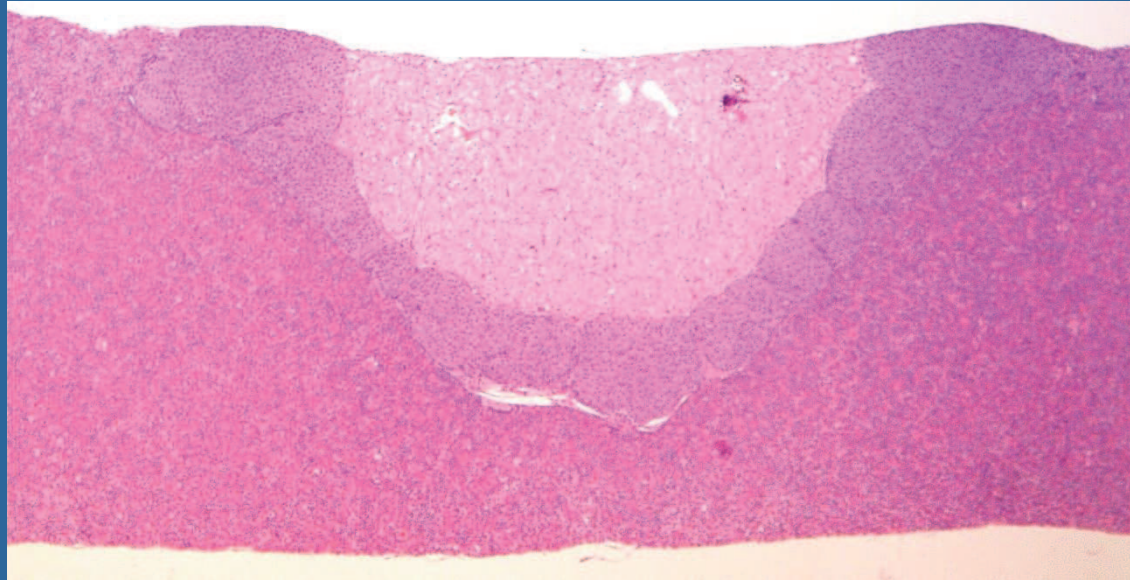


# PITUITARY IN PRECLINICAL TOXICOLOGY



**Dr. S. K. Vijayasarithi**  
**Head, Pathology**  
**Advinus, Bangalore**

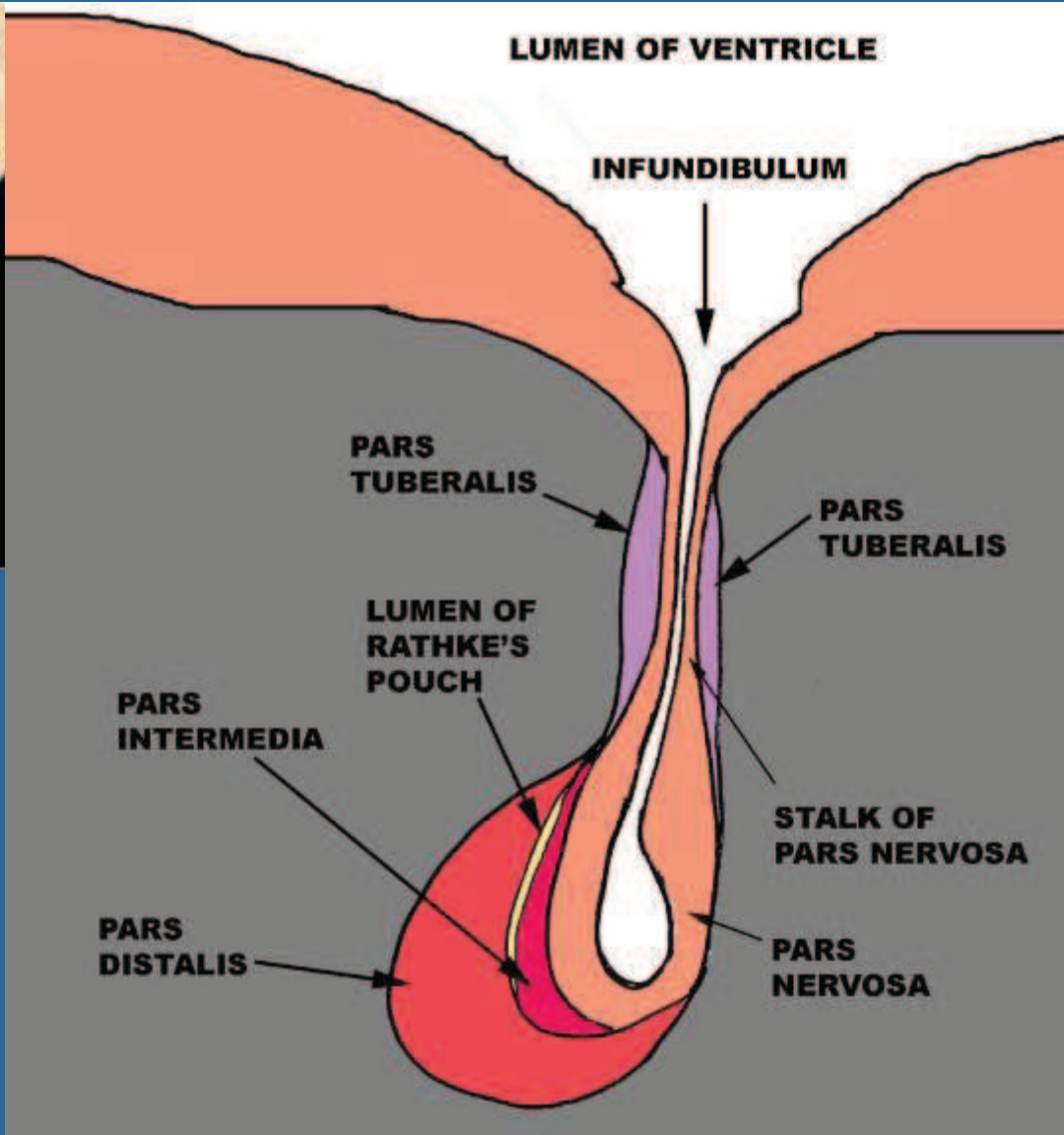
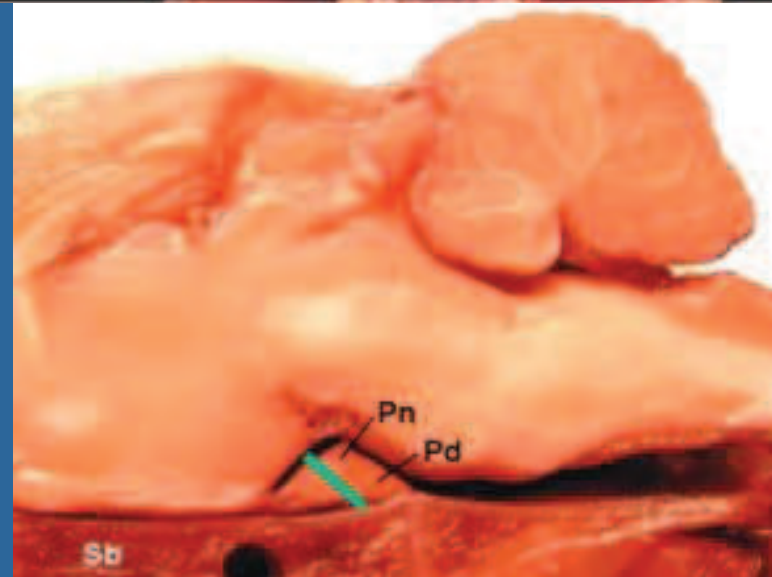
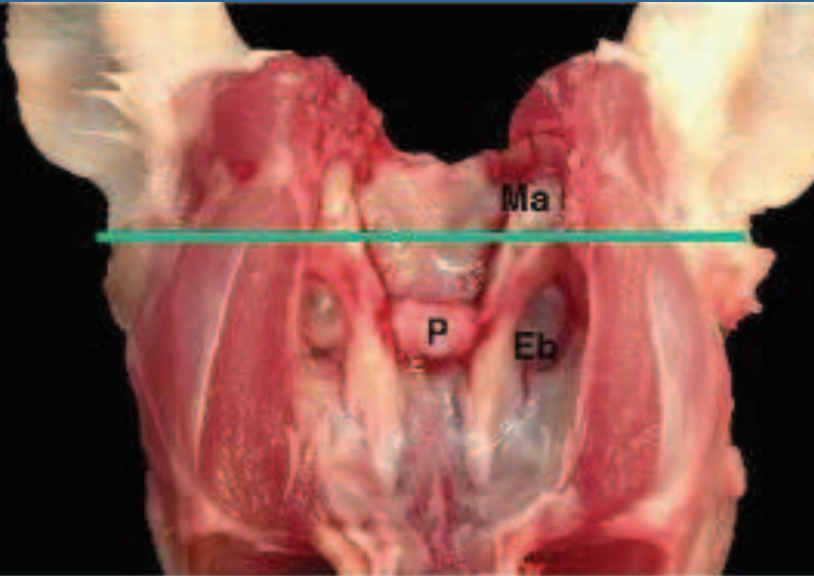


# Disclaimer

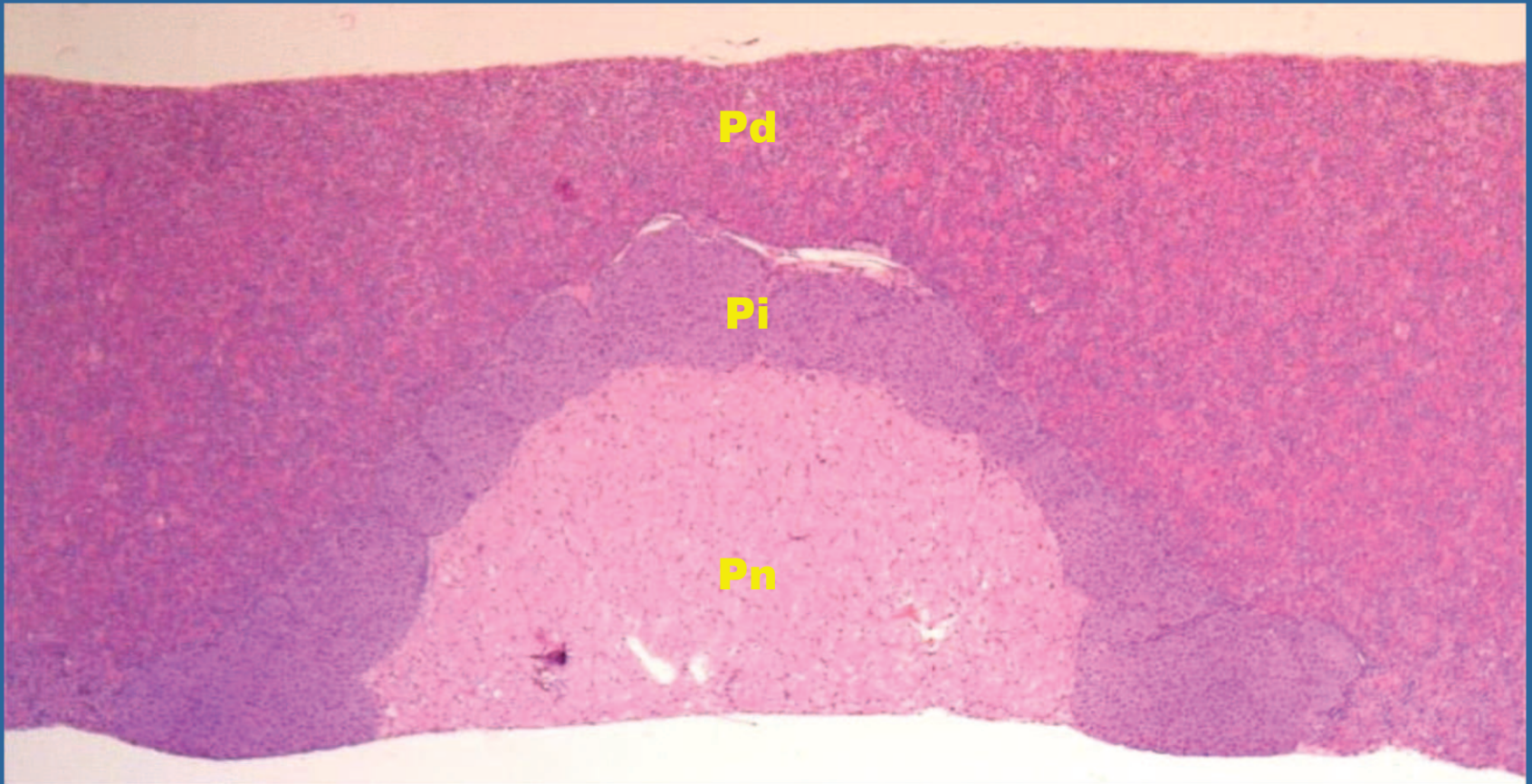
**The ideas and thoughts expressed in this presentation are purely that of the presenter and do not necessarily reflect the thinking of the organization or represented by the presenter.**



