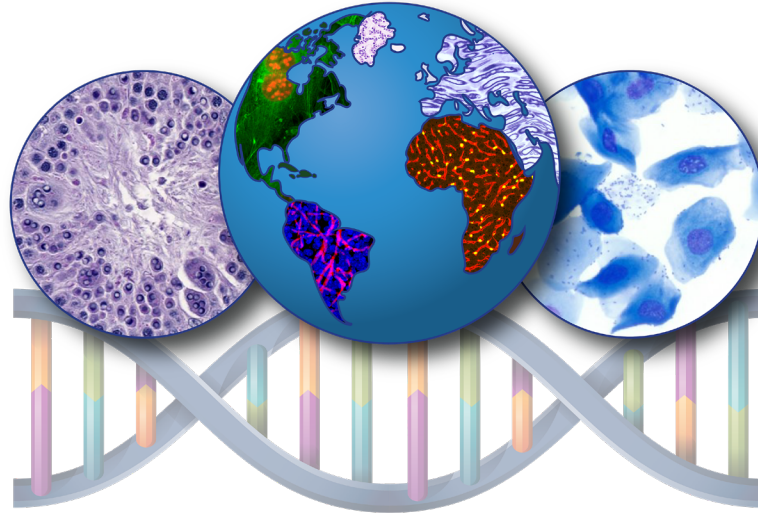




National Institute of
Environmental Health Sciences
Division of Translational Toxicology

Nonproliferative Lesions of the Rodent Thyroid 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 Thyroid Gland

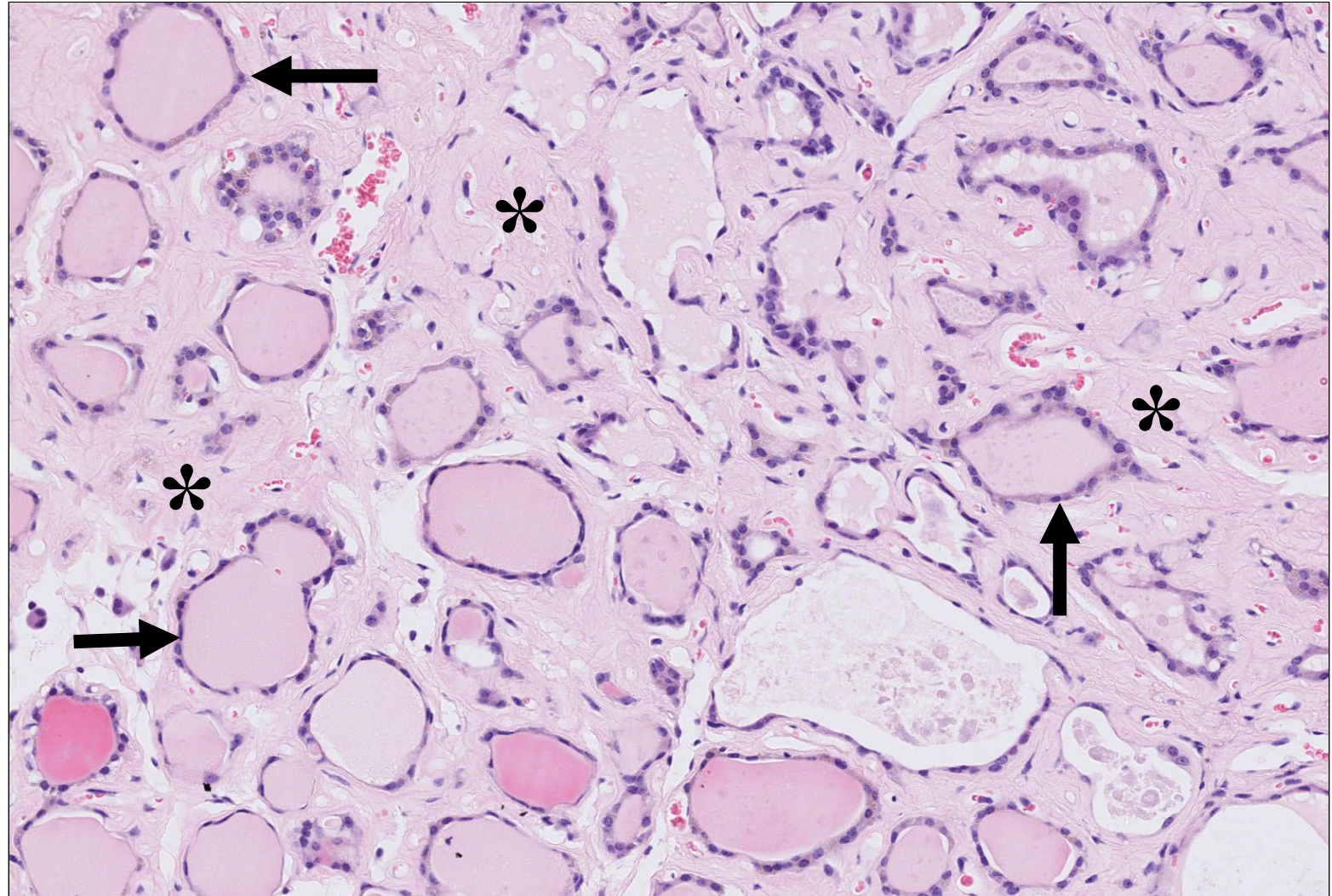
- Amyloid
- Atrophy
- Colloid Alteration
- Cystic Follicle
- Dilatation, Follicular, Diffuse
- Hypertrophy, Follicular Cell
- Infiltrate, Inflammatory Cell
- Inflammation
- Mineralization
- Pigment

Thyroid Gland – Amyloid

- Accumulation of abnormal material that is part of a localized or systemic disease.
 - Characterized by the extracellular deposition of polypeptides derived from immunoglobulins or serum proteins in one or more 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.

