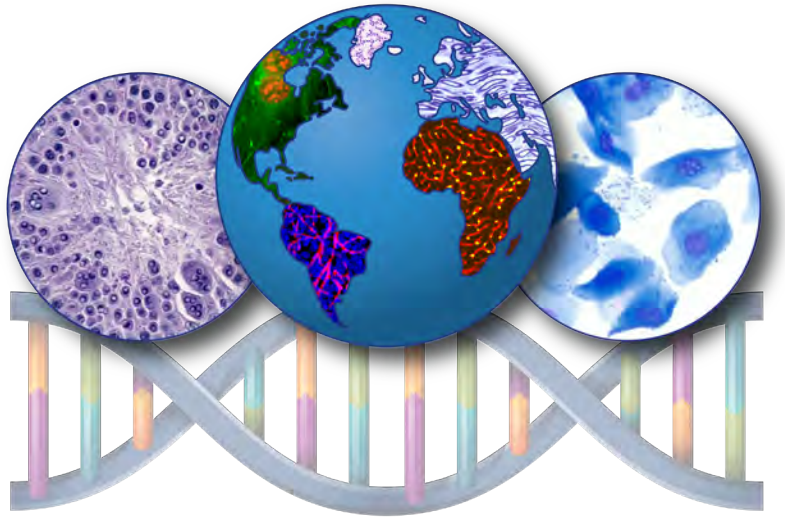
Proliferative Lesions in the Rodent Uterus



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 Uterus

Overview

- **Hyperplastic Lesions**
  - Hyperplasia, Endometrial Stromal
  - Hyperplasia, Glandular, Cystic
  - Hyperplasia, Glandular, Focal
- **Benign Tumors**
  - Adenoma, Endometrium
  - Leiomyoma
  - Papilloma, Squamous Cell
  - Polyp, Endometrial Stromal
  - Polyp, Glandular
  - Schwannoma, Benign
- **Malignant Tumors**
  - Adenocarcinoma, Endometrium
  - Carcinoma, Adenosquamous
  - Carcinoma, Squamous Cell
  - Histiocytic Sarcoma
  - Leiomyosarcoma
  - Sarcoma, Endometrial Stromal
  - Schwannoma, Malignant

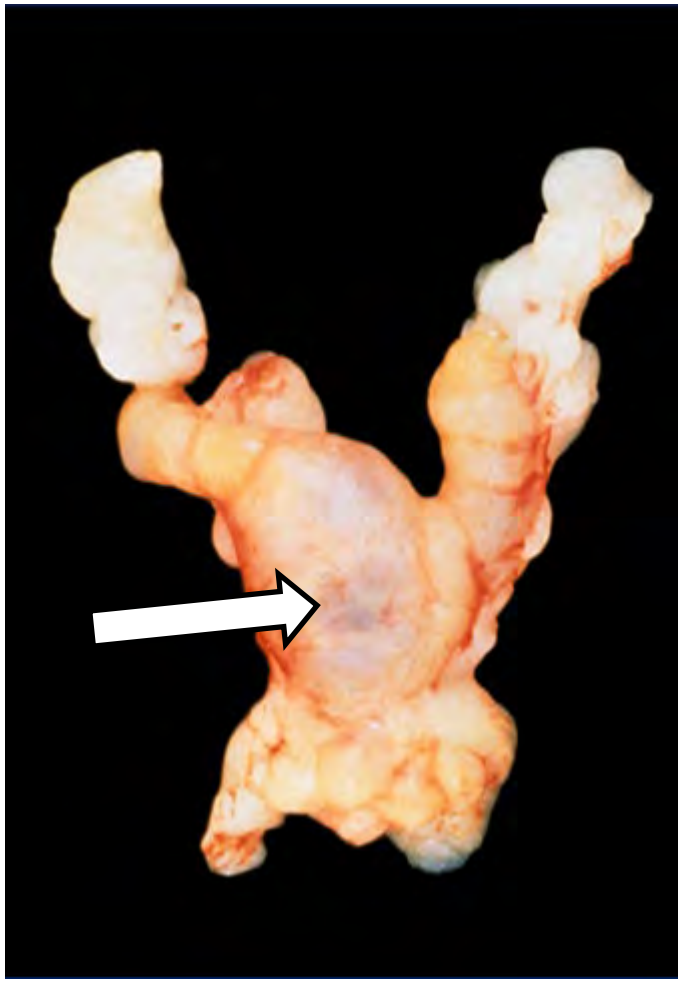
Uterus – Hyperplasia, Endometrial Stromal

- Increased stromal component.
- Proliferation of spindle/stellate stromal cells.
- Variable amount of intercellular collagen depending on age of lesion (older lesions have dense collagen stroma or fibrosis).
- Oriented around normal anatomical structures; not associated with gross anatomical abnormalities or tissue distortion.
- Non-invasive.
- Endometrial glands absent or sparse.
- Mitoses and vascularization may be prominent.
- Common finding in aged mice and rats.

Dixon et al., 2014

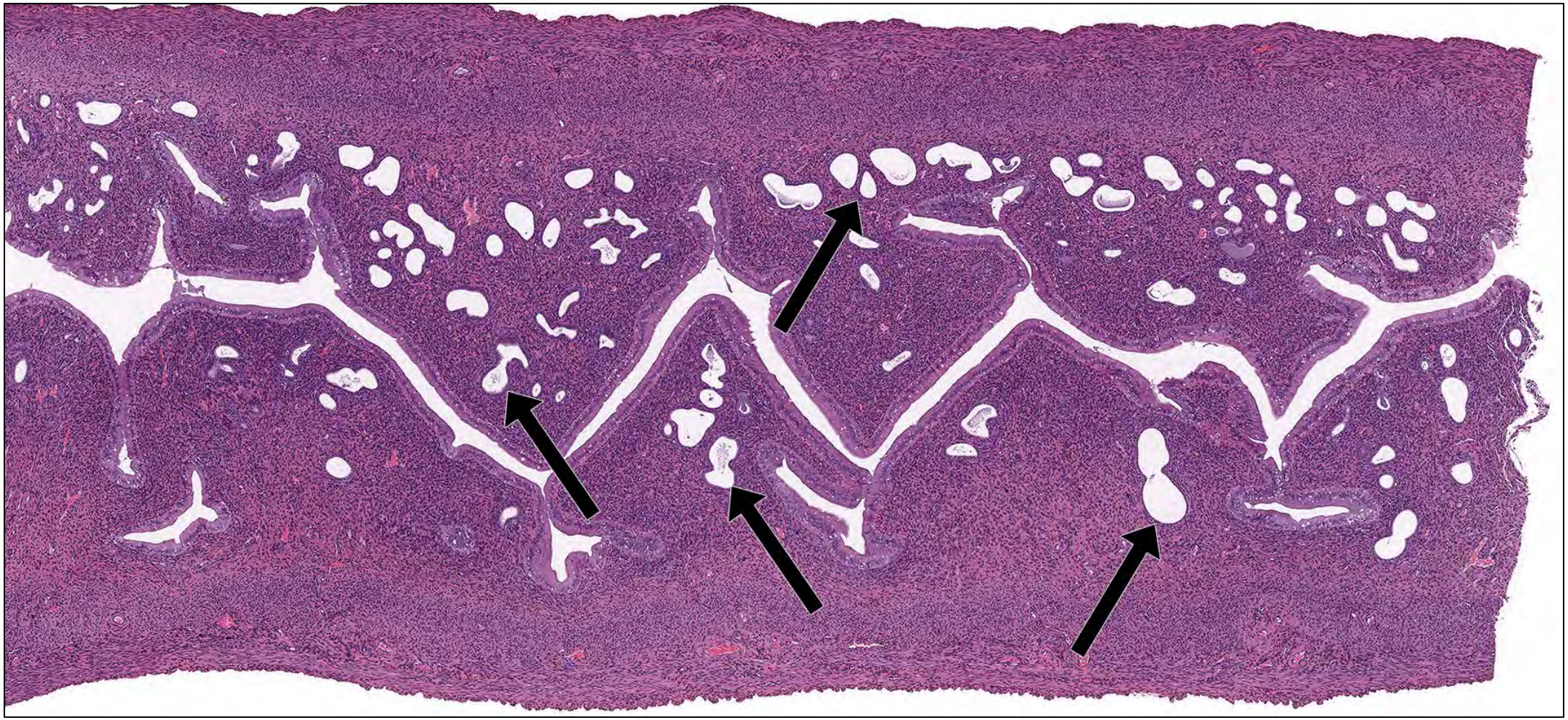
Uterus – Hyperplasia, Glandular, Cystic

- Formerly known as cystic endometrial hyperplasia (CEH).
- Generally diffuse, but may be focal, increase in the number of glands, which become variably and progressively dilated and usually cystic (Hobbie and Dixon, 2020).
- The glands are individualized and separated by increased or decreased amounts of stroma (Hobbie and Dixon, 2020).
- Mitotic figures and cellular atypia can be observed.
- Often brought about by prolonged estrogen stimulation and is not believed to be preneoplastic (Dixon et al., 2018).
- Most common spontaneous age-related lesion in the uterus of mice and rats (Dixon et al., 2018).
- More common in mice than rats.



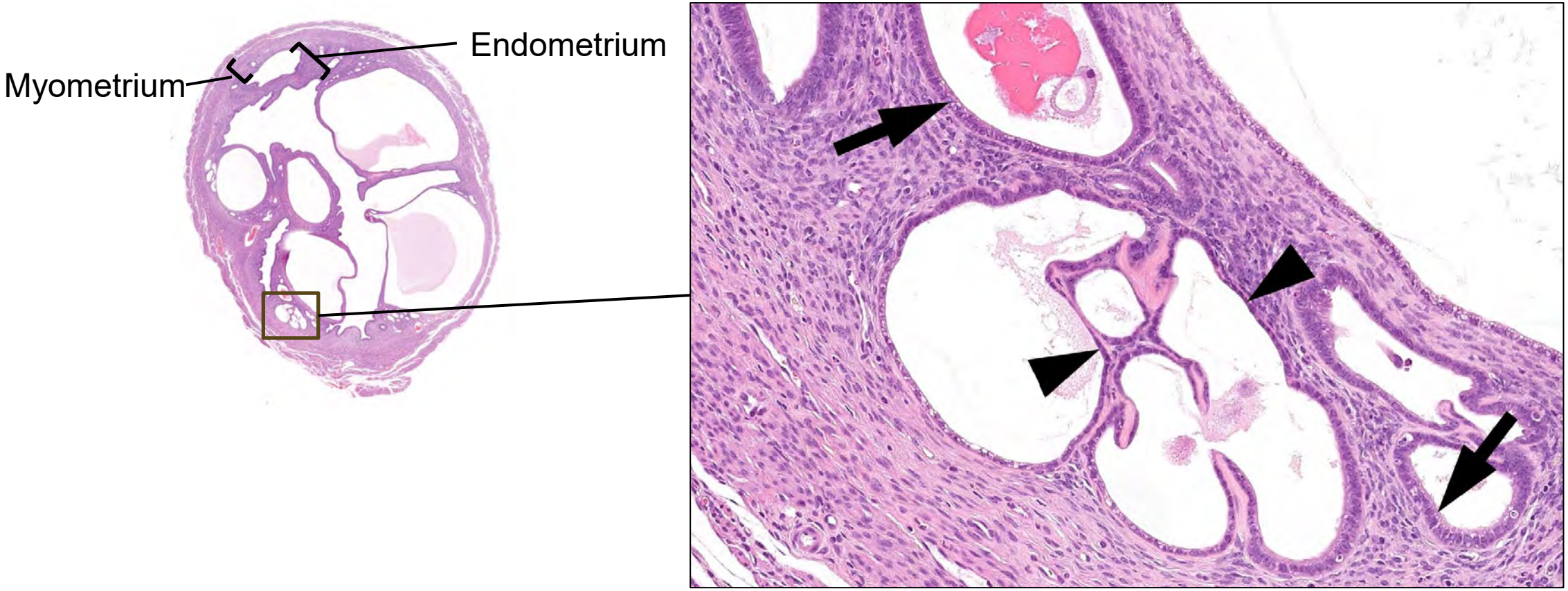
Uterine horn is distorted by cystic glandular hyperplasia (arrow).
Image courtesy of Dr. Ron Herbert.

Uterus – Hyperplasia, Glandular, Cystic



Note from this longitudinal uterine section that the change is diffuse, with increased amounts of dilated (cystic) and tortuous (irregularly winding / twisting) glands throughout the stroma (arrows).

Uterus – Hyperplasia, Glandular, Cystic

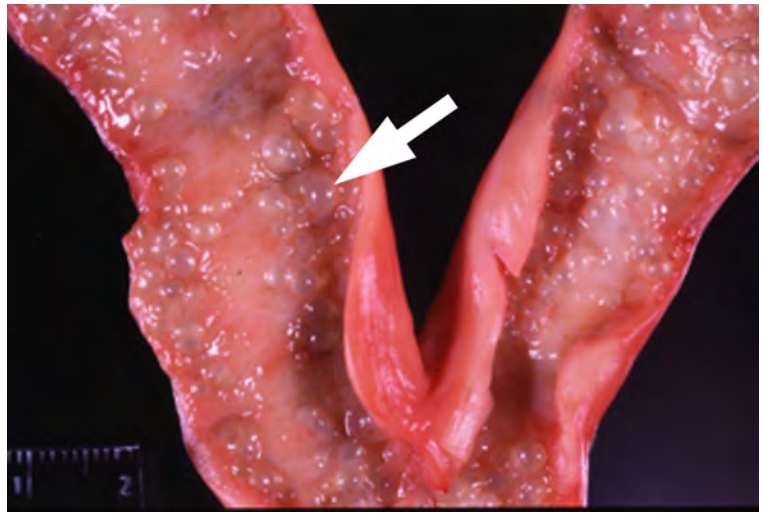


Uterus – Hyperplasia, Glandular, Cystic, mouse.