# Anatomy and Histology

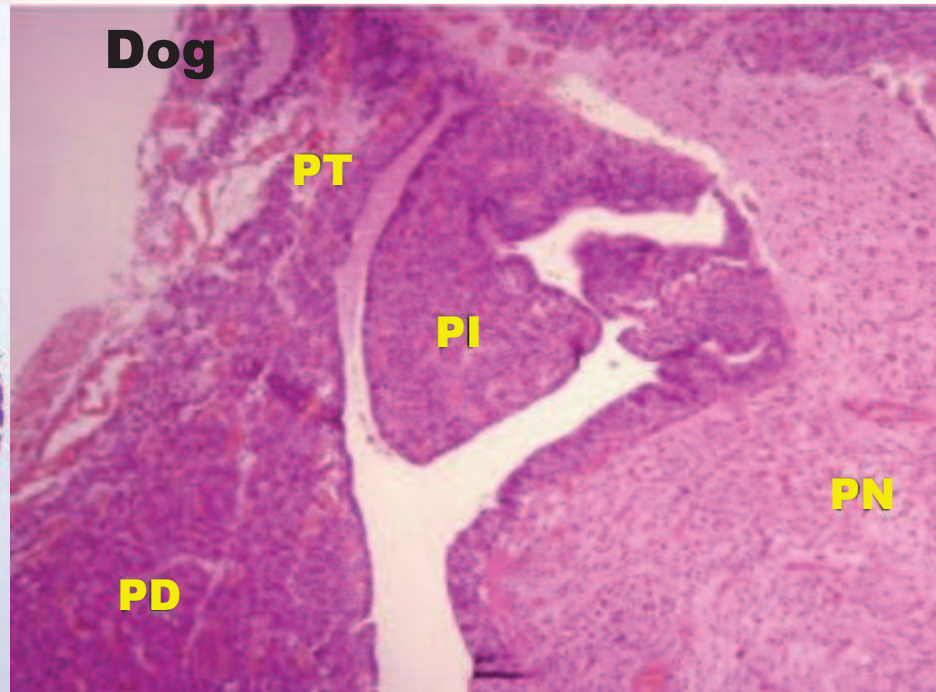
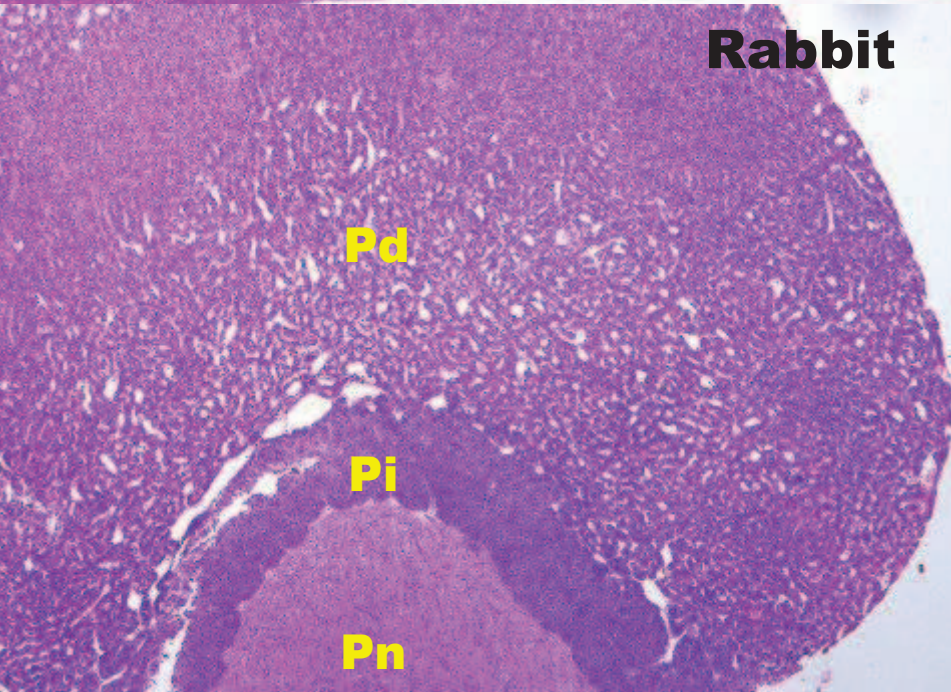
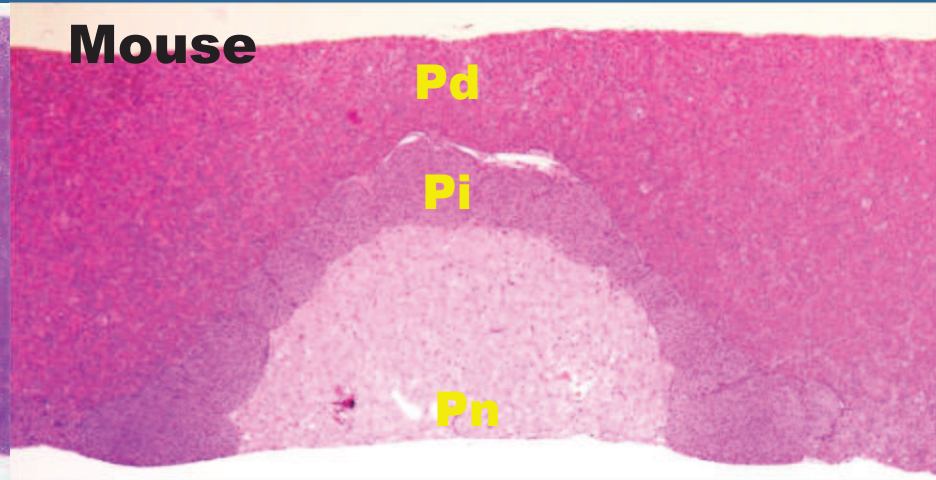
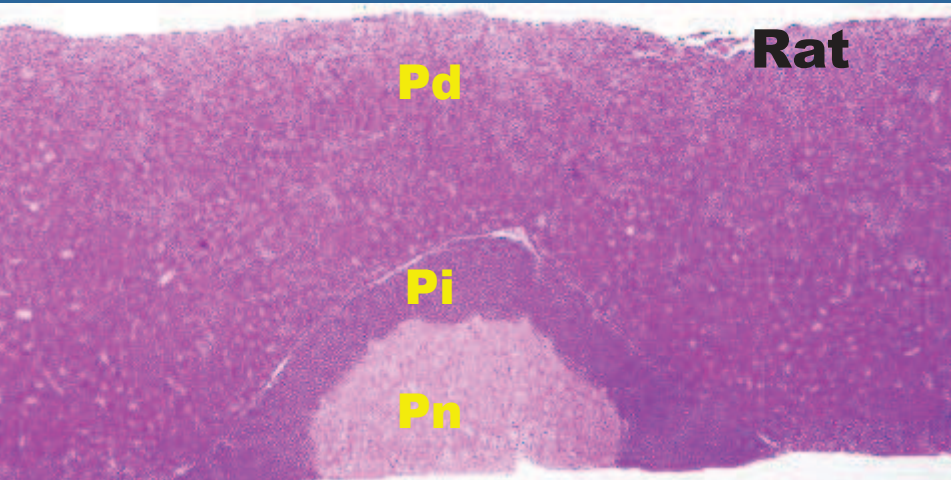


# Normal Pituitary Gland

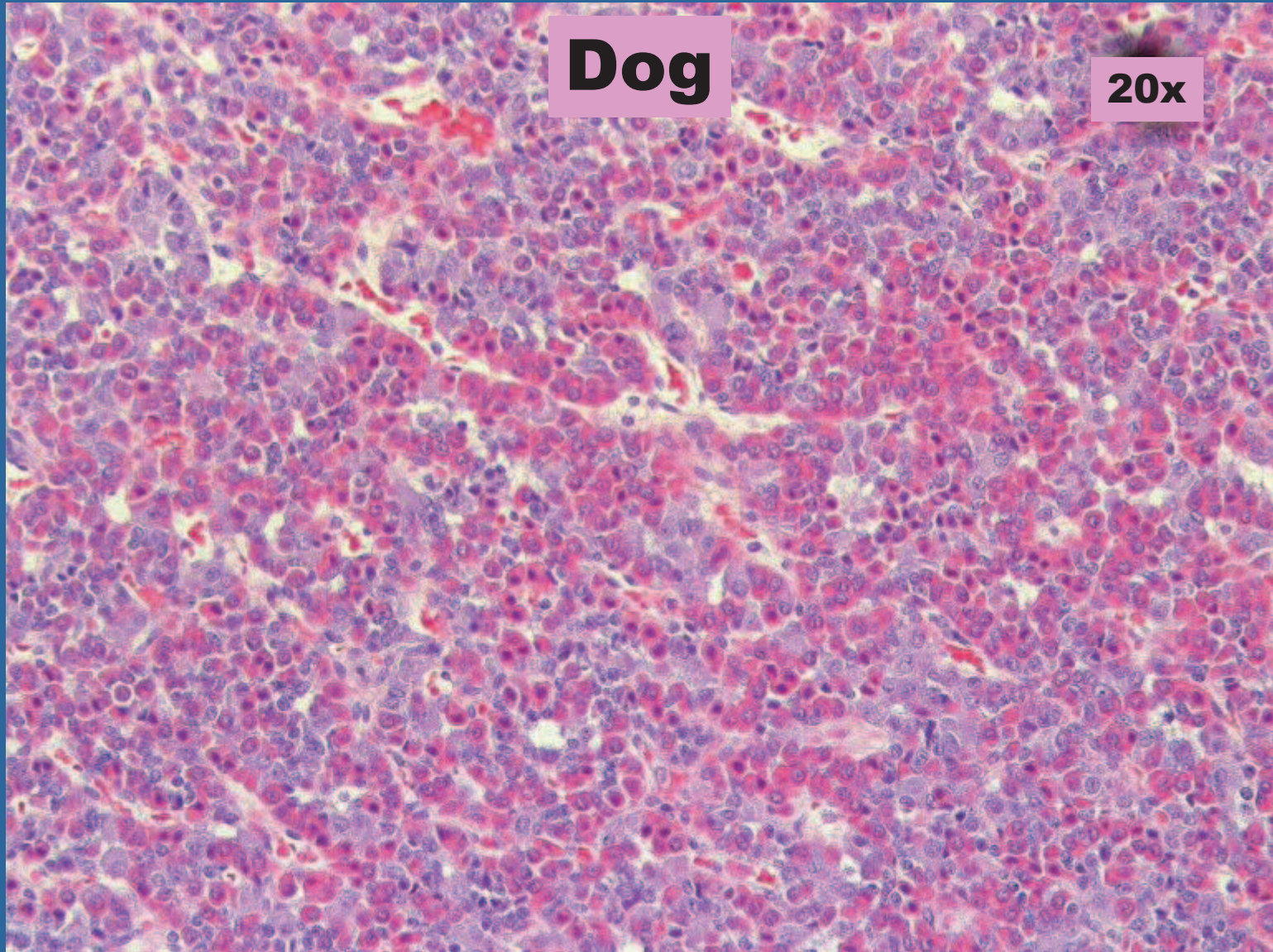


**Pn: pars nervosa, Pi: pars intermedia, Pd: pars distalis**

# Histology Comparison

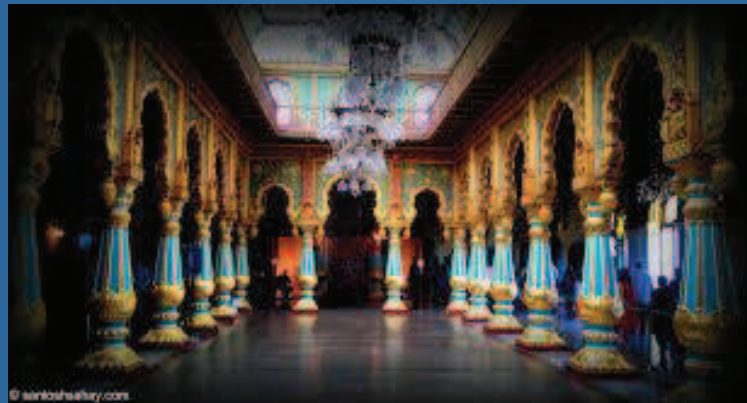
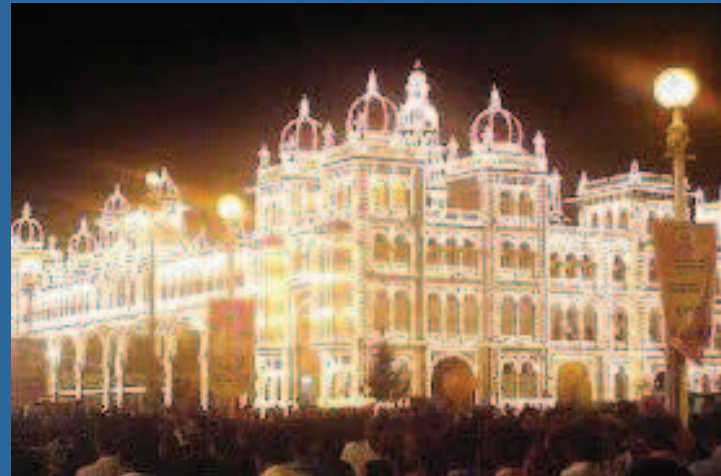


