

# Pituitary, endocrine pancreas, and adrenal pathology

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**Learning Objectives:**

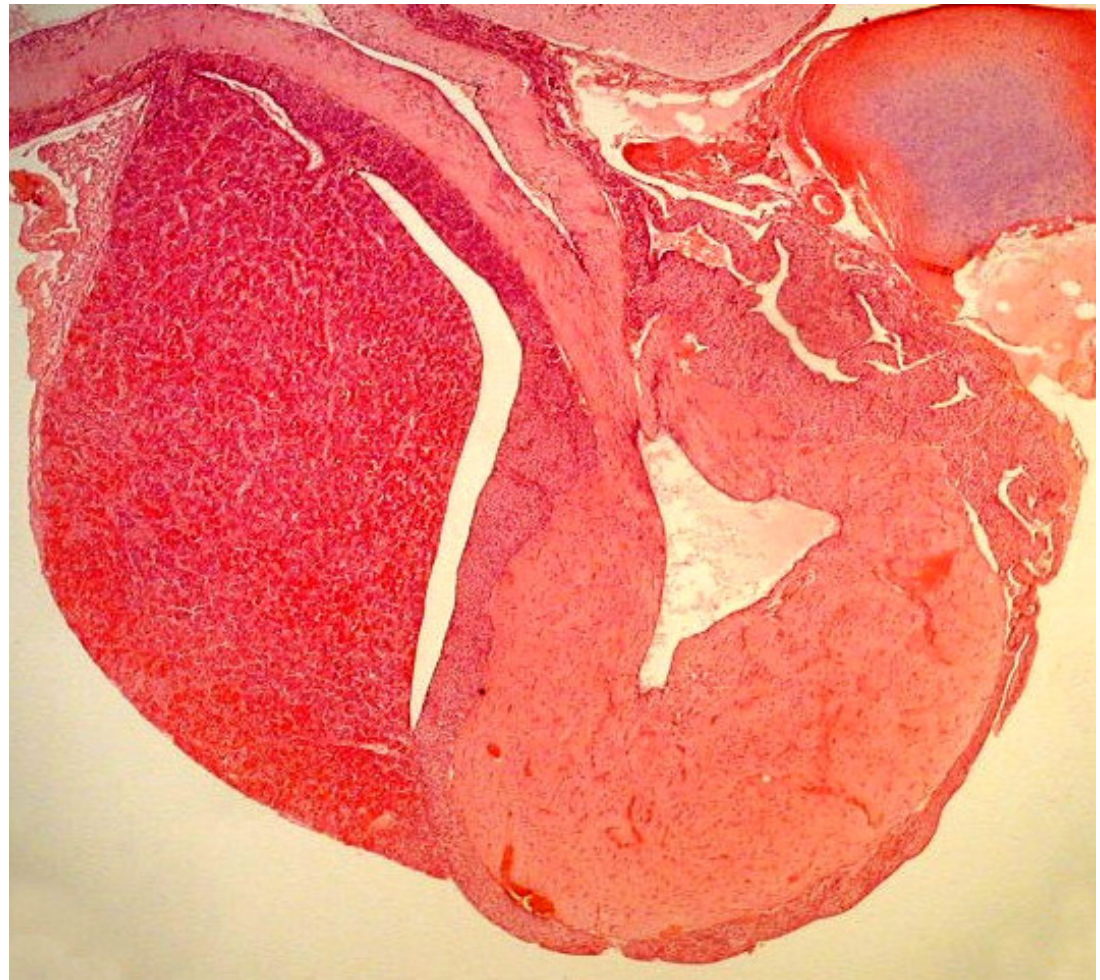
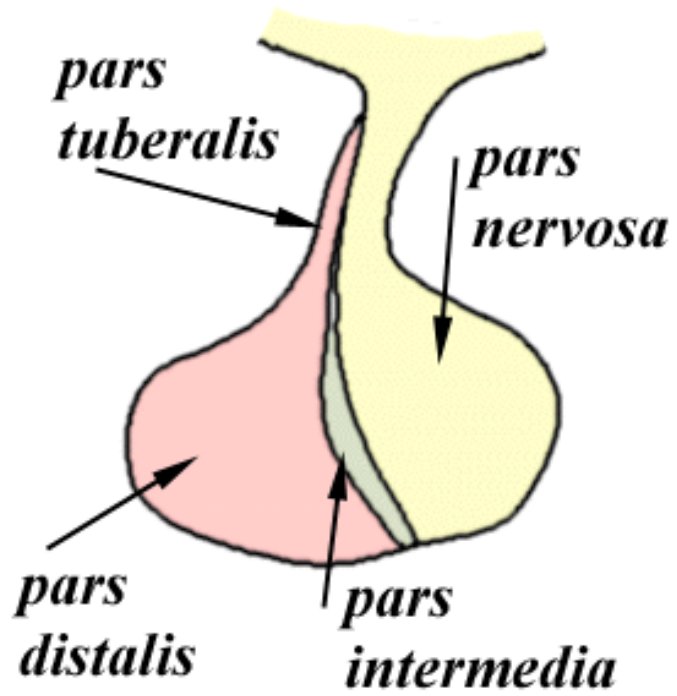
1. Describe the histogenesis and normal anatomy of the pituitary gland.
2. Itemize the distinguishing features of normal and neoplastic pituitary parenchyma.
3. Describe the histologic features of various sellar/suprasellar epithelial lesions.
4. Describe the functional and malignant potentials of pancreatic islet-cell tumors.
5. Name the major causes of adrenocortical hyperfunction and insufficiency

**Reading:** Robbins and Cotran pathologic basis of disease.

Ninth edition Online: The Endocrine system, pp 1074-1082, 1105-1134

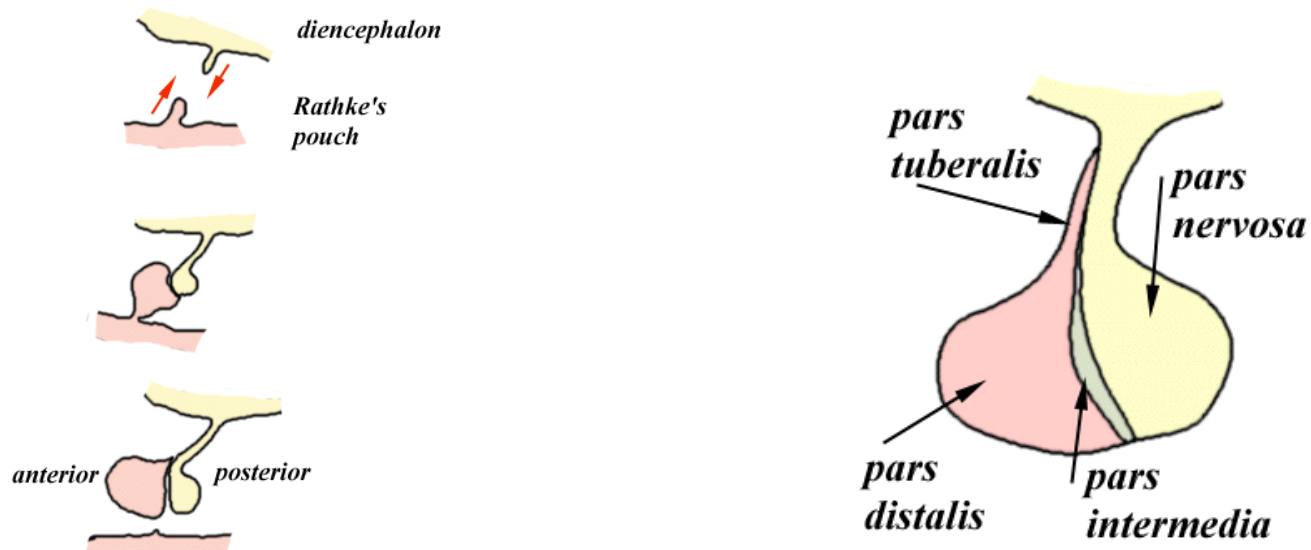
# Pituitary Anatomy

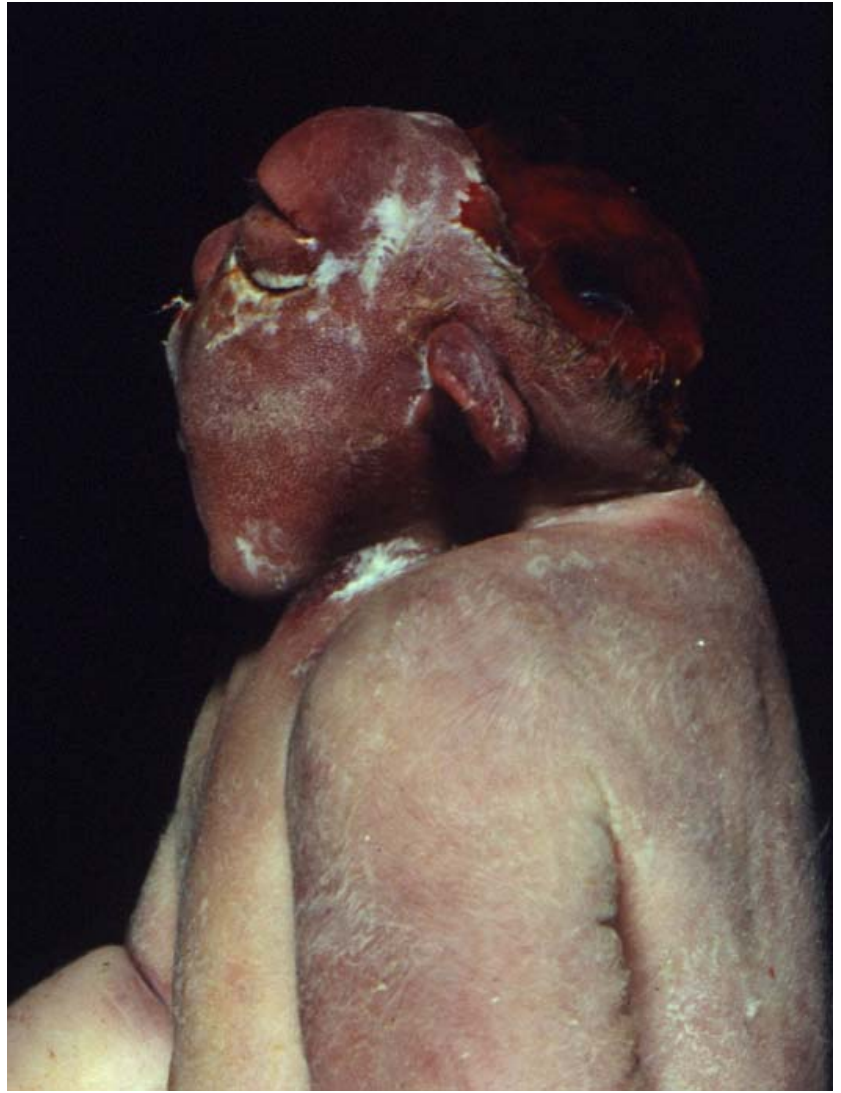
- Anterior pituitary
  - Pars distalis (adenohypophysis)
  - Pars intermedia
  - Pars tuberalis
- Posterior pituitary (neurohypophysis, pars nervosa)
- Stalk



# Histogenesis

- Anterior pituitary (adenohypophysis)
  - Arises from invagination of Rathke's pouch
  - Residual small cystic epithelial lined remnants are common at interface with posterior pituitary
- Posterior pituitary (neurohypophysis)
  - Composed of nerve fibers (arising in hypothalamic nuclei), axon terminals and stromal cells

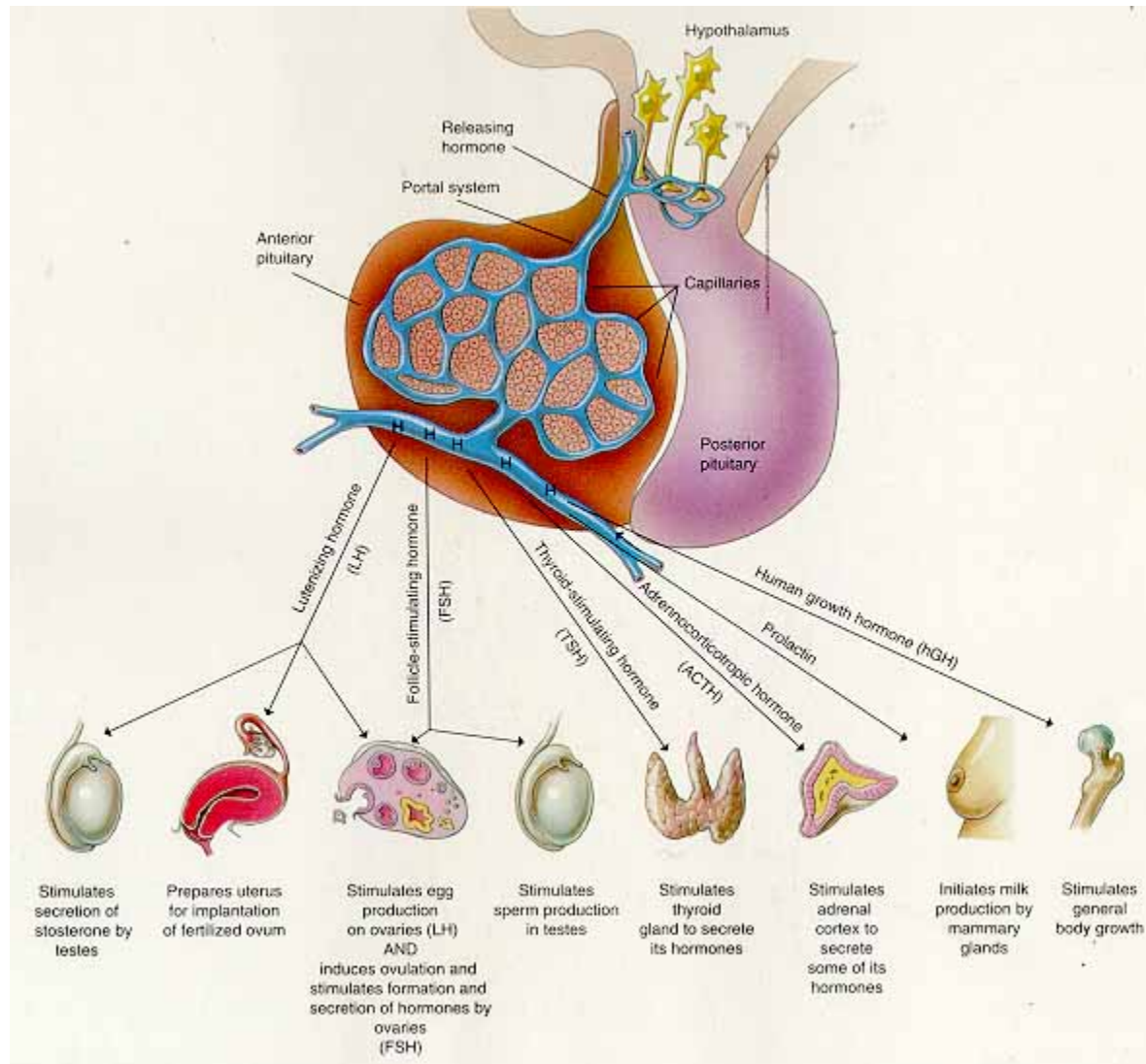




Anencephaly



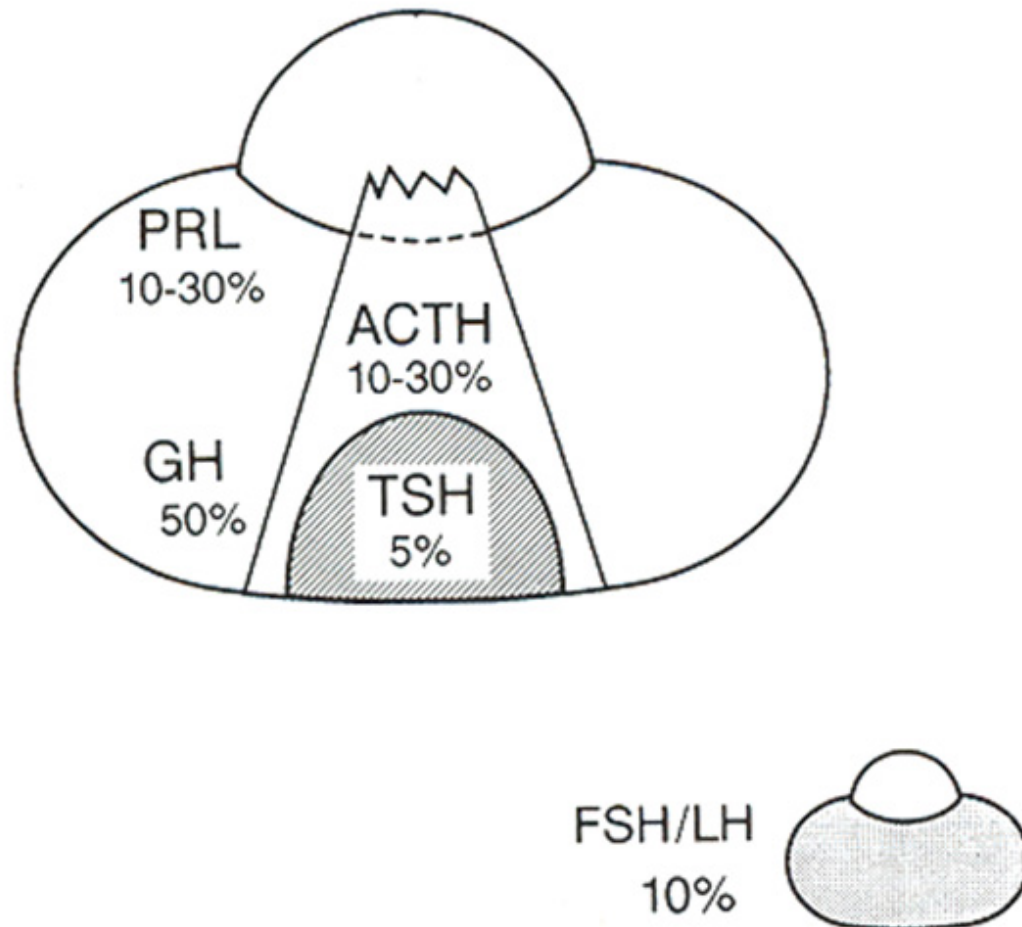
Area cerebrovasculosa + anterior pituitary