Higher magnification (right panel) of transverse section (left panel) of uterus. The dilated glands (arrows) are lined by normal / uniform cuboidal to low columnar epithelium. The epithelium may be attenuated in particularly dilated or cystic glands (arrowheads).

Comparative Pathology: Hyperplasia, Glandular, Cystic (Cystic Endometrial Hyperplasia)

- Dog: Cystic endometrial hyperplasia (CEH) is associated with pyometra, usually secondary to estrogen-priming/progesterone-induction and opportunistic bacterial infection (Bigliardi et al., 2004; Schlafer and Foster, 2007)
- Cattle: CEH is associated with ovarian follicular cysts or granulosa cell tumors → hyperestrogenism (Schlafer and Foster, 2007)
- Rabbit: Endometrial hyperplasia is age-related and second most common uterine lesion, often glandular/cystic (Bertram et al., 2018)
- Non-human Primates (NHPs) / Humans: Endometrial hyperplasia arises with prolonged estrogen exposure (estrogen replacement therapy, polycystic ovarian syndrome, granulosa cell tumors) (Cline et al, 2008)



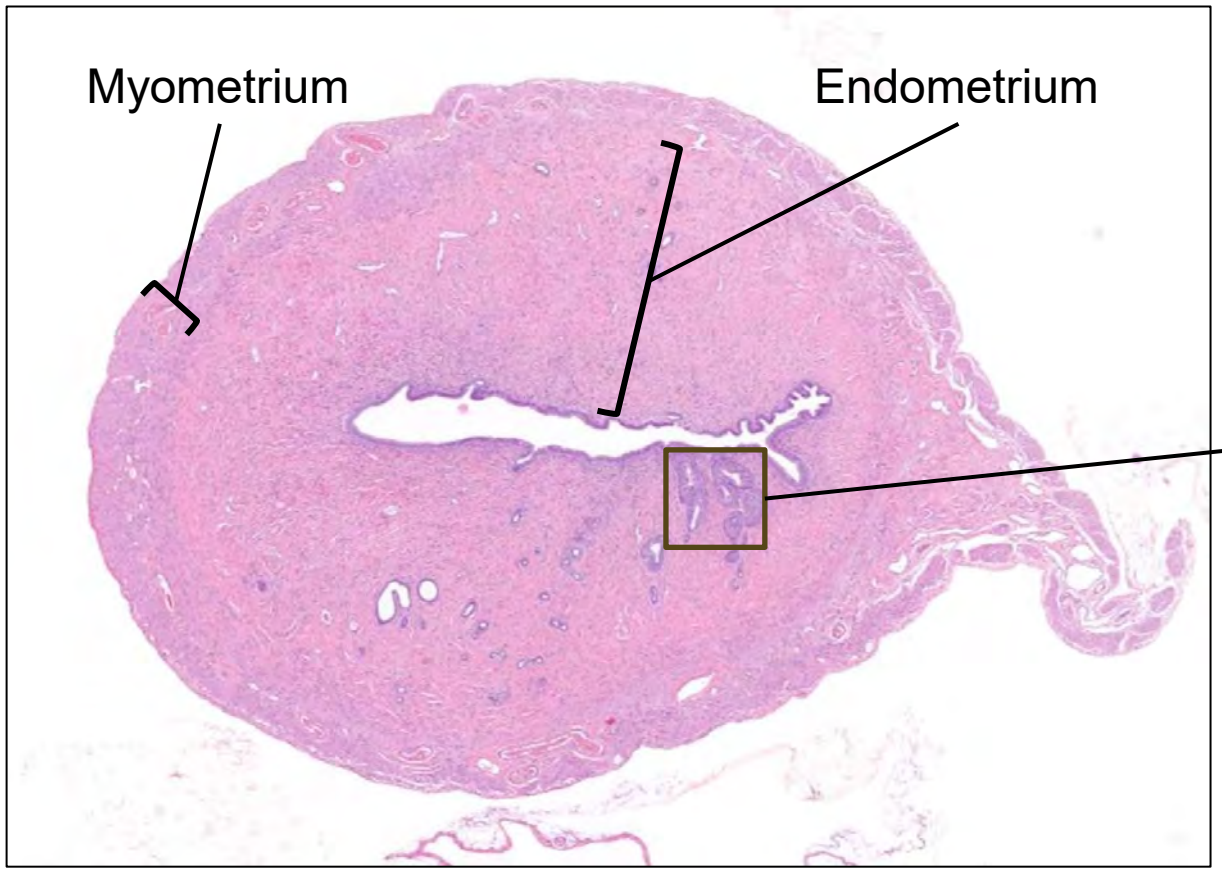
Canine uterus – cystic endometrial hyperplasia (arrow)

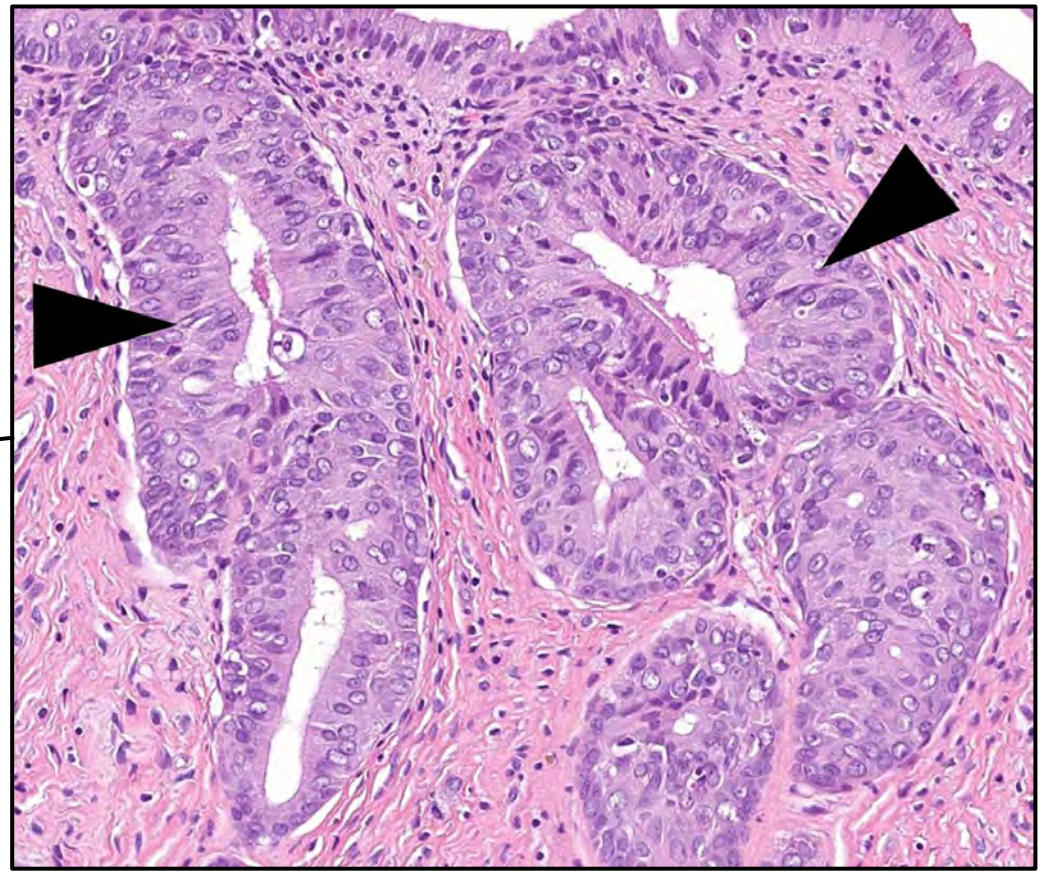
Image courtesy of Noah's Arkive

Uterus – Hyperplasia, Glandular, Focal

- Formerly known as atypical glandular hyperplasia or adenomatous hyperplasia.
- Rarely spontaneous; most often induced by experimental compounds (uterine carcinogens) (Dixon et al., 2014).
- Considered a preneoplastic lesion, and its differentiation from neoplasia is often difficult in advanced cases.
- Consists of a focal proliferation of endometrial glands, often crowded or “back-to-back” without intervening stroma, that display pleomorphism (variation in shapes and sizes of the nuclei or cytoplasm) and atypia (structural abnormality in a cell).
- Glandular epithelial cells may be stratified (multi-layered) and abundant mitotic figures may be present.
- Found within the normal morphological boundaries of the endometrium.

Uterus – Hyperplasia, Glandular, Focal





Uterus – Hyperplasia, Glandular, Focal, rat.

Endometrial glands are closely apposed with increased gland-to-stroma ratio. Glandular epithelial cells are stratified (arrowheads) with cellular atypia. DTT nomenclature is Uterus – Hyperplasia, Atypical.

Comparative Pathology: Humans – Endometrial Intraepithelial Neoplasia (EIN)

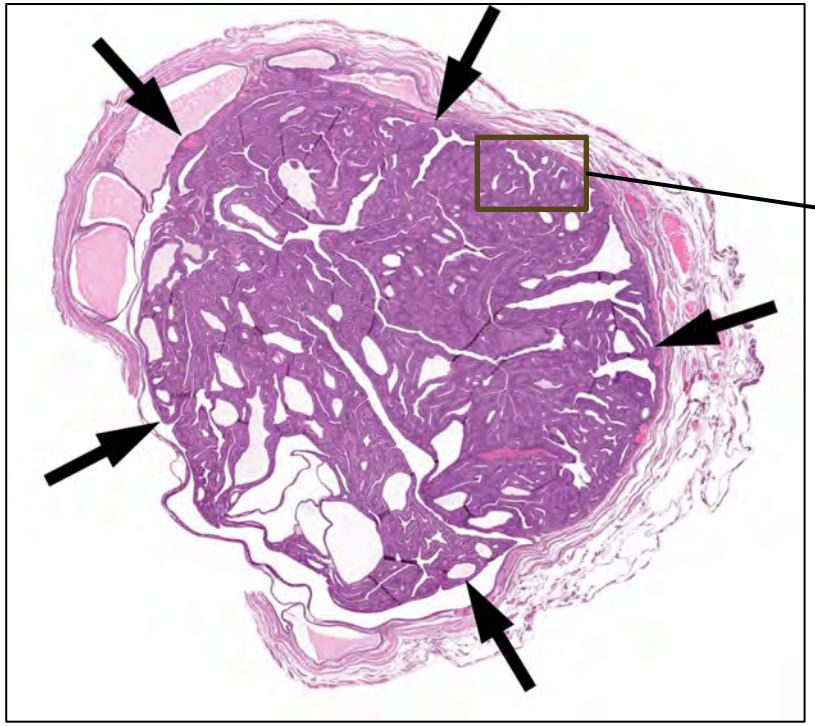
- The classification of endometrial hyperplasia in humans was simplified from 4 categories (WHO 1994) to 2 categories (WHO 2014) (Sanderson et al., 2017; Ring et al., 2022).
  - Endometrial hyperplasia without atypia (benign hyperplasia).
  - Endometrial hyperplasia with atypia (endometrial intraepithelial neoplasia).
- Endometrial Intraepithelial Neoplasia (EIN).
  - Previously known as atypical endometrial hyperplasia (Ring et al., 2022).
  - Considered a precursor lesion for endometrioid endometrial carcinoma.
  - Criteria includes glandular crowding with cytologic atypia beyond expected in proliferative endometrium; glandular volume exceeding that of stroma; atypical glands cytologically distinguished from surrounding normal glands (Ring et al., 2022; Semere et al., 2011).