# Histology Comparison



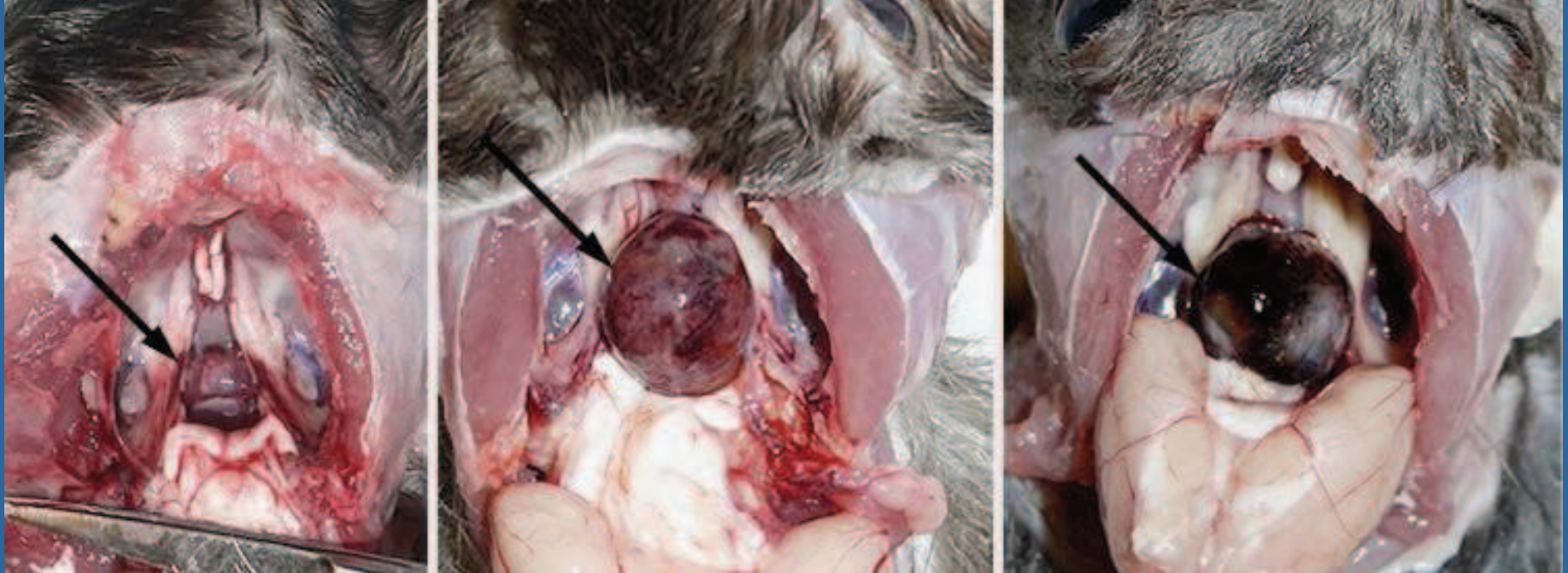
# Pituitary Gross Lesions

- ✓ **Discoloration**
- ✓ **Focus/foci**
- ✓ **Enlarged**
- ✓ **Mass**





# Gross Lesions



# Common Histopathological Findings



## ➤ NON-PROLIFERATIVE LESIONS

### ➤ Congenital changes

- ✓ Dilatation/Persistence of Rathke's Pouch / Cleft
- ✓ Stomatodeal remnants in neurohypophysis

### ➤ Vascular changes

- ✓ Hemangiectasis
- ✓ Hemorrhage
- ✓ Thrombosis

### ➤ Inflammatory changes

- ✓ Inflammation

### ➤ Miscellaneous changes

- ✓ Cysts/Hemocyst



## ➤ **PROLIFERATIVE LESIONS**

### □ **Pars Distalis**

- ✓ **Focal hypertrophy**
- ✓ **Focal hyperplasia**
- ✓ **Adenoma**
- ✓ **Carcinoma**

### □ **Pars Intermedia**

- ✓ **Hyperplasia**
- ✓ **hypertrophy**
- ✓ **Adenoma**

### □ **Pars Nervosa**

- ✓ **Pituicytoma**

## ➤ **Tumor of Embryonic Remnant**

- ✓ **Craniopharyngioma**



# Induced Lesions

## □ **Pars Distalis/Pars Intermedia**

- ✓ **Hypertrophy/hyperplasia**
- ✓ **Atrophy**
- ✓ **Increased no. of vacuolated cells**

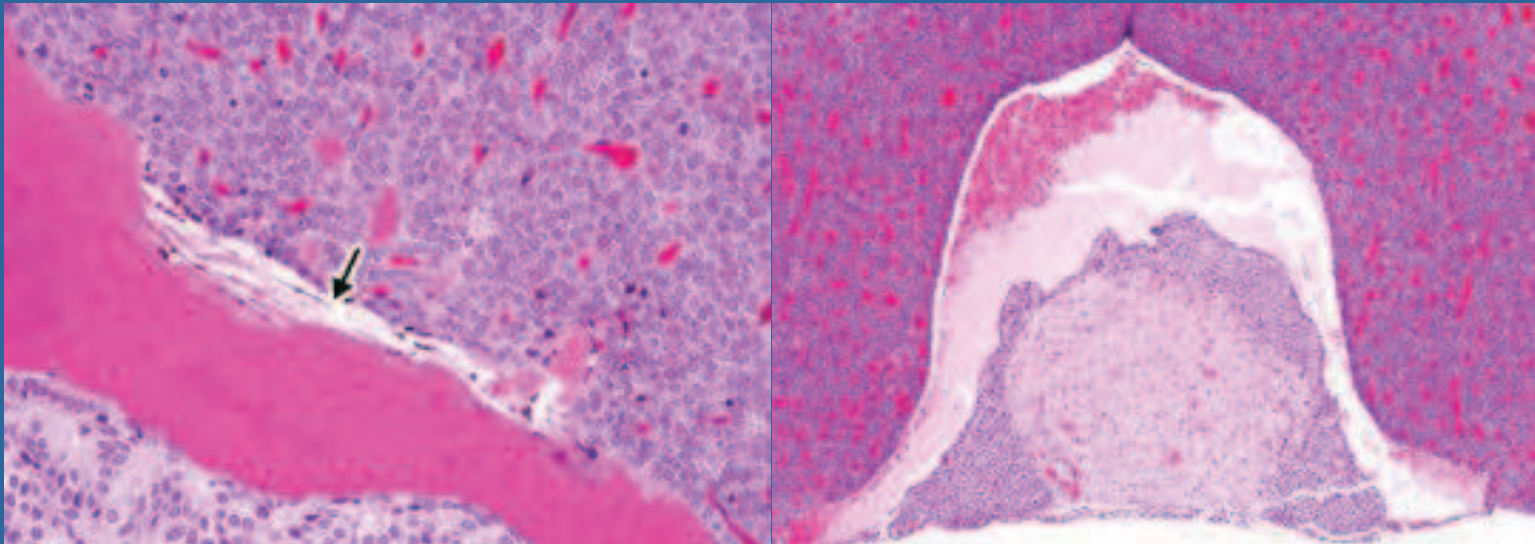


# Congenital changes

## ➤ **Dilatation/Persistence of Rathke's Pouch / Cleft**

- ✓ **May be located in pars distalis, pars intermedia, or pars nervosa**
- ✓ **Often associated with Rathke's cleft**
- ✓ **Epithelial lining is usually ciliated but can be squamous, cuboidal, or columnar – occasional lesion**

# Congenital changes

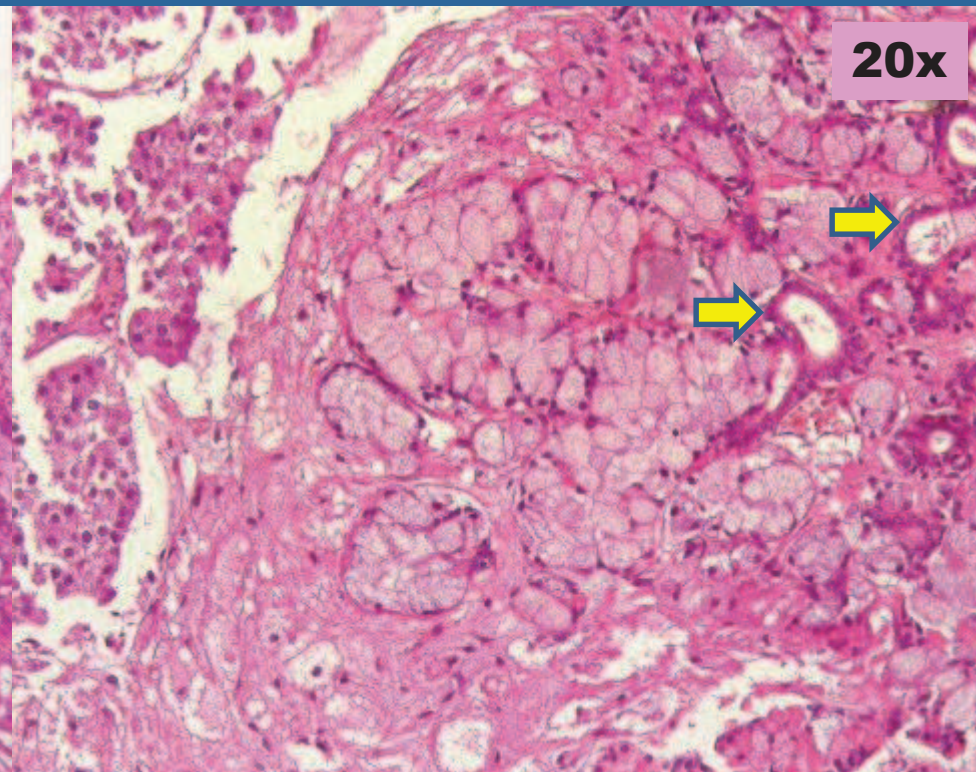
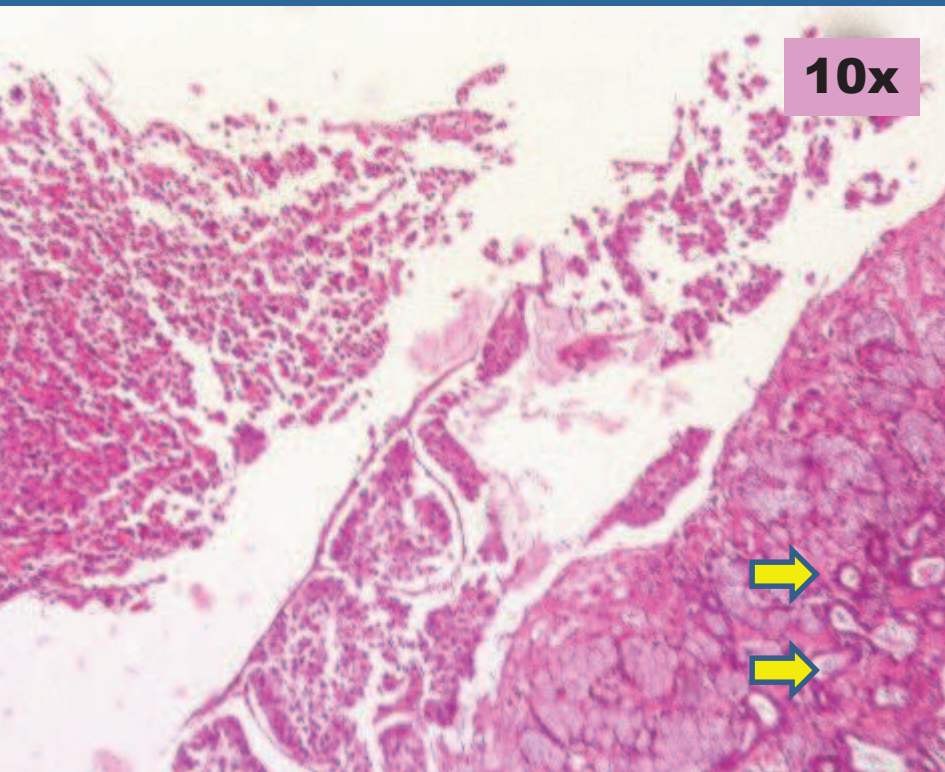


**Persistence of Rathke's Pouch**

# Congenital changes

- **Stomatodeal remnants in neurohypophysis**
  - ✓ **Consisting of duct like structure of varying sizes**
  - ✓ **Lined by cuboidal/columnar type of epithelium**
  - ✓ **Occasionally lumen may contains secretions**

# Congenital changes



**Stomatodeal remnants in neurohypophysis**

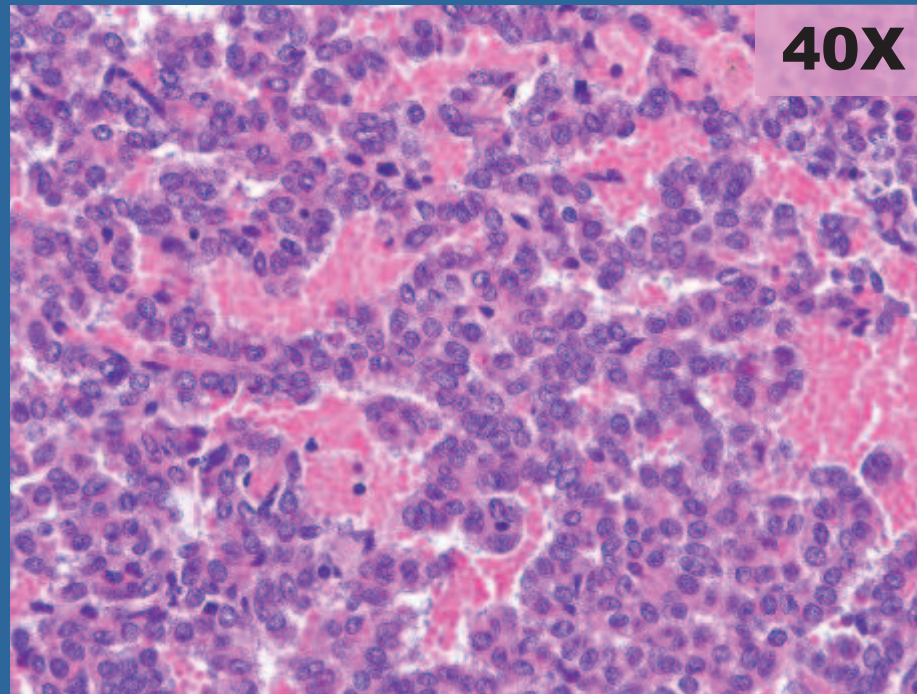


# Vascular changes

## ➤ Hemangiectasis

- ✓ Dilated, blood-filled spaces lined by endothelium
- ✓ Usually present in pars distalis
- ✓ May be accompanied by proteinaceous fluid or hemorrhage

