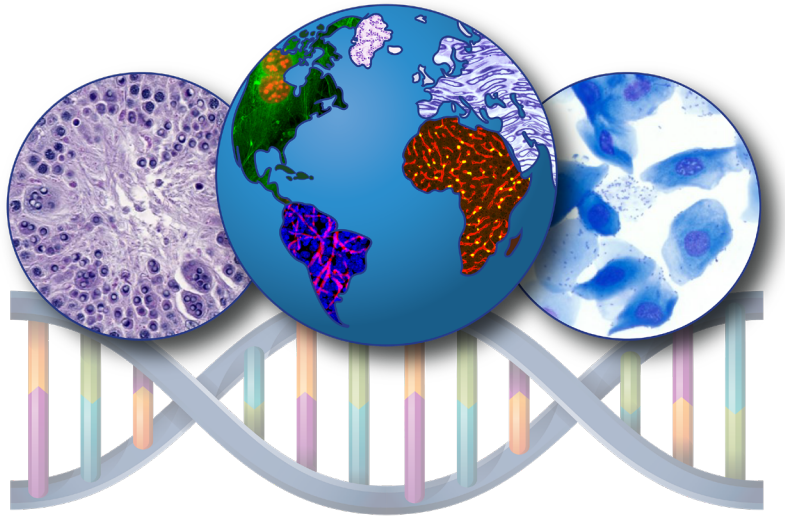
National Institute of
Environmental Health Sciences
Division of Translational Toxicology

Proliferative 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

Proliferative Lesions of the Parathyroid Gland

- Hyperplastic Lesions
  - Hyperplasia
- Benign Tumors
  - Adenoma
- Malignant Tumors
  - Carcinoma

Proliferative Lesions of the Parathyroid Gland

Introduction

- In general, proliferative lesions of the parathyroid gland are uncommon.
  - However, parathyroid gland hyperplasia is more common among rats and mouse strains other than B6C3F1/N mice.
  - Diffuse, bilateral parathyroid gland hyperplasia is usually associated with chronic progressive nephropathy and is therefore common in aging rats (especially males).
- As with many other tissues, hyperplasia in the parathyroid gland can either be **diffuse** (affecting the entire gland) or **focal** (one or more discrete areas within a gland) and affect one or both glands (bilateral).
  - In both focal and diffuse hyperplasia, cells are also usually enlarged (hypertrophy) and cytoplasm is eosinophilic to vacuolated.