Thyroid Gland – Amyloid

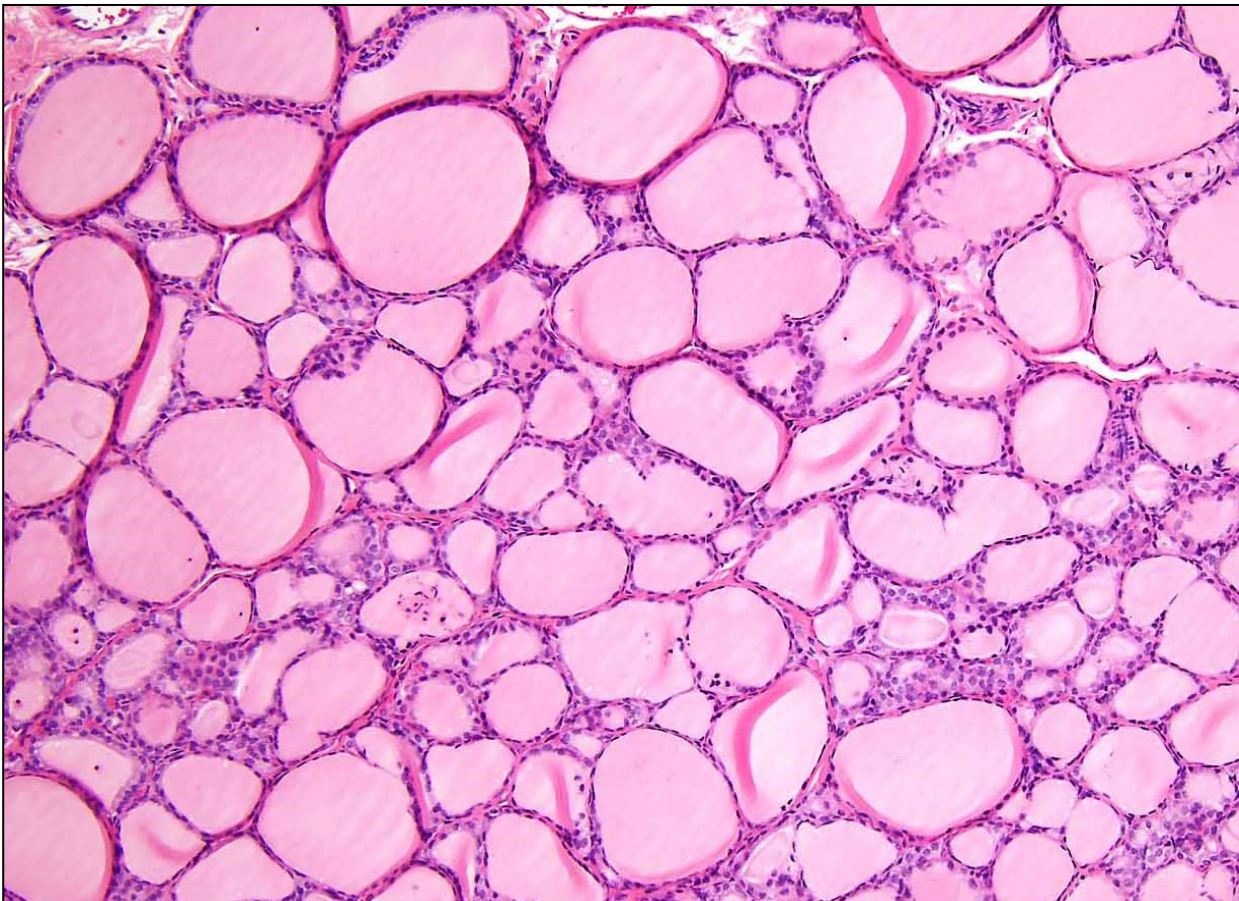
- Amyloid in the thyroid gland of a mouse.
 - Interstitial deposition of pale eosinophilic, amorphous material (*).
 - The amyloid expands the interstitium and separates the preexisting follicles (arrows).



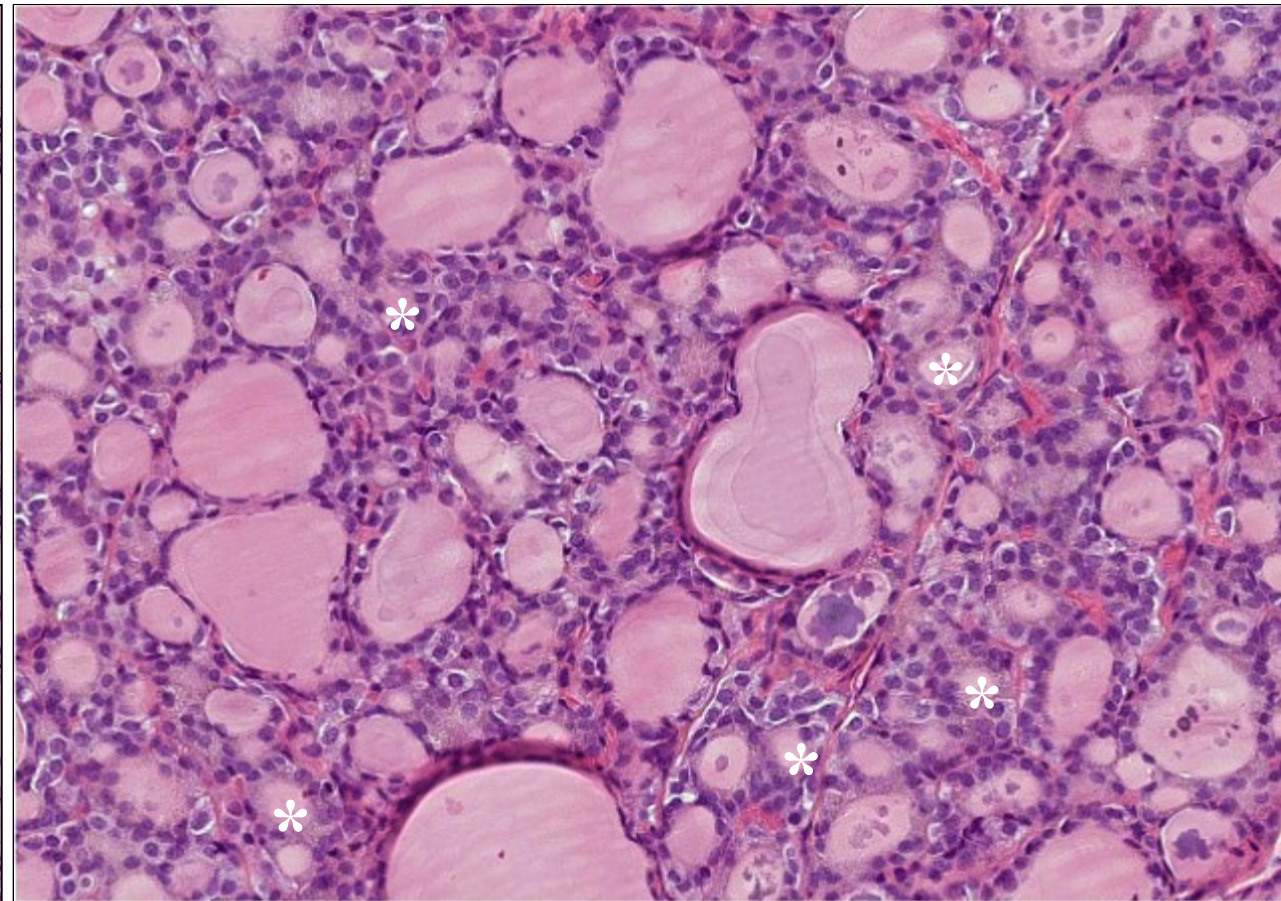
Thyroid Gland – Atrophy

- Diagnostic features:
 - Small follicles that contain decreased amounts colloid.
 - Follicular epithelial cells are decreased in size.
 - Entire gland usually is affected (diffuse).
 - May be associated with inflammation.
- May be due to lack of thyroid stimulating hormone (TSH) from the pituitary gland or thyrotropin releasing hormone (TRH) from the hypothalamus.
- Occurs in mice and rats.

Thyroid Gland – Atrophy



Normal thyroid gland from a rat.



