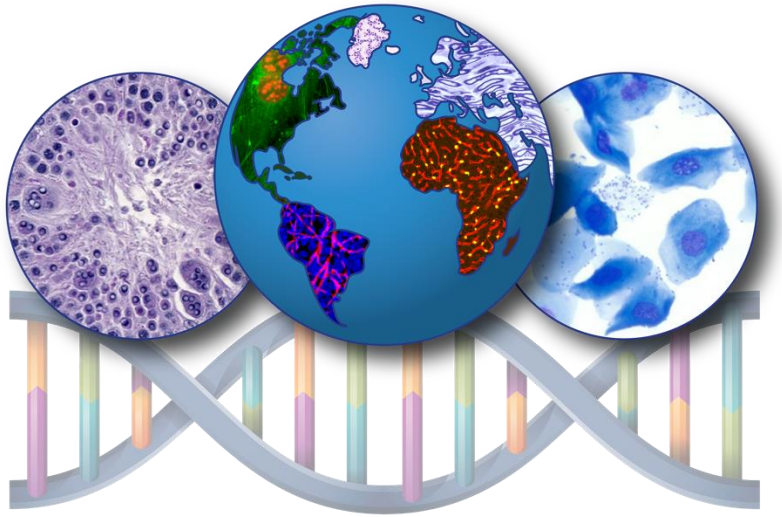
Nonproliferative Lesions of the Rodent Parathyroid Gland



Division of Translational Toxicology Global Toxicologic Pathology Training Program

National Institutes of Health • U.S. Department of Health and Human Services

Nonproliferative Lesions of the Parathyroid Gland

Nonproliferative Lesions in Rats and Mice

- Amyloid
- Angiectasis
- Atrophy
- Fibrosis
- Hypertrophy
- Infiltrate, Inflammatory Cell
- Inflammation
- Multinucleated Giant Cells

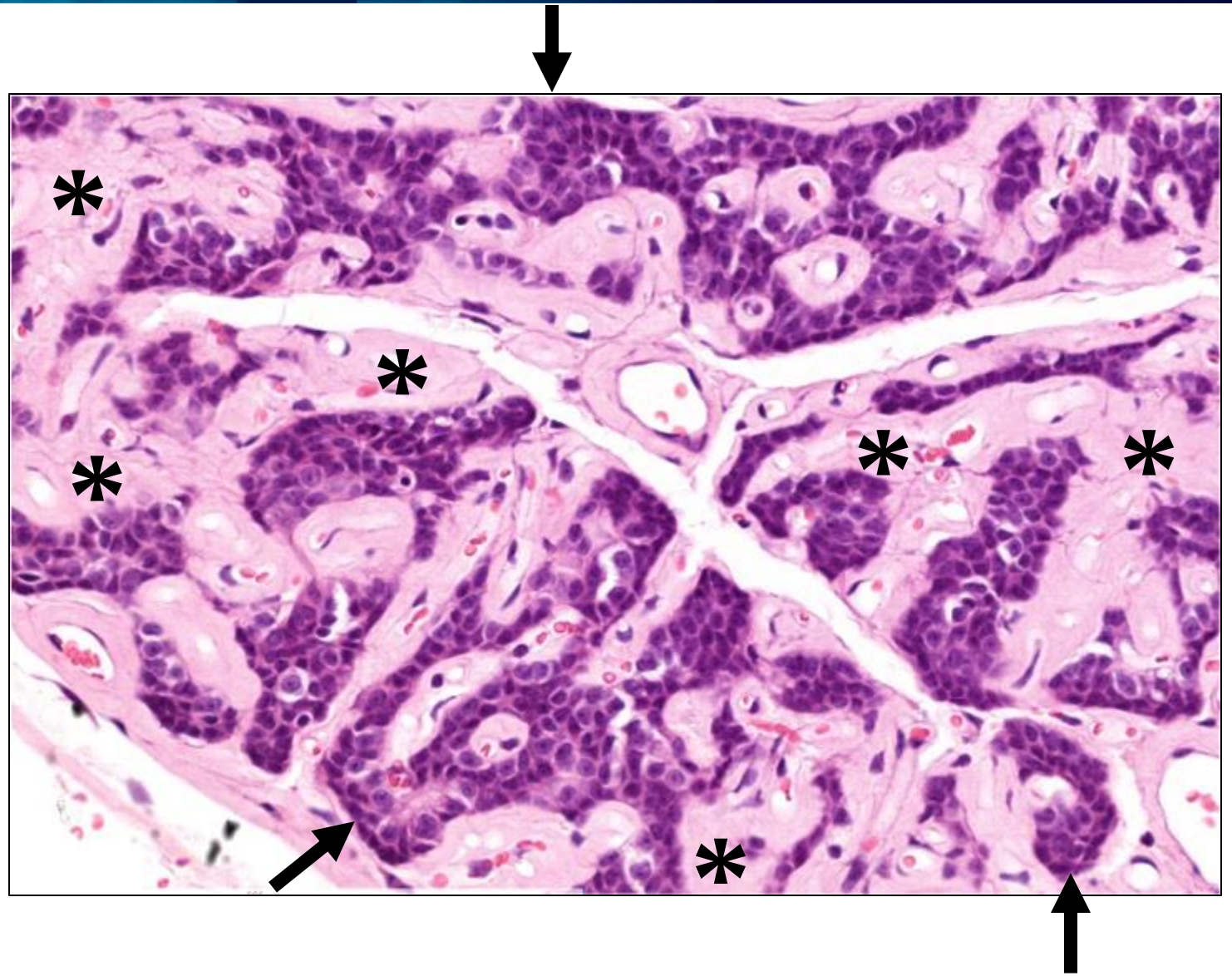
Parathyroid Gland – Amyloid

- Accumulation of abnormal material that is part of a systemic disease
  - Characterized by the extracellular deposition of polypeptides derived from immunoglobulins or serum proteins in multiple tissues
- Diagnostic features
  - Extracellular deposition of amorphous material that stains pale eosinophilic with hematoxylin and eosin (H&E)
  - Green birefringence (double refraction of light) using polarized light with Congo red stain
  - Yellow to yellow-green under fluorescent microscope with Thioflavin T stain
- Incidence increases with age
- Common in some strains of mice (CD-1 and C57BL/6) and rare in B6C3F1 mice and in rats

Parathyroid Gland – Amyloid

Amyloid

- Expansion of interstitium due to deposition of pale eosinophilic, amorphous material (amyloid)* in the parathyroid gland of a mouse
- The amyloid deposition results in increased prominence of chief cell cords (arrows)



