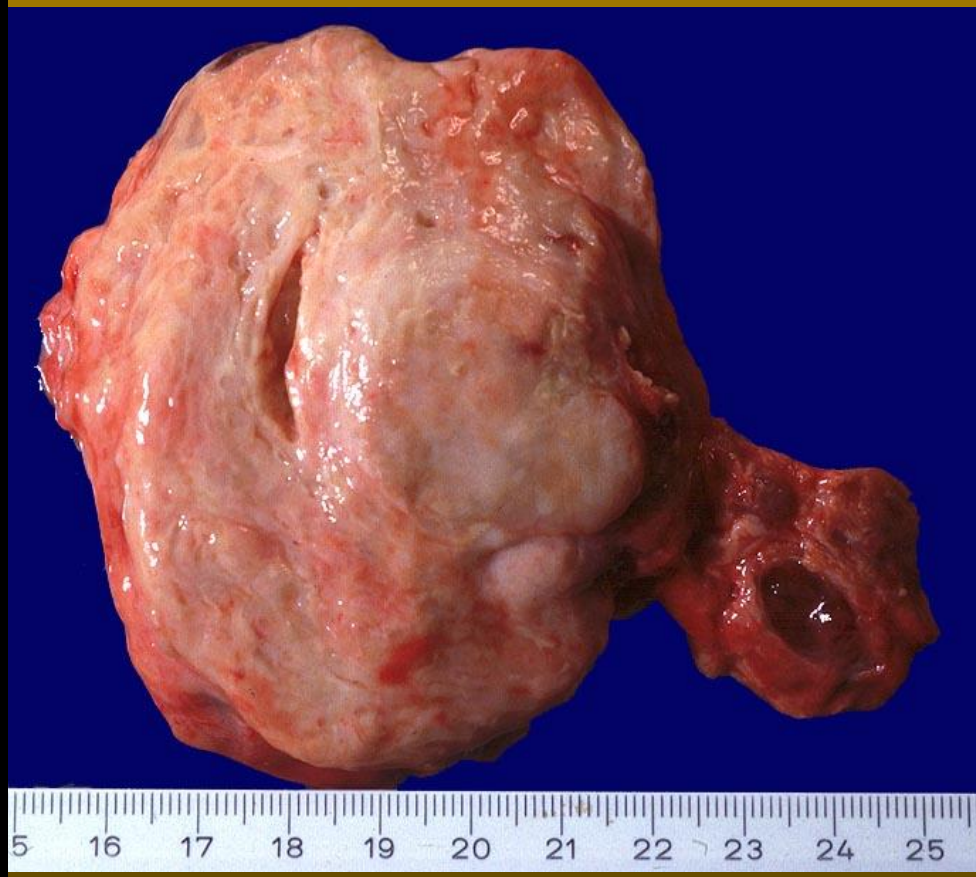
CARCINOMA MEDULLARE **(MEDULLARY CARCINOMA FROM C CELLS) - AMYLOID →**

ANAPLASTIC CARCINOMA

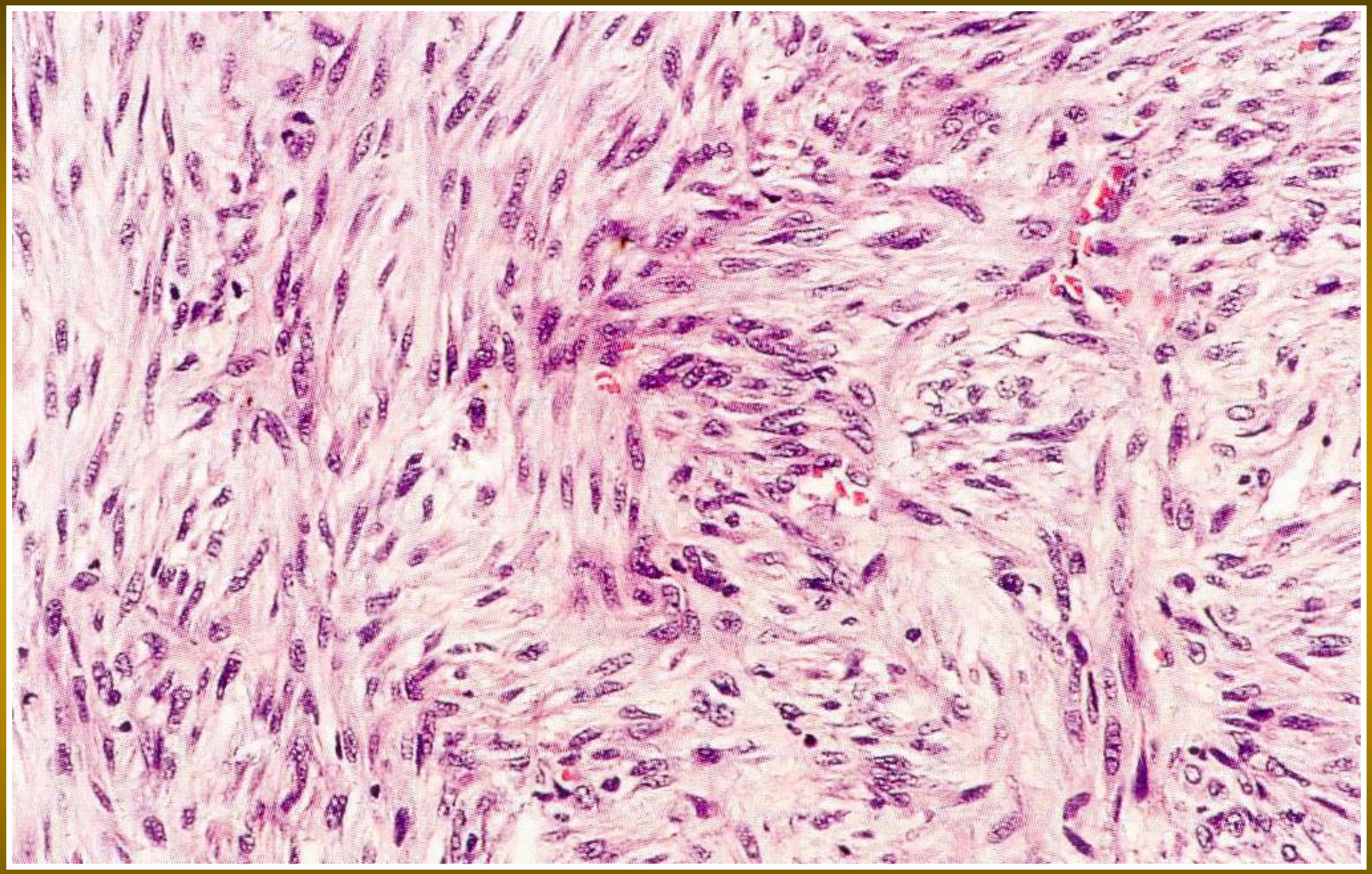
- **Undifferentiated (high grade) carcinoma of thyroid gland**
- 2 - 5% of thyroid cancers but 40% of thyroid cancer deaths
- Rapidly enlarging, bulky neck mass invades adjacent structures causing hoarseness, dysphagia, dyspnea

ANAPLASTIC CARCINOMA





THYROID GLAND TUMORS



***CARCINOMA INDIFFERENTIATUM (ANAPLASTICUM)* – ANAPLASTIC CARCINOMA - FUSOCELLULAR TYPE**

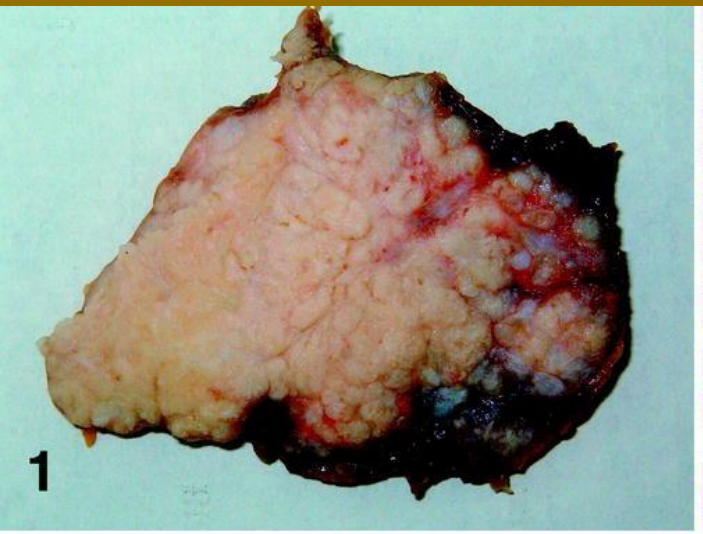
CASTLE

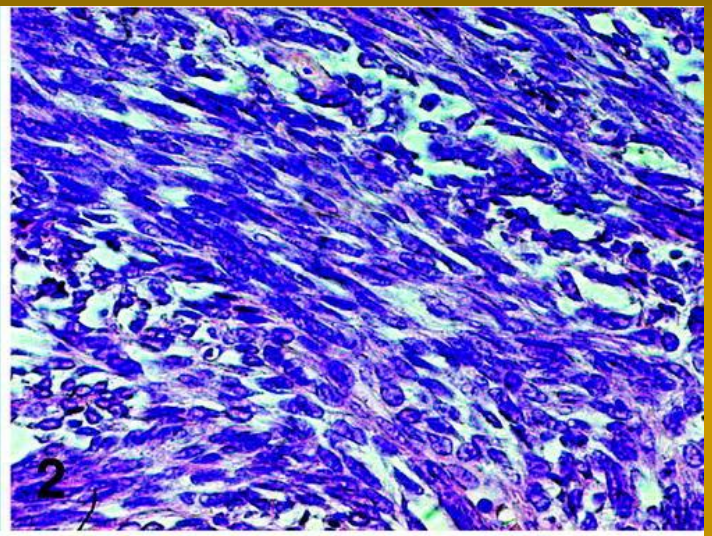
- CArcinoma Showing Thymus-Like differentiation
- Terminology first used in 1991 (Hum Pathol 1991;22:349)
- Also known as intrathyroidal (ectopic) thymic carcinoma
- Commonly involves the lower pole of the thyroid and surrounding soft tissue