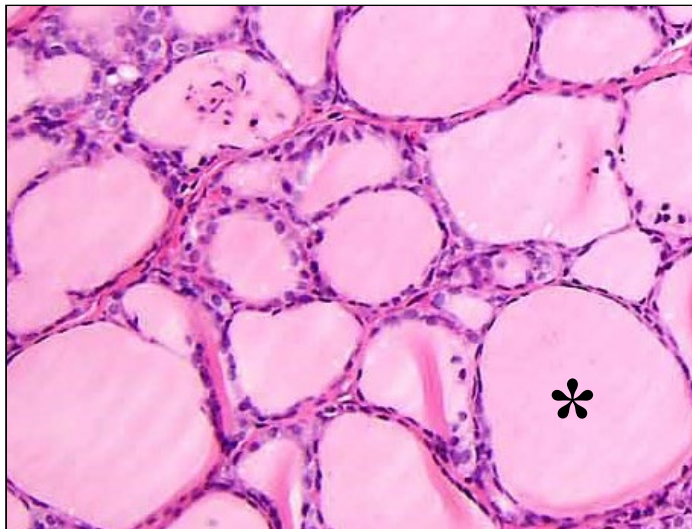
Atrophy in a rat thyroid gland (not all follicles affected in this case). There are many small follicles with decreased colloid (*). Note the tinctorial difference between the two images is due to staining artifact.

Thyroid Gland – Colloid Alteration

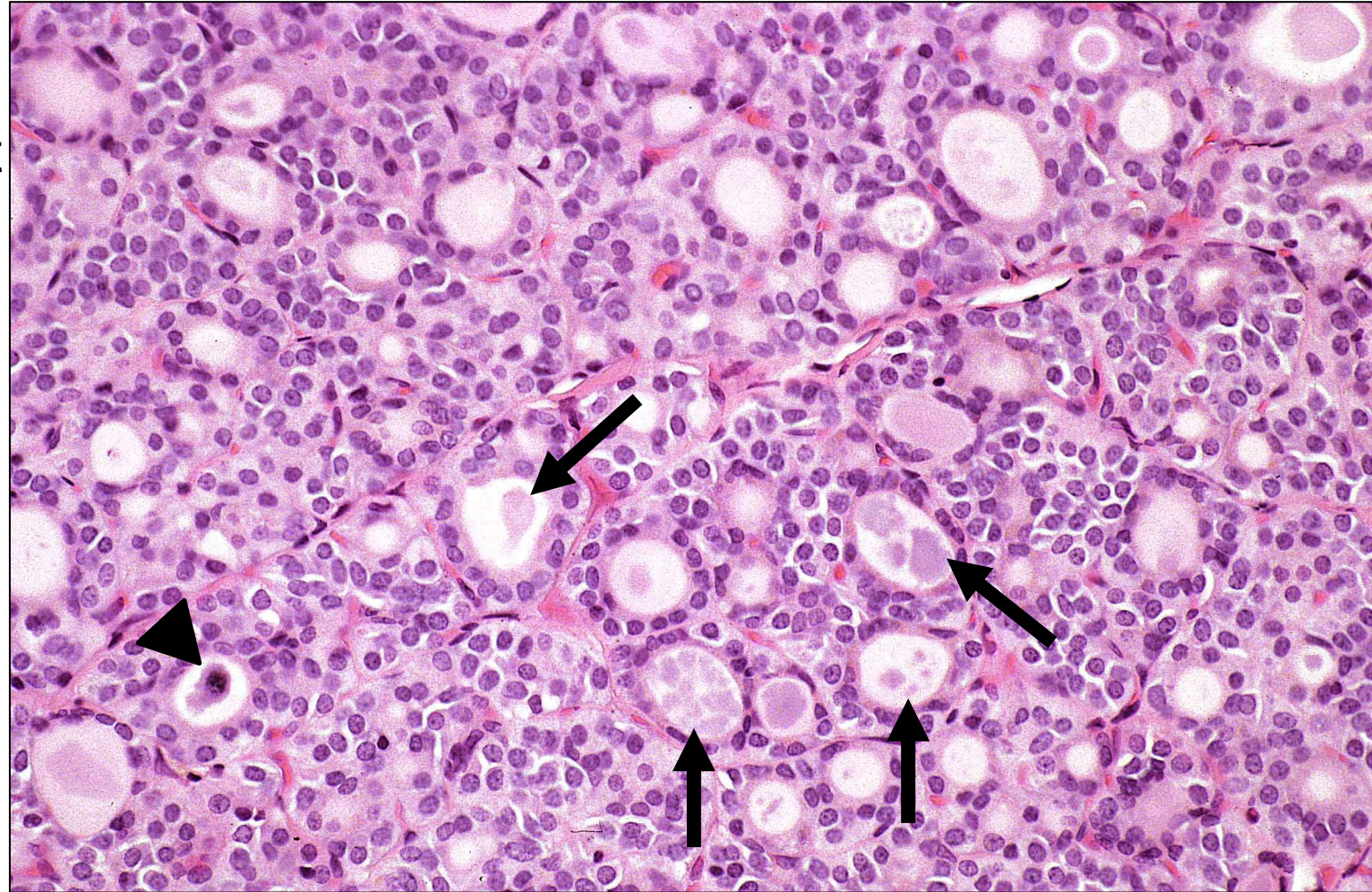
- Degeneration of colloid in follicles.
- Diagnostic features:
 - Stippled or clumped colloid with variable staining.
 - Colloid may contain mineralized material and desquamated (cells that flake off into the colloid) follicular cells.
- Usually associated with thyroid stimulation.
- Increases with age.
- Usually not diagnosed unless pronounced or test article-related.
- Occurs in rats, likely due to their normally rapid turnover of colloid.

Thyroid Gland – Colloid Alteration

- Colloid alteration in the thyroid gland from a rat.
- Some follicles contain colloid that is clumped with variable staining (arrows).
- Colloid in one follicle contains a focus of mineralized material (arrowhead).



Normal
thyroid
gland
showing
normal
colloid (*).