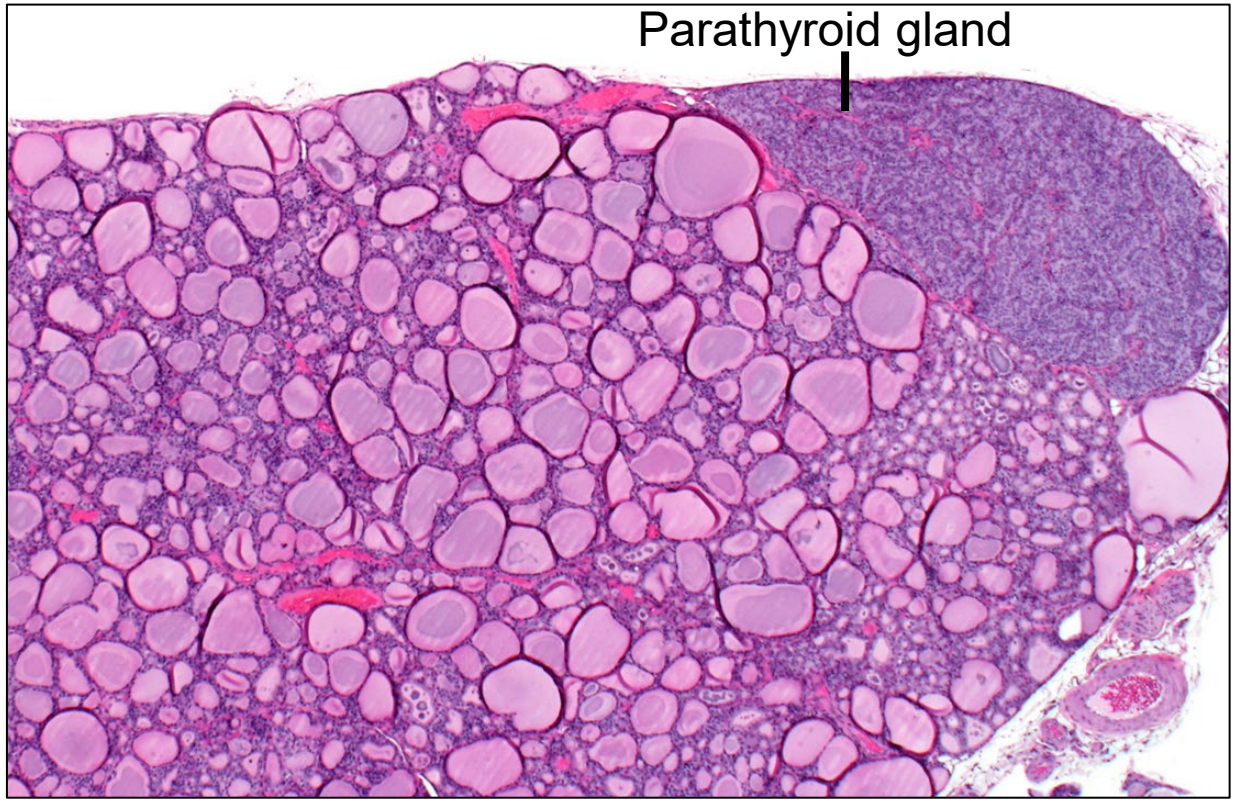
Parathyroid Gland – Hyperplasia

Hyperplasia, Diffuse

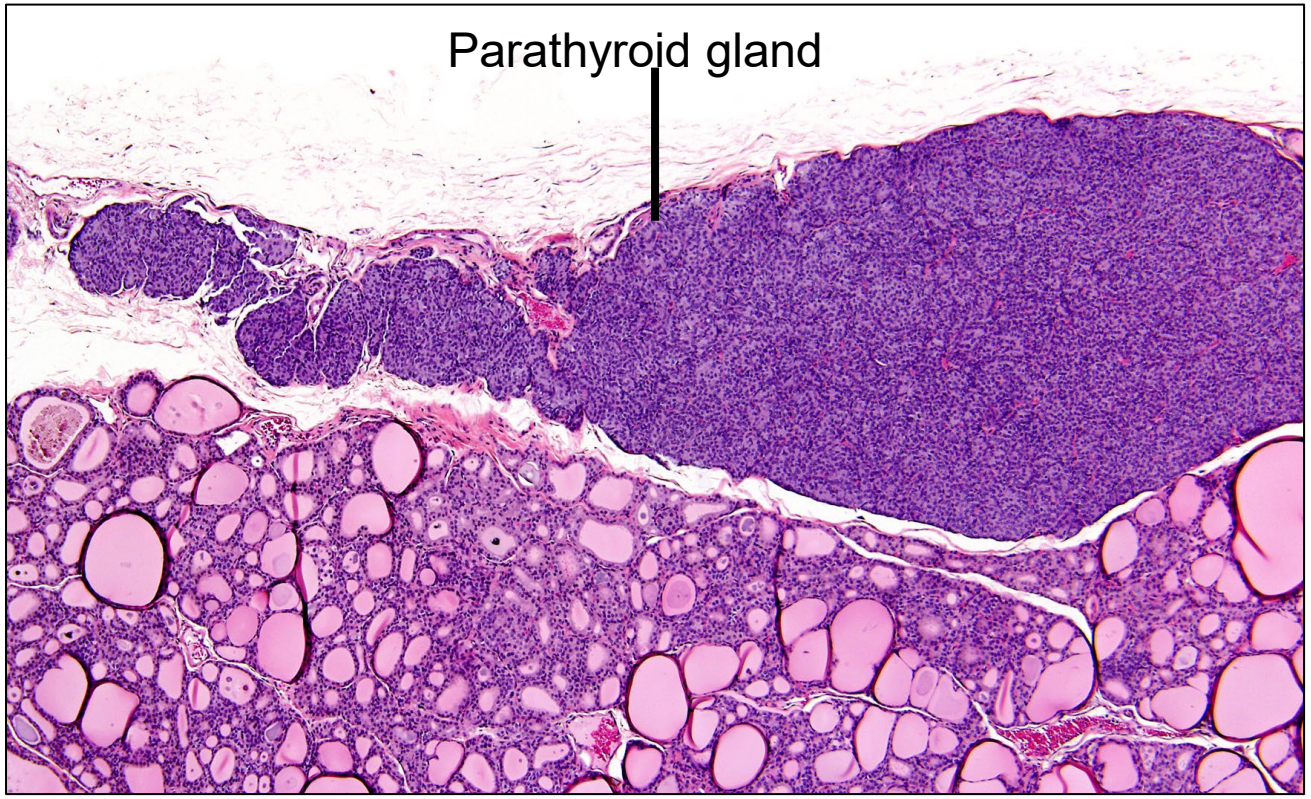
- Diagnostic features:
  - Chief cells are increased in number and uniformly enlarged (hypertrophy).
  - Both parathyroid glands are similarly affected and diffusely enlarged.
  - May cause compression of adjacent thyroid parenchyma.
  - Chief cells are polygonal to elongated.
  - Nuclei are round or elongated and are often larger than normal.
- Associated with conditions that alter calcium metabolism.
  - Chronic renal disease.
  - Diet with inadequate calcium or incorrect calcium to phosphorus ratio.
  - Low serum calcium leads to secondary hyperparathyroidism.
  - Diffuse hyperplasia is reversible if underlying issue is corrected.
- Ultrastructurally, there are increased interdigitations between cells, enlarged mitochondria, increased ribosomes, prominent Golgi.
- Differentiate from adenoma, which is well demarcated with clear compression of surrounding chief cells and affects only one parathyroid gland.

Parathyroid Gland – Hyperplasia

Hyperplasia, Diffuse



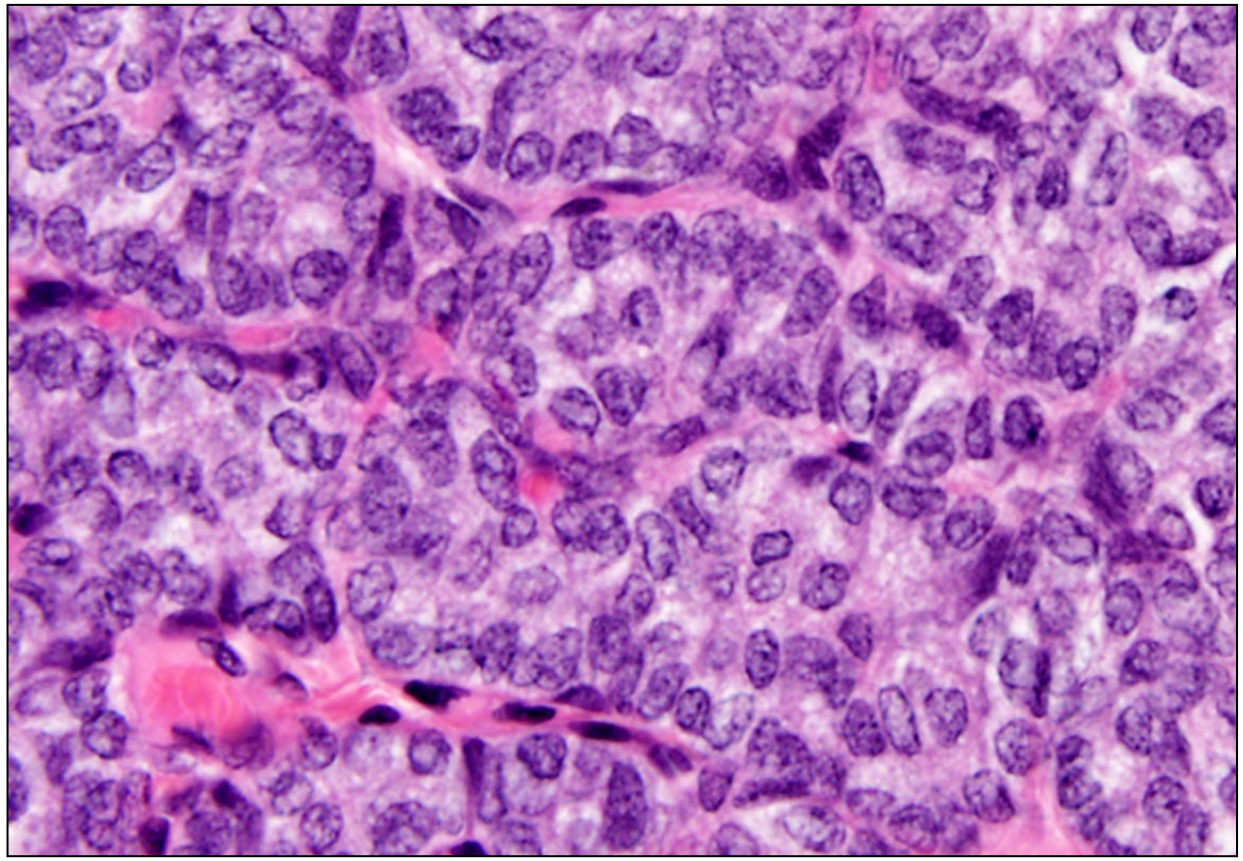
Normal parathyroid gland from a rat.