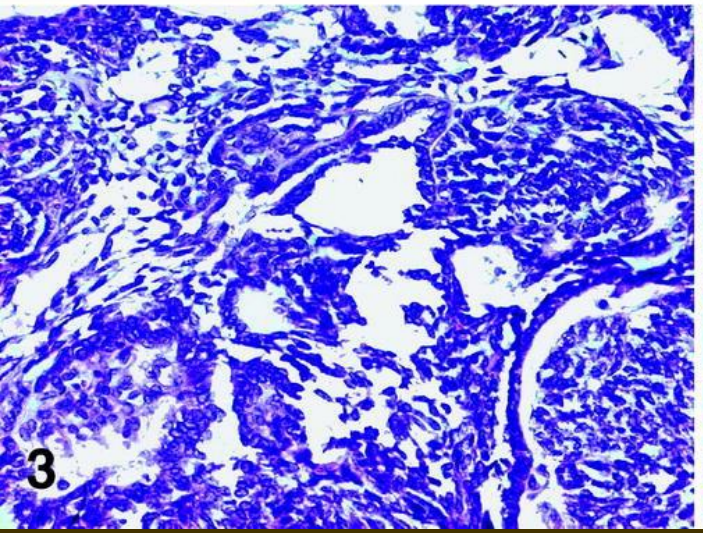
Thyroid gland
Other carcinoma
SETTLE

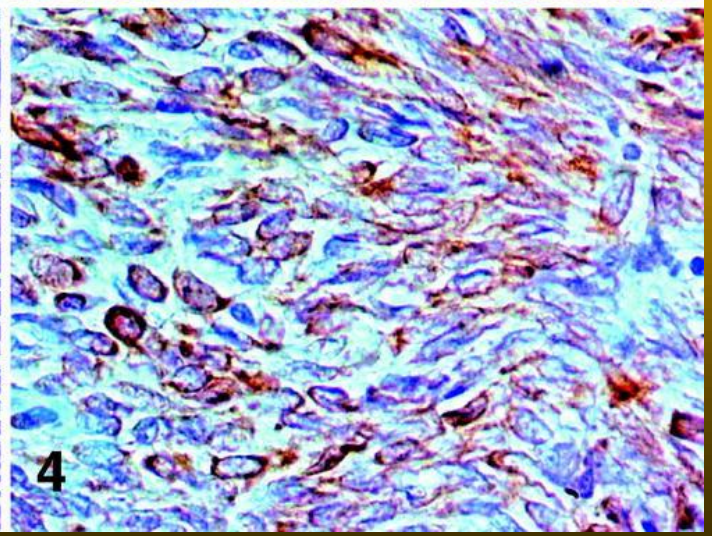
- **Spindle Epithelial Tumor with Thymus-Like Differentiation**
- Rare initially indolent tumor of neck in young patients (4 - 59 years old, median age 18 years), with delayed (after 5 years) metastases to lymph nodes or lungs, indolent even with metastasis

Thyroid gland
Other carcinoma
SETTLE







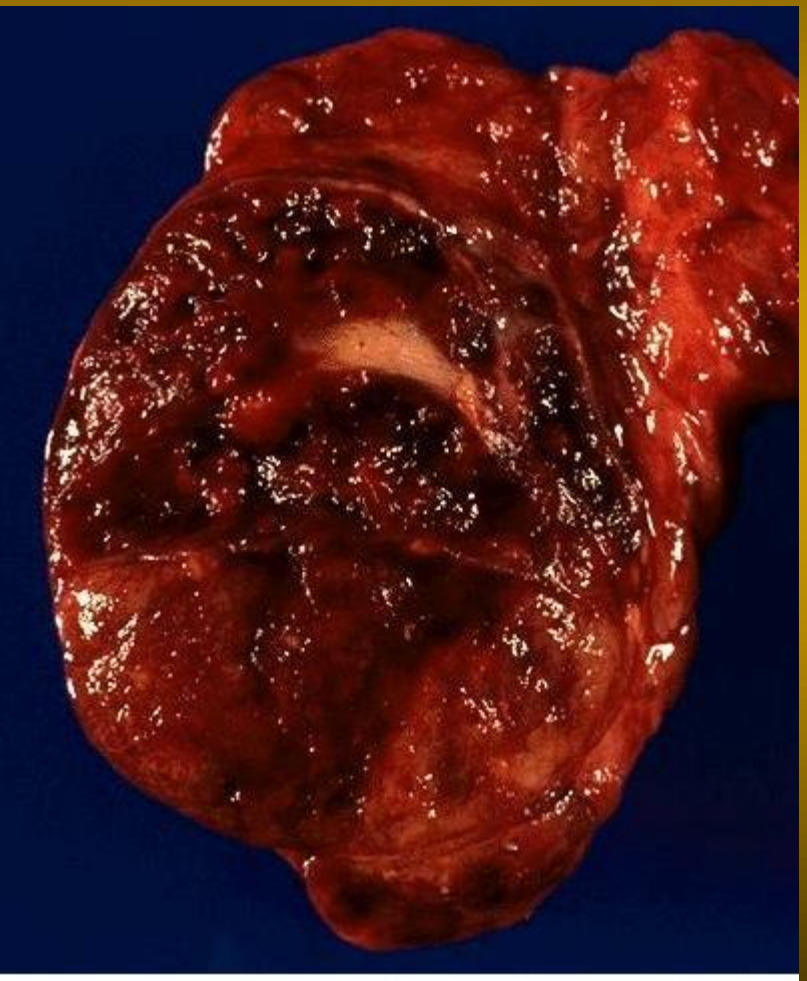


cut surface is white and lobulated by fibrous capsule

Thyroid gland
Other thyroid carcinoma
Oncocytic (Hürthle cell) tumors

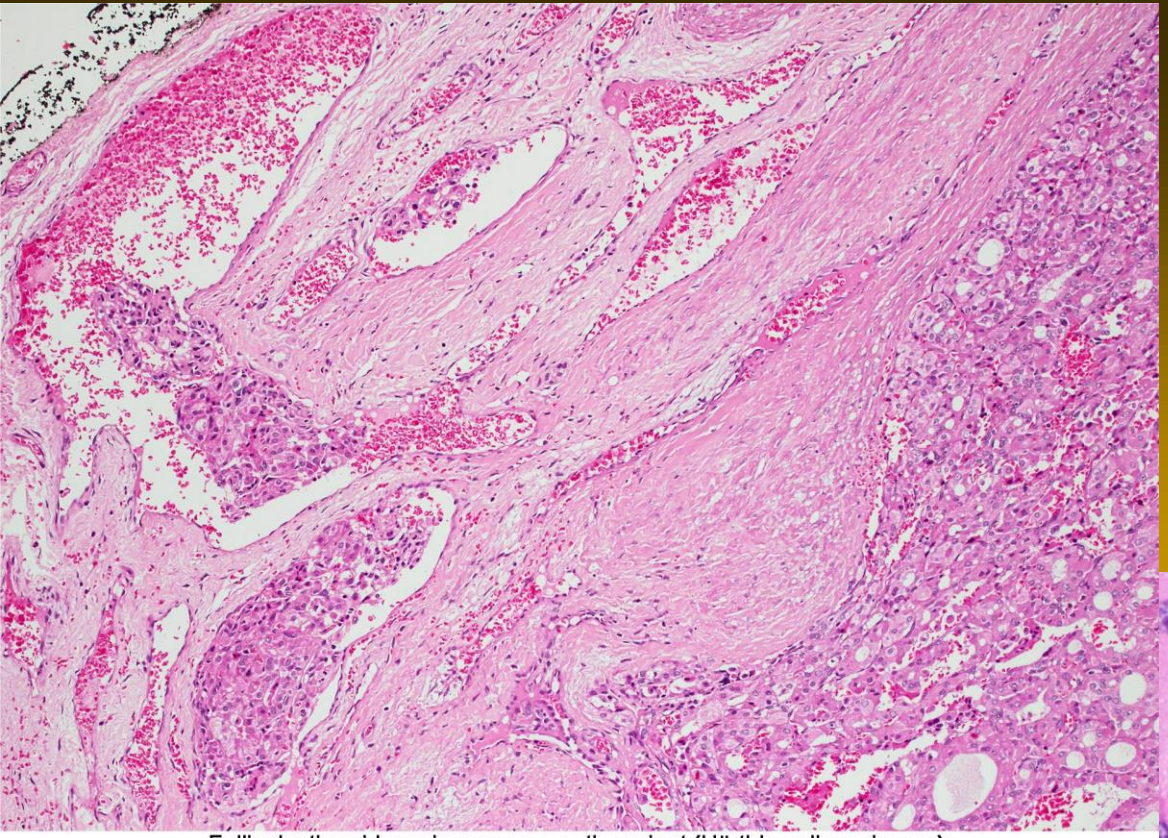
- Follicular neoplasm with more than 75% oncocytic tumor cells
- Oncocytic appearance is due to accumulation of dysfunctional mitochondria
- Malignant if capsular and / or vascular invasion
- Tumor size, nuclear atypia, multinucleation, pleomorphism, mitoses or histologic pattern of the lesion are not determinants of malignancy