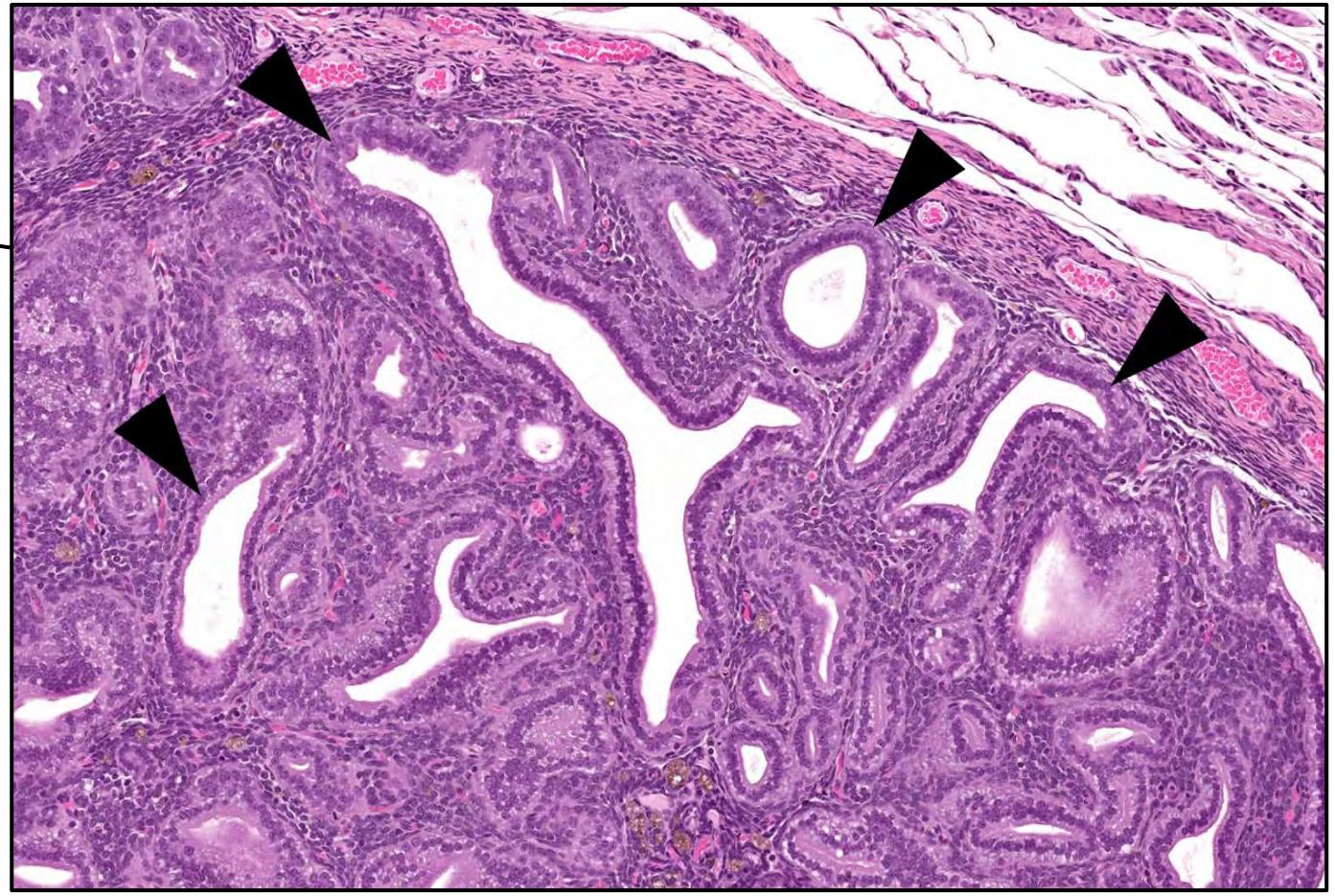
Uterus – Adenoma, Endometrium

- Benign (non-cancerous) neoplastic proliferation of uterine epithelial elements.
  - Arise from the luminal endometrial epithelium and may have a broad base or delicate stalk.
  - Solitary and well-demarcated (sharp, regular border) mass that may compress, but not invade, adjacent tissue.
  - No evidence of invasion of surrounding tissues or metastasis (spread to distant sites).
- Often exophytic (grow outward) or papillary (if papillary, use the modifier “papillary”).
  - Less frequently, endophytic (growing inward) and glandular (Dixon et al., 2018).
- Cells are typically well-differentiated, cuboidal to columnar.
  - Cells form glandular or tubular structures or papillary fronds that extend into the uterine lumen.
  - Intervening stroma is scant between neoplastic glands.
  - Low numbers of mitotic figures.
- Decidual reaction is occasionally observed in or associated with endometrial neoplasms (Dixon et al., 2018).

Dixon et al., 2014

Uterus – Adenoma, Endometrium





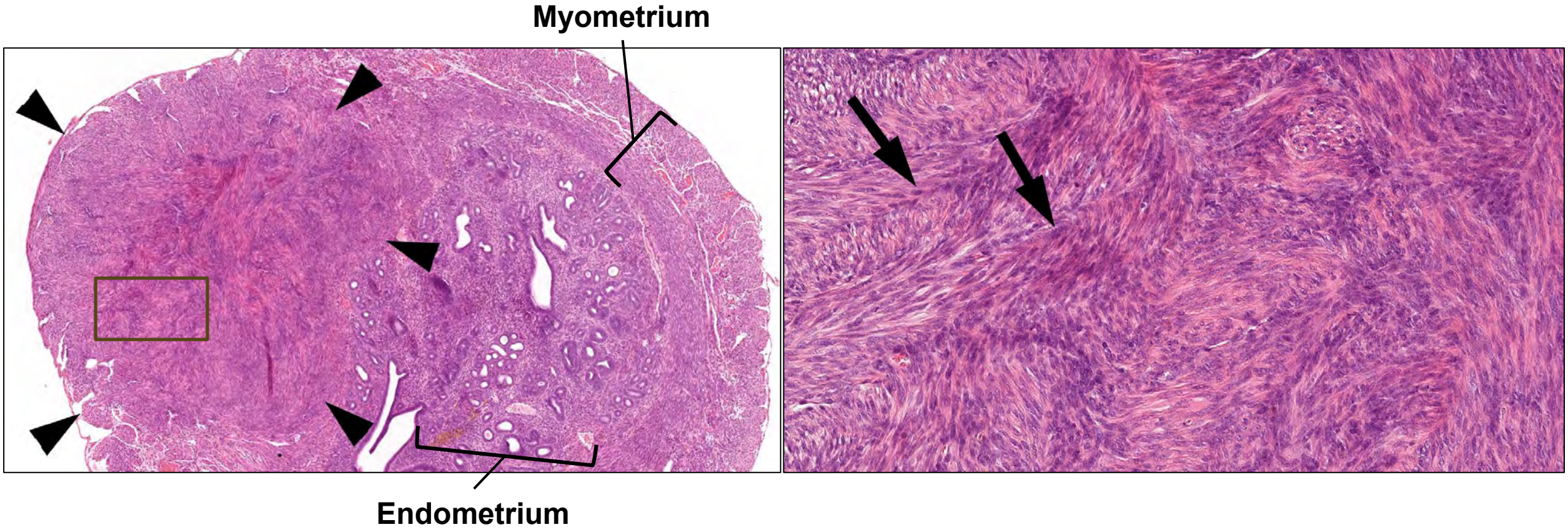
Uterus – Adenoma, Endometrium, mouse.

Mass is exophytic (arrows) and fills the uterine lumen. Mass is comprised of well-differentiated, cuboidal to columnar epithelium forming often dilated or tortuous glandular structures (arrowheads).

Uterus – Leiomyoma

- A benign tumor arising from the smooth muscle cells of the myometrium as solitary or multiple, well-circumscribed masses that may compress adjacent tissues (Dixon et al., 2014).
- Well-differentiated spindle cells arranged in interlacing bundles and whorls in a delicate collagenous stroma.
- Tumor cells have abundant eosinophilic cytoplasm, distinct borders and “cigar-shaped” or blunt-ended nuclei.
- There is minimal nuclear pleomorphism and mitotic figures are rare.
  - Differentiate from leiomyosarcoma: cellular and nuclear pleomorphism, poorly circumscribed and invasive, prominent nucleoli and mitotic figures.
- Leiomyomas have been induced following Diethylstilbestrol (DES) exposure in CD-1 mice (Dixon et al., 2014).
- Most leiomyoma cells are immunoreactive for desmin (muscle) and alpha smooth muscle actin (α-SMA, smooth muscle) and stain positive with phosphotungstic acid-hematoxylin (PTAH, differentiates muscle from other tissues).

Uterus – Leiomyoma

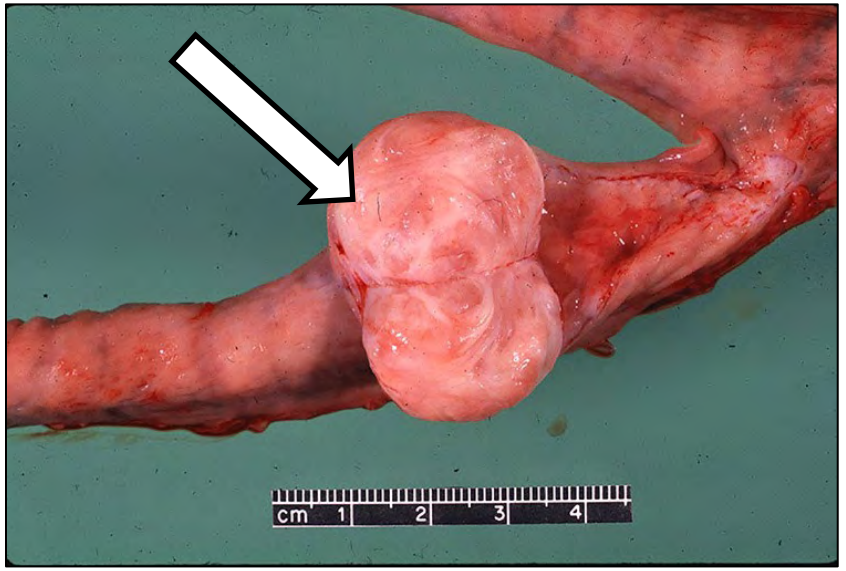


Uterus – Leiomyoma, mouse.

A solitary mass (arrowheads) expands the myometrium and compresses the adjacent endometrium. The mass is comprised of interlacing bundles (arrows) of well-differentiated neoplastic spindle cells.

Uterus – Leiomyoma: Comparative Pathology Dogs

- Leiomyomas are the most common uterine tumors of dogs, rare in other domestic species (Schlafer & Foster, 2016).
  - Upper image: canine uterine leiomyoma.
  - Lower image: sectioned-surface, note the pale-tan whorls and bundles (arrow).
- Hormonally-responsive and may regress following neutering.
- Can differentiate from other mesenchymal neoplasms by IHC staining with alpha smooth-muscle actin (α-SMA, smooth muscle) and desmin (muscle).



Images courtesy of Noah's Arkive

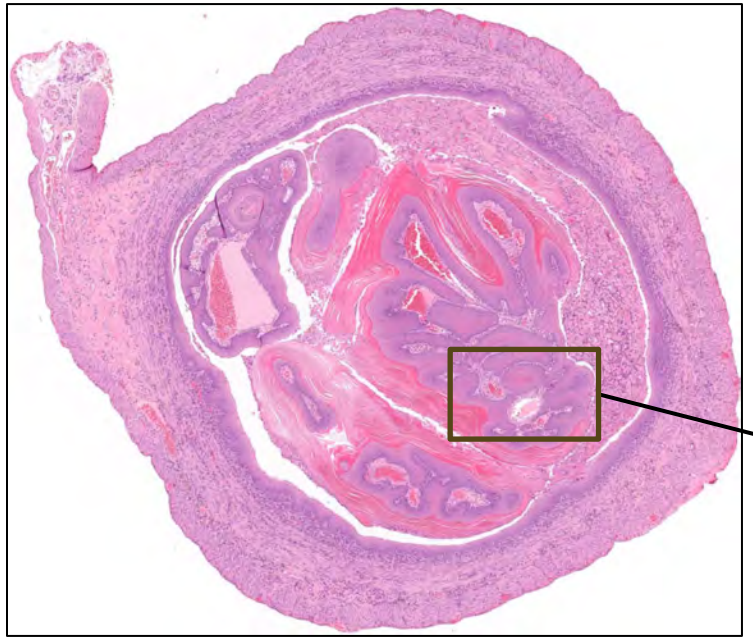
Uterus - Leiomyoma: Comparative Pathology Humans and NHPs