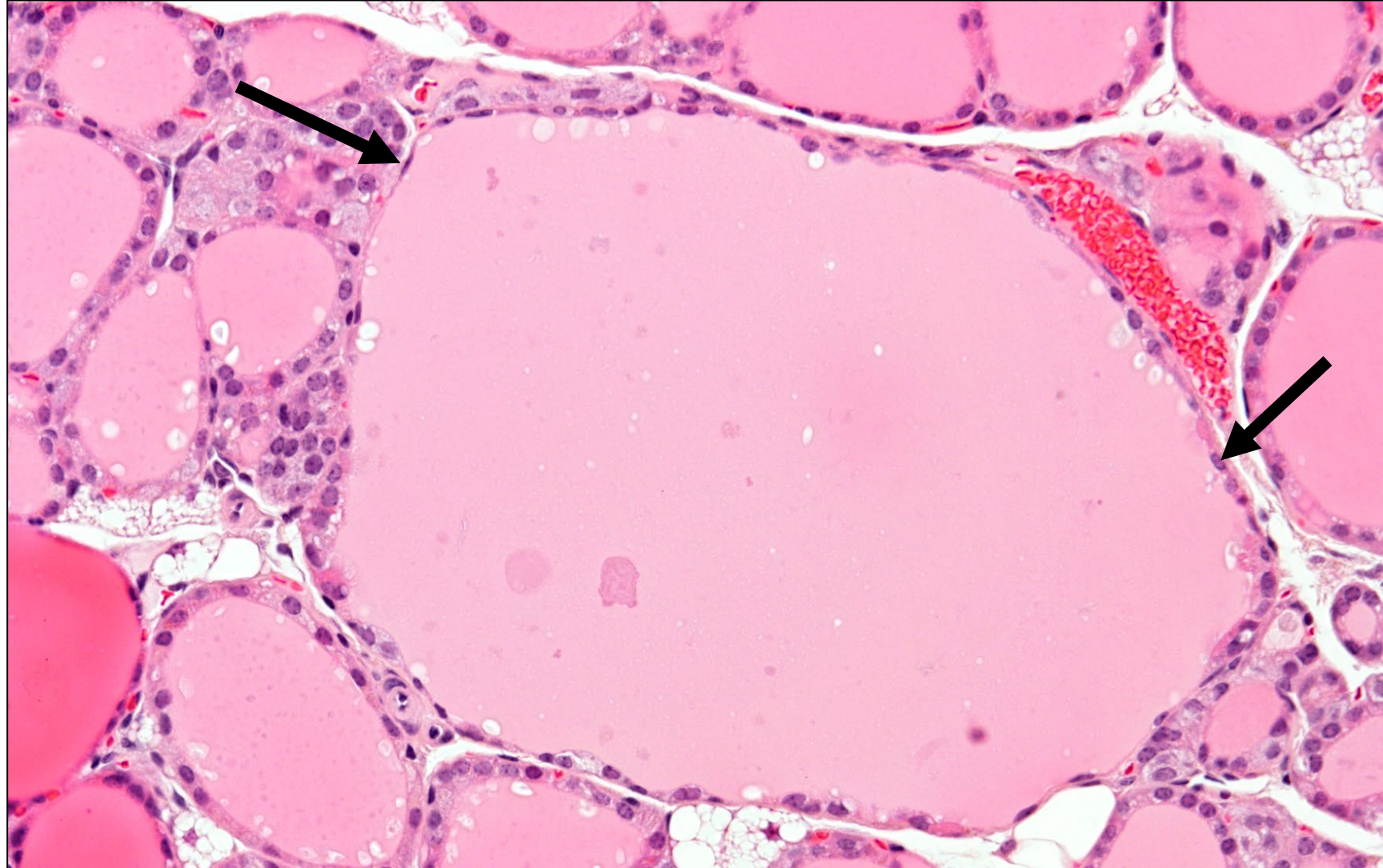


Thyroid Gland, Follicle – Cyst (DTT terminology)

- Degenerative change characterized by dilated follicle(s).
- Diagnostic features:
 - Dilated follicles many times larger than normal that are lined by single layer of flattened follicular epithelial cells.
 - Epithelium does not form papillary structures.
 - Usually focal.
 - Often compresses adjacent follicles.
- Must be distinguished from normal physiologic follicle enlargement in older mice and the often-enlarged peripheral follicles of a normal thyroid gland.
- Occurs in rats and mice.

Thyroid Gland – Cystic Follicle

- Cystic follicle from a rat.
- Lined by a single layer of flattened follicular epithelial cells (arrows).



Thyroid Gland, Follicle – Dilation, Diffuse (DTT terminology)

- Accumulation of colloid in enlarged follicles.
- Diagnostic features:
 - Enlargement of most follicles, which are filled with eosinophilic colloid.
 - Follicles are lined by low cuboidal to flattened epithelial cells.
- Indicative of inactive thyroid gland in euthyroid (state of normal thyroid hormone levels) animals.
- May occur in animals with an excess of iodide or in animals that have recovered from dietary or chemical-induced hypothyroidism.
- Must be distinguished from normal physiologic follicle enlargement in older mice and often enlarged peripheral follicles of the normal thyroid gland.
- Differentiate from cystic follicle, which affects a single follicle.
- Occurs in rats and mice.

Thyroid Gland – Dilatation, Follicle, Diffuse

- Diffuse follicular dilatation in the thyroid gland of a rat.
- Most follicles are variably enlarged and filled with eosinophilic colloid (*).
- Follicular epithelial cells are low cuboidal to flattened (arrows).