Thyroid gland
Other thyroid carcinoma
Oncocytic (Hürthle cell) tumors

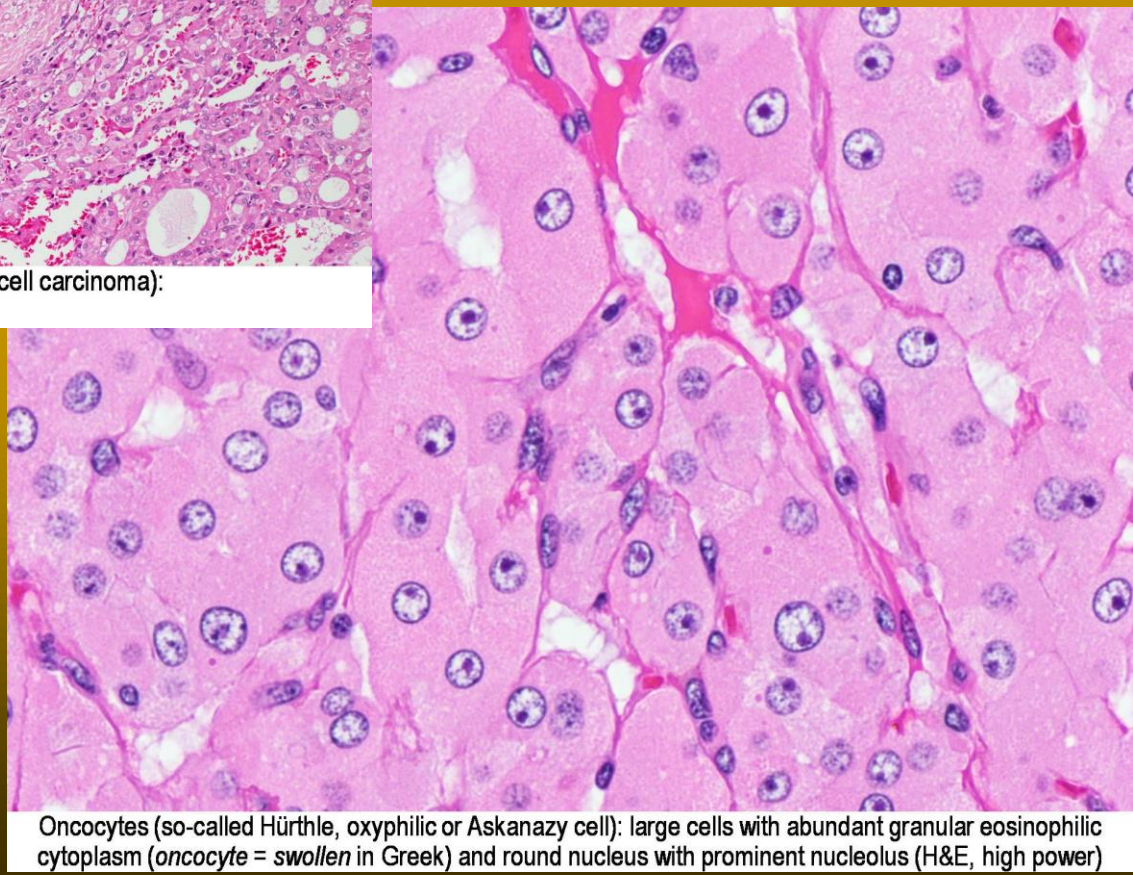


Carcinoma has focal capsular invasion, brown cut surface, hemorrhage, necrosis

At least 75% of tumor cells are oncocytes with large size, distinct cell borders, deeply eosinophilic and granular cytoplasm, large nucleus with prominent nucleolus, complete loss of cell polarity
Follicular, trabecular, solid or papillary growth patterns
Occasional nuclear grooves or nuclear pseudoinclusions

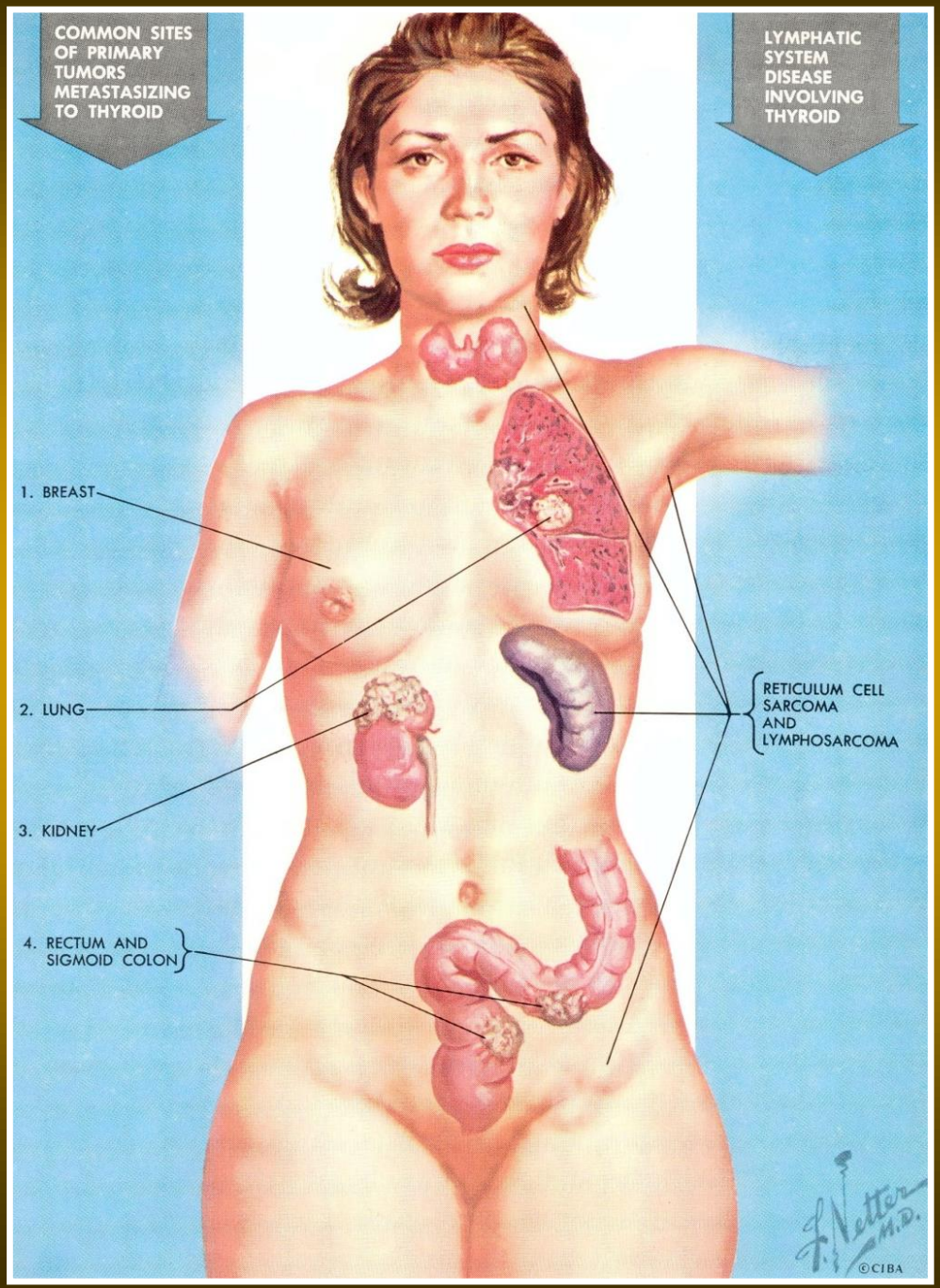


Follicular thyroid carcinoma, oncocytic variant (Hürthle cell carcinoma): vascular invasion (H&E, high power)



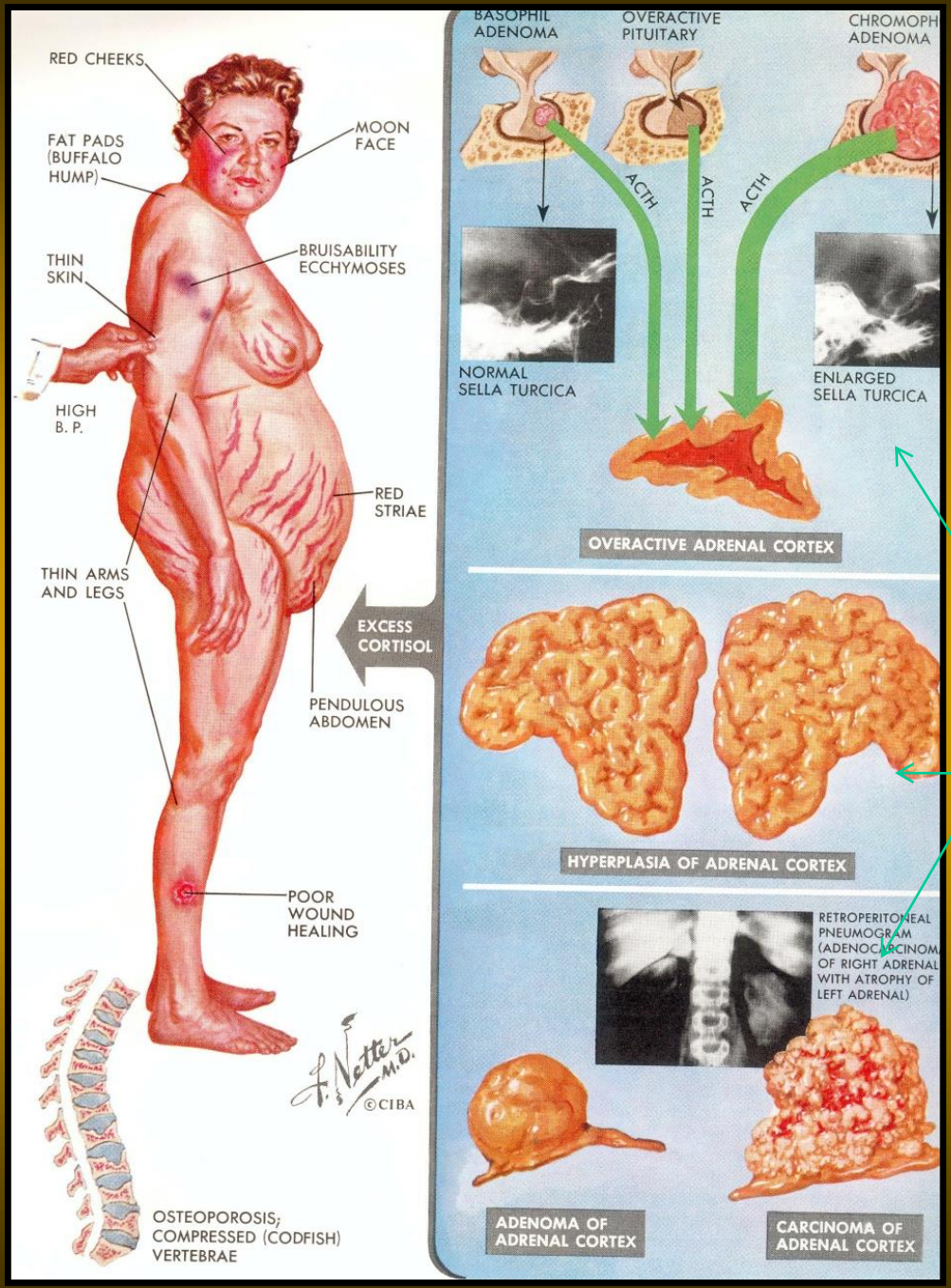
Oncocytes (so-called Hürthle, oxyphilic or Askanazy cell): large cells with abundant granular eosinophilic cytoplasm (*oncocyte* = *swollen* in Greek) and round nucleus with prominent nucleolus (H&E, high power)