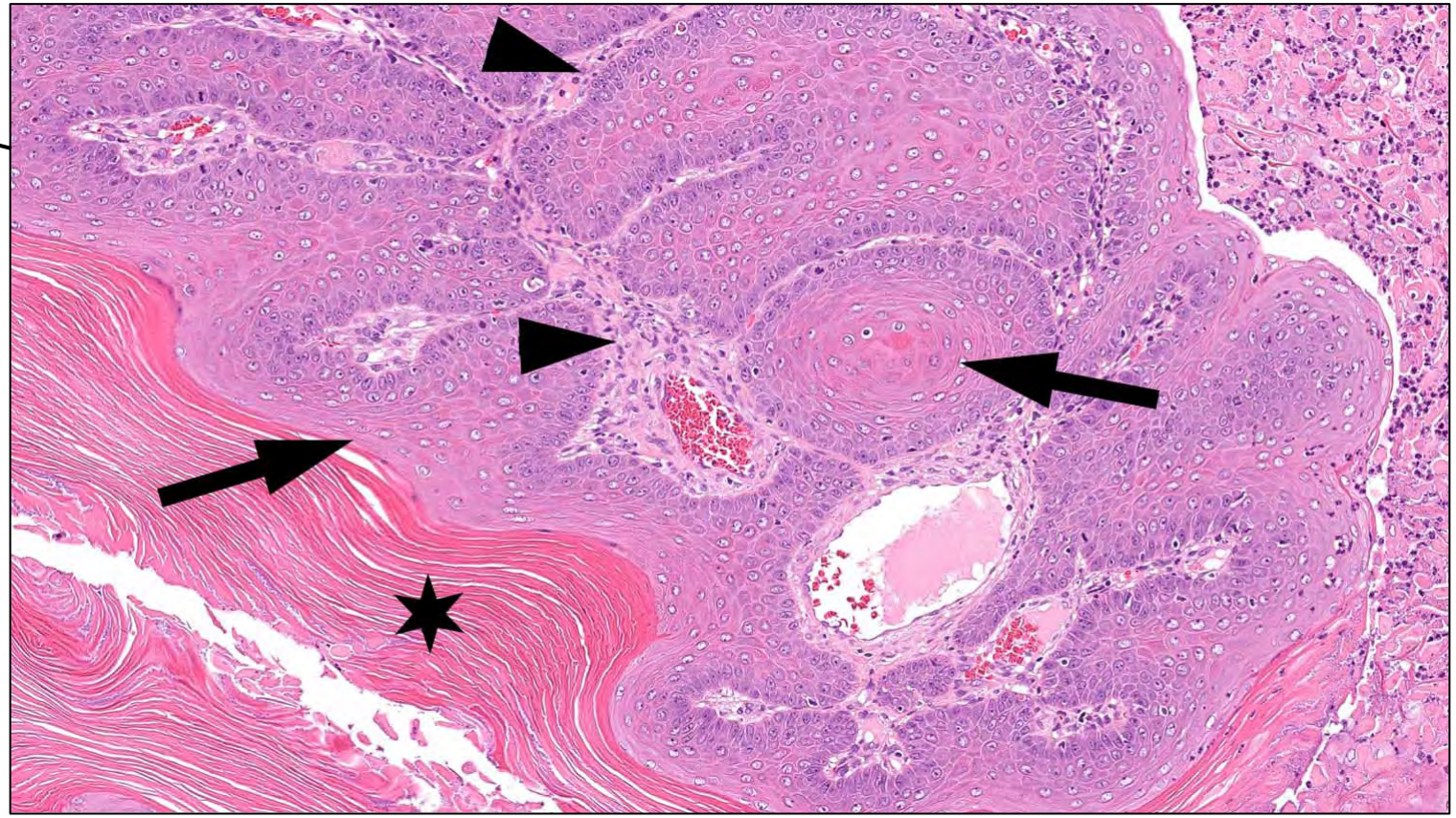
- Uterine leiomyoma (often called a “fibroid”) is the most common tumor in women (Ellenson & Pirog, 2010).
- Malignant transformation is extremely rare.
- Uterine leiomyomas are common, benign neoplasms in adult and aging macaques (Cline et al., 2008).
  - In nonhuman primates, was the most common uterine neoplasm in one review of 2 large primate centers (Kirejczyk et al., 2021).
  - As in humans, leiomyomas may be associated with infertility, and express receptors for both estrogen and progesterone and are hormonally-responsive (Cline et al., 2008).

Uterus – Papilloma, Squamous Cell

- Benign tumor arising from the surface epithelium.
- Marked papillary/exophytic proliferation of the uterine mucosa with squamous cell differentiation (Dixon et al., 2014).
- Has a moderately dense fibrovascular core that comprises less of the lesion than the squamous epithelial component.
- Squamous cells are well differentiated with no atypia or invasion of the underlying stroma.
  - Differentiate from squamous cell carcinoma, in which the cells have atypia and often invade the submucosa and muscularis and/or serosa.
- Squamous cell papillomas are frequently associated with chronic suppurative inflammation.
- Modifiers: keratinizing or non-keratinizing.

Uterus – Papilloma, Squamous Cell





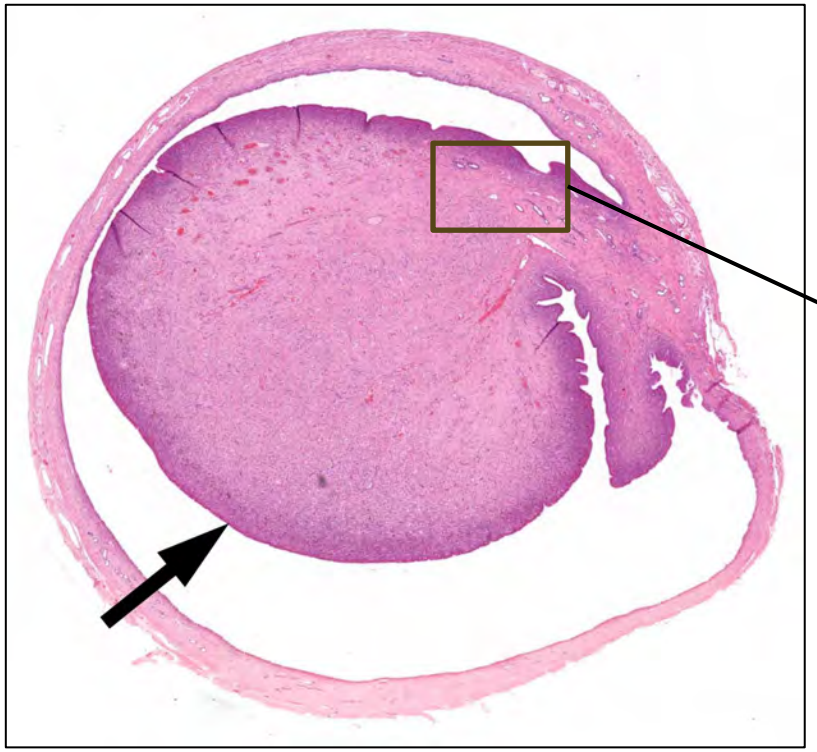
Uterus – Papilloma, Squamous Cell, rat.

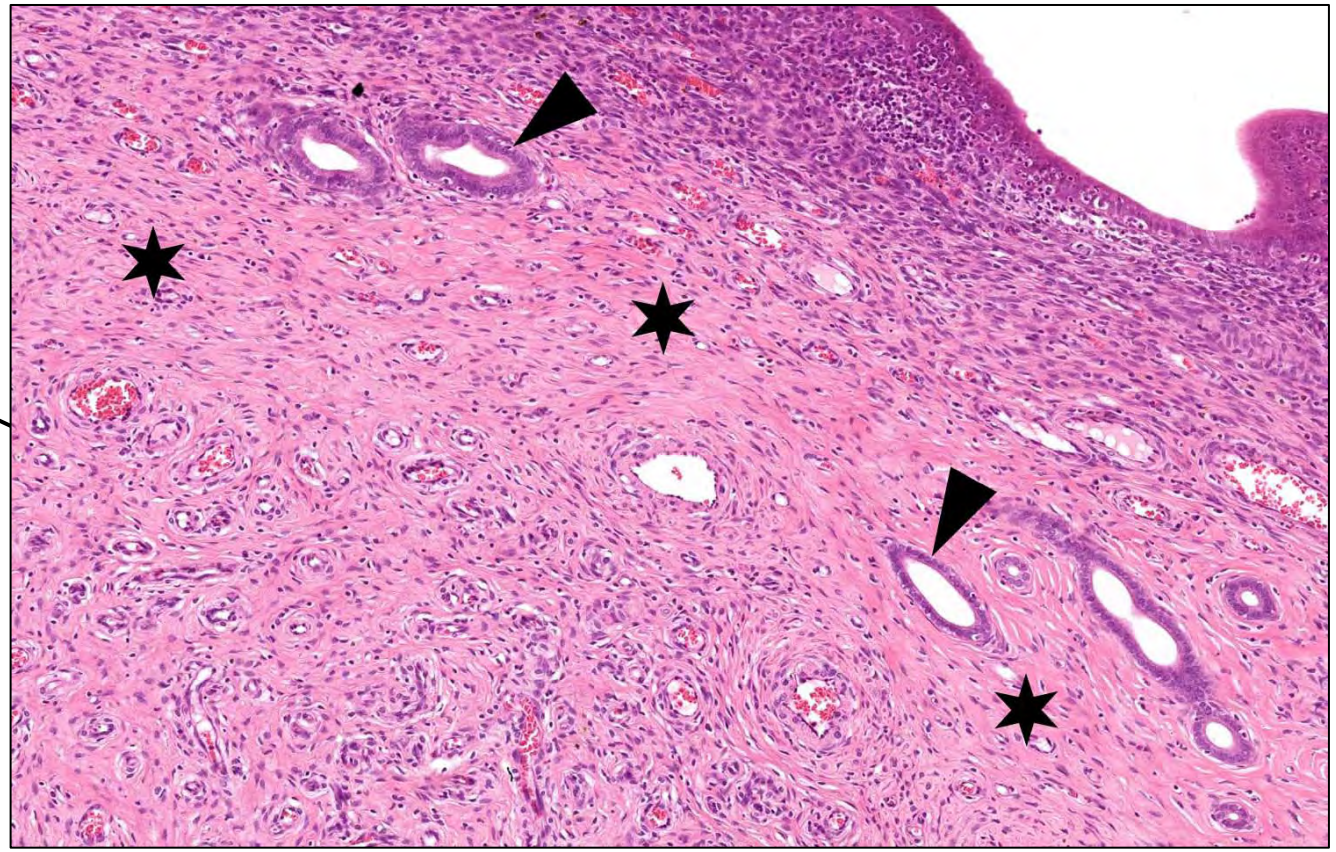
The stalk of this papillary mass (above image) is not observed in section. The mass is comprised of proliferative squamous cell epithelium (arrows) lining a fibrous core (arrowheads). There is abundant keratin (asterisk) in the uterine lumen.

Uterus – Polyp, Endometrial Stromal

- Age-related benign tumor in rodents; the most common spontaneous reproductive tract lesion in aged nulliparous (have not given birth to live offspring) female rats (Davis, 2012).
- Solitary or multiple polypoid masses that protrude into the uterine lumen but may arise from the uterine cervix or extend into the vaginal lumen (Dixon et al., 2014).
  - Polyps extending into the vaginal lumen may be edematous, inflamed, ulcerated, and/or infarcted (localized regions of necrosis due to poor or impeded blood flow).
- Composed predominantly of loosely organized, stromal spindle-shaped or stellate cells with collagen and small blood vessels; may have a few entrapped endometrial glands (Dixon et al., 2014).
  - Differentiating from a glandular polyp: a glandular endometrial polyp has prominent and often hyperplastic glands in most of the polyp.
- Covered by cuboidal to columnar epithelium, which is continuous with the endometrial lining epithelium (Dixon et al., 2014).
  - Differentiating from a vaginal polyp: A polyp that arises from the vagina will be covered by vaginal epithelium (stratified squamous).
- Occasionally, endometrial stromal sarcomas arise from polyps (Davis, 2012; Dixon et al., 2014).

Uterus – Polyp, Endometrial Stromal





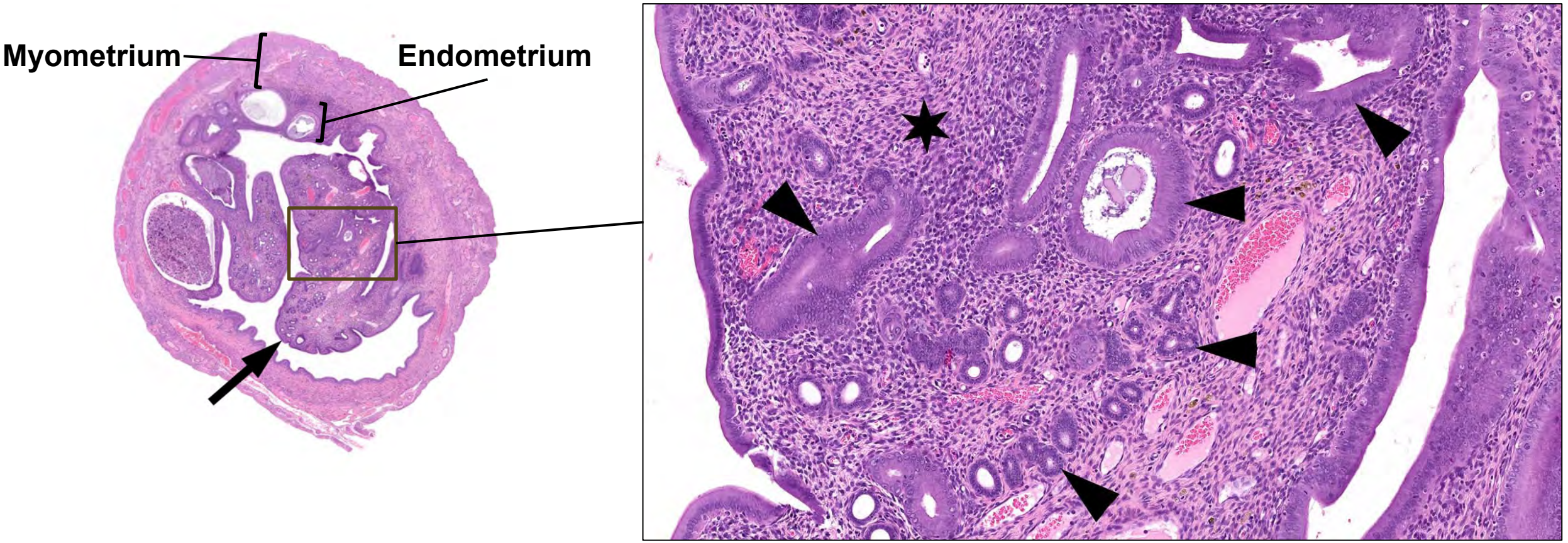
Uterus – Polyp, Endometrial Stromal, rat.

Polypoid mass of endometrial stroma protruding into the uterine lumen (arrow). Composed predominantly of dense endometrial stroma (asterisks) and small blood vessels with few entrapped endometrial glands (arrowheads). Uterine wall is thin due to luminal dilatation.