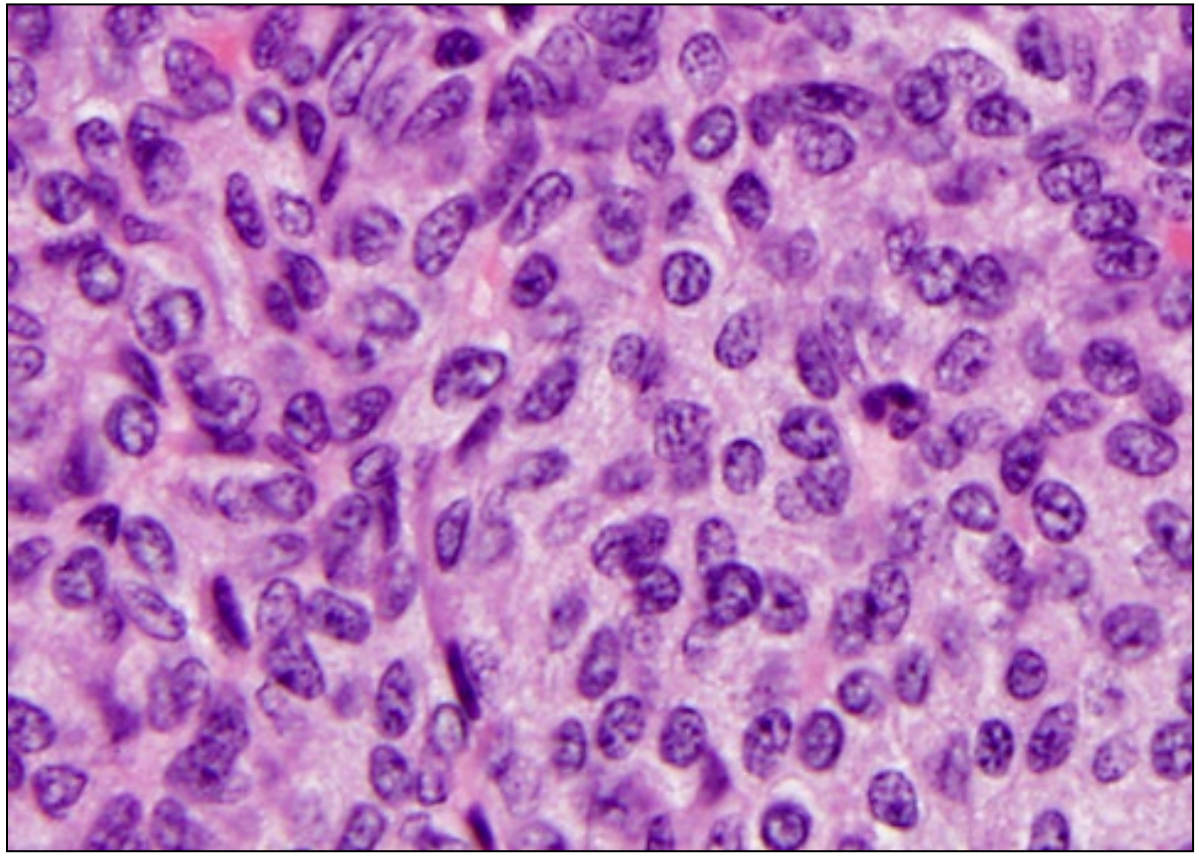
Diffuse parathyroid gland hyperplasia in a rat. The parathyroid gland is diffusely increased in size and would also be observed in the other parathyroid gland (bilateral).

Parathyroid Gland – Hyperplasia

Hyperplasia, Diffuse



Normal chief cells from a rat.



Enlarged (hypertrophied) chief cells from a diffusely hyperplastic parathyroid gland from a rat.

Parathyroid Gland – Hyperplasia

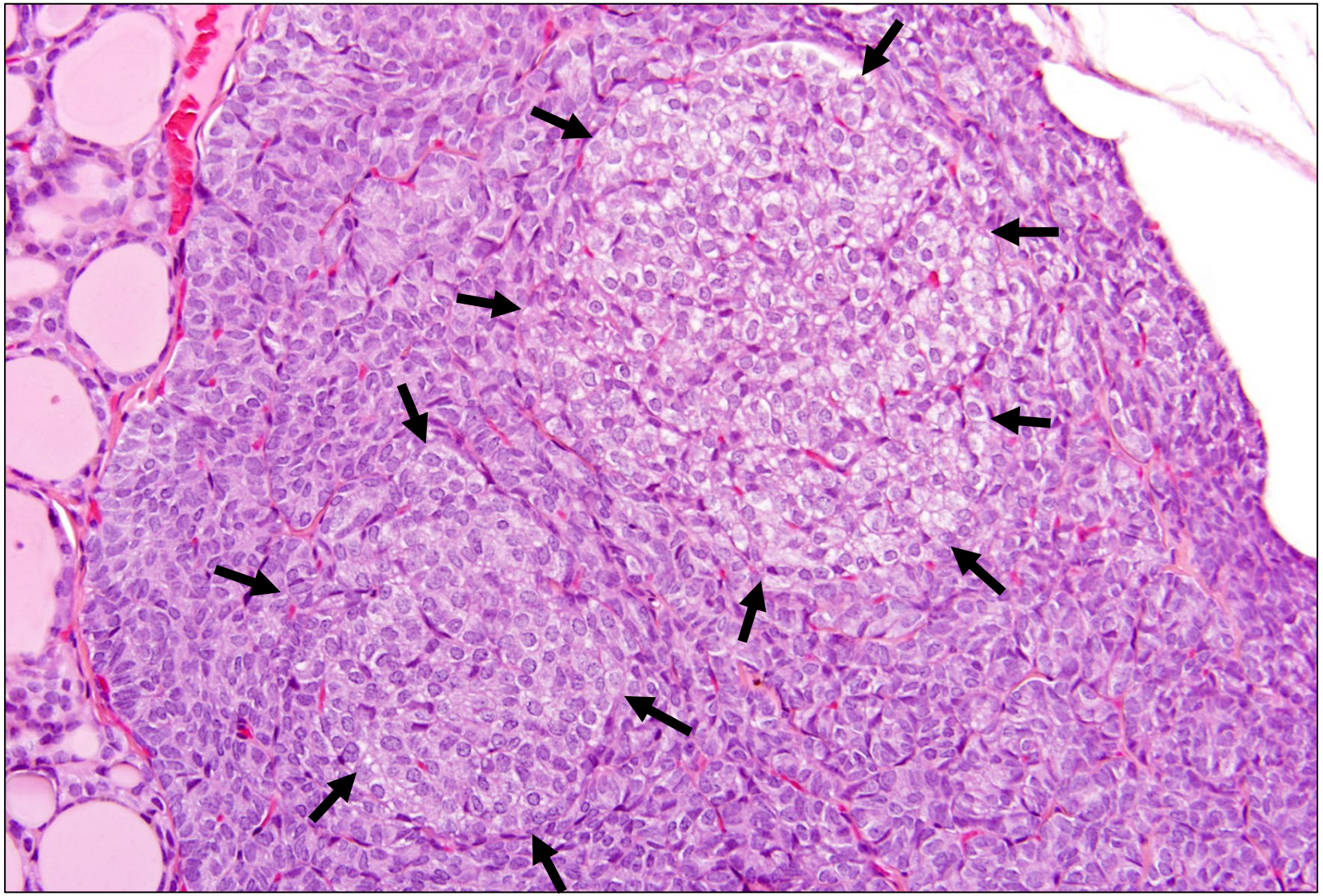
Hyperplasia, Focal

- Diagnostic features:
  - Nodular area(s) within an otherwise normal-looking parathyroid gland.
    - Unencapsulated and poorly demarcated with minimal or no compression of surrounding chief cells.
    - Occur in one or both parathyroid glands.
  - Alteration in growth pattern and/or differential tinctorial staining of cells causes foci to stand out from surrounding parenchyma.
  - Enlarged cells are increased in number in a single focus or multifocal areas.
  - Cellular characteristics are similar to those in diffuse hyperplasia.
    - Cytoplasm is eosinophilic and sometimes vacuolated.
    - Cytoplasm to nuclear ratio can be increased or decreased.
- Focal hyperplasia is usually nonfunctional and is potentially preneoplastic (potential to progress to a tumor).
- Differentiate from adenoma, which is a solitary, well-demarcated nodule with compression of surrounding parathyroid parenchyma or thyroid gland that may or may not have a capsule.
- Much less frequent than diffuse, bilateral hyperplasia.

