

STOMACH IN PRECLINICAL TOXICOLOGY

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Disclaimer

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Anatomy



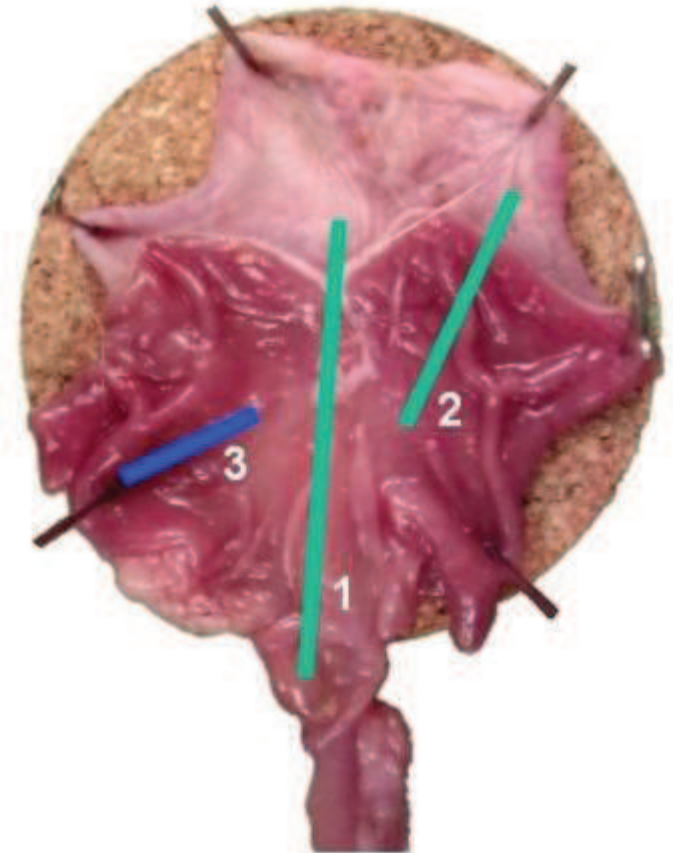
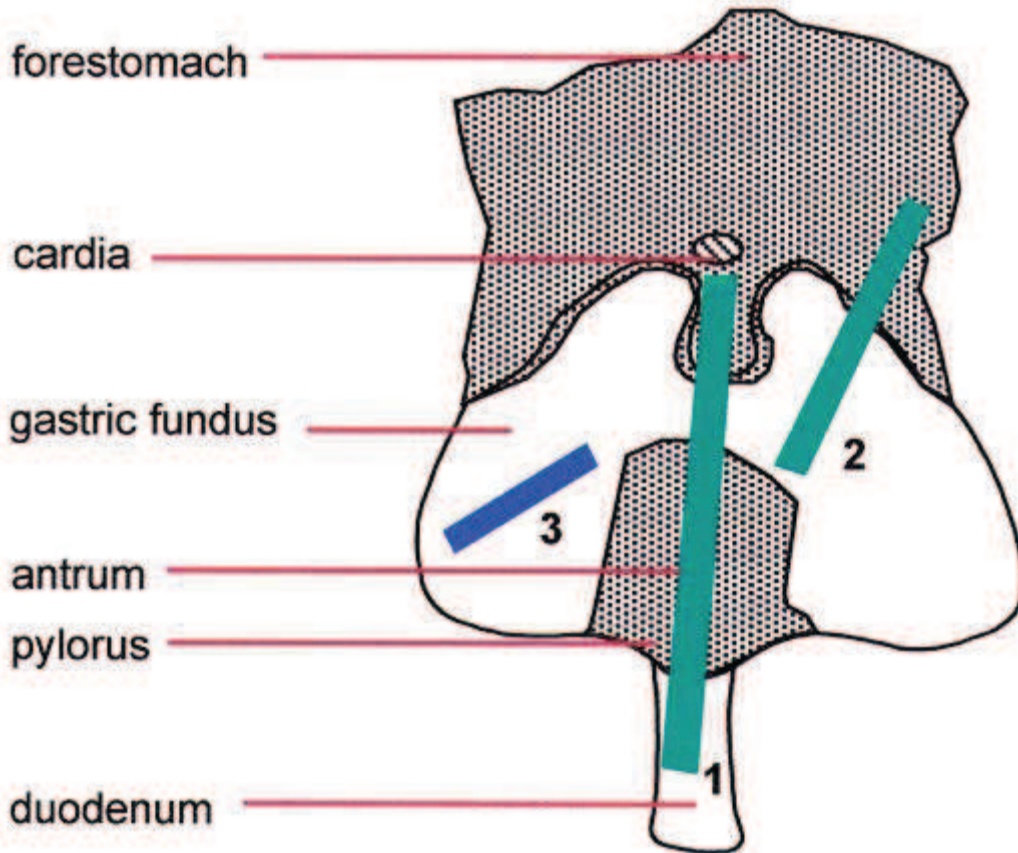
Rat

Anatomy



Mouse

Trimming Guidelines

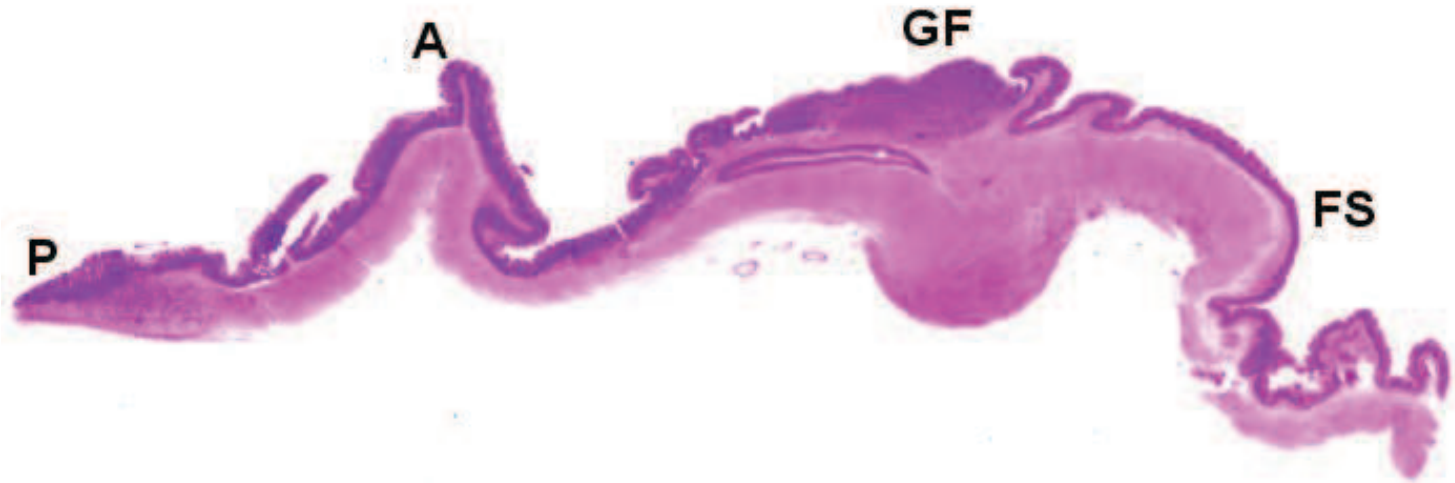


1: Forestomach (FS), gastric fundus (GF), antrum (A), pylorus (P).

2: Forestomach (FS), gastric fundus (GF)

3: Optional section - fundus

Trimming Guidelines



1: Forestomach (FS), gastric fundus (GF), antrum (A), pylorus (P).

Trimming Guidelines



2: Forestomach (FS), gastric fundus (GF)

Trimming Guidelines

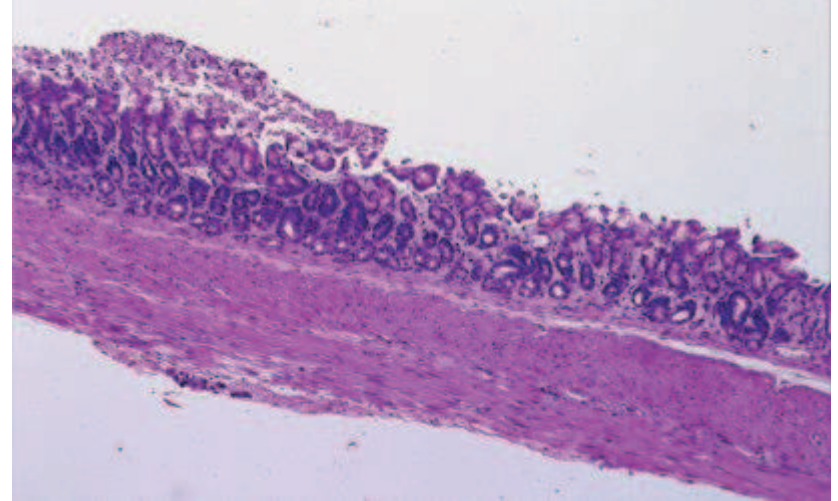
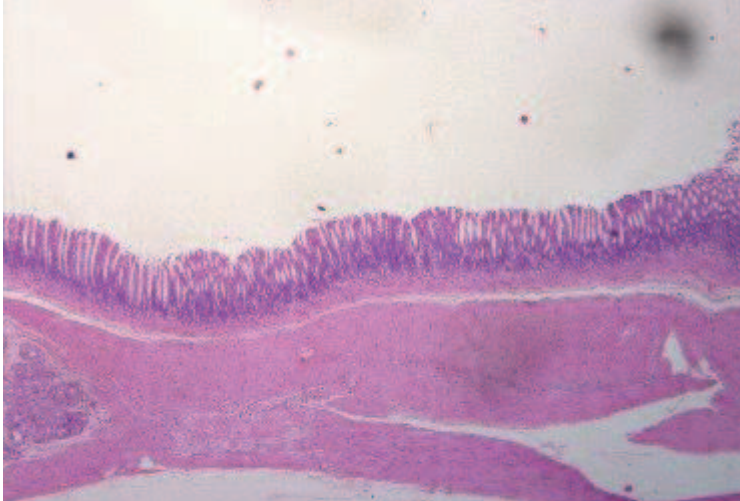
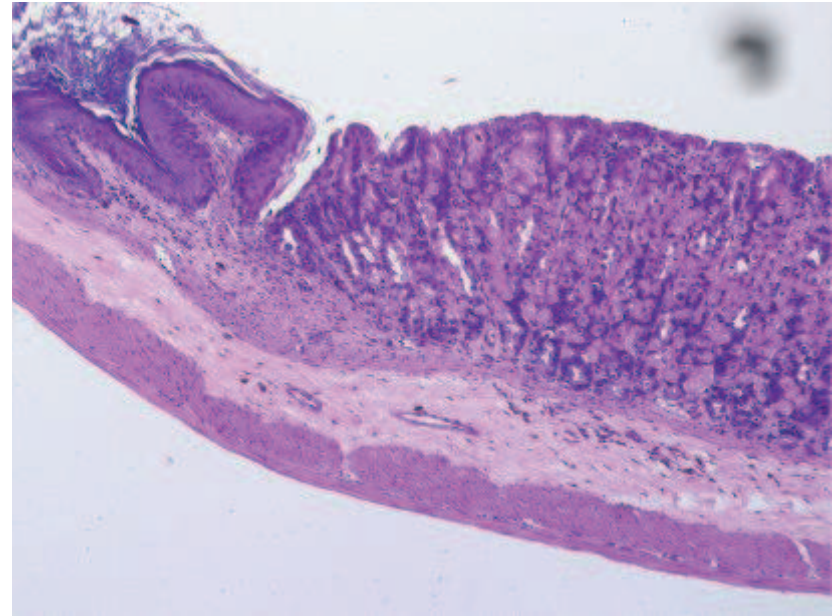
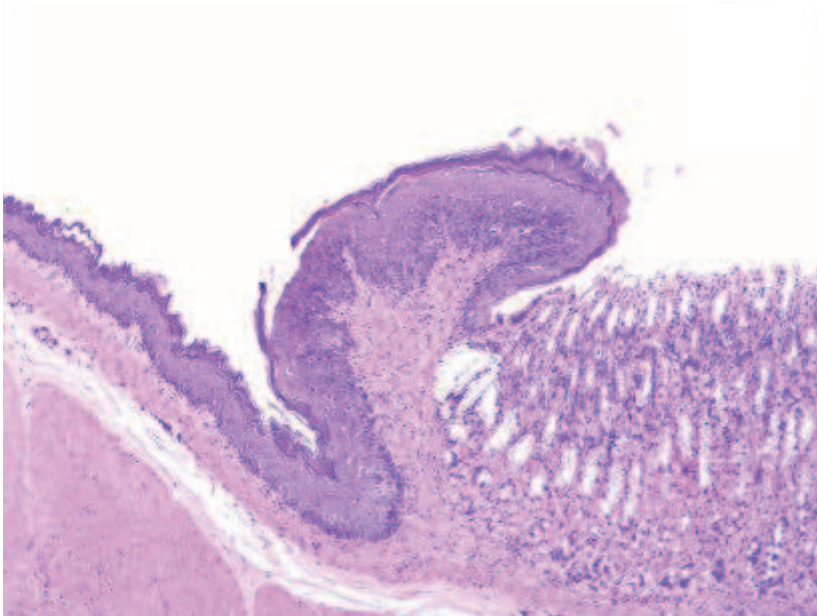


3: Optional section - fundus

Histology Comparisons

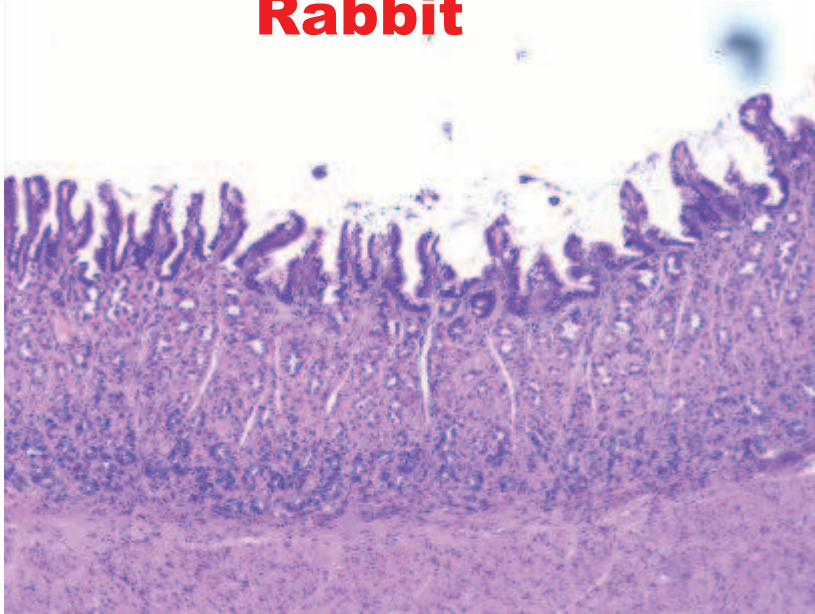
Rat

Mouse

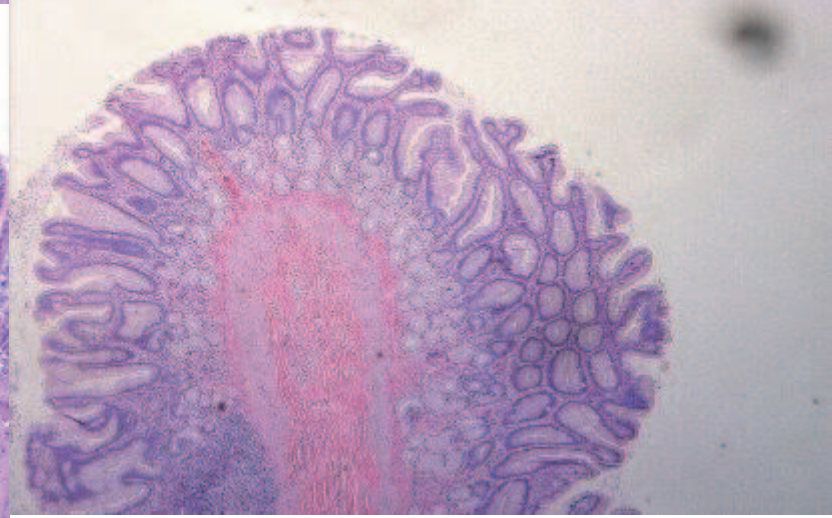
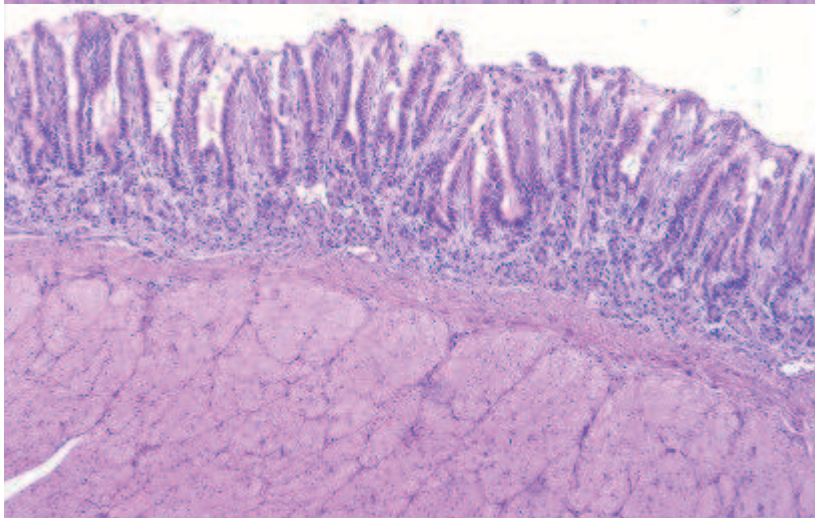
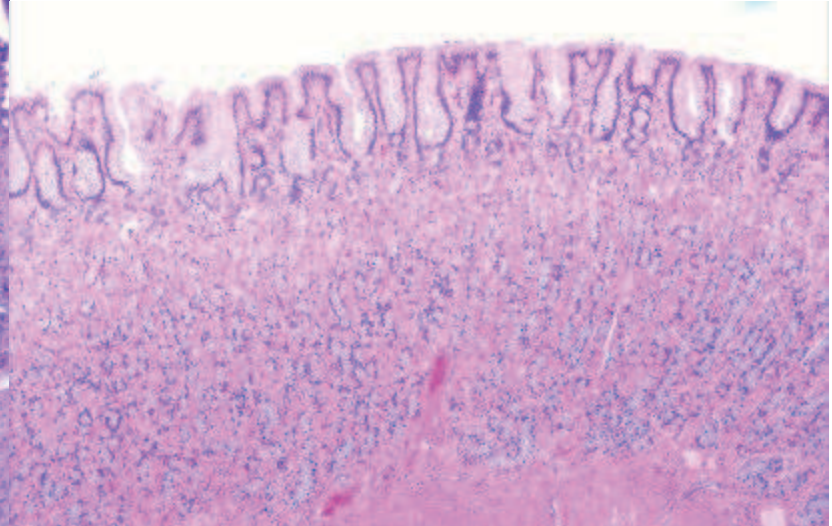