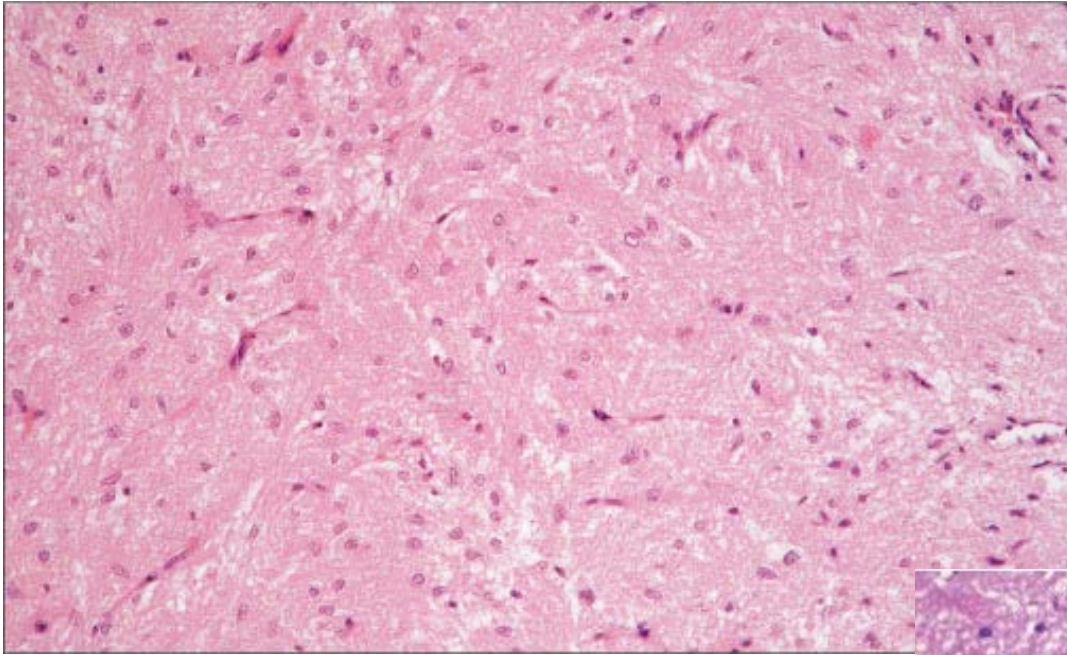


# Adenohypophysis

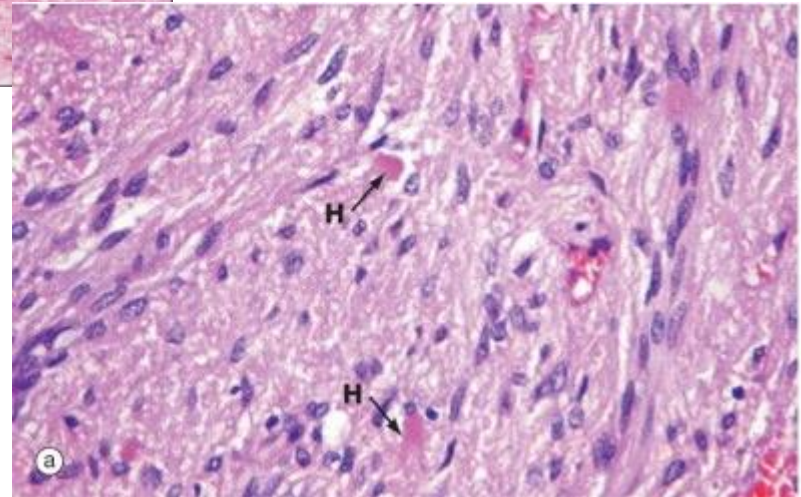
Cell type predominance and distribution

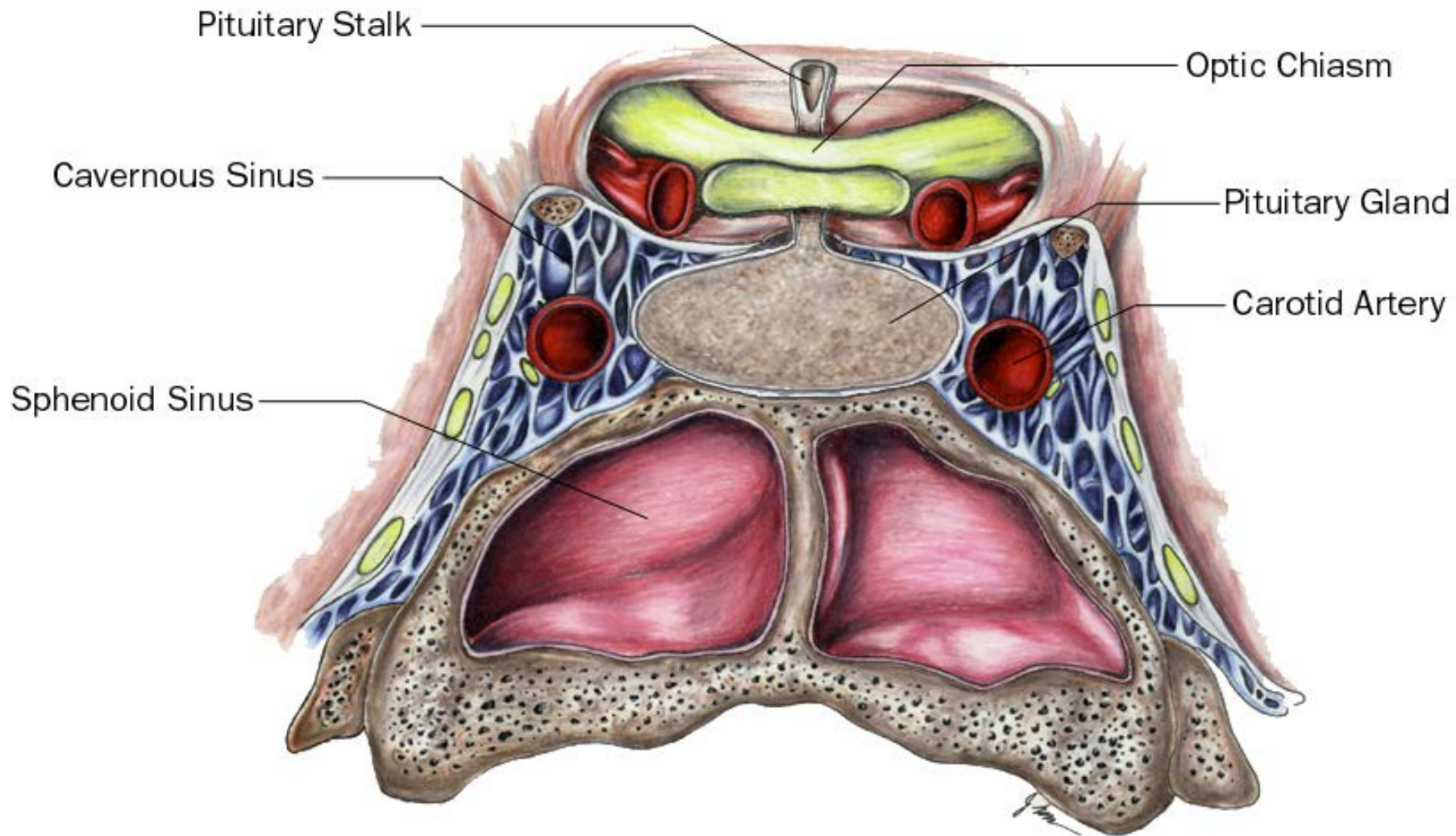


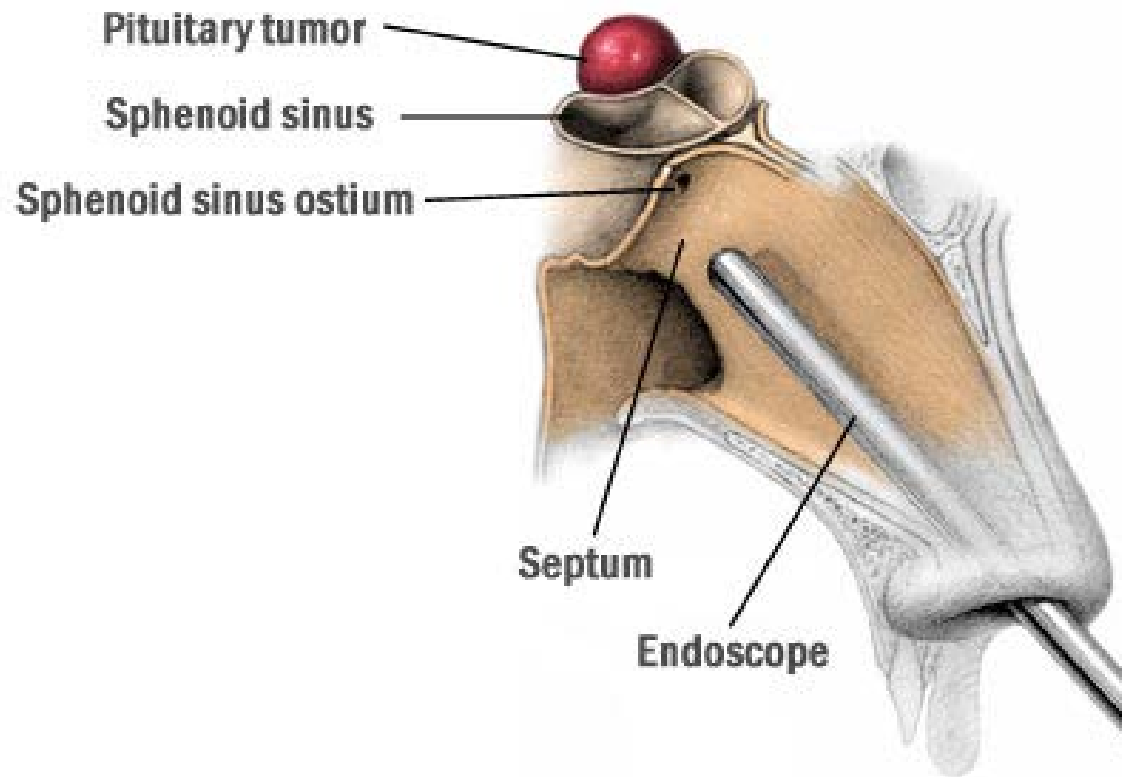
# Neurohypophysis

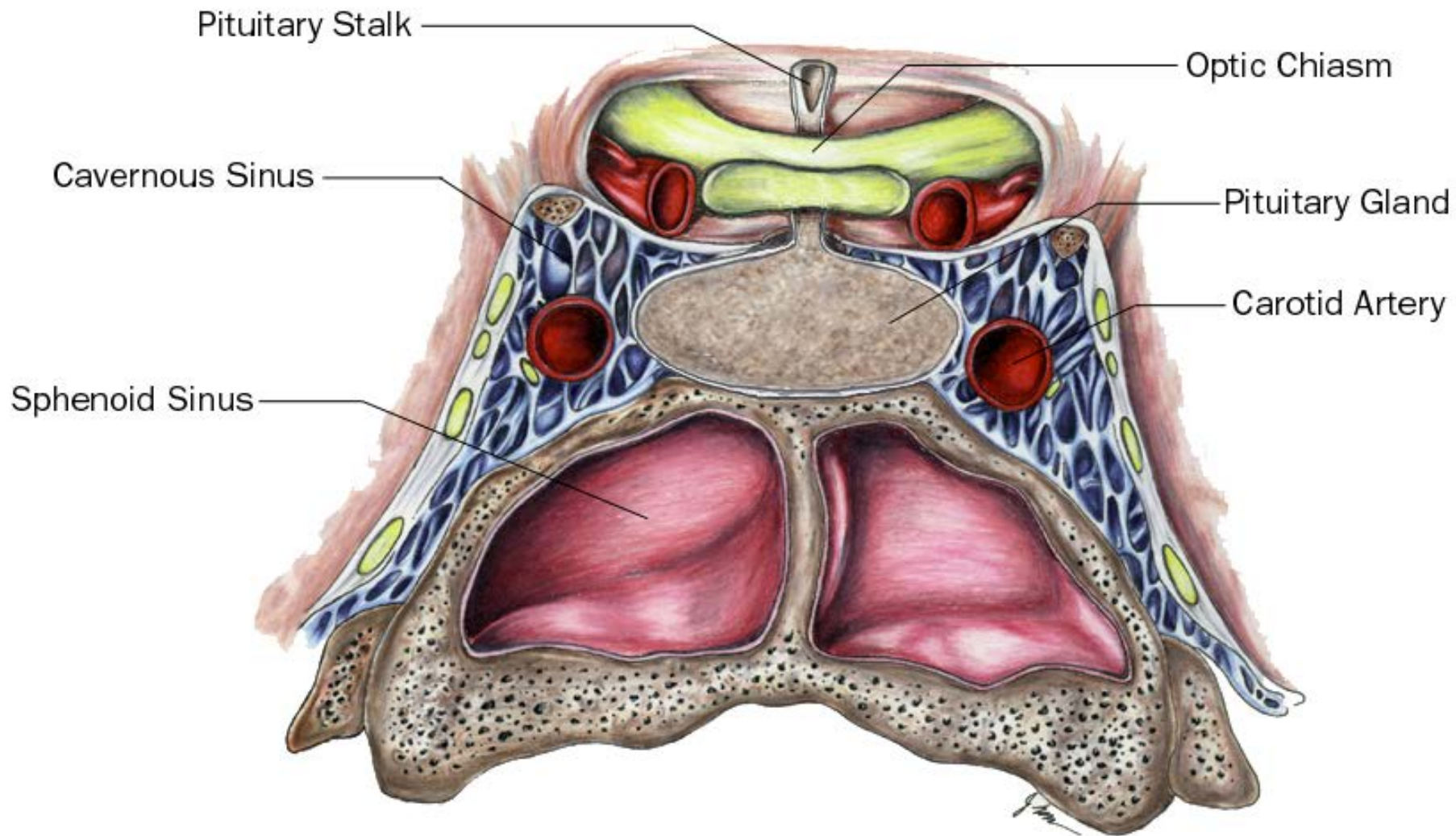


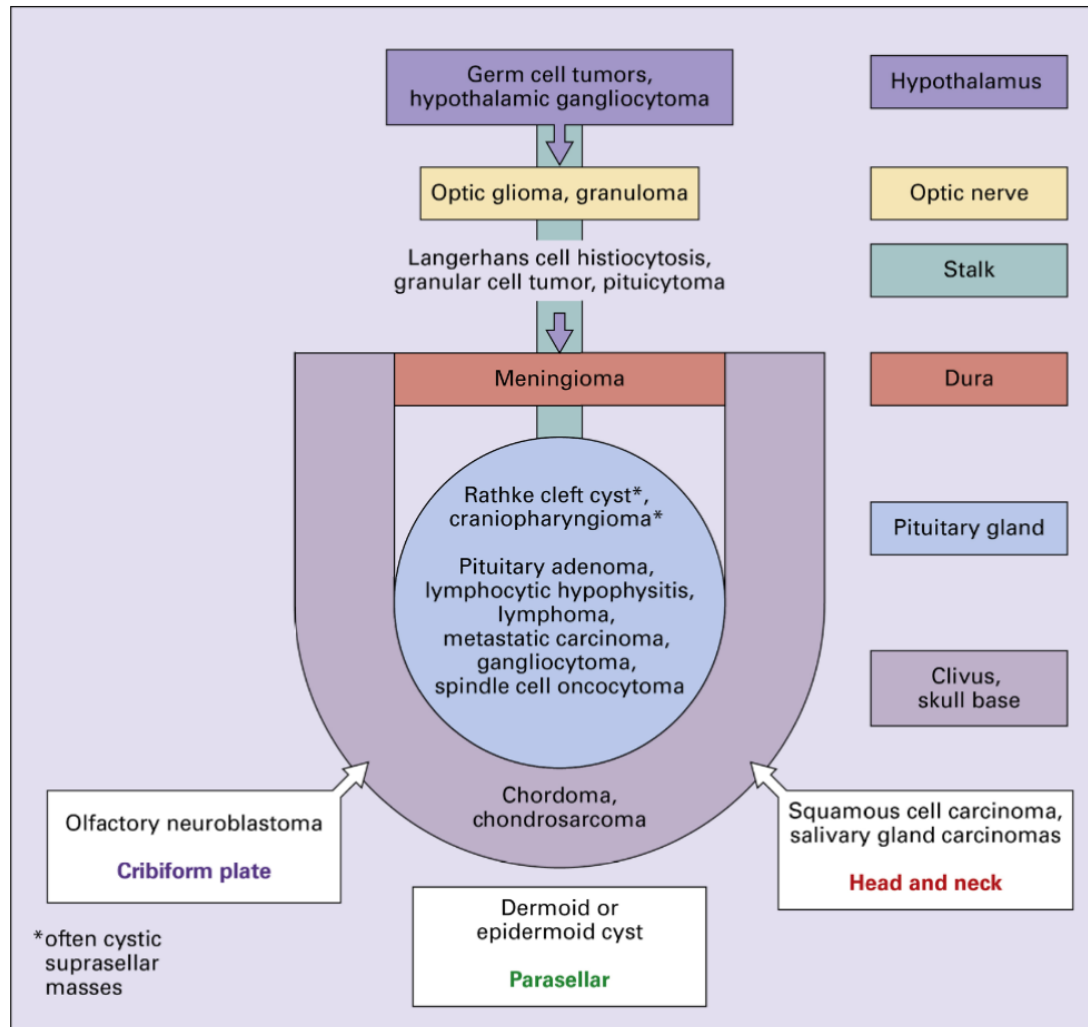
- Composed of nerve fibers, few astrocytes
- Herring bodies – eosinophilic intracellular secretory material







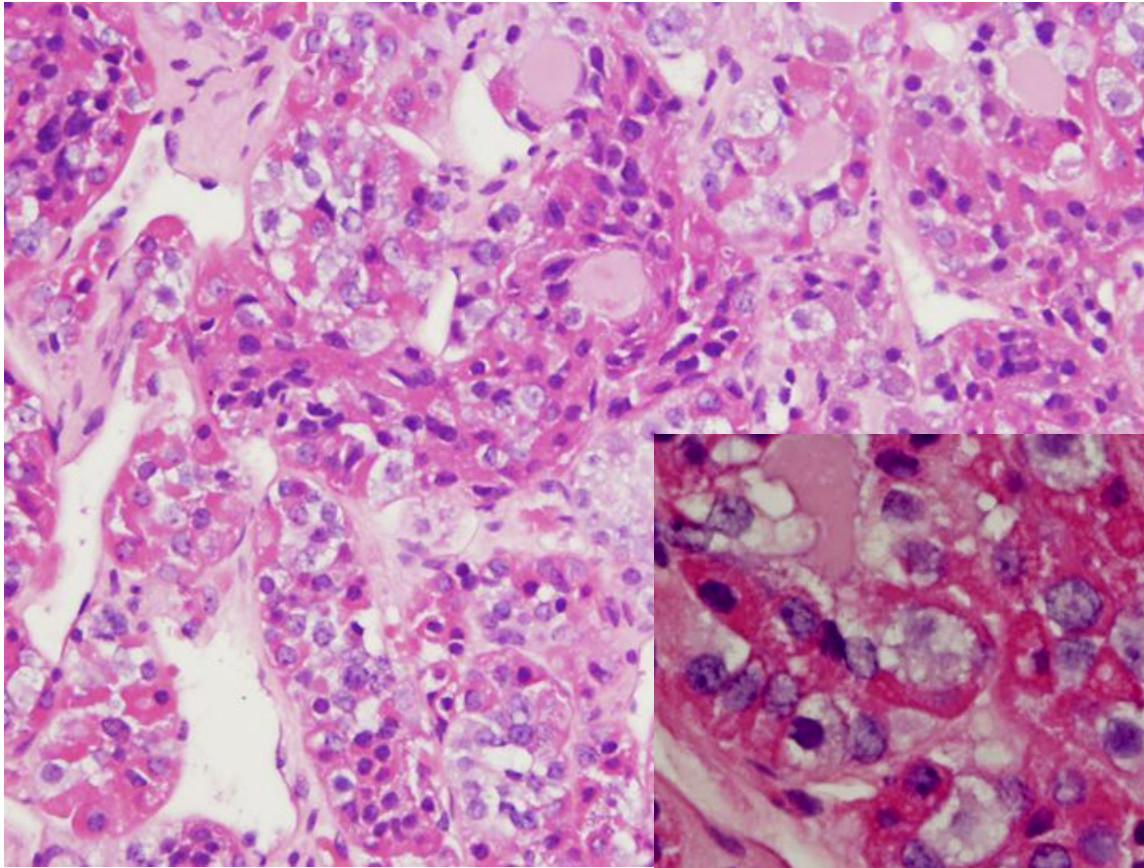




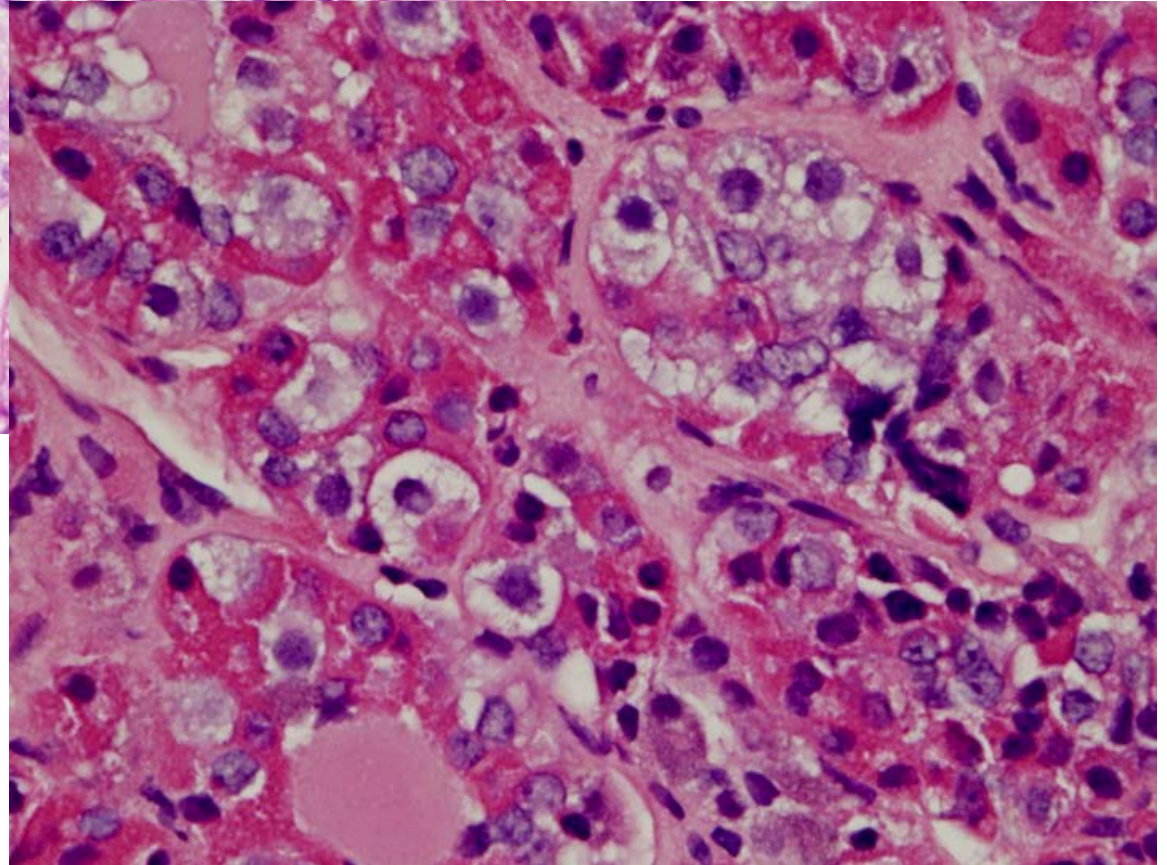