Parathyroid Gland – Angiectasis

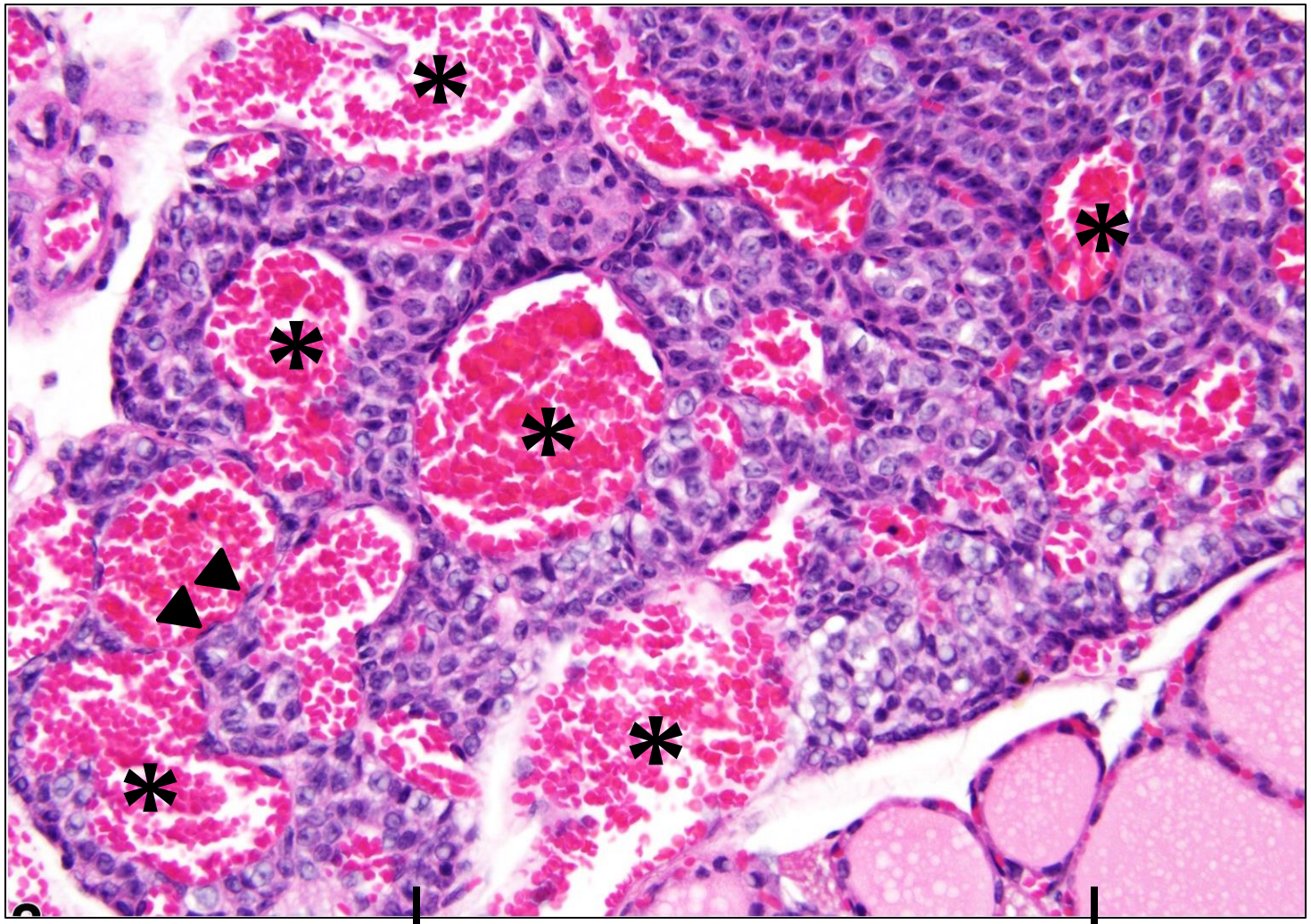
- Dilation of blood vessels
  - Variably sized, blood-filled vascular spaces
  - Lined by single layer of well-differentiated endothelial cells
  - Causes distortion of the architecture of the tissue (differentiates from congestion, in which diffusely dilated, blood-filled vessels do not distort the architecture)
  - Vascular spaces are preexisting and loosely distributed (unlike hemangioma, which is a well-circumscribed mass of newly formed vascular structures)
- Angiectasis may accompany hyperplasia or adenoma
- Rare lesion in mice and rats

Parathyroid Gland – Angiectasis

- Angiectasis in the parathyroid gland of a mouse
- Multiple dilated blood-filled vascular structures (*)

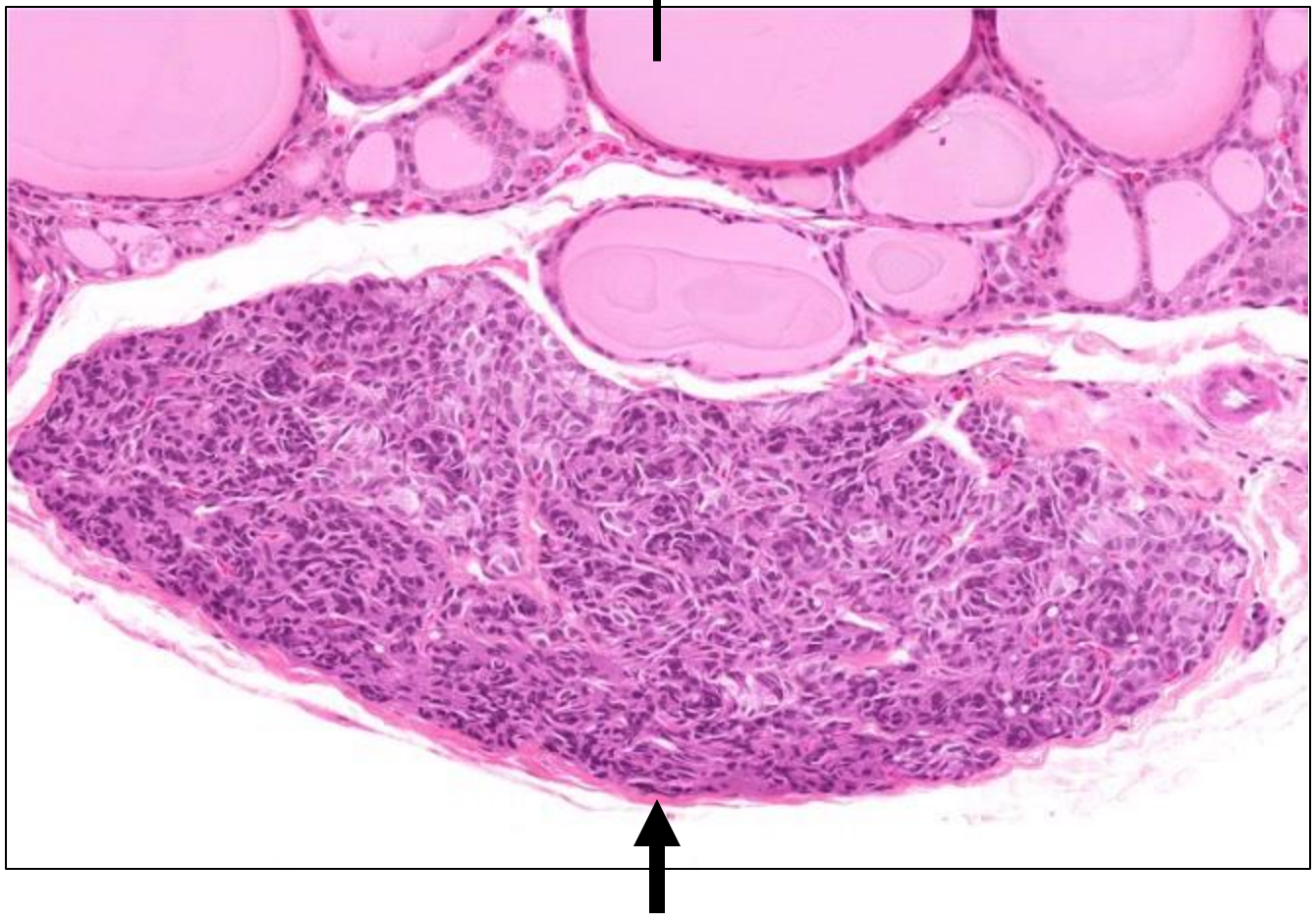
Parathyroid Gland – Angiectasis

Multiple dilated blood-filled vascular structures (*) lined by well-differentiated endothelial cells (arrowheads) in the parathyroid of a mouse