Histology Comparisons

Rabbit



Dog



Commonly Affected Regions

- ✓ **In the decreasing order**
 - ✓ **Non glandular stomach in rats-frequency more**
 - ✓ **Glandular stomach in mice**
 - ✓ **Non glandular stomach in mice**
 - ✓ **Glandular stomach in rats**
 - ✓ **Dogs**
 - ✓ **Rabbits**

Common Factors Influencing Stomach Findings

- ✓ **Gavage/feeding studies**
- ✓ **Feed Quality/texture , contamination**
- ✓ **Duration of exposure**
- ✓ **Species difference**

Gross Lesions



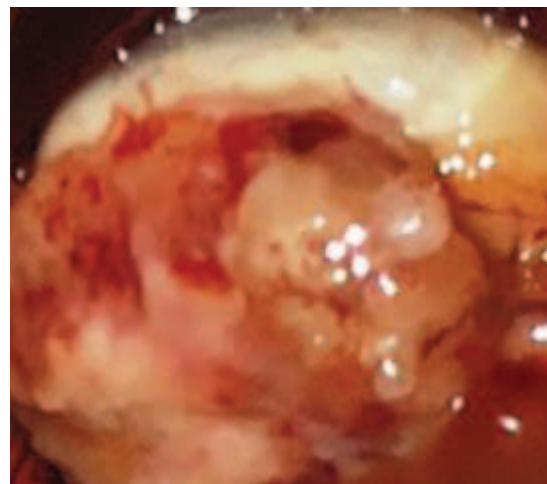
Non-glandular mucosa, white, focus



Glandular mucosa-raised focus



Glandular mucosa, Ulcer



Non glandular - Mass

Recording Gross Lesions

- ✓ **Foci-depressed/white/raised**
- ✓ **Discolouration**
- ✓ **Mucosal thickening**
- ✓ **Thinning of mucosa**
- ✓ **Distension**
- ✓ **Texture of contents**

Gross & Micro Correlation



- **Foci**
- **Discoloration**
- **Distended stomach**
- **Mucosal Thickening**
- **Adhesions**
- **Masses/nodular growth**

Common Microscopic Lesions- Short Term Studies

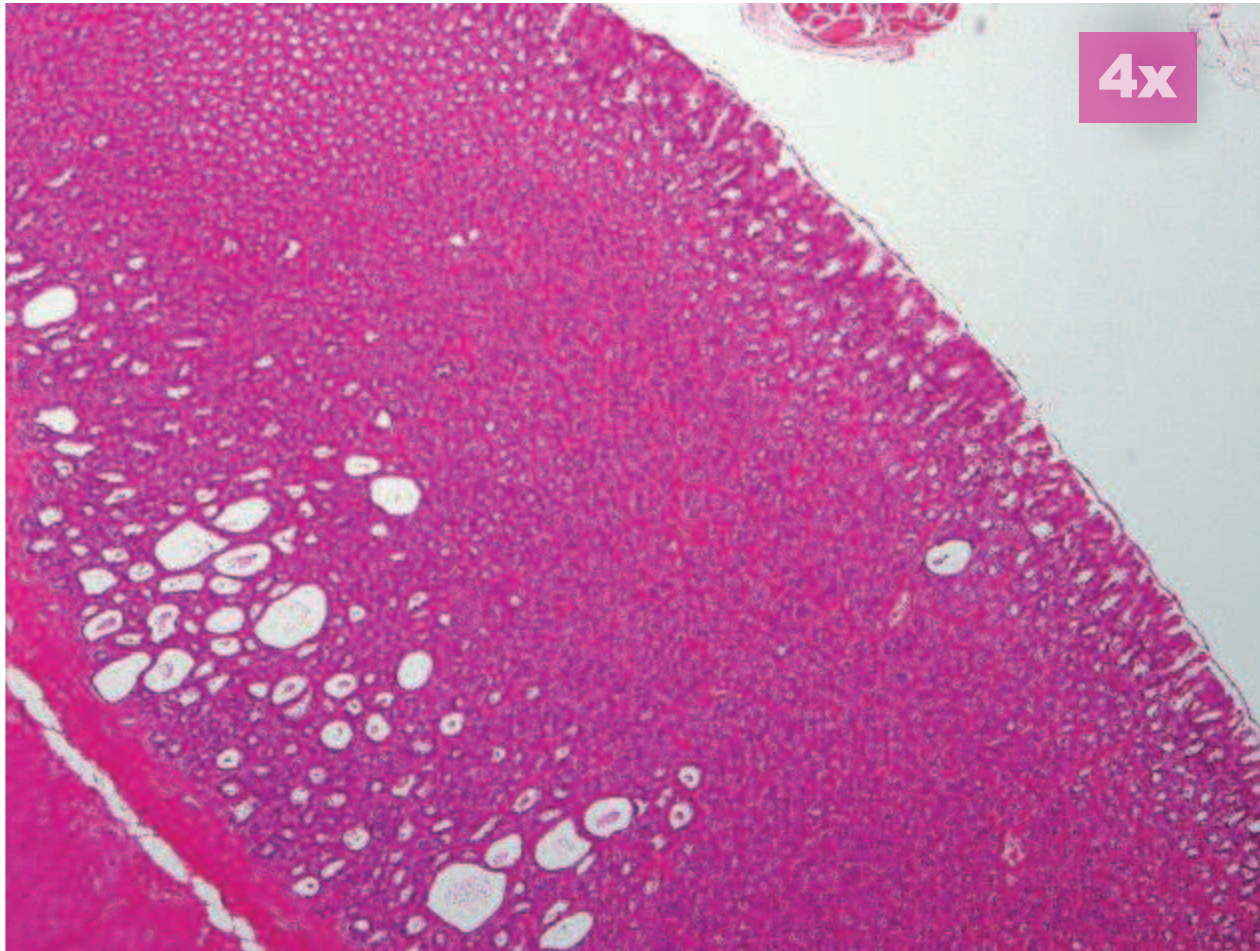
- ✓ **Dilated/distended glands**
- ✓ **Vacuolar changes/degeneration-non glandular stomach-limiting ridge**
- ✓ **Inflammation-glandular mucosa/submucosa**
- ✓ **Submucosal leukocytic infiltration**
- ✓ **Epithelial degeneration-eosinophilic droplets in fundic mucosa—HE, PAS**
- ✓ **Epithelial hyperplasia**
- ✓ **Ectopic pancreas/keratin cyst**

Common Induced Lesions. Short Term Studies- Rat

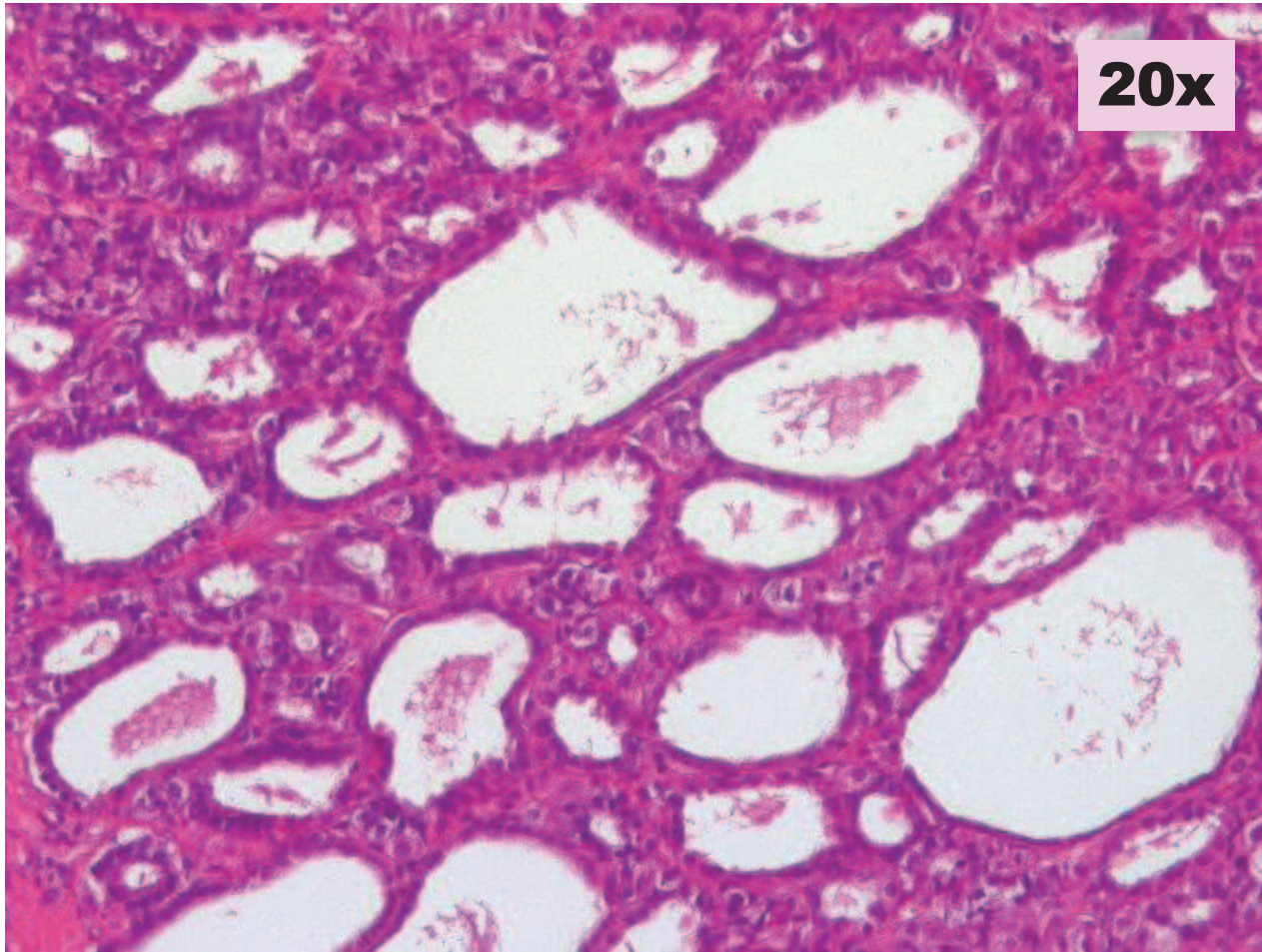


- ✓ **Non glandular-epithelial hyperplasia, mucosal necrosis/erosion/ulceration**
- ✓ **Glandular-individual cell necrosis/epithelial degeneration/mucosal necrosis/ulceration**
- ✓ **Mineralization**