Types and sources of neoplasm that can  
affect the pituitary gland

# Adenohypophysis

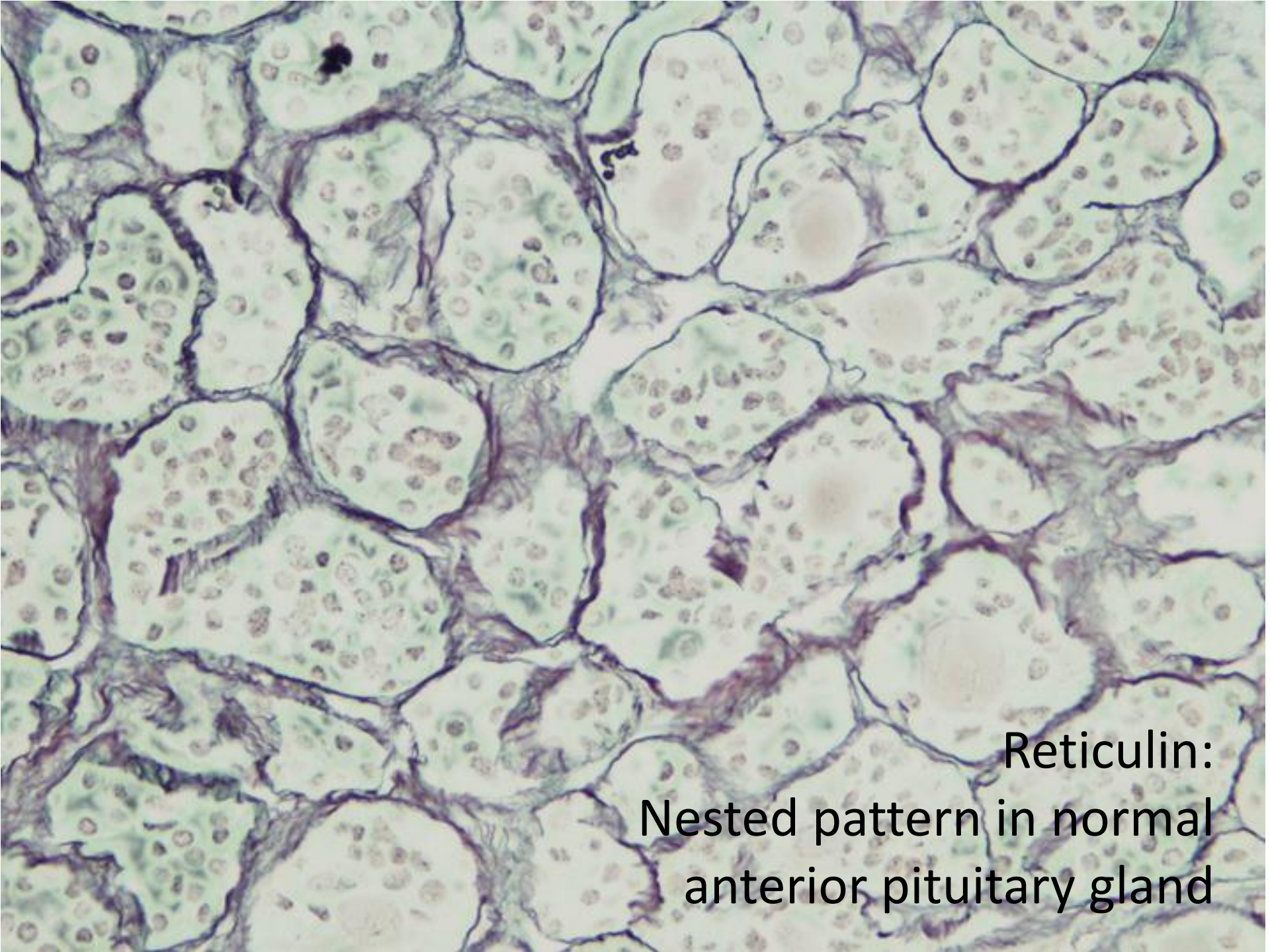
Cell Type	Hormone Stain
Somatotroph	Growth Hormone (GH)
Mammosomatotroph	GH, Prolactin (PRL)
Lactotroph	PRL
Thyrotroph	Thyroid stimulation hormone (TSH)
Corticotroph	ACTH
Gonadotroph	Luteinizing hormone (LH) Follicle stimulating hormone (FSH)



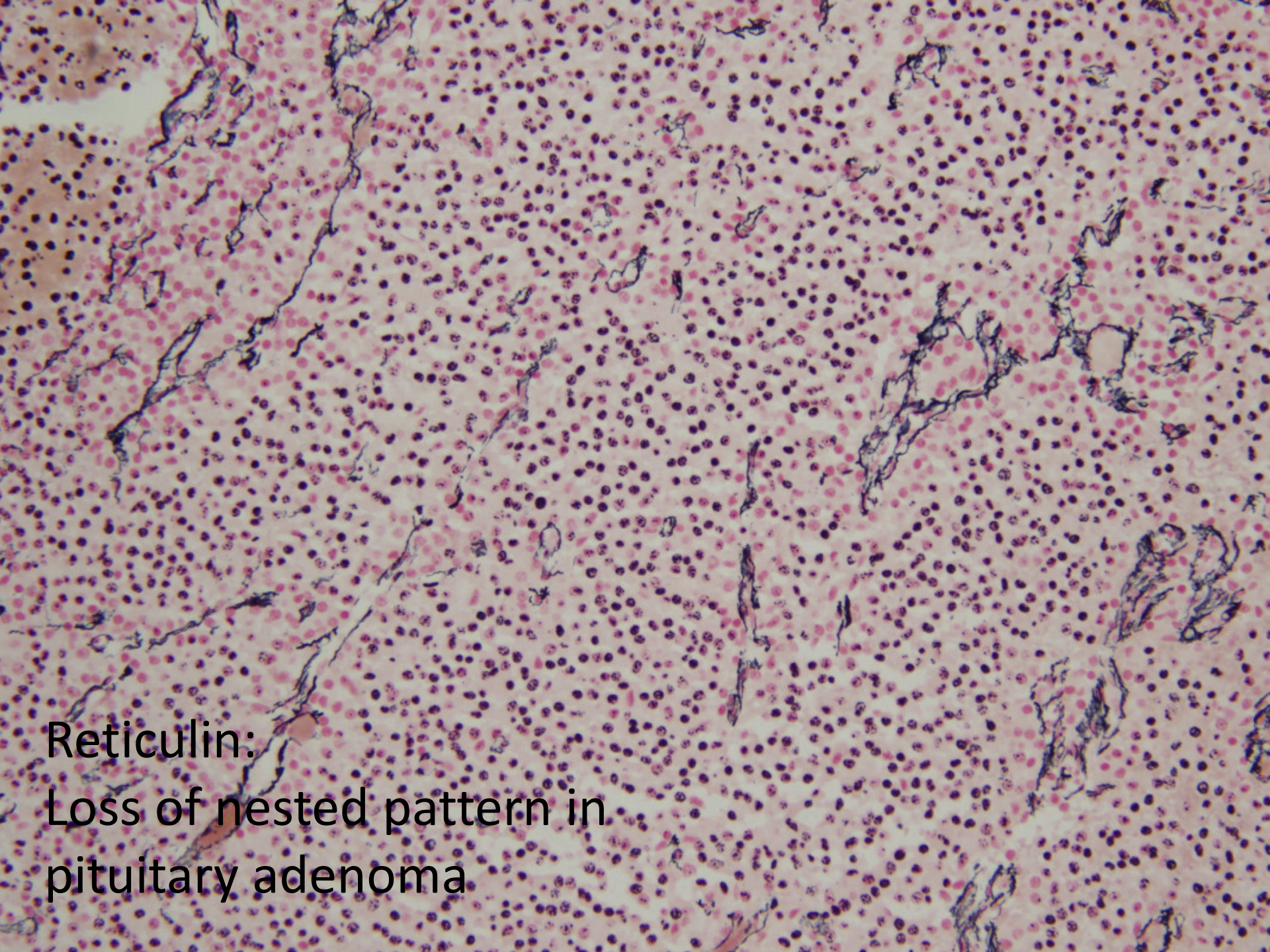
Non-neoplastic  
anterior pituitary:  
Nested pattern  
with different cell types