Parathyroid Gland – Atrophy

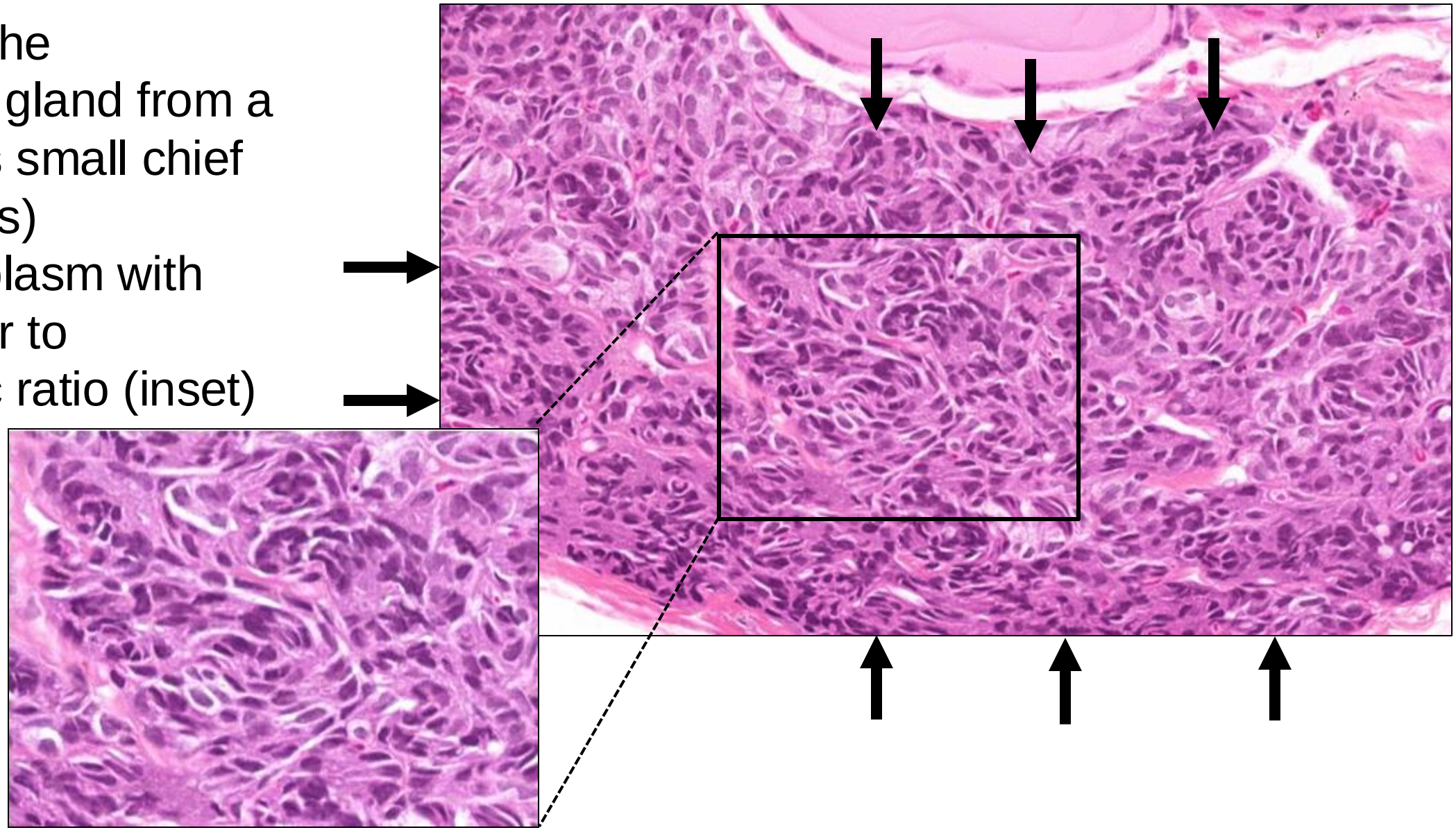
- Small (atrophied) chief cells with scant cytoplasm and high nuclear to cytoplasmic ratio
- Pathogenesis: Suppression of parathyroid hormone synthesis caused by increased serum ionized calcium concentration or excessive vitamin D supplementation in mice and rats



Atrophy of the parathyroid gland from a rat

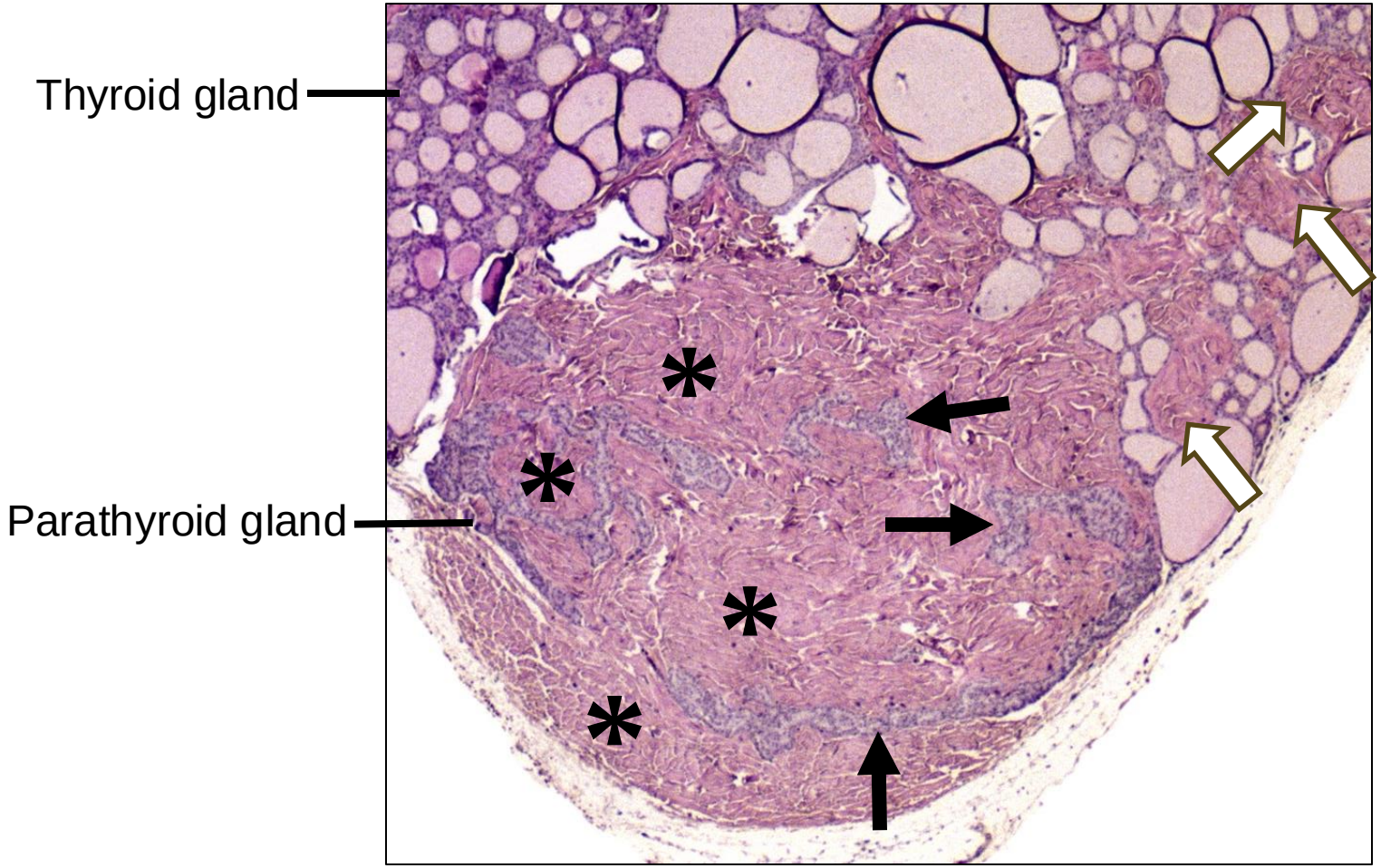
Parathyroid Gland – Atrophy

- Atrophy of the parathyroid gland from a rat, seen as small chief cells (arrows)
- Scant cytoplasm with high nuclear to cytoplasmic ratio (inset)