# Vascular changes



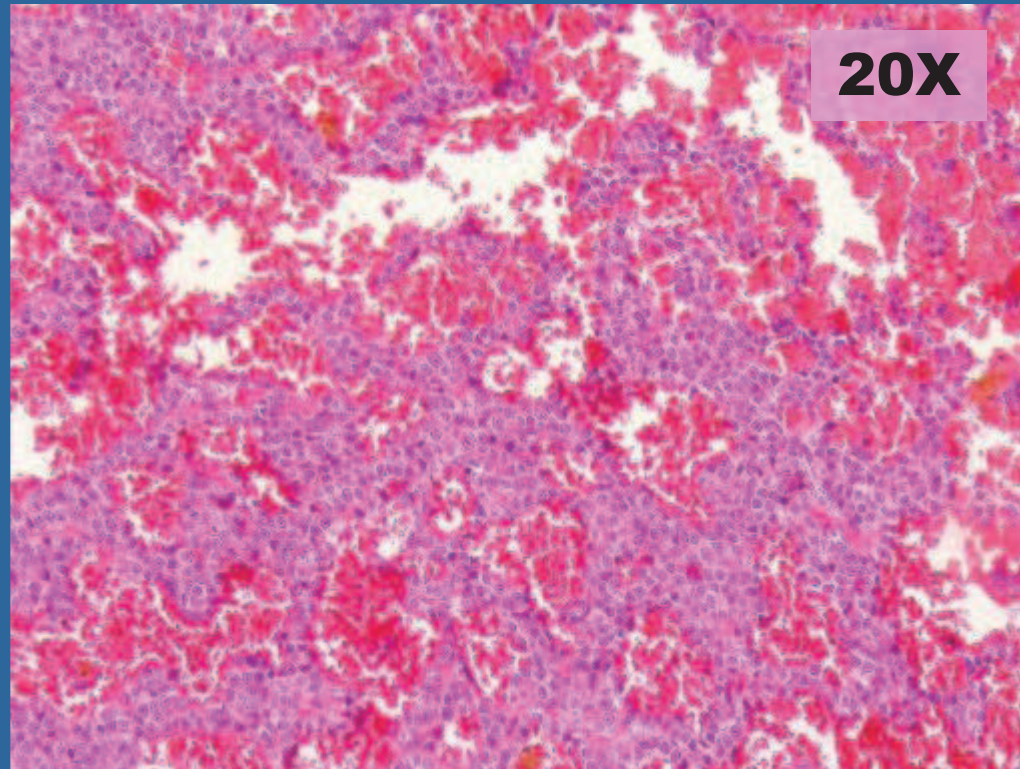
**Hemangiectasis**

# Vascular changes

## ➤ Hemorrhage

- ✓ **Free erythrocytes outside of vascular channels**
- ✓ **May be accompanied by hemosiderin-laden macrophages, cholesterol clefts, and fibrosis if long-standing**

# Vascular changes



**Hemorrhage - pars distalis**

# Vascular changes

## ➤ Thrombosis

- ✓ Solid mass within lumen of blood vessels
- ✓ Composed of fibrin and platelets, and may contain trapped erythrocytes



# Inflammatory changes

## ➤ Inflammation - Rare

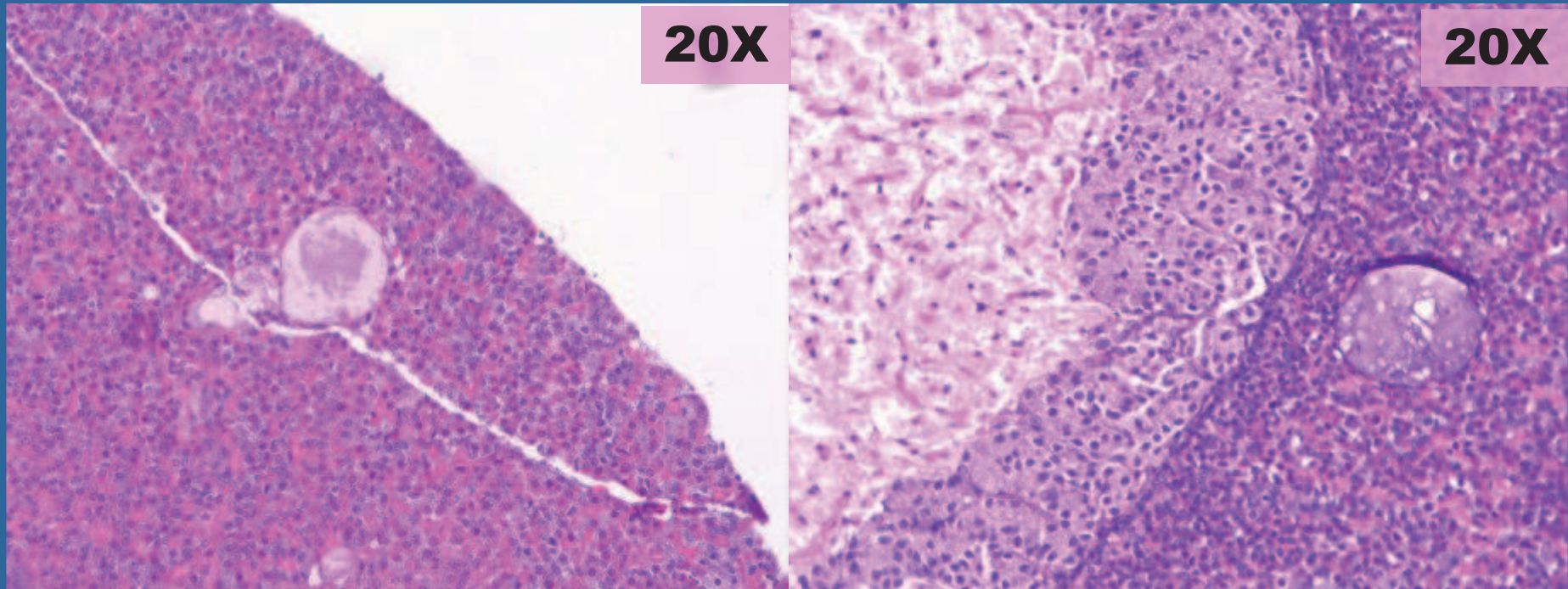
- ✓ Inflammatory cellular infiltrate
- ✓ In acute cases, inflammatory cells are predominantly neutrophils
- ✓ In chronic cases, inflammatory cells are plasma cells and lymphocytes
- ✓ Cell degeneration or loss

# Miscellaneous changes

## ➤ **Cysts/hemocyst**

- ✓ **Simple or multilocular**
- ✓ **Common in pars distalis**
- ✓ **Usually contain eosinophilic to amphophilic mucoproteinaceous material**
- ✓ **Single layer of cuboidal to columnar epithelium**
- ✓ **Epithelial lining is generally ciliated and contain mucous cells**

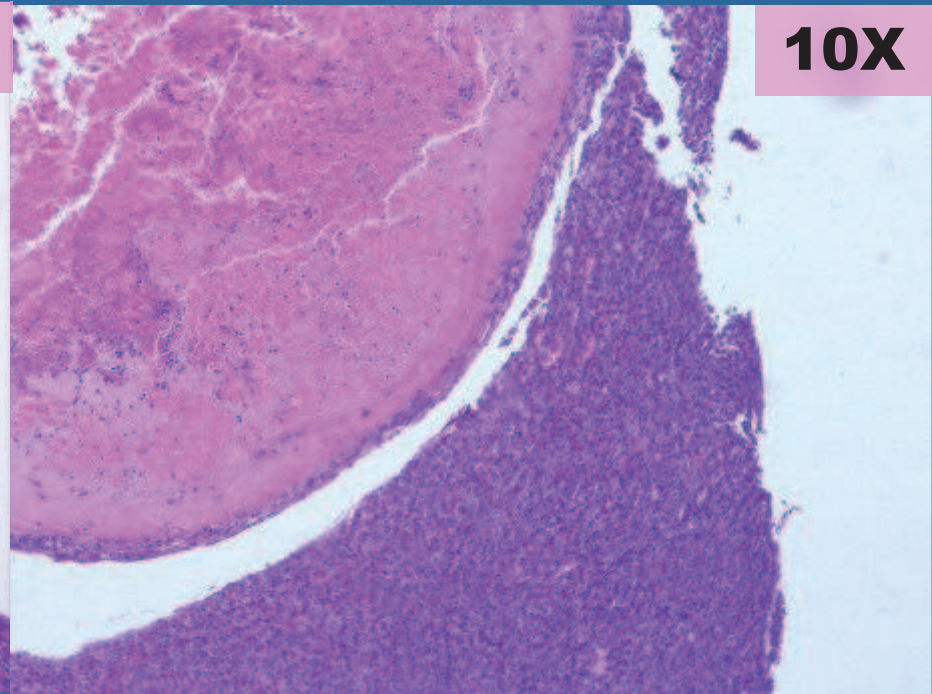
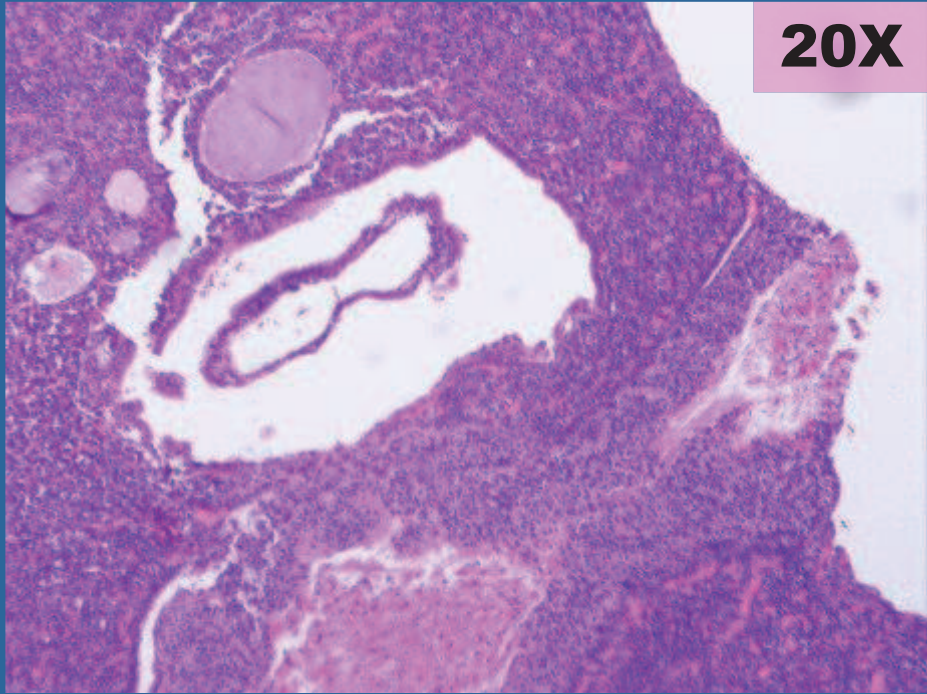
# Miscellaneous changes