Reticulin:  
Nested pattern in normal  
anterior pituitary gland

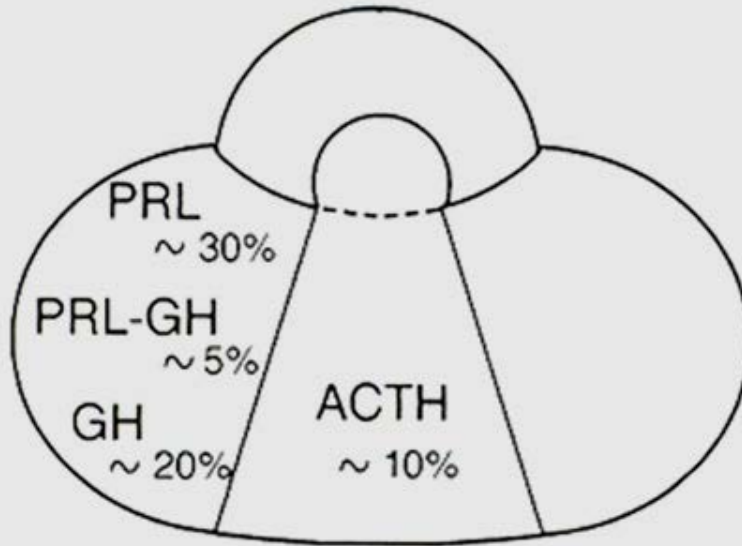


Reticulin:  
Loss of nested pattern in  
pituitary adenoma

# Adenoma characterization

- Clinical features and syndromes (e.g. MEN I)
- Adenomas with no clinical endocrinologic abnormalities are more likely to reach large sizes before clinically recognized
- Histology
  - Appearance in H & E stained section (acidophil, basophil, chromophobe)
- Electron microscopy
  - Appearance and size of granules
- Immunohistochemistry
  - Hormone-specific antibodies

# Pituitary adenomas - frequencies

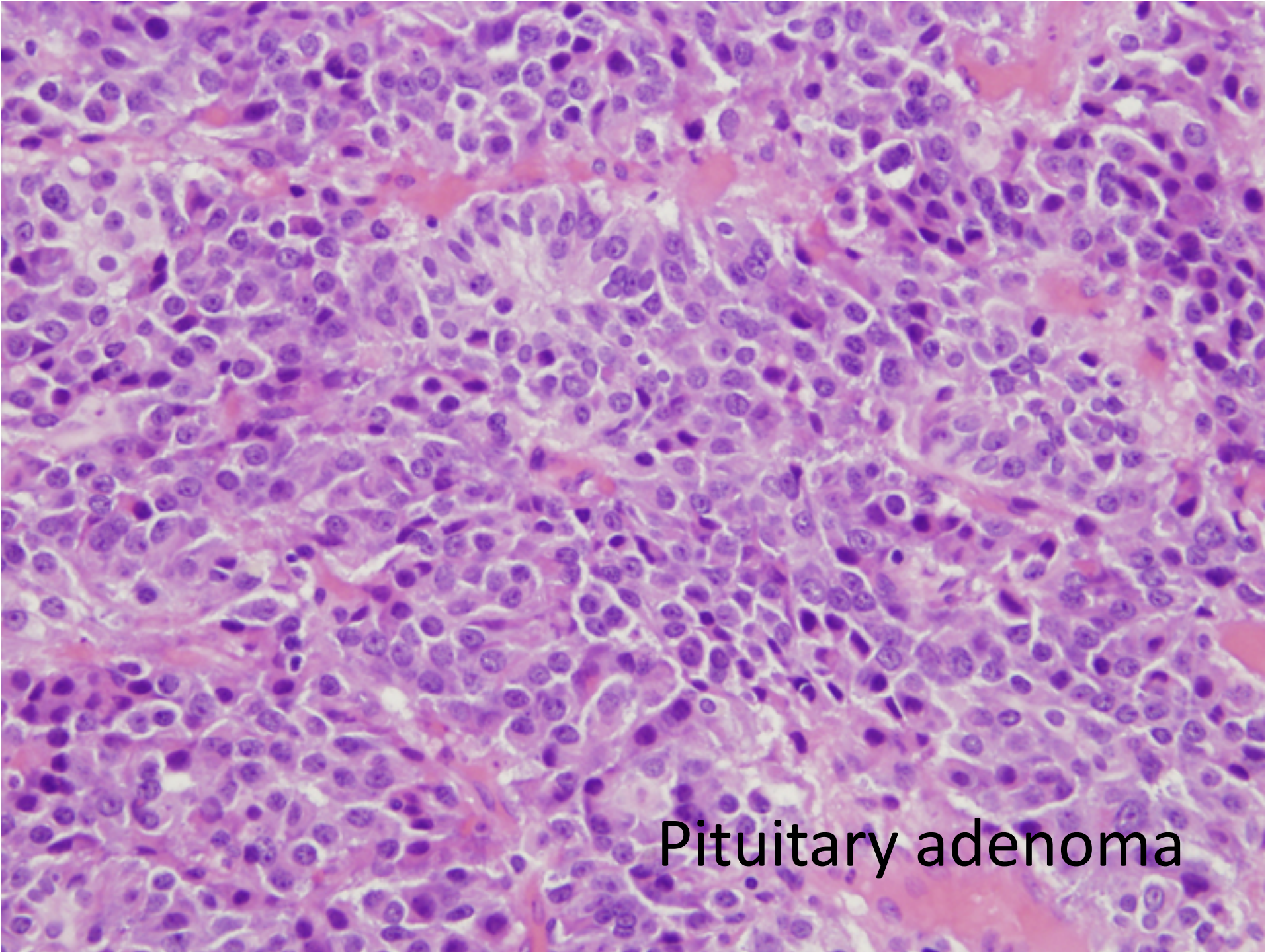


Acidophil stem cell	2%
ACTH (silent)	2%
FSH/LH	10%
TSH	1%
Null cell	20%

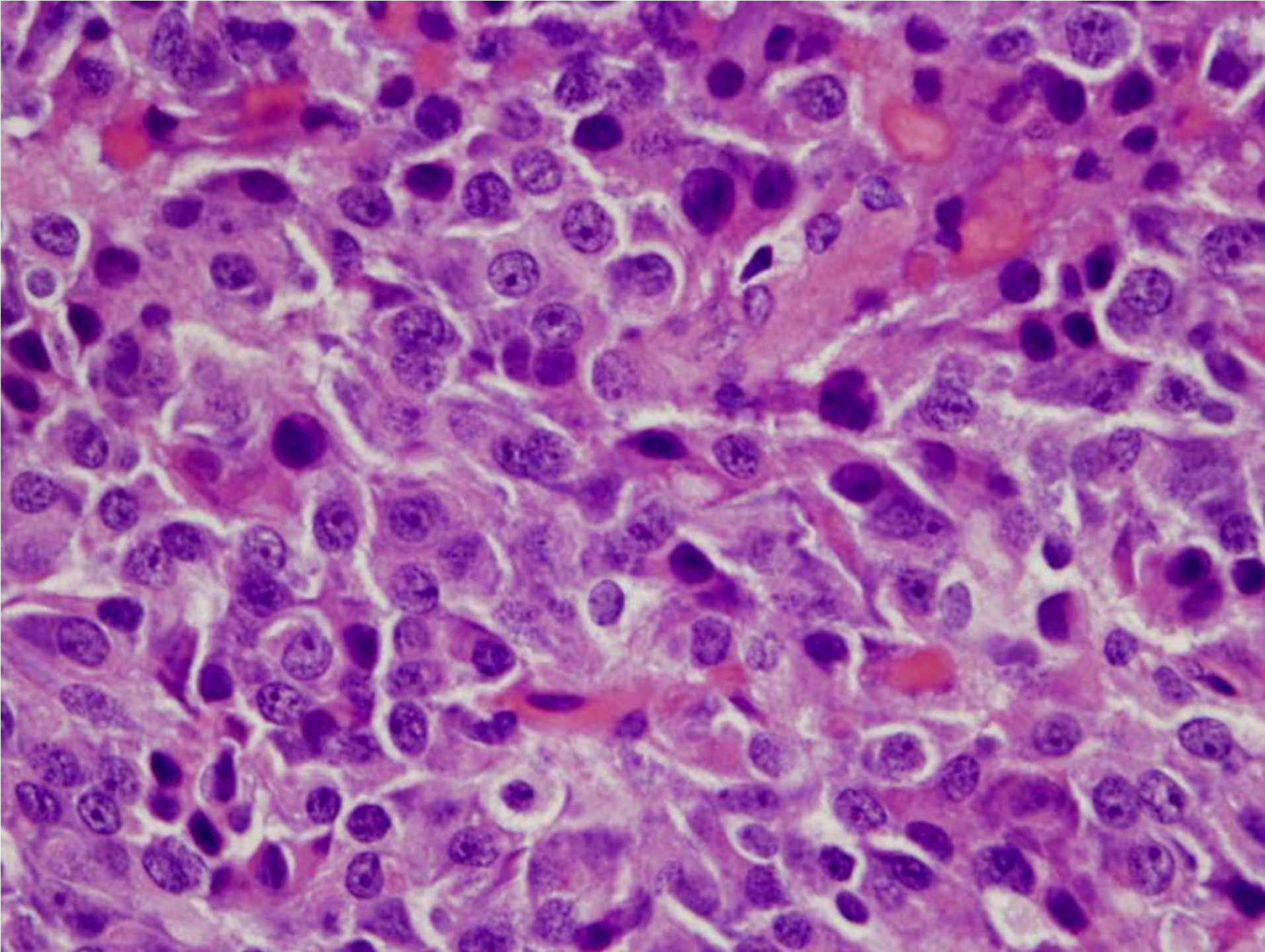
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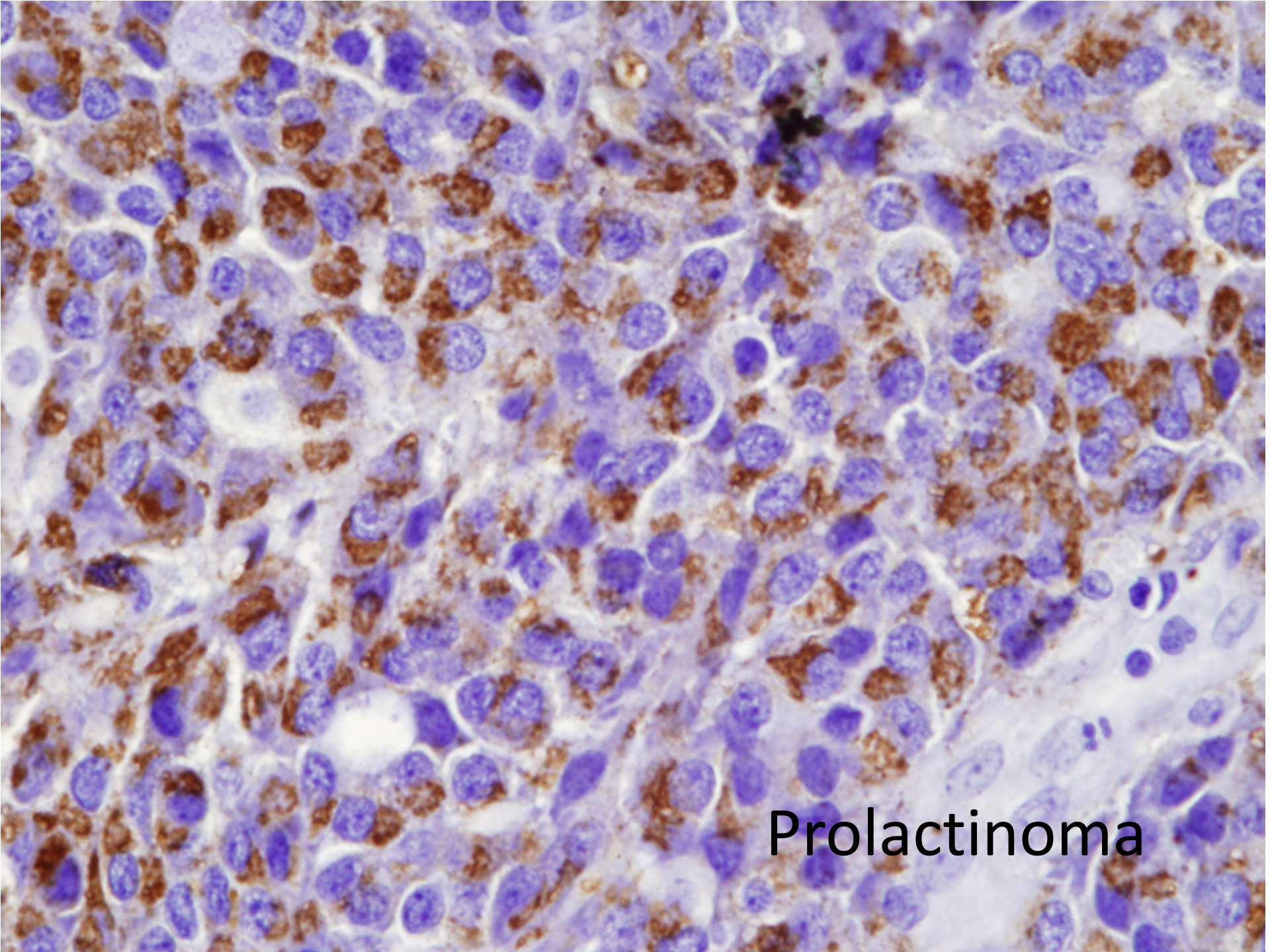
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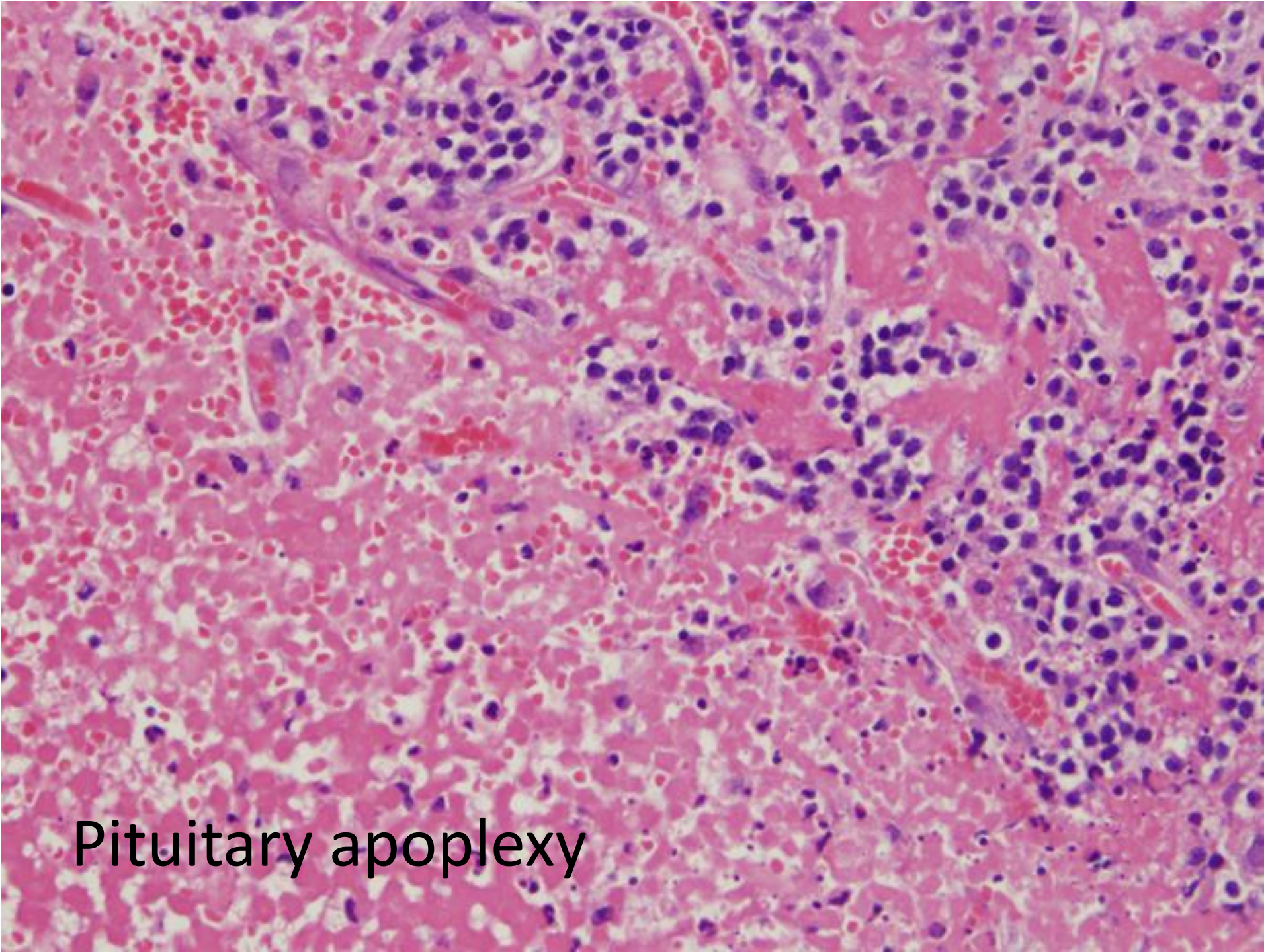