Parathyroid Gland – Hyperplasia

Hyperplasia, Focal

- Focal hyperplasia in the parathyroid gland of a rat.
- Two focal areas of hyperplasia with increased numbers of pale, enlarged chief cells (arrows).
- There is little to no compression of surrounding tissue.

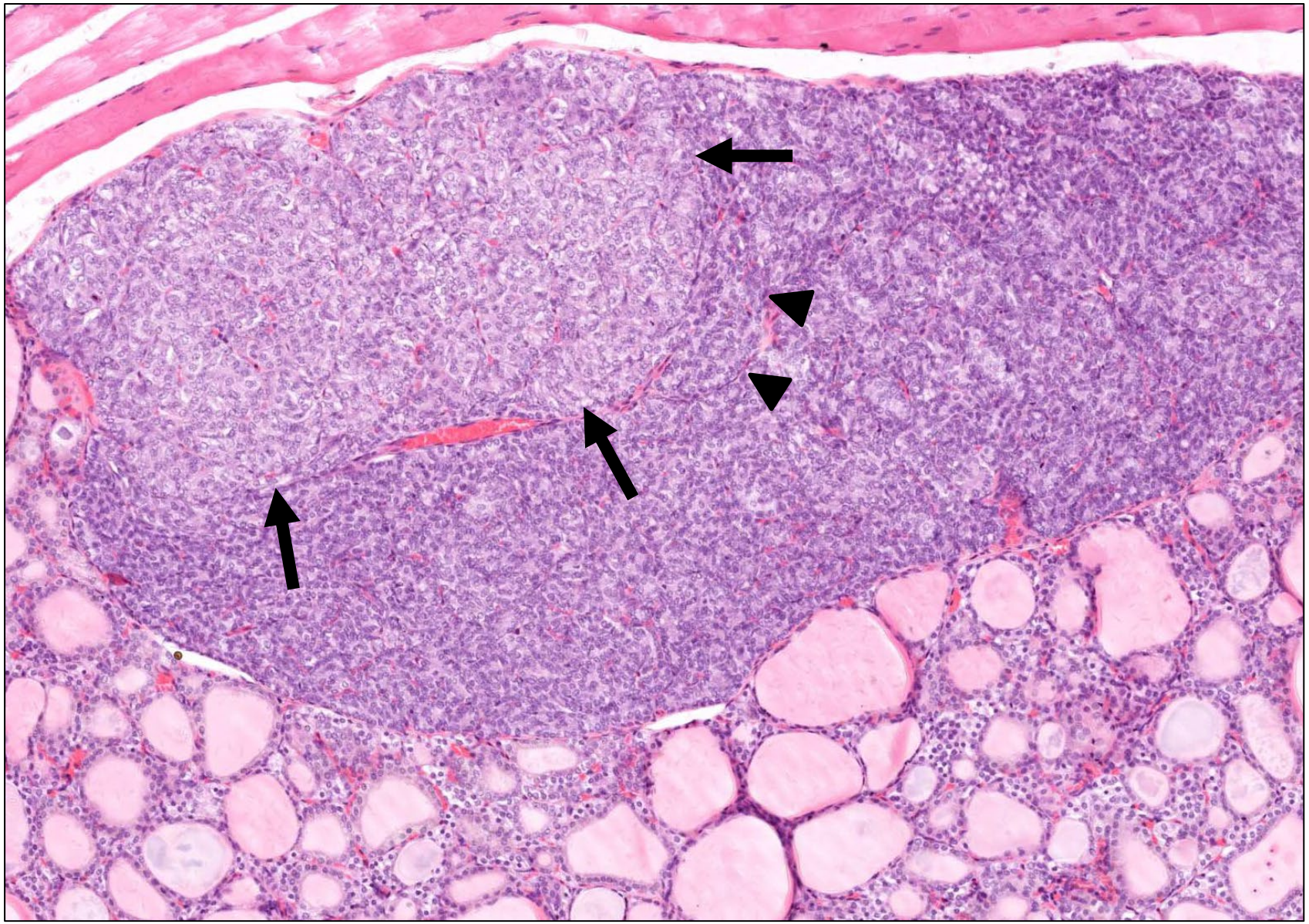


Parathyroid Gland – Adenoma

- Benign tumor of chief cells of the parathyroid gland.
- Diagnostic features:
  - Solitary, well-demarcated, nodule that may or may not be encapsulated, with compression of adjacent chief cells or thyroid gland.
  - Composed of chief cells with nuclear pleomorphism, sometimes mitoses, and either an increased or decreased cytoplasm to nuclear ratio.
  - Usually solid growth pattern but may have papillary, acinar, or cystic pattern.
    - Papillary = projections on a fibrovascular core.
    - Acinar = round to oval glandular structures with central luminal spaces.
    - Cystic = formation of cyst-like spaces.
- Adenoma likely progresses from focal hyperplasia but does not progress from diffuse hyperplasia.
- May rarely arise from ectopic parathyroid tissue in the mediastinum.
- Uncommon in rats, rare in mice.

