Neoplasms of the Rodent Female Reproductive System

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In Cooperation with

BSL Scientific Laboratories GmbH,

Planegg, Germany

Classification

- Harmonization: http://www.toxpath.org/nomen/
- Dixon et al., 1999, Proliferative Lesions of the ovary, Uterus, Vagina, Cervix and Oviducts in Rats. In: Guides for Toxicologic Pathology, STP/ARP/AFIP. Washington, DC
- Mann, P.C. et al., 1996, Proliferative Lesions of the Mammary Glands in Rats. In: Guides for Toxicologic Pathology, STP/ARP/AFIP. Washington, DC
- Boorman et al., 1990. Pathology of the Fisher Rat.
 Academic Press
- Maronot et al., 1999. Pathology of the Mouse, Cache River Press
- Mohr, U (ed): 2001. International Classification if Rodent Tumors. The Mouse. Springer Verlag.

Classification: Ovary - Recommendations http://www.toxpath.org/nomen/

- Hyperplasia: tubulostromal, cystic/papillary, sex cord stromal (diffuse mixed type, granulosa cell, mixed Sertoli cell, theca cell)
- Adenoma, tubulostromal and Adenocarcinoma, tubulostromal
- Mesothelioma, malignant
- Cystadenoma and Cystadenocarcinoma
- Tumor, granulosa cell, benign and malignant
- The coma, benign and malignant
- Luteoma, benign
- Tumor, Sertoli cell, benign and malignant
- Tumor, sex cord stromal, mixed, benign and malignant
- Dysgerminoma (teratoma, benign or malignant)
- Carcinoma, yolk sac
- Choriocarcinoma

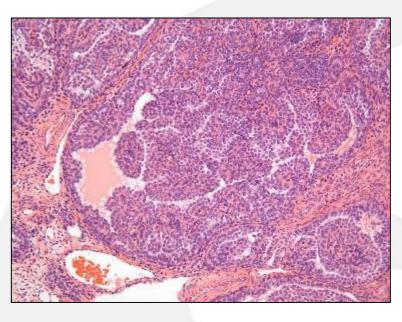
Classification: Ovarian Lesions

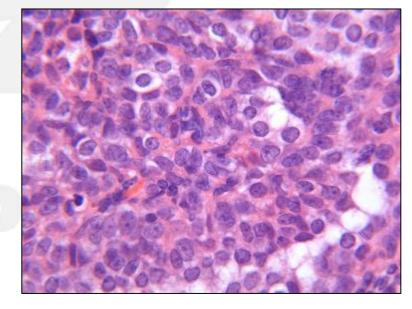
- Only organ specific tumors are recommended (harmonized), i.e. neoplasms arising in mesenchymal tissues are not listed under particular organs in the, International Harmonization of Rat Nomenclature' but under, Soft Tissues and Others'
- Differentiation between hyperplastic and neoplastic stromal sex cord lesions:
 - Focal hyperplasia: focal small, 2-3 mm
 - Diffuse hyperplasia: 2-3fold increased size of a normal ovary

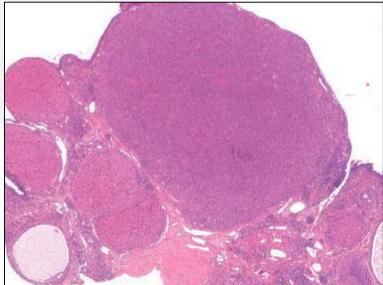
Ovary-Sex Cord Neoplasms: Granulosa Cell Tumor

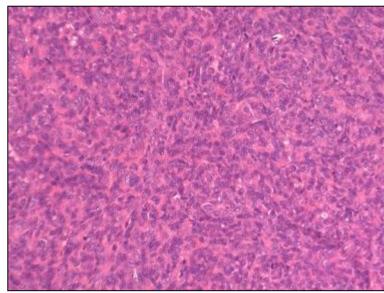
- Variety of patterns: solid, cystic, tubular, occasionally sertoliform
- Resemble normal granulosa cells with round nucleus and coarse stippled chromatin
- Cytoplasm may become luteinized
- Malignancy: pleomorphism, increased mitosis, necrosis, invasion
- Differential Diagnose: Hyperplasia, Luteoma, Thecoma

Rat: Granulosa Cell Tumor, benign

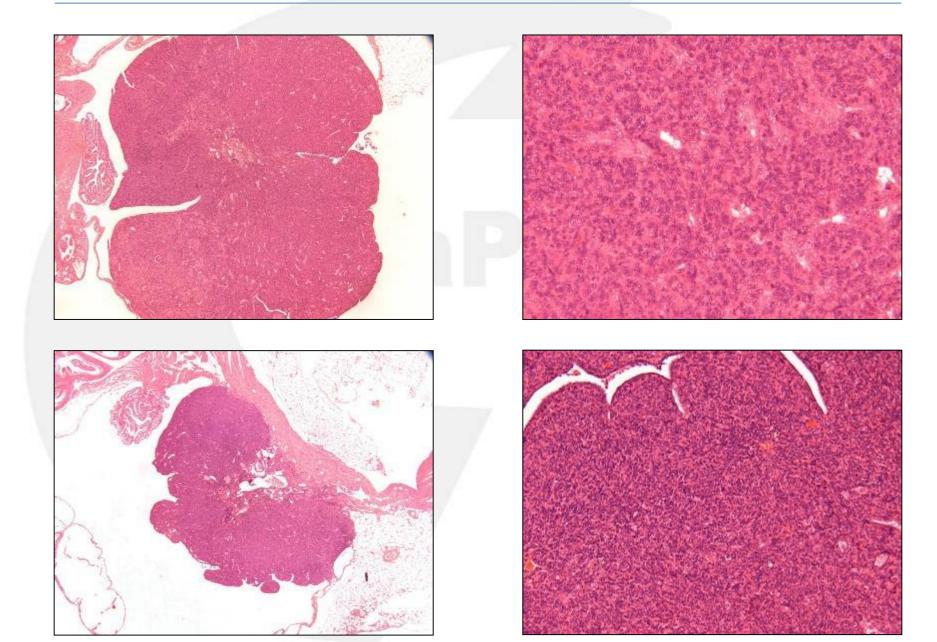




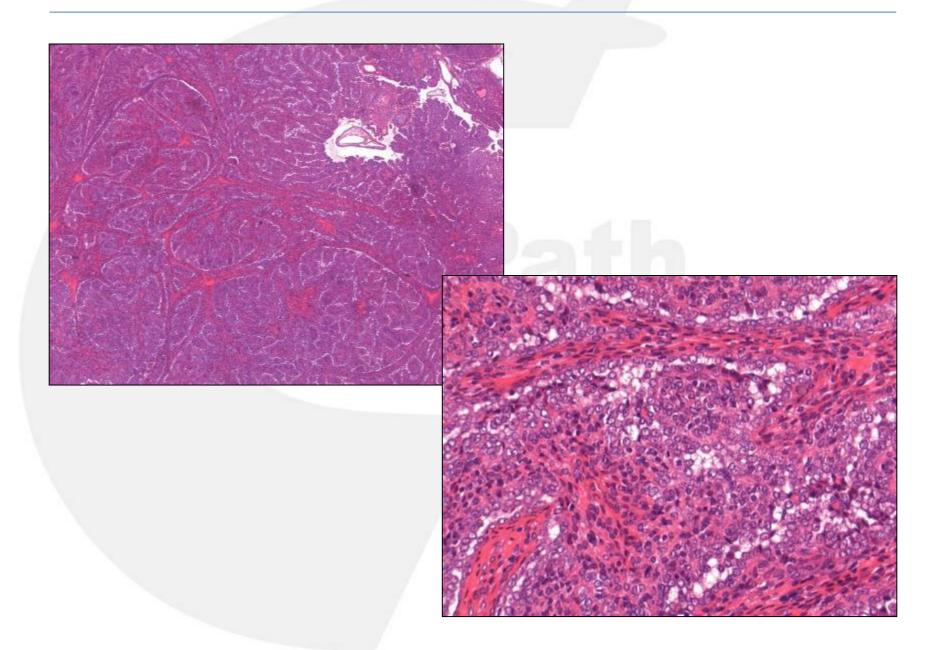




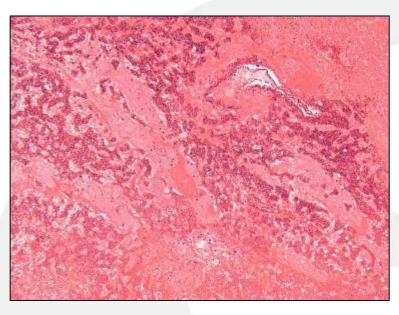
Mouse: Granulosa Cell Tumor, benign

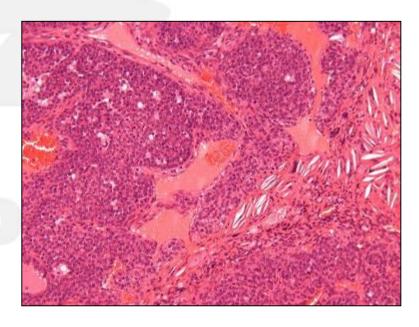


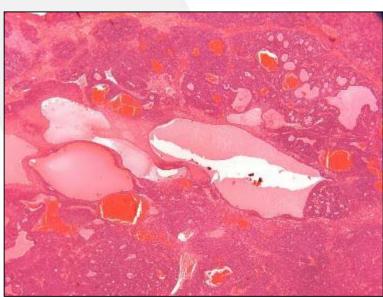
Rat: Granulosa Cell Tumor, malignant

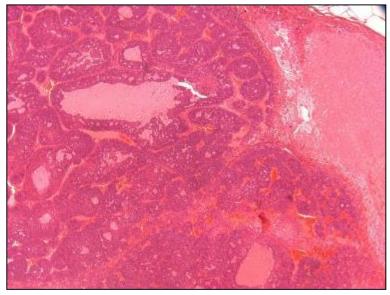


Mouse: Granulosa Cell Tumor, malignant





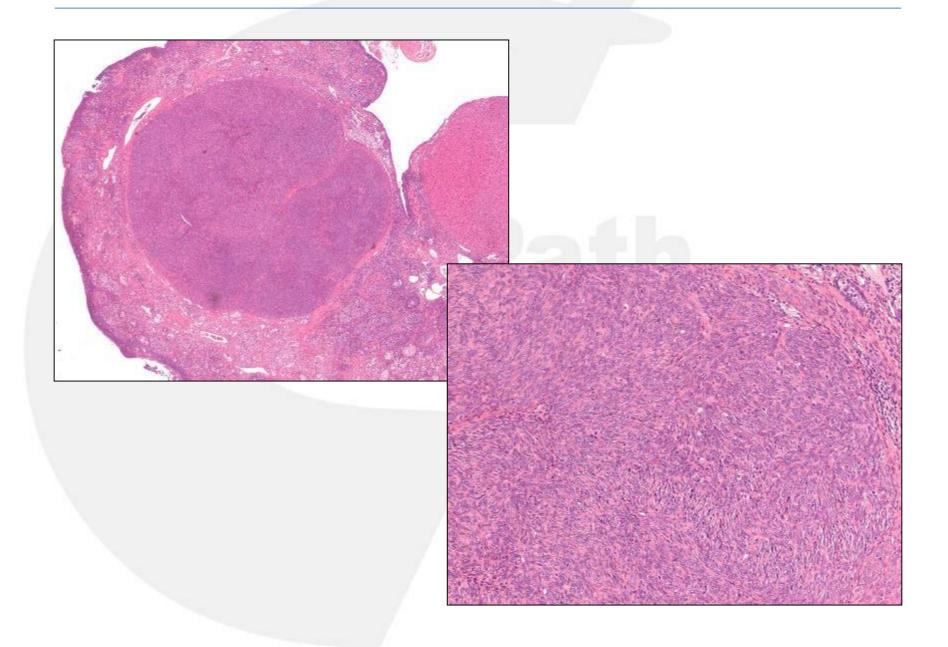




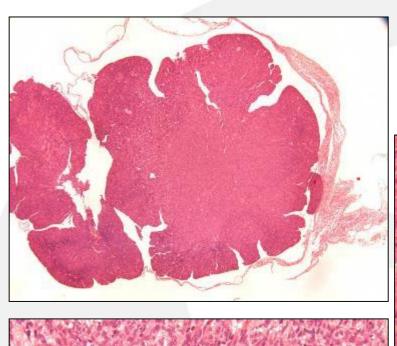
Ovary-Sex Cord Neoplasms: Thecoma

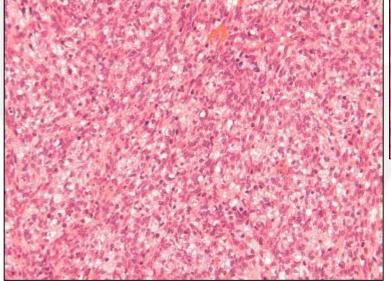
- Densely packed masses
- Fusiform, spindle-shaped cells in whorls and nodular
- Areas of vacuolated cells may be present
- Malignancy: infiltrative growth pattern, invasion, atypia
- Differential Diagnose: Hyperplasia, Fibroma, Granulosa cell tumor, Luteoma