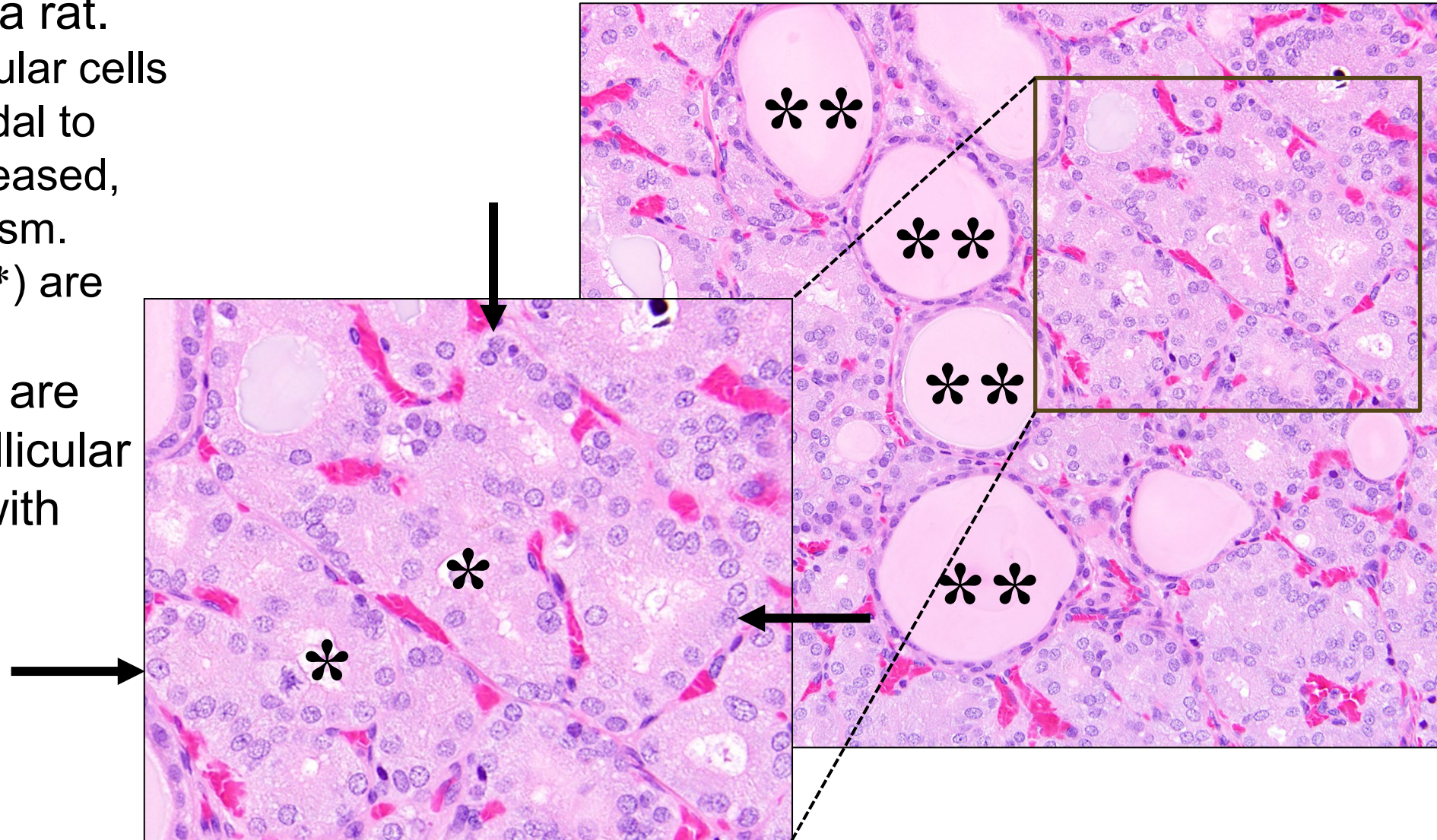


Thyroid Gland – Hypertrophy, Follicular Cell

- Diagnostic features:
 - Follicular epithelial cells are enlarged and cuboidal to columnar.
 - Cytoplasm is often pale eosinophilic and may contain vacuoles.
 - Follicular lumen is typically small and contains normal staining to pale colloid, which may be mineralized.
 - Distribution is usually diffuse.
 - Epithelium does not form papillary structures (may be present in Hyperplasia, Follicular Cell).
- Prolonged hypertrophy (increased size) can progress to hyperplasia (increased number) and often occur together.
- May be induced by chemicals or hormones that stimulate follicular cell activity.
- Common in rats and rare in mice.

Thyroid Gland – Hypertrophy, Follicular Cell

- Follicular cell hypertrophy in the thyroid gland of a rat.
 - The enlarged follicular cells (arrows) are cuboidal to columnar with increased, vacuolated cytoplasm.
 - Follicular lumens (*) are small.
- Normal follicles (**) are lined by flattened follicular cells and are filled with intraluminal colloid.

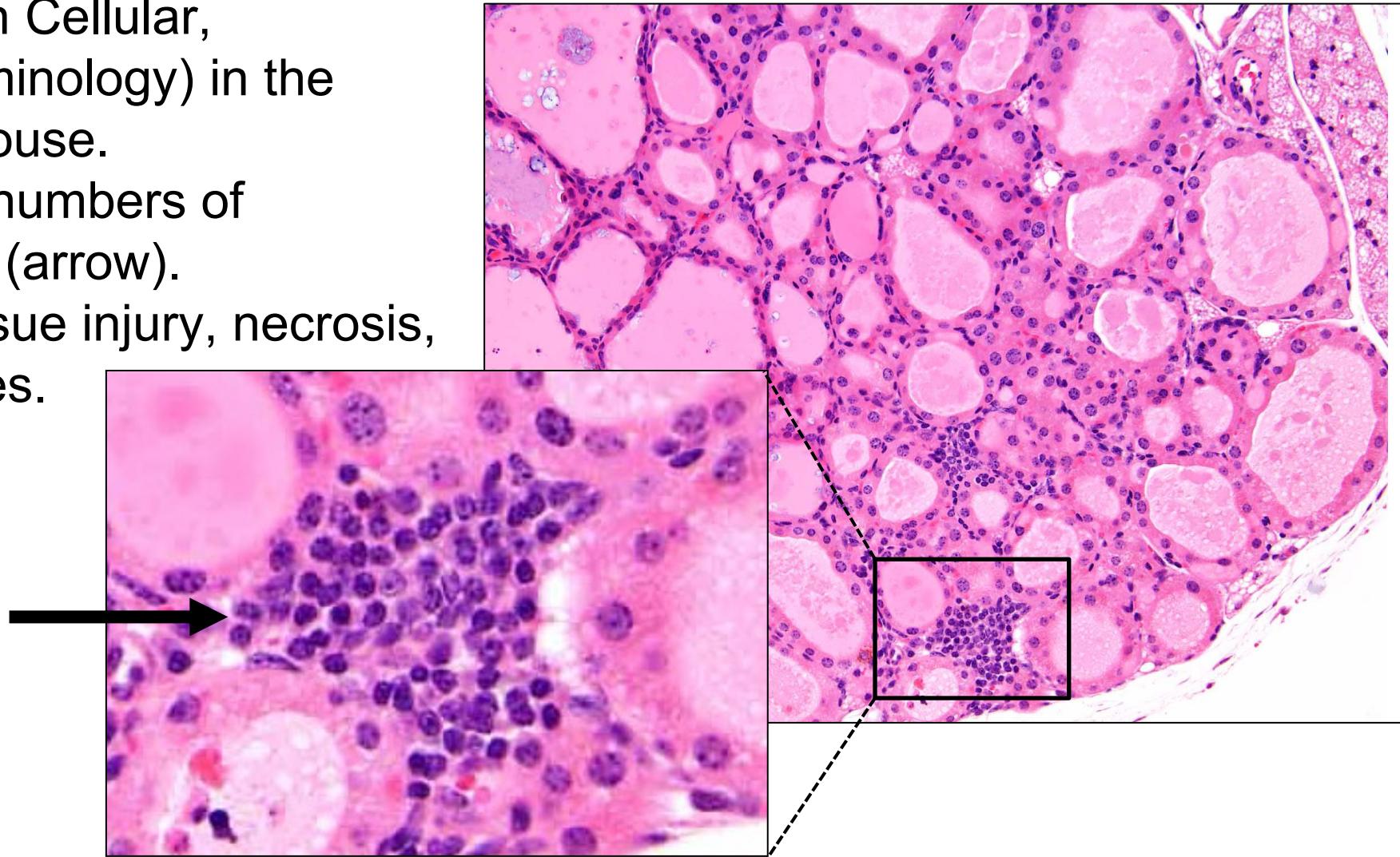


Infiltration Cellular (DTT terminology)

- Diagnostic features:
 - Inflammatory cells within the interstitium.
 - Not associated with tissue injury or damage, and/or vascular changes.
 - Usually mononuclear cells but there may be small numbers of neutrophils.
- Specify cell type as a modifier: mononuclear cell, lymphocyte, neutrophil, mixed cell, eosinophil.
- May be due to a local immune response or other unidentified process.
- Differentiate from inflammation, which is usually more extensive and associated with tissue damage and/or vascular changes (such as congestion).

Thyroid Gland – Infiltrate, Inflammatory Cell

- “Infiltrate, mononuclear cell” (INHAND terminology)/“Infiltration Cellular, Lymphocyte” (DTT terminology) in the thyroid gland from a mouse.
- Accumulation of small numbers of interstitial lymphocytes (arrow).
- Not associated with tissue injury, necrosis, and/or vascular changes.