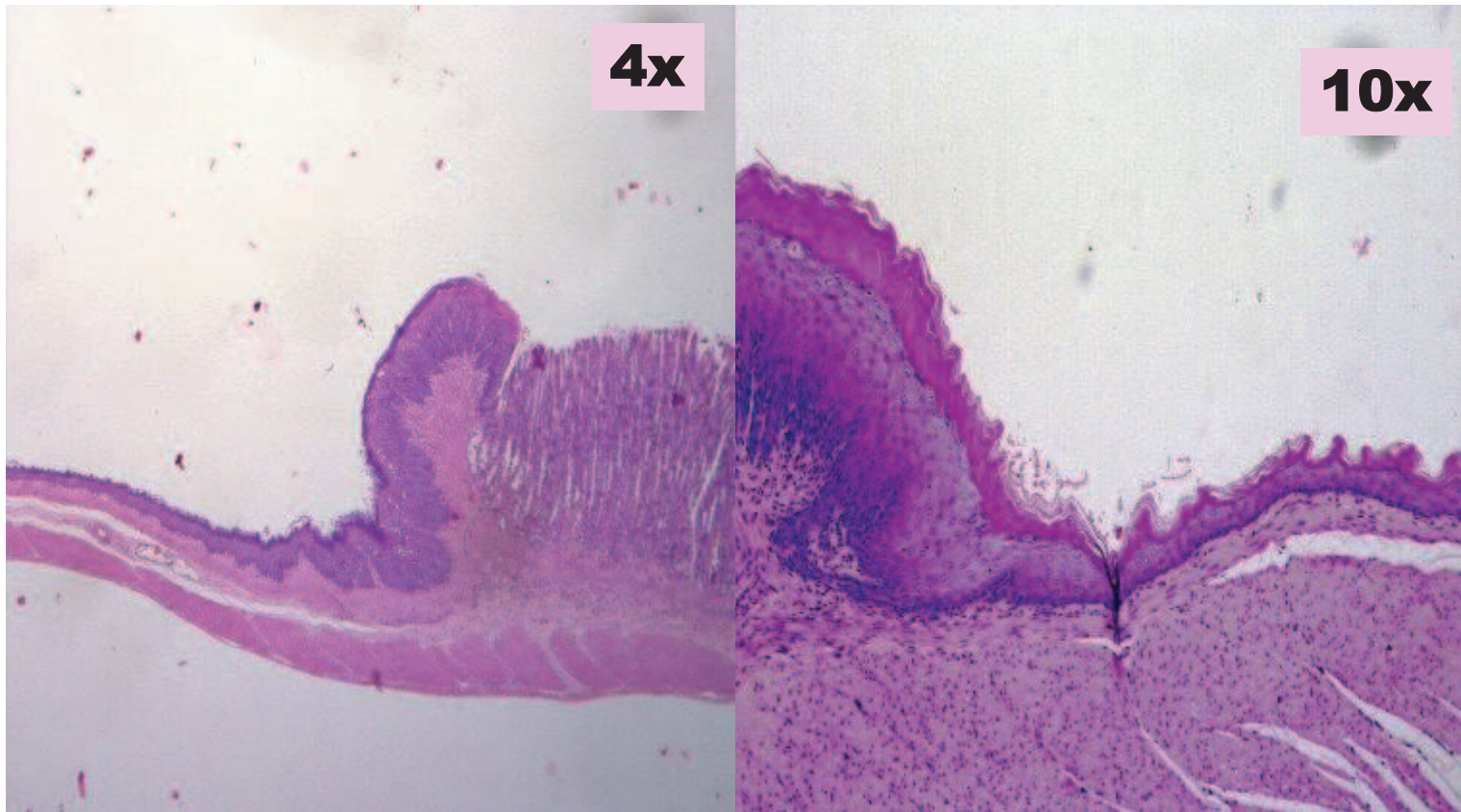
Dilated/Distended Glands - Rat



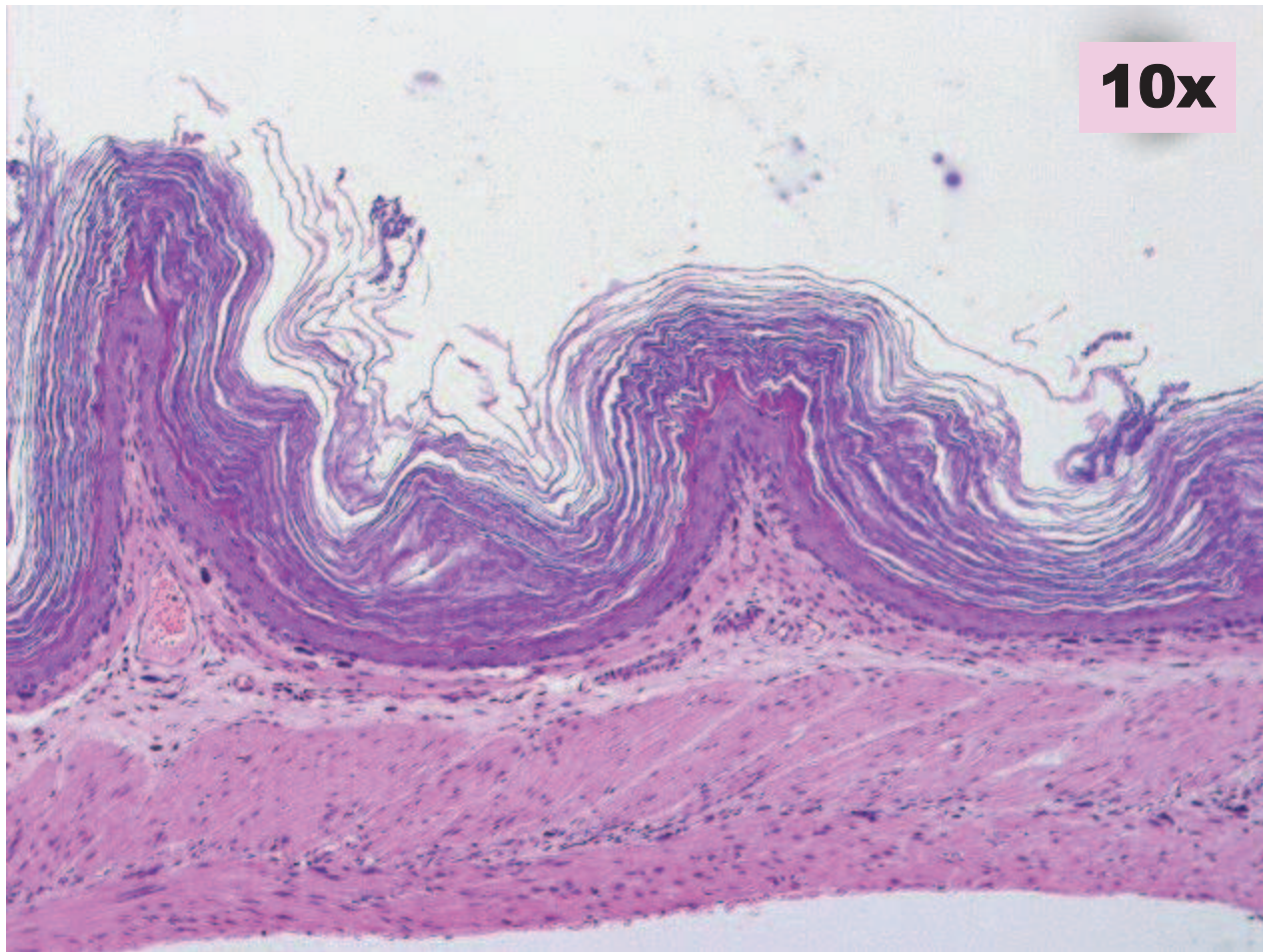
Dilated/Distended Glands - Rat



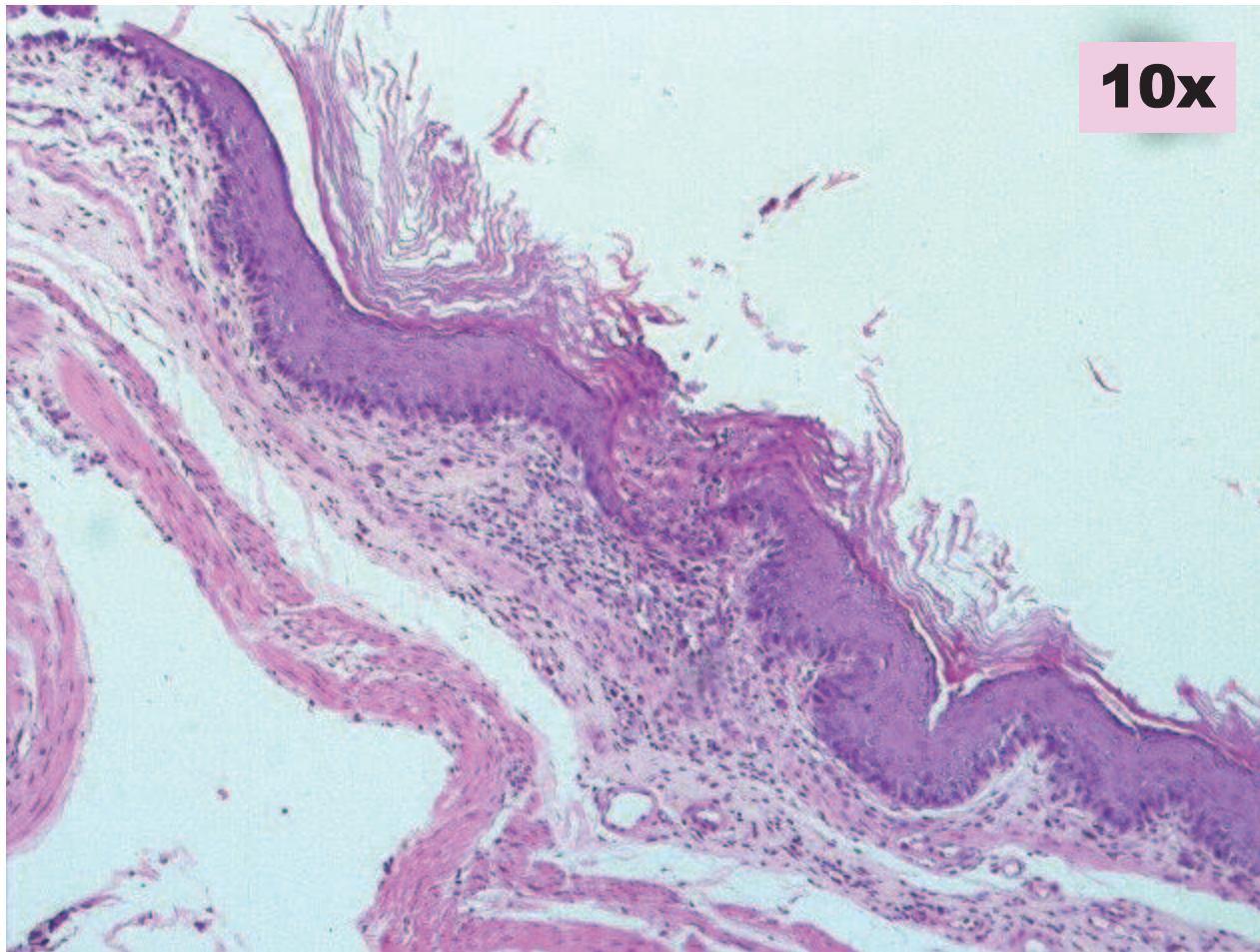
Epithelial Cell Vacuolation- Limiting Ridge- Rat



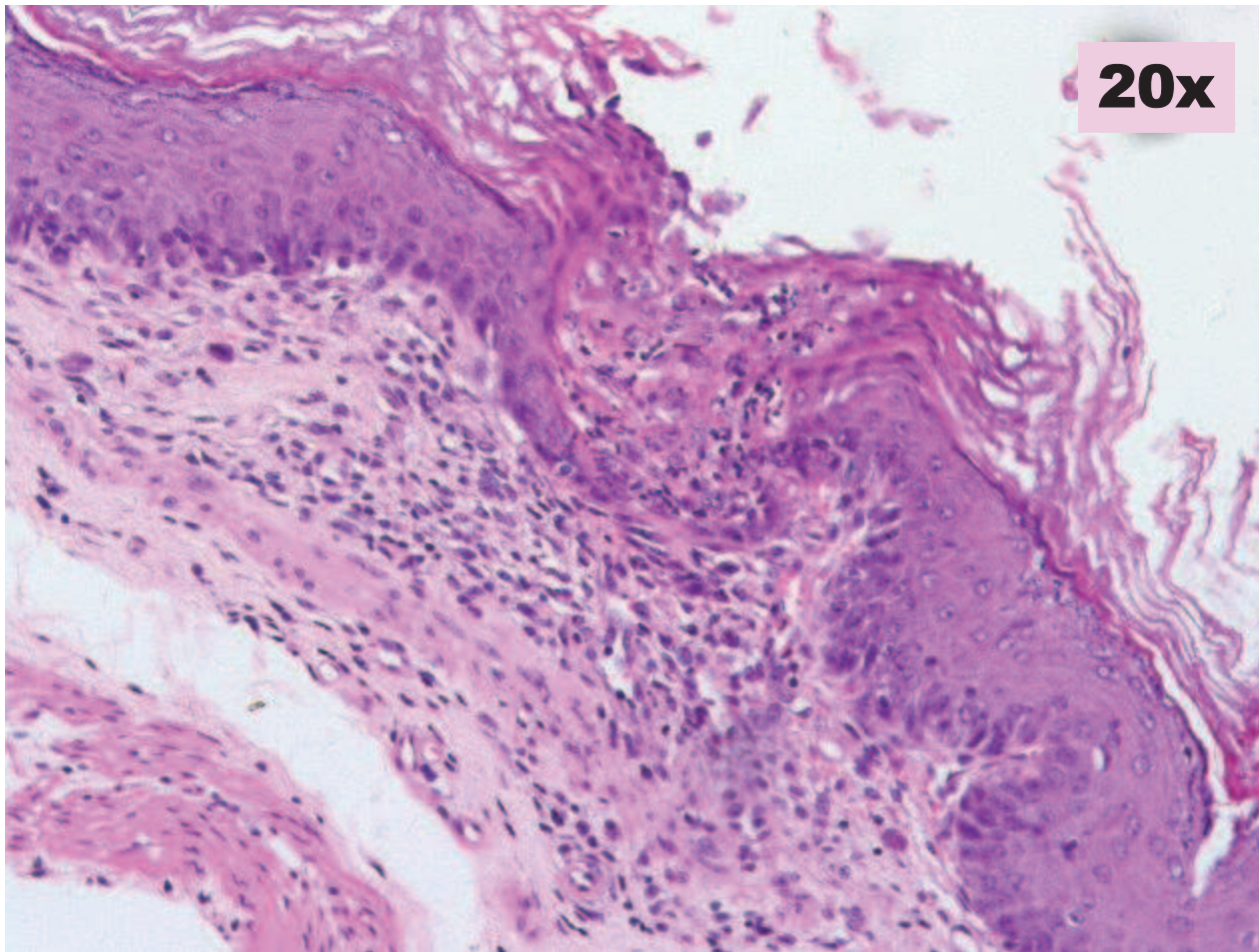
Hyperkeratosis – Non-glandular - Mouse



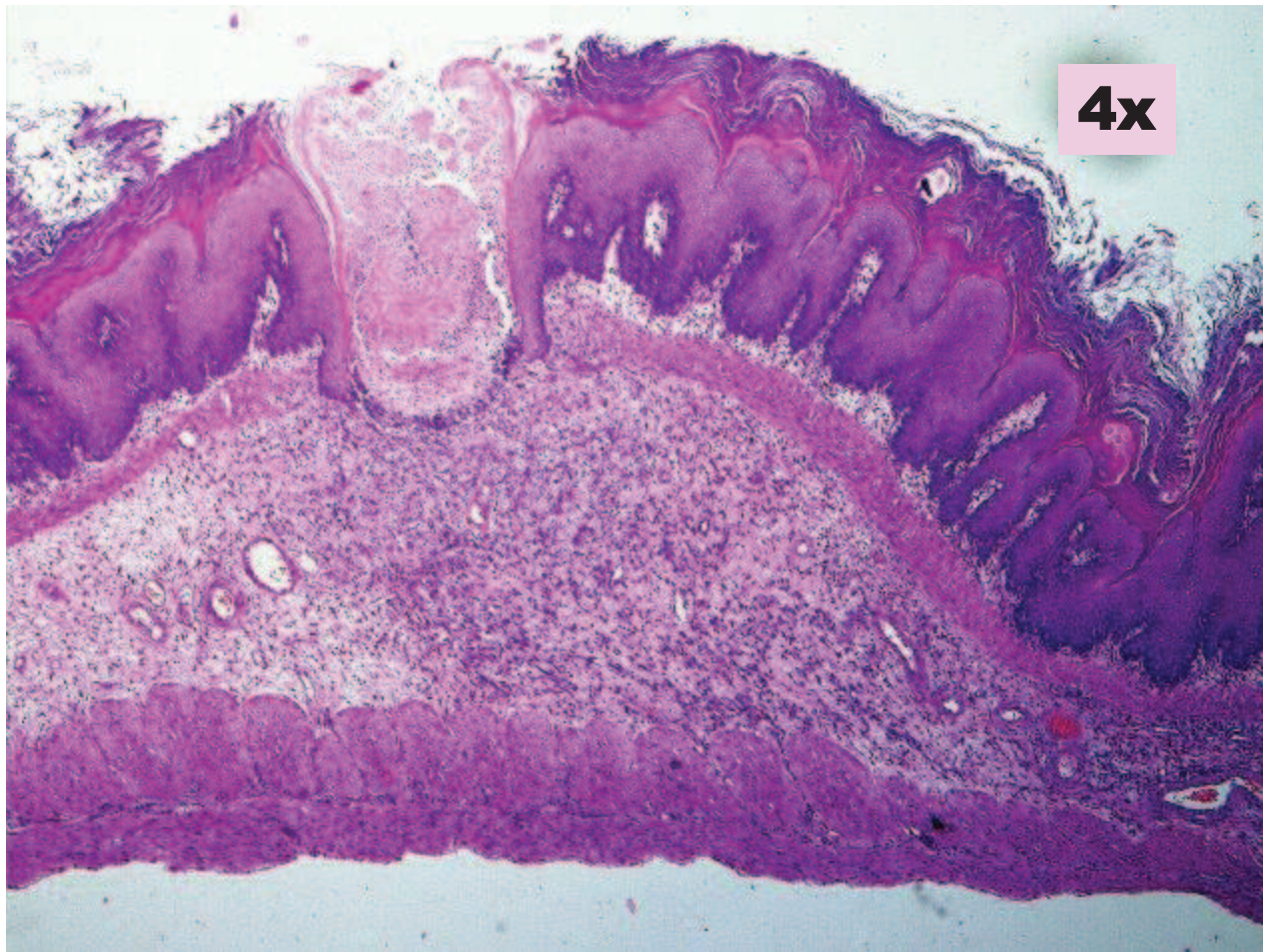
Mucosal Necrosis/Ulcer – Non-glandular - Mouse



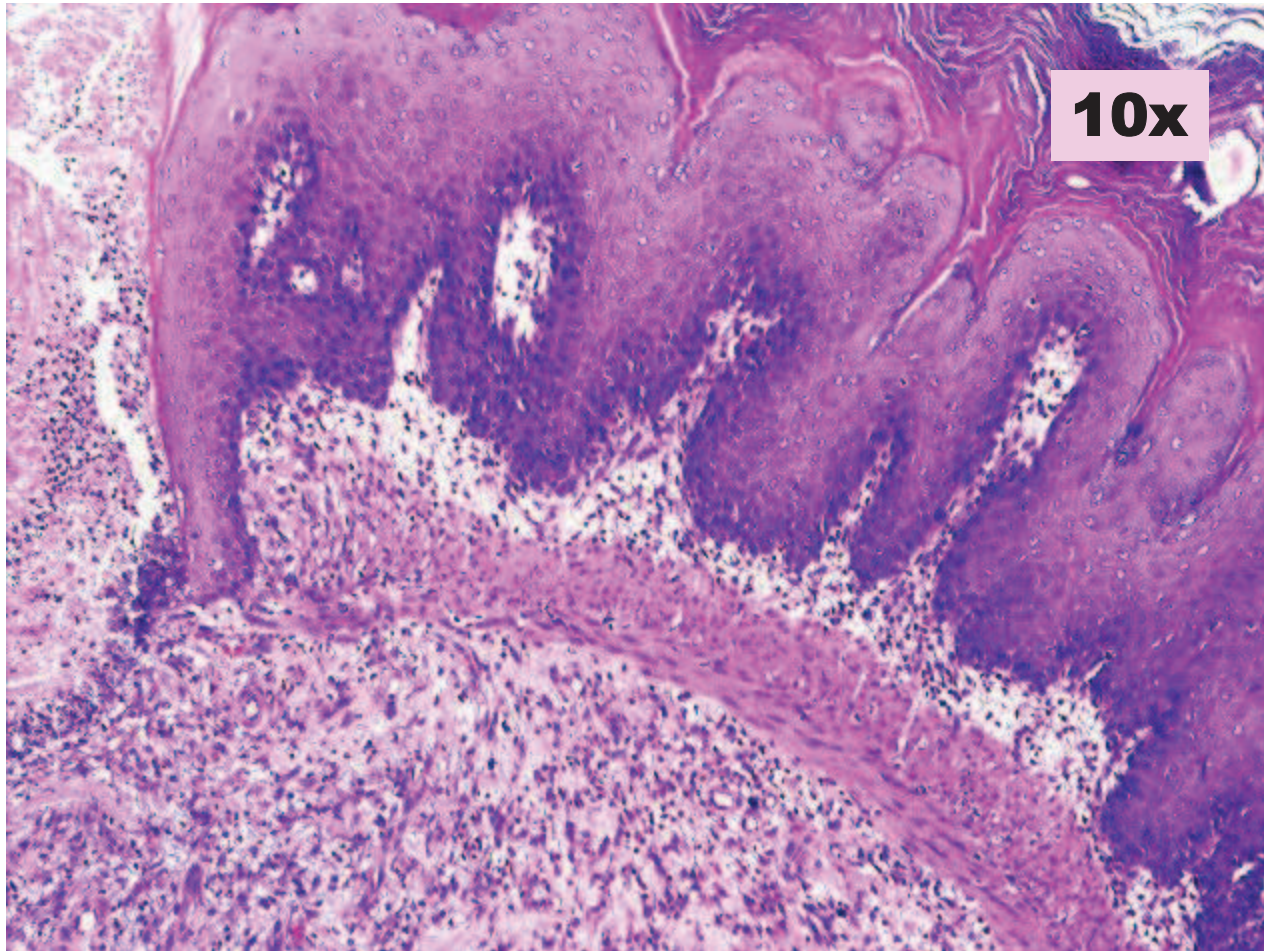
Mucosal Necrosis/Ulcer - Non-glandular - Mouse