**Cyst**



# Miscellaneous changes



**Multiple Cyst**

**Hemocyst**



# PROLIFERATIVE LESIONS



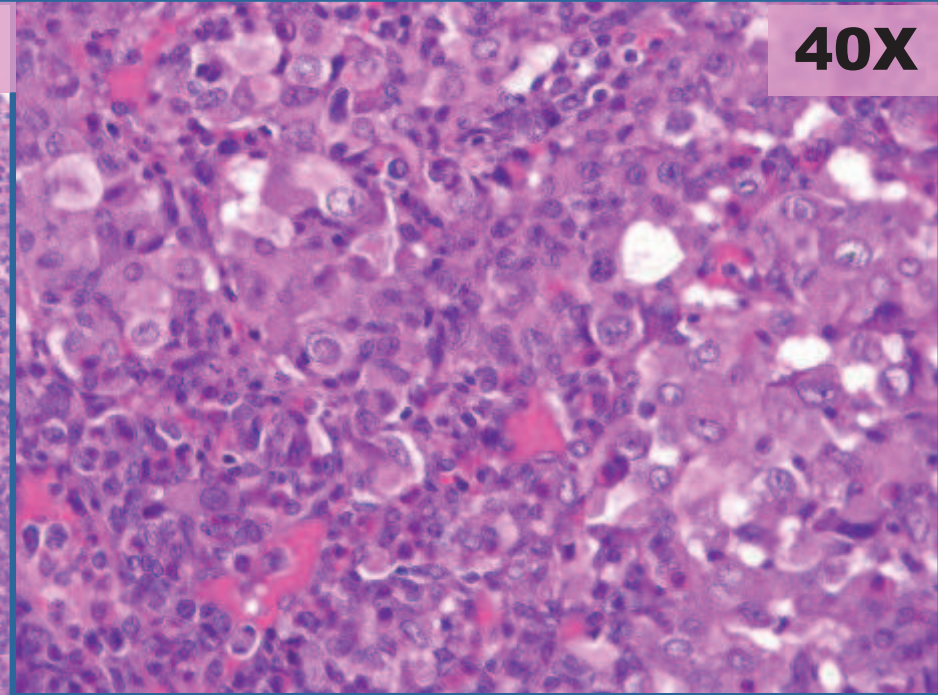
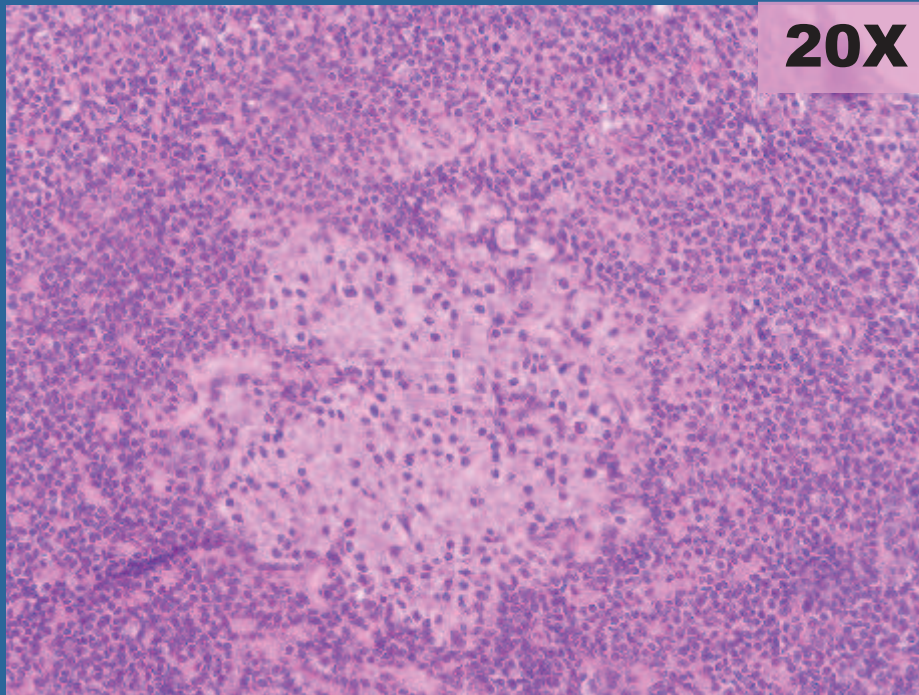
- **In routine long-term rat studies neoplasms of the pituitary gland are among the most commonly encountered in most strains**
- **The vast majority of these neoplasms occurs in the pars distalis**

# PARS DISTALIS

## ➤ **Focal hypertrophy**

- ✓ **Slightly delineated focus or area**
- ✓ **No apparent compression**
- ✓ **Indistinct borders**
- ✓ **Cells enlarged due to increase in eosinophilic cytoplasm-droplets or vacuoles**
- ✓ **Nuclei normal or enlarged**

# PARS DISTALIS



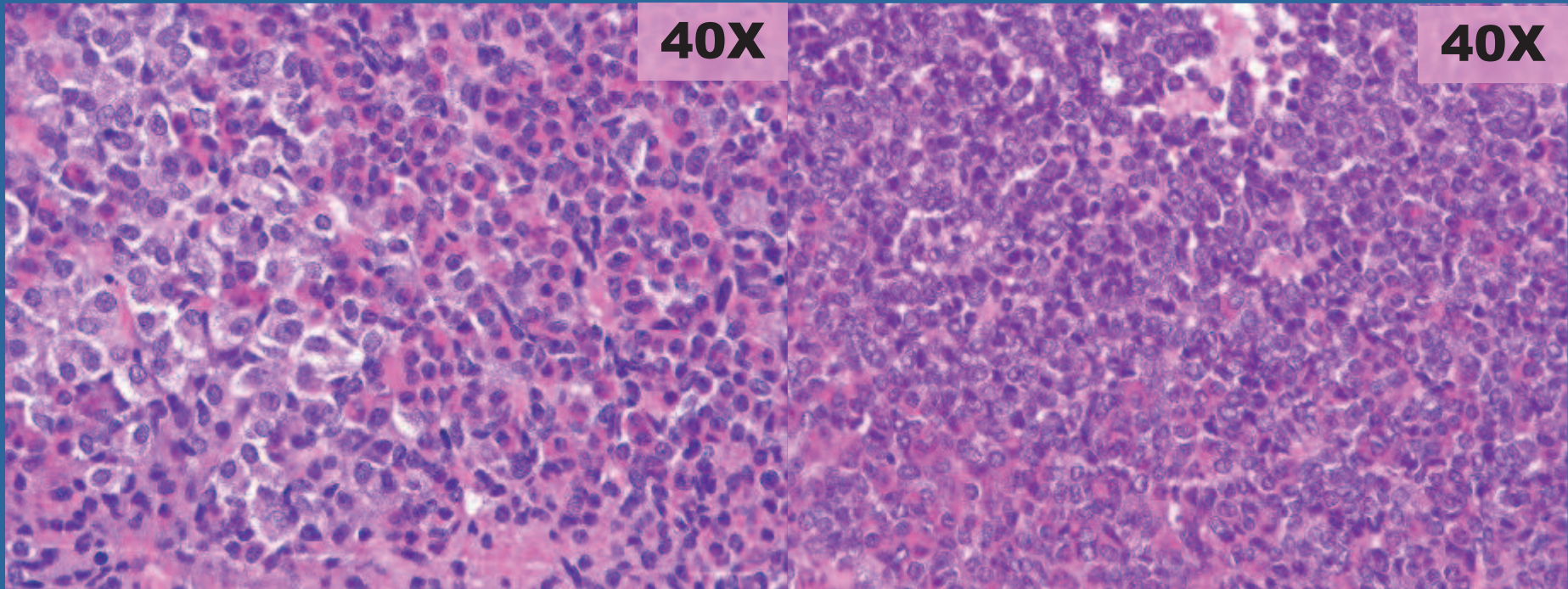
**Focal hypertrophy- Pars distalis**

# PARS DISTALIS

## ➤ **Focal hyperplasia**

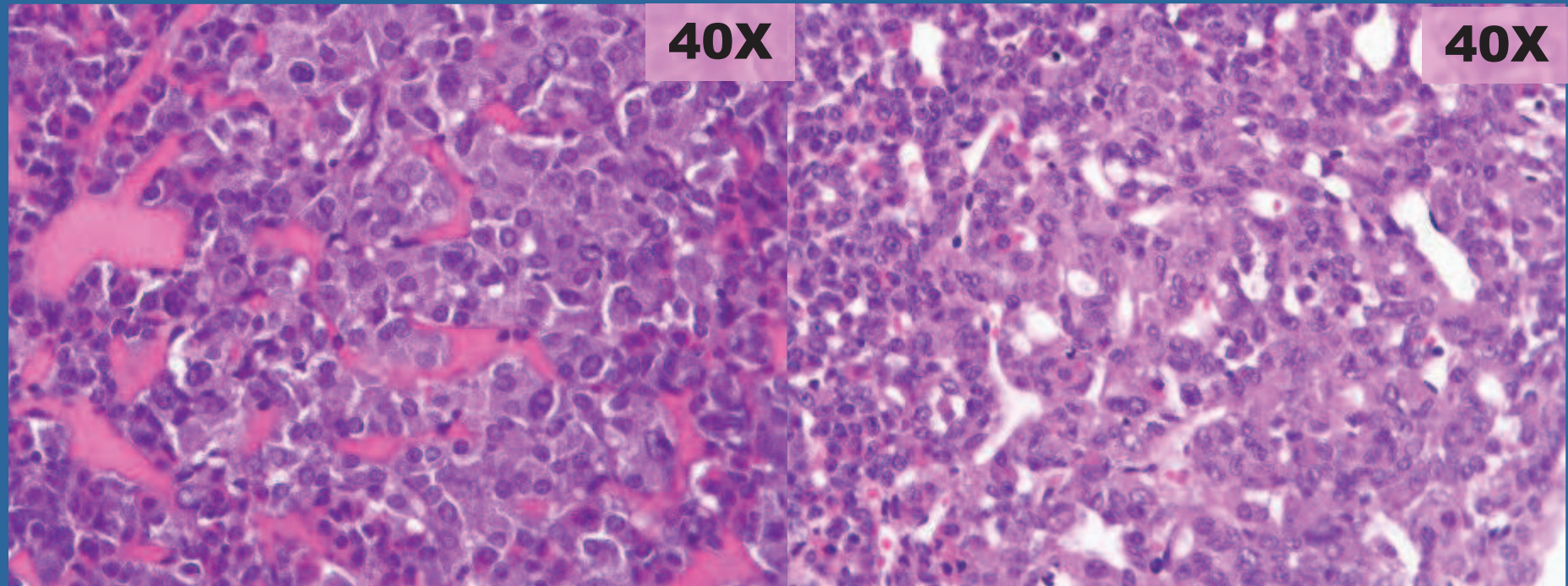
- ✓ **Focal proliferation**
- ✓ **Little or no compression**
- ✓ **Relatively indistinct borders**
- ✓ **Cells slightly larger and paler than normal**
- ✓ **Nuclei often similar to normal cells**
- ✓ **Occasional "normal" cell types interspersed in focus**