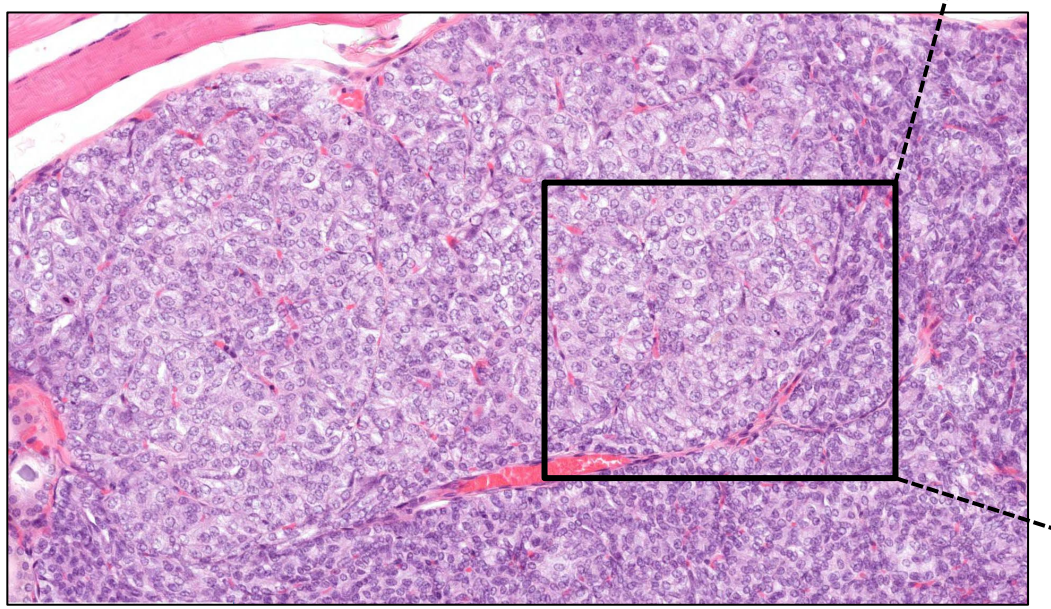
Parathyroid Gland – Adenoma

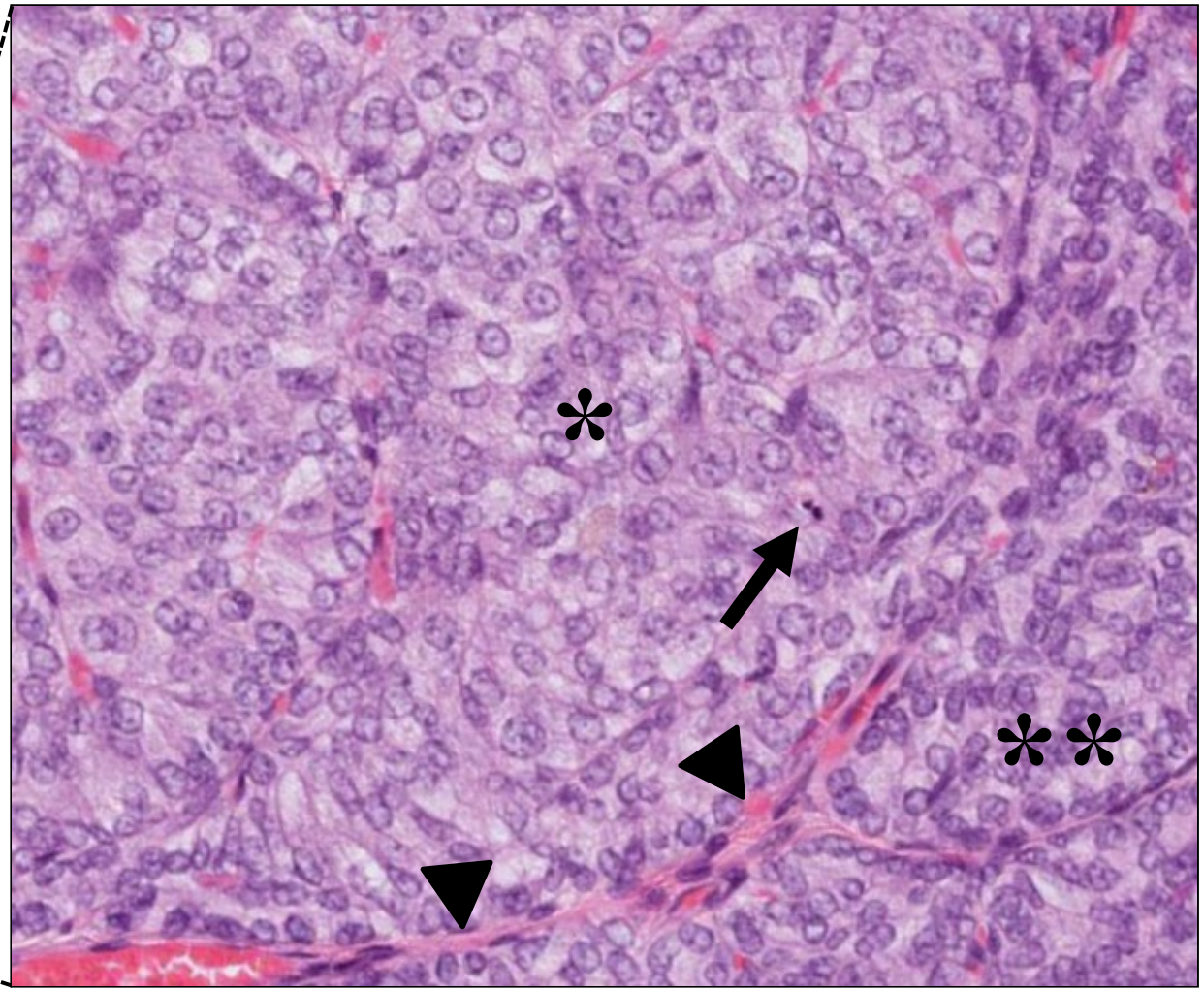
- Adenoma (arrows) in the parathyroid gland of a rat.
- Well demarcated, expansile nodule causing slight compression of the surrounding chief cells (arrowheads).
- Neoplastic chief cells form a solid growth pattern and have pale cytoplasm in comparison with surrounding chief cells.



Parathyroid Gland – Adenoma

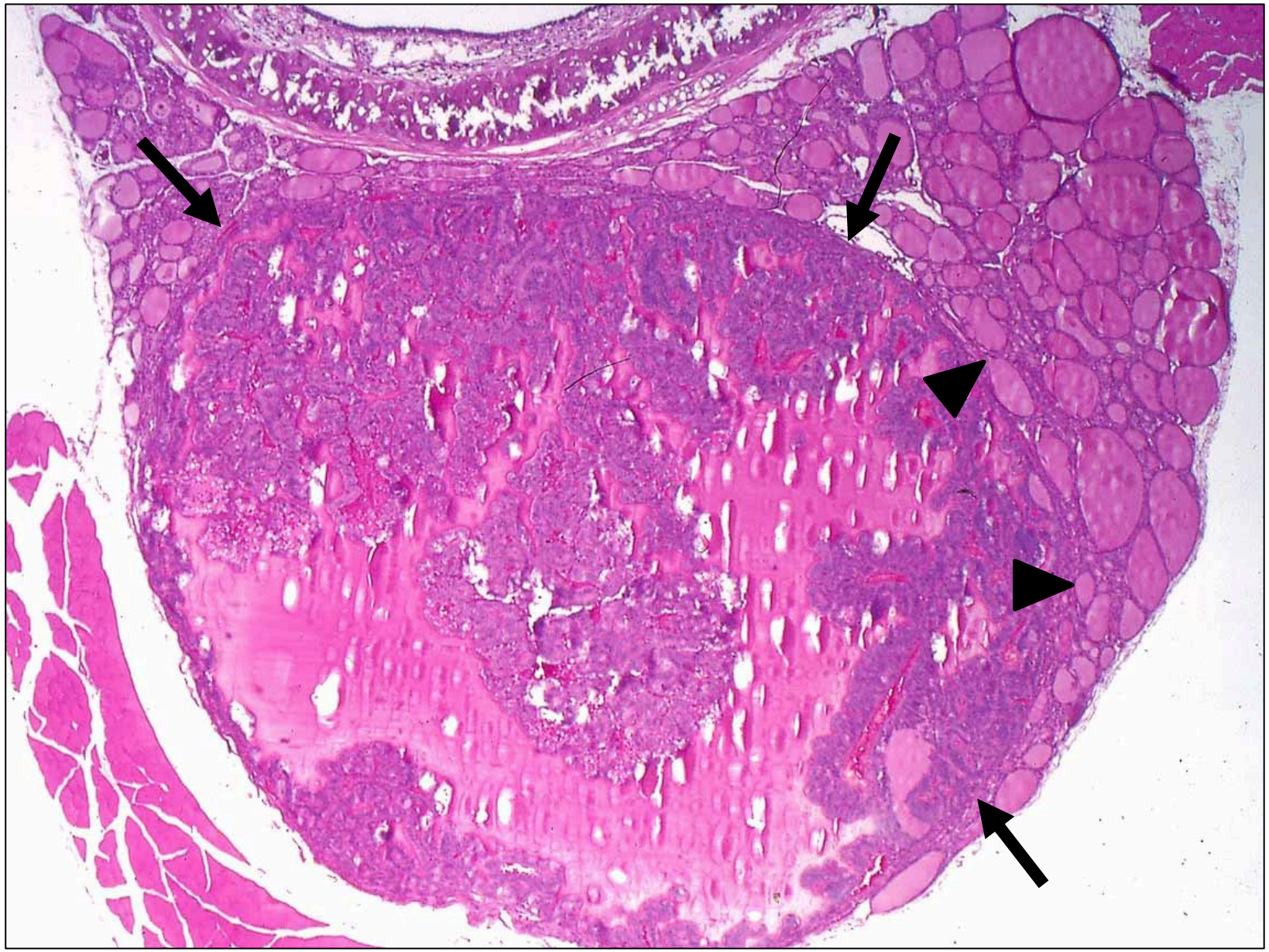
- Higher magnification of adenoma from previous slide.
- There is partial encapsulation by a rim of fibrous connective tissue (arrowheads).
- Neoplastic cells (*) have large nuclei and abundant cytoplasm in comparison with surrounding normal chief cells (**).
- Mitotic activity is present (arrow).