Ulcer/Epithelial Hyperplasia- Non-glandular - Rat



Ulcer/Epithelial Hyperplasia- Non-glandular - Rat

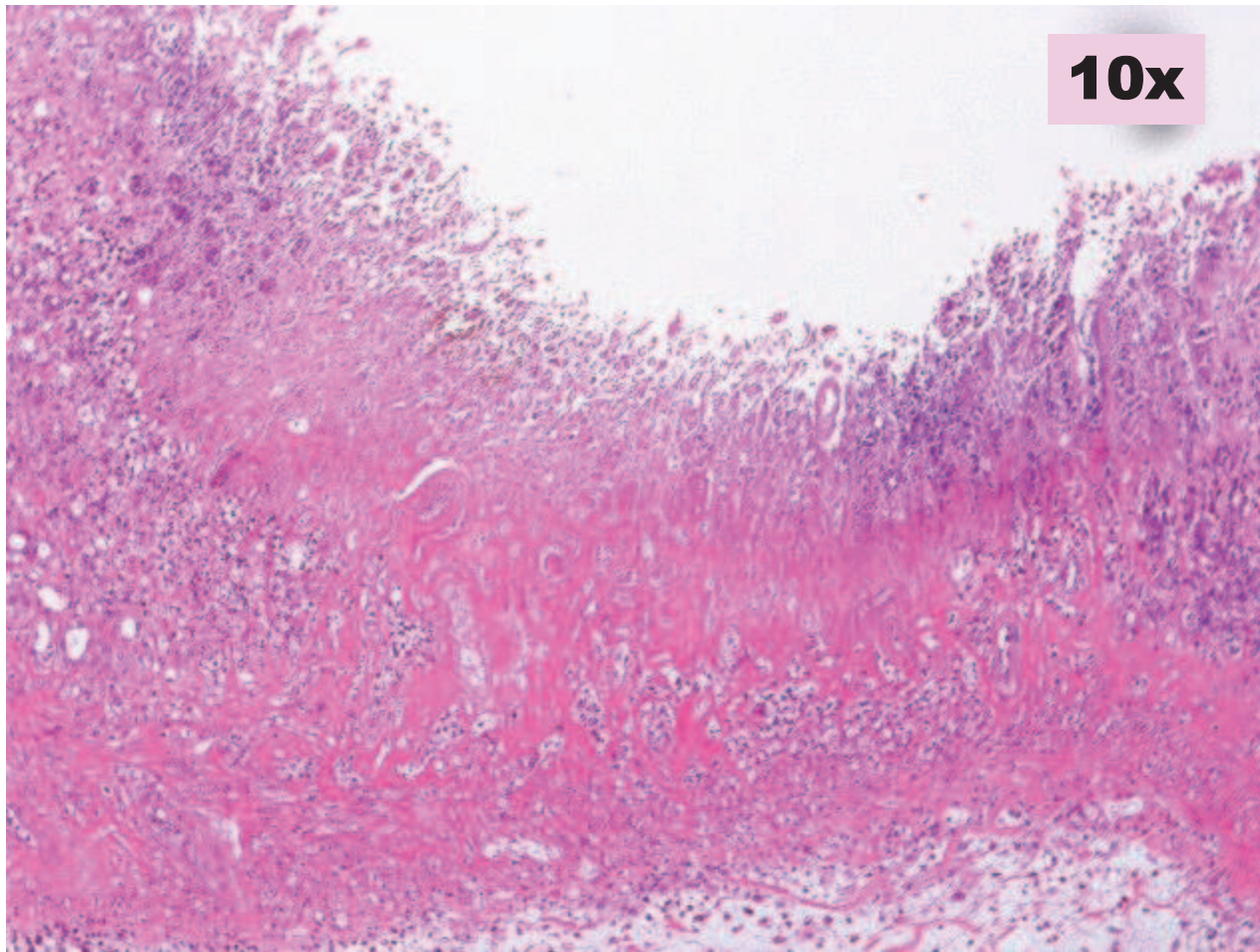


Epithelial Hyperplasia/Ulcer- Glandular

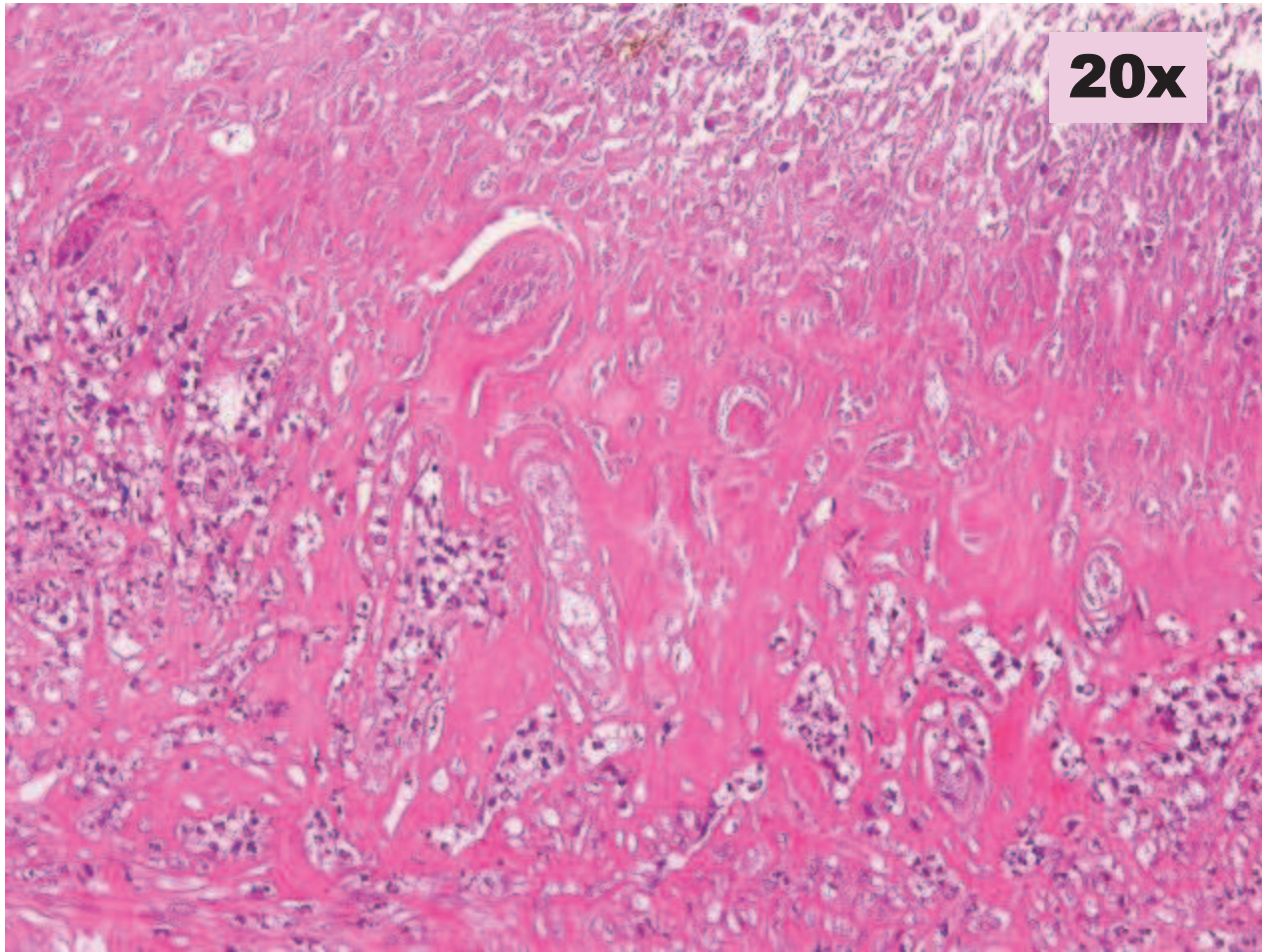


- **HMG Co-A inhibitors**
- **Irritant potential of test substance**
- **Not related to pharmacodynamic properties of test substance**
- **Long stasis of test substance**
- **Stress/starvation**
- **Biochemical changes- BUN/Urea**
- **Hematology changes- altered leukocyte count**

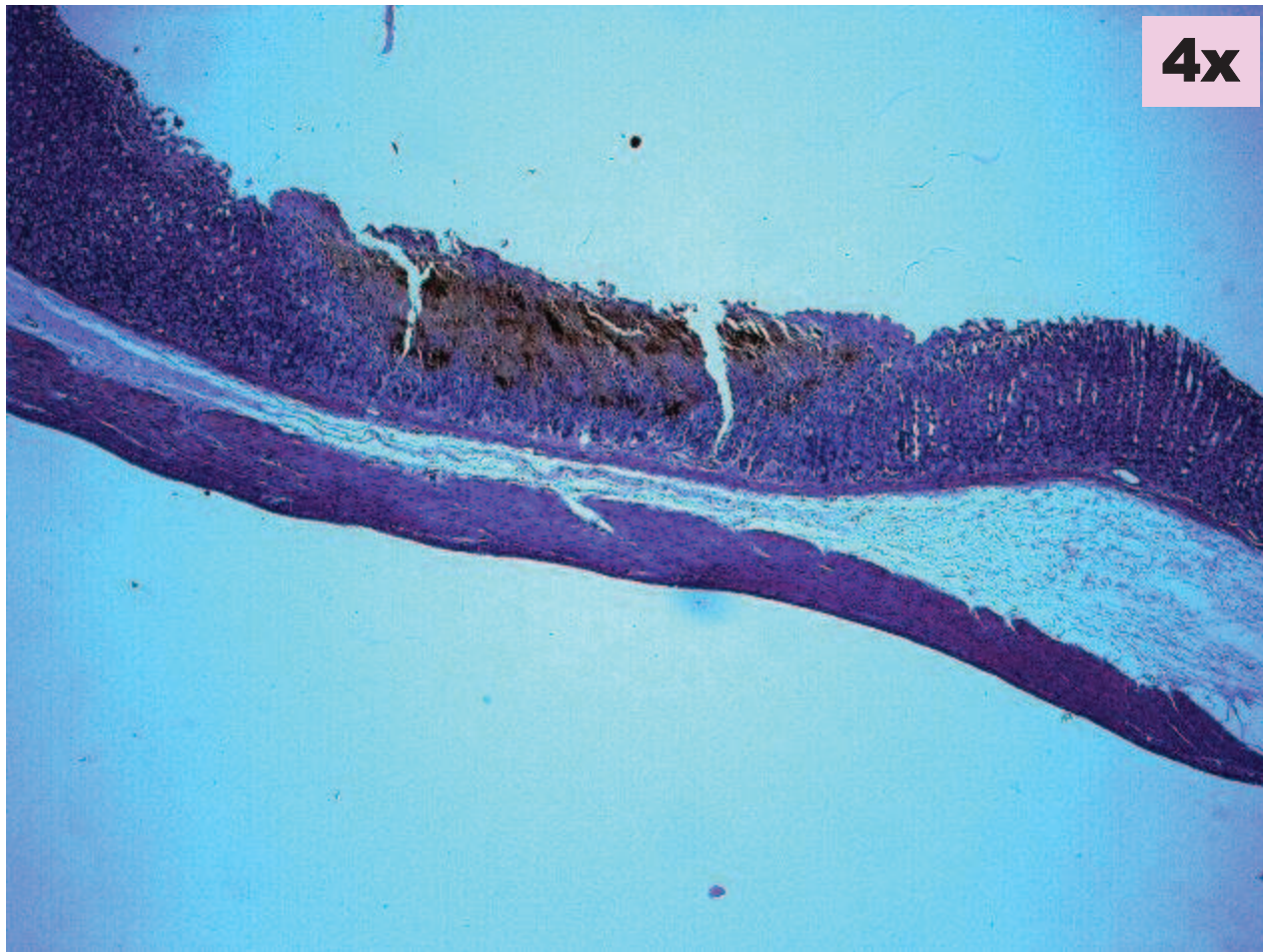
Ulcer- Glandular Stomach- Rat



Ulcer-Glandular stomach – Rat



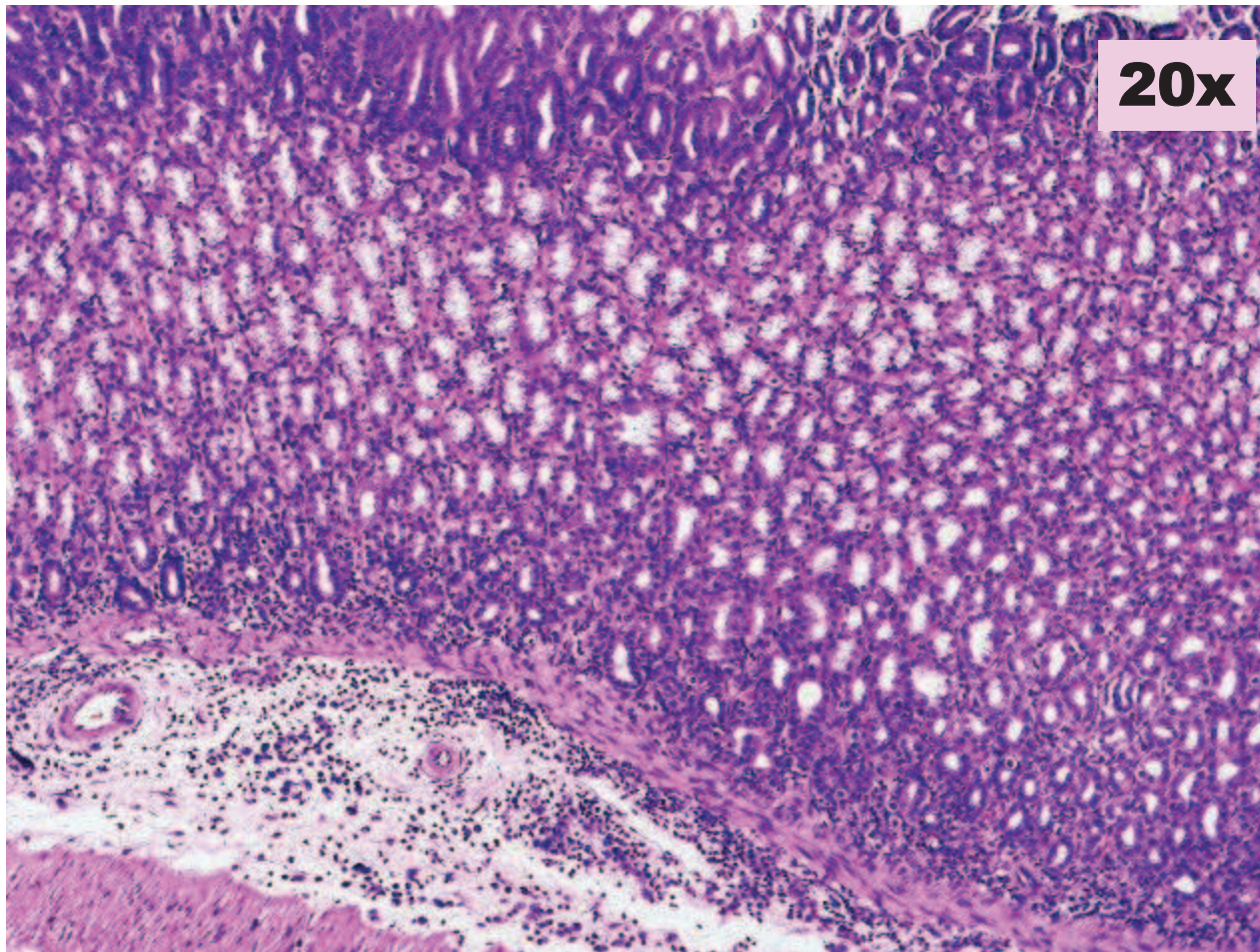
Mucosal Necrosis and Pigmentation – Glandular - Rat



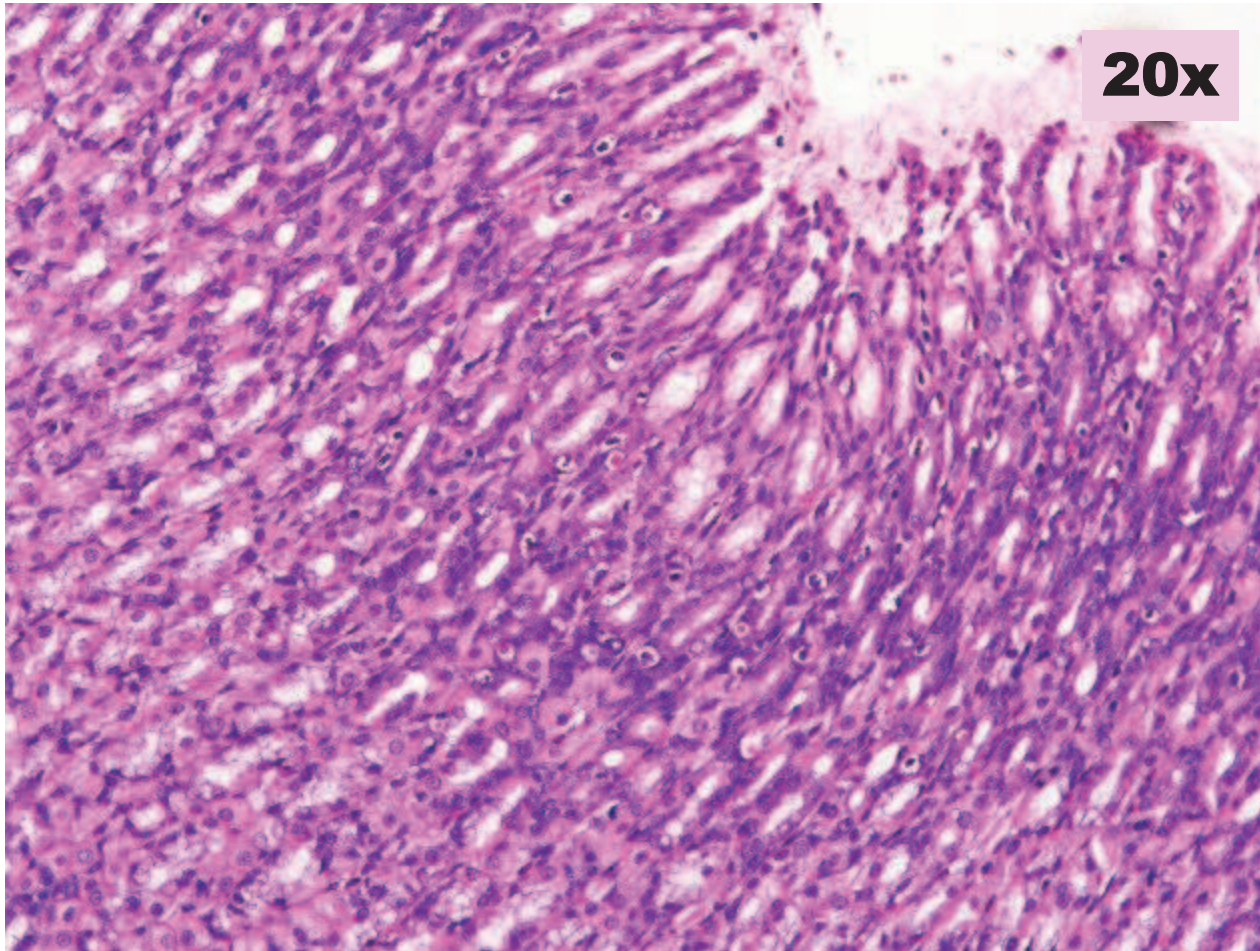
Ulcer-glandular stomach

- **Non seroidal anti-inflammatory drugs**
- **Stress**
- **High doses of ACE inhibitors**
- **Biochemical changes**
- **Hematology changes- associated hemorrhage**