# PARS DISTALIS



**Focal hyperplasia- Pars distalis**

# PARS DISTALIS



**Focal hyperplasia- Pars distalis**



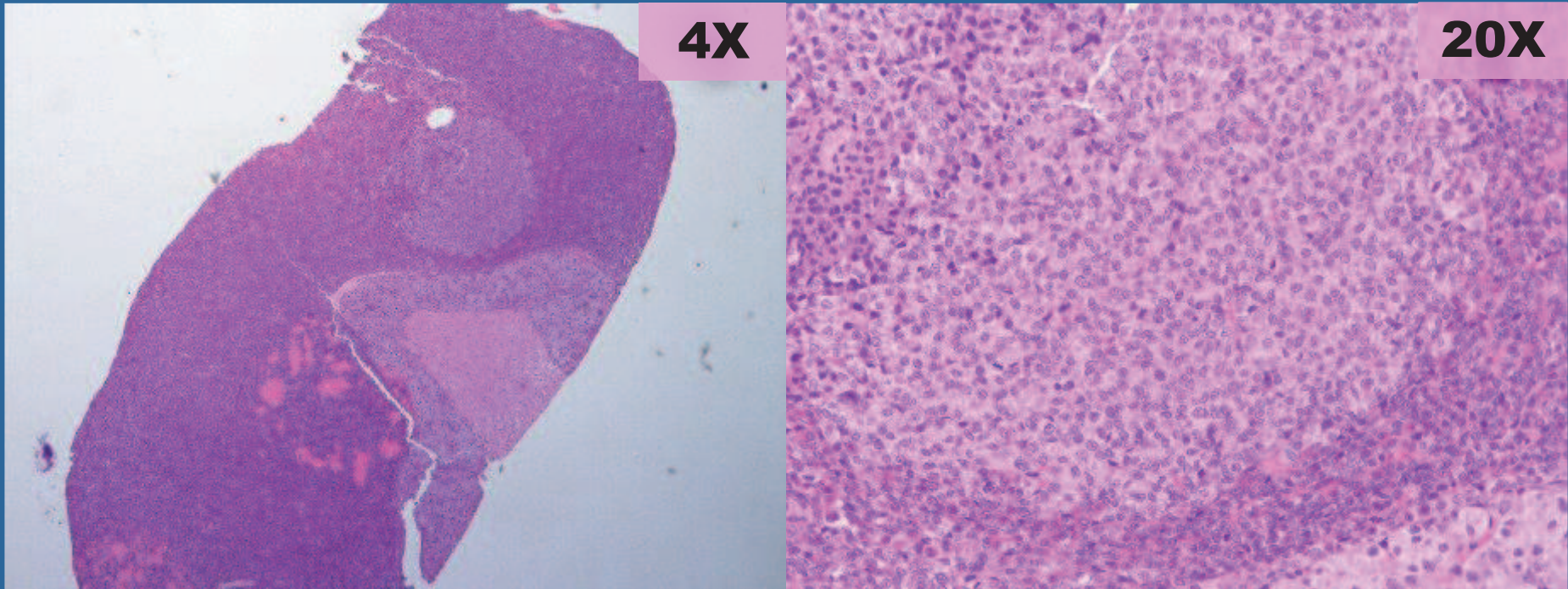
# PARS DISTALIS



## ➤ Adenoma

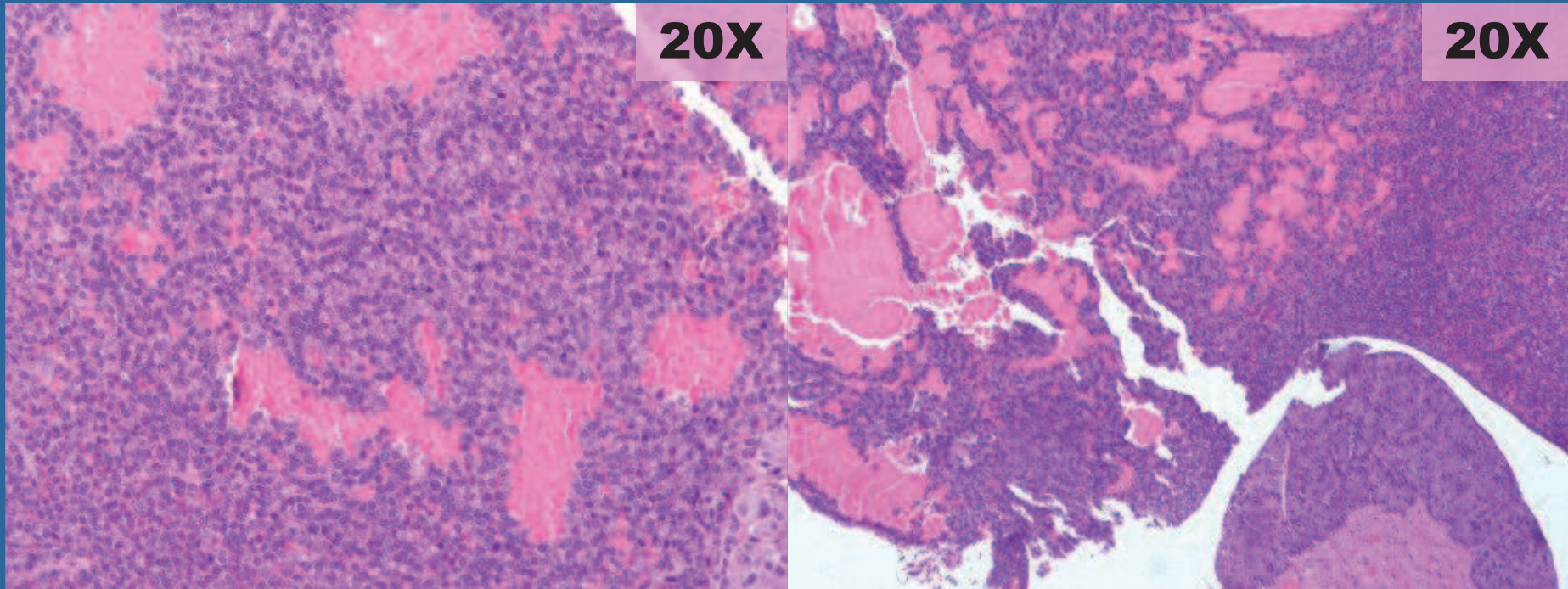
- ✓ **Growth by expansion with prominent compression**
- ✓ **Sharp delineation from normal areas**
- ✓ **Cells usually larger with abundant, pale cytoplasm**
- ✓ **Nuclei more vesicular**
- ✓ **Variety of architectural patterns — diffuse, angiomatous, glandular, pseudofollicular. Pleomorphic**

# PARS DISTALIS



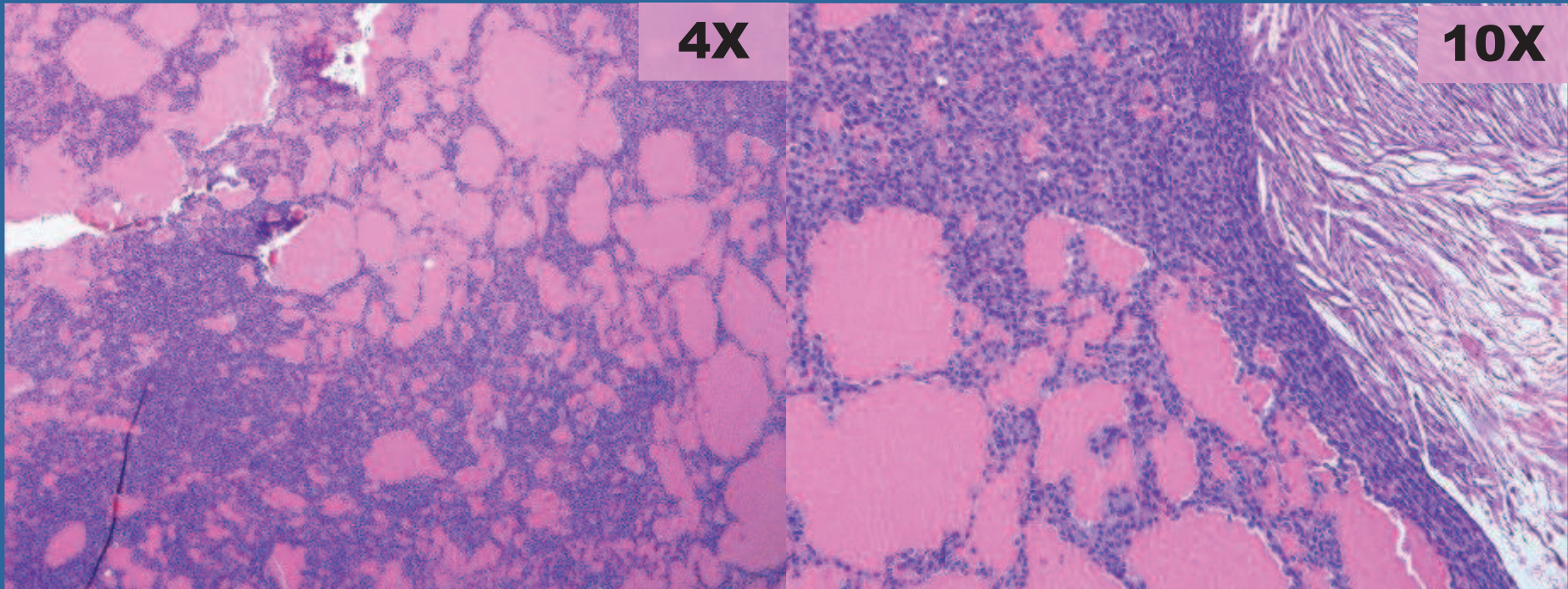
**Adenoma – Pars distalis**

# PARS DISTALIS



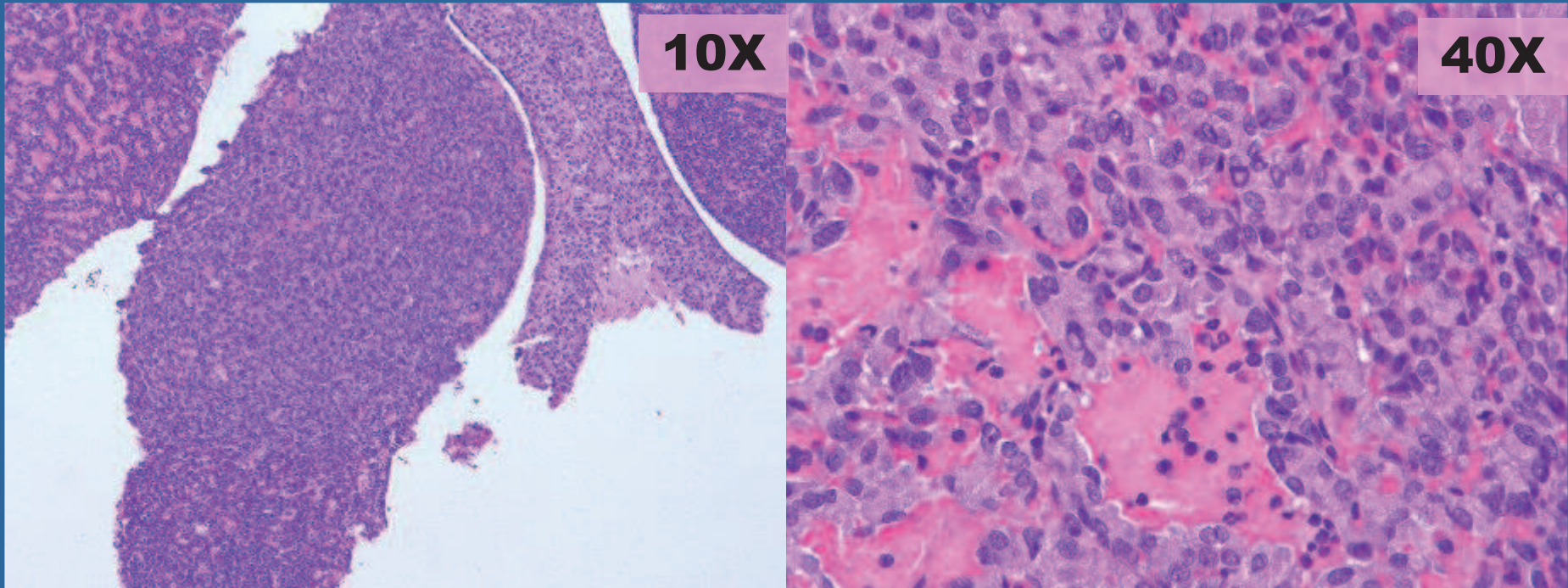
**Adenoma – Pars distalis**

# PARS DISTALIS



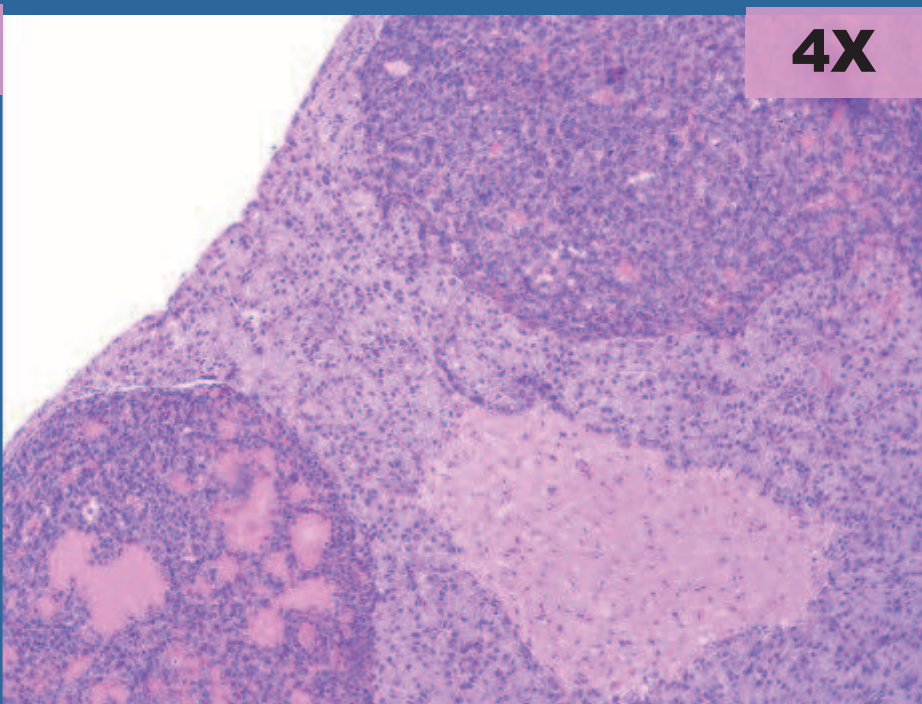
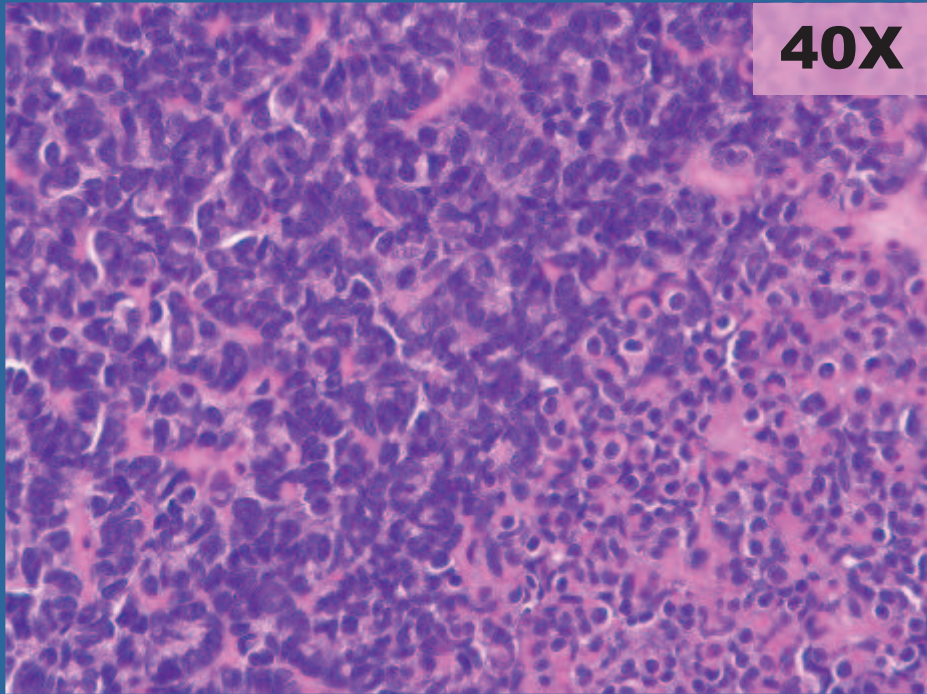
**Adenoma – Pars distalis**

# PARS DISTALIS



**Adenoma – Pars distalis**

# PARS DISTALIS



**Adenoma – Pars distalis**

# PARS DISTALIS

## ➤ Carcinoma

- ✓ Morphologically similar to adenoma
- ✓ Rarely metastasize
- ✓ Local invasion into brain



# PARS INTERMEDIA

## ➤ **Atrophy**

- ✓ **Decreased width/small sized cells**

## ➤ **Hypertrophy**

- ✓ **Diffuse broadening of intermediate zone**
- ✓ **Large sized cells**
- ✓ **Pale in color**

## ➤ **Hyperplasia**

- ✓ **Diffuse broadening of intermediate zone**
- ✓ **Normal cell morphology**
- ✓ **Presence of mitotic figure**