Pituitary adenoma





Prolactinoma



Pituitary apoplexy



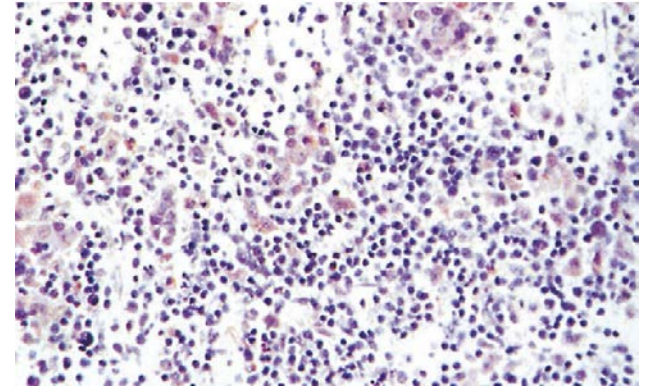
# Non-neoplastic v. Adenoma

Non-neoplastic	Adenoma
Heterogeneous cell population	Monomorphic or little pleomorphism
Nests of cells	Non-nested (varied appearances)
Reticulin deposition	Loss of reticulin
Heterogeneous immunoreactivity	Uniform immunoreactivity or loss

## Inflammatory diseases may present as a mass in the pituitary fossa

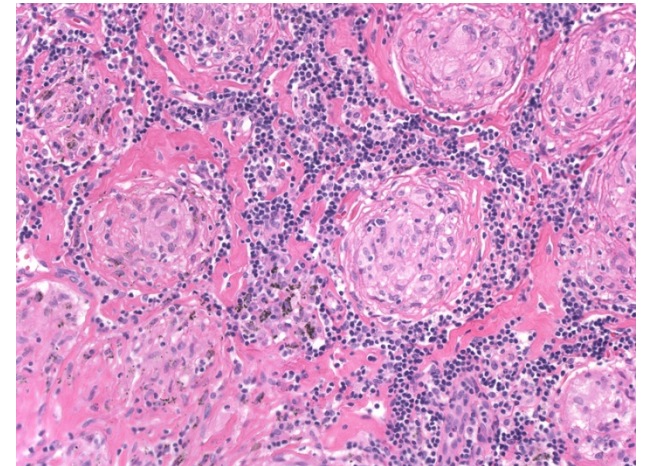
### Lymphocytic hypophysitis

- Occurs almost exclusively in women
- Usually occurs in pregnancy or the postpartum period
- Often presents with pituitary insufficiency
- Characterized by a mixed infiltrate of inflammatory cells, mainly lymphocytes



### CNS sarcoidosis

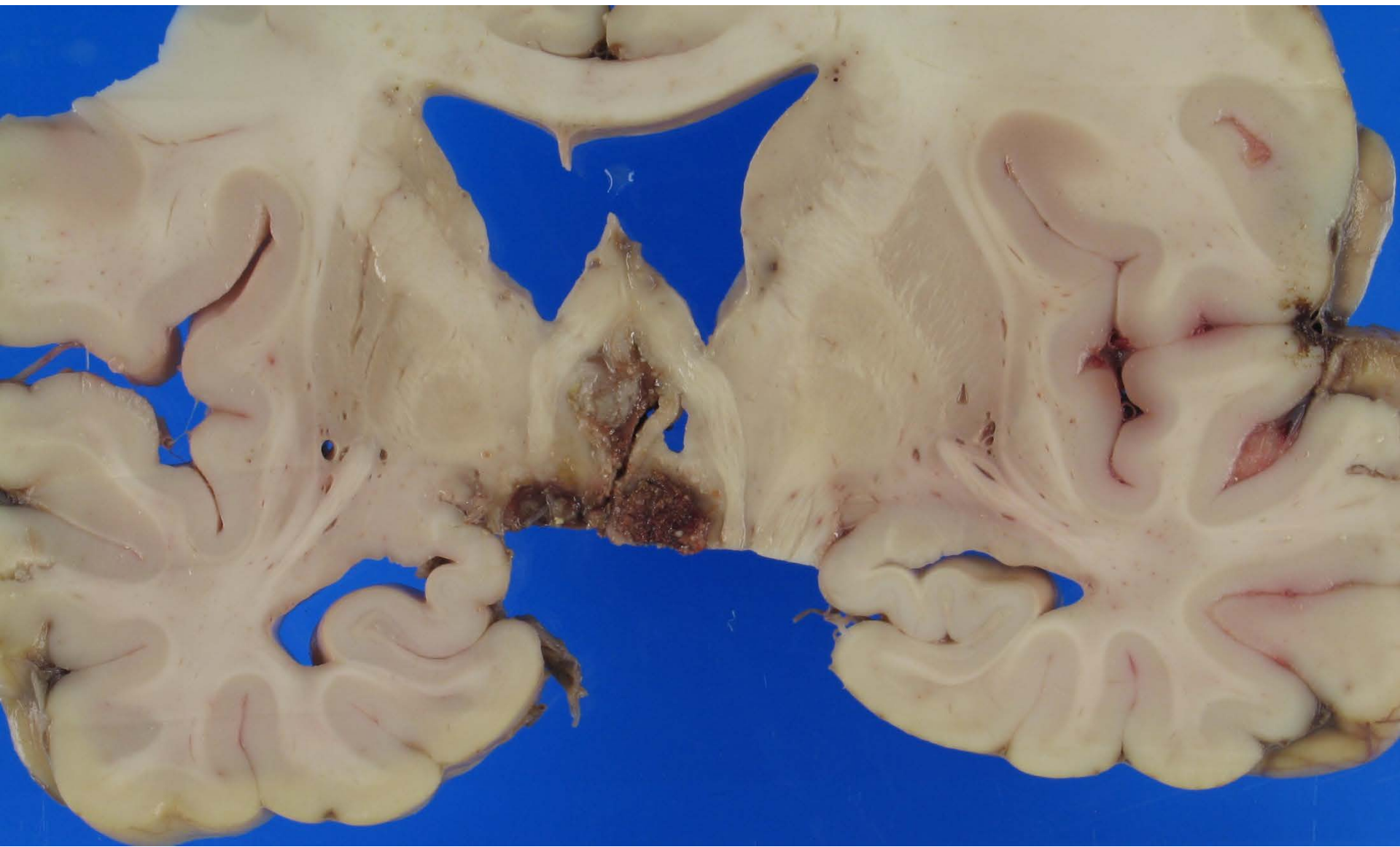
- Often associated with systemic sarcoidosis
- Preferentially affects structures in the suprasellar region
- Produces non-caseating, granulomatous inflammation with multinucleated giant cells
- More widespread than granulomatous hypophysitis



# Epithelial Lesions

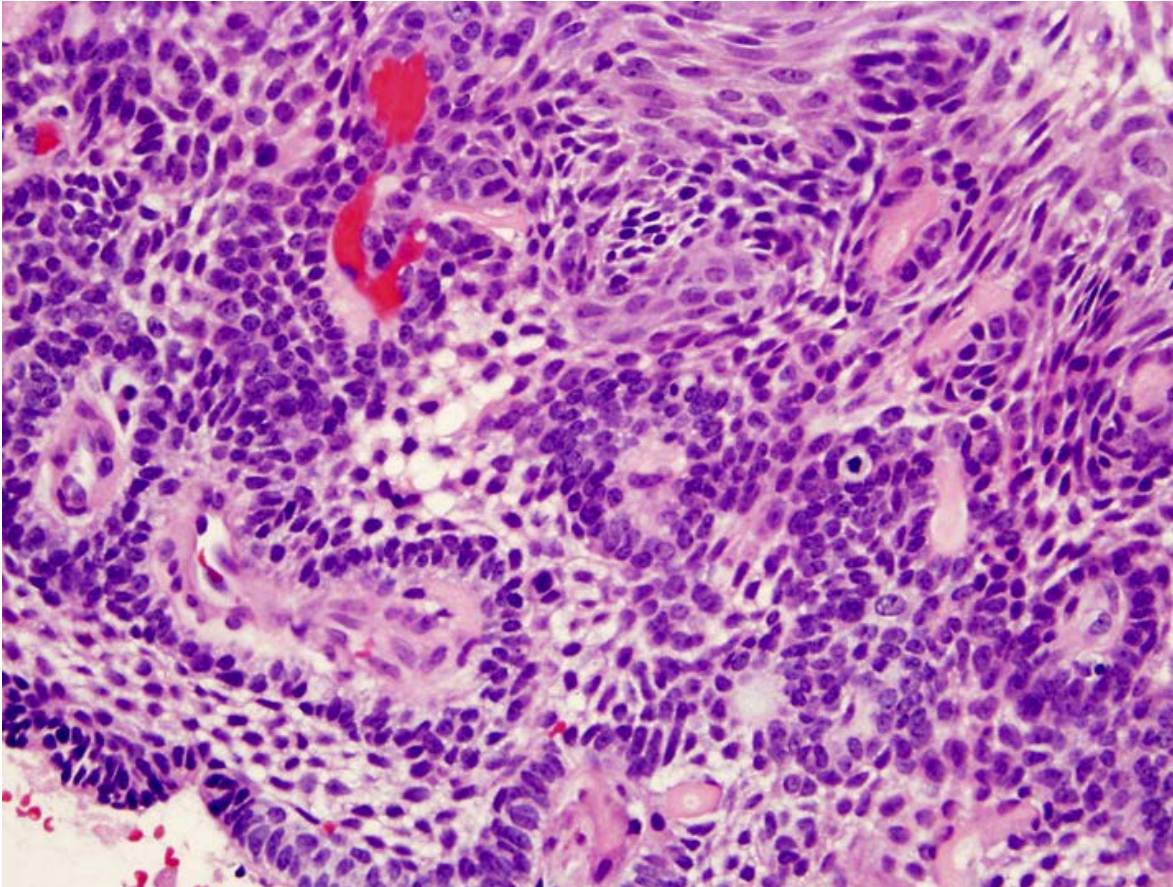
- Craniopharyngioma
  - Adamantinomatous – occur in adults and children
  - Papillary – occur in adults
- Rathke's cleft cyst
- Epidermoid cyst