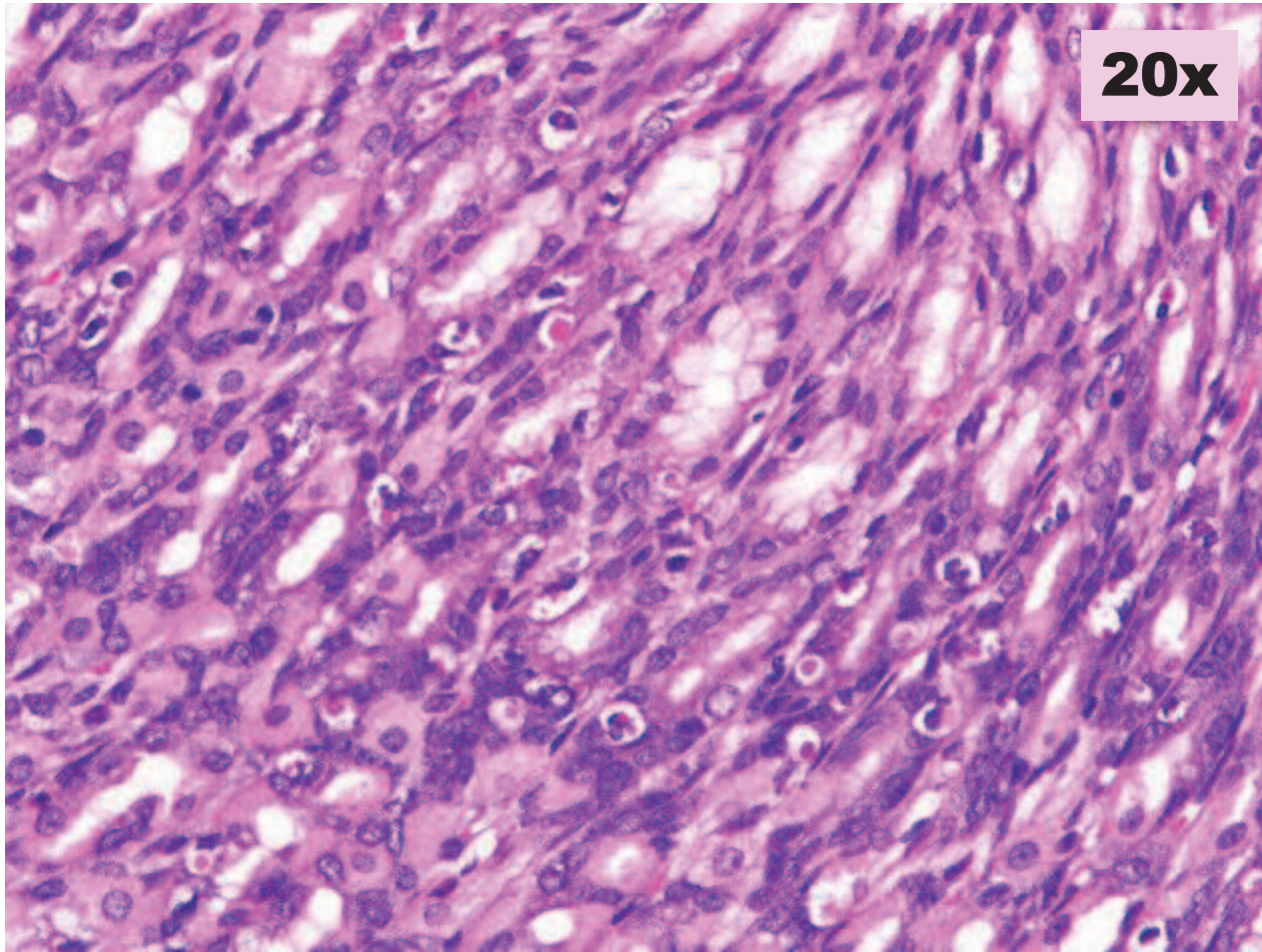
Leukocytic Infiltration Glandular Stomach - Rat



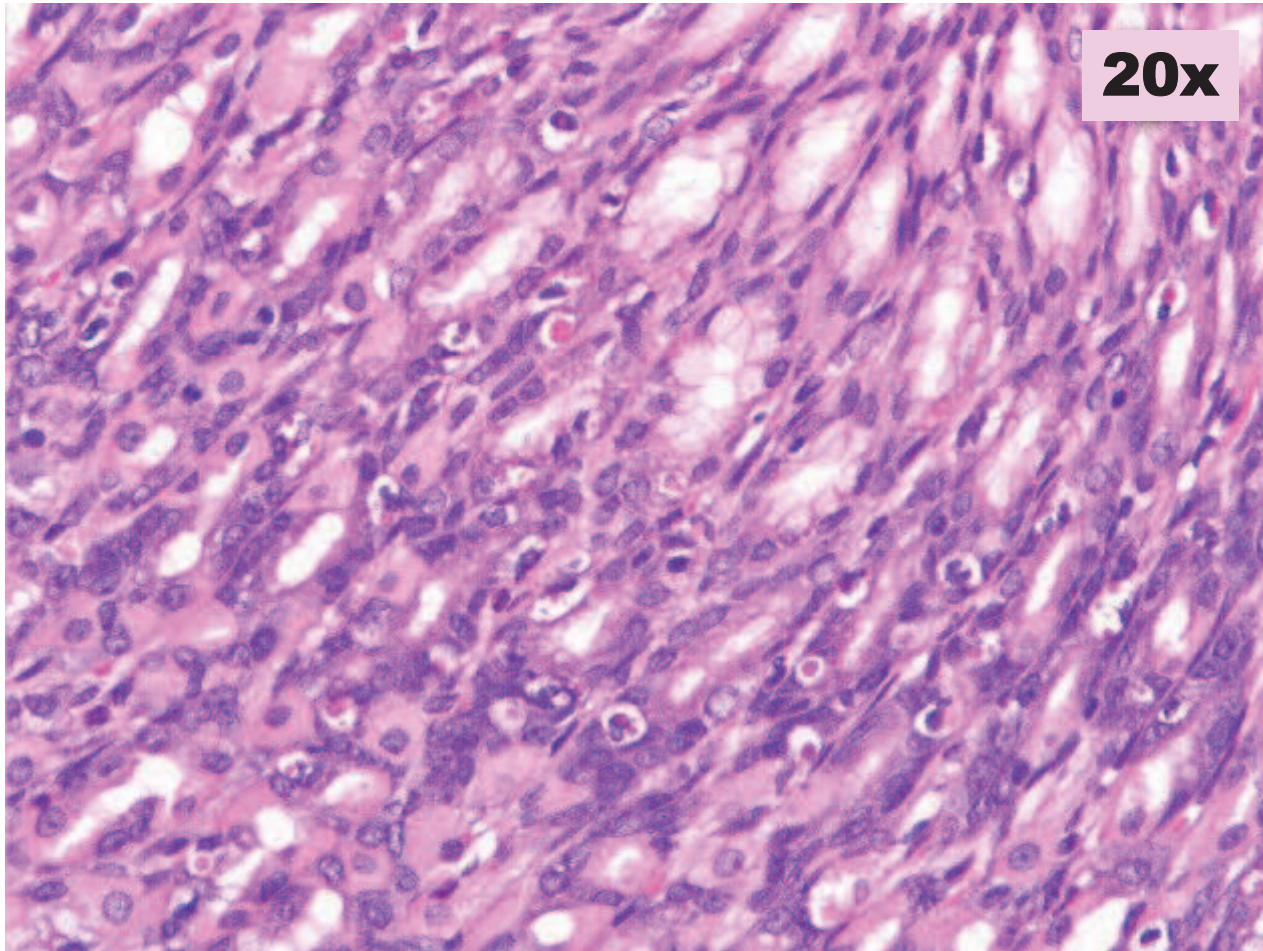
Epithelial degeneration Glandular Stomach - Rat



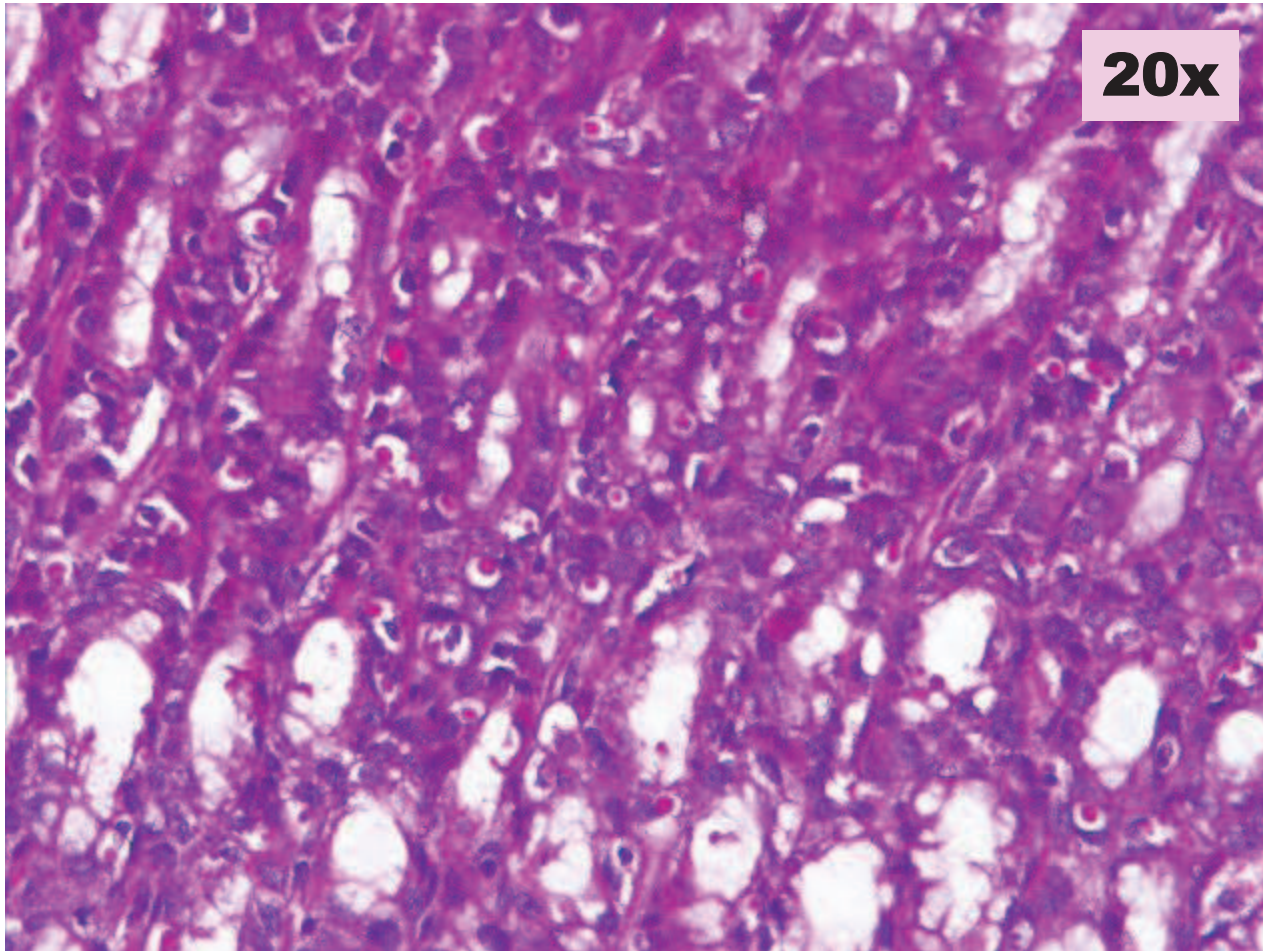
Epithelial degeneration Glandular Stomach - Rat



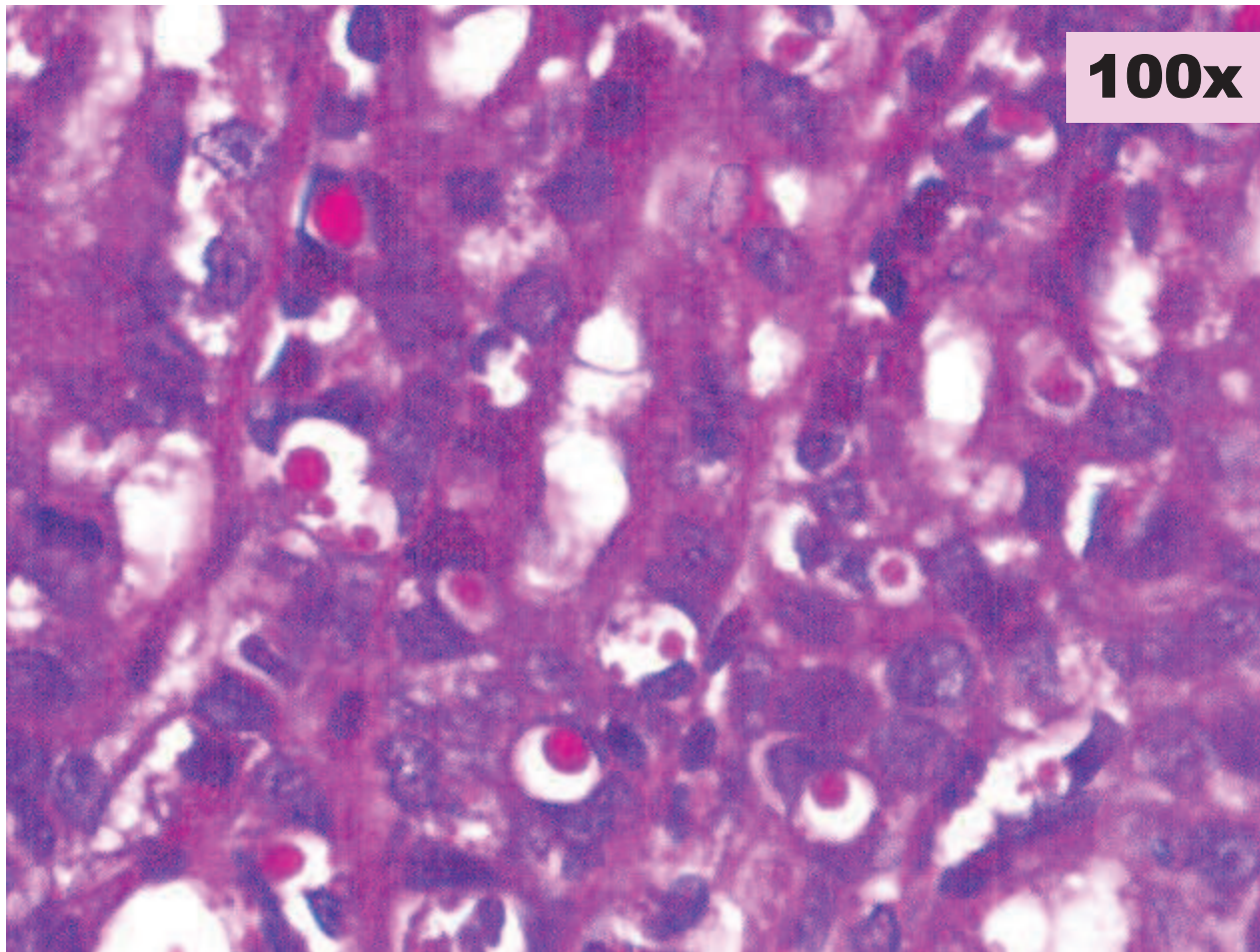
Epithelial degeneration Glandular Stomach - Rat



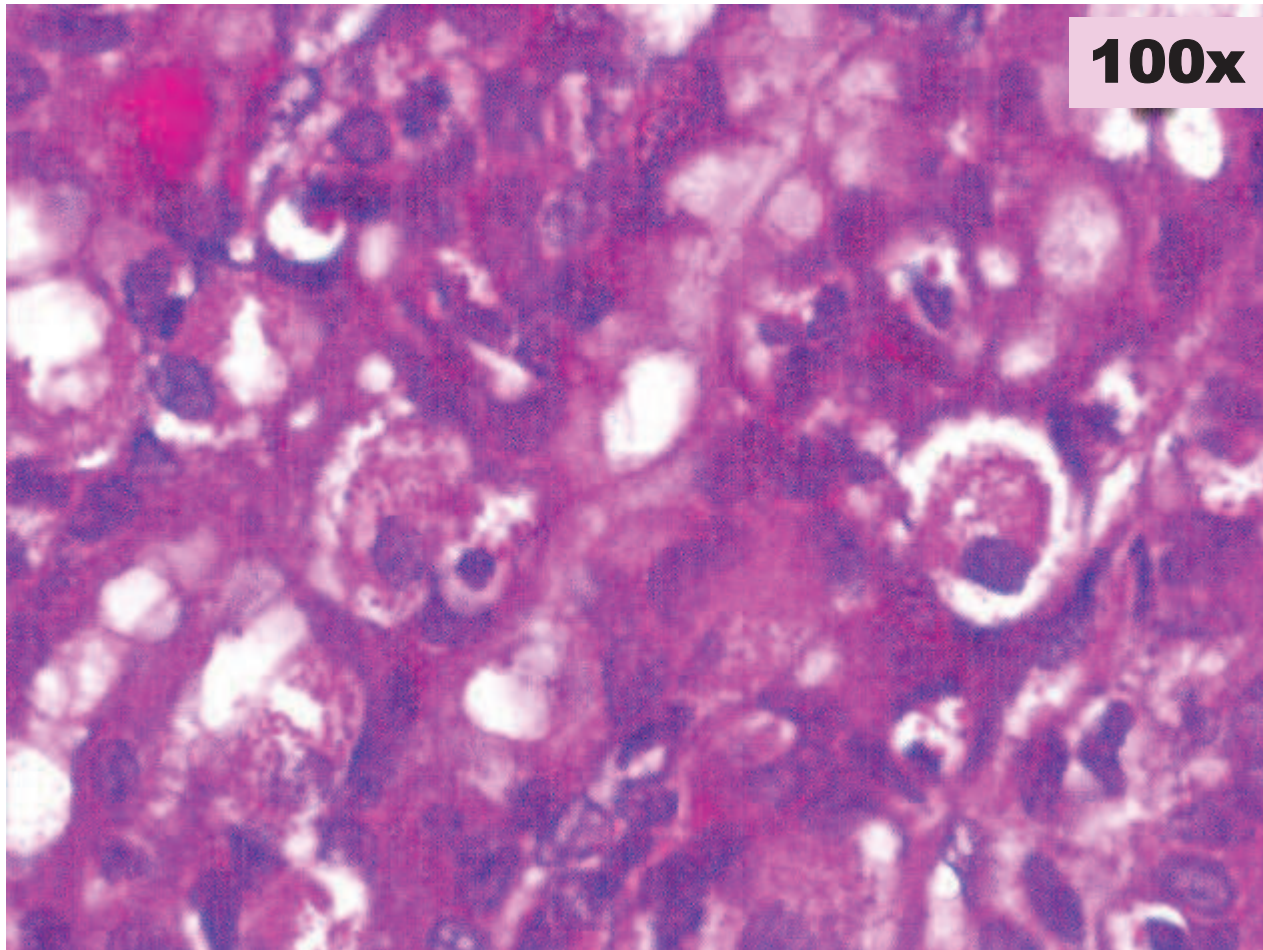
Epithelial degeneration Glandular Stomach - Rat