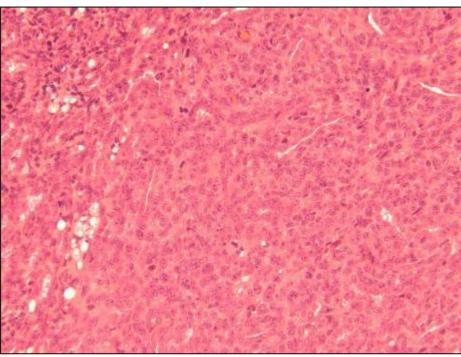
Rat: Thecoma, benign



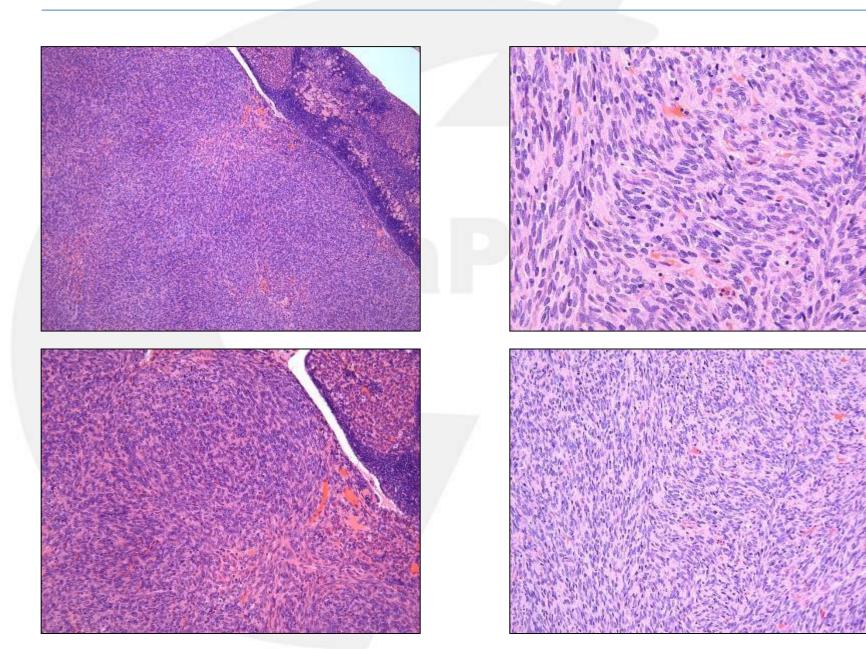
Mouse: Thecoma, benign



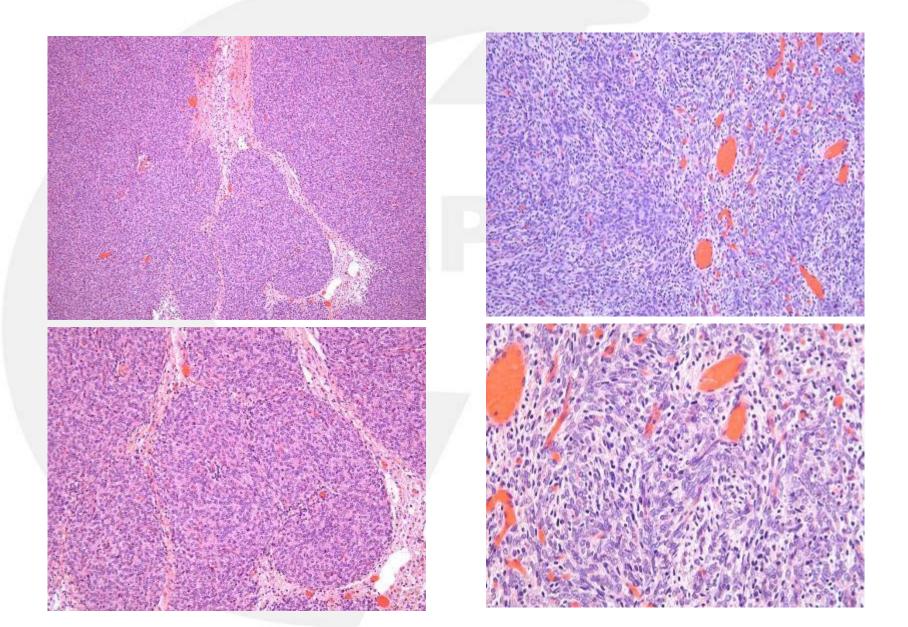




Hamster: Thecoma, benign



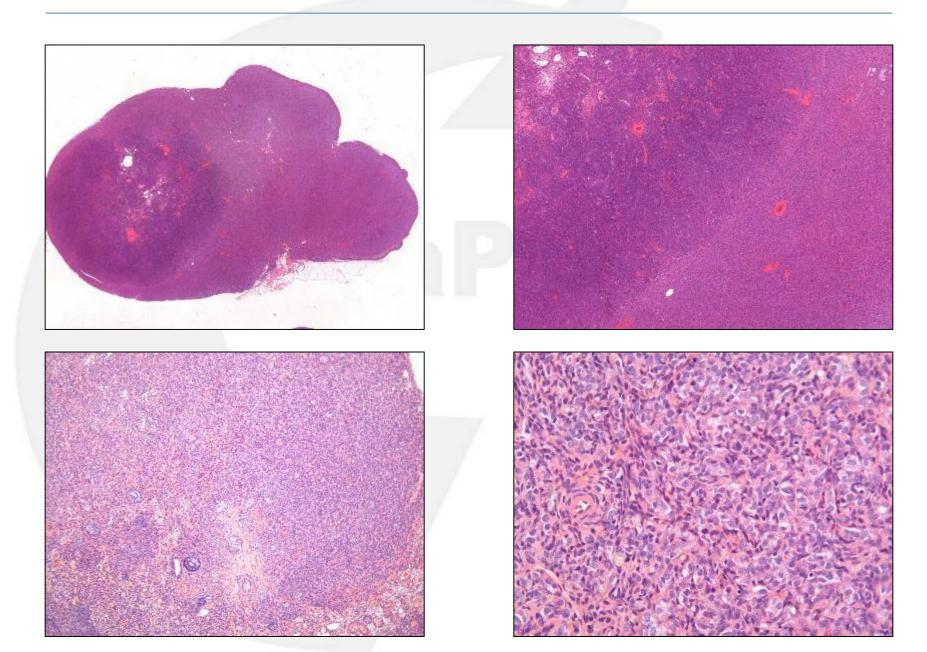
Hamster: Thecoma, malignant



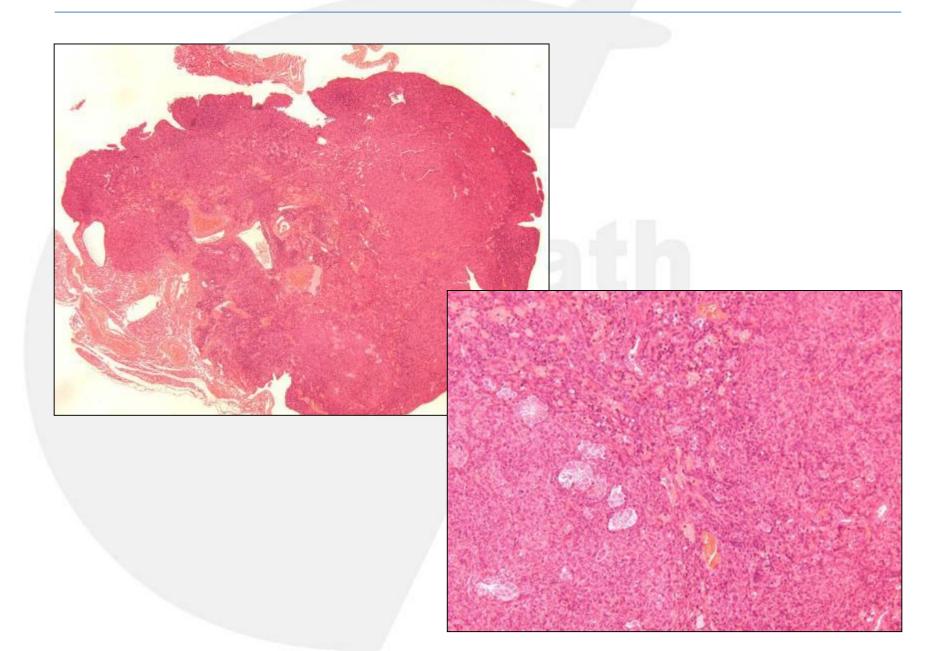
Ovary-Sex Cord Neoplasms: Granulosa-Theca Cell Tumor

- Mixed neoplasm
- Partly dense areas of a particular cell type
- Differential Diagnose: Hyperplasia, Granulosa cell tumor, Thecoma

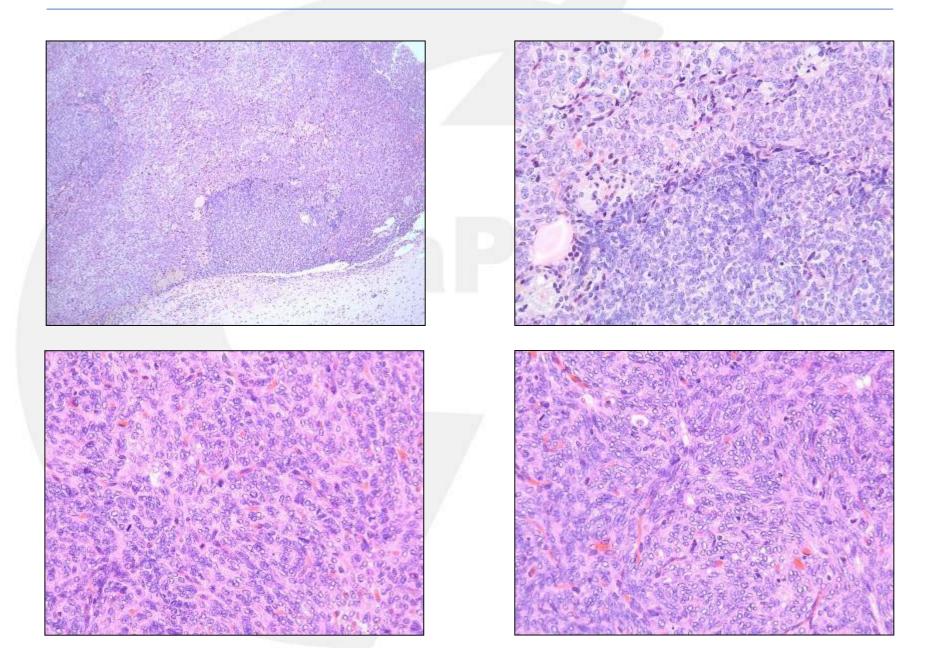
Rat: Granulosa-Theca Cell Tumor, benign



Mouse: Granulosa-Theca Cell Tumor, benign



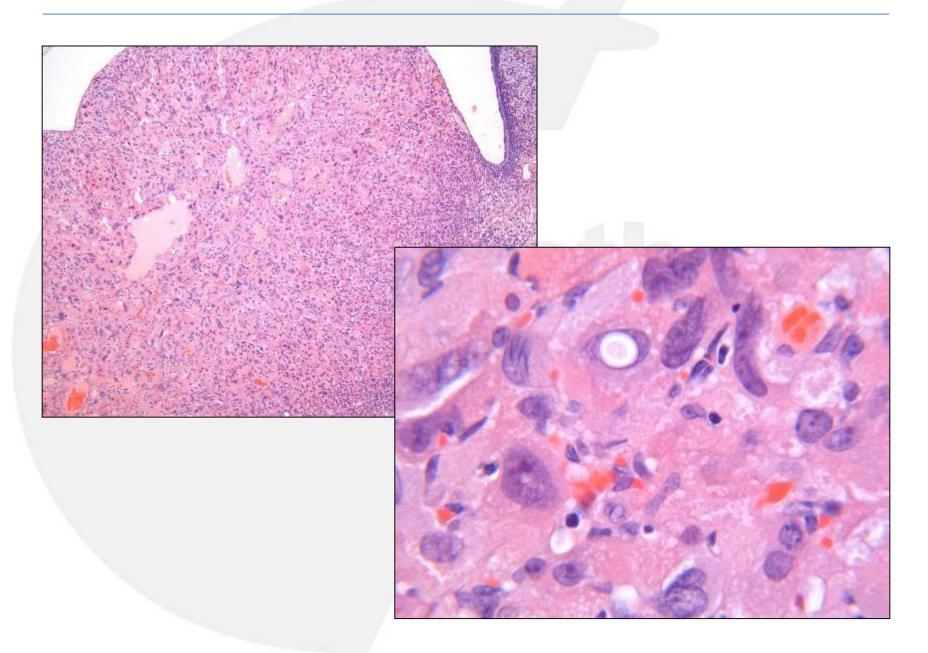
Hamster: Granulosa-Theca Cell Tumor, benign



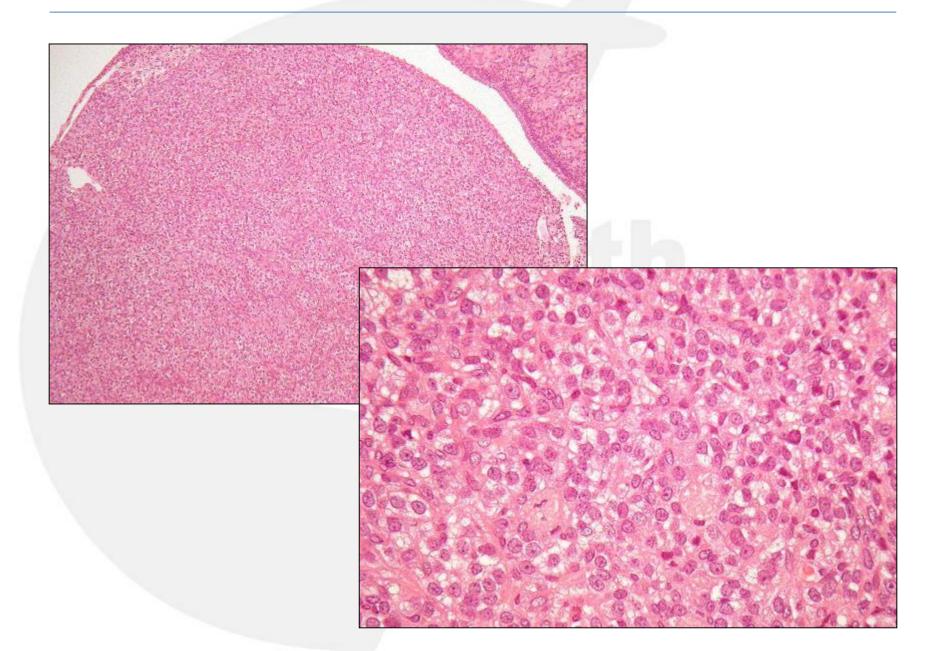
Ovary-Sex Cord Neoplasms: Luteoma

- Similar to granulosa cell tumor
- Neoplastic cells with abundant eosinophilic or vacuolated cytoplasm
- Intranuclear cytoplasmic invaginations
- Lobulation of tumor mass
- Differential Diagnose: Granulosa cell tumor, Thecoma