Parathyroid Gland – Fibrosis

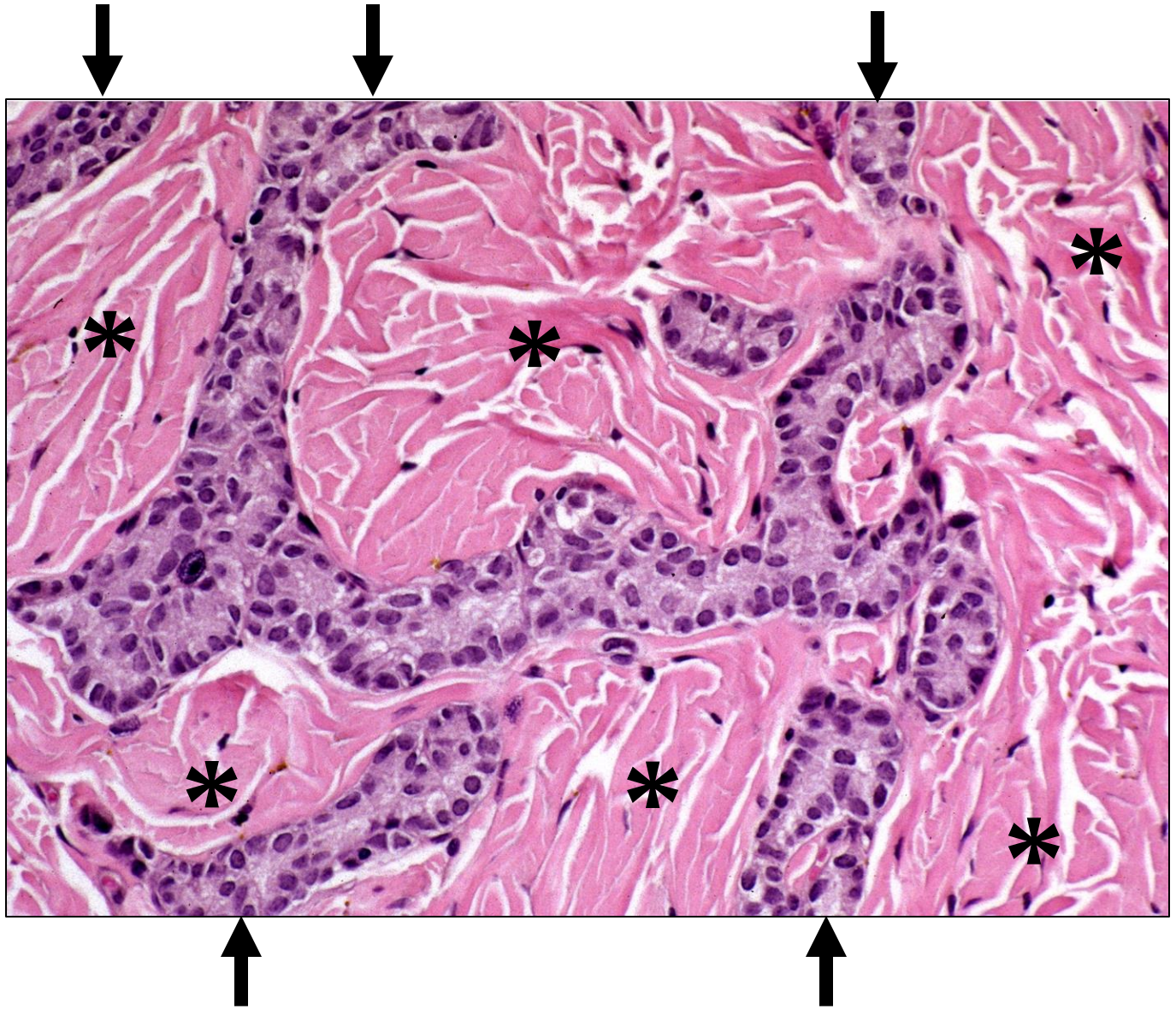
- Increased amounts of mature collagen expands the interstitium
- Replaces the glandular parenchyma and may extend into adjacent thyroid gland when severe
- Significance is unknown
- Rare lesion in mice and rats



Fibrosis (*) in the parathyroid gland of a rat has replaced much of the glandular parenchyma (black arrows) and extends into the adjacent thyroid gland (white arrows)

Parathyroid Gland – Fibrosis

- Fibrosis in parathyroid gland of a rat
- An increased amount of mature collagen (*) expands the interstitium, replacing much of the glandular parenchyma and leaving small residual cords of chief cells (arrows)