THYROID GLAND TUMORS



METASTASES TO THYROID GLAND

CUSHING SYNDROM



CORTISOL OVERPRODUCTION

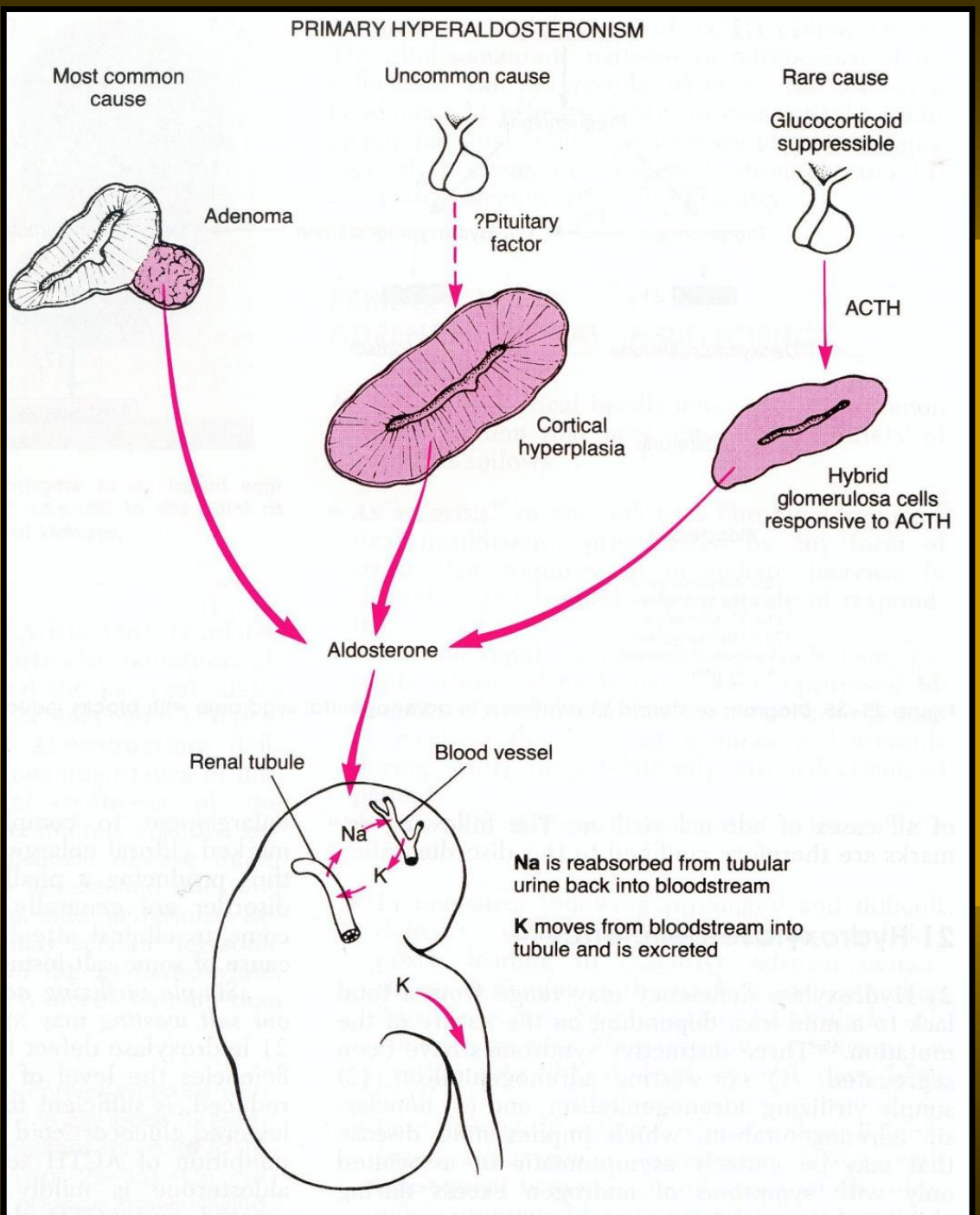
PATHOGENESIS:

OVERPRODUCTION OF ACTH IN HYPOPHYSIS,

ECTOPIC PRODUCTION OF ACTH,

HYPERSECRETION IN ADRENALS

SYMPTOMS: OBESITY – MOON FACE, HIGH BLOOD PRESSURE, HIRSUTISM, DIABETES, RED STRIAE



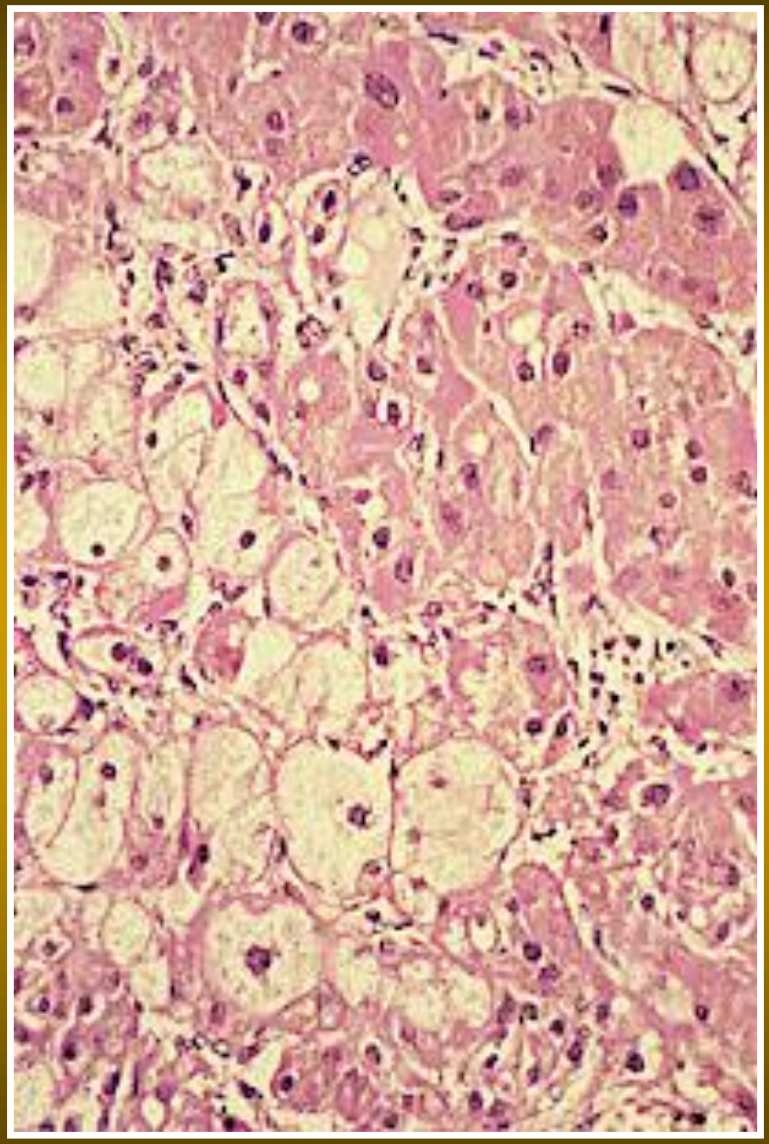
CONN SYNDROME

PRIMARY HYPERALDOSTERONISM PATHOGENESIS: OVERPRODUCTION OF ALDOSTERONE

SYMPTOMS: LOW PLASMA ACTIVITY OF RENIN, HYPOKALEMIA, NATRIUM RETENTION, HIGH BLOOD PRESSURE

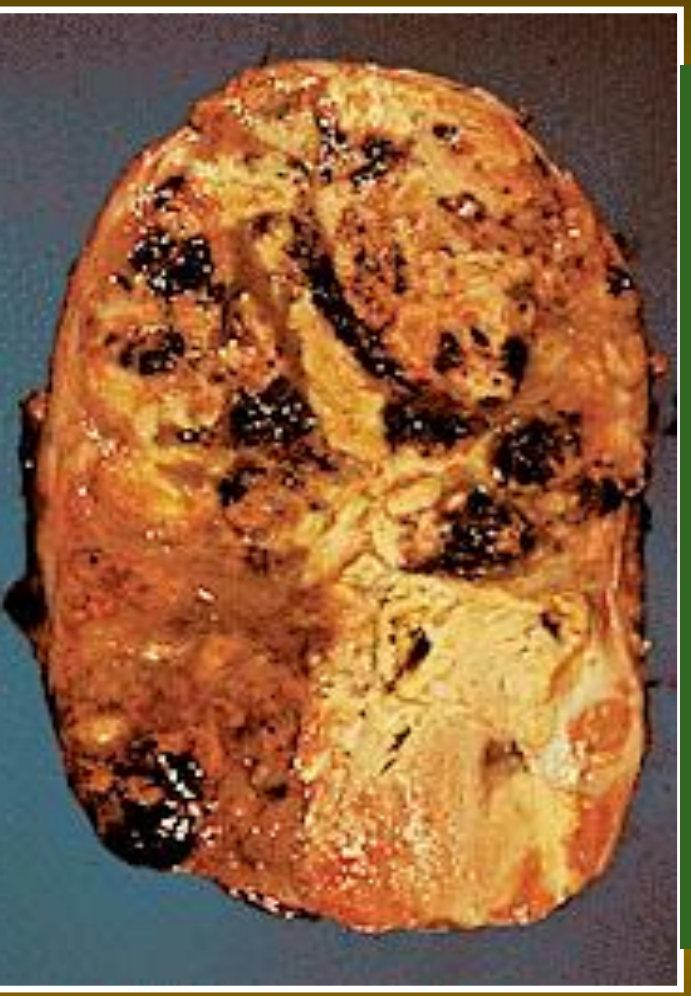
CAUSES: CORTICAL ADENOMA OR HYPERPLASIA

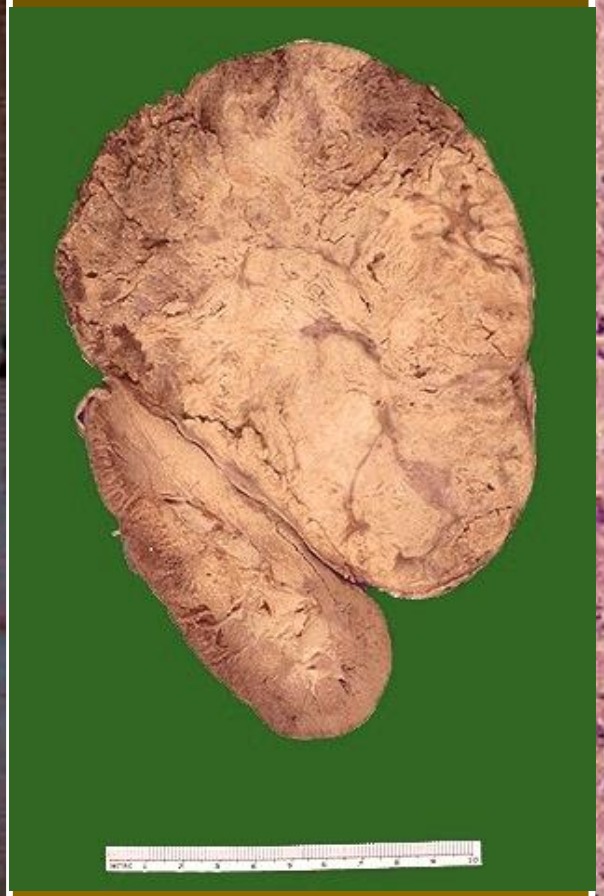
ADRENAL GLAND TUMORS

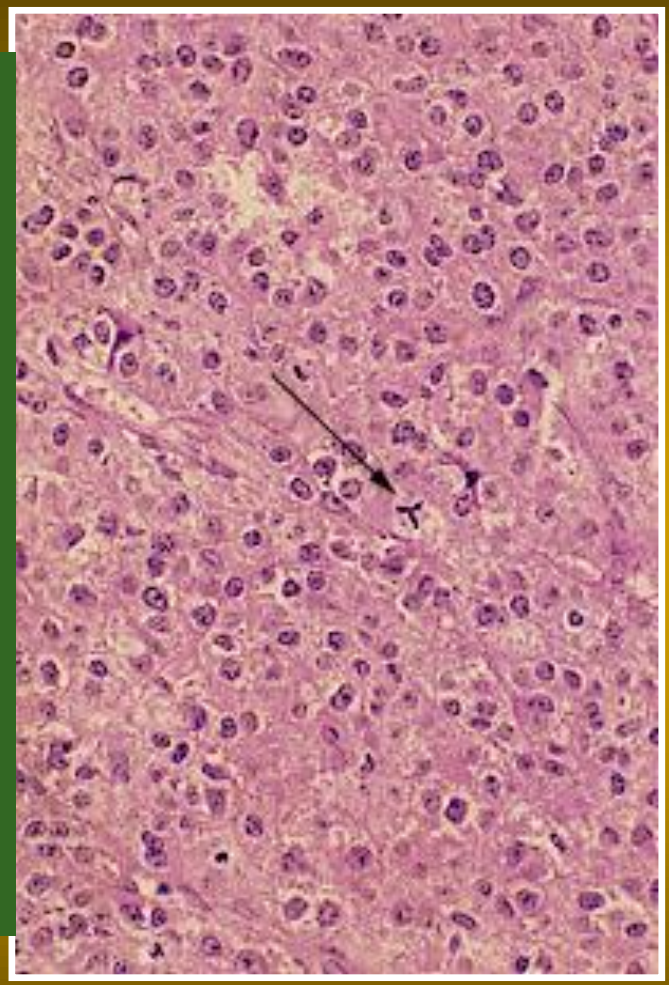


ADRENAL GLAND ADENOMA WITH CUSHING SYNDROME

ADRENAL GLAND TUMORS







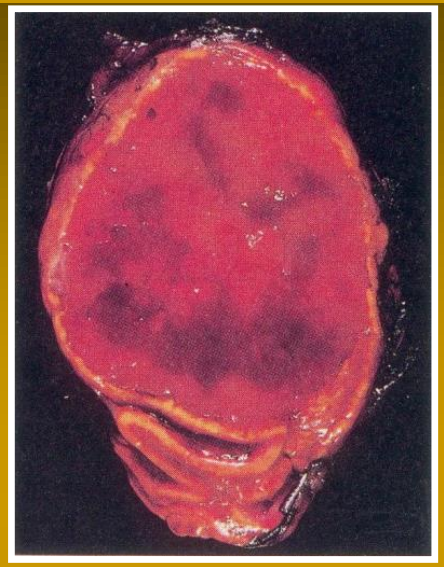
ADRENOCORTICAL CARCINOMA – MODERATE POLYMORPHISM OF CELLS

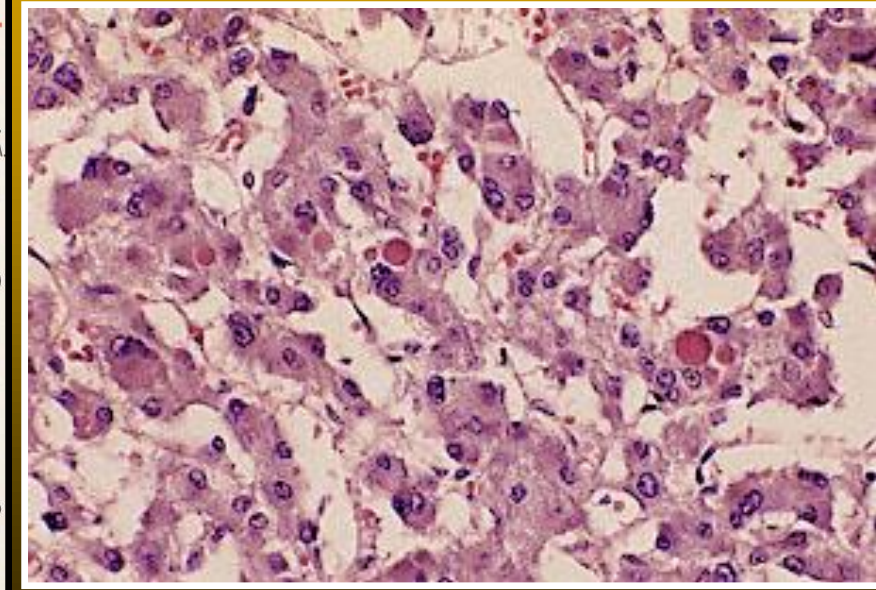
Adrenal gland tumors
Adrenocortical carcinoma

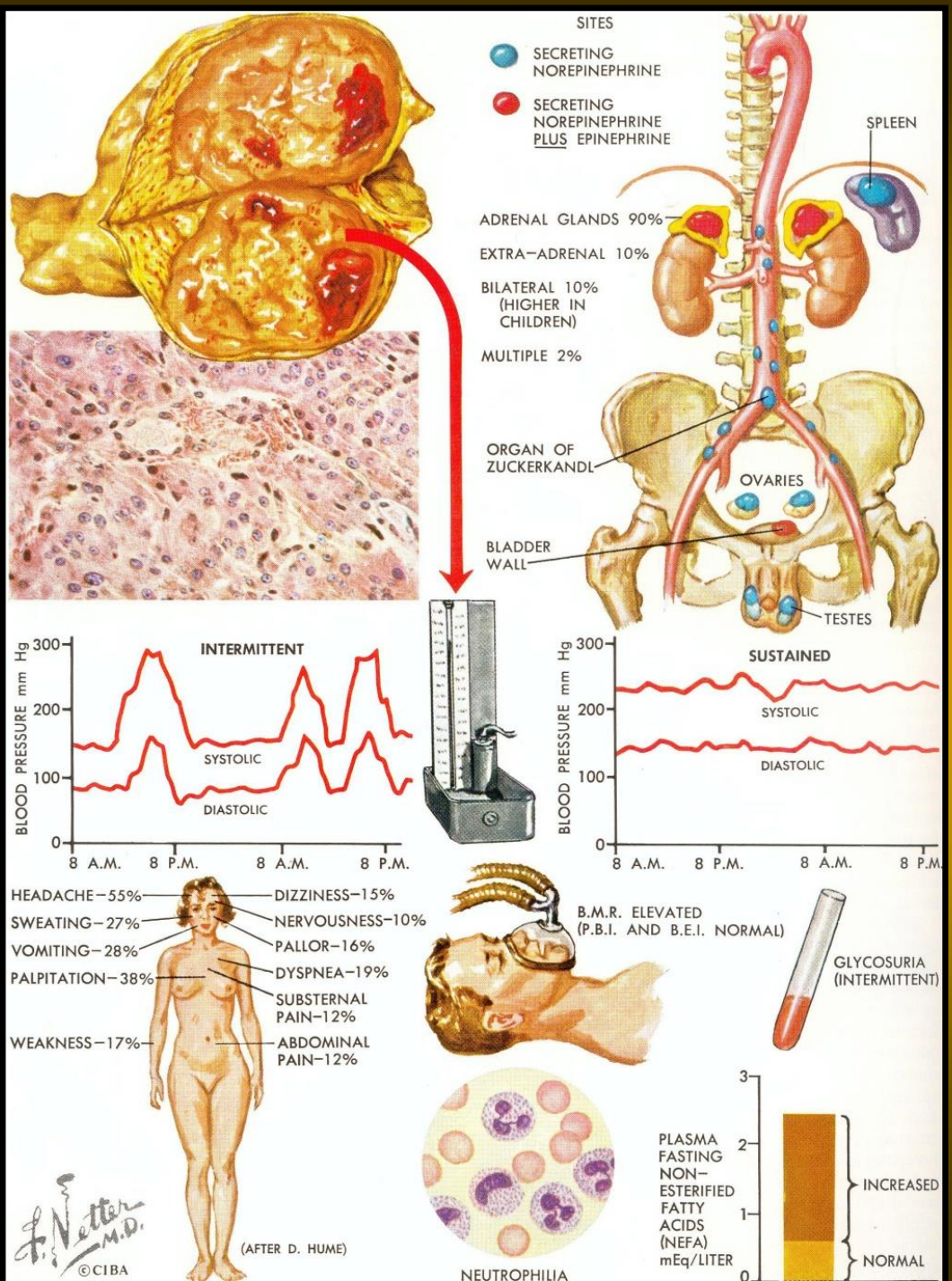
- **Rare, 0.5 to 2 cases per million annually in U.S.**
- No gender preference, bimodal age distribution with first peak in childhood, second peak in 4th - 5th decade of life
- Associated with Li Fraumeni syndrome, Beckwith-Wiedemann syndrome, congenital adrenal hyperplasia