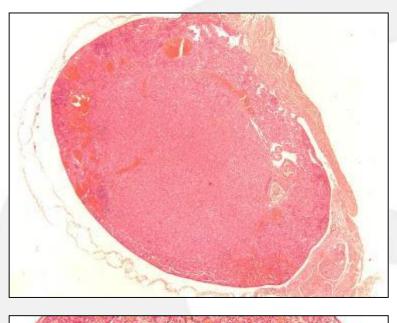
Rat: Luteoma, benign

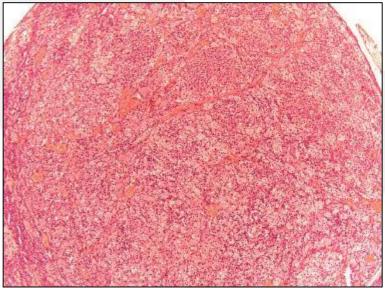


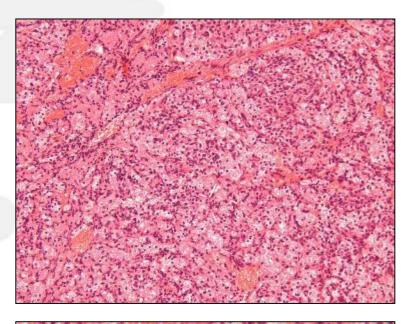
Rat: Luteoma, benign

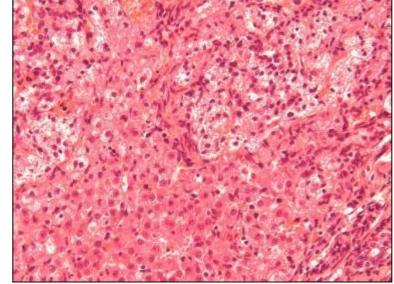


Mouse: Luteoma, benign





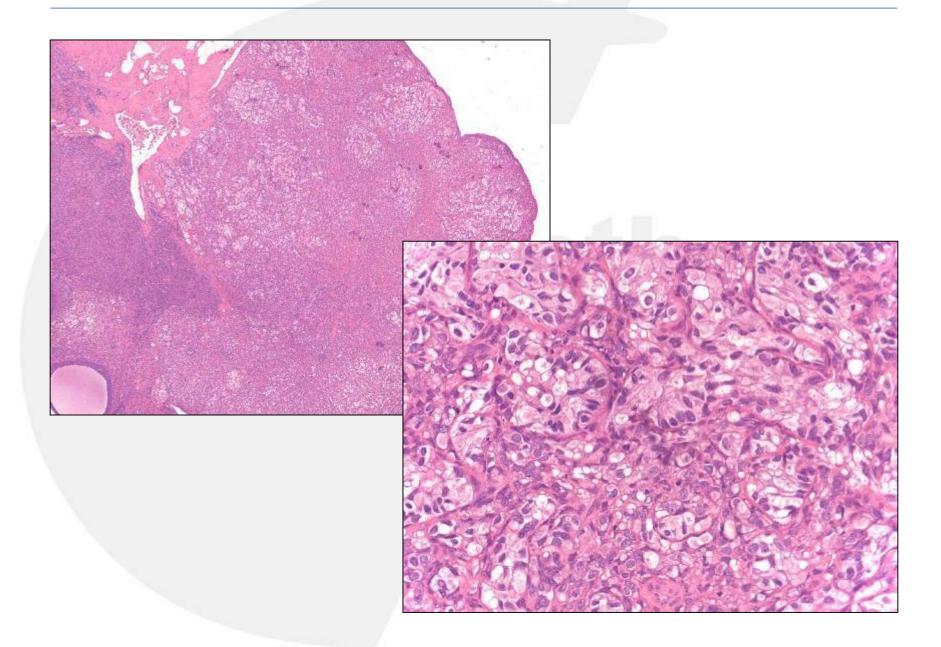




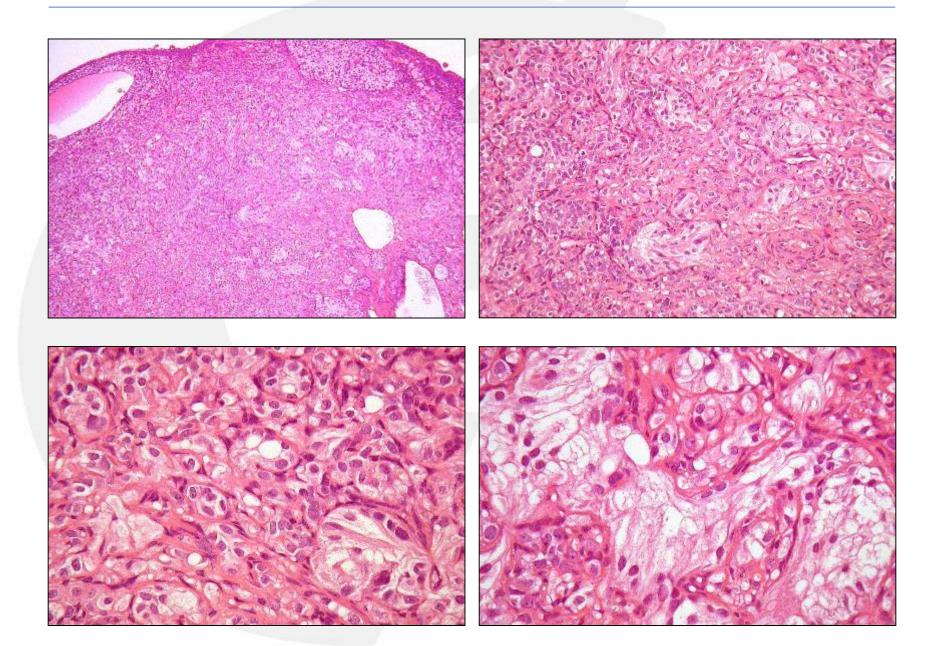
Ovary-Sex Cord Neoplasms: Sertoli's Cell Tumor

- Usually well circumscribed
- Irregular lobules
- Tubules composed of pale, vacuolated cells with indistrict cell boundaries, seminiferous-like
- Malignancy: pleomorphism, increased mitosis, necrosis, invasion
- Differential Diagnose: Hyperplasia, Granulosa cell tumor,
 Thecoma

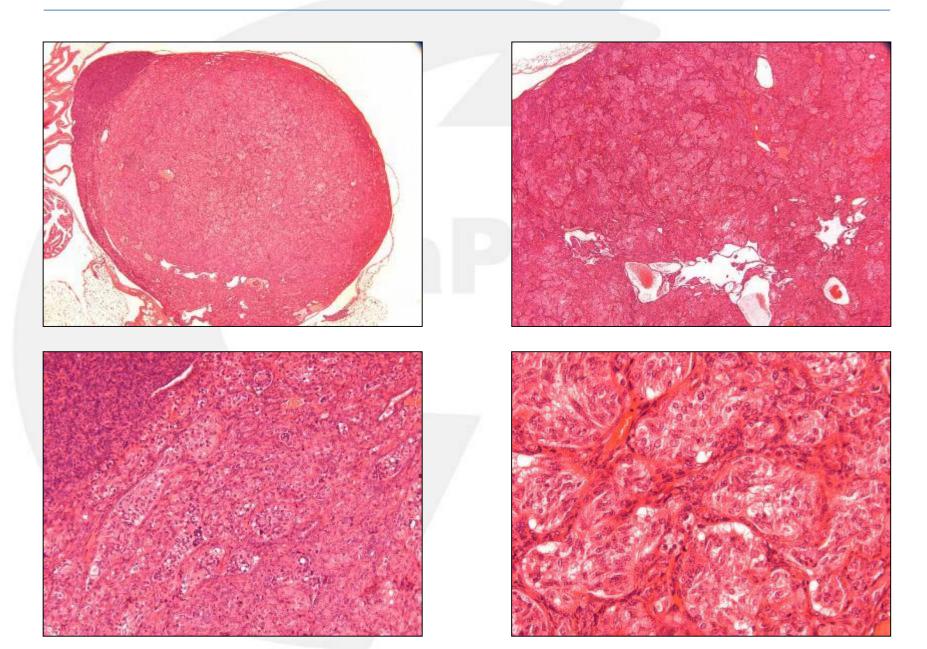
Rat: Sertoli`s Cell Tumor, benign



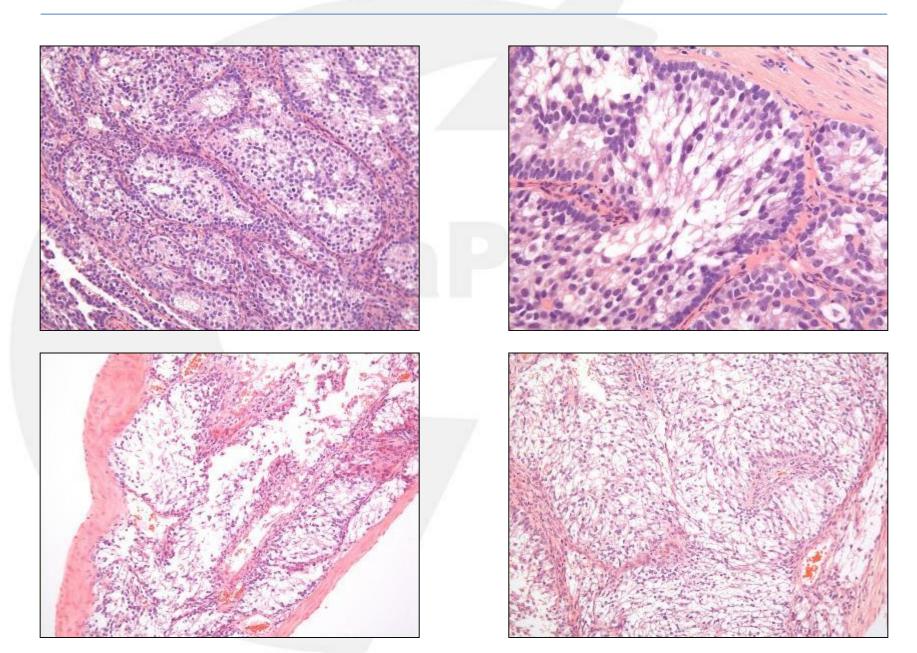
Rat: Sertoli's Cell Tumor, benign



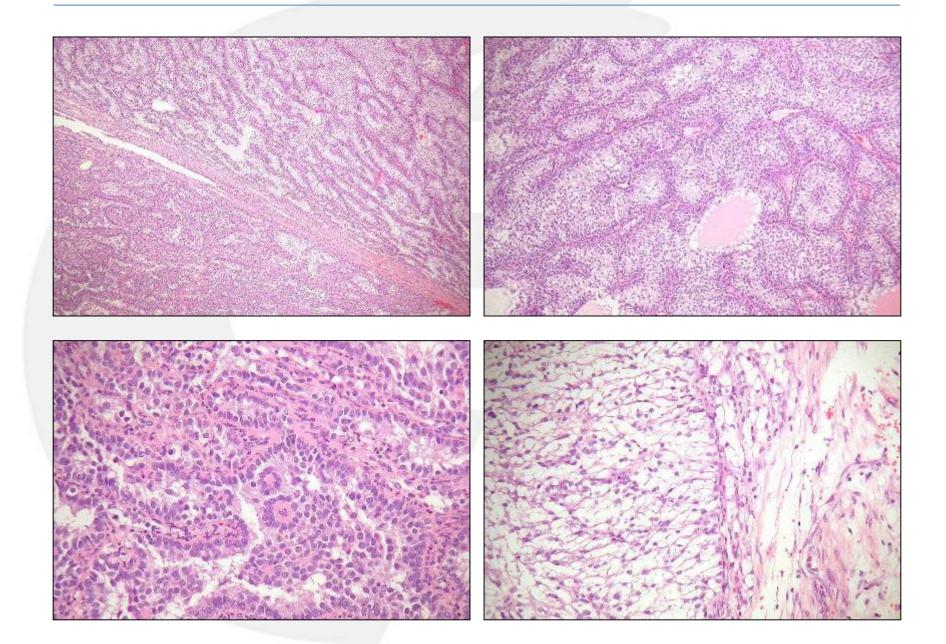
Mouse: Sertoli's Cell Tumor, benign



Rat: Sertoli's Cell Tumor, malignant



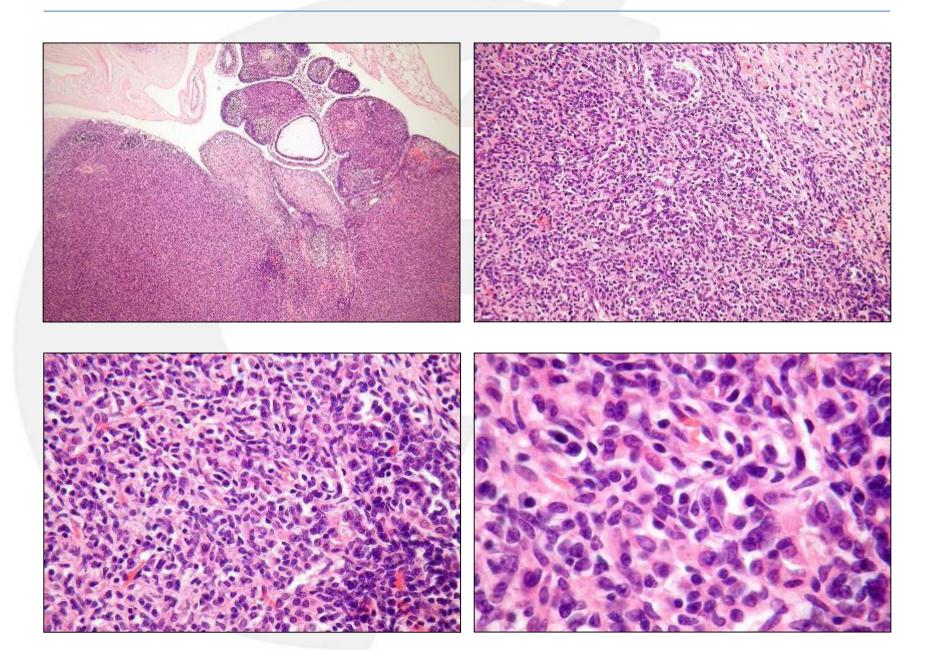
Rat: Sertoli's Cell Tumor, malignant



Ovary-Epithelial Neoplasms: Mixed Sex-Cord Stromal Tumor

- Consist of a mixture of granulosa, theca, sertoli and stromal cells of varying degree
- Differential Diagnose: Sex cord stromal hyperplasia,
 Granulosa cell tumor, Sertoli cell tumor, Thecoma

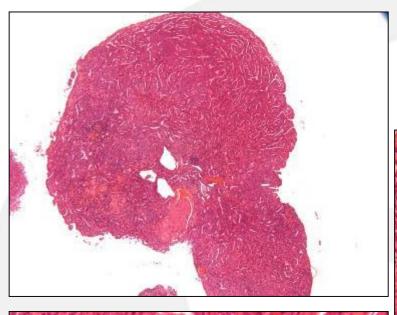
Ovary, Rat: Mixed Sex-Cord Stromal Tumor, benign

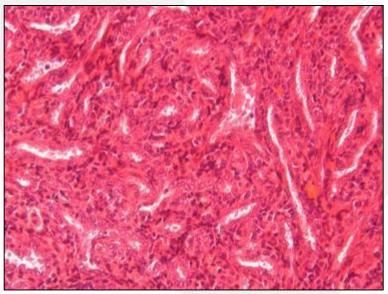


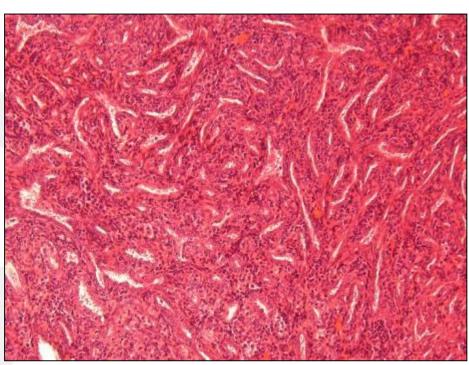
Ovary-Epithelial Neoplasms: Tubulostromal Tumor

- Nodular, usually well circumscribed
- Tubules lined by cuboidal epithelium (resemble mesothelium)
- Tubules separated by packets of cells (sex stromal cord?)
- Occassionally sertoliform structures
- Malignancy: pleomorphism, increased mitosis, necrosis, invasion
- Differential Diagnose: Tubulostromal hyperplasia, Cystadenoma, Cystadenocarcinoma

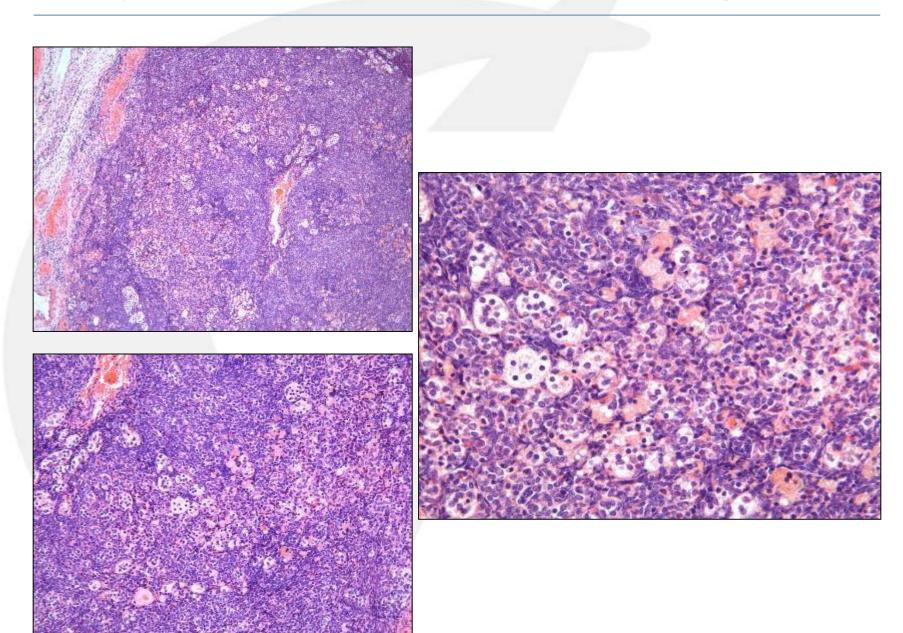
Ovary, Mouse: Tubulostromal Tumor, benign