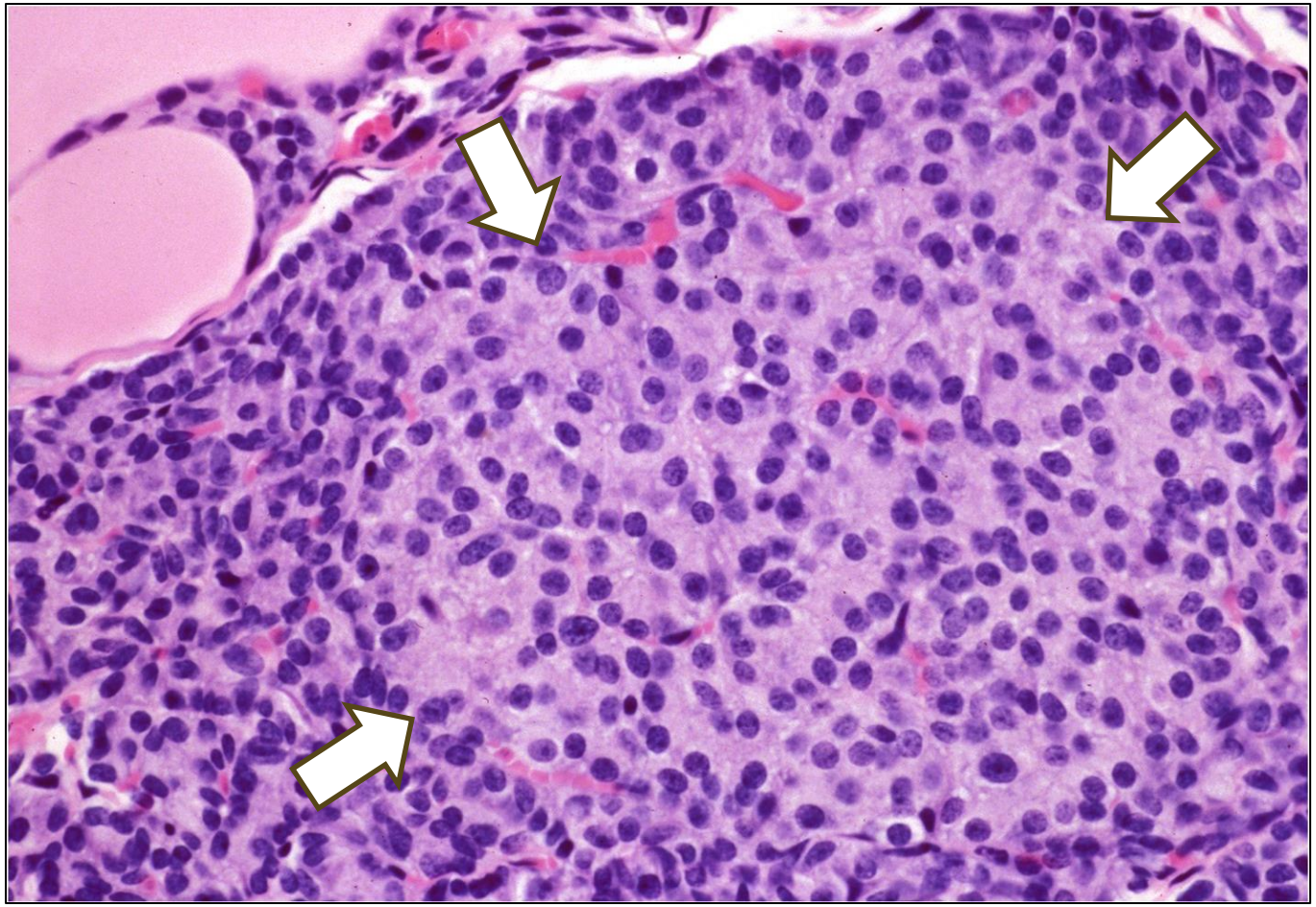
Parathyroid Gland – Hypertrophy

- Enlarged chief cells containing increased cytoplasm
  - Cytoplasm is eosinophilic and may be vacuolated
- May be focal or diffuse
- Hypertrophy (increased cell size) may occur in conjunction with hyperplasia (increased number of cells)

Parathyroid Gland – Hypertrophy

Hypertrophy, Focal

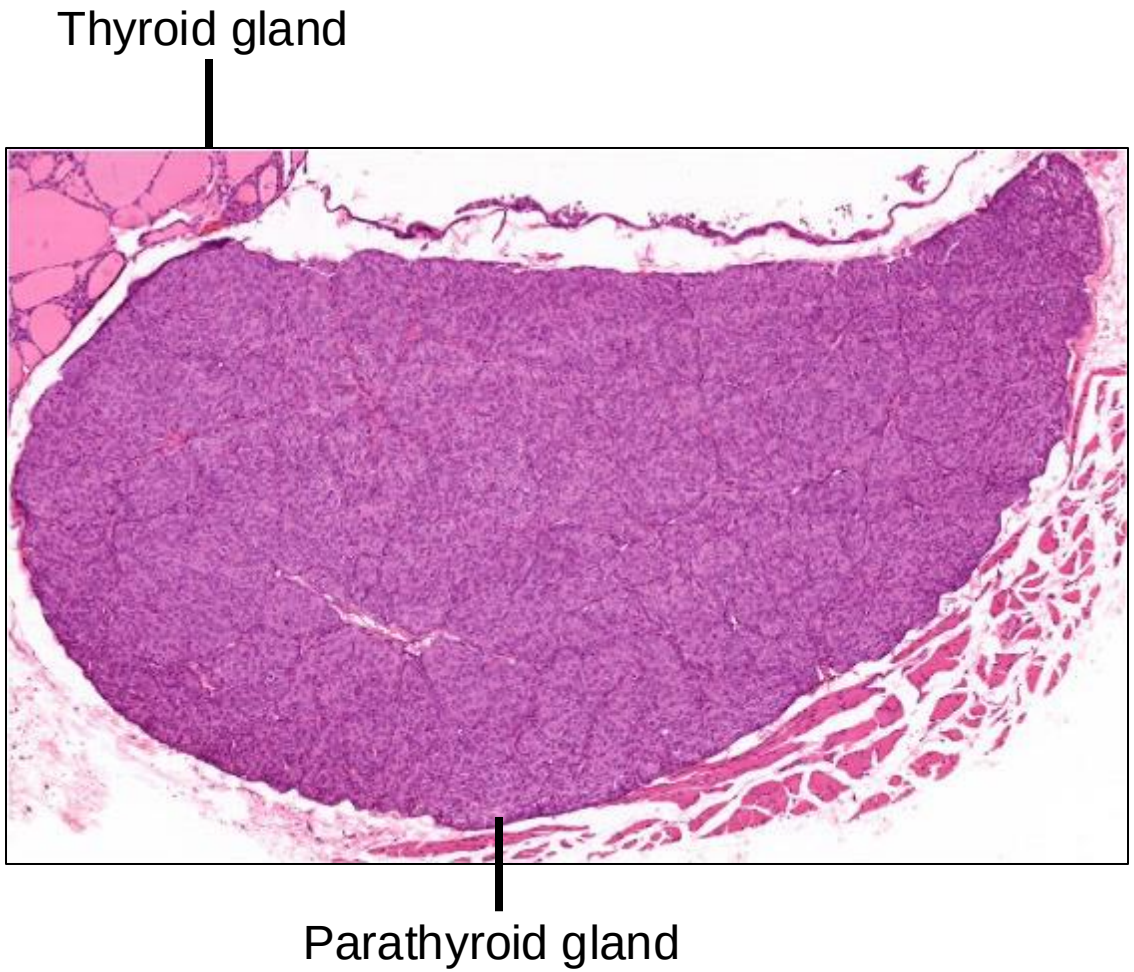
- Focal hypertrophy in the parathyroid gland of a rat (white arrows)
- One or more clusters of enlarged chief cells
- Lacks compression of surrounding parenchyma