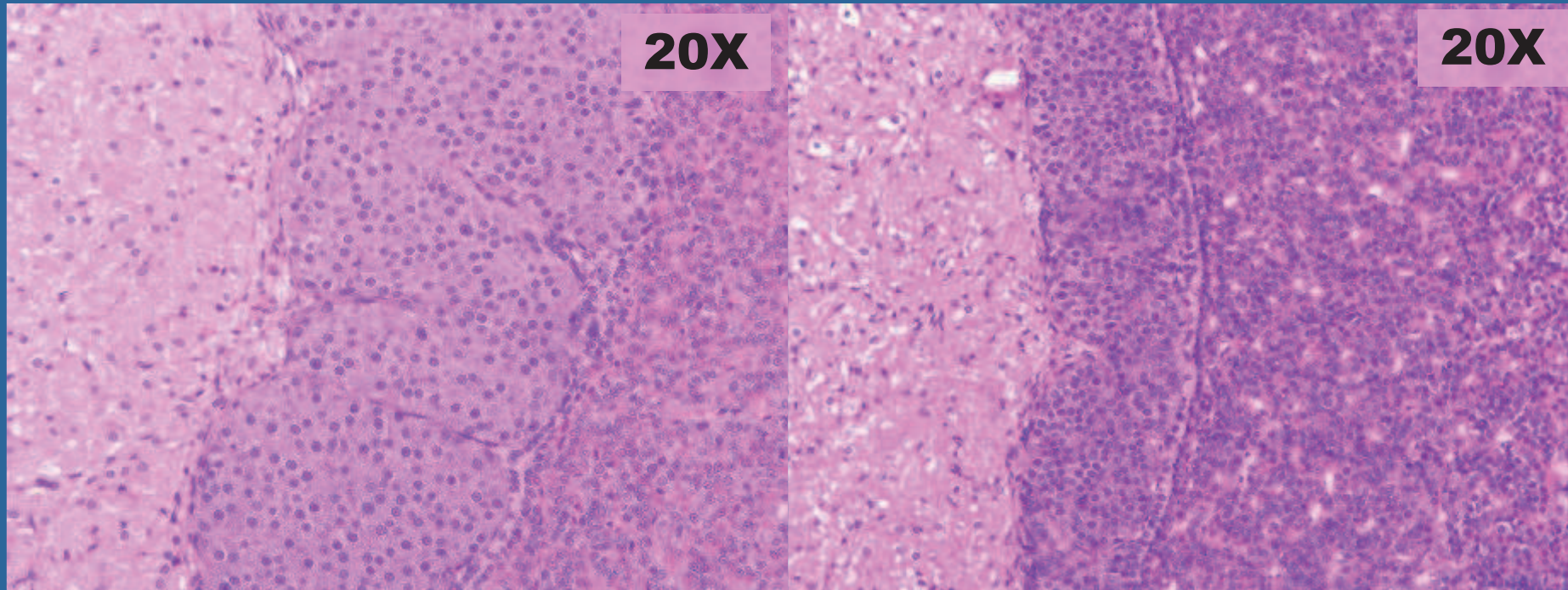


# PARS INTERMEDIA

## ➤ Adenoma

- **Non-encapsulated and poorly circumscribed**
- **Cells extend into other /ones of gland**
- **Cells larger and more basophilic than normal**
- **Nuclear pleomorphism common**
- **Lobular or whorled pattern**
- **Single/multiple**

# PARS INTERMEDIA



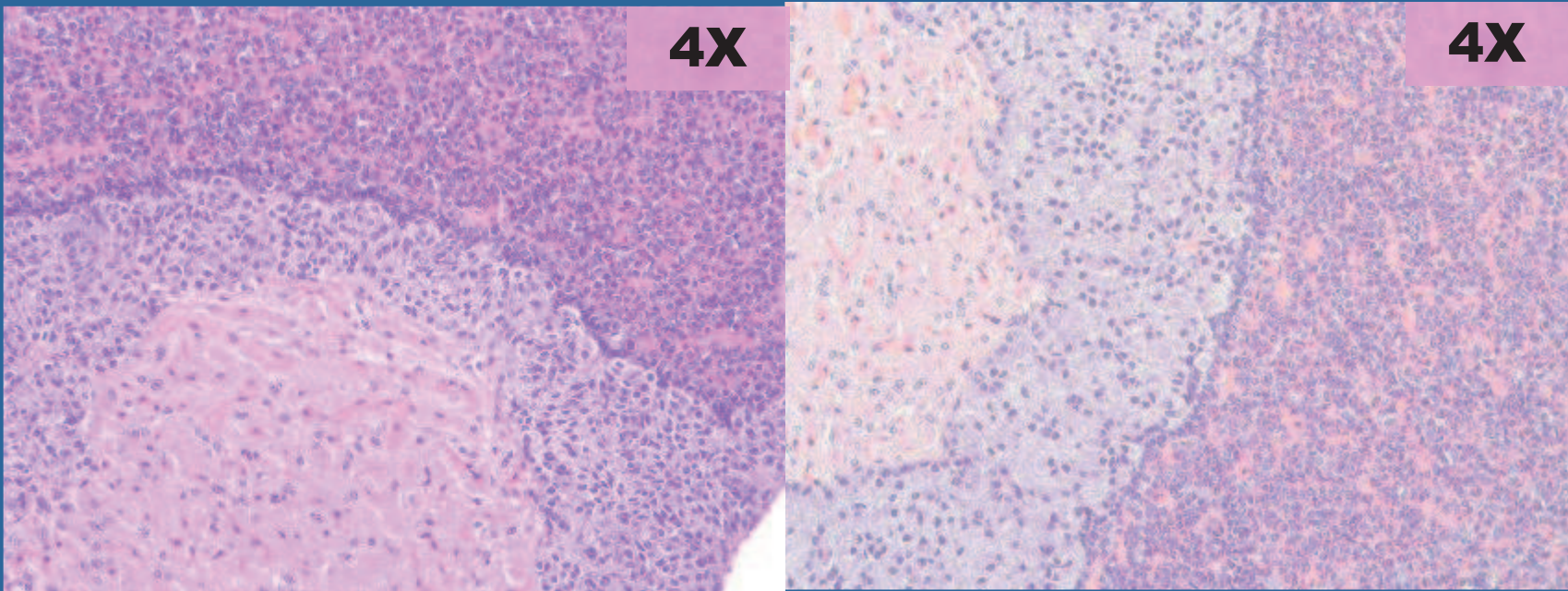
**Normal**

**Atrophy**

**Atrophy – Pars intermedia**

# PARS INTERMEDIA

Male Mice



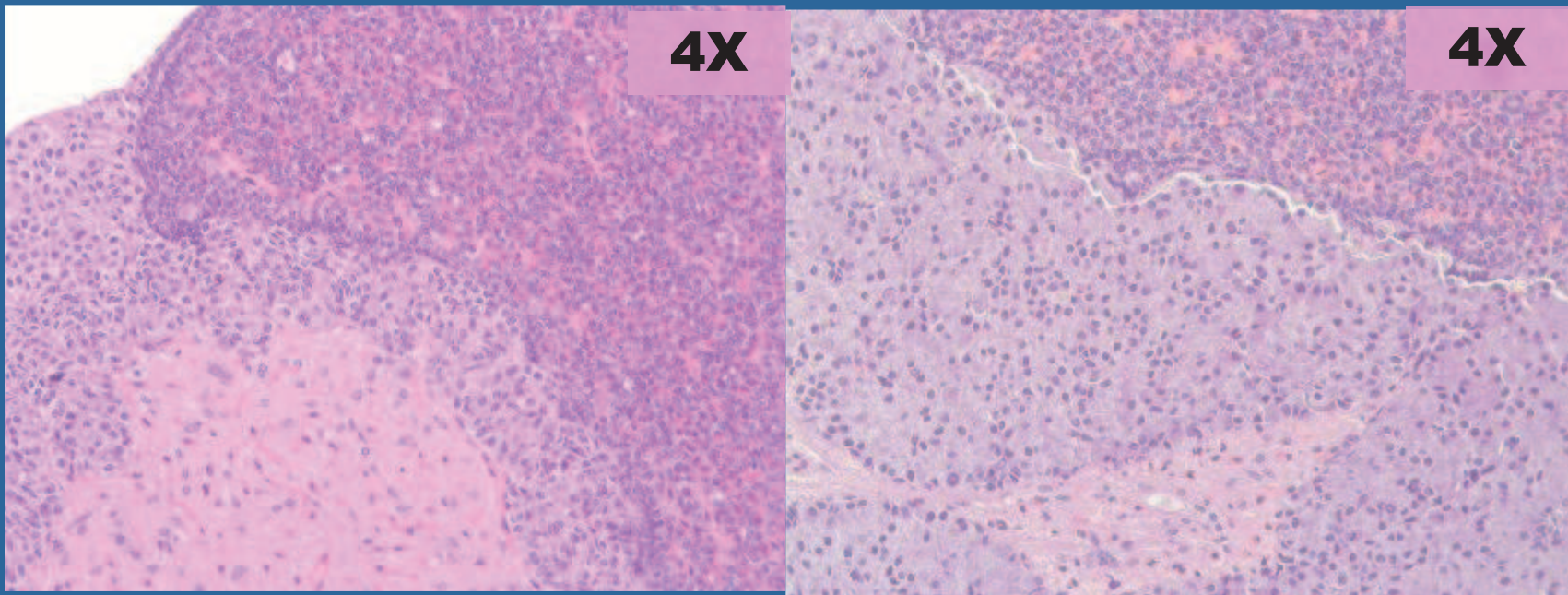
Normal

Hypertrophy

**Hypertrophy – Pars intermedia**

# PARS INTERMEDIA

## Female Mice

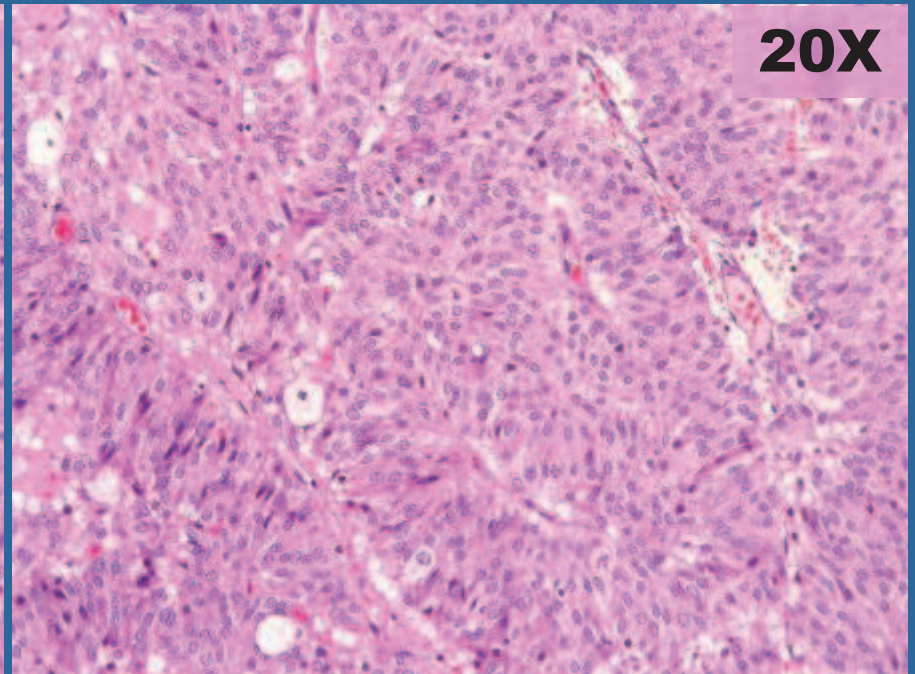
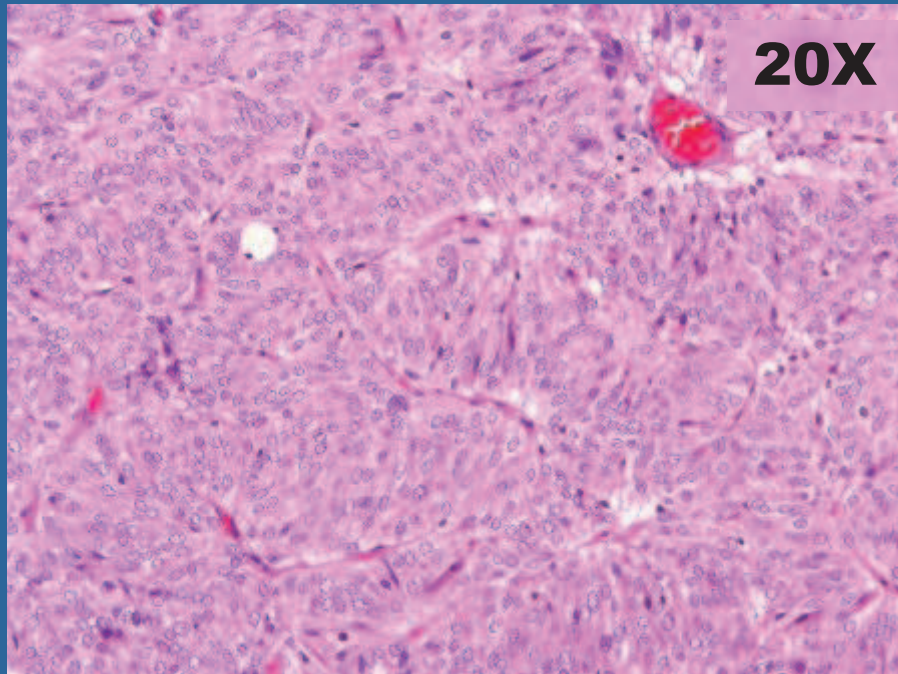