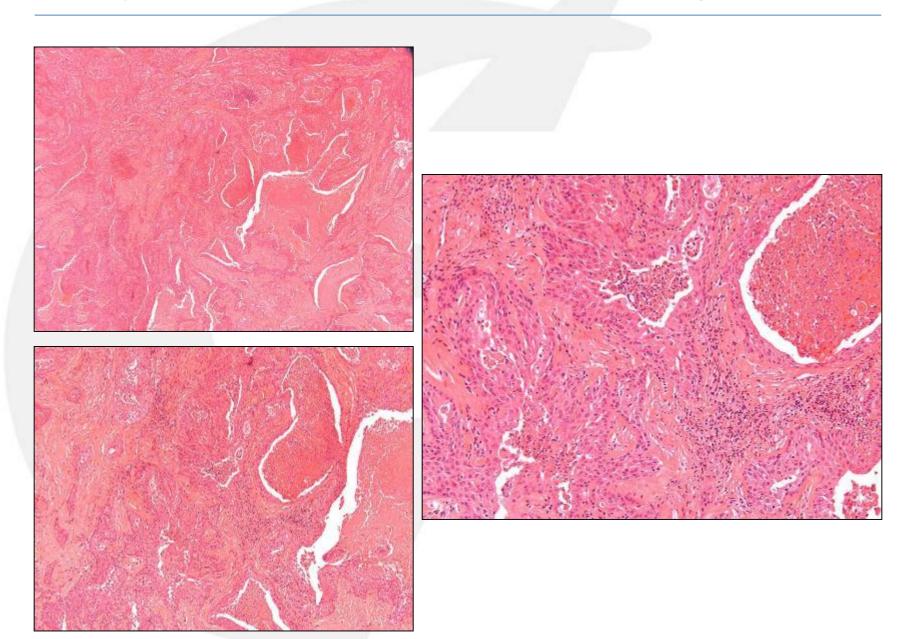




Ovary, Hamster: Tubulostromal Tumor, benign



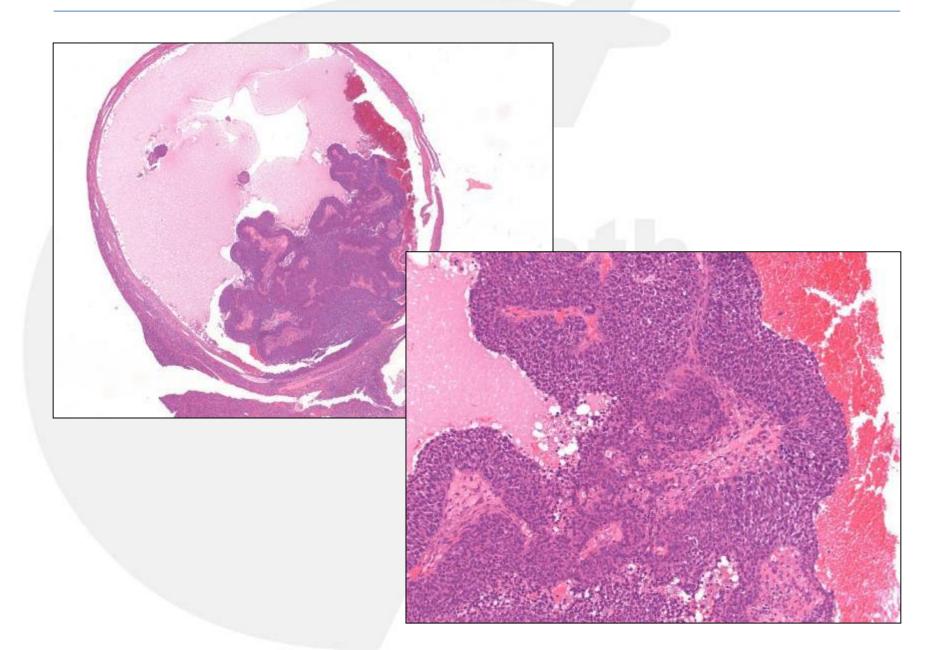
Ovary, Mouse: Tubulostromal Tumor, malignant



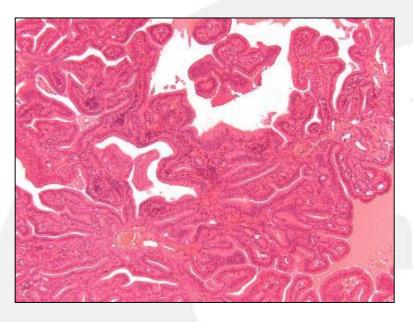
Ovary-Ephitelial Neoplasms: Cystadenoma

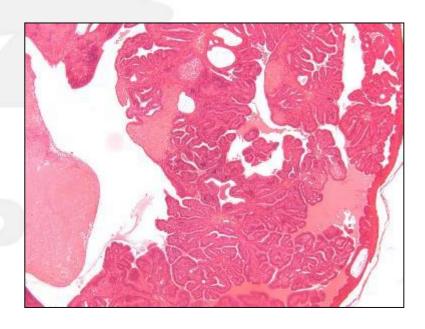
- Often within cyst lined by cuboidal epithelium
- Folds, projections
- Delicate stroma
- Malignancy: pleomorphism, increased mitosis, necrosis, invasion
- Differential Diagnose: Hyperplasia, Tubulostromal Adenoma and Adenocarcinoma,

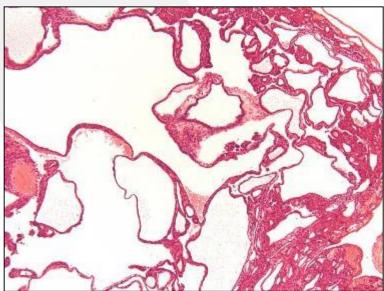
Ovary, Rat: Cystadenoma

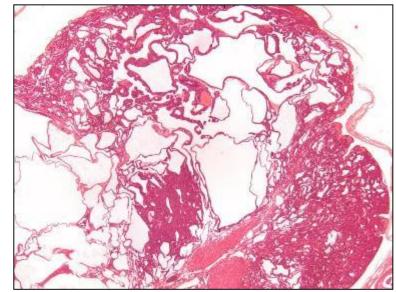


Ovary, Mouse: Cystadenoma





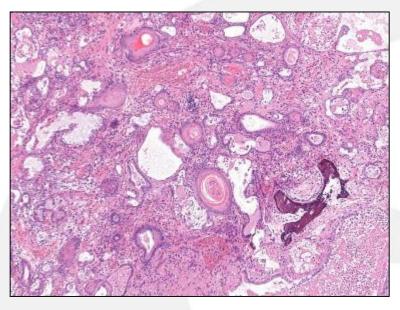


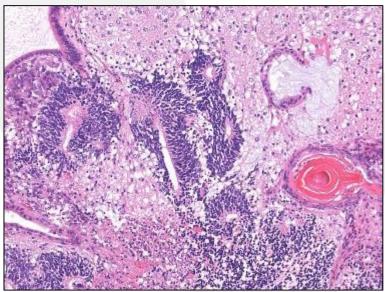


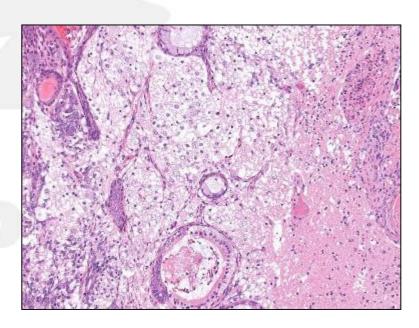
Ovary-Dysgerminoma (Teratoma)

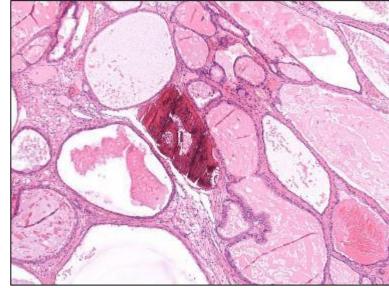
- Contains tissues from three germ layers
- Tissues well differentiated
- Benign tumors often with cysts
- Differential Diagnose: Muellerian tumor

Ovary-Teranoma: Mouse





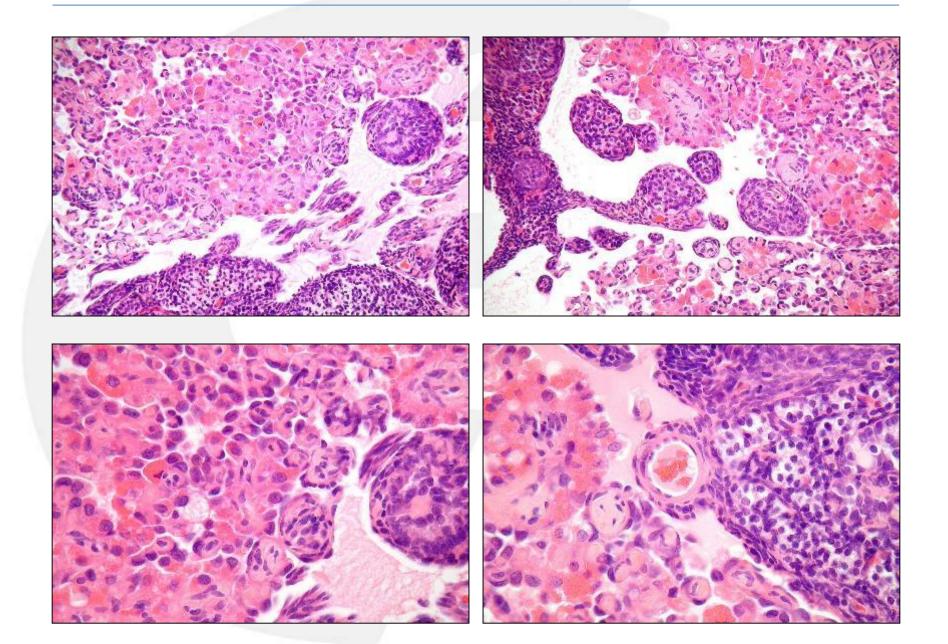




Ovary-Mesothelioma

- Papillary structures
- Local invasion
- Solid areas composed of epithelial-like cells with foamy or vacuolated cytoplasm and large nuclei
- Differential Diagnose: Adenoma, Adenocarcinoma

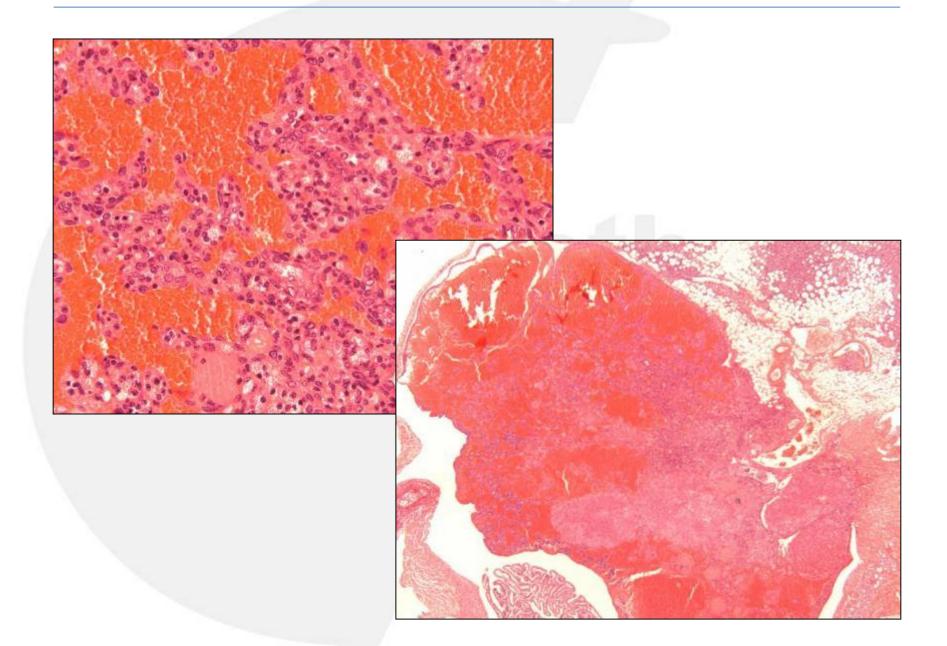
Ovary, Rat: Mesothelioma (combined with Granulosa cell tumor)



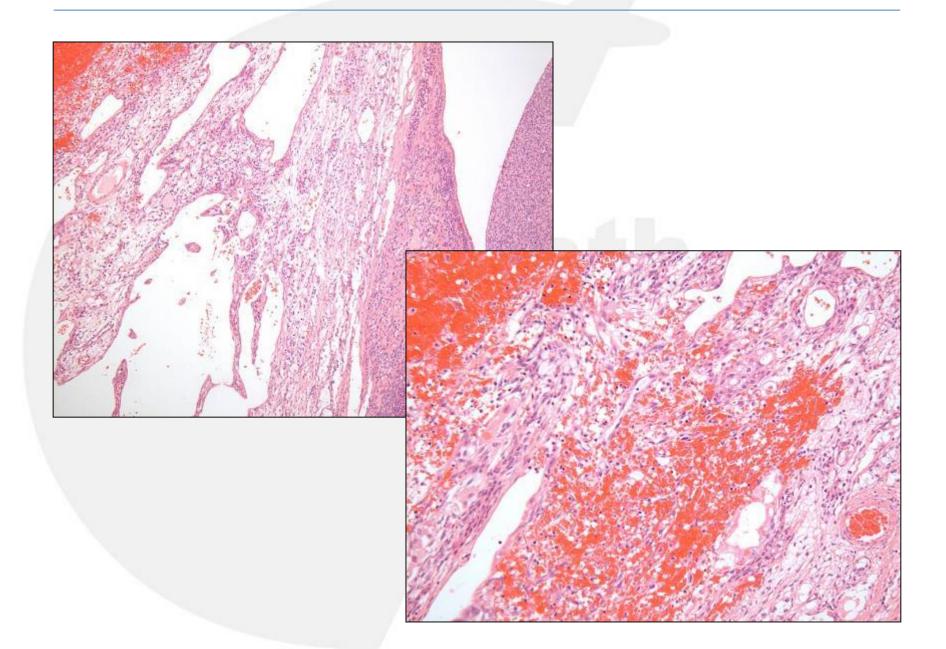
Ovary-Mesenchymal Neoplasms: Hemangioma, Hemangiosarcoma

- Hemangioma compressing surrounding tissue
- Hemangioma rarely encapsulated
- Monolayer of endothelial cells with prominent nuclei
- Hemangiosarcoma with atypical endothelium

Mouse, Ovary: Hemangioma



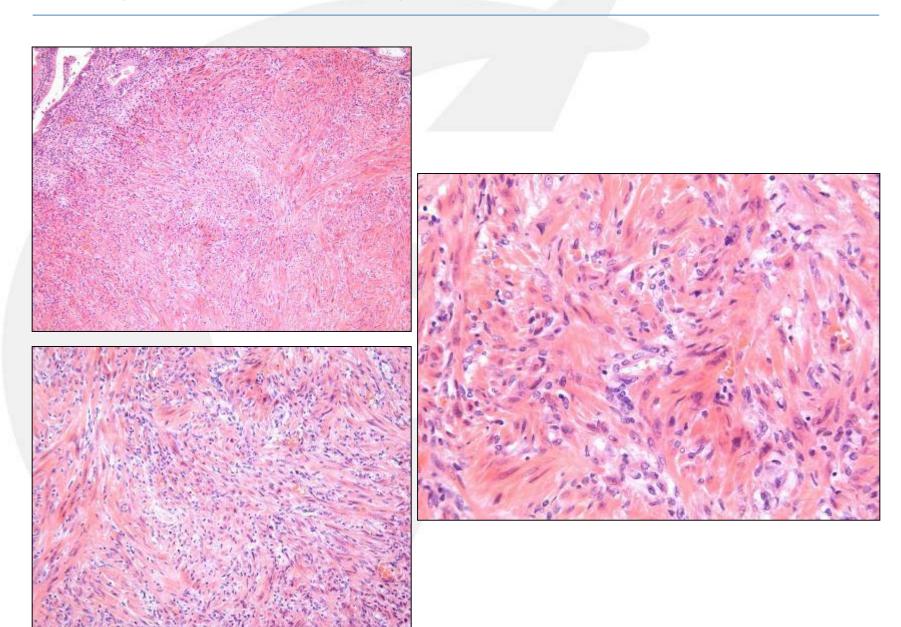
Rat, Ovary: Hemangiosarcoma



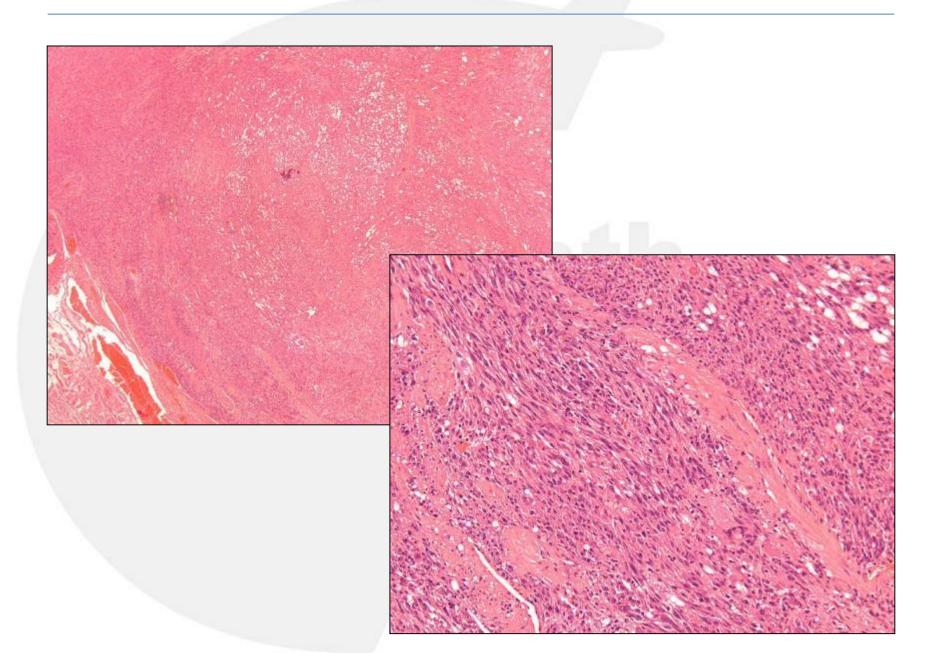
Ovary-Mesenchymal Neoplasms: Leiomyoma, Leiomyosarcoma