Uterus – Polyp, Glandular

- Primarily a polypoid mass that protrudes into the uterine lumen but may arise from the uterine cervix or extend into the vaginal lumen (Dixon et al., 2014).
  - Polyps extending into the vaginal lumen may be edematous, inflamed, ulcerated, and/or infarcted.
- Endometrial glands, lined by cuboidal to columnar epithelium, which are often cystic and hyperplastic, are prominent within the stroma.
  - Differentiating from a stromal polyp: an endometrial stromal polyp has no or very few entrapped glands.
- Stroma composed of spindle-shaped or stellate cells with variable amounts of collagen and small blood vessels.
- Epithelium lining the glandular polyp is often hyperplastic and is continuous and similar in appearance to the endometrial lining epithelium.

Uterus – Polyp, Glandular



Uterus – Polyp, Glandular, rat.

Polypoid mass of endometrial glands and stroma that protrudes into the uterine lumen (arrow). Composed of increased numbers of endometrial glands (arrowheads), many of which are lined by hyperplastic epithelium, within loosely organized endometrial stroma (asterisk). The polyp epithelium is continuous with the endometrial epithelial lining.

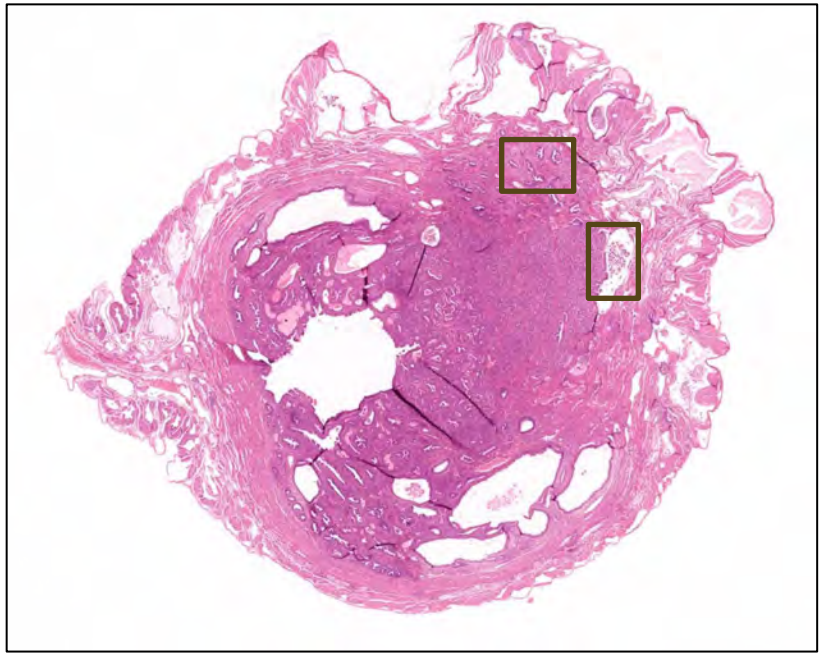
Uterus – Schwannoma, Benign

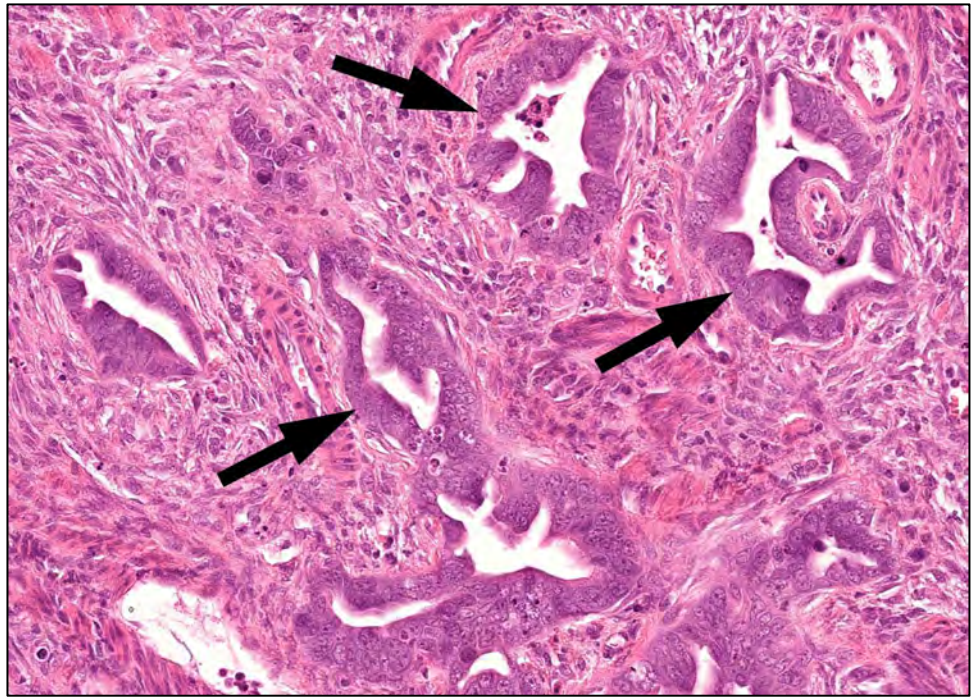
- Benign tumor arising from Schwann cells (Dixon et al, 2014).
  - Schwann cell considered to be neuroectodermal (gives rise to nervous tissue) with facultative (gives rise under certain conditions) mesenchymal features.
- Expansile, compressive and usually encapsulated.
- Elongated neoplastic cells with indistinct borders arranged in an interlacing or whorling pattern, or more loosely arranged cells within a clear matrix.
- Two patterns of growth; both patterns may or may not be present within the neoplasm.
  - **Antoni Type A:** more dense cellular arrangement; shows nuclear palisading sometimes forming Verocay bodies (palisading nuclei surrounding homogeneous, eosinophilic intercellular material).
  - **Antoni Type B:** more loose cellular arrangement; often containing cystic spaces.
- Positive for S-100 IHC stain (neural); presence of basement membrane with electron microscopy supports the diagnosis of schwannoma.

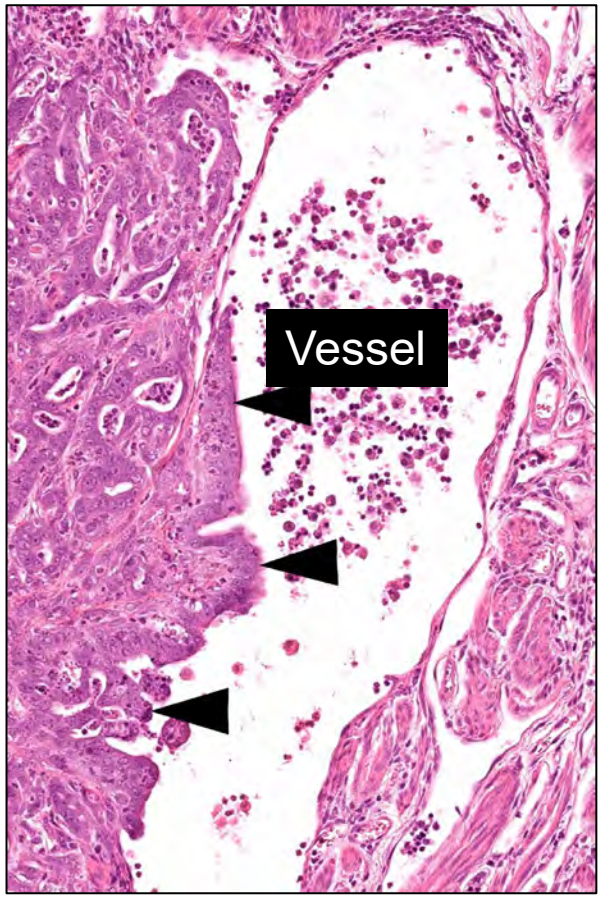
Uterus – Adenocarcinoma, Endometrium

- Typically, a poorly circumscribed, neoplastic, malignant (cancerous) tumor of atypical epithelial elements with invasion into the myometrium; arises from endometrial epithelium (Dixon et al., 2014).
  - May extend into and occlude the uterine lumen and may extend beyond the serosa into the peritoneum.
  - May metastasize locally to cervix or to distant sites (e.g., lung).
  - May show vascular invasion; may have focal areas of squamous differentiation, necrosis, or hemorrhage; may have prominent scirrhous (proliferative fibrous tissue) response.
- Tumor cells form solid nests, cords, papillary or acinar (glandular) structures.
  - Cells may be well-differentiated or may be anaplastic (cellular/nuclear atypia, pleomorphism).
  - Cells typically cuboidal to columnar and usually 1-2 cell layers thick (may be more).
  - Mitotic figures can be frequent.
  - May have rare areas of squamous differentiation; <10% squamous metaplasia still considered adenocarcinoma and not adenosquamous carcinoma.

Uterus – Adenocarcinoma, Endometrium



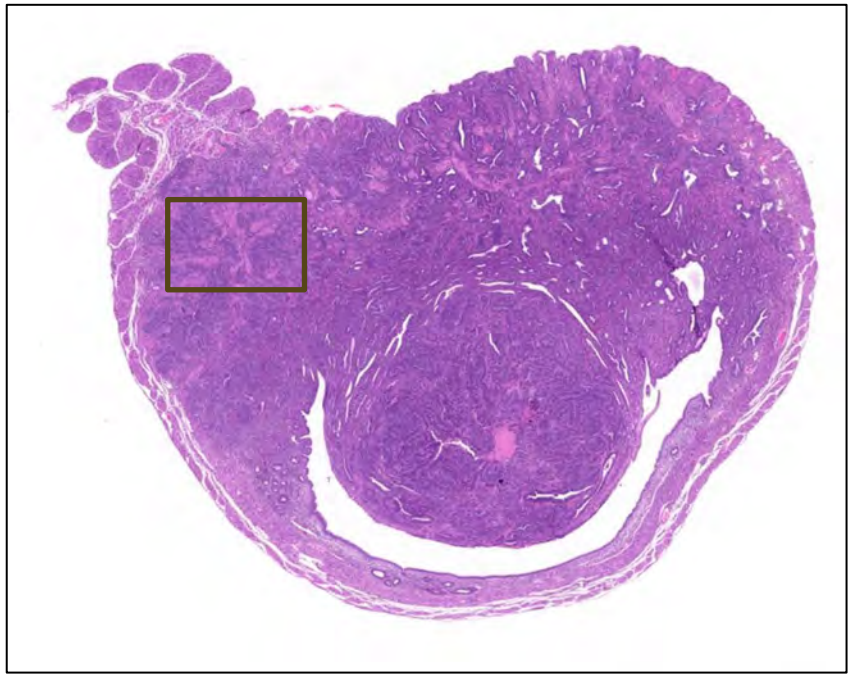


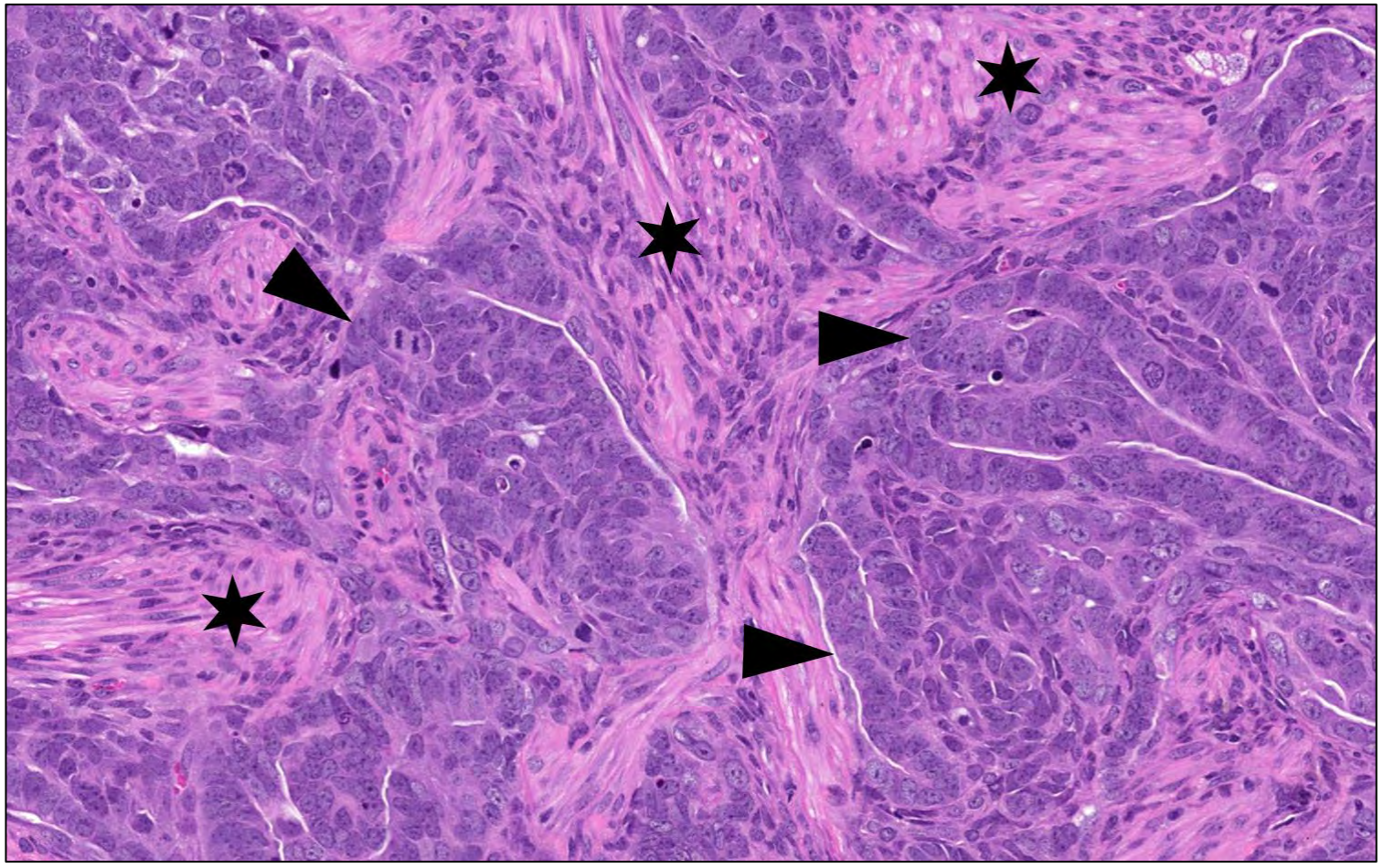


Uterus – Adenocarcinoma, Endometrium, mouse.