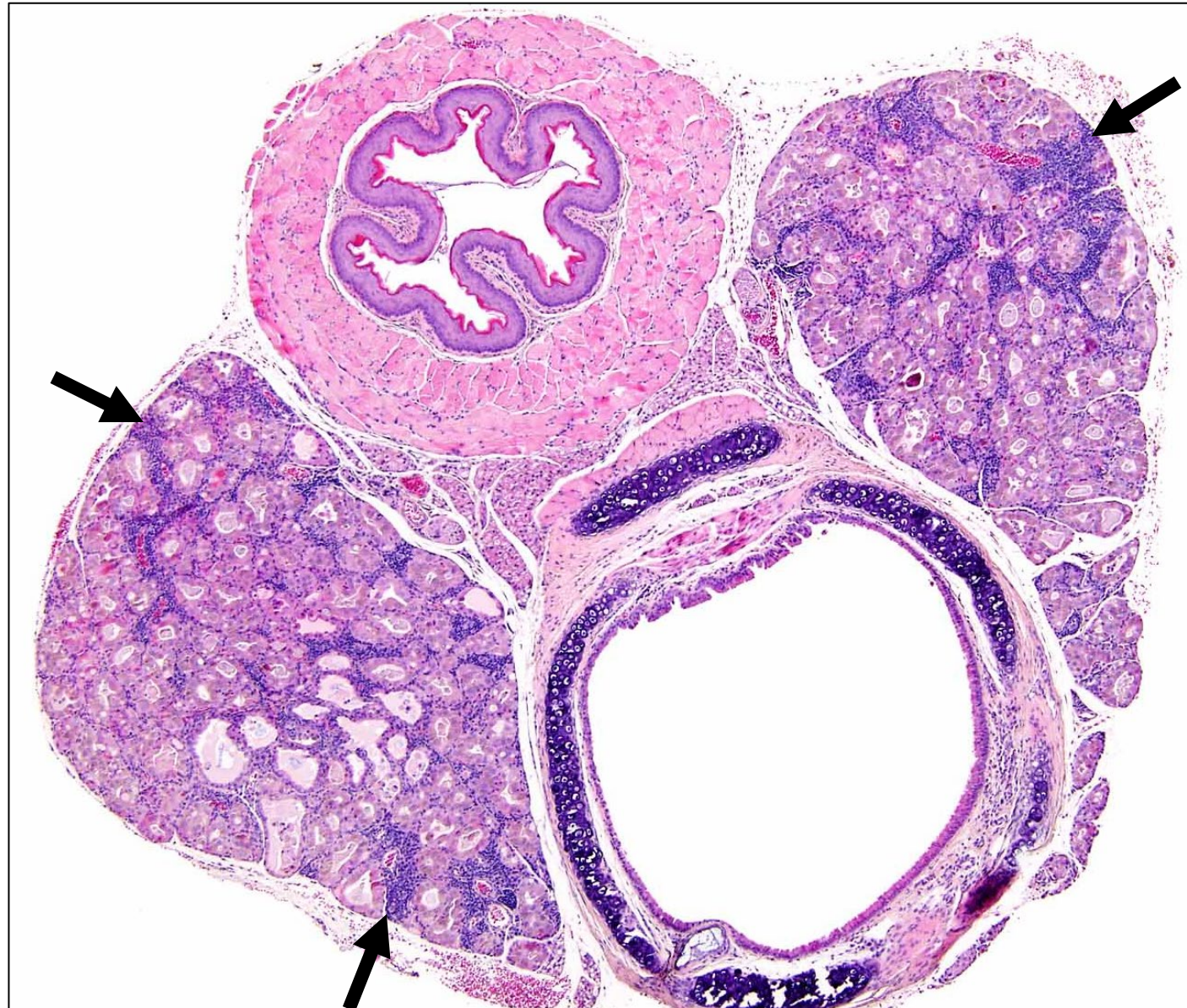
Thyroid Gland – Inflammation

- Diagnostic Features:
 - Multifocal to diffuse accumulation of variable combinations of lymphocytes, plasma cells, and macrophages; neutrophilic infiltration is less common.
 - Associated with some degree of tissue damage and/or vascular changes.
 - Thyroid follicles may be fewer and smaller and have colloid depletion.
 - Follicular cells may be hyperplastic in affected areas.
- Usually classified according to cell type: mononuclear cell, lymphocyte, neutrophil, mixed cell, eosinophil, granulomatous.
- May arise secondary to systemic disease or extension from adjacent tissues
- Spontaneous lymphocytic inflammation may rarely occur in some rat strains and may also be test article-induced.
- Differentiate from infiltrate, inflammatory cell; which is not associated with tissue injury and/or vascular changes.
- Uncommon in rats and mice.

Thyroid Gland – Inflammation

Inflammation, Mononuclear Cell

- Mononuclear cell inflammation (arrows) in the thyroid gland of a rat.
- Inflammatory cells consist of lymphocytes and plasma cells.

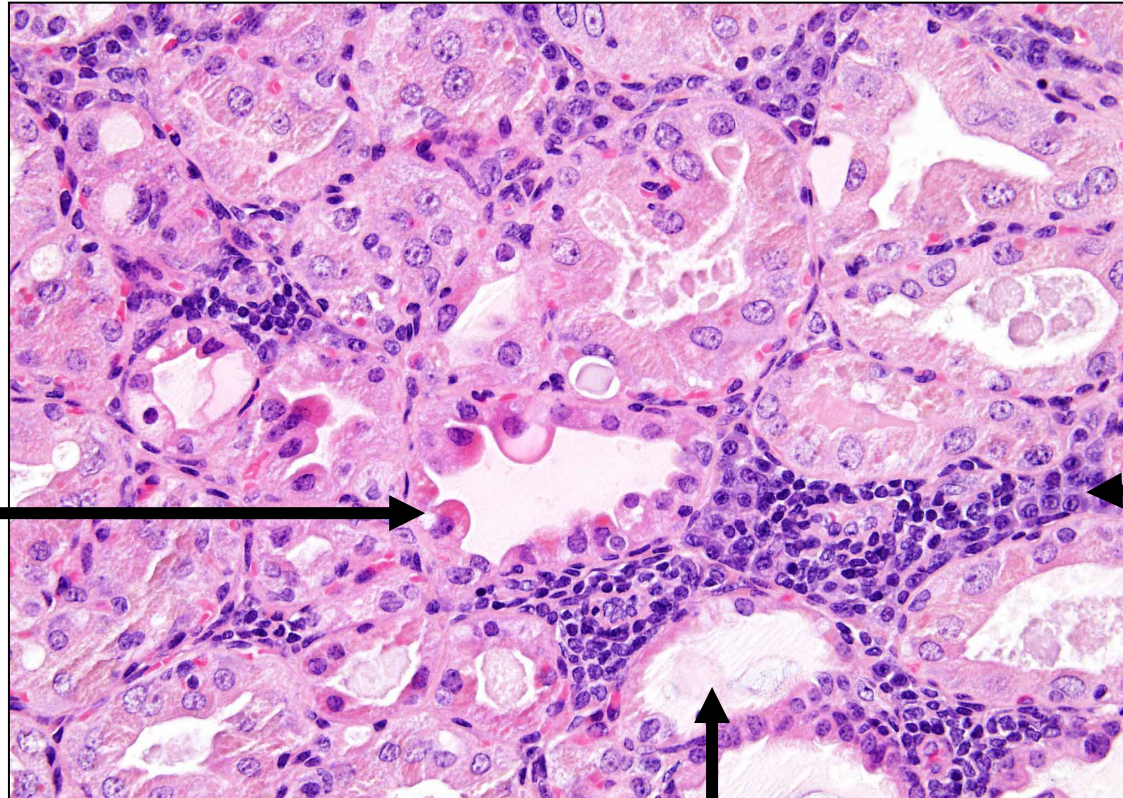


Thyroid Gland – Inflammation

Inflammation, Mononuclear Cell

- Inflammatory infiltration by lymphocytes and plasma cells in the thyroid gland of a rat.
- Predominantly interstitial infiltration.
- Associated with tissue injury and/or vascular changes and possibly other findings (e.g., follicular cell degeneration, colloid depletion).