- Leiomyoma: well circumscribed
- Interlacing bundles and whorls (often criss-cross)
- Often abundant eosinophilic cells
- Cells often with perinuclear space
- Leiomyosarcoma: ill defined
- Heterogenous pattern
- Often necrosis, mineralization
- Differential Diagnose: Fibroma, Fibrosarcoma, Histiocytic sarcoma, Schwannoma

Ovary, Hamster: Leiomyoma



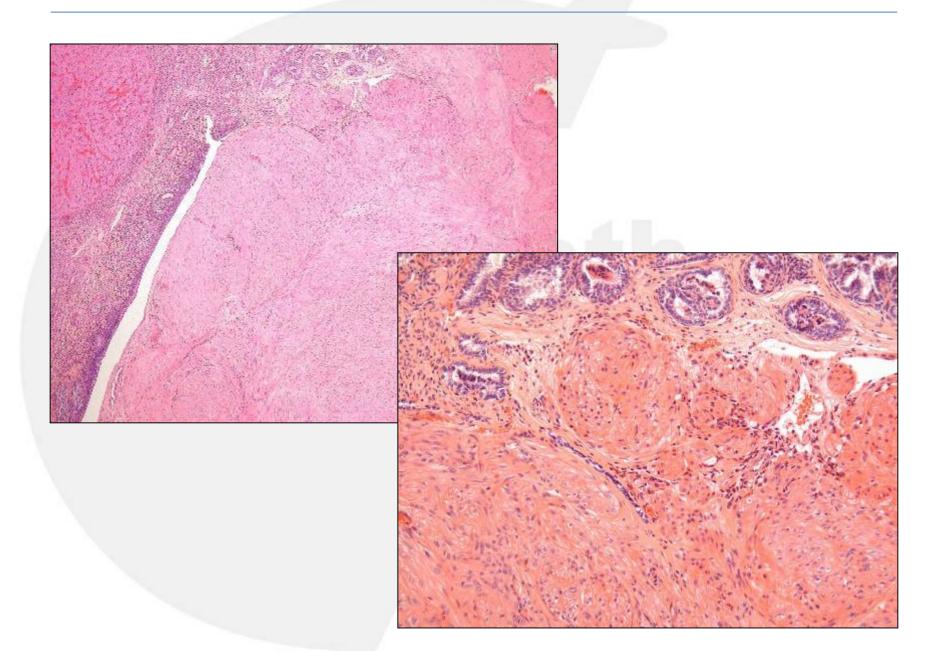
Ovary, Mouse: Leiomyosarcoma



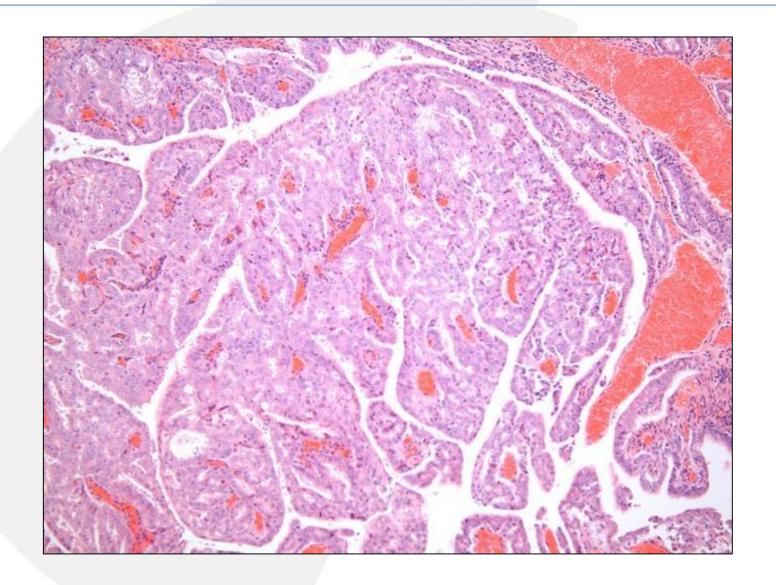
Ovary-Mesenchymal Neoplasms: Fibroma, Fibrosarcoma

- Fibroma: poorly or moderately cellular tumor compressing surrounding tissue
- Interlacing bundles of well-differentiated fibroblasts
- Bands of mature collagen
- Fibrosarcoma: pleomorphic spindelshaped cells
- Often herringbone features
- Occassionally myxomatous
- There may be necrosis, hemorrhage, invasion
- Differential Diagnose: Reactive Fibroplasia, Leiomyoma, Leiosarcoma, Schwannoma

Ovary, Rat: Fibroma



Ovary-Metastasis: Hamster (Metastasizing Uterine Carcinoma)



Classifications: Uterus – Recommendations

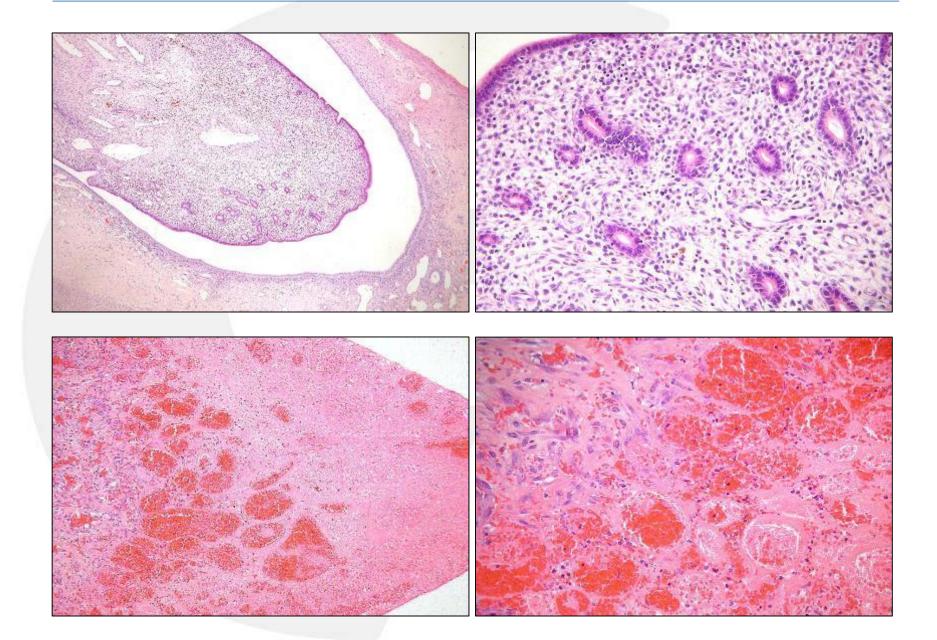
http://www.toxpath.org/nomen/

- Hyperplasia, endometrial (epithelial, glandular, stromal)
- Adenoma and Adenocarcinoma, endometrial
- Papilloma, squamous cell (keratinizing, non-keratinizing)
- Carcinoma, squamous cell (keratinizing, non-keratinizing)
- Carcinoma, adenosquamous
- Polyp, glandular
- Polyp, endometrial stromal
- Tumor, endometrial stromal, benign
- Sarcoma, endometrial stromal
- Carcinoma, yolk sac
- Choriocarcinoma
- Tumor, Muellerian, mixed, benign and malignant (heterologous, homologous)
- Carcinoma, embryonal
- Keratoacanthoma

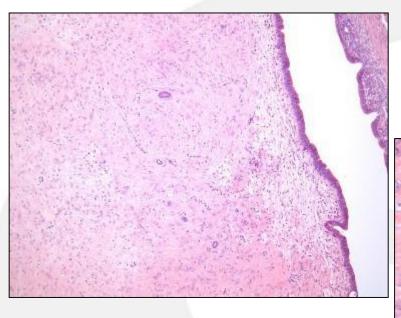
Uterus-Epithelial Neoplasms: Polyp

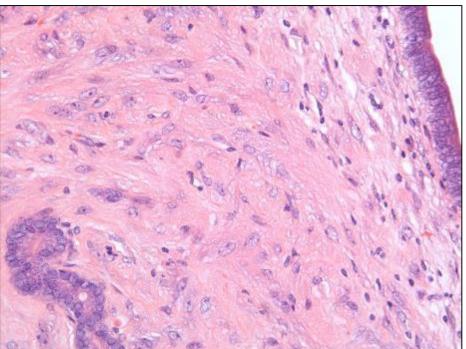
- Stomal polyp: mass protruding into uterine lumen
- covered by cuboidal to columnar epithelium
- Stroma composed of spindle-shaped cells, collagen and rarely endometrial glands
- Glandular polyp: like stromal polyp but endometrial glands are predominating
- large tumors may reveal hemorrhagic necrosis
- Differential Diagnose: Papillary adenoma, Stromal sarcoma, Vascular tumors

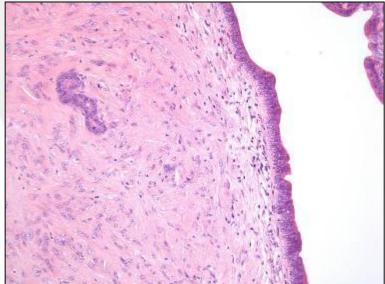
Uterus, Rat: Stromal Polyp



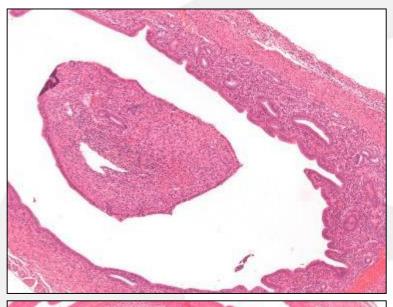
Uterus, Hamster: Stromal Polyp



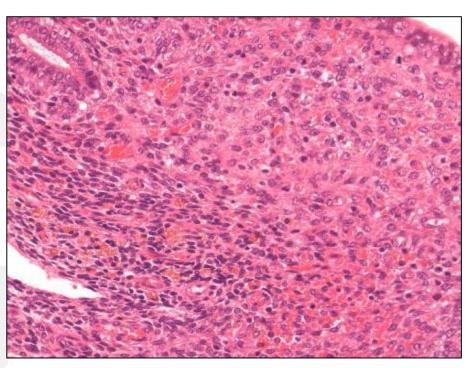




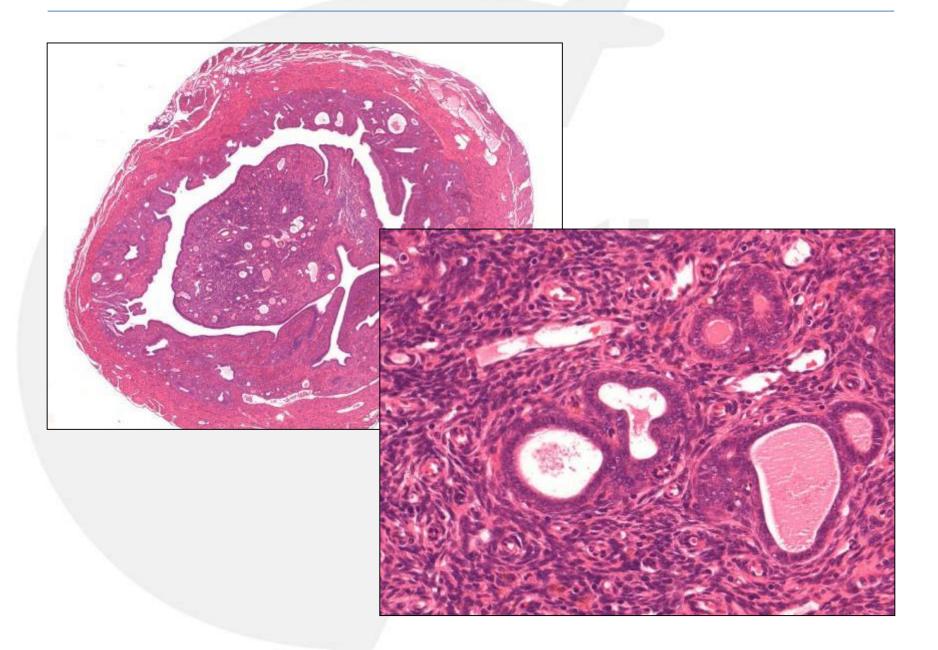
Uterus, Mouse: Stromal Polyp







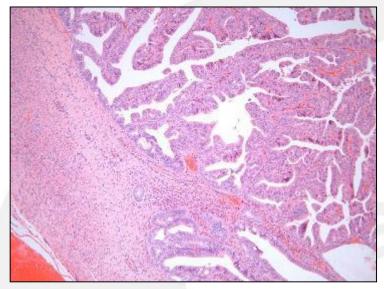
Uterus, Mouse: Glandular Polyp

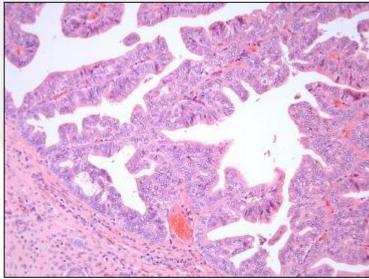


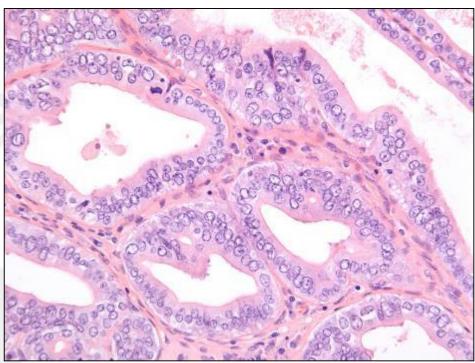
Uterus-Epithelial Neoplasms: Adenoma and Adenocarcinoma

- Arrising from surface epithelium
- Epithelium arranged in papillary, glandular or tubular structures
- In some glandular structures secretion
- Cells often eosinophilic
- Delicate stroma in adenoma
- Often desmoplastic stromal reaction in adenocarcinoma with necrosis and hemorrhage
- Differential Diagnose: Glandular polyp, Endometrial hyperplasia, Glandular hyperplasia, Adenomyosis, Squamous cell carcinoma