Poorly circumscribed malignant uterine neoplasm comprised of haphazardly arranged acini that invade the myometrium (left image). Acinar epithelial cells demonstrate cellular atypia (arrows; left inset). Similar neoplastic cells invade a vessel (arrowheads; right inset).

Uterus – Adenocarcinoma, Endometrium





Uterus – Adenocarcinoma, Endometrium, mouse.

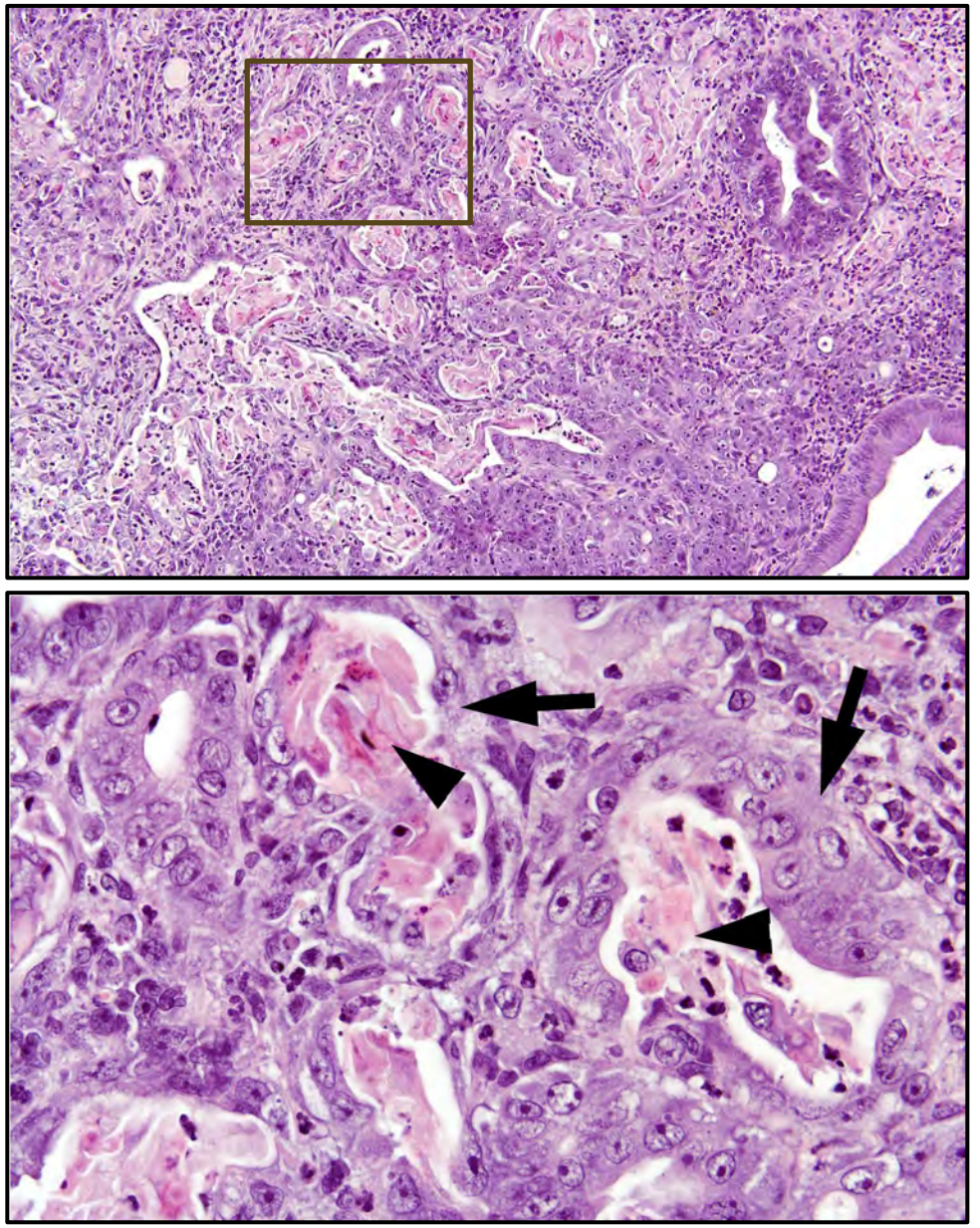
This invasive neoplasm comprised of neoplastic epithelial acini, islands and cords (arrowheads) that has a prominent scirrhous response (extensive fibrous reaction; asterisks).

Uterus – Adenocarcinoma, Endometrium: Comparative Pathology

- Relatively uncommon as a spontaneous lesion in rats and mice, apart from certain rat strains (Donryu, BDII/Han, and Wistar Han) (Dixon et al., 2014).
- Decreased body weight gain due to dietary restriction is associated with higher incidence of uterine tumors in Wistar rats (Harleman et al., 2012).
- Rare in domestic animals but occur more frequently in cattle and often have prominent fibrous component / desmoplastic response (Schlafer & Foster, 2016).
- Most common spontaneous neoplasm in older rabbits, with an incidence of up to 80% in 5 to 6 years-old does (Barthold et al, 2016).
- Endometrial carcinoma most common invasive cancer of the female genital tract in humans (Ellenson and Pirog, 2010).
  - Cervical carcinoma used to be the most common, but earlier detection of precursor lesions and a rise in endometrial carcinoma frequency has changed this commonality.
  - Accounts for 7% of all invasive cancers in women, excluding skin cancer.
- Despite the similarities between the female reproductive tracts of macaques and humans, especially in the ease of which endometrial hyperplasia can be induced, endometrial carcinoma is exceedingly rare in macaques (Cline et al., 2008).

Uterus – Carcinoma, Adenosquamous

- Adenocarcinoma with foci or zones of squamous epithelial differentiation (Dixon et al., 2014).
- At least 10% or greater of the lesion should have squamous differentiation.
- Adenosquamous carcinoma has primarily glandular tubular structures versus the solid growth pattern in squamous cell carcinoma.



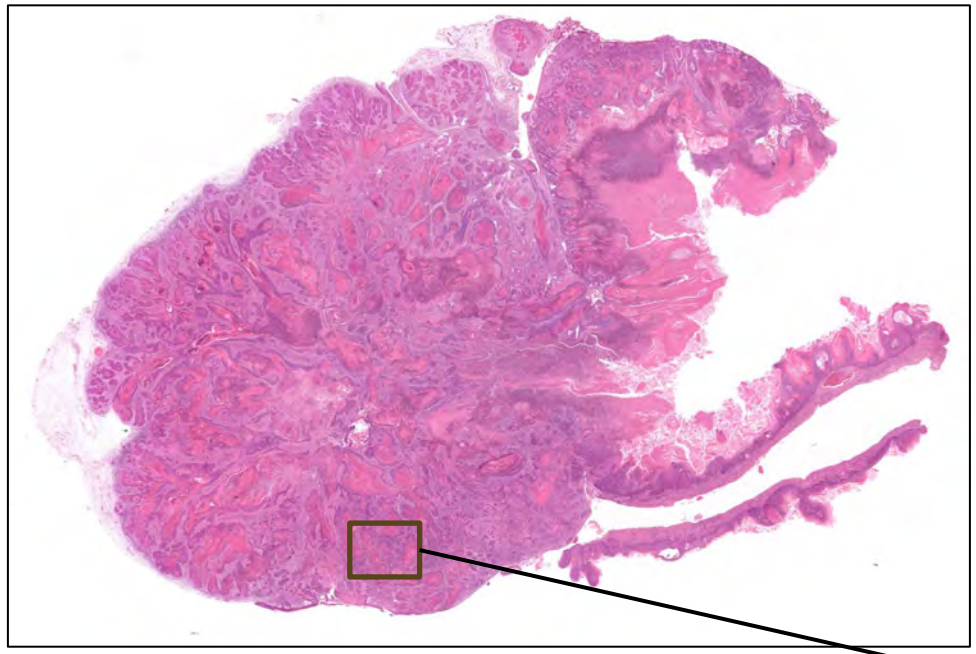
Uterus – Carcinoma, Adenosquamous, rat.

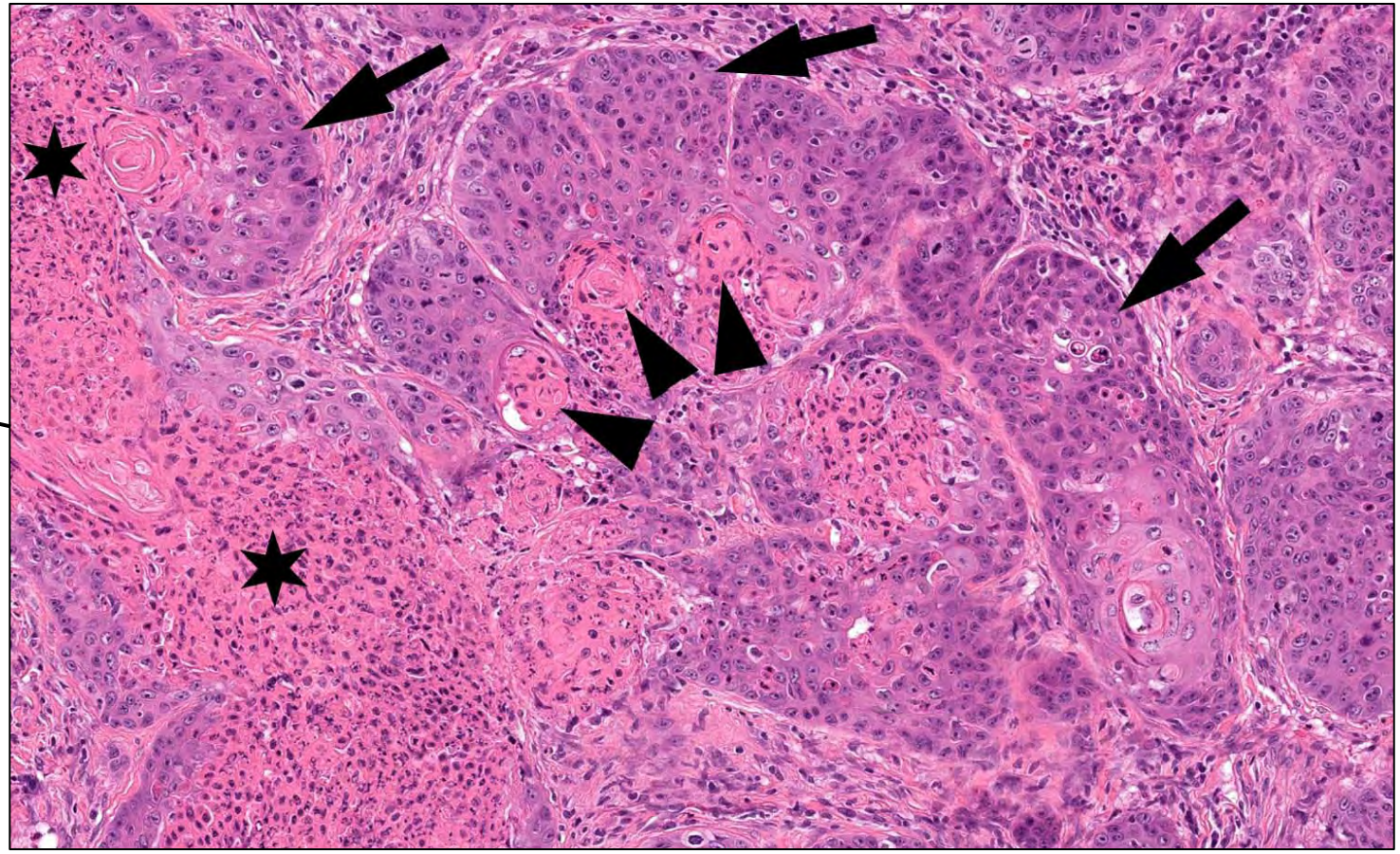
Malignant neoplasm (top photo) is comprised of variably sized tubules (arrows, inset) with squamous epithelial differentiation and keratinization (arrowheads, inset).

Uterus – Carcinoma, Squamous Cell

- A malignant tumor that may have an exophytic growth pattern and/or invade the endometrial stroma, myometrium, serosa or contiguous organs (share a border) (Dixon et al., 2014).
- Tumor cells are large and polygonal with prominent vesicular (vesicle-like) nuclei containing one or more nucleoli.
- Tumor cells arranged in cords and nests; may demonstrate stratification (layers).
- Neoplastic epithelium on the surface may be markedly thickened, dysplastic (abnormal growth), and/or keratinized.
  - Keratin or keratin pearls (typically concentric whorls of keratin) may be on the surface or deeper in the tumor.
- Tumors can be composed of well- to poorly-differentiated squamous epithelium and infiltrated with leukocytes.
- Stroma may be scant or abundant giving a scirrhous reaction.
- Need to be distinguished from squamous cell carcinoma arising from the vaginal or cervical epithelium.
- Modifiers: keratinizing or non-keratinizing.