Normal

Hypertrophy

**Hypertrophy – Pars intermedia**

# PARS INTERMEDIA



**Adenoma – Pars intermedia**

# PARS NERVOSA



## ➤ **Pituicytoma**

- ✓ **Circumscribed, nonencapsulated**
- ✓ **Dense packets of spindle cells**
- ✓ **Indistinct cords and interlacing bundles**
- ✓ **Dark ovoid to round nuclei and minimal indistinct cytoplasm**
- ✓ **Nuclear pleomorphism seen in some regions**
- ✓ **Foci of mineralization sometimes present**

# Tumor of Embryonic Remnant

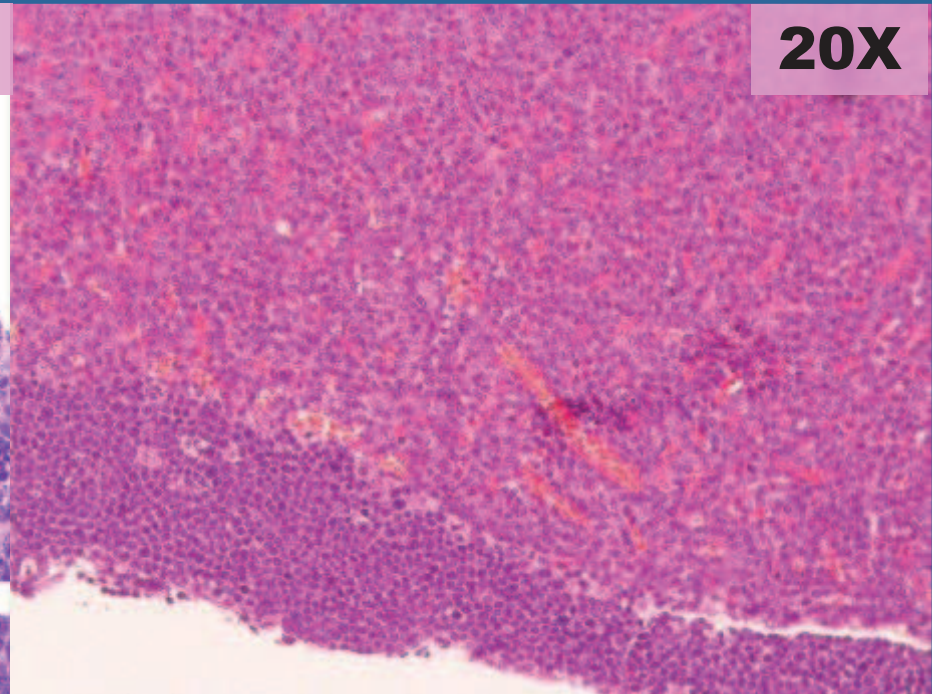
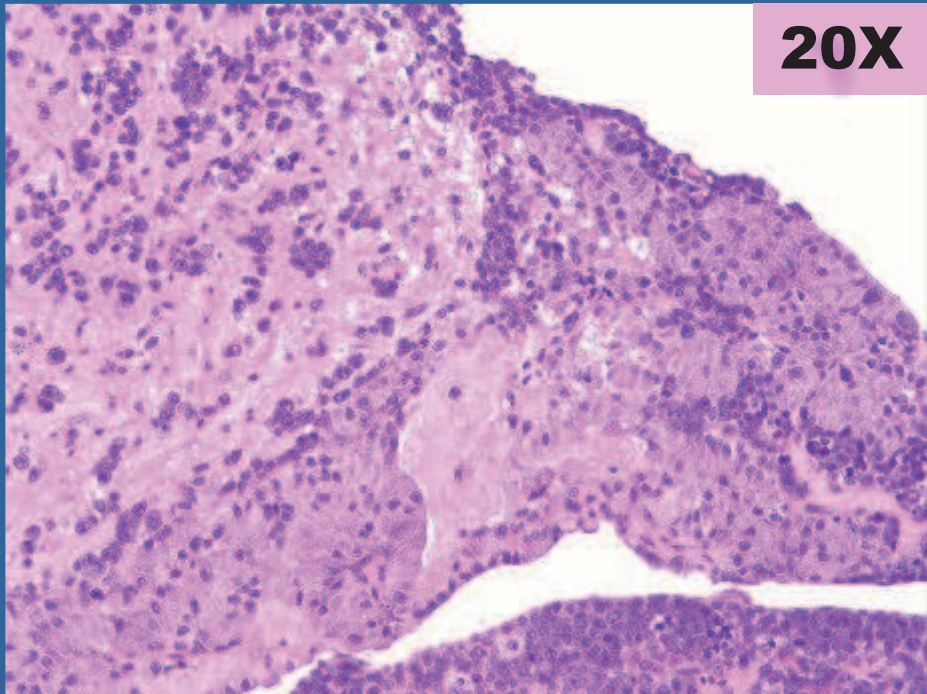


## ➤ Craniopharyngioma

- ✓ Keratinizing squamous epithelium
- ✓ Cells arranged in cords, columns, nests
- ✓ Cystic spaces filled with keratin and debris
- ✓ Invasion of brain or pituitary tissue



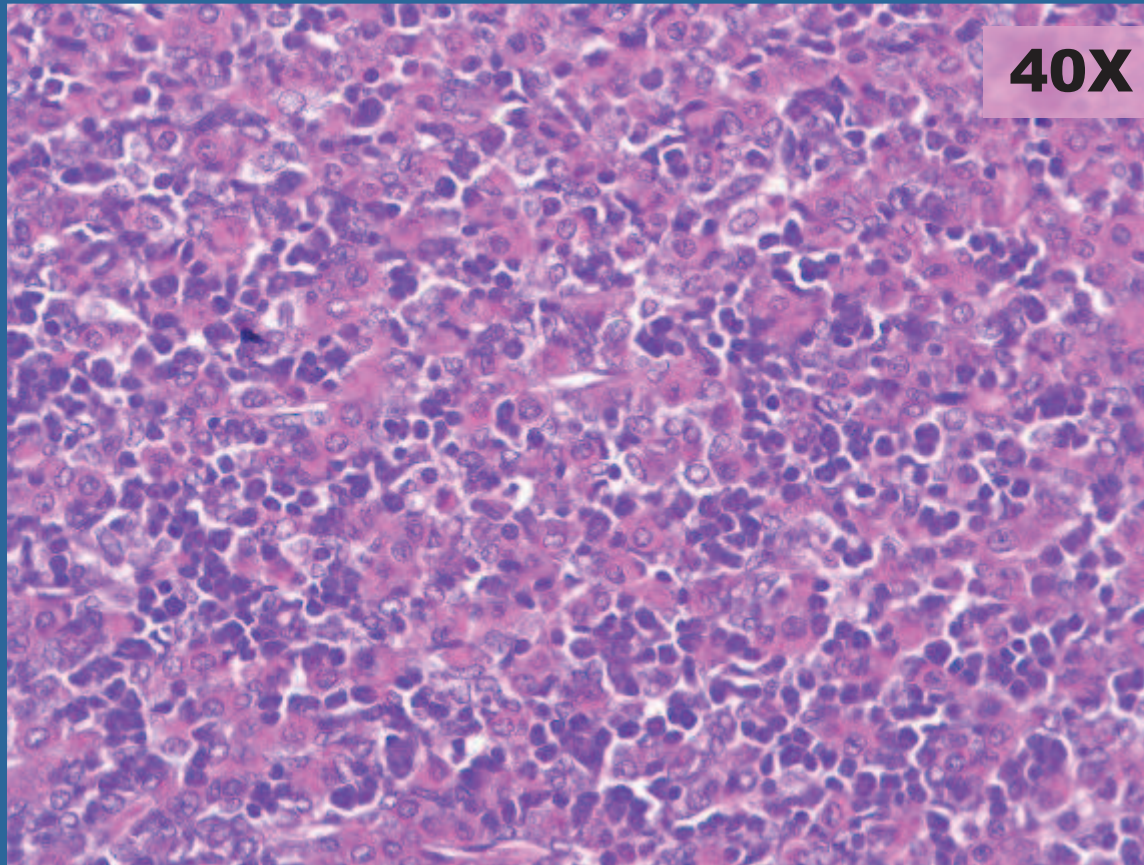
# LYMPHORETICULAR/ HEMOPOIETIC SYSTEM TUMOR



**Lymphoma; malignant; multicentric**

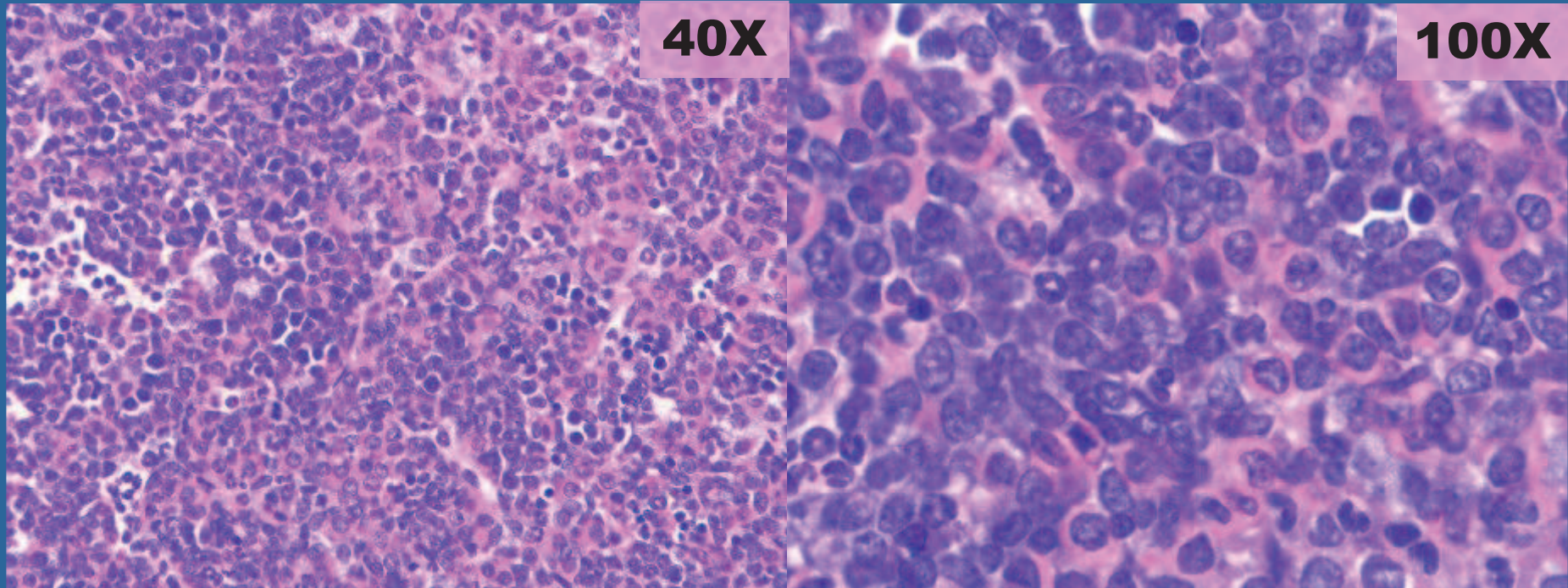


# LYMPHORETICULAR/ HEMOPOIETIC SYSTEM TUMOR



**Lymphoma; malignant; multicentric**

# LYMPHORETICULAR/ HEMOPOIETIC SYSTEM TUMOR



**Myeloid leukemia; malignant; multicentric**

# NTP Historical Controls Data - June 2013

## All Routes & Vehicles - Overall Incidence



Location	Lesion	Species/Strain									
		Rats/ Fischer 344N		Rats/ Fischer 344N TAC		Rats/ Wistar Han		Rats/ Harlan Sprague Dawley		Mice/ B6C3F1	
		M	F	M	F	M	F	M	F	M	F
Pars Distalis or Unspecified Site	Adenoma	408/698 (58.45%)	411/699 (58.8%)	53/100 (53%)	52/100 (52%)	54/149 (36.24%)	88/150 (58.67%)	5/50 (10%)	35/102 (34.31%)	3/933 (0.32%)	72/933 (7.72%)
	Carcinoma	4/698 (0.57%)	11/699 (1.57%)	----	----	----	----	0/50 (0%)	2/102 (1.96%)	0/933 (0%)	1/933 (0.11%)
	Carcinoma or Adenoma	412/698 (59.03%)	422/699 (60.37%)	53/100 (53%)	52/100 (52%)	54/149 (36.24%)	88/150 (58.67%)	5/50 (10%)	37/102 (36.27%)	3/933 (0.32%)	73/933 (7.82%)
	Ganglio- neuroma	1/698 (0.14%)	1/699 (0.14%)	----	----	----	----	----	----	----	----
Pars Intermedia	Adenoma	2/698 (0.29%)	3/699 (0.43%)	----	----	5/149 (3.36%)	7/150 (4.67%)	----	----	2/933 (0.21%)	7/933 (0.75%)
	Carcinoma or Adenoma	2/698 (0.29%)	3/699 (0.43%)	----	----	5/149 (3.36%)	7/150 (4.67%)	----	----	2/933 (0.21%)	7/933 (0.75%)
Pars Nervosa	Cranio- pharyngioma	0/698 (0%)	1/699 (0.14%)	----	----	----	----	----	----	----	----

\*: Denominator is number of animals with tissues examined microscopically

<http://ntp.niehs.nih.gov/results/dbsearch/historical/ntp2000/index.html>



*Thank You*