Parathyroid Gland – Hypertrophy

Hypertrophy, Diffuse

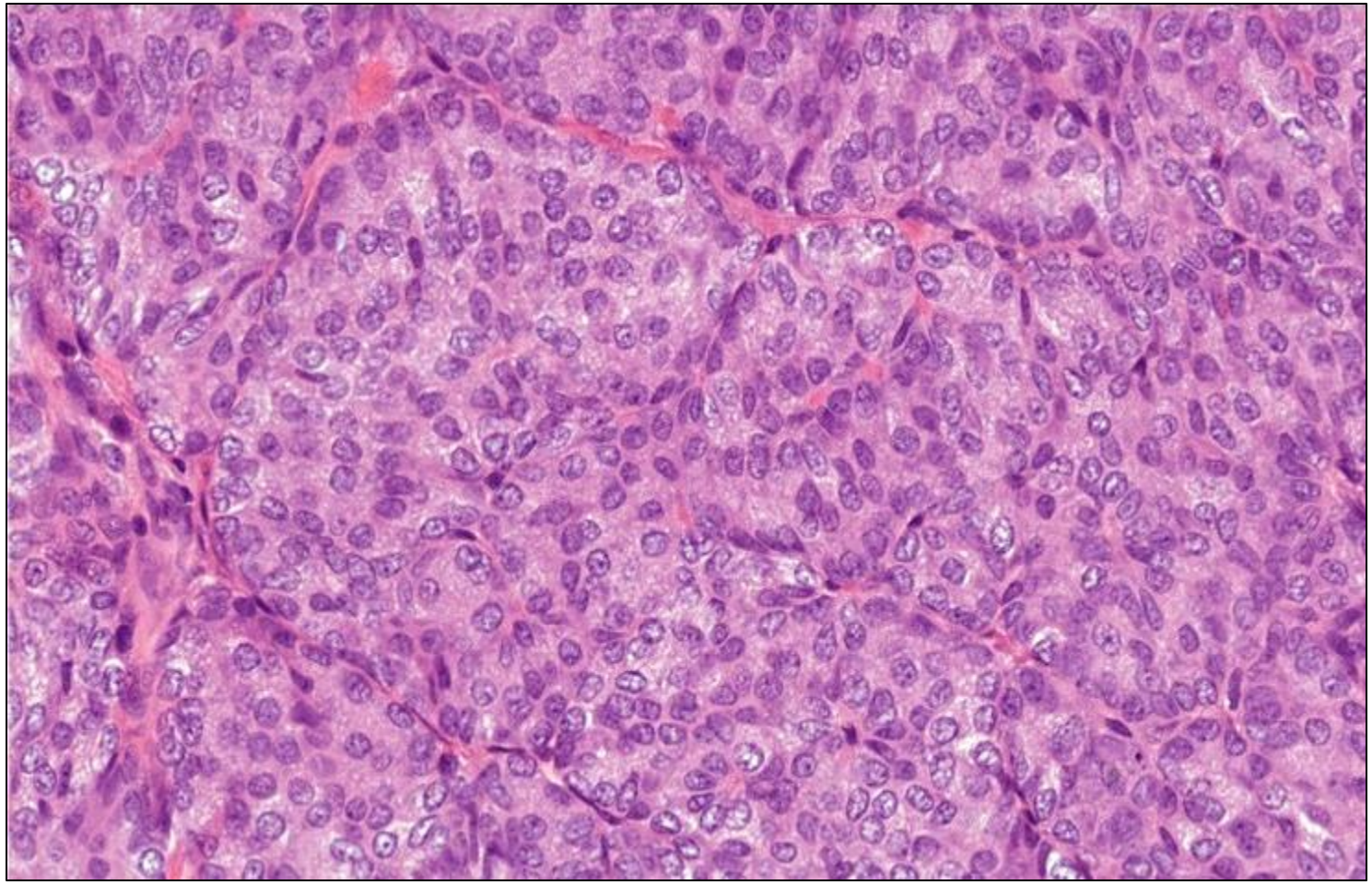
- Chief cells of both glands are diffusely enlarged
- Cells contain increased cytoplasm
- Early stage of physiological stimulation of chief cells
  - Causes include hypocalcemia and decreased calcitriol (active form of vitamin D)
  - May progress to hyperplasia (enlarged chief cells that are also increased number)



Parathyroid Gland – Hypertrophy

Hypertrophy, Diffuse

- Diffuse hypertrophy in the parathyroid gland from a rat
- All chief cells are enlarged with increased eosinophilic cytoplasm



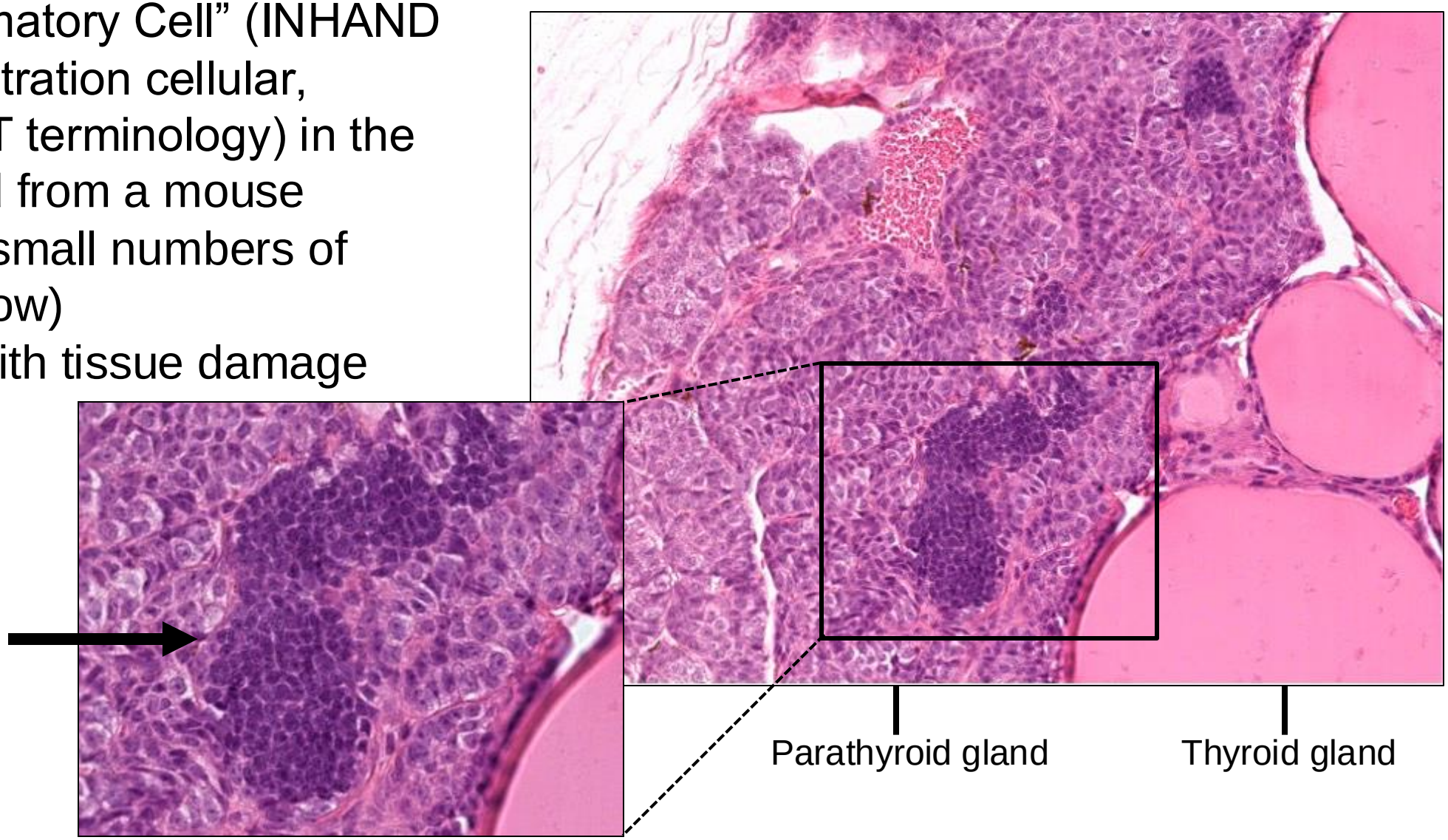
Parathyroid Gland – Infiltrate, Inflammatory Cell

Infiltrate, Inflammatory Cell (INHAND terminology)
Infiltration Cellular (DTT terminology)

- Inflammatory cell infiltrates within the interstitium
  - Not associated with tissue damage
  - Cell infiltrates usually consist of mononuclear cells but may include small numbers of neutrophils
- If possible, specify cell type if using DTT terminology (e.g., “Infiltration Cellular, Lymphocyte” or “Infiltration Cellular, Mononuclear Cell”)
- May be due to a local immune response or other unidentified process
- Differentiate from inflammation, which is associated with tissue damage and/or vascular changes (such as congestion, edema)

Parathyroid Gland – Infiltrate, Inflammatory Cell

- “Infiltrate, Inflammatory Cell” (INHAND terminology)/“Infiltration cellular, lymphocyte” (DTT terminology) in the parathyroid gland from a mouse
- Accumulation of small numbers of lymphocytes (arrow)
- Not associated with tissue damage