Uterus – Carcinoma, Squamous Cell





Uterus - Carcinoma, Squamous Cell, rat.

This exophytic mass is comprised of variably sized nests of stratified polygonal neoplastic epithelial cells (arrows). There is abundant keratin (asterisks) associated with the neoplastic cells. Whorls of keratin (keratin pearls) are often present (arrowheads).

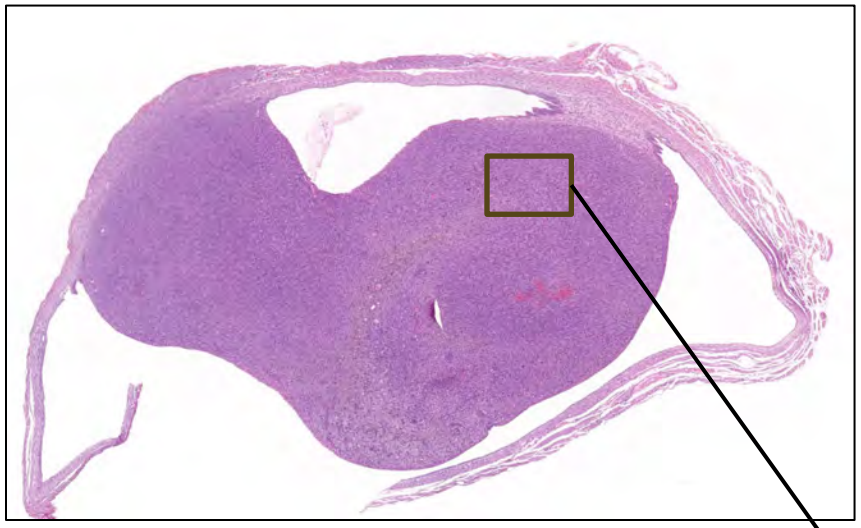
Uterus – Histiocytic Sarcoma

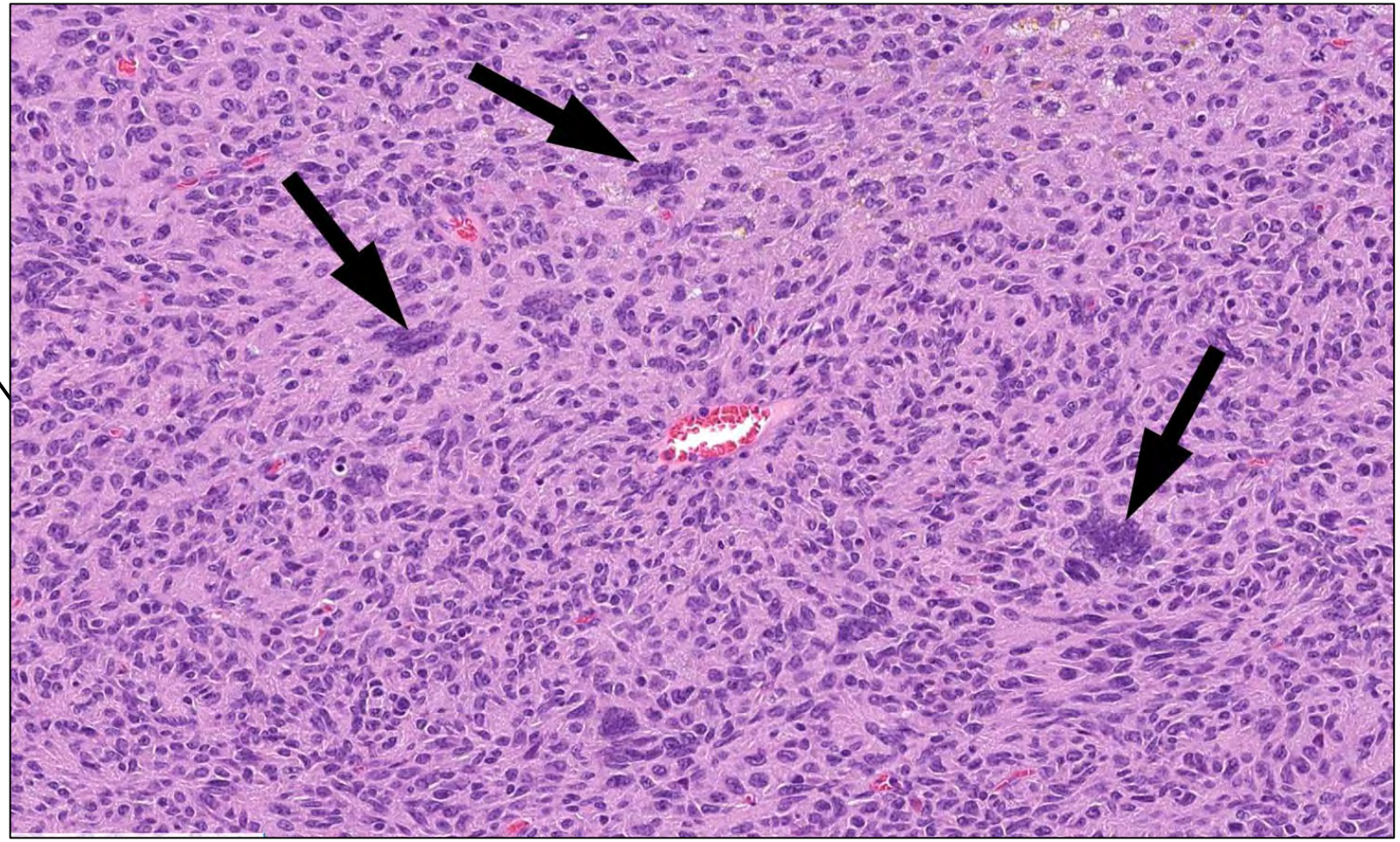
- May be observed in the uterus of mice and rats but will also frequently affect other tissues such as liver (almost always involved, Dixon et al., 2014) and spleen.
- Observed less frequently in rats than mice.
- Neoplastic histiocytes form sheets or circumscribed nodular aggregates.
- Uniform population histiocytic cells with abundant eosinophilic cytoplasm and indistinct cell borders.
  - Cells are often pleomorphic (oval to spindle-shaped).
  - Nuclei are often dark, pleomorphic, slightly elongated, reniform (kidney-shaped), or folded.
  - Many cells may be multinucleated.
- Focal necrosis surrounded by palisaded neoplastic histiocytes is characteristic, and mitotic rate may be high.
- Neoplastic cells in the uterine wall tend to be particularly elongated (Barthold et al., 2016).
- Kidneys often have an increase in intracytoplasmic eosinophilic hyaline granules (hyaline droplets) in the proximal tubules, which may help confirm diagnosis in unclear cases (Willard-Mack et al., 2019).

Uterus – Histiocytic Sarcoma

- May be difficult to differentiate from lymphoma in some cases.
  - Especially histiocyte-rich subsets (e.g., histiocyte-associated diffuse large B-cell lymphomas) (Hao et al., 2010; Barthold et al., 2016).
  - Staining with histiocyte-specific immunohistochemical (IHC) markers may aid in diagnosis (Willard-Mack et al., 2019).
    - Mice: F4/80, Lysozyme, MAC-2.
    - Rats: ED1 (CD68), ED2 (CD163), Lysozyme.
  - With lymphoma, cell cytoplasm is less eosinophilic, giant cells are absent, and lymph nodes are also involved.
- Differentiating from malignant schwannoma: lack giant cells and abundant eosinophilic cytoplasm, stain positive with S-100 (neural).

Uterus – Histiocytic Sarcoma





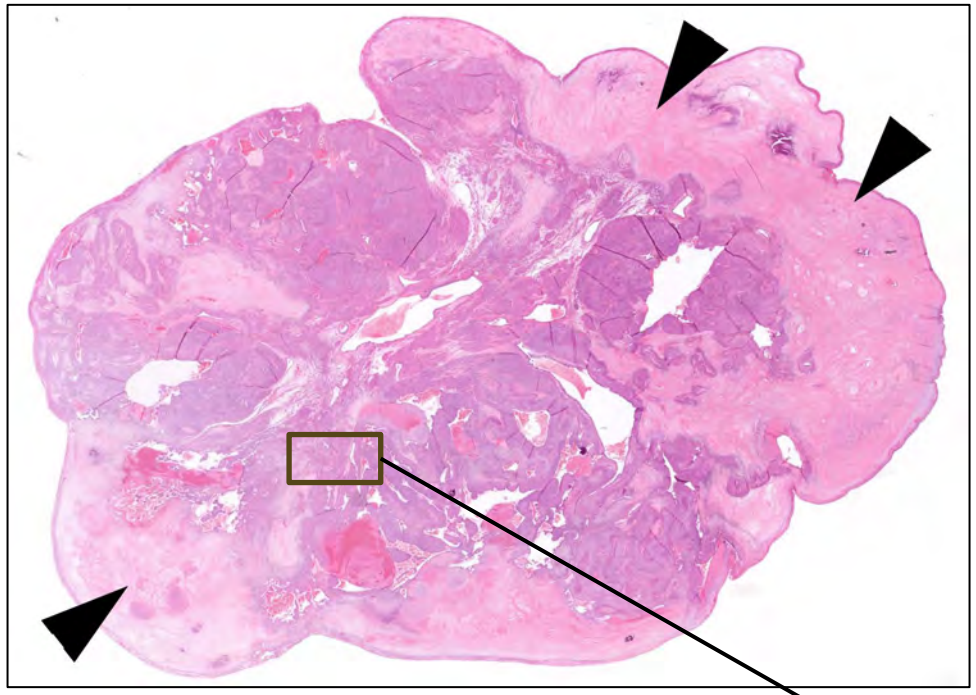
Uterus – Sarcoma, Histiocytic, mouse.

Neoplastic histiocytes are oval to spindle-shaped and arranged in sheets. Multinucleated neoplastic cells (giant cells) are present (arrows).

Uterus – Leiomyosarcoma

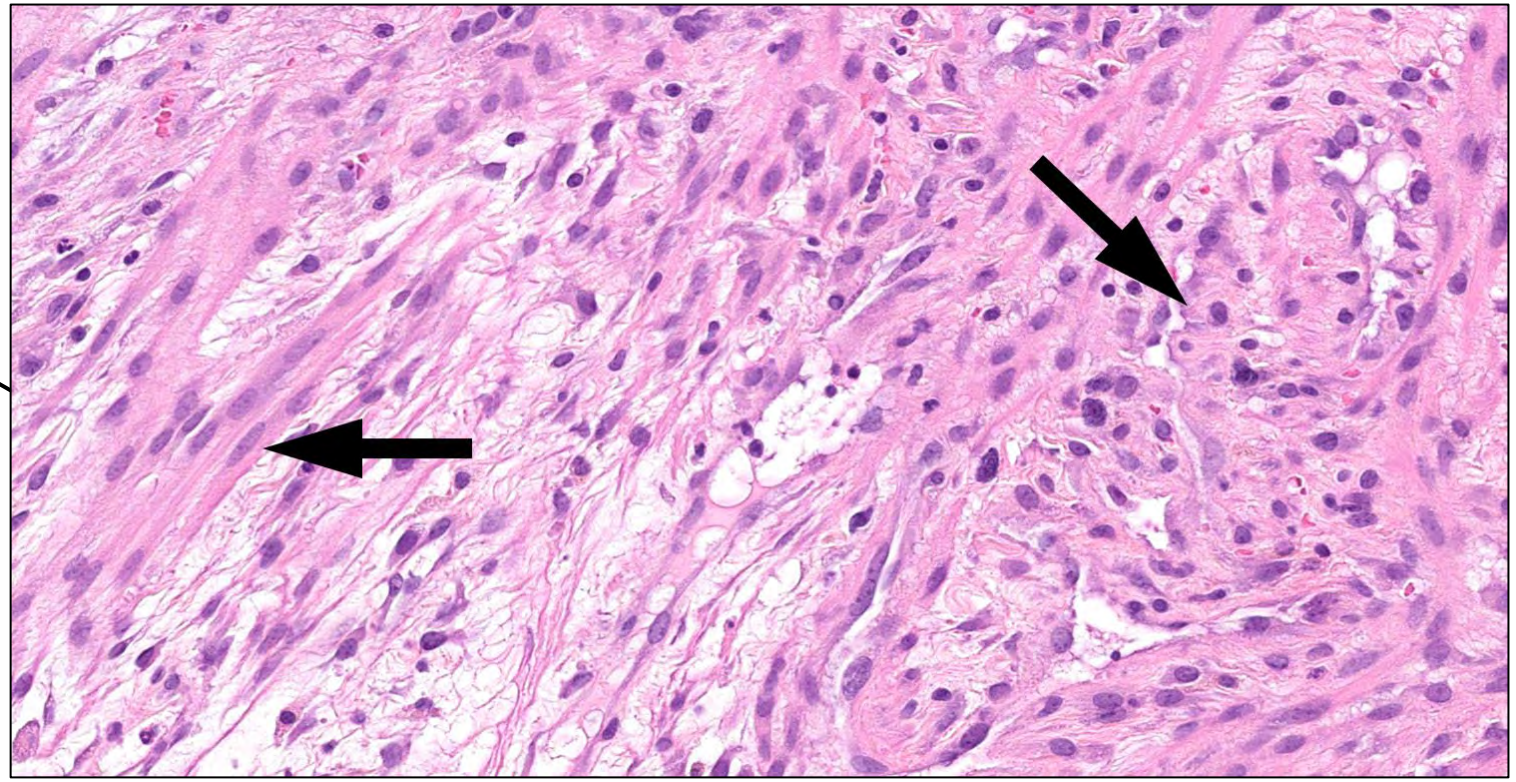
- Poorly delineated malignant tumor arising from pluripotent mesenchymal stem cells or smooth muscle cells with disorganized and invasive growth patterns (Dixon et al., 2014).
  - Metastasis is not common.
- Appear very cellular due to decreased amount of eosinophilic cytoplasm of the cells.
- Composed of anaplastic spindle cells with variable amounts of eosinophilic cytoplasm with blunt-ended to oval nuclei.
  - Nuclei may be pleomorphic and have high mitotic activity, prominent nucleoli.
  - Multinucleated tumor cells may be present.
- Bundles of neoplastic spindle cells are disorganized or not apparent; some collagenous stroma present.
- Focal areas of necrosis or hemorrhage may be present.
- Cells will likely stain with α-smooth muscle actin (smooth muscle) and desmin (muscle), which can help differentiate from other poorly differentiated mesenchymal tumors; stain positive with phosphotungstic acid-hematoxylin (PTAH, differentiates muscle from other tissues).