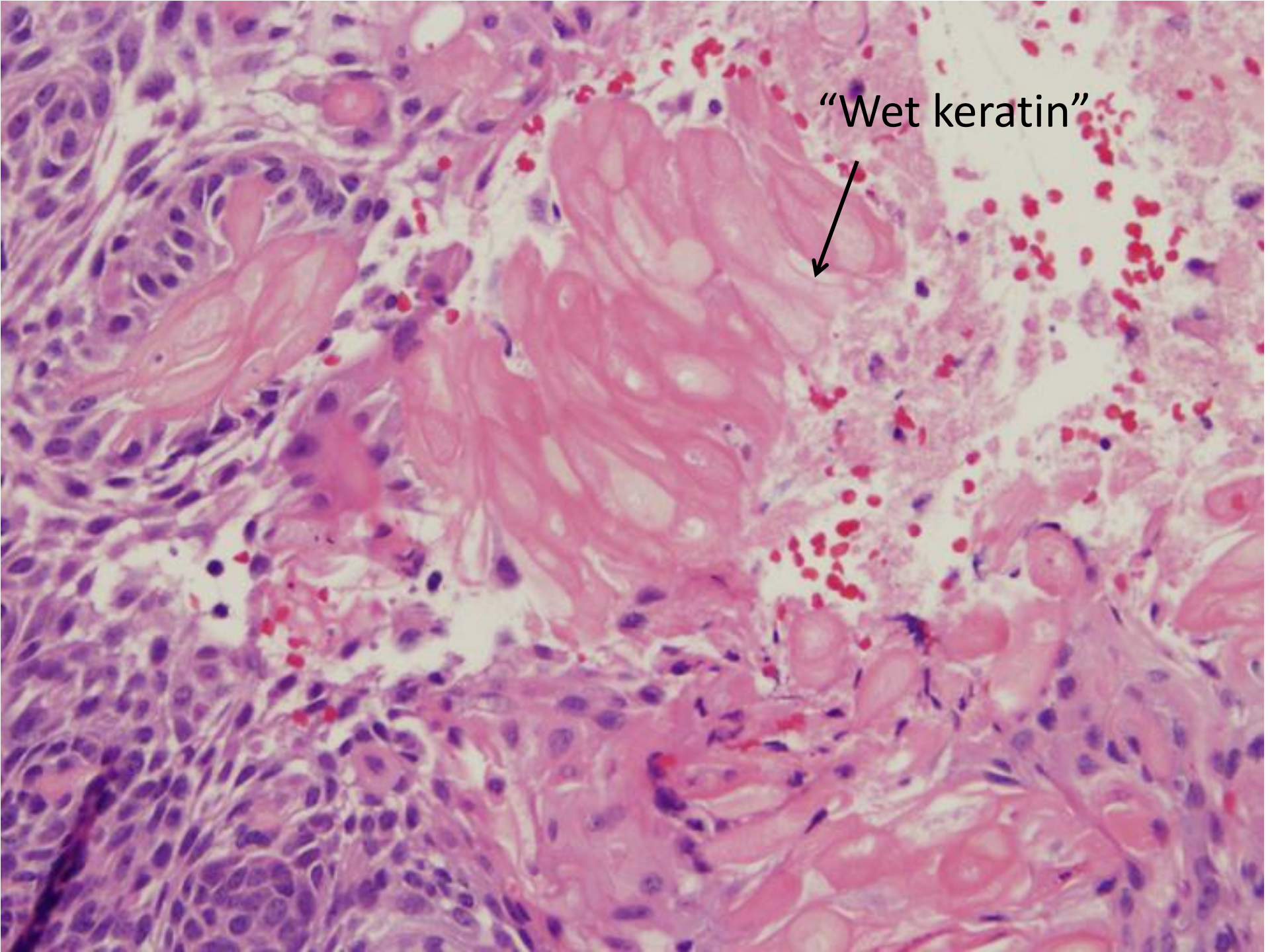


# Adamantinomatous craniopharyngioma

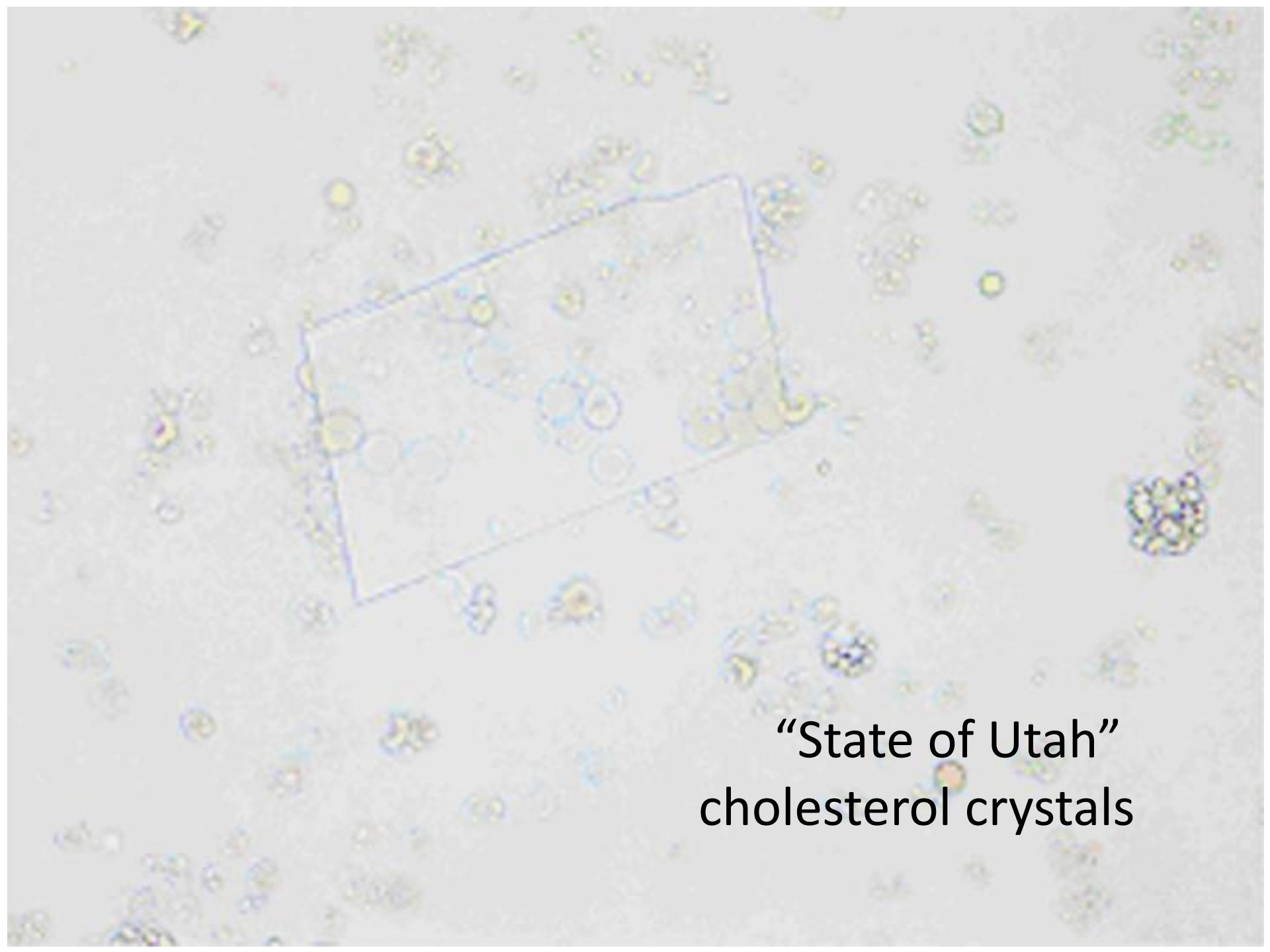


- Squamous cells with peripheral palisades
- Stellate reticulum
- Calcification
- Cysts with “machine oil” contents

“Wet keratin”

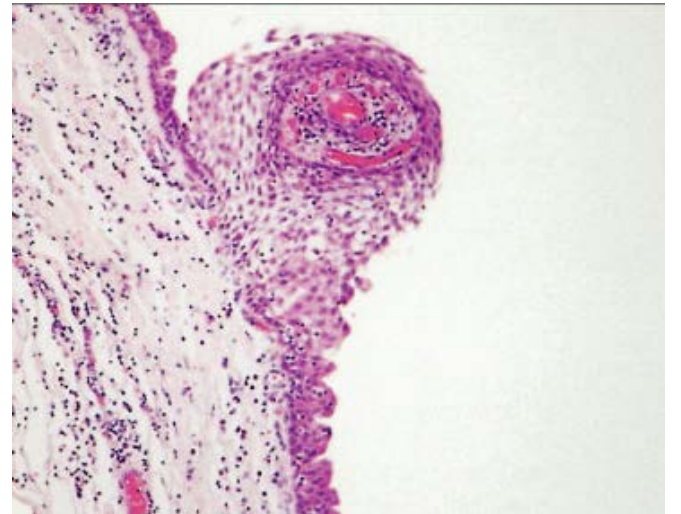
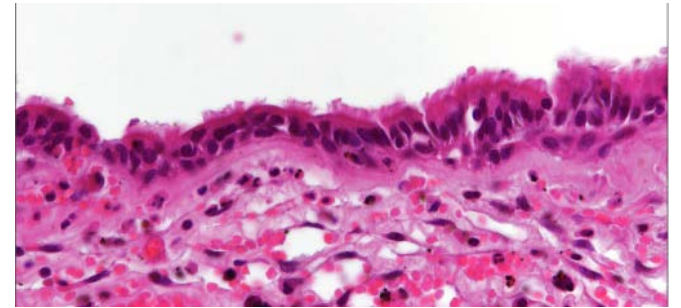
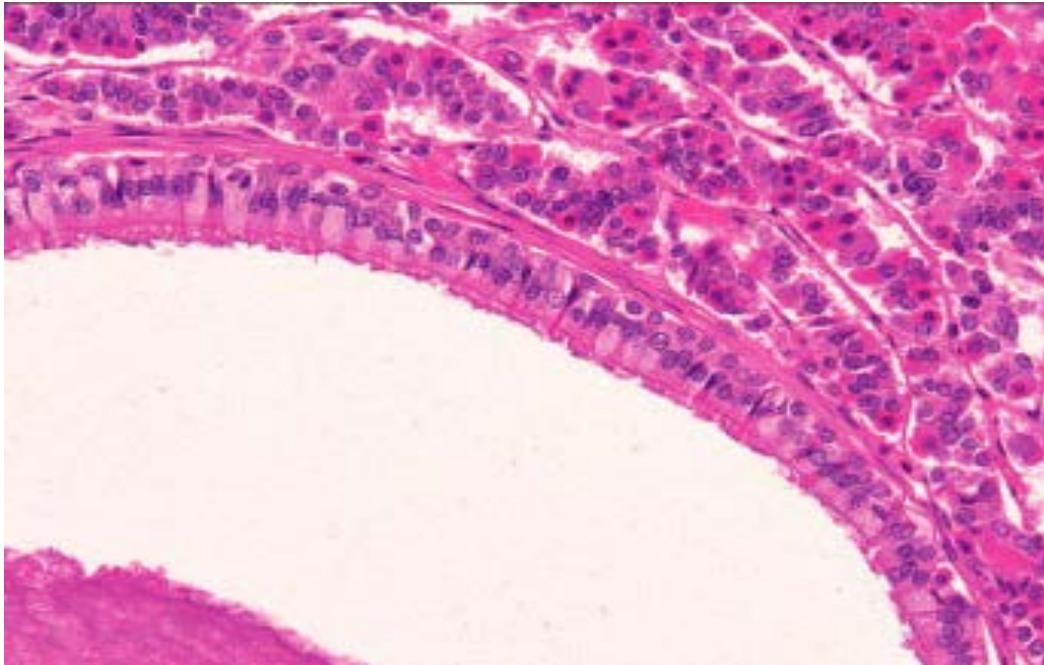


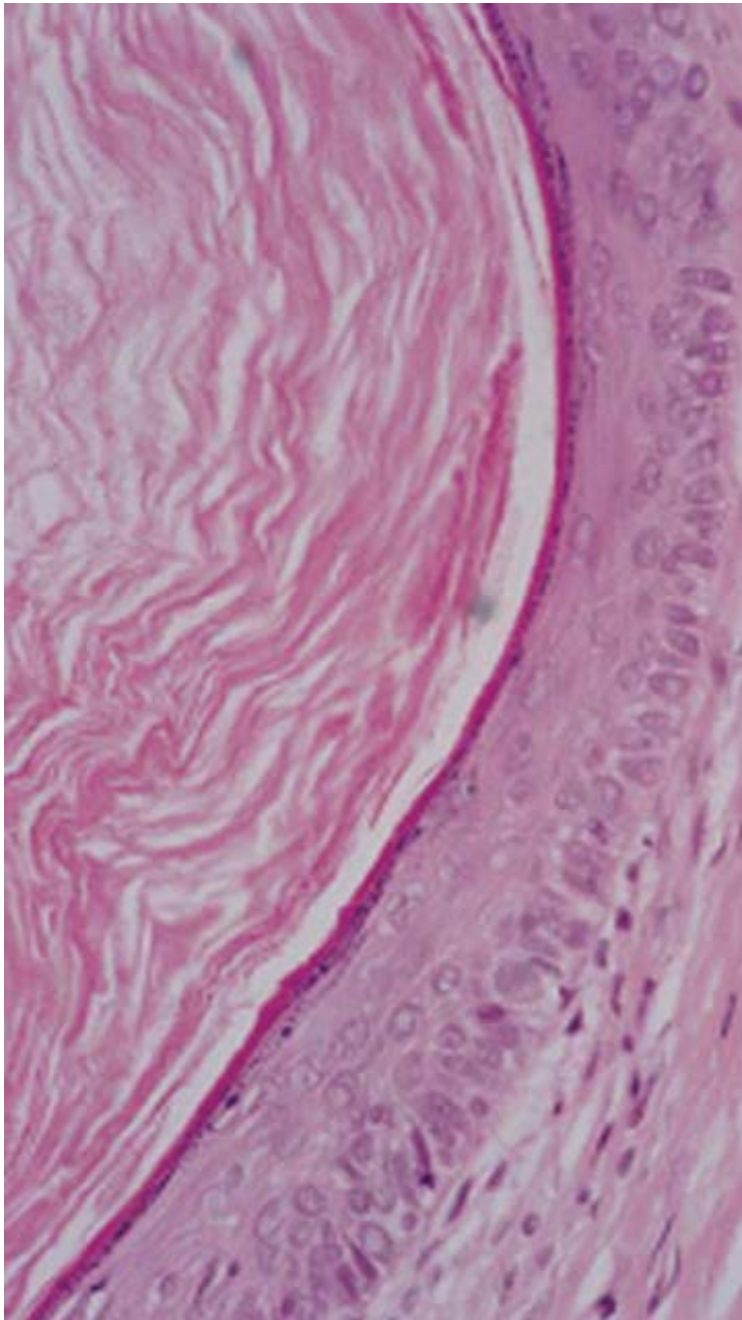




“State of Utah”  
cholesterol crystals

# Rathke's cleft cyst





# Epidermoid cyst

- Keratinizing squamous epithelium
- “Dry keratin”
- No epidermal appendages

Questions. Thank you M-208!

## Room M-208

<p>Group 1</p>  <p>Aalipour, Amin</p>	<p>Group 1</p>  <p>Fletcher, Will</p>	<p>Group 1</p>  <p>Maheshwari, Akshay</p>	<p>Group 1</p>  <p>Sotelo Leon, Daniel</p>
<p>Group 2</p>  <p>Becker, Winston</p>	<p>Group 2</p>  <p>Hodgkinson, Luqman</p>	<p>Group 2</p>  <p>Ober-Reynolds, Benjamin</p>	<p>Group 2</p>  <p>Vaca, Silvia</p>
<p>Group 3</p>  <p>Connolly, Sara</p>	<p>Group 3</p>  <p>Lamsam, Layton</p>	<p>Group 3</p>  <p>Rajeshuni, Nitya</p>	<p>Group 3</p>  <p>Yu, Caroline</p>

Anencephaly is a condition in which there is loss of major portions of the forebrain and its derivatives due to a defect in neural tube closure. Which of the following structures is not derived from the developing central nervous system and would be intact in anencephaly?

- A. Anterior pituitary (adenohypophysis)
- B. Posterior pituitary (neurohypophysis)
- C. Optic nerves
- D. Hypothalamus
- E. Pineal gland

Correct answer A.

You are called by a neurosurgeon in order to determine whether resected tissue from the vicinity of a presumed pituitary adenoma is adenoma or non-neoplastic anterior pituitary tissue. Which of the following features would lead you to conclude that the specimen represents non-neoplastic anterior pituitary tissue?

- A. Non-nested cells
- B. Heterogenous cell population
- C. Loss of reticulin
- D. Glial tissue with Herring bodies
- E. Pituitary apoplexy

Correct answer: B

An intrasellar cystic lesion with calcification on CT scan in a 6 year old female with delayed growth is partially resected. Among the following choices, which is the most likely?

- A. Epidermoid cyst
- B. Craniopharyngioma
- C. Rathke's cleft cyst
- D. Pituitary adenoma
- E. Colloid cyst