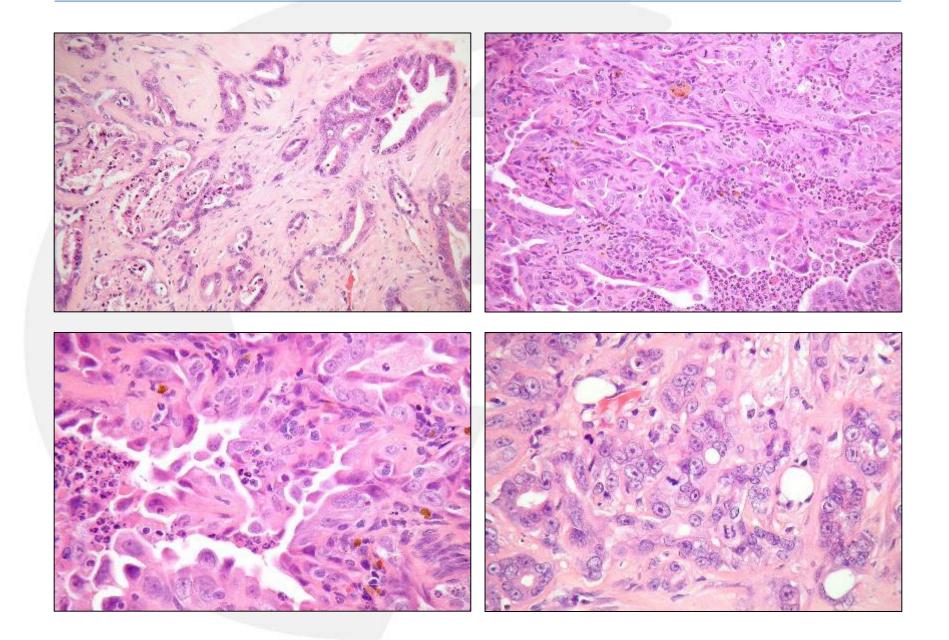
Uterus, Hamster: Adenoma



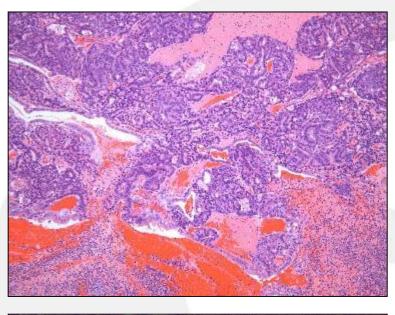


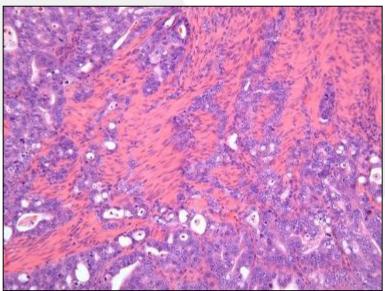


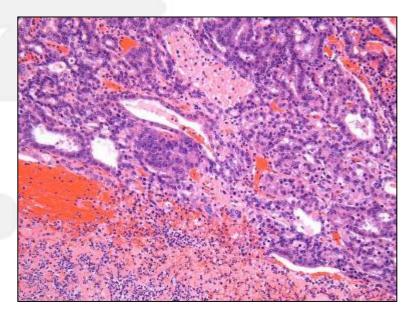
Uterus, Rat: Adenocarcinoma

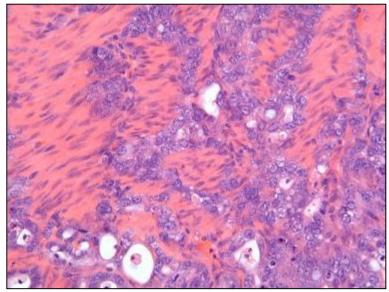


Uterus, Hamster: Adenocarcinoma

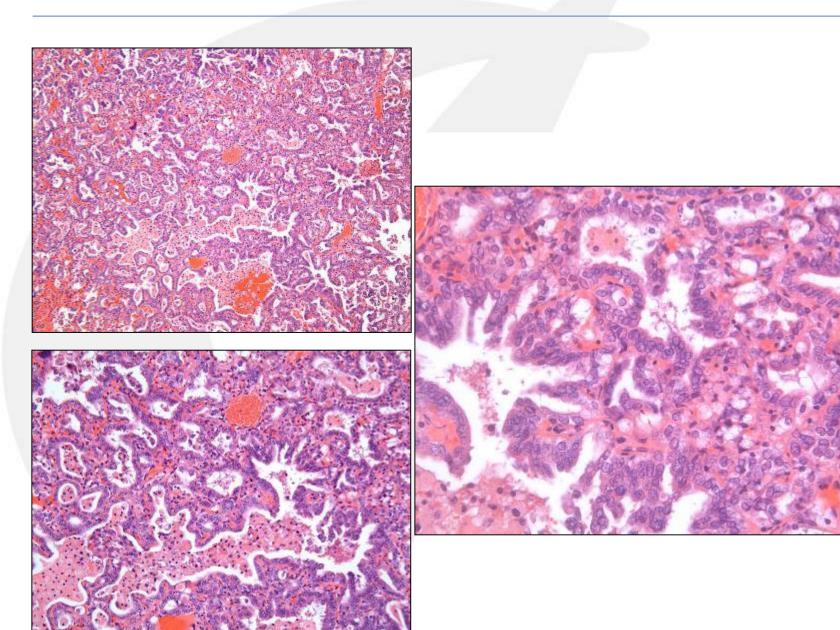




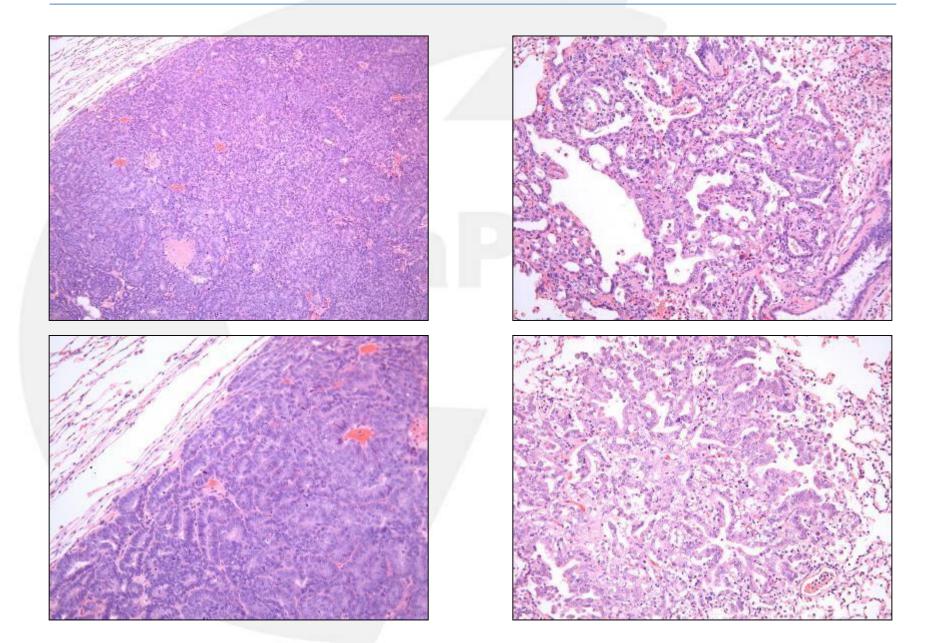




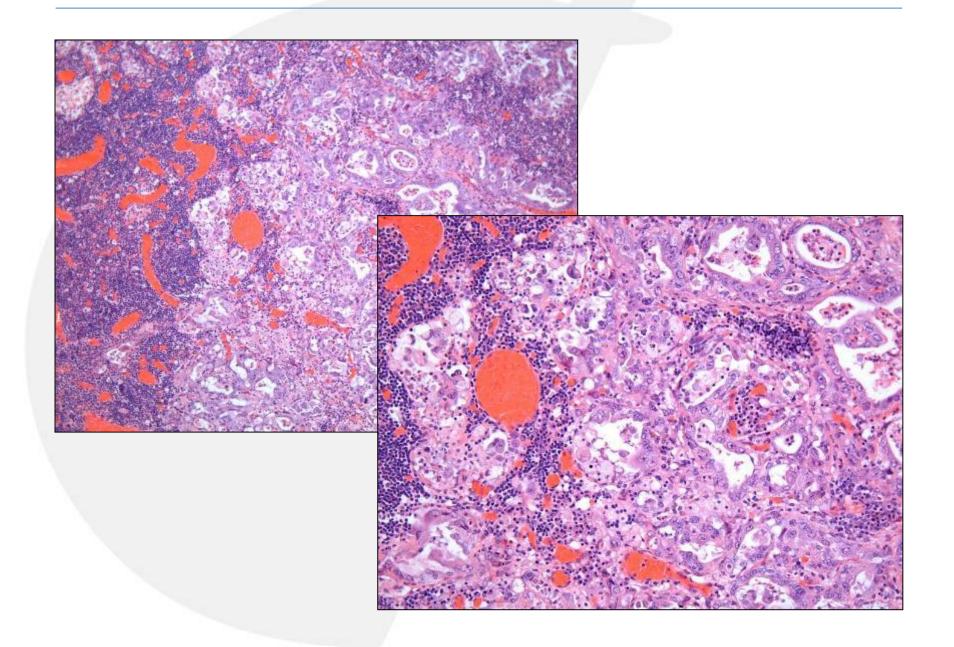
Uterus, Hamster: Adenocarcinoma



Lung Metastases, Hamster: Uterine Adenocarcinoma



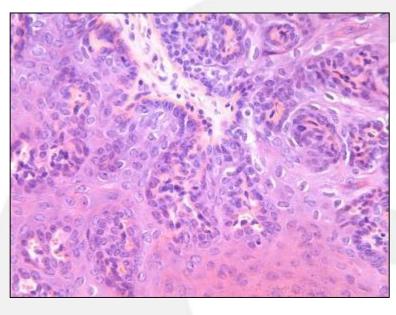
Lymph Nodes, Metastases, Hamster: Uterine Adenocarcinoma

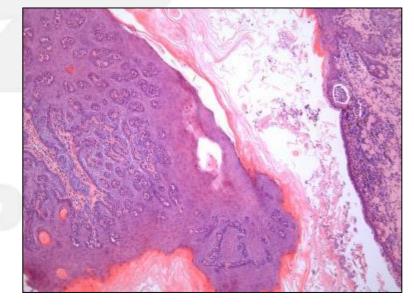


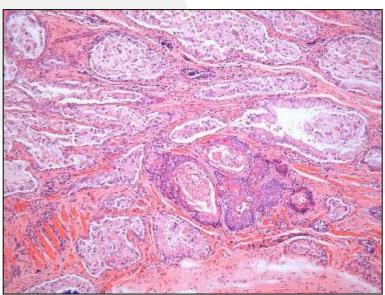
Uterus-Mesenchymal Neoplasms: Squamous Carcinoma

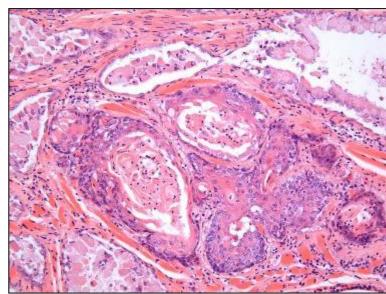
- Most often in cervical region
- Usually well-differentiated
- Often non-keratinizing
- Occassionally keratin perls
- Stroma scant or abundant
- Differential Diagnose: Squamous papilloma, Adenocarcinoma

Uterus-Cervix, Hamster: Squamous Carcinoma





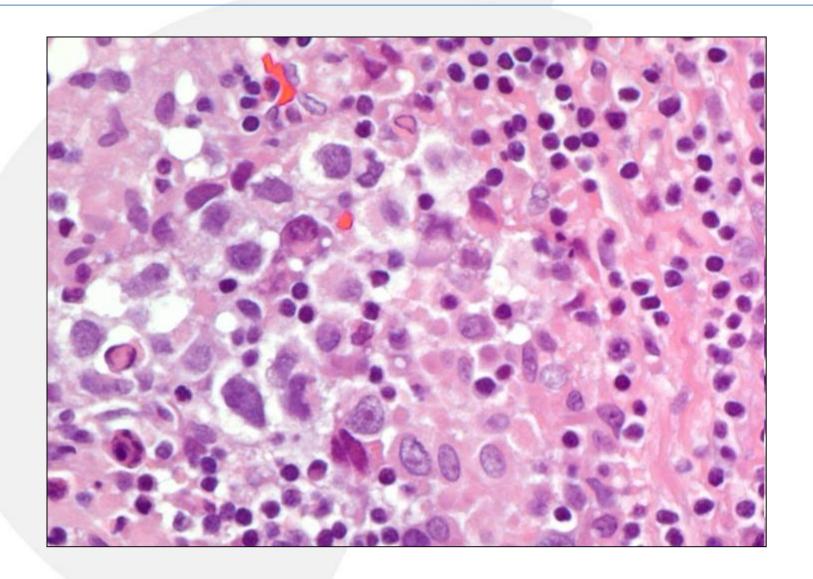




Uterus-Epithelial Neoplasms: Yolk Sac Carcinoma

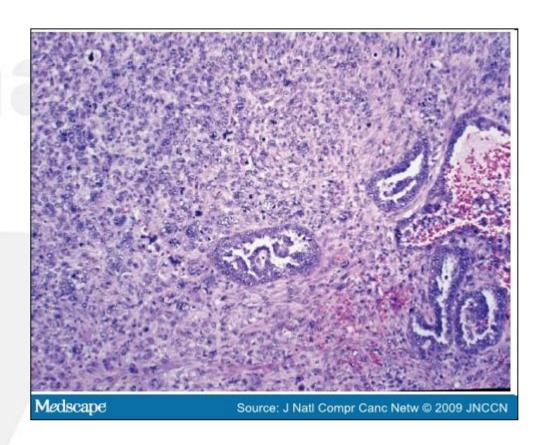
- Rosettes, nest, cords or papillary structures of cells
- Eosinophilic, hyalinized ground substance (PAS-positive)
- Cytoplasm often vacuolated and often with droplets of a compound similar to the ground substance (extracellular matrix)
- Rare!
- Differential Diagnose: Adenocarcinoma

Uterus-Epithelial Neoplasms: Yolk Sac Carcinoma



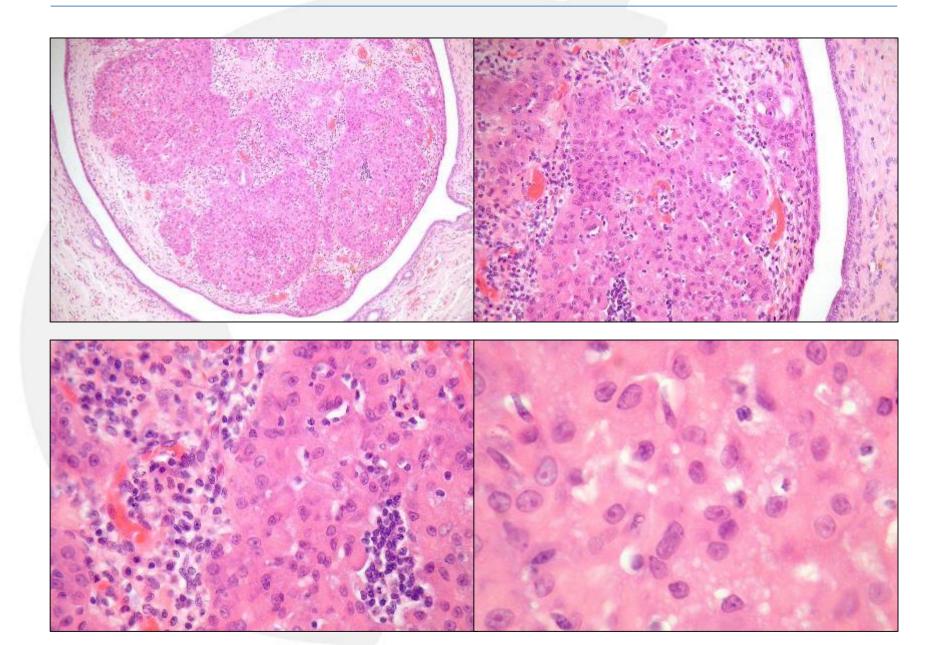
Uterus-Epithelial Neoplasms: Muellerian Tumor