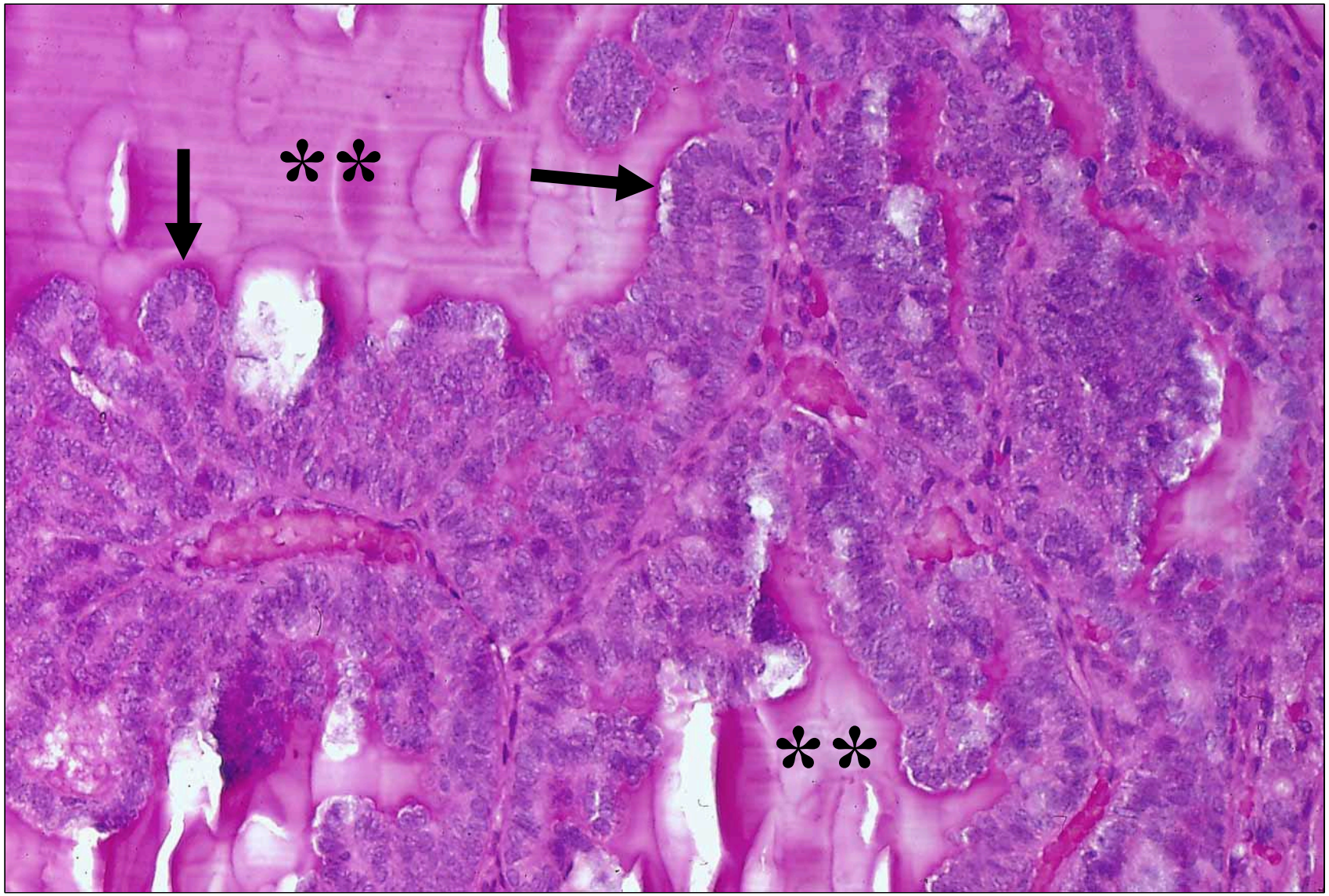
Parathyroid Gland – Adenoma

- Adenoma (arrows) in the parathyroid gland of a rat.
- Well demarcated, expansile nodule causing slight compression of the surrounding thyroid follicles (arrowheads).
- Neoplastic chief cells form a cystic (fluid-filled) papillary (finger-like projections) growth pattern.



Parathyroid Gland – Adenoma

- Higher magnification of adenoma from previous slide showing cystic papillary growth pattern.
- Neoplastic chief cells form papillary projections (arrows) into eosinophilic-staining cystic fluid (**).