Epithelial degeneration Glandular Stomach - Rat



Epithelial degeneration Glandular Stomach - Rat



Epithelial Degeneration

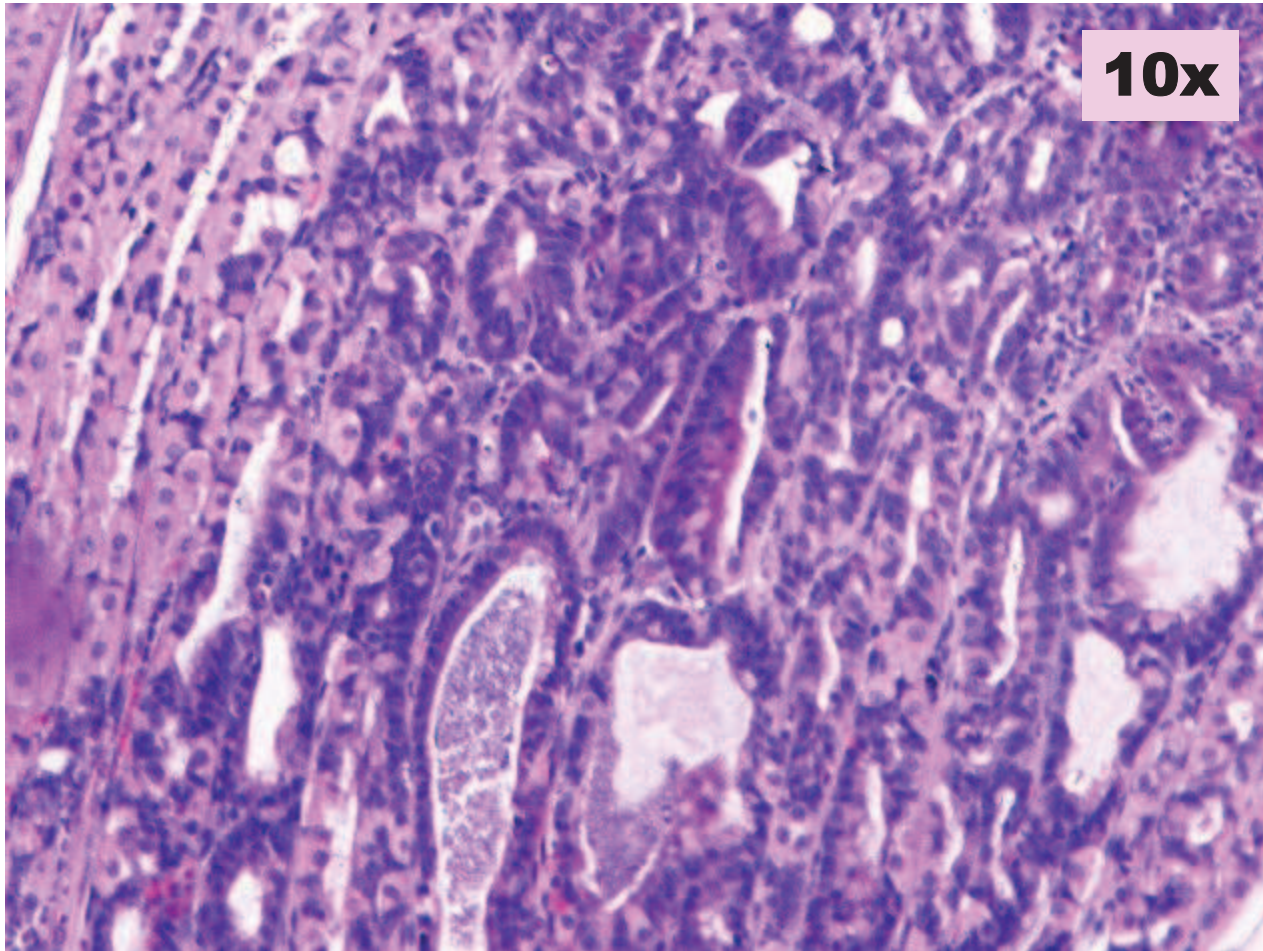
- ✓ **Common in feeding studies**
- ✓ **Allergic gastritis**
- ✓ **Eosinophilic gastritis**
- ✓ **Eosinophilic droplets/ capillaries**
- ✓ **Industrial chemicals**
- ✓ **Not observed with Pharmaceutical compounds**
- ✓ **Enzyme preparations-fermentation**

Epithelial Degeneration

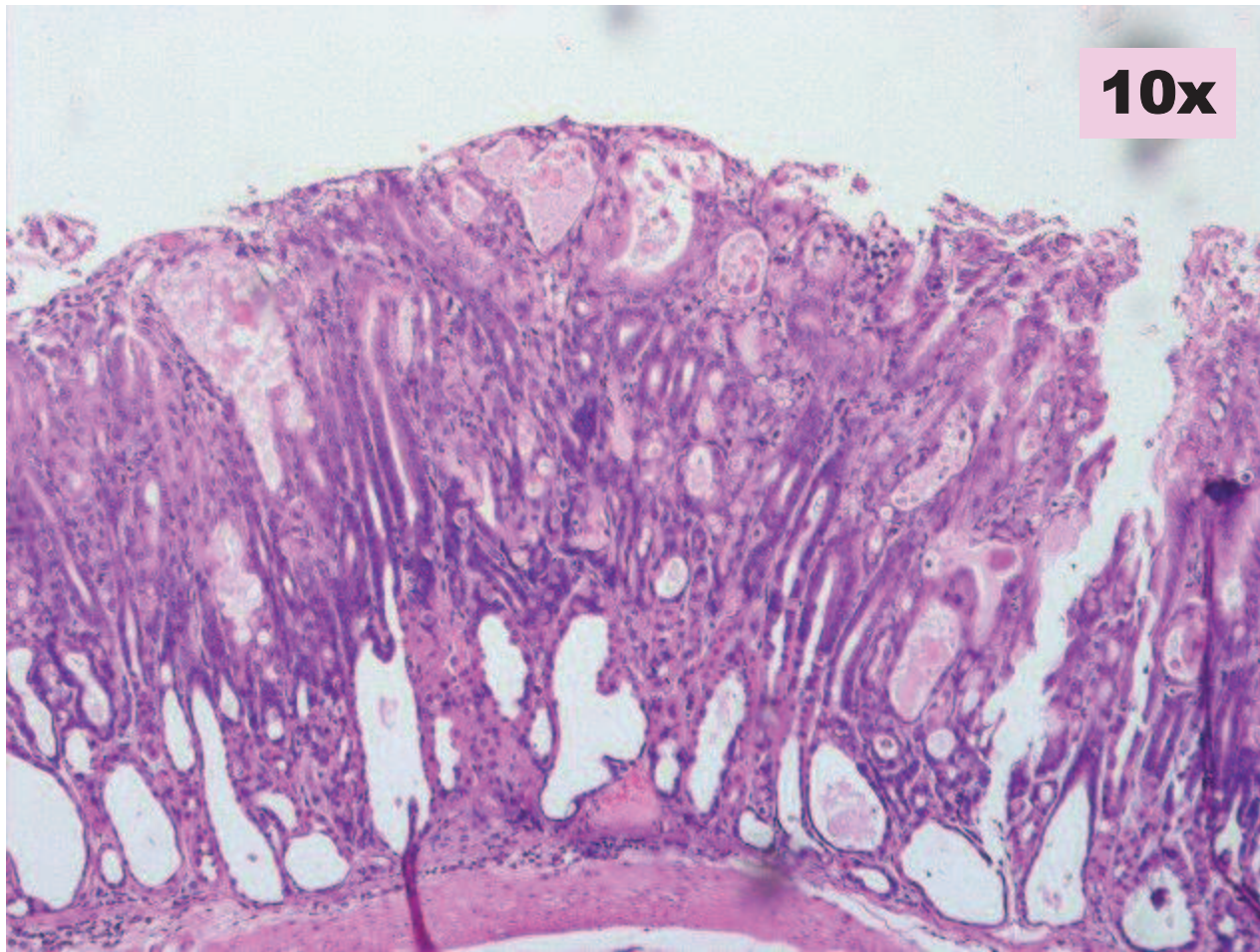
Associated/primary changes

- **Non glandular epithelial hyperplasia**
- **Lekocytic infiltration**
- **Edema in submucosa**
- **Foveolar epithelial hyperplasia**
- **Increased mucosal thickness- fundic**

Epithelial Hyperplasia Glandular Stomach - Rat



Epithelial Hyperplasia Glandular Stomach - Mouse

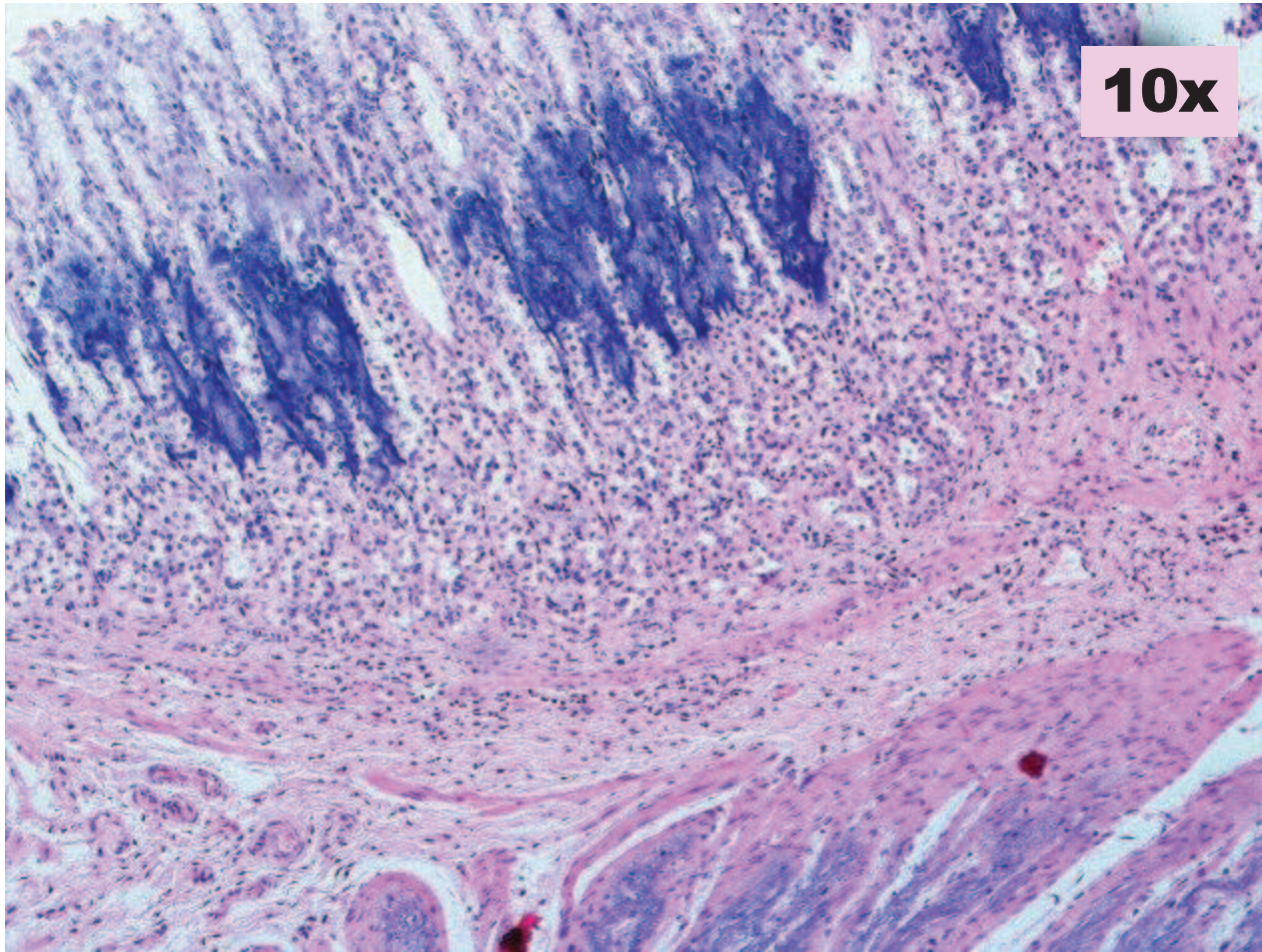


Epithelial Hyperplasia- Glandular stomach

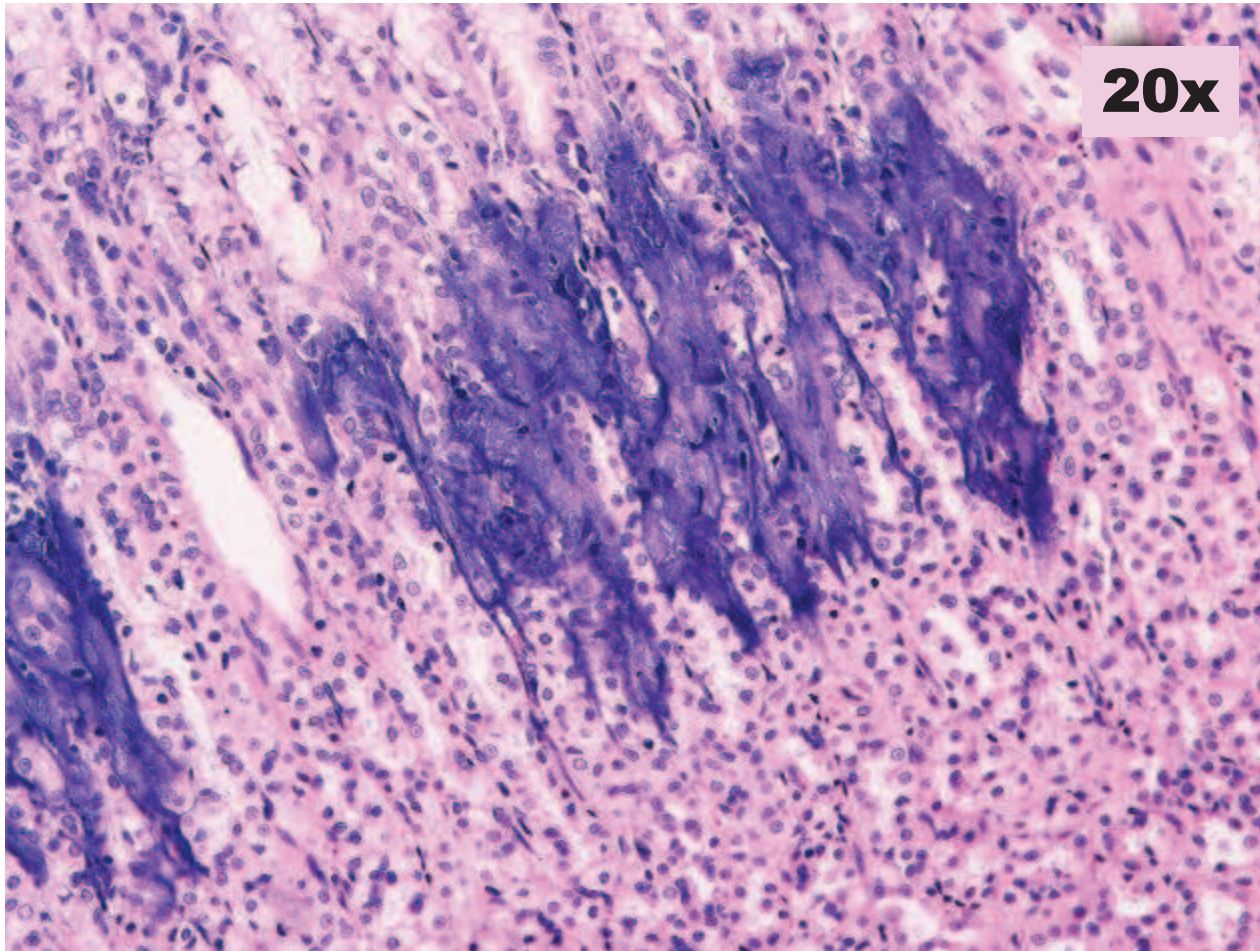
- **Common in aged mice**
- **Rats- discrete lesion and the incidence rat is low, basophilic cells**
- **Mice-to differentiate for the dilated/distended glands**
- **To differentiate adenoma/glandular polyp**
- **Gastric acid inhibitors, H2 antagonists**