- Carcinosarcoma type
- Polypoid with local invasion
- Epithelial and mesenchymal elements
- Very rare!!!
- Differential Diagnose:
 Teratoma

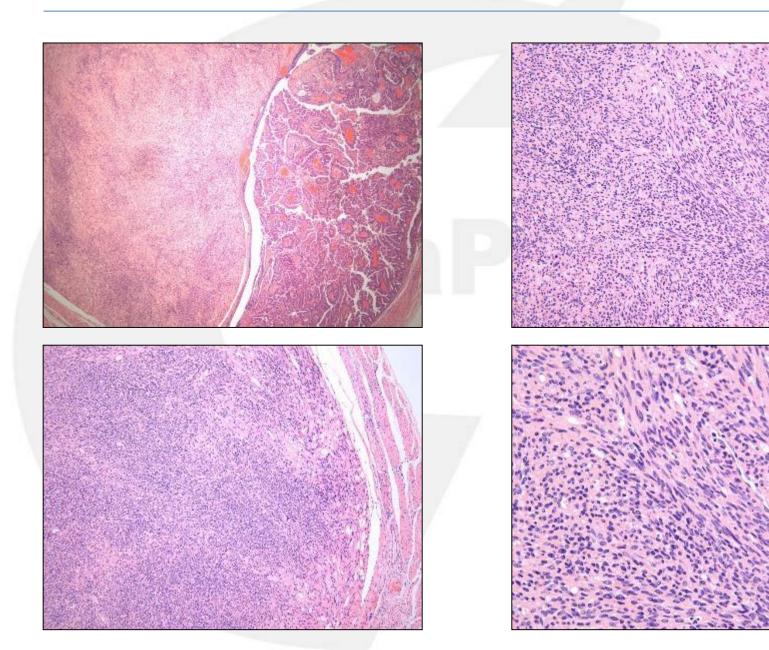


- As described under 'Ovaries' as myometrial nodules
- Leiomyoma: nuclei usually elongated with round ends but when abundant cytoplasm, the nuclei may be round up)
- Leiomyosarcoma: nuclei may be pleomorphic
- Differential Diagnose: Malignant schwannoma, Histiocytic sarcoma, Stromal sarcoma

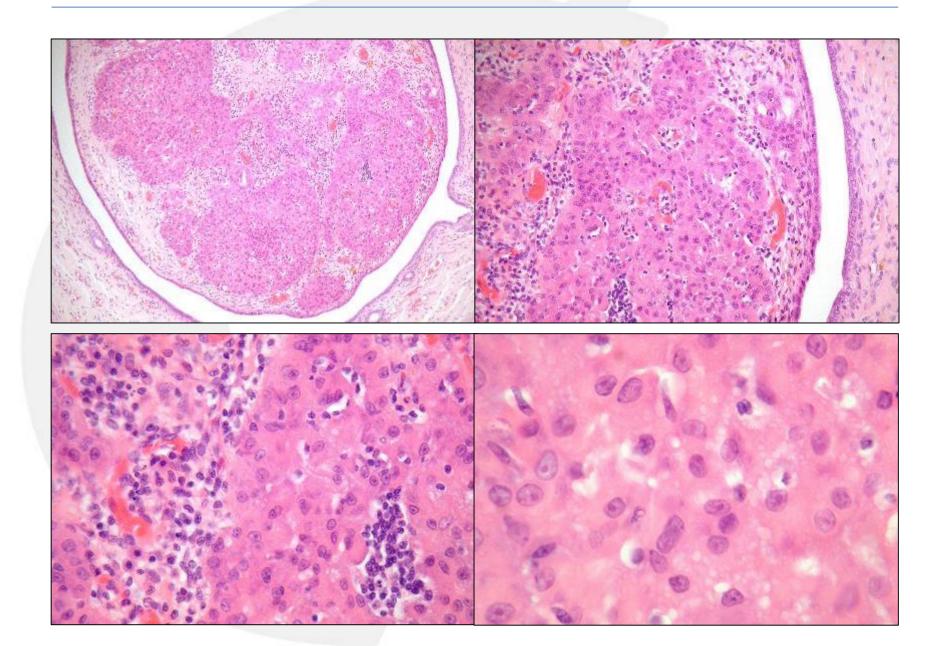
Uterus; Rat: Leiomyoma (Growth in Stromal Polyp)



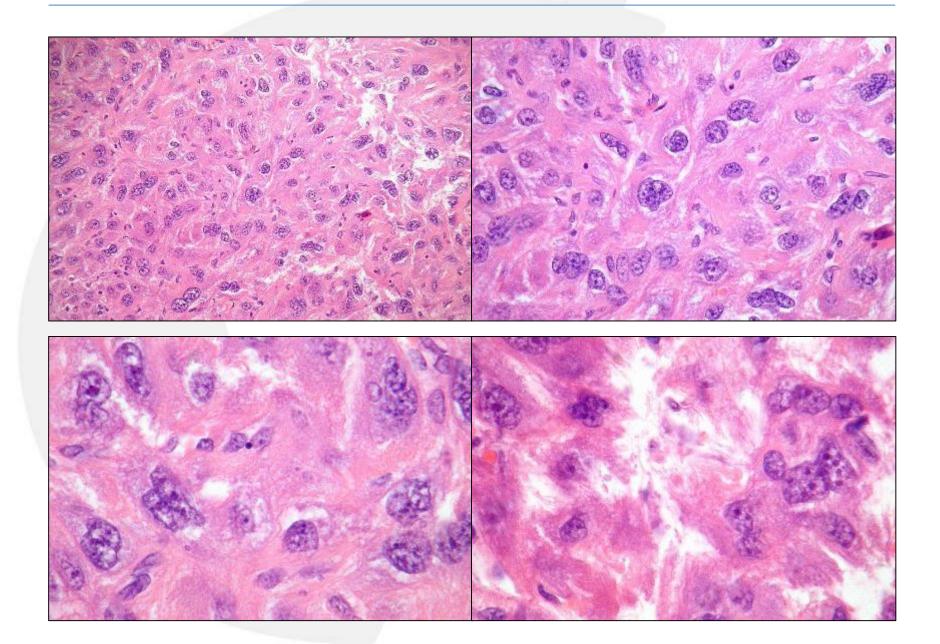
Uterus; Hamster: Leiomyoma



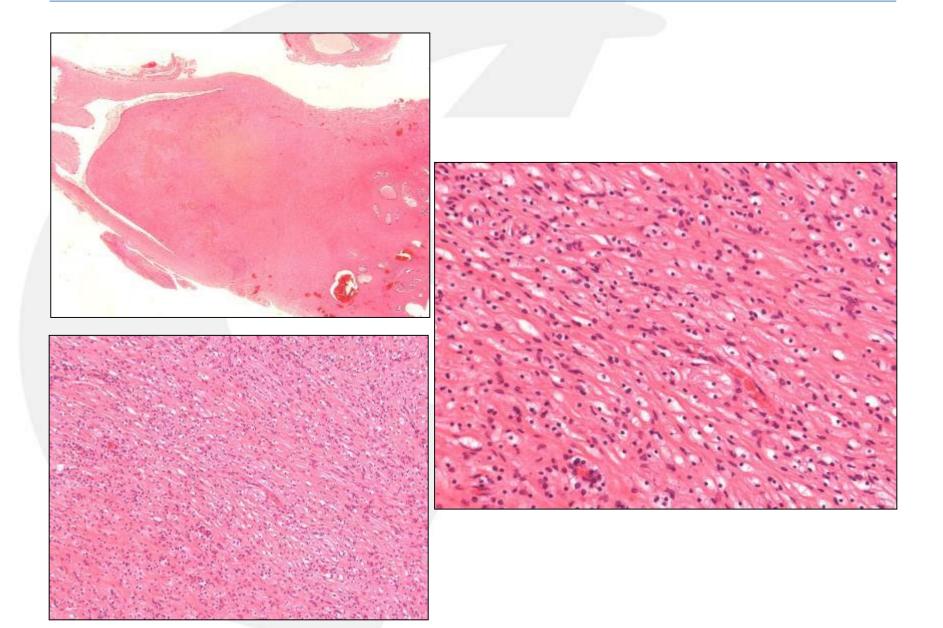
Uterus; Rat: Leiomyoma (Growth in Stromal Polyp)



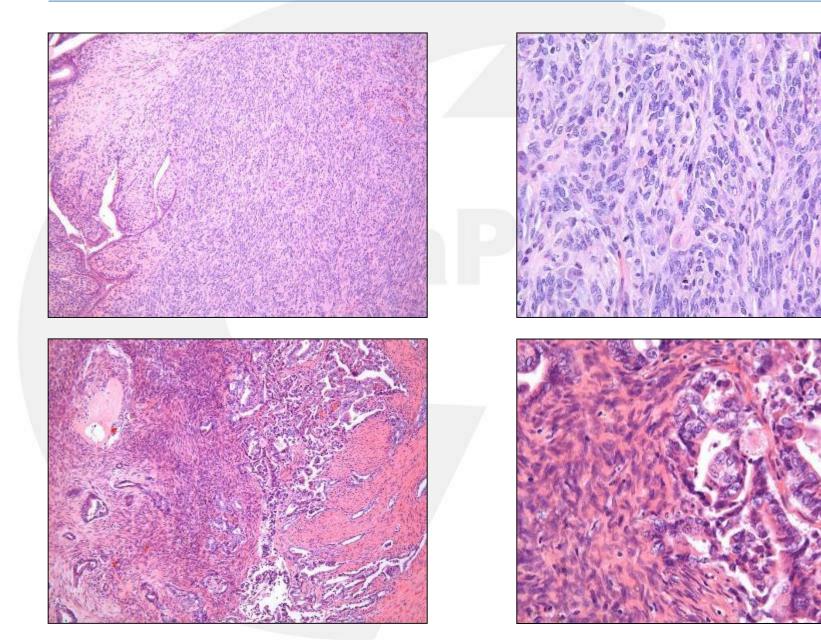
Uterus; Rat: Leiomyomsarcoma



Uterus; Mouse: Leiomyomsarcoma



Uterus; Hamster: Leiomyomsarcoma

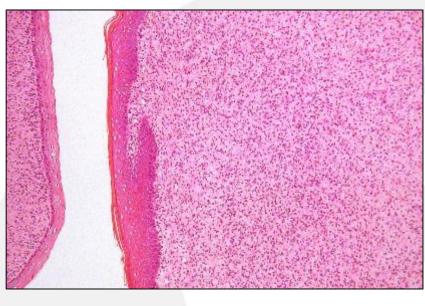


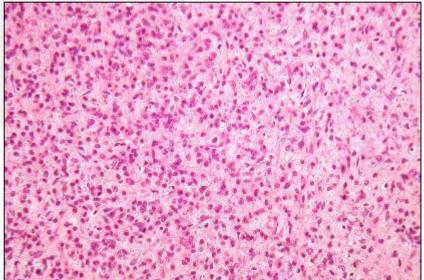
Uterus-Mesenchymal Neoplasms: Stromal Sarcoma

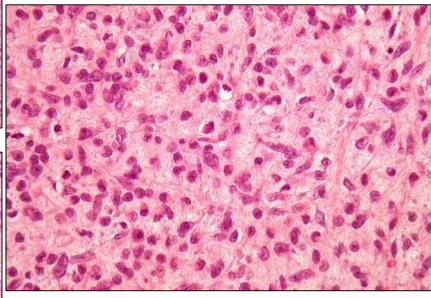
- Slightly spindle-shaped plump cells
- Nuclei elliptical and hyperchromatic
- Cell borders indistinct
- Slight pleomorphism
- May arise in stromal polyps
- Occasionally cystic and haemorrhagic areas

 Differential Diagnose: Stromal polyp, Schwannoma, Leiomyoma, Leiomyosarcoma, Fibroma, Fibrosarcoma