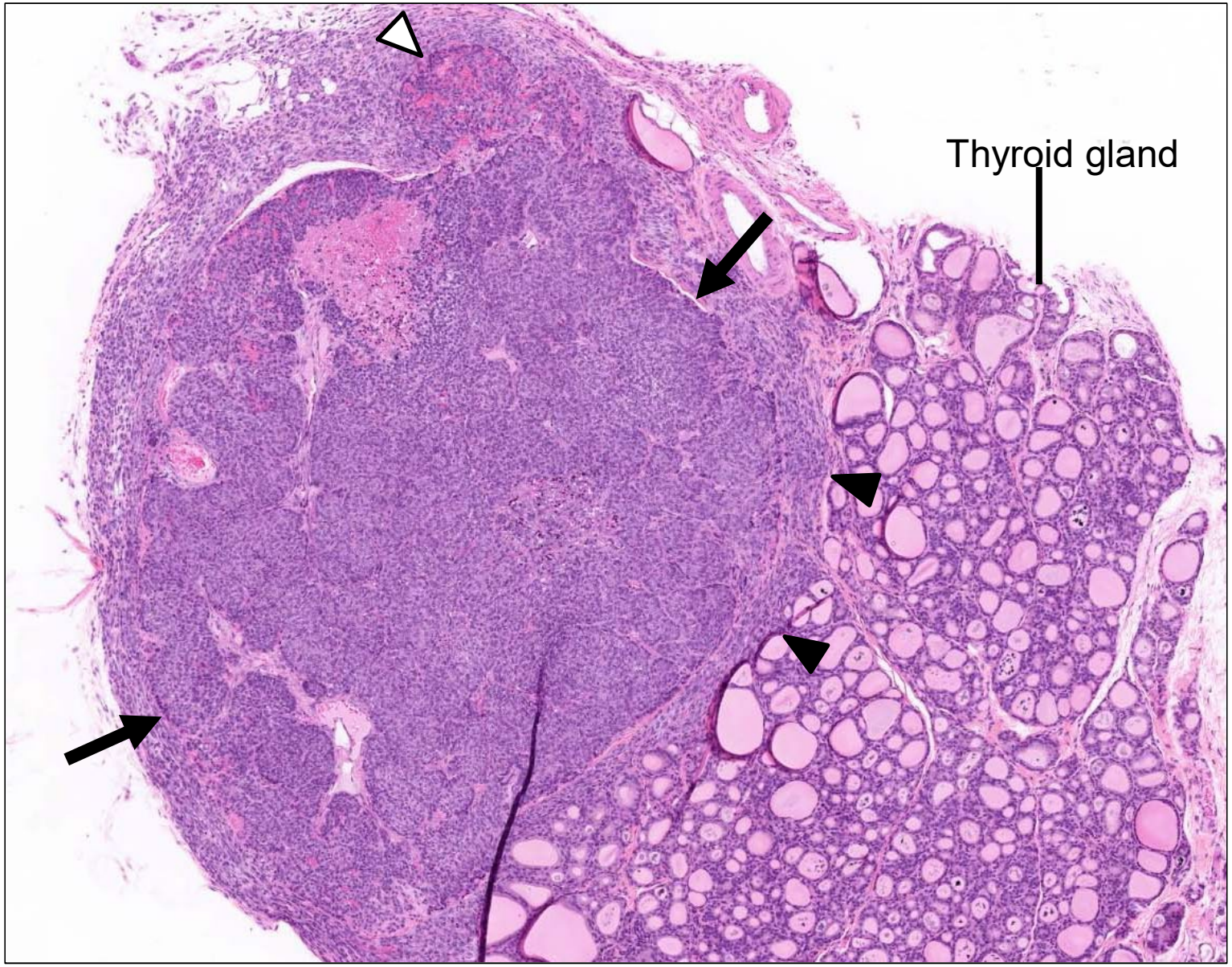


Parathyroid Gland – Carcinoma

- Malignant tumor of chief cells of the parathyroid gland.
- Diagnostic features:
  - Large mass, often as large or larger than the normal parathyroid gland.
    - Usually has a solid growth pattern.
    - Causes compression of the normal adjacent chief cells.
  - Capsular, vascular, or intrathyroidal invasion.
    - Metastases most commonly occurs to regional lymph nodes or lungs; however, metastasis has not been described in rats.
  - Polygonal or elongated proliferative chief cells with nuclear pleomorphism and mitoses.
- Uncommon to rare in rats and mice.
- Differentiate from adenoma in that there is no invasion or metastasis with adenoma.

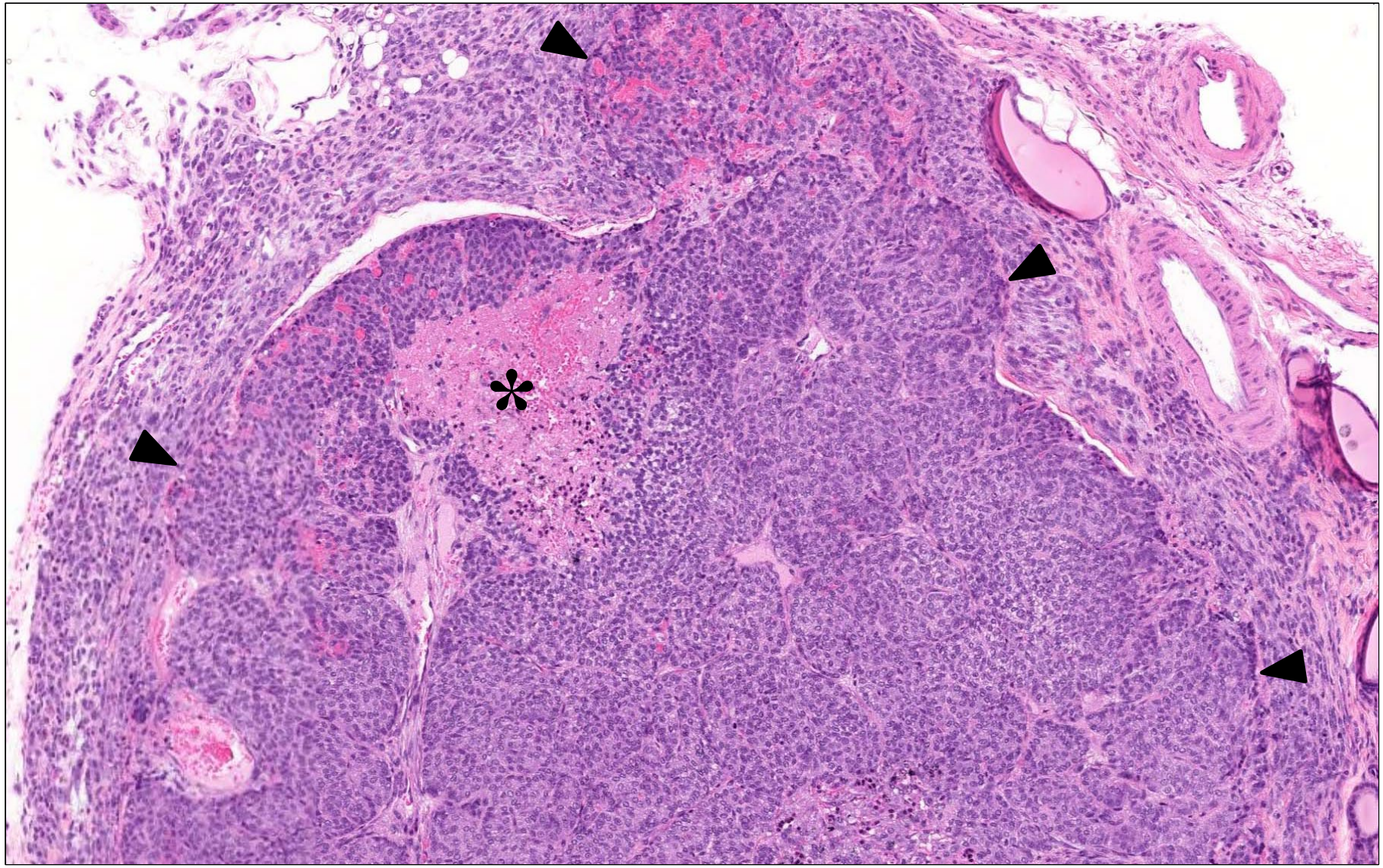
Parathyroid Gland – Carcinoma

- Carcinoma (arrows) in the parathyroid gland of a rat.
- Large, poorly demarcated neoplastic proliferation of chief cells.
- Invasion of neoplastic cells into surrounding capsule (white arrowhead) and adjacent thyroid gland (black arrowheads).
- Predominantly solid growth pattern.