Follicular cell degeneration (cell swelling, cytoplasmic vacuolation).



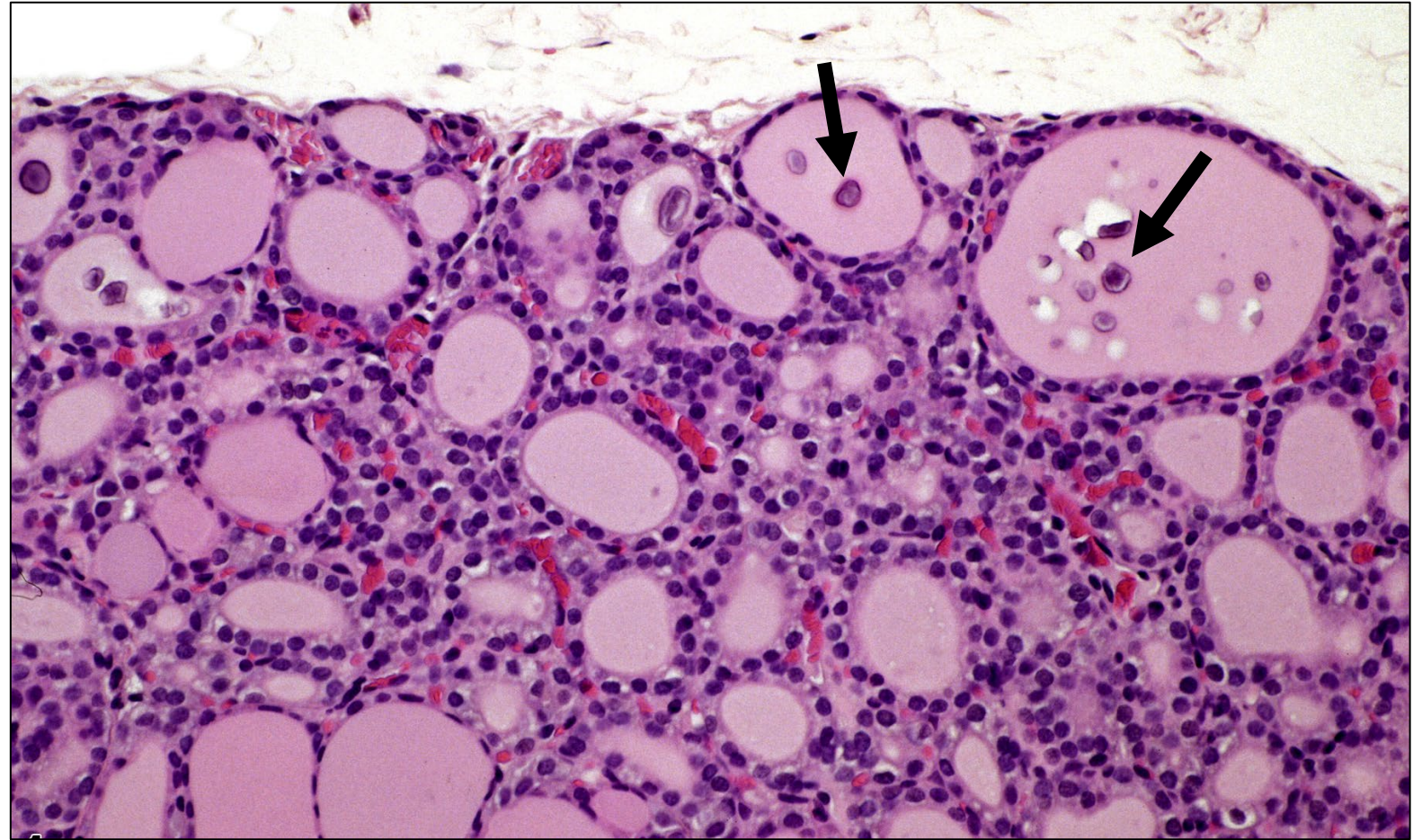
Interstitial infiltrates of lymphocytes and plasma cells.

Colloid depletion (reduced colloid).

Thyroid Gland –Mineralization

Thyroid Gland – Mineral (DTT terminology)

- Degenerative change.
- Diagnostic feature: Irregular basophilic clumps of mineral within follicular colloid.
- Incidental finding not usually diagnosed unless severe or suspected of being treatment-related.
- Differentiate from colloid alteration, which may have small mineral clumps as a minor component, but not as the predominant lesion.
- May be an aging change.
- Occurs in mice and rats.



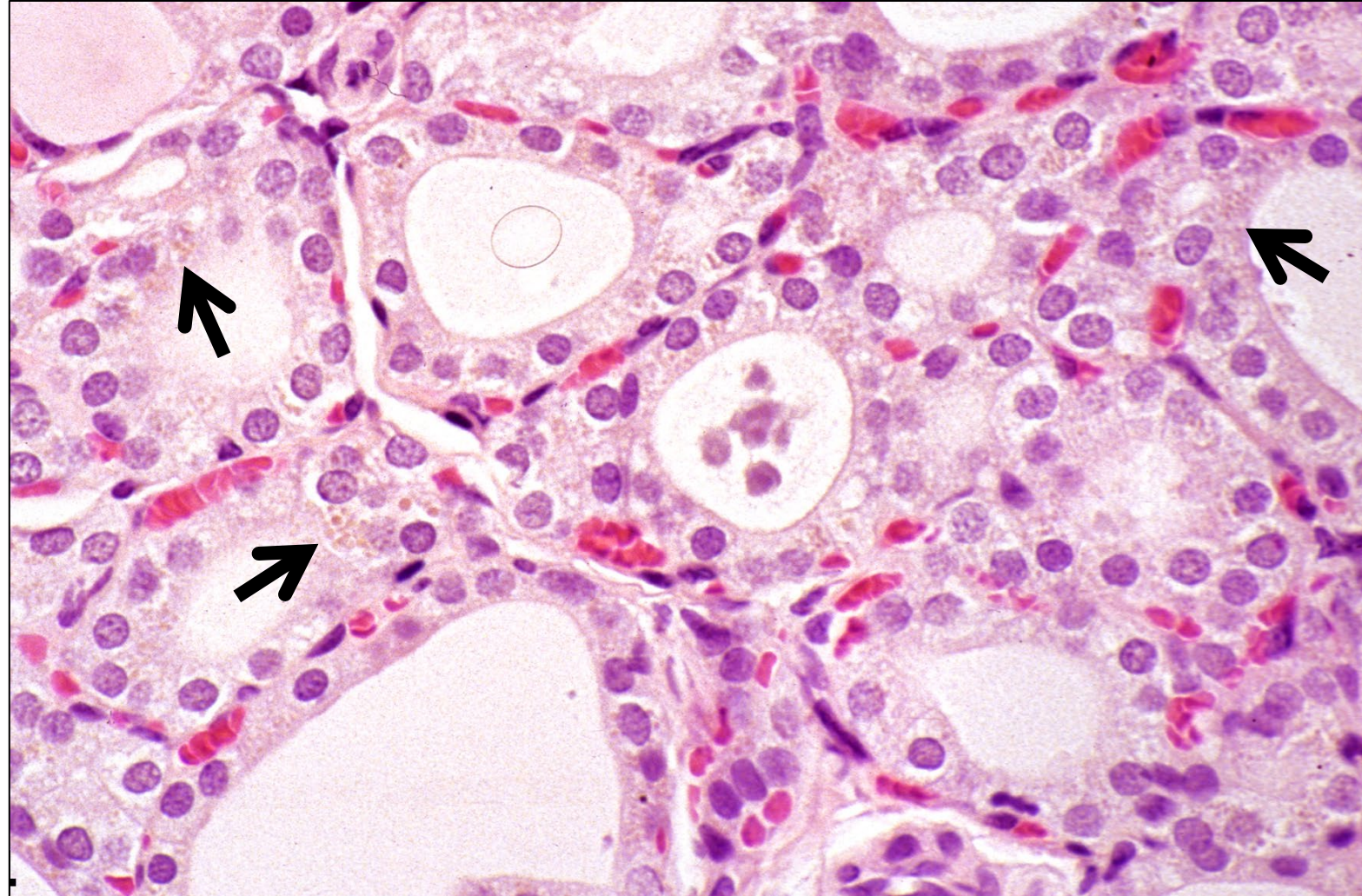
Basophilic clumps of mineral (arrows) within the colloid of follicles in the thyroid gland of a rat.