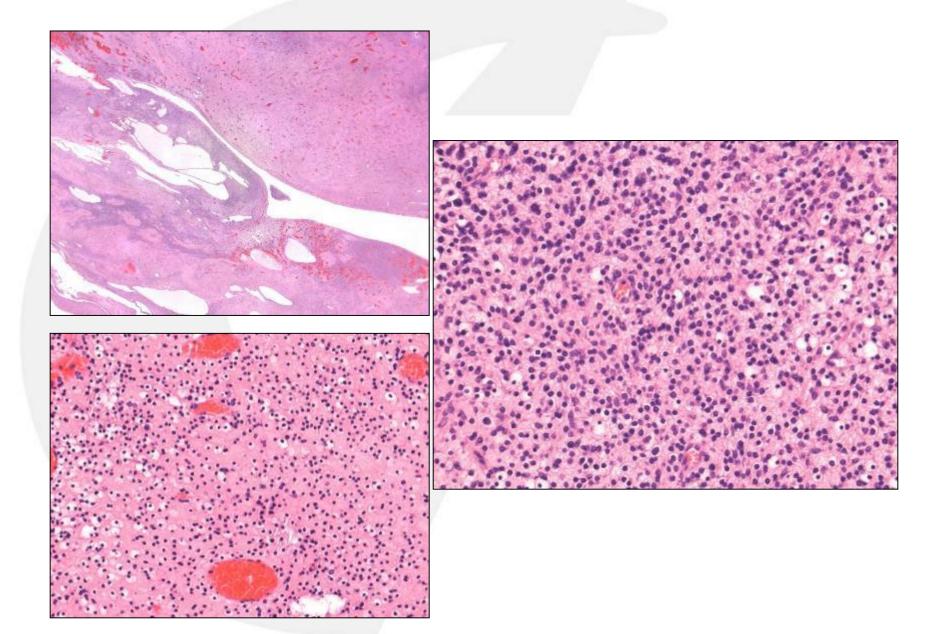
Uterus; Rat: Stromal Sarcoma







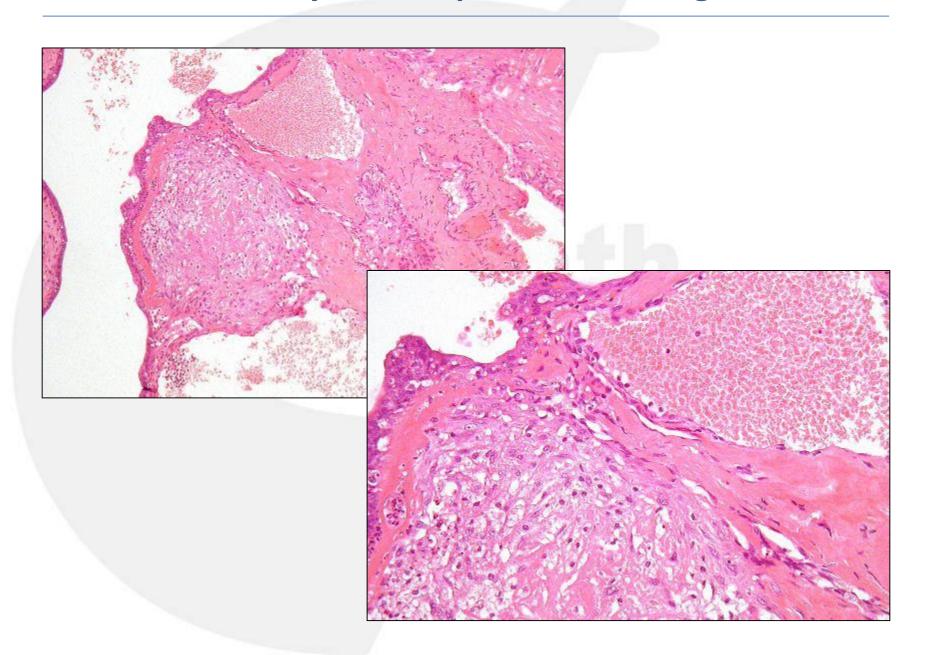
Uterus; Mouse: Stromal Sarcoma



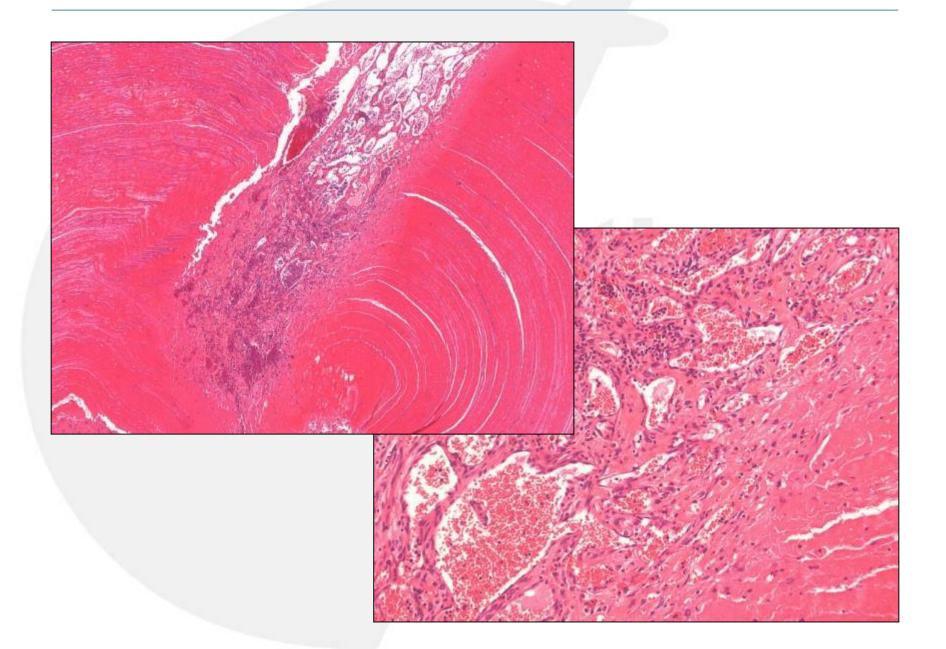
Uterus-Mesenchymal Neoplasms: Hemangioma and Hemangiosarcoma

- As described under 'Ovaries'
- Differential Diagnose: Stromal sarcoma and Malignant schwannoma with large necrotic areas, Torsion of polyps with hemorrhagic necrosis

Uterus-Mesenchymal Neoplasms: Hemangiosacoma



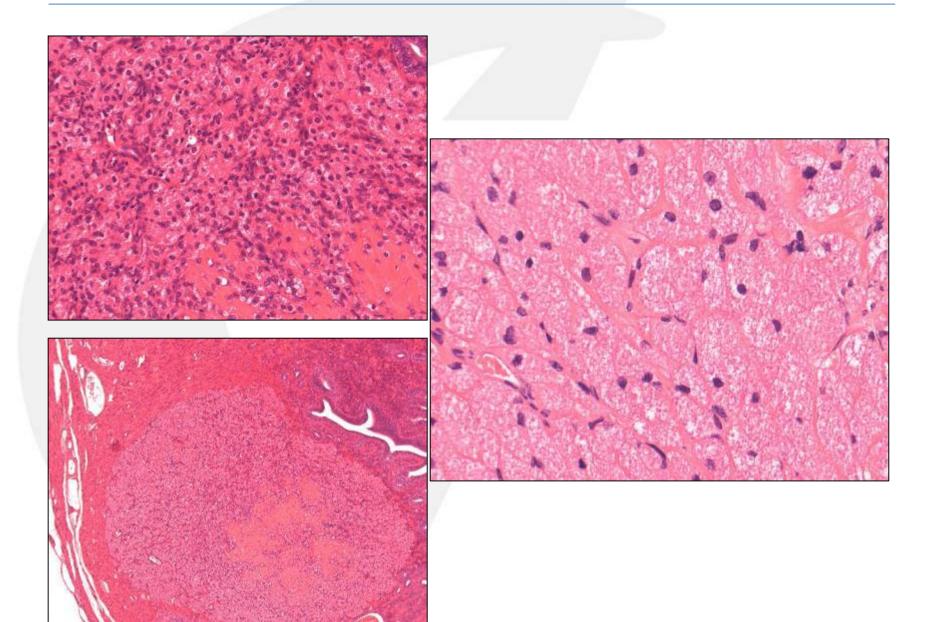
Uterus; Mouse: Hemangiosarcoma



Uterus-Mesechymal Neoplasms: Granular Cell Tumor

- Typical nodular mass with large cells
- Abundant cytoplasm containing PAS-positive granules
- Benign and malignant tumors

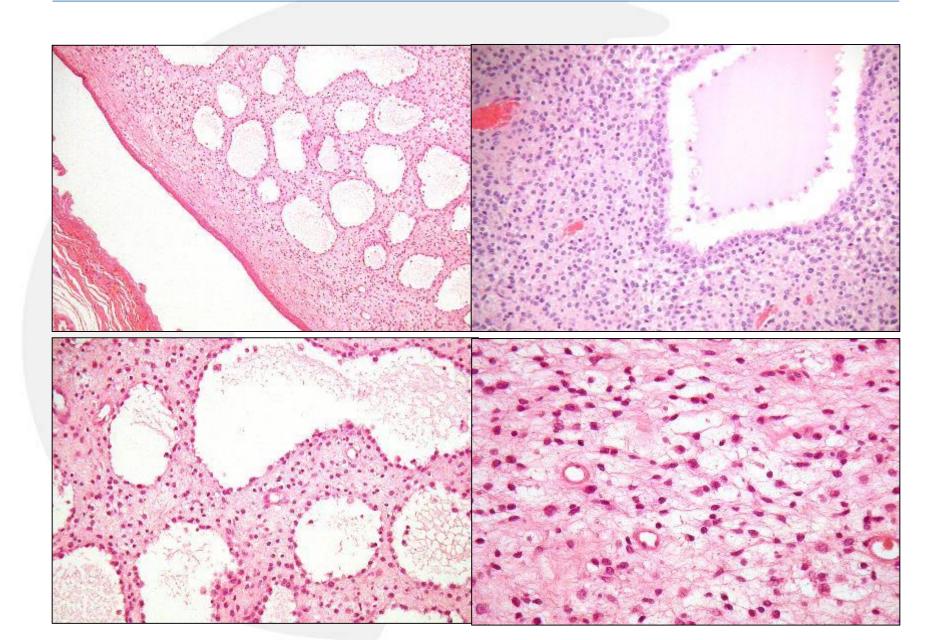
Uterus; Mouse: Granular Cell Tumor



Uterus-Mesenchymal Neoplasms: Malignant Schwannoma

- Antoni type A (Verocay-bodies with whorls)
- Antoni type B (cystic areas)
- Differential diagnose: Stromal sarcoma, Leiomyosarcoma

Uterus; Rat: Malignant Schwannoma



Classisfication: Oviduct - Recommendations

- Adenoma (papillary)
- Adenocarcinoma
- Carcinoma, yolk sac
- Choriocarcinoma

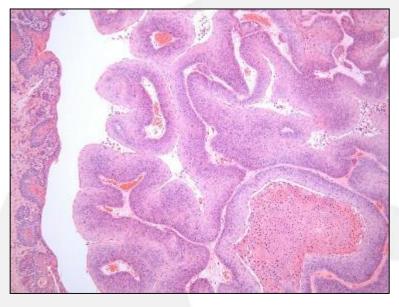
Classification: Vagina - Recommendations

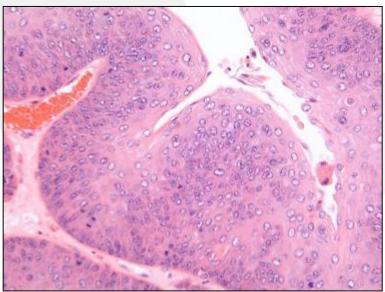
- Hyperplasia, squamous cell (keratinizing, non-keratinizing)
- Papilloma, squamous cell (keratinizing, non-keratinizing)
- Carcinoma, squamous cell (keratinizing, non-keratinizing)
- Keratoacanthoma
- Polyp, vaginal

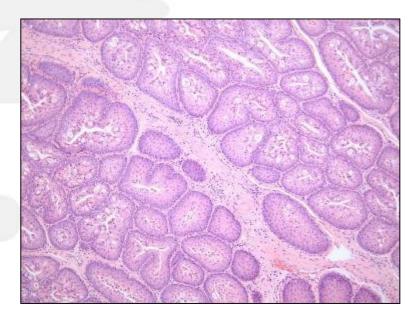
Classification: Clitoral Gland - Recommendations

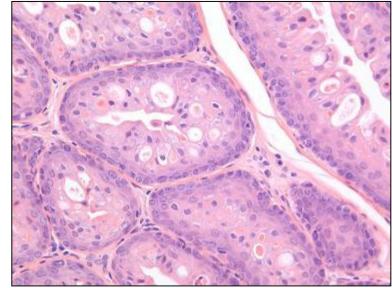
- Hyperplasia, acinar cell
- Hyperplasia, squamous cell
- Adenoma (cystic, papillary, solid)
- Papilloma, squamous cell (keratinizing, non-keratinizing)
- Adenocarcinoma (cystic, papillary, solid)
- Carcinoma, squamous cell (keratinizing, non-keratinizing)
- Tumor, basal cell, benign and malignant

Vagina, Hamster: Papilloma

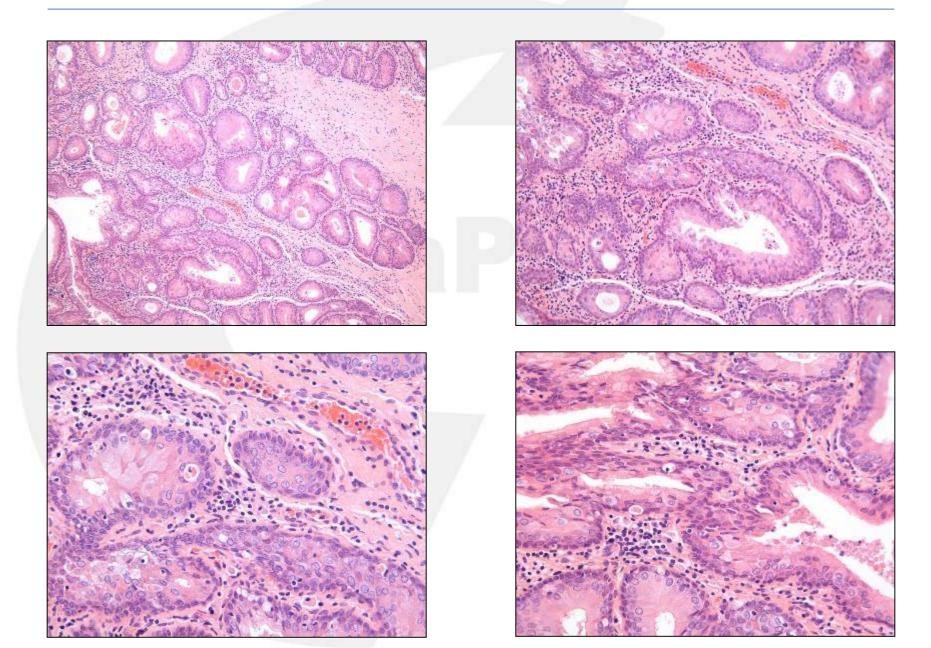






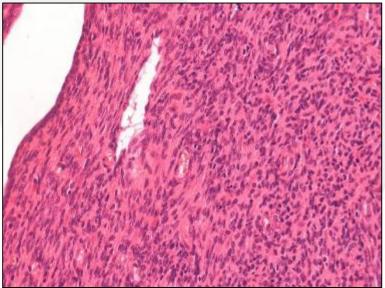


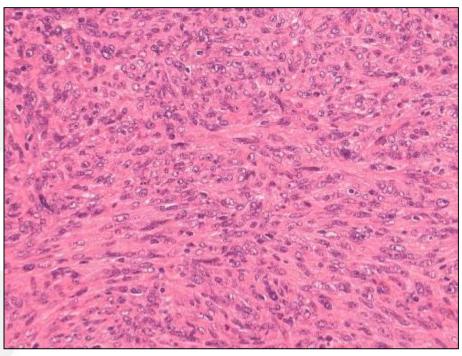
Vagina, Hamster: Squamous Carcinoma



Vagina, Mouse: Leiomyoma



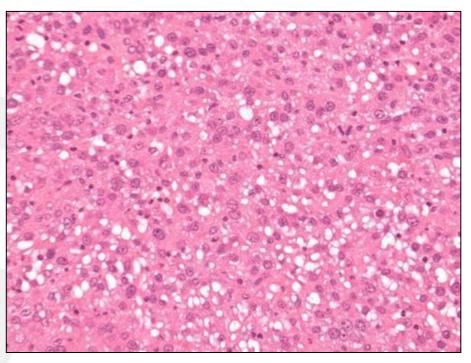




Vagina, Mouse: Liposarcoma







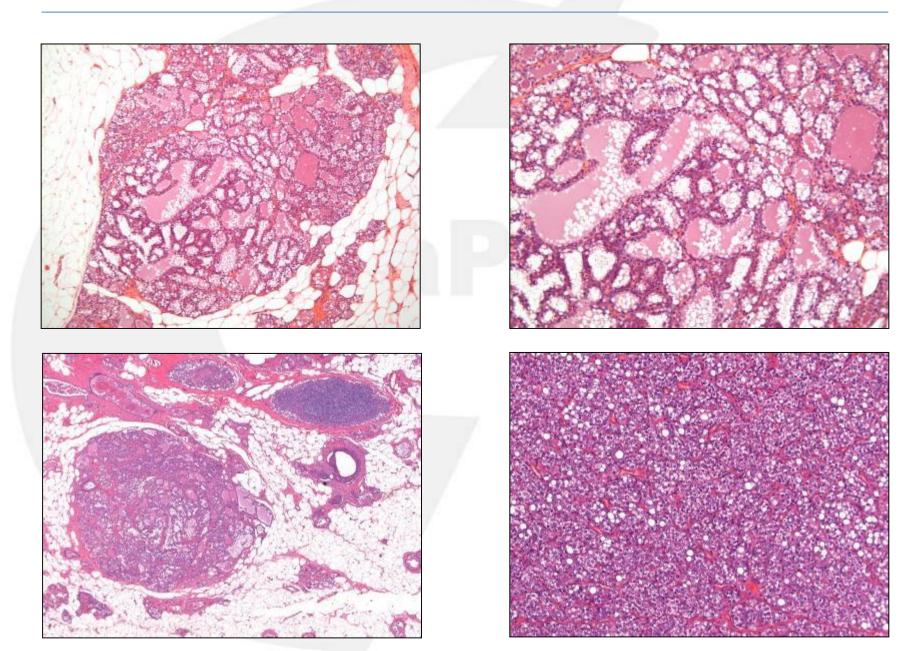
Classification: Mammary Gland - Recommendations

- Hyperplasia (focal with atypia, lobular, ductal)
- Adenoma (alveolar, cystic, papillar, tubular)
- Fibroadenoma (adenomatous, fibromatous) (B)
- Adenocarcinoma (alveolar, comedo, cribriform, cystic, medullary, papillary, scirrhous, solid, spindle cell, tubular)
- Adenocarcinoma arising in fibroadenoma
- Tumor, mixed, benign (adenolipoma type) and malignant (carcinosarcoma type)