Uterus – Leiomyosarcoma



Uterus – Leiomyosarcoma, rat.

This poorly circumscribed mass invades and effaces (replaces) the normal uterine architecture. There are multiple areas of necrosis (arrowheads). Neoplastic spindle cells are haphazardly arranged (arrows), in contrast to the organized interlacing bundles of the leiomyoma.

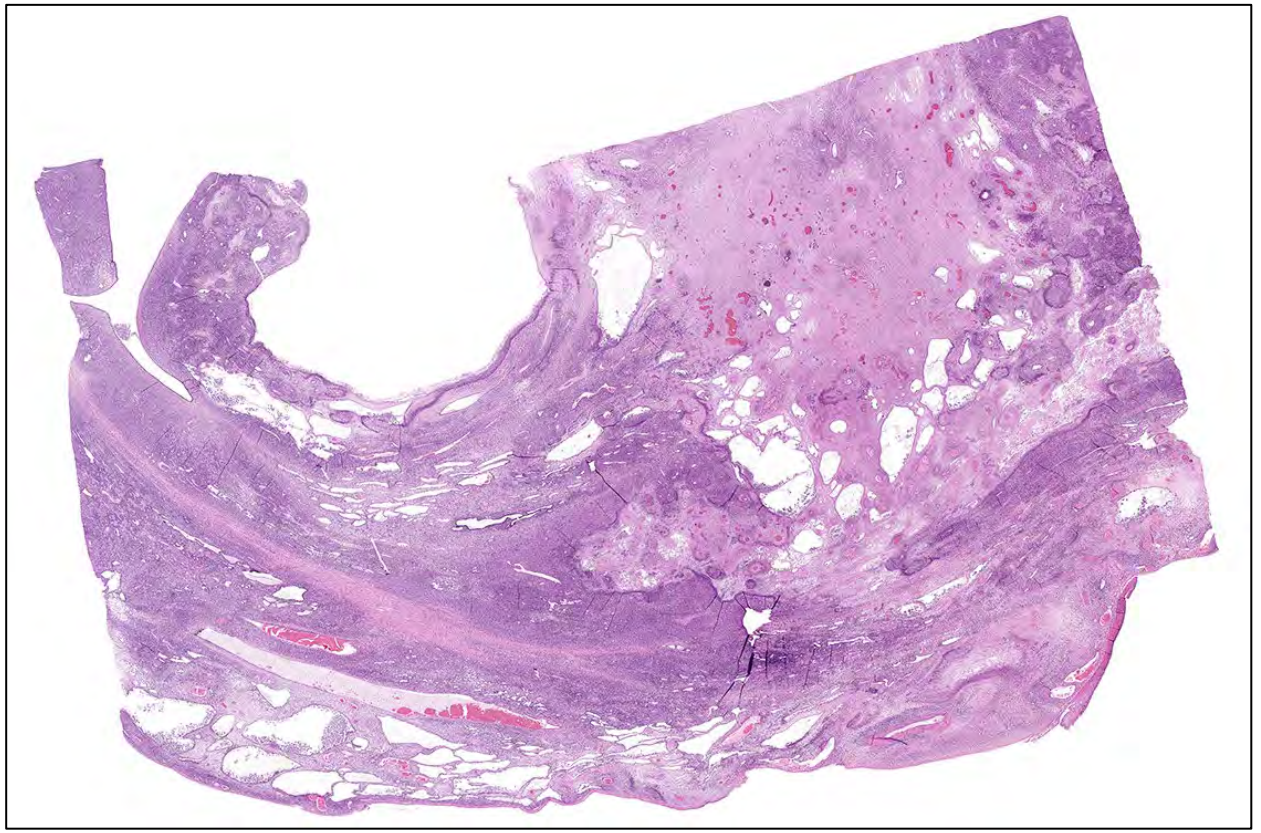


Uterus – Sarcoma, Endometrial Stromal

- Malignant tumor arising from endometrial stroma; may originate within a stromal polyp (Davis, 2012; Dixon et al., 2014).
  - Metastasis is rare.
  - May be found in uterine wall or as polypoid masses protruding into the uterine lumen.
- Composed of stromal spindle-shaped cells with variable amounts of collagen and endothelial-lined vascular spaces.
  - Cells are poorly differentiated, often pleomorphic, and have indistinct cell borders with variable amounts of eosinophilic cytoplasm and elliptical or elongated nuclei.
- Characterized by infiltrative growth and high mitotic index.
  - Infiltrative growth pattern does not follow existing anatomical structures, leading to gross distortions.
- Focal areas of hemorrhage and necrosis may be present.
- May be positive for S-100 (neural) and vimentin (mesenchymal), negative for desmin (muscle) and α-SMA (smooth muscle).

Uterus – Schwannoma, Malignant

- Malignant tumor with expansile, poorly delineated borders and an invasive growth pattern.
- Generally infiltrative growth pattern into the adjacent tissues.
- Elongated neoplastic cells with indistinct borders arranged in an interlacing or whorling pattern, or more loosely arranged cells within a clear matrix (Dixon et al., 2014).
  - Antoni A and Antoni B growth patterns.
  - Both patterns may or may not be present in same neoplasm.
- High mitotic activity, mitotic or cellular atypia, necrosis and/or distant metastases are all indicative of malignancy.
- Positive for S-100 IHC stain (neural).

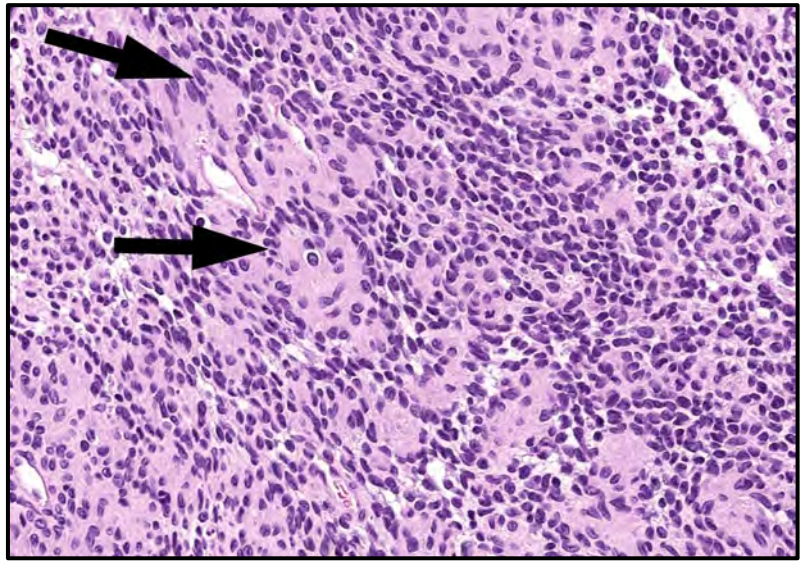


Uterus – Schwannoma, Malignant, rat.

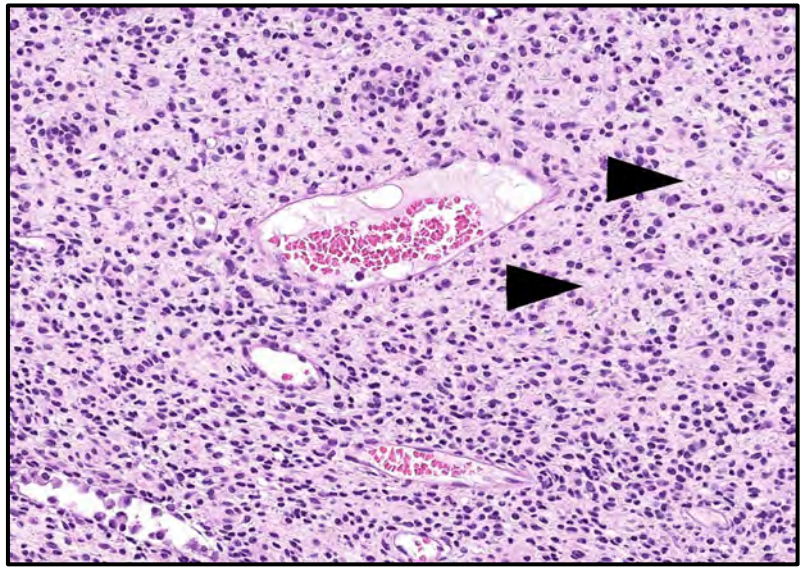
The uterus is effaced by this invasive neoplasm.

Uterus – Schwannoma, Malignant

- Composed of fibrillar tissue arranged in **Antoni type A** or **Antoni type B** patterns.
- **Type A:** (densely-cellular): Palisaded bundles of cells associated with whorls and knot-like formations resembling Verocay bodies (stacks of nuclei).
- **Type B:** (lower cellular density): Loosely arranged cells within a delicate stroma in which there may be cystic spaces.
- IHC staining for Schwann cell-specific markers proteolipid protein (PLP) and peripheral myelin protein 22 kDA (PMP22) can be helpful for confirmation (Bradley et al., 2018).



Type A
Neoplastic cells in this region are densely packed and form slightly disorganized streams and bundles. In some areas, the nuclei form roughly linear stacks reminiscent of “Verocay bodies” (arrows).



Type B
Neoplastic cells in the region depicted here are loosely-spaced within a delicate stroma (arrowheads) and the fine-filamentous cytoplasmic extensions typical of the cells can be seen.

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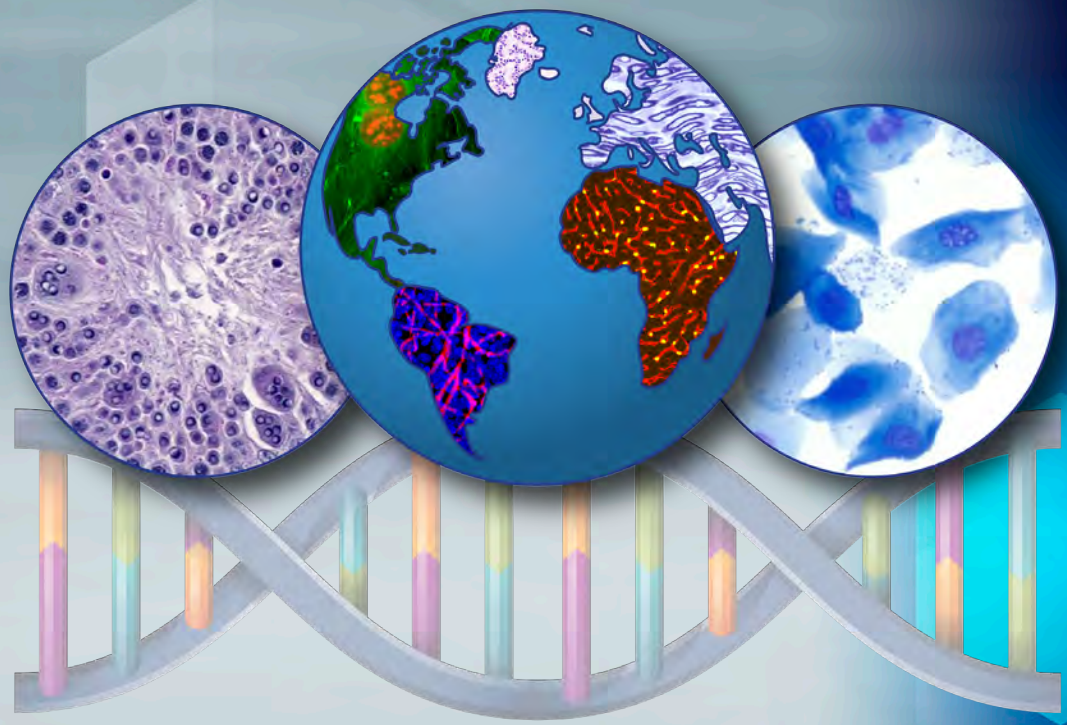

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