Thyroid Gland – Pigment

- Accumulation of colored substances from deposition of iron, lipofuscin, or various chemicals or their metabolites in follicular epithelial cells or within colloid.
- Diagnostic features:
 - Pigment is commonly brown and granular.
 - May stain positive for iron or lipofuscin.
- Definitive pigment identification is difficult, even with special stains, and is not usually necessary.
- Lipofuscin pigment accumulation may increase with age or after prolonged thyroid gland stimulation.
- Occurs in rats and mice.

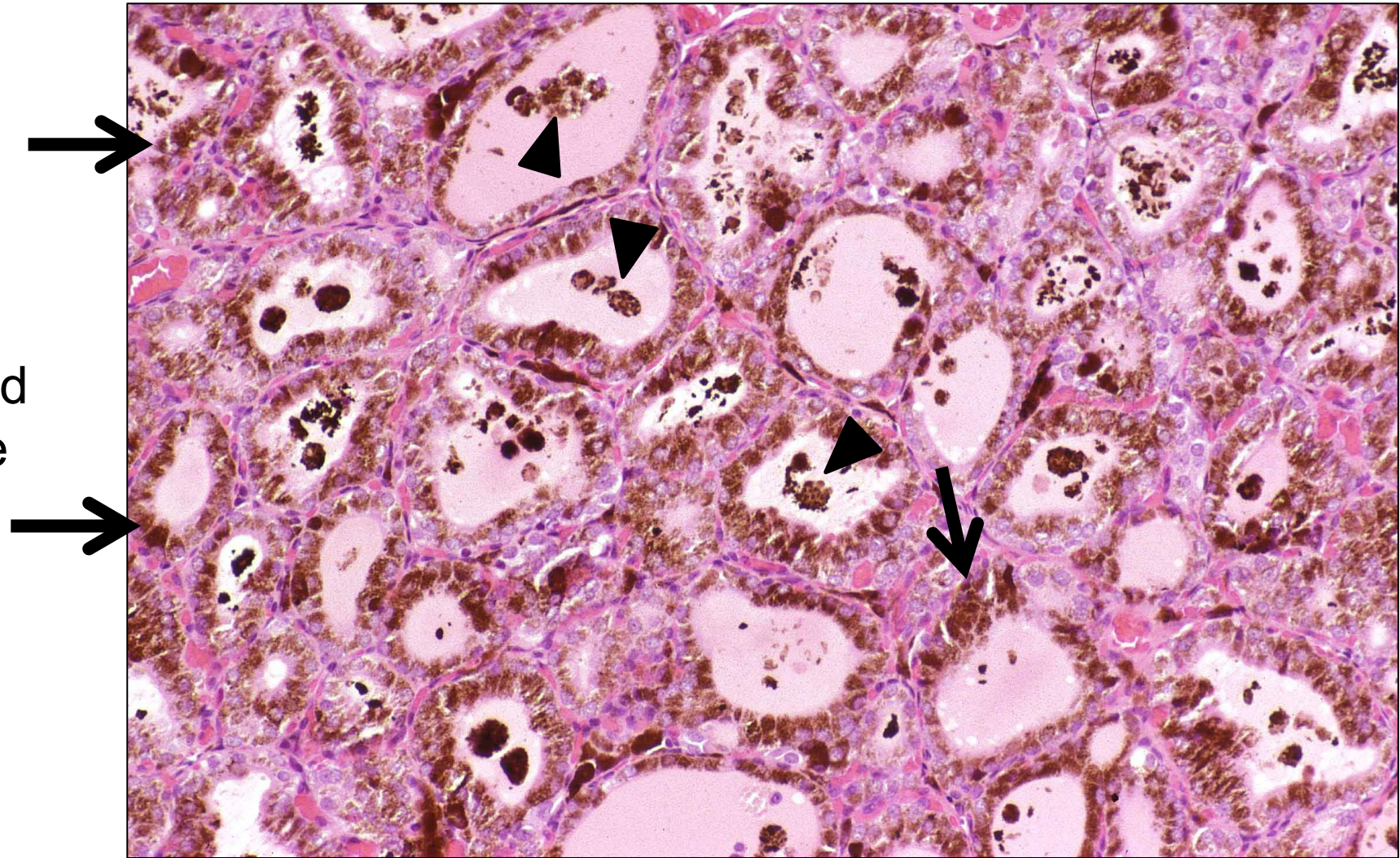
Thyroid Gland – Pigment

Brown granular pigment accumulation (arrows) in the cytoplasm of follicular epithelial cells in the thyroid gland of a rat.



Thyroid Gland – Pigment

Brown granular pigment accumulation in follicular epithelial cells (arrows) and colloid (arrowheads) in the thyroid gland of a rat.



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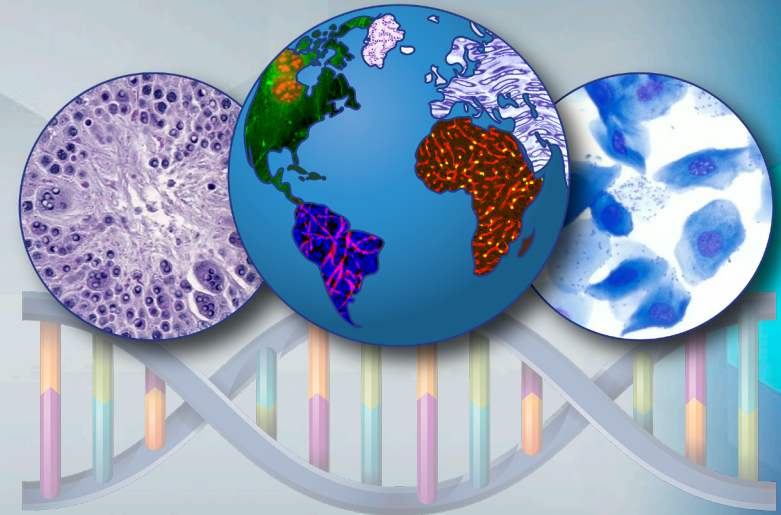
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