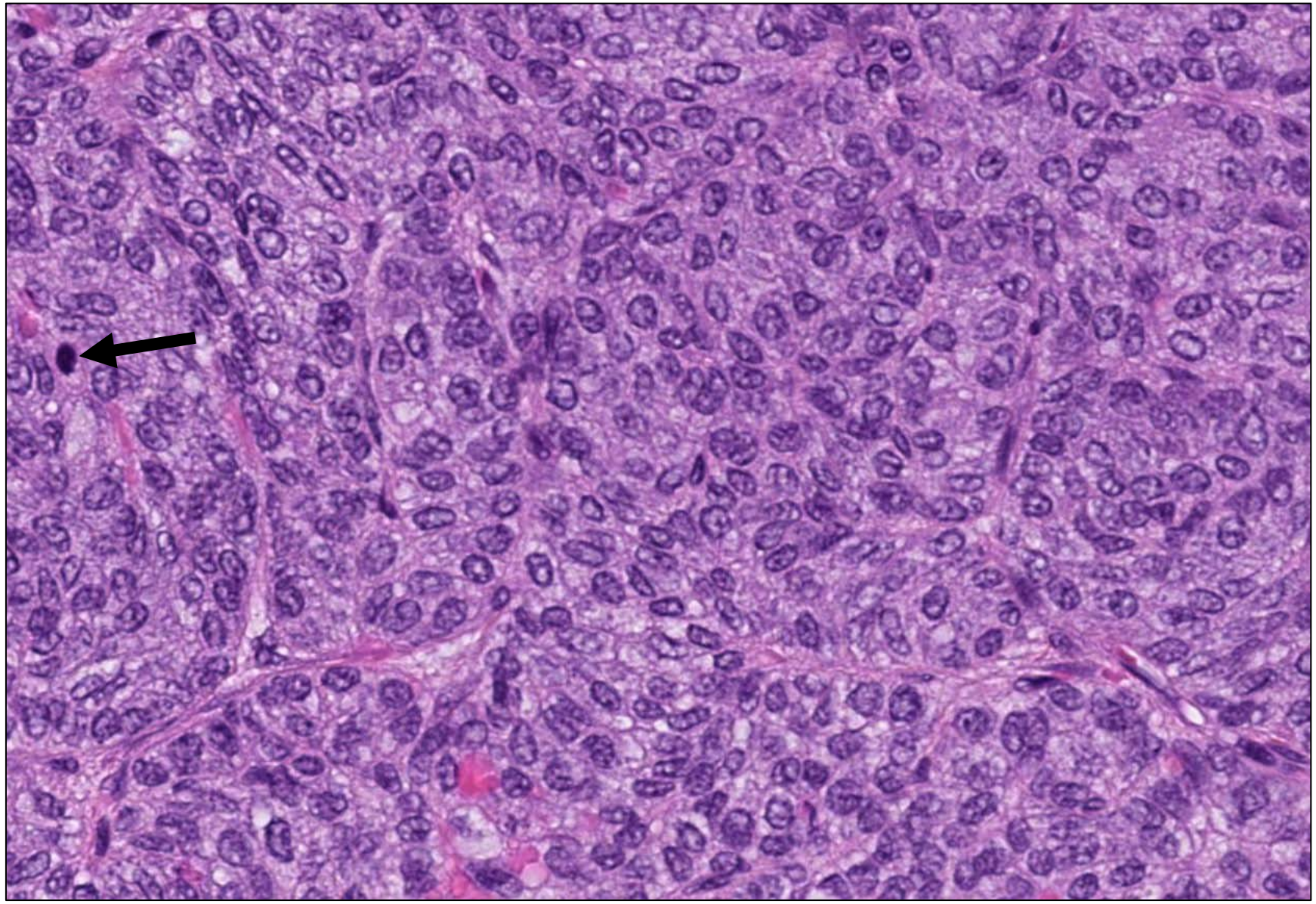
Parathyroid Gland – Carcinoma

- Higher magnification of carcinoma from previous slide showing invasion of neoplastic cells into surrounding capsule and extrathyroidal tissue (black arrowheads).
- Area of necrosis (*) within neoplasm.



Parathyroid Gland – Carcinoma

- Higher magnification of carcinoma from previous slide.
- Neoplastic cells have large nuclei and amphophilic (purple) cytoplasm with slight variation in nuclear size and shape (pleomorphism).
- Mitotic activity is present (arrow).



References

- Brandli-Baiocco A, Balme E, Bruder M, Chandra S, Hellmann J, Hoenerhoff MJ, Kambara T, Landes C, Lenz B, Mense M, Rittinghausen S, Satoh H, Schorsch F, Seeliger F, Tanaka T, Tsuchitani M, Wojcinski Z, Rosol TJ. (2018). Nonproliferative and proliferative lesions of the rat and mouse endocrine system. Toxicol Pathol 31 (3 Suppl): 1S-95S

- Hardisty JF, Boorman GA (1999). Thyroid and Parathyroid Glands. In Maronpot RR (ed.) *Pathology of the Mouse,* pp. 537 – 554. Cache River Press. Vienna, IL.

- Maronpot RR, Hill GD. 2014. Parathyroid Gland. In: Cesta MF, Herbert RA, Brix A, Malarkey DE, Sills RC (Eds.), National Toxicology Program Nonneoplastic Lesion Atlas. Available: https://ntp.niehs.nih.gov/atlas/nnl/endocrine-system/parathyroid-gland.

- Mense MG, Rosol TJ (2018). Parathyroid Gland. In Suttie AW (ed.) *Boorman's Pathology of the Rat,* pp. 687 – 693. Academic Press. Cambridge, MA.

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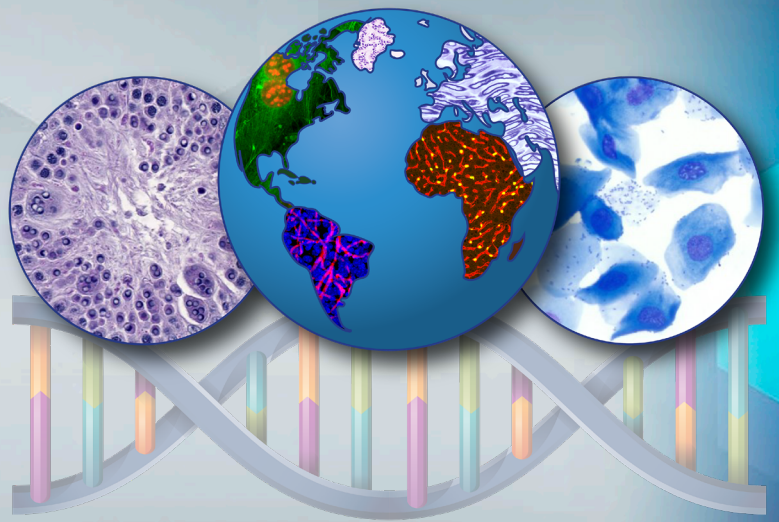

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