Correct answer: B

# Tumors of the Endocrine Pancreas

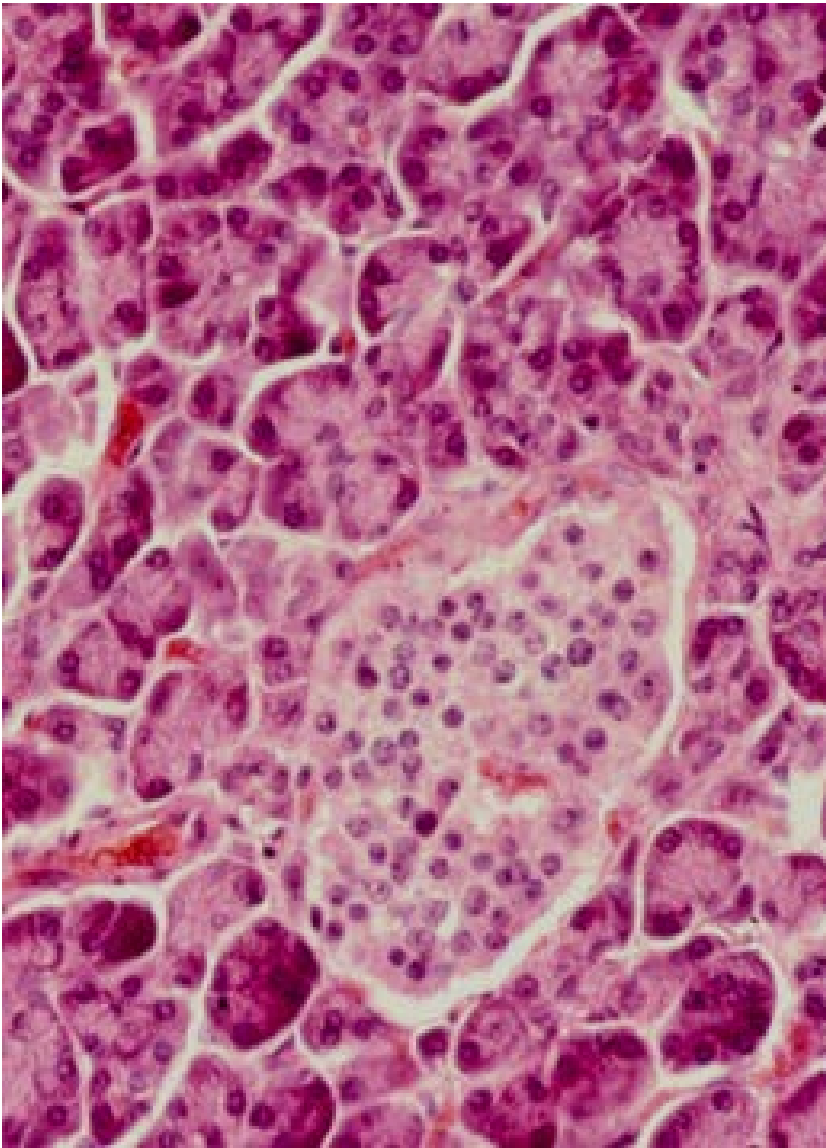


# Pancreatic endocrine tumors

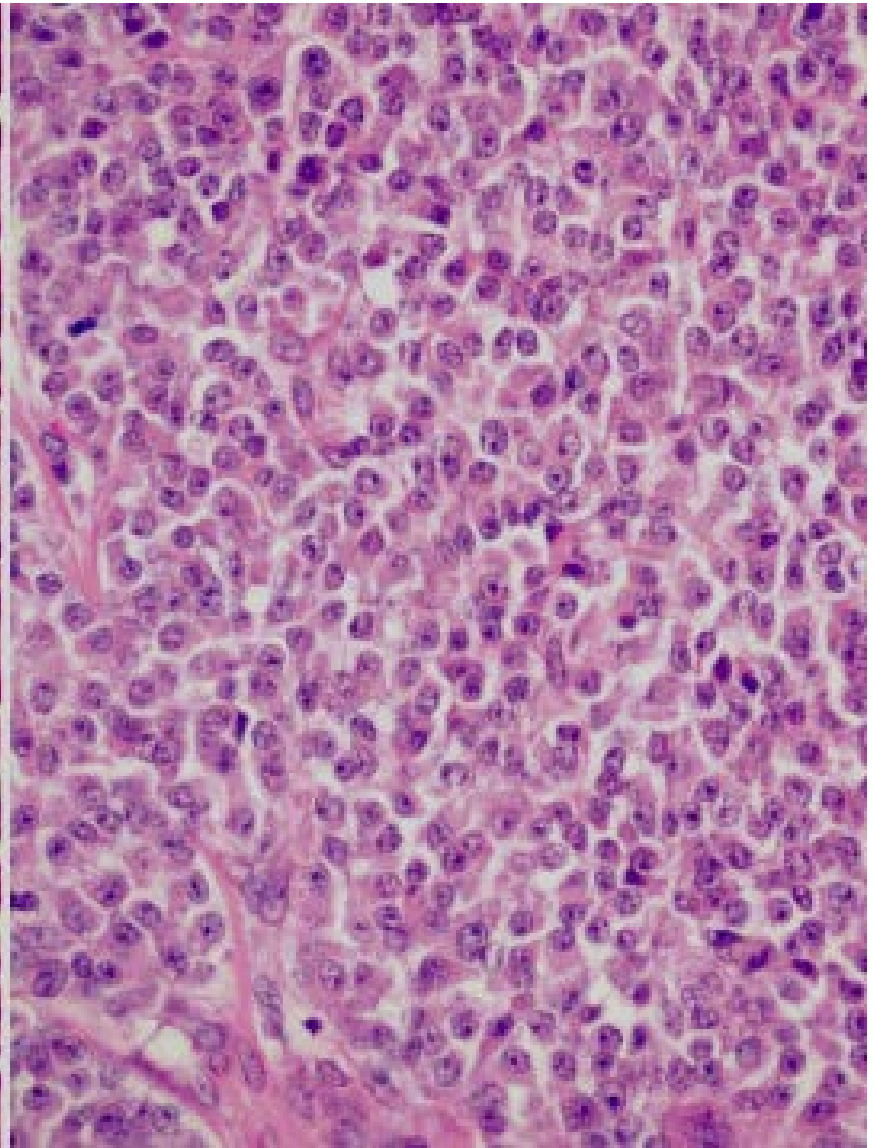
- Islet cell tumors are rare in contrast to carcinoma of the exocrine pancreas
- Have a variable clinical course, including curative resection

# Islet cell tumors

- Non-functional vs. functional
- Malignant when there is metastasis or infiltration of extra pancreatic tissue
- Malignant potential can not be determined by light microscopy (“endocrine anaplasia”)



Non-neoplastic islet cells



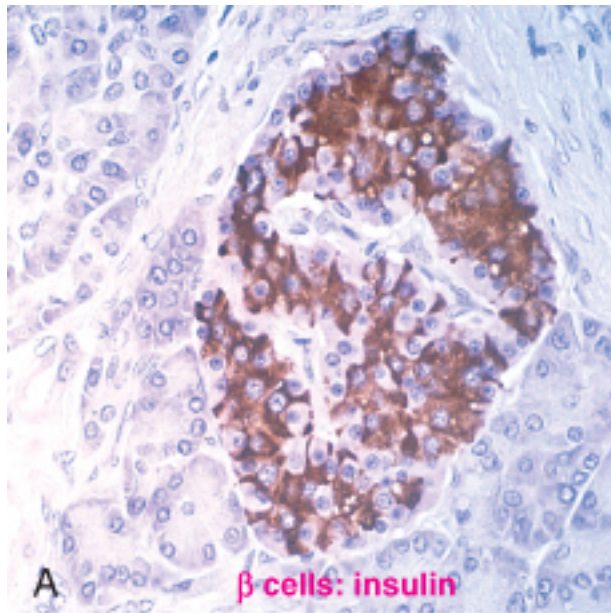
Islet cell tumor

# Characterization of tumors

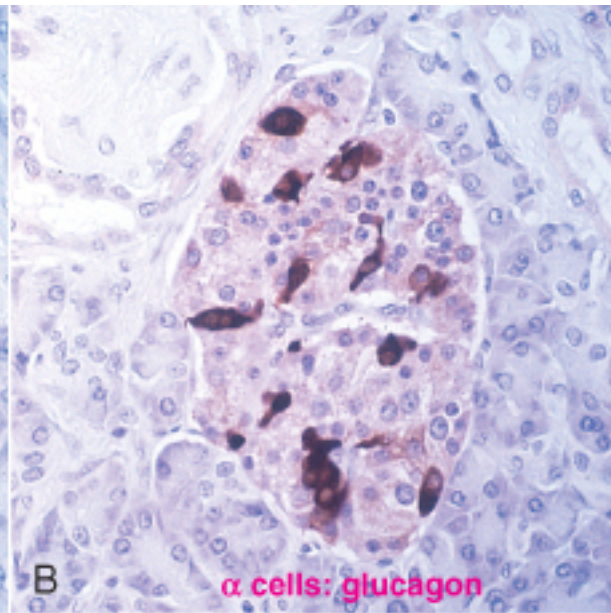
- Radioimmunoassay or immunohistochemistry
  - Insulin
  - Gastrin
  - Glucagon
  - VIP producing
  - Carcinoid tumor
  - ACTH or MSH (rare)
  - Somatostatin
- Tumors producing more than one hormone are common

# Characterization of tumors

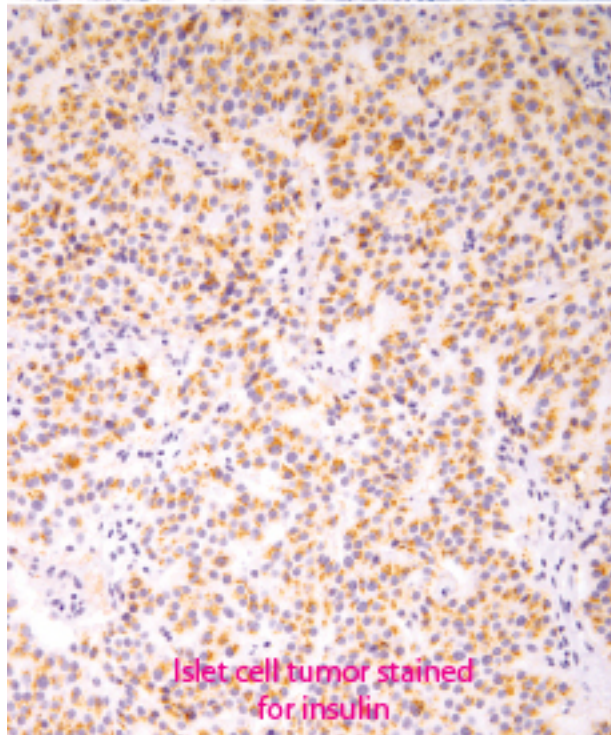
- Clinical syndromes
  - Gastrinomas – Zollinger-Ellison Syndrome (multiple peptic ulcers)
  - Insulinomas – hypoglycemic episodes
  - VIPoma – WDHA (watery diarrhea, hypokalemia, achlorhydria) syndrome
  - Carcinoid (serotonin) – vasomotor (e.g. flushing), GI (e.g. diarrhea), bronchoconstriction



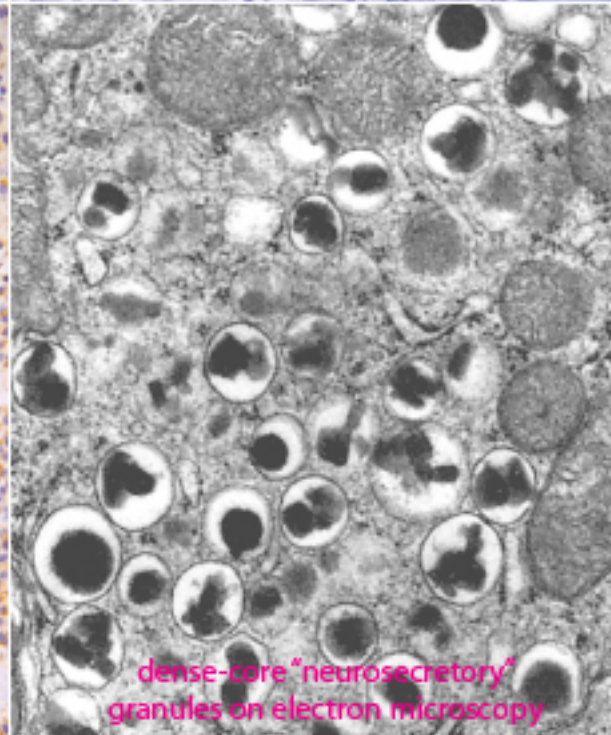
$\beta$  cells: insulin



$\alpha$  cells: glucagon

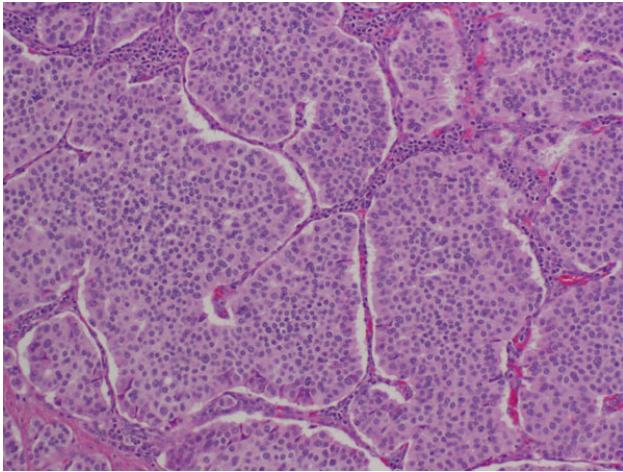


Islet cell tumor stained for insulin



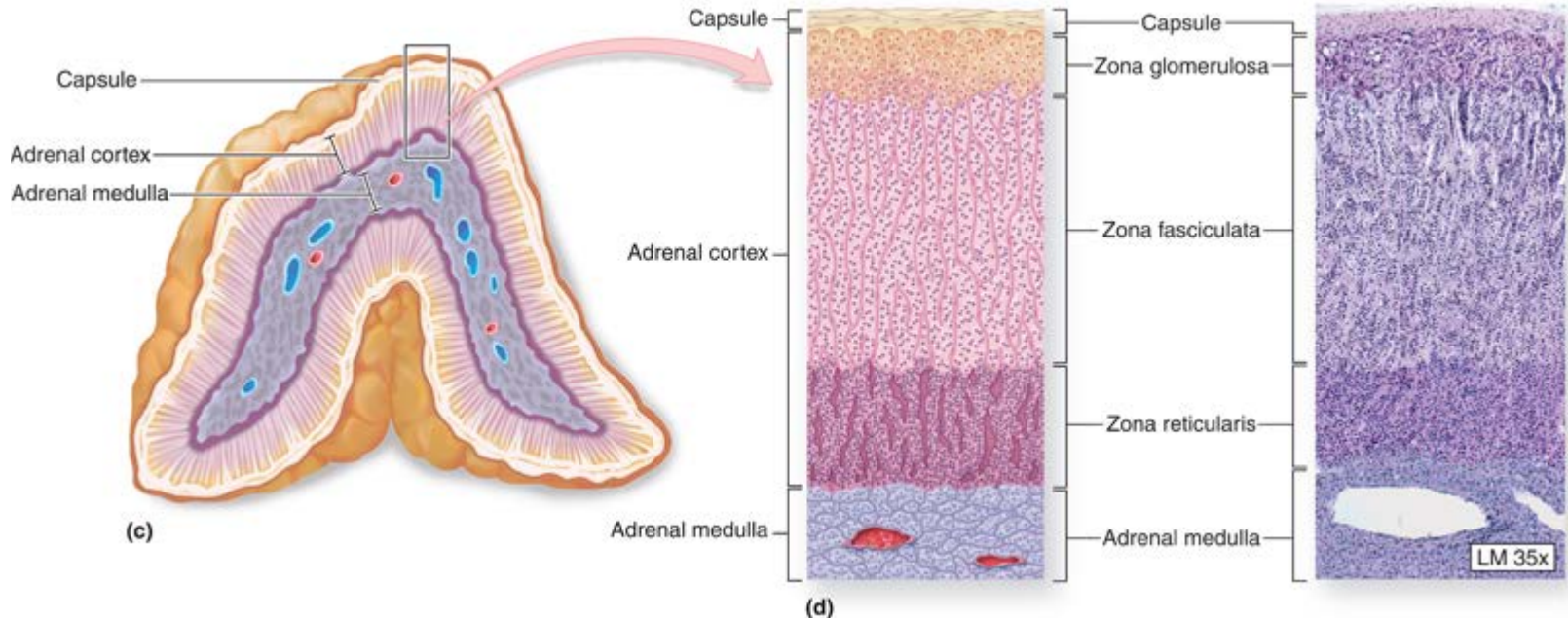
dense-core "neurosecretory" granules on electron microscopy

A pancreatic tumor in a patient with watery diarrhea is resected and shows the following histological appearance. Among the following choices, which is the most likely based upon the symptoms and histology?