ADRENAL GLAND TUMORS

PHEOCHROMOCYTOMA







PHEOCHROMOCYTOMA

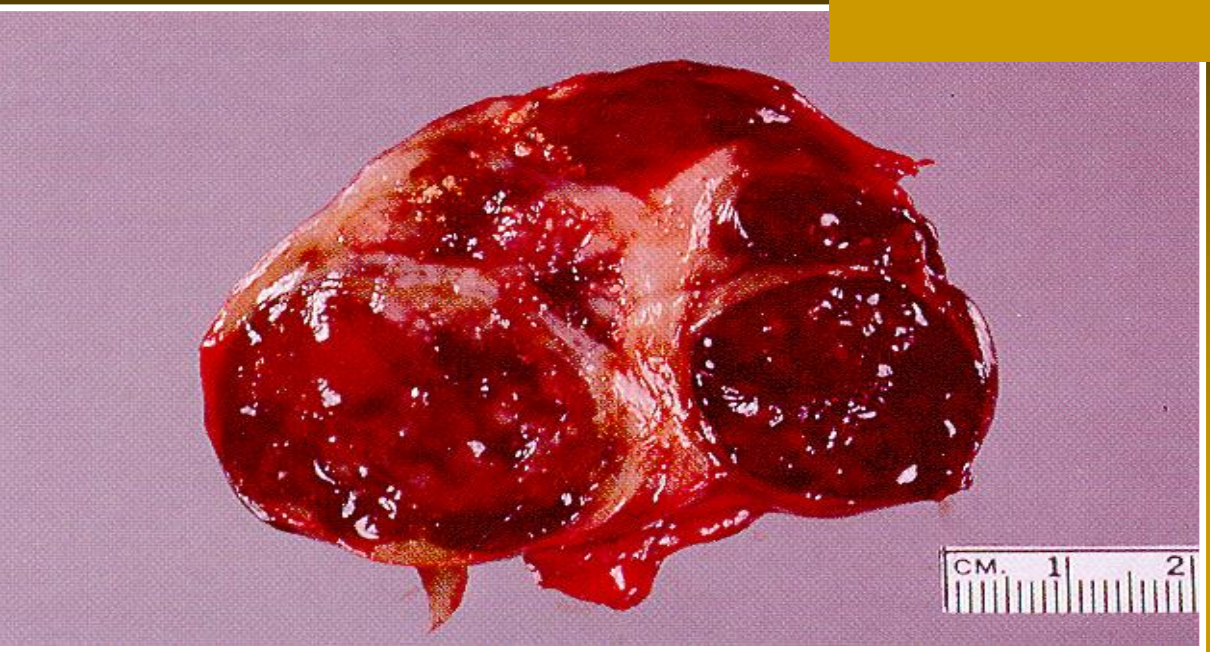
- **Causes surgically correctable hypertension (also aldosterone-secreting tumors, renal artery stenosis)**
- Represents 0.1% of patients with hypertension, but may be fatal
- Mean age 47 years in one series, range 3-81 years
- Called 10% tumor: 10% bilateral (probably higher), 10% outside adrenal medulla, 10% metastasize (probably higher), 10% in children
- Extra-adrenal tumors secrete only norepinephrine, have 20% malignancy rate
- In children, usually extra-adrenal, bilateral and associated with MEN 2a/2b

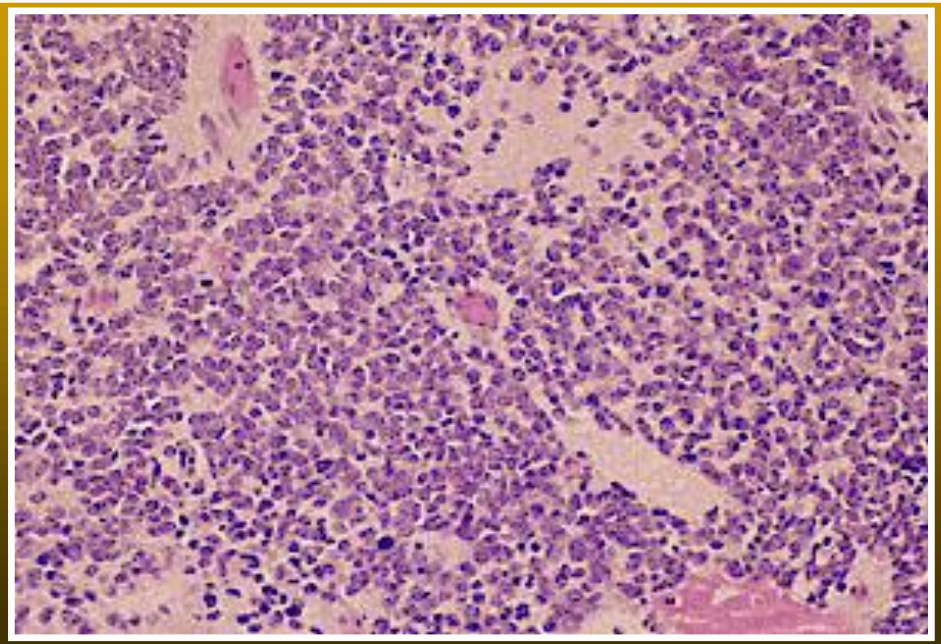
PHEOCHROMOCYTOMA

- **Also called paraganglioma of adrenal medulla** (extra-adrenal tumors are called extra-adrenal paragangliomas)
- Rare catecholamine secreting tumor (0.005% to 0.1% of unselected autopsies)
- Described by Poll in 1905 as having cut surface with dusky [pheo] color [chromo]

ADRENAL GLAND TUMORS

NEUROBLASTOMA





ADRENAL GLAND MEDULLA IS ONE OF THE MOST FREQUENT SITES OF THIS TUMOR (35%).

INFANT TUMOR;

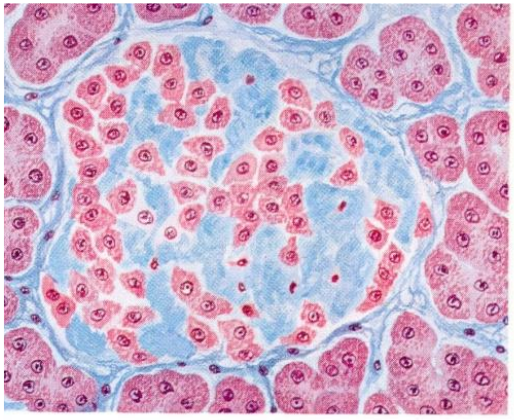
DIFFERENTIATION IS VARIOUS.

CHROMOSOMES: DELETION OF THE SHORT ARM OF CHROMOSOME 1 (OR 13 OR 14).