Mineralization

Glandular Stomach - Rat



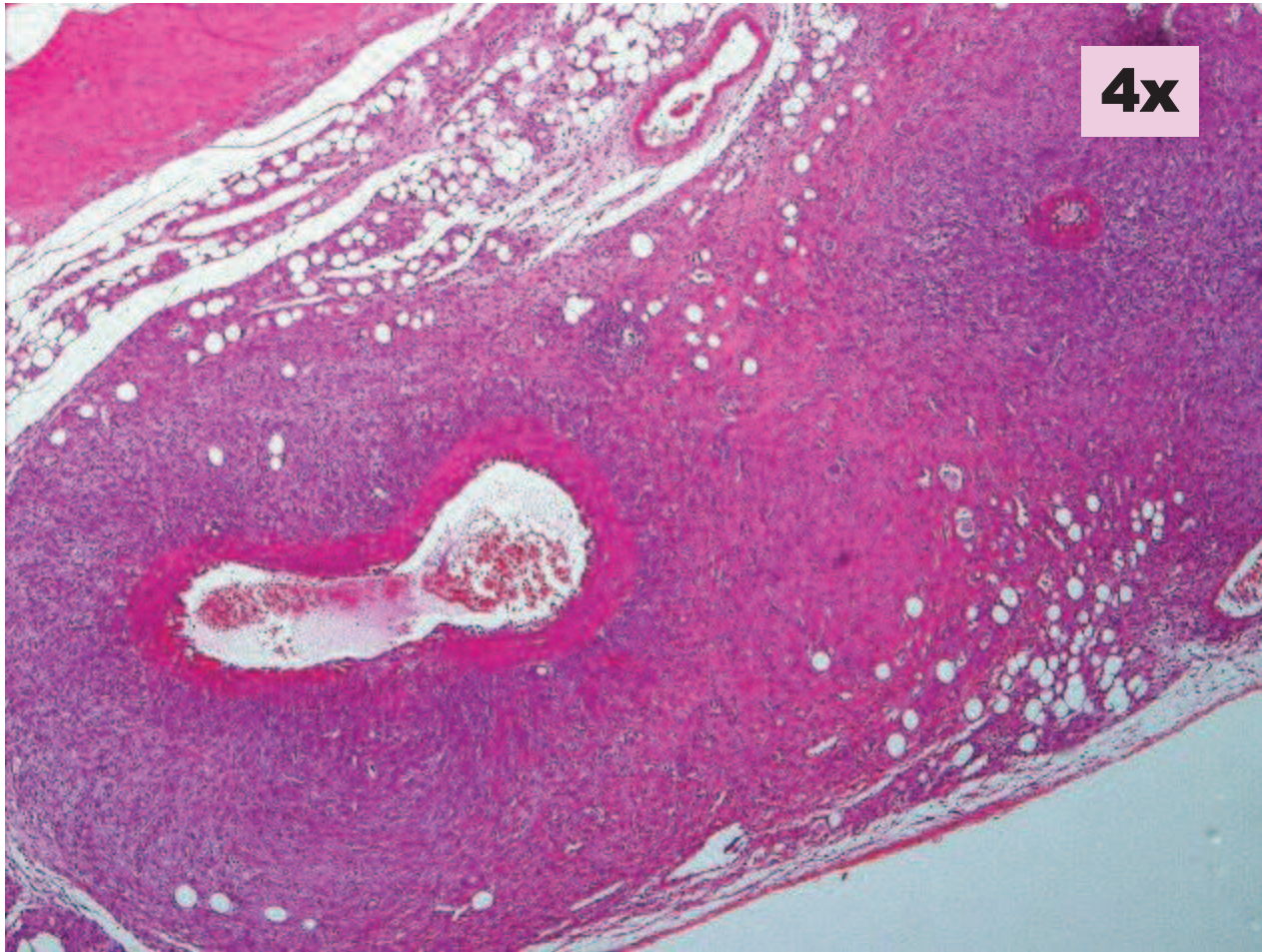
Mineralization Glandular Stomach - Rat



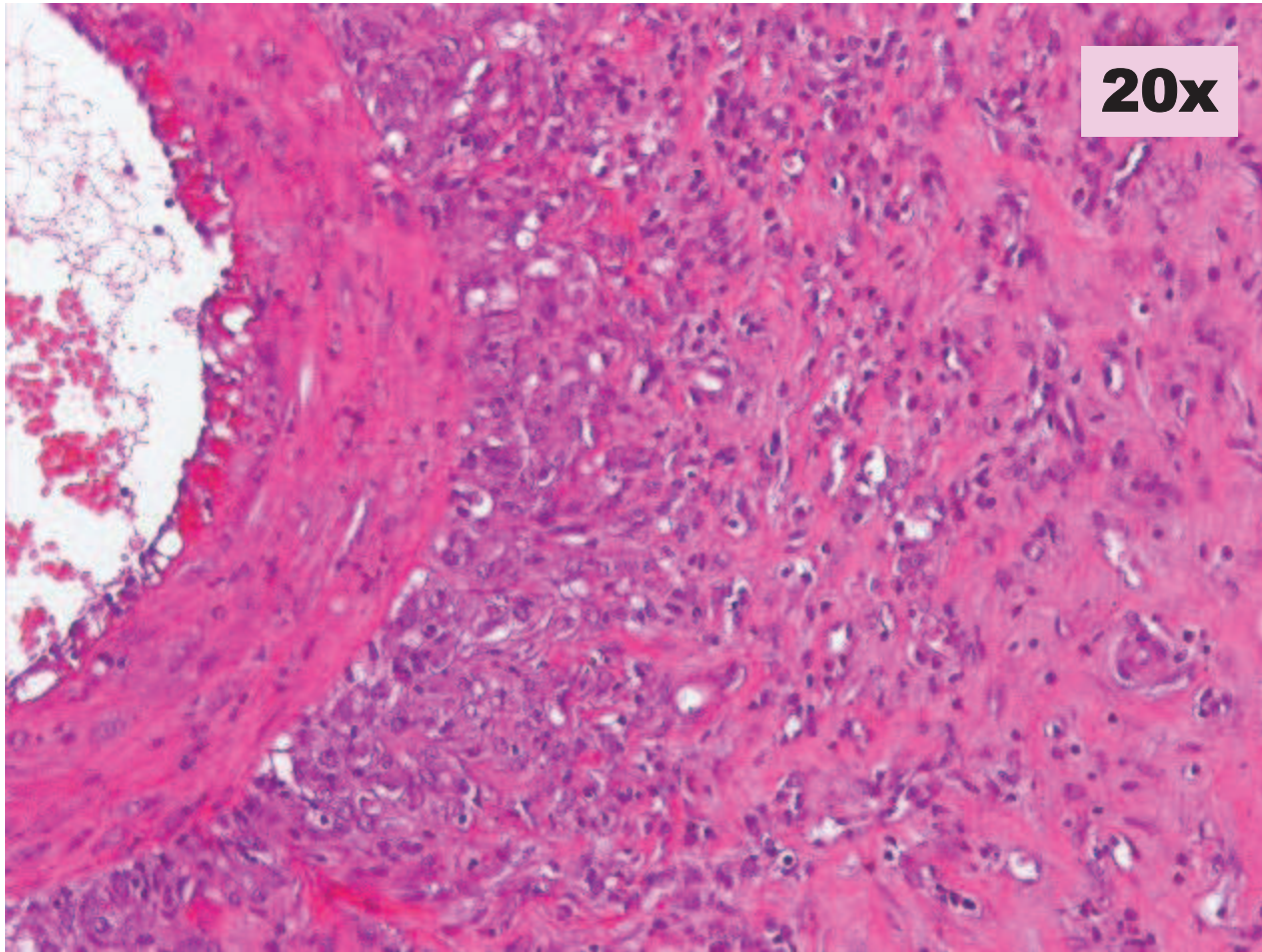
Mineralization- Glandular stomach

- ✓ **Metastatic calcium salt deposits**
- ✓ **Kidney injury and parathyroid hyperplasia**
- ✓ **Dystrophic**
- ✓ **Associated changes**
- ✓ **Confirmation of metastatic mineral deposits**
- ✓ **Basement membrane of blood vessels**
- ✓ **Tyrosine kinase inhibitors(fibroblast growth factor inhibitor)**

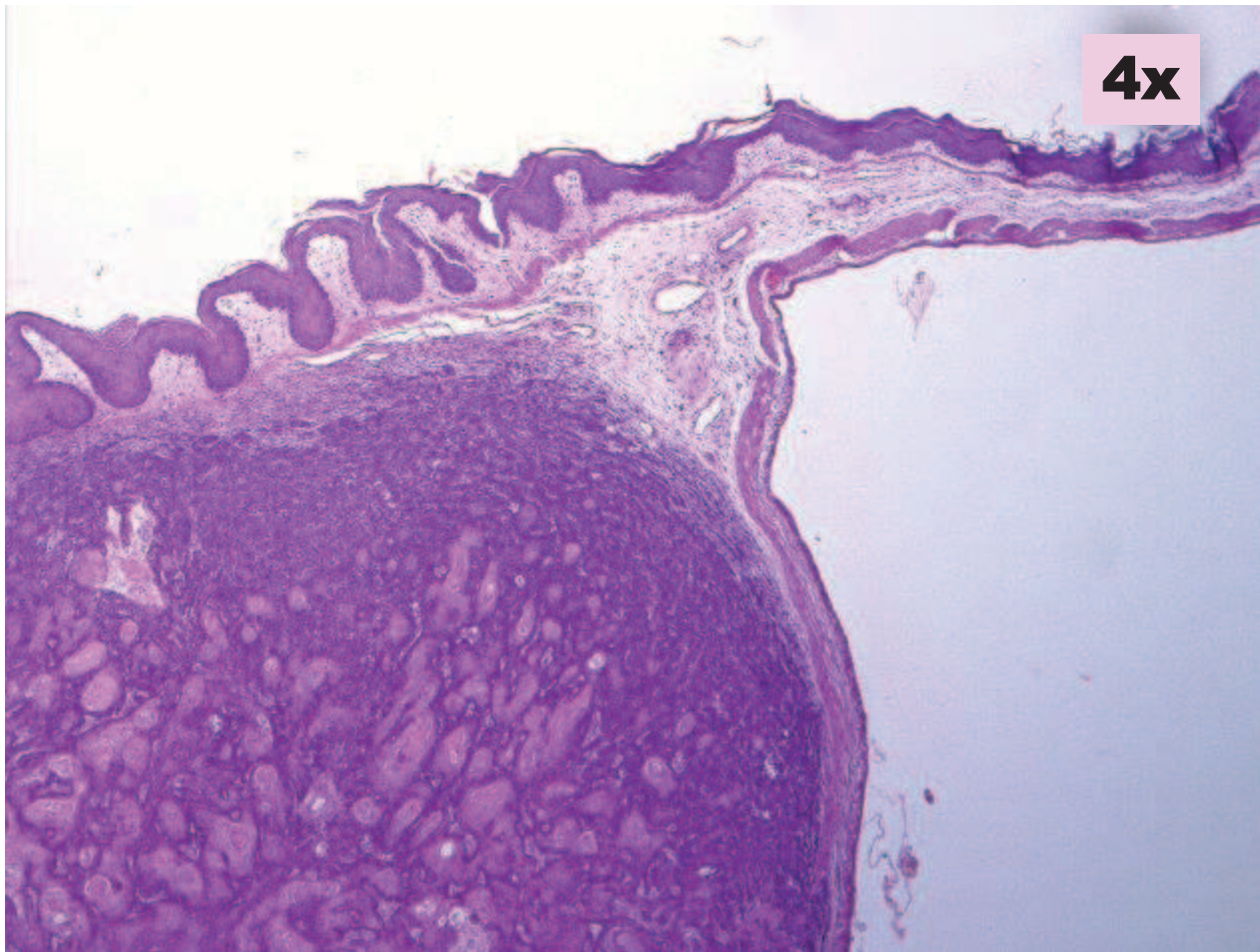
Vasculitis/Perivasculitis - Serosa - Rat



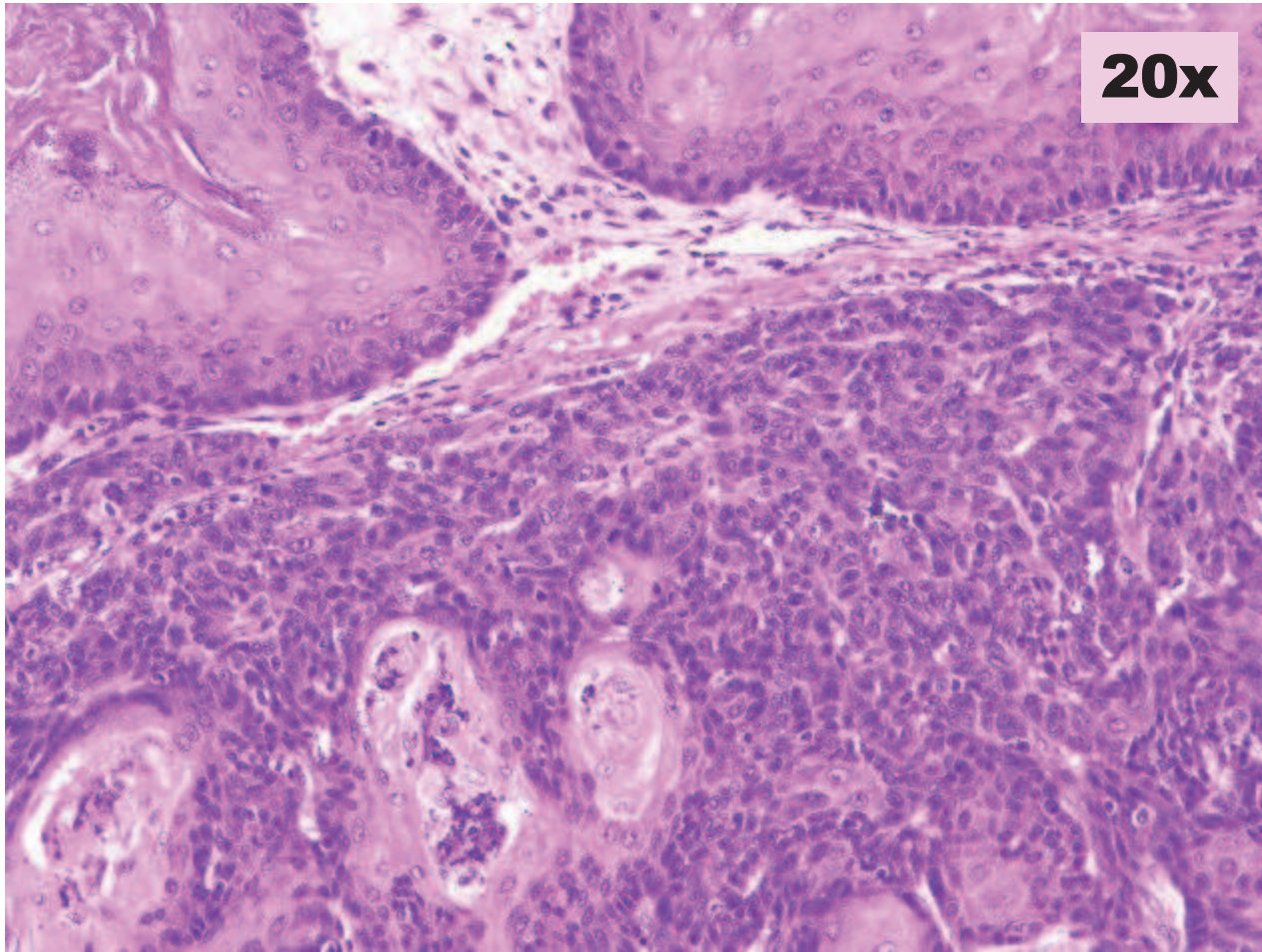
Vasculitis/Perivasculitis - Serosa - Rat



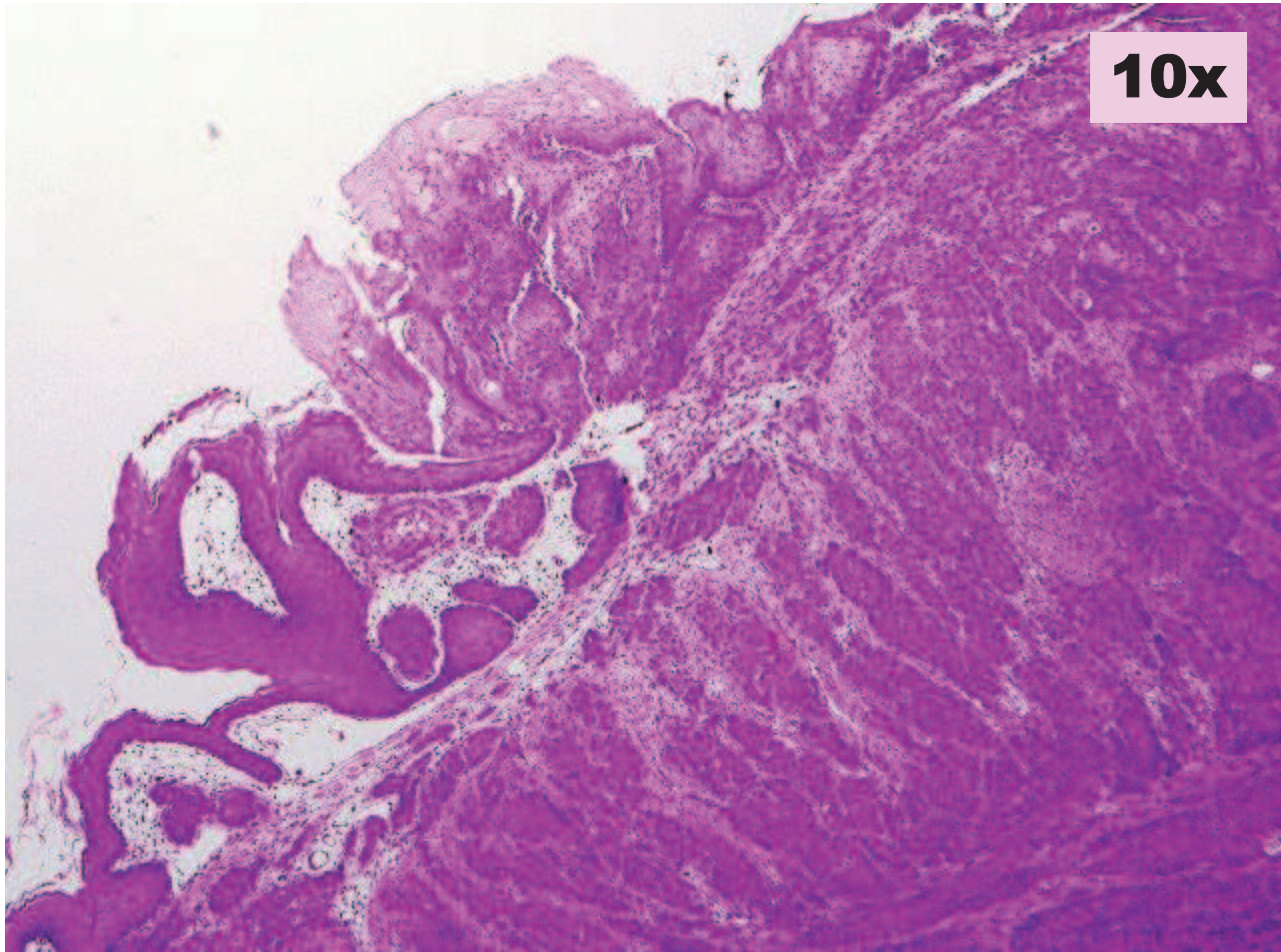
Squamous Cell Carcinoma - Non-glandular - Mouse