- A. Insulinoma
- B. Glucagonoma
- C. VIPoma
- D. Zollinger-Ellison syndrome
- E. Pheochromocytoma

Correct answer: C



*Adrenal glands:* paired endocrine organs consisting of both cortex and medulla

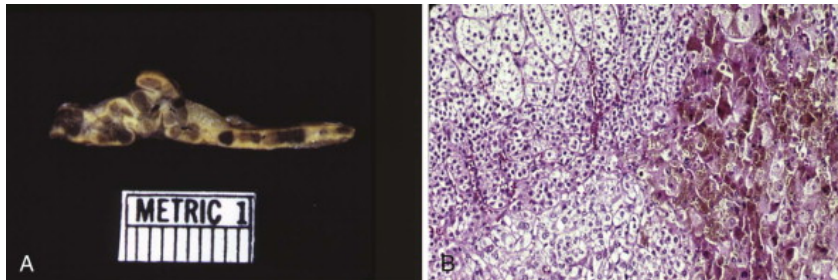
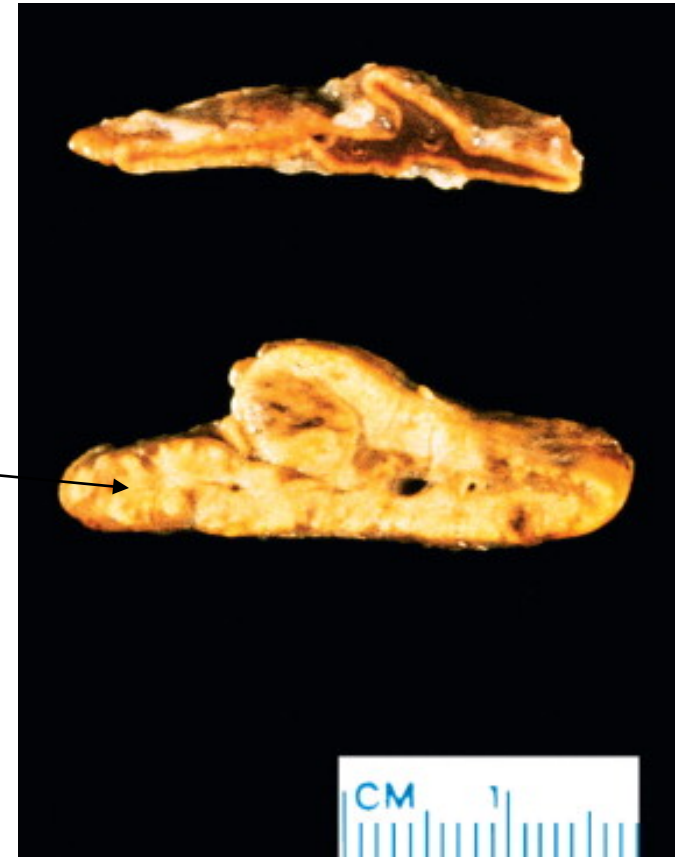
Diseases of the adrenal cortex can be conveniently divided into those associated with **hyperfunction** vs. **hypofunction**

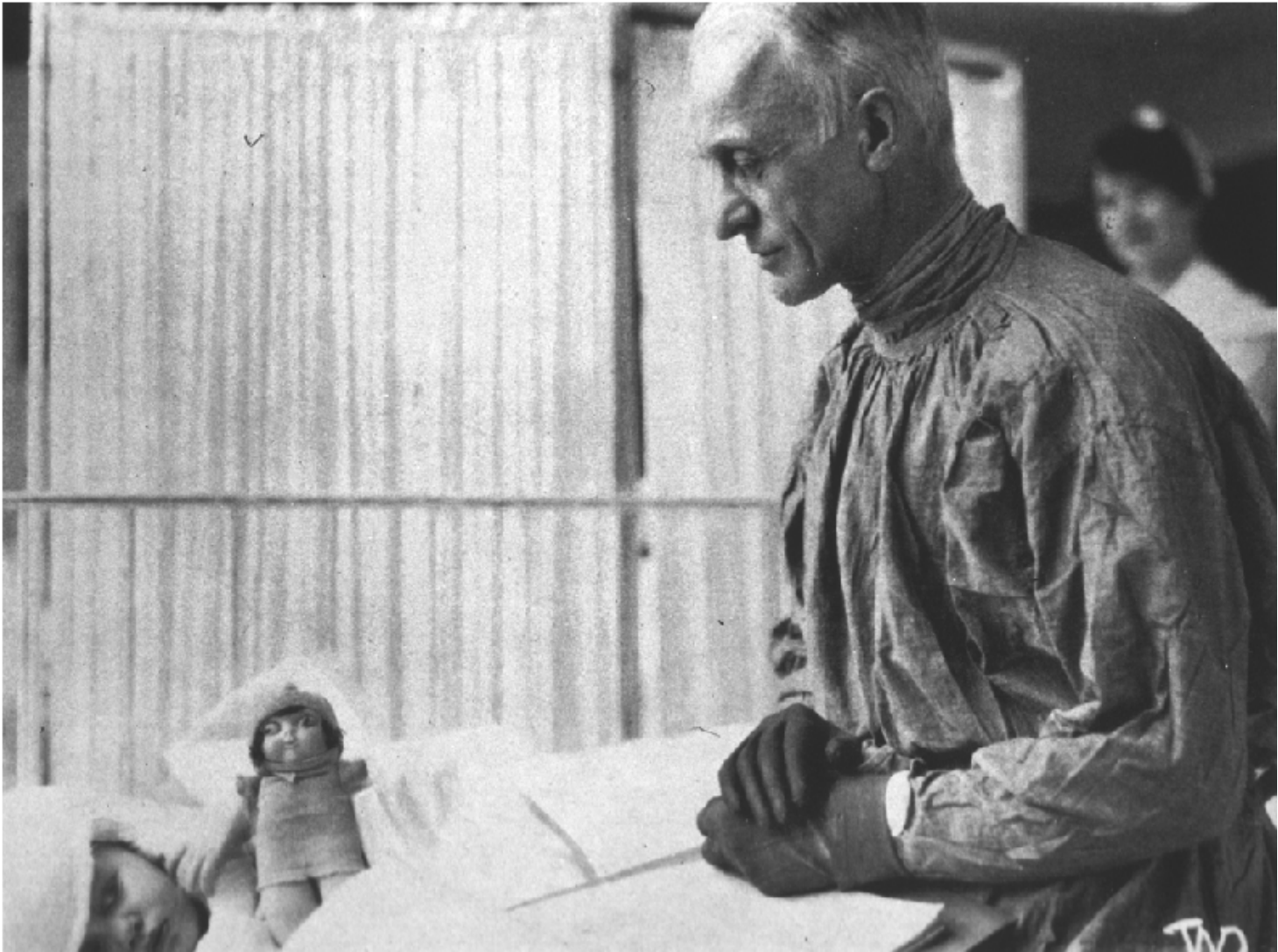


# Adrenal hyperfunction

Depending on the cause of the hypercortisolism the **adrenals** have one of the following abnormalities:

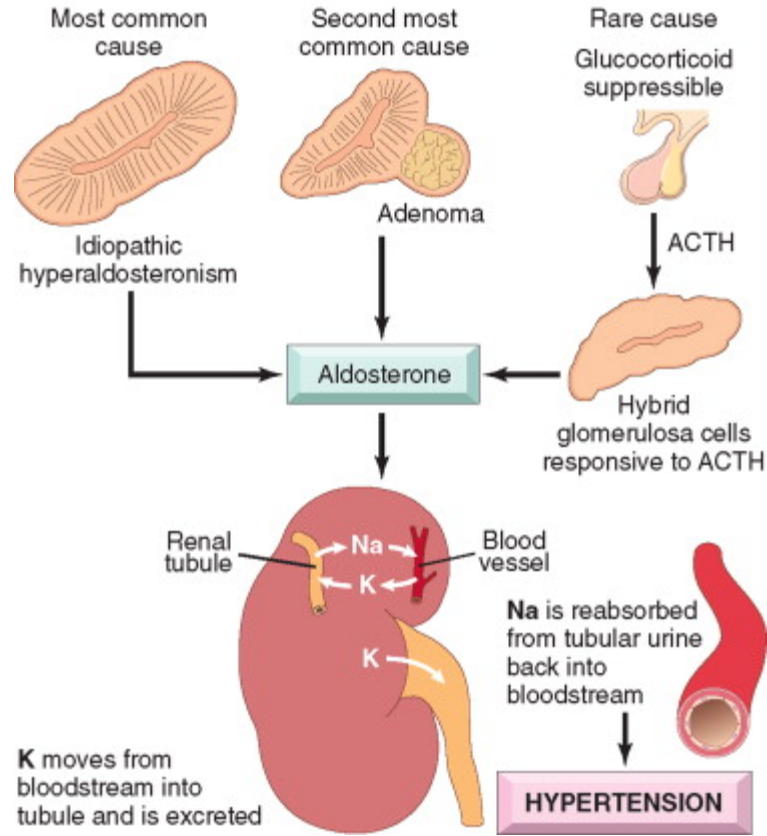
1. cortical atrophy
2. diffuse hyperplasia
3. macronodular or micronodular hyperplasia, and
4. an adenoma or carcinoma





Harvey Cushing

## PRIMARY HYPERALDOSTERONISM



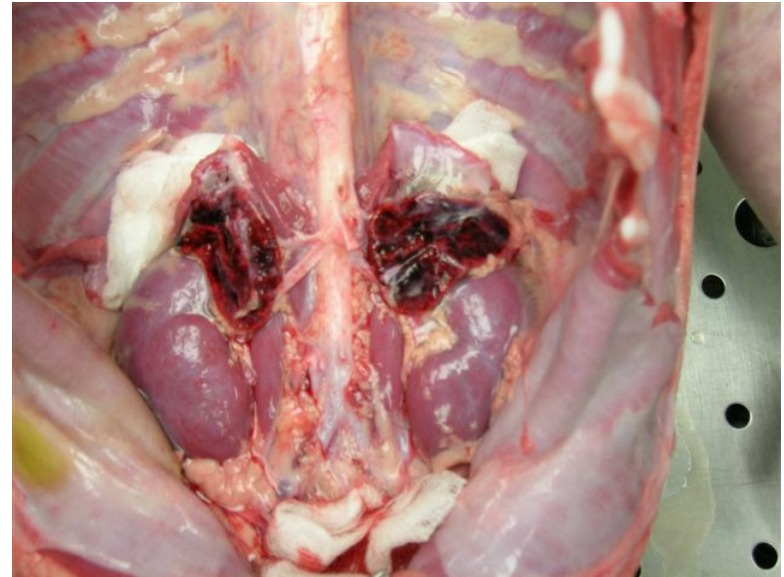
**Aldosterone-producing adenomas** are almost always solitary, small (<2 cm in diameter), well-circumscribed lesions, more often found on the left than on the right. They tend to occur in the 30s and 40s, and in women more often than in men.

# Adrenal hypofunction/insufficiency

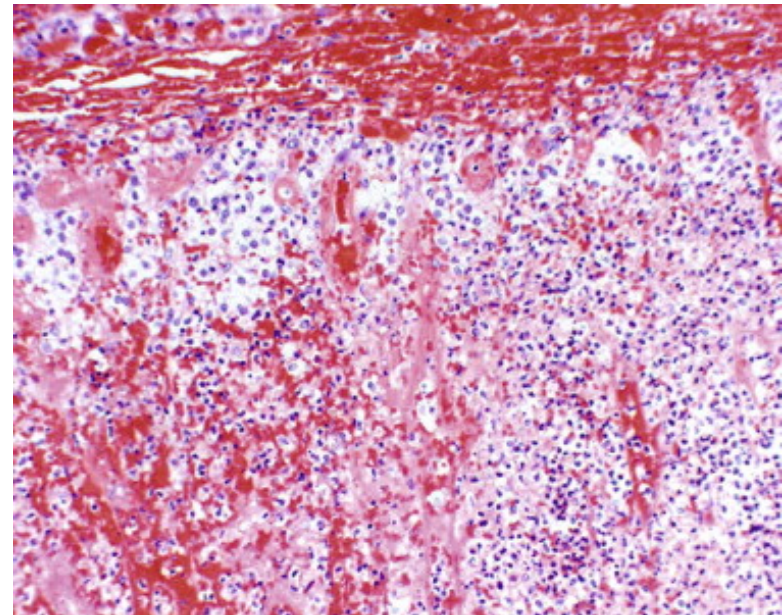
- May be caused by either primary adrenal disease (primary hypoadrenalism) or decreased stimulation of the adrenals due to a deficiency of ACTH (secondary hypoadrenalism)
- The patterns of adrenocortical insufficiency:
  1. primary *acute* adrenocortical insufficiency (adrenal crisis)
  2. primary *chronic* adrenocortical insufficiency (*Addison disease*)
  3. secondary adrenocortical insufficiency.

## Primary acute adrenocortical insufficiency

1. In patients maintained on exogenous corticosteroids, in whom *rapid withdrawal of steroids* or failure to increase steroid doses in response to an acute stress may precipitate an adrenal crisis, as a result of the inability of the atrophic adrenals to produce glucocorticoid hormones
2. As a result of *massive adrenal hemorrhage*, which damages the adrenal cortex sufficiently to cause acute adrenocortical insufficiency—as occurs in newborns following prolonged and difficult delivery with considerable trauma and hypoxia. Newborns are particularly vulnerable because they are often deficient in prothrombin for at least several days after birth
3. It also occurs in some patients maintained on anticoagulant therapy, in postsurgical patients who develop disseminated intravascular coagulation and consequent hemorrhagic infarction of the adrenals, and as a complication of bacteremic infection; in this last setting, it is called *Waterhouse-Friderichsen syndrome*



*Waterhouse-Friderichsen syndrome*



# Primary chronic adrenocortical insufficiency (Addison disease)

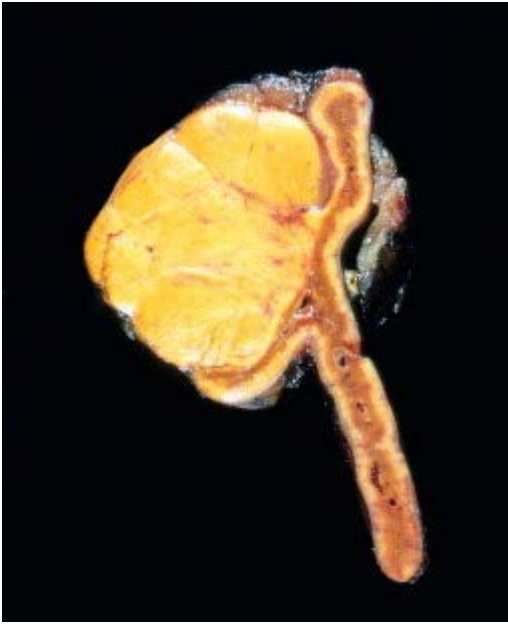
A large number of diseases may affect the adrenal cortex, including:

- Lymphomas
  - Amyloidosis
  - Sarcoidosis
  - Hemochromatosis
  - Fungal infections
  - Adrenal hemorrhage
- 
- More than 90% of all cases are attributable to one of four disorders: *autoimmune adrenalitis, tuberculosis, AIDS, or metastatic cancers*

# Adrenal cortical tumors

- Functional adrenal neoplasms may be responsible for any of the various forms of hyperadrenalism
- Adenomas and carcinomas are about equally common in adults; in children, carcinomas predominate
- While most cortical neoplasms are sporadic, two familial cancer syndromes are associated with a predisposition for developing adrenocortical carcinomas:
  - Li-Fraumeni syndrome: germline *p53* mutations
  - Beckwith-Wiedemann syndrome: an imprinting disorder
- *Functional adenomas are most commonly associated with hyperaldosteronism and Cushing syndrome, whereas a virilizing neoplasm is more likely to be a carcinoma*
- Not all adrenocortical neoplasms elaborate steroid hormones
- *Functional and nonfunctional adrenocortical neoplasms cannot be distinguished on the basis of morphologic features*

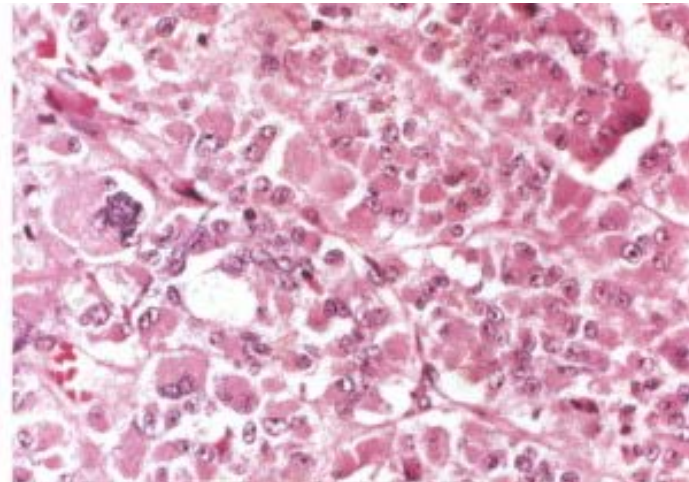
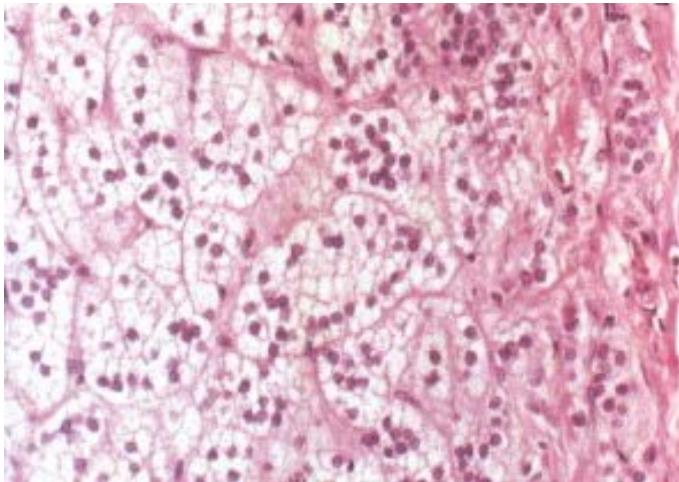




Adrenal cortical adenoma



Adrenal cortical carcinoma



A 4 year old boy experiences the sudden onset of fever, irritability, and a purpuric rash. He becomes unresponsive and upon evaluation in an emergency room is noted to have a blood pressure of 75/40. Which of the following conditions is most likely to be occurring in this clinical scenario?

- A. Addison disease
- B. Cushing syndrome
- C. Waterhouse-Friderichsen syndrome
- D. Diabetic ketoacidosis
- E. Hemophilia

Correct answer: C