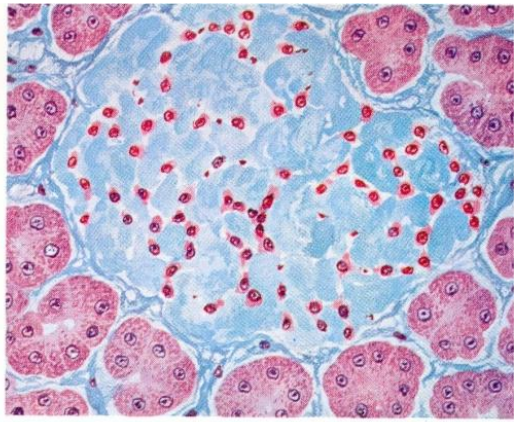
VARIOUS CLINICAL COURSE

PATHOLOGY OF ISLET CELLS

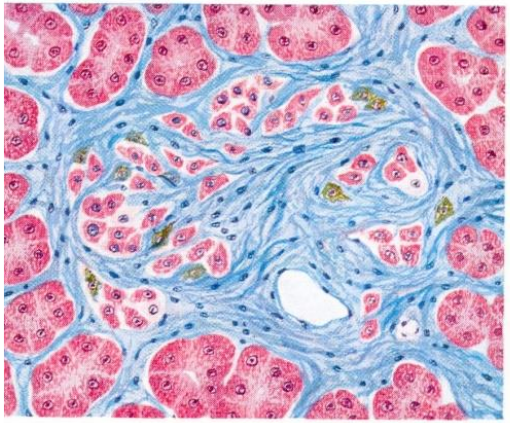
DIABETES MELLITUS



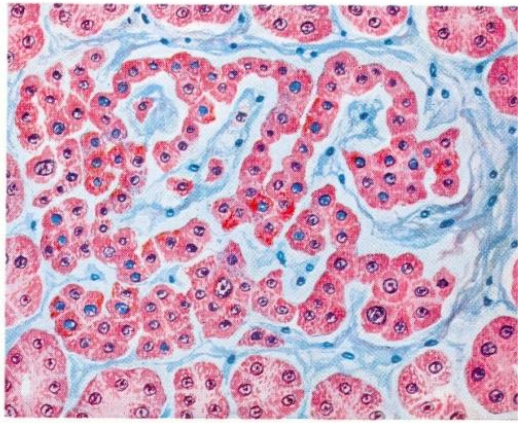
PARTIAL HYALINIZATION
(MALLORY'S ANILINE BLUE STAIN)



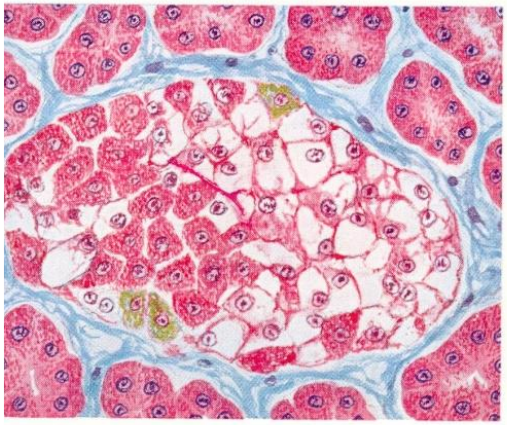
COMPLETE HYALINIZATION
(MALLORY'S ANILINE BLUE STAIN)



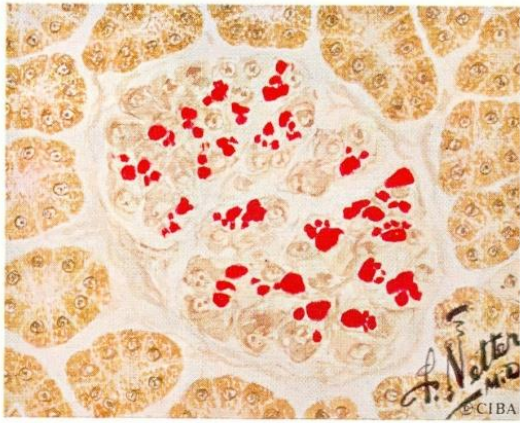
FIBROSIS
(MALLORY'S ANILINE BLUE STAIN)



CORDLIKE FORMATION
(MALLORY'S ANILINE BLUE STAIN)



HYDROPIC CHANGE (VACUOLIZATION)
GOMORI'S ALDEHYDE FUCHSIN AND PONCEAU STAIN)

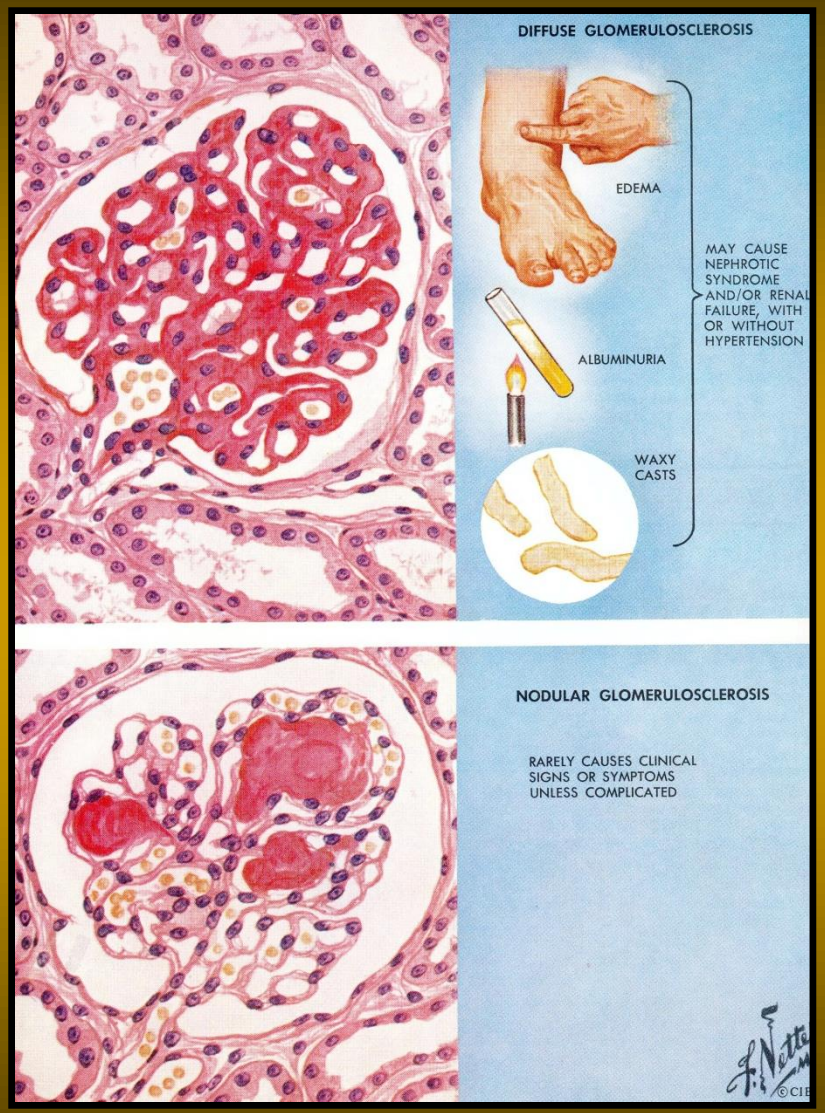


GLYCOGEN DEMONSTRATED IN VACUOLES
BY PERIODIC ACID SCHIFF REAGENT

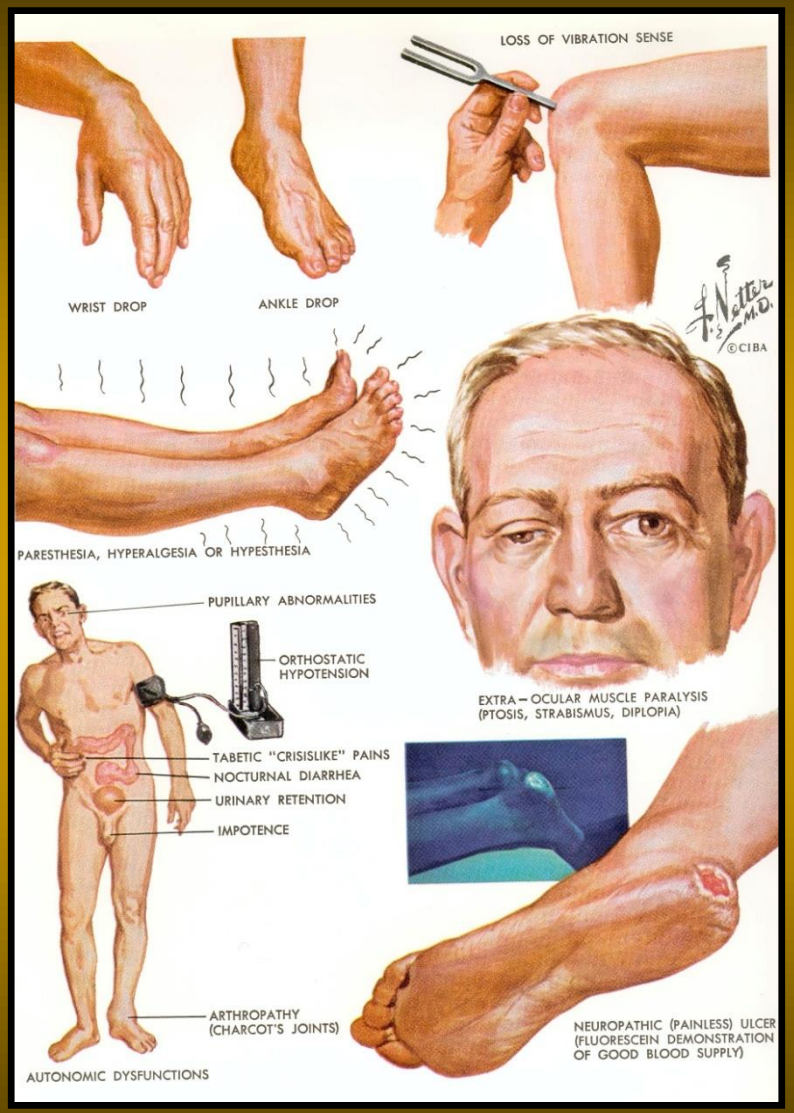
CHANGES IN MORPHOLOGY OF ISLET CELLS <u>ARE VERY RARE</u>