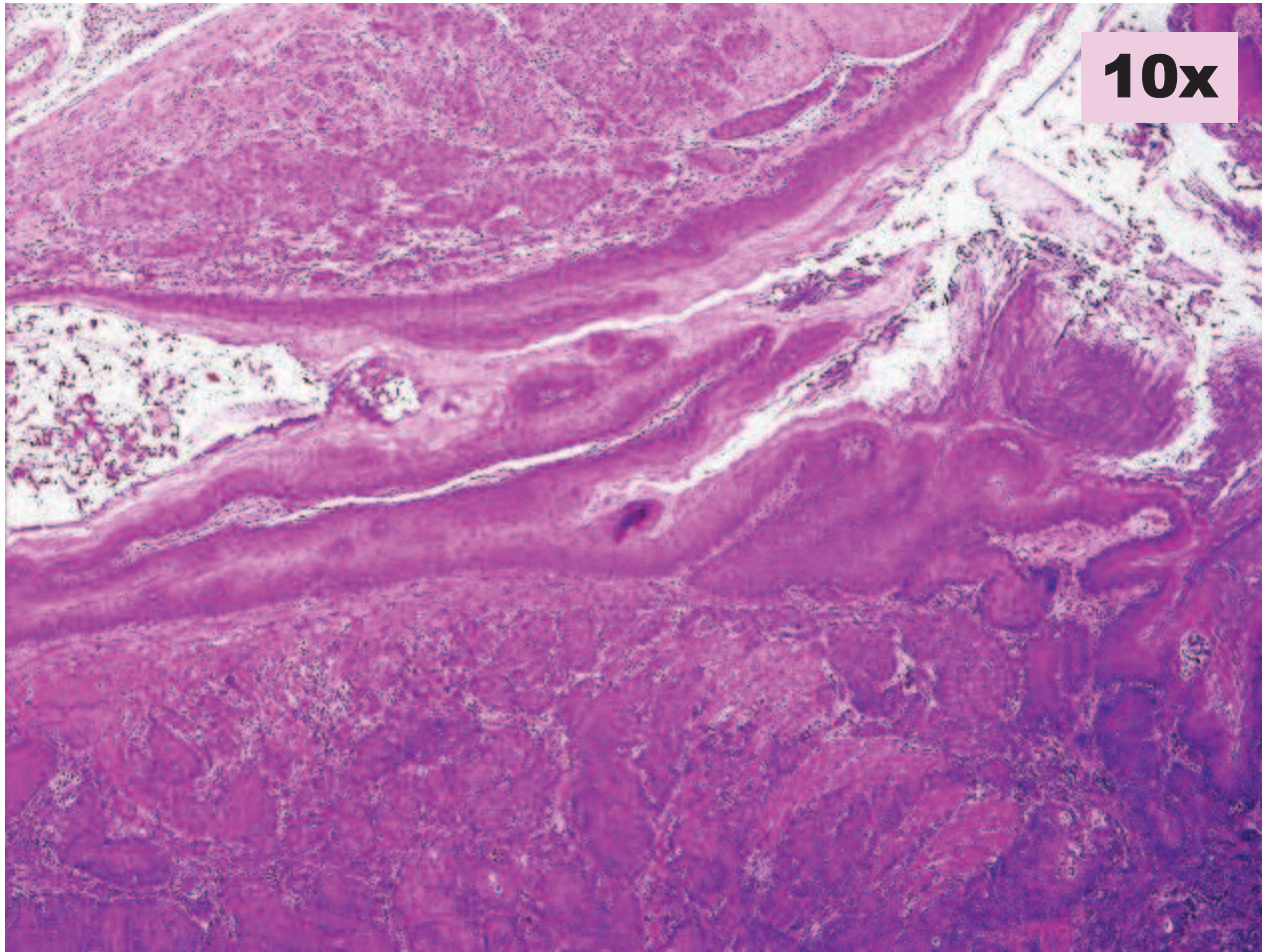
Squamous Cell Carcinoma - Non-glandular - Mouse



Squamous Cell Carcinoma – Mouse



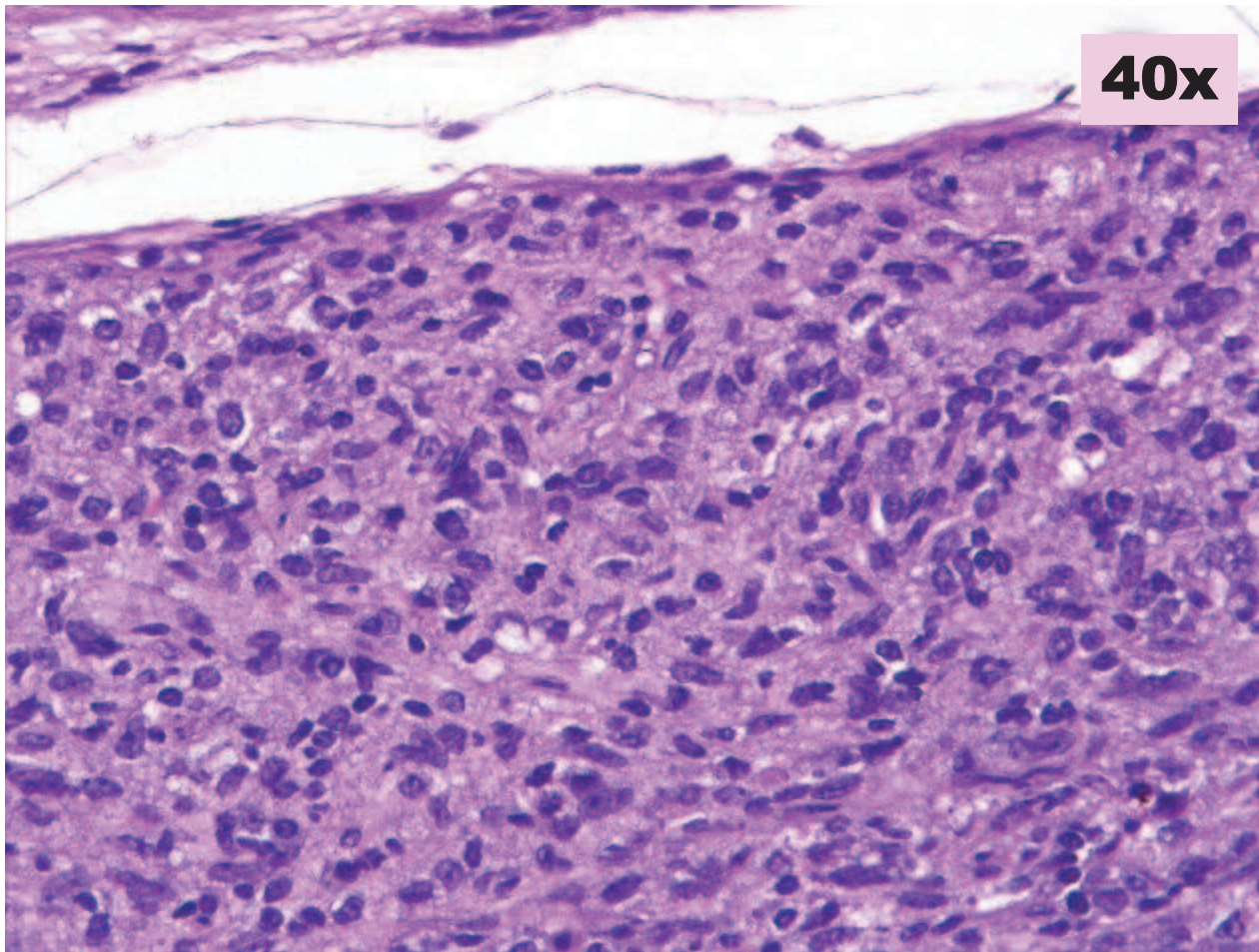
Squamous Cell Carcinoma – Mouse



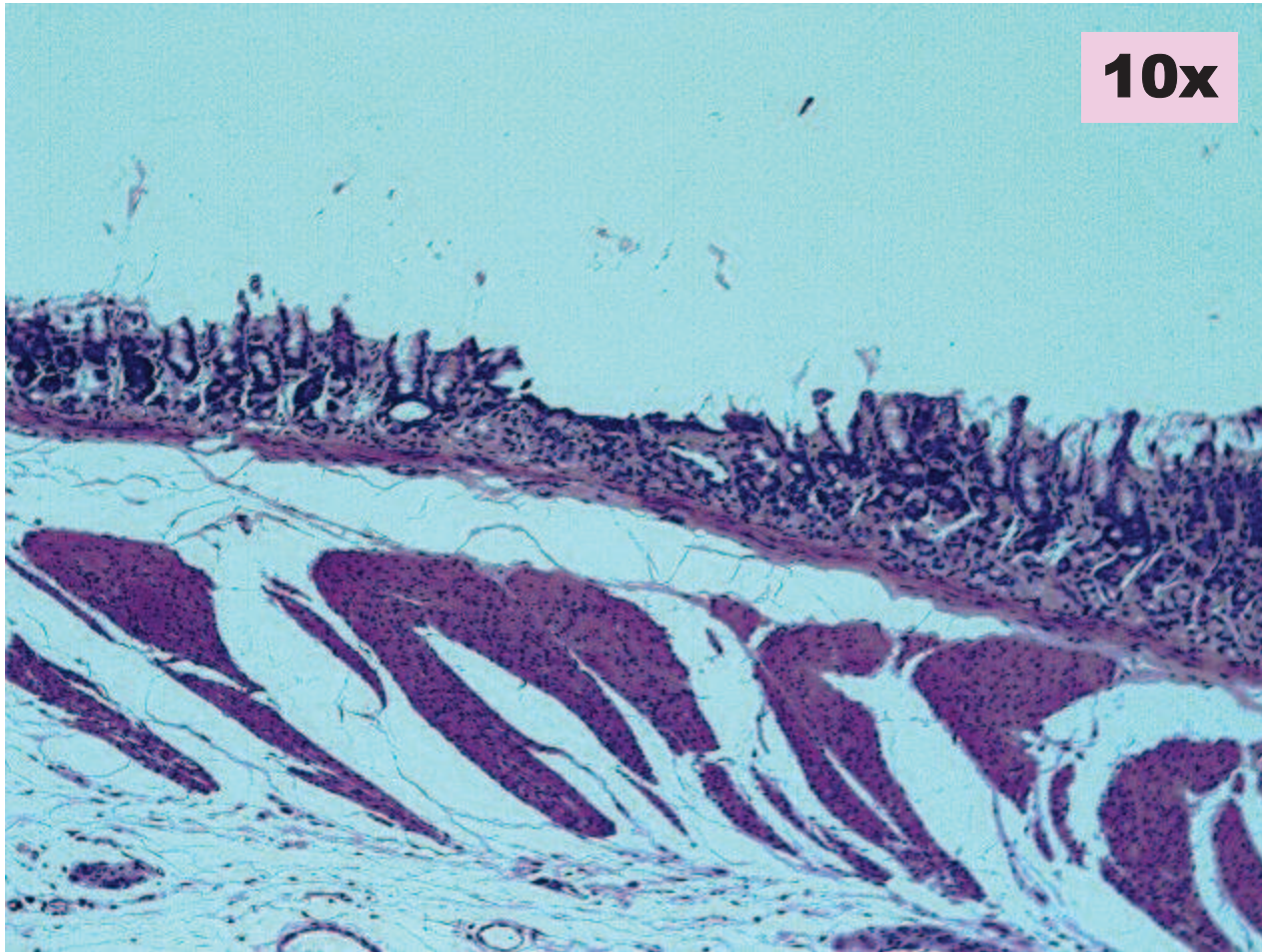
Histiocytic Sarcoma Mouse



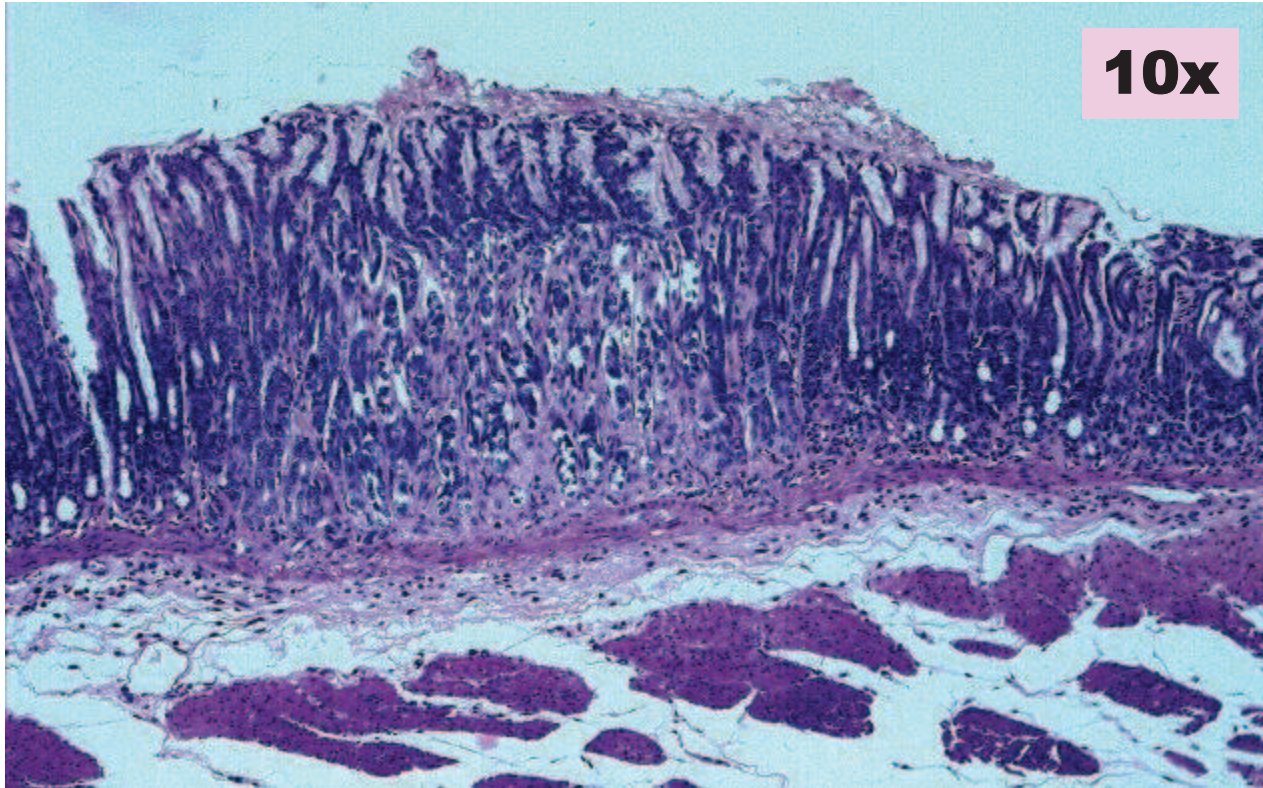
Histiocytic Sarcoma Mouse



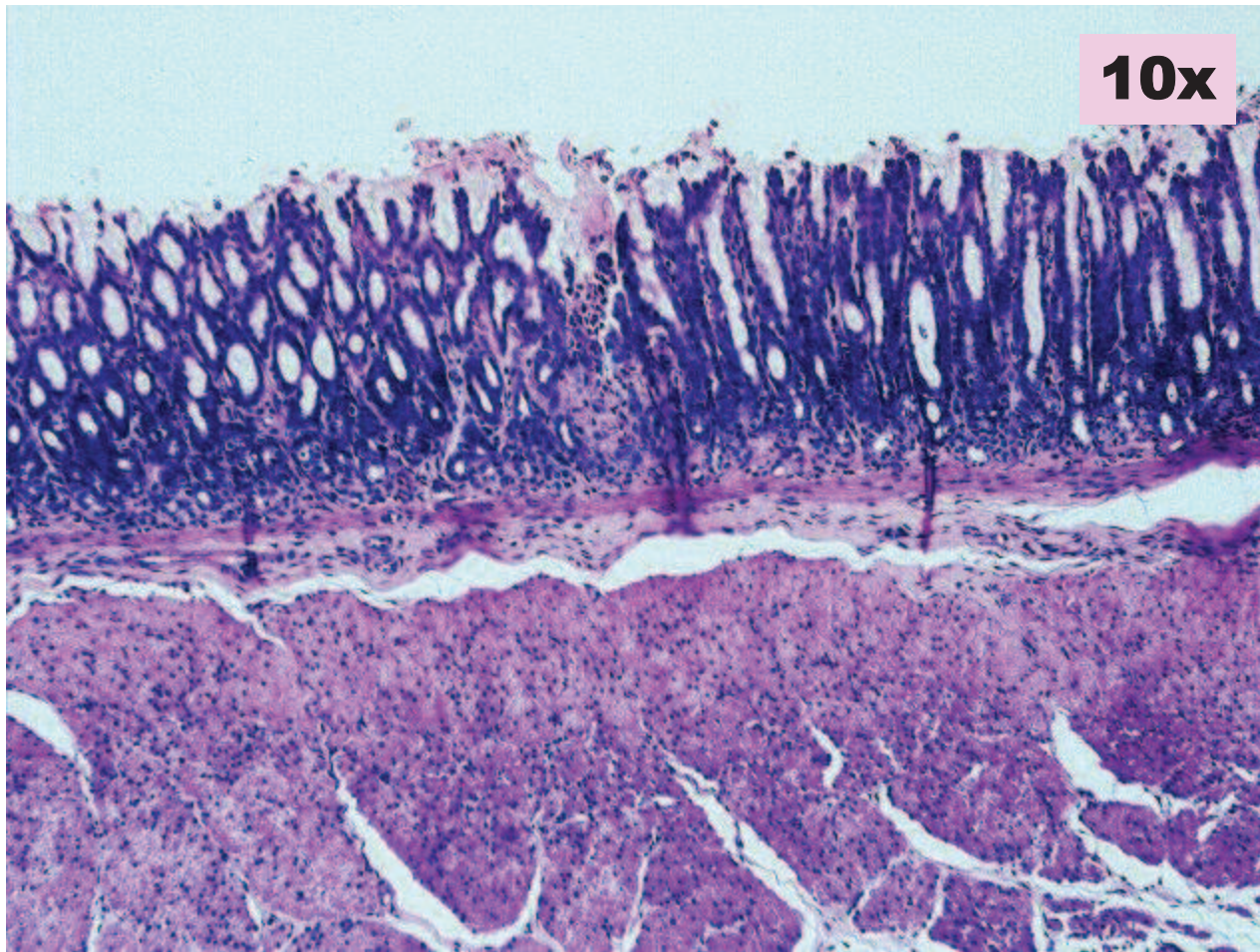
Artifact/Erosion - Glandular Stomach - Rat



Artifact- Glandular Stomach - Rat



Artifact- Glandular Stomach - Rat





Thank You