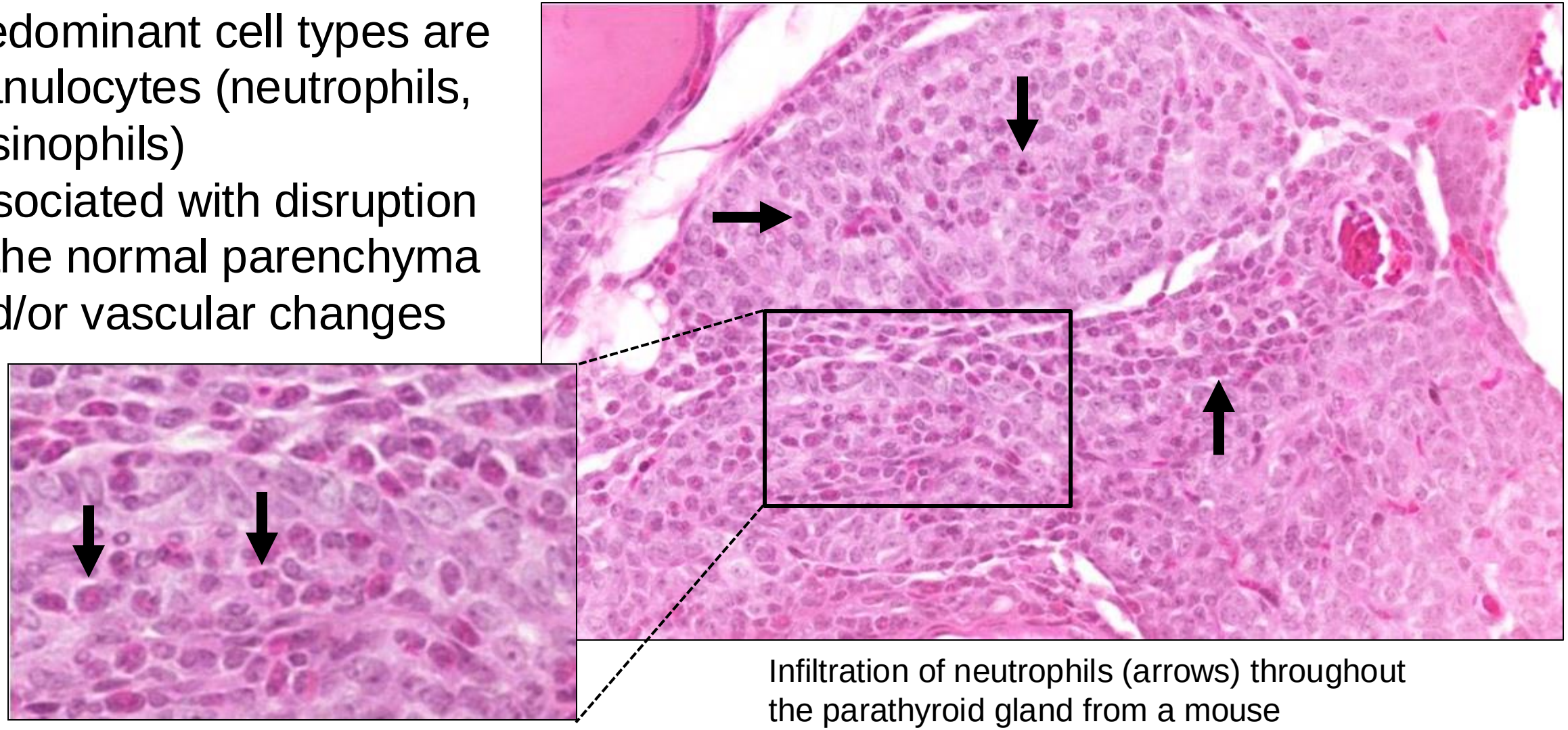
Parathyroid Gland – Inflammation

- Infiltration of variable combinations of lymphocytes, plasma cells, macrophages, and neutrophils
- Tissue damage and/or vascular changes are present
  - Differentiate from infiltrate, inflammatory cell: not associated with tissue damage and/or vascular changes
- Usually classified as acute, subacute , chronic, chronic-active, or granulomatous
- Most often acute or chronic in parathyroid gland
- Rare parathyroid lesion in rats and mice

Parathyroid Gland – Inflammation

Inflammation, Acute

- Predominant cell types are granulocytes (neutrophils, eosinophils)
- Associated with disruption of the normal parenchyma and/or vascular changes

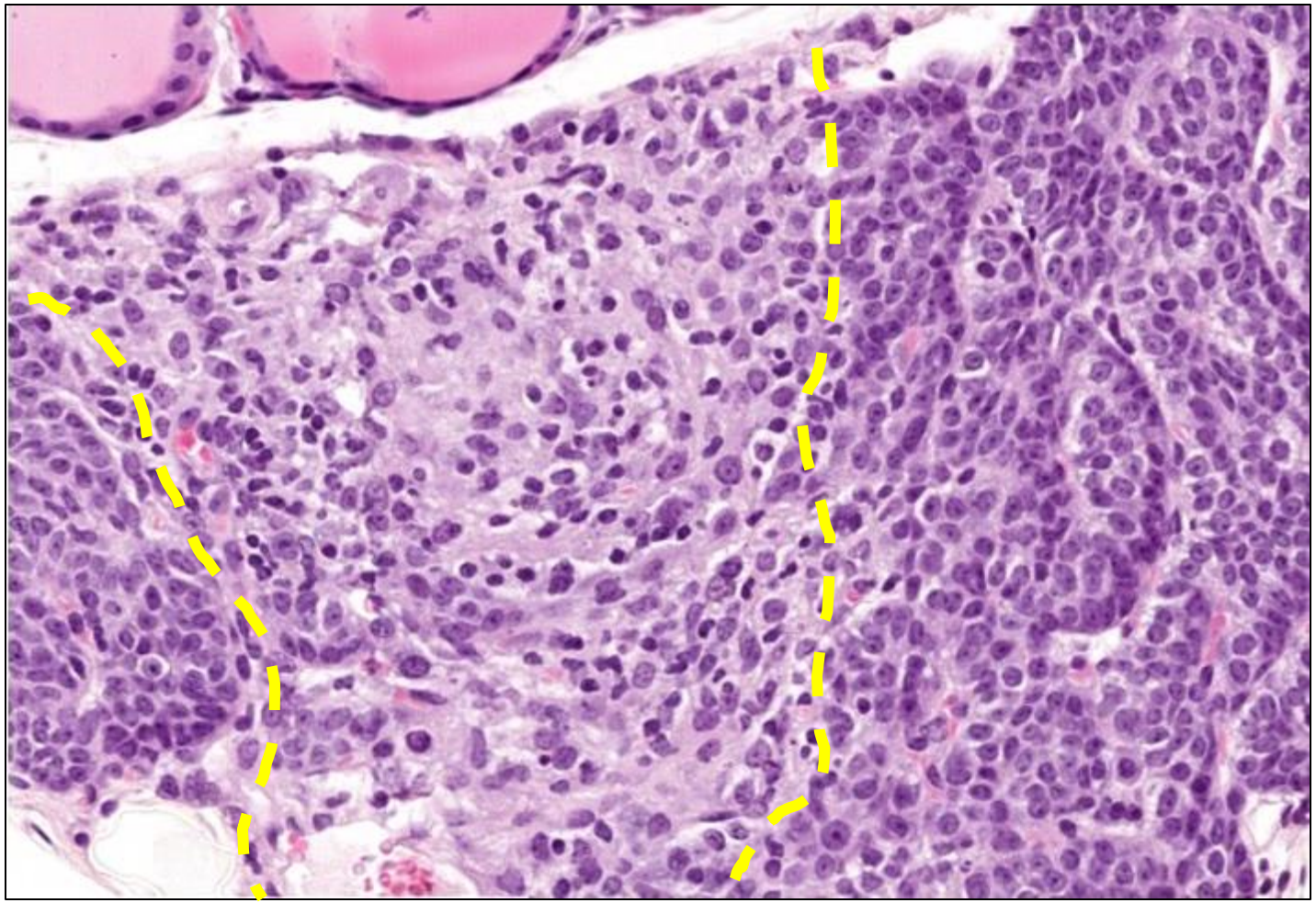


Infiltration of neutrophils (arrows) throughout the parathyroid gland from a mouse