PATHOLOGY OF ISLET CELLS

COMPLICATIONS IN DIABETES MELLITUS

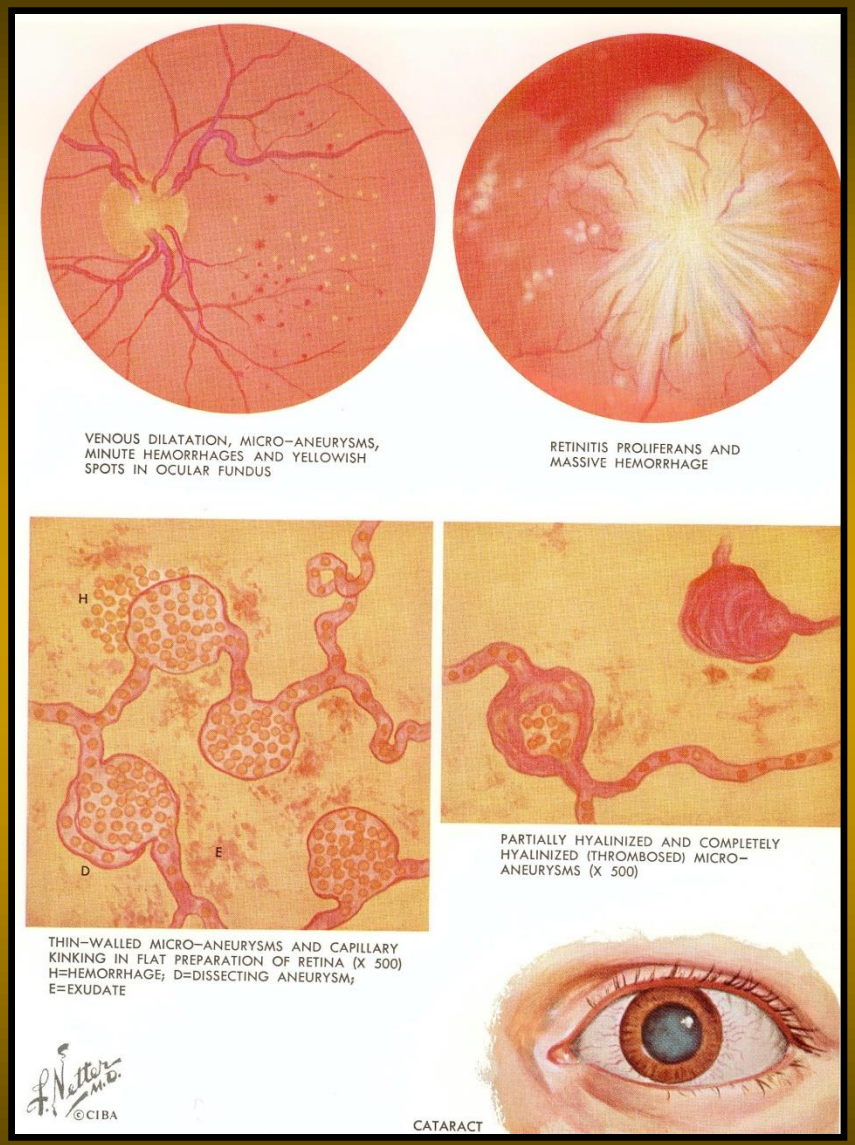


DIABETIC GLOMERULOPATHY

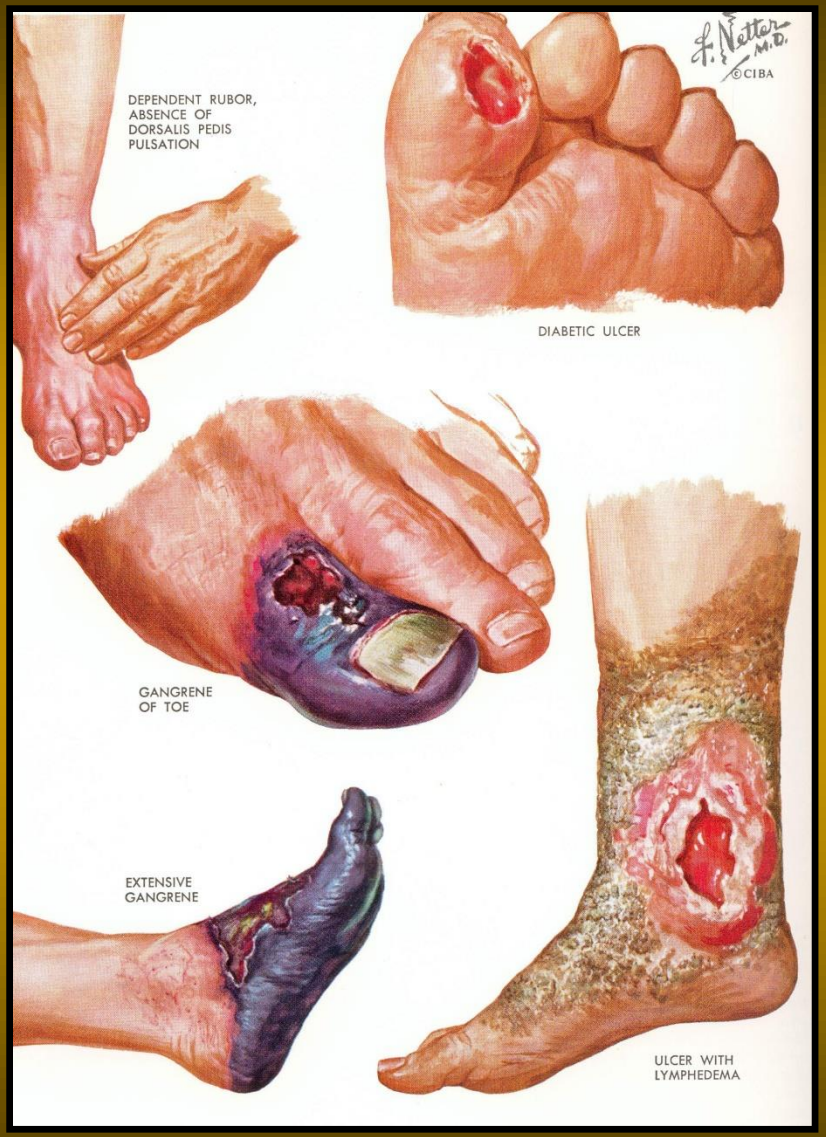


DIABETIC NEUROPATHY

PATHOLOGY OF ISLET CELLS



DIABETIC RETINOPATHY – FUNDUS OF THE EYE



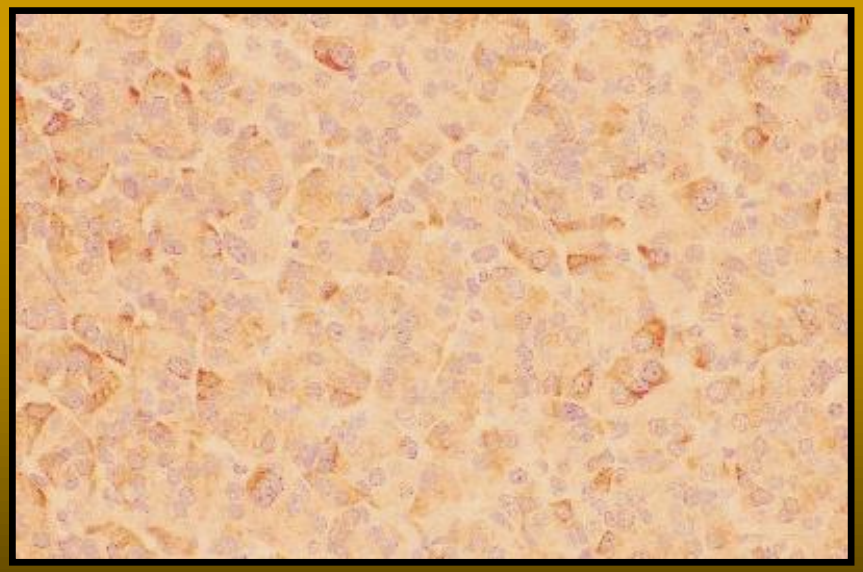
DIABETIC ANGIOPATHY

PATHOLOGY OF ISLET CELLS

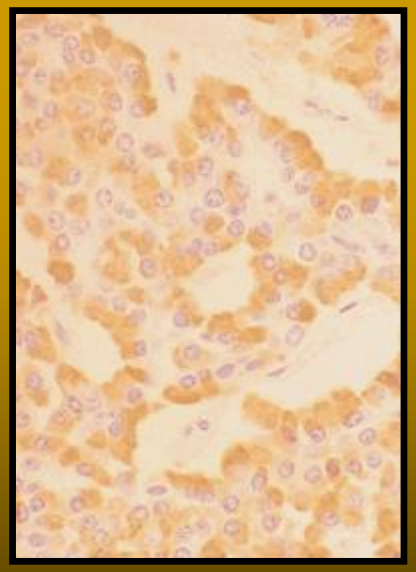
TUMORS OF ISLET CELLS - INSULOMAS

THESE TUMORS PRODUCE NUMEROUS HORMONES

INSULIN-PRODUCING TUMOR – INSULINOMA;
GASTRIN-PRODUCING TUMOR (HYPERSECRETION IN THE GASTRIC MUCOSA AND PEPTIC ULCERS – ZOLLINGER-ELLISON SYNDROME) – GASTRINOMA;
OTHERS: SOMATOSTATINOMA → DIABETES, DIARRHEA
GLUCAGONOMA → DIABETES



INSULINOMA



GLUCAGONOMA

IMMUNOHISTOCHEMICAL STAININGS REVEAL THE CELLULAR STRUCTURE OF THESE TUMORS

MULTIPLE ENDOCRINE NEOPLASIA (MEN)

Table 25–7. MULTIPLE ENDOCRINE NEOPLASIA SYNDROMES

	MEN I (WERMER'S SYNDROME)	MEN II OR IIa (SIPPLE'S SYNDROME)	MEN IIb OR III
Pituitary	Adenomas		
Parathyroid	Hyperplasia^{+++}	Hyperplasia^{+}	Hyperplasia
	Adenomas^{+}	Adenomas	
Pancreatic islets	Hyperplasia^{+}		
	Adenomas^{+++}		
	Carcinoma^{++}		
Adrenal	Cortical hyperplasia^{++}	Pheochromocytoma^{++}	Pheochromocytoma^{+++}
Thyroid	C-cell hyperplasia$^{\pm}$	Medullary carcinoma^{+++}	Medullary carcinoma^{++}
Extraendocrine changes			Mucocutaneous ganglioneuromas
			Marfanoid habitus
Mutant gene locus	11q11-13	10 (near centromere)	Unknown

Relative frequency; +, uncommon; +++, common.

THANK YOU