Parathyroid Gland – Inflammation

Inflammation, Chronic-Active

- Predominant cell types are mononuclear cells (lymphocytes and plasma cells +/- macrophages) and neutrophils
- Associated with disruption of the normal parenchyma
- Loss of chief cells



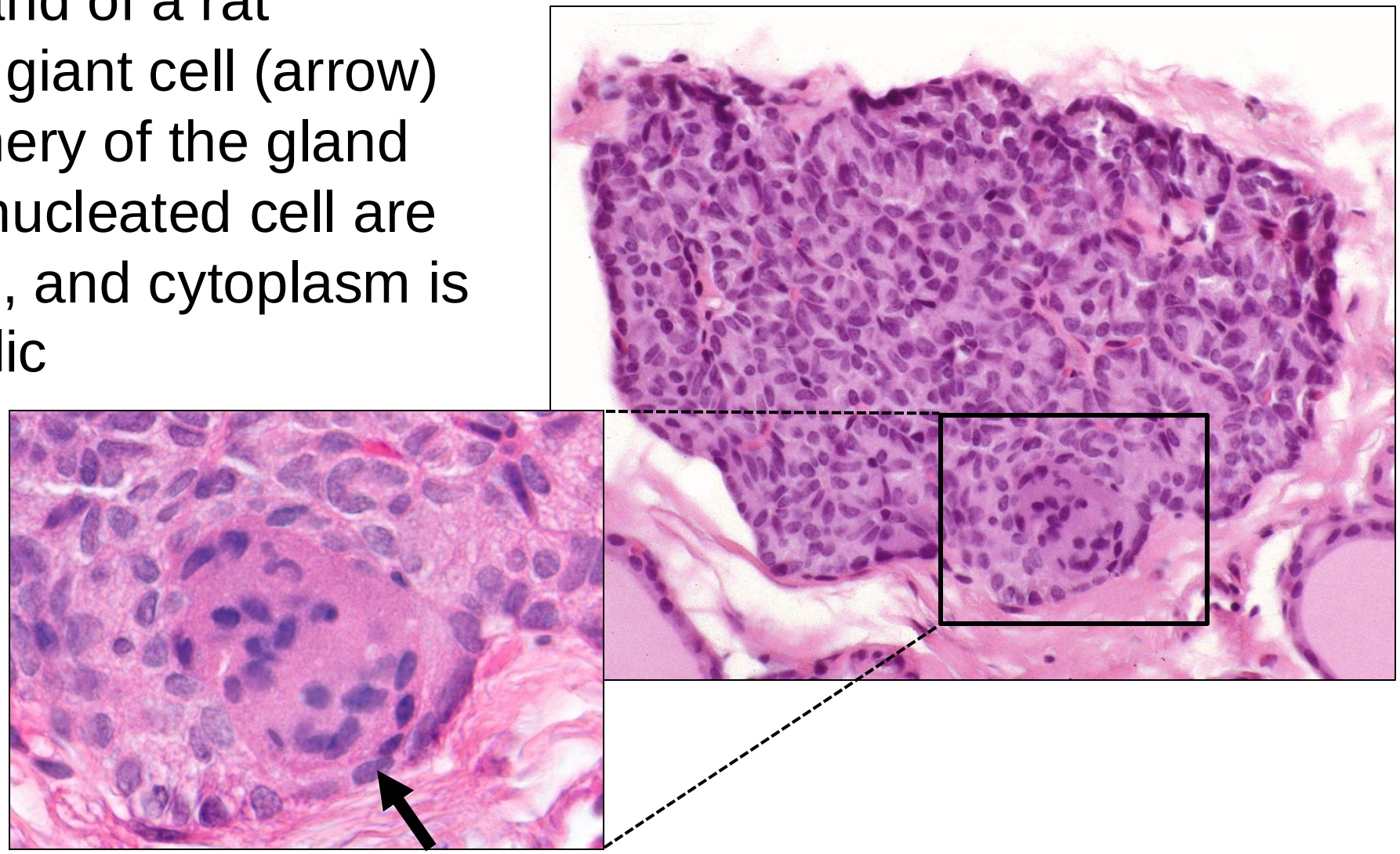
Infiltration of mononuclear cells and neutrophils within a region (area delineated between dashed yellow lines) of the parathyroid gland from a rat

Parathyroid Gland – Multinucleated Giant Cells

- Large, multinucleated syncytial cells
- Believed to form via the fusion of several chief cells
- Significance is unknown but some consider them to be fixation artifacts
- Uncommon; may be observed near periphery of the gland
- Occurs in the rat

Parathyroid Gland – Multinucleated Giant Cells

- Parathyroid gland of a rat
- Multinucleated giant cell (arrow) near the periphery of the gland
- Nuclei of multinucleated cell are dark basophilic, and cytoplasm is dark eosinophilic



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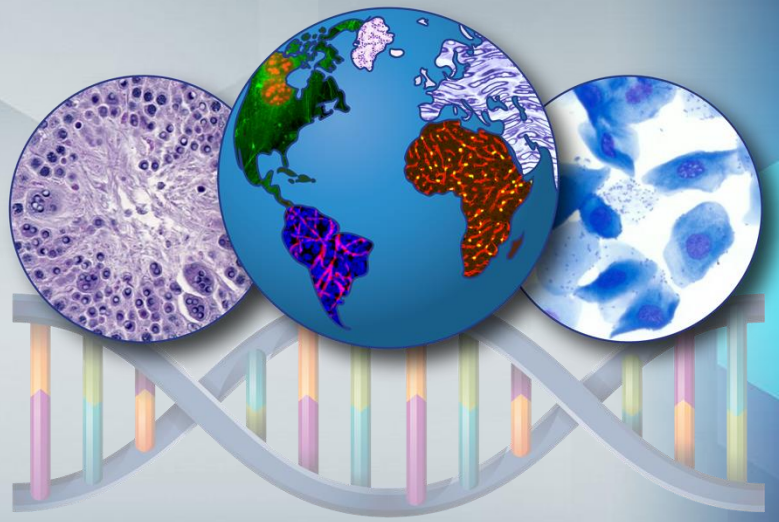
National Institute of Environmental Health Sciences
Division of Translational Toxicology

Author
- Rebecca Moore, DVM, DACVP – Inotiv-RTP

Reviewers
- Beth Lubeck, PhD, MBA – Division of Translational Toxicology, NIEHS
- Cynthia Willson, MS, PhD, DVM, DACVP, DABT – Inotiv-RTP
- William O. Iverson, DVM, DACVP – Charles River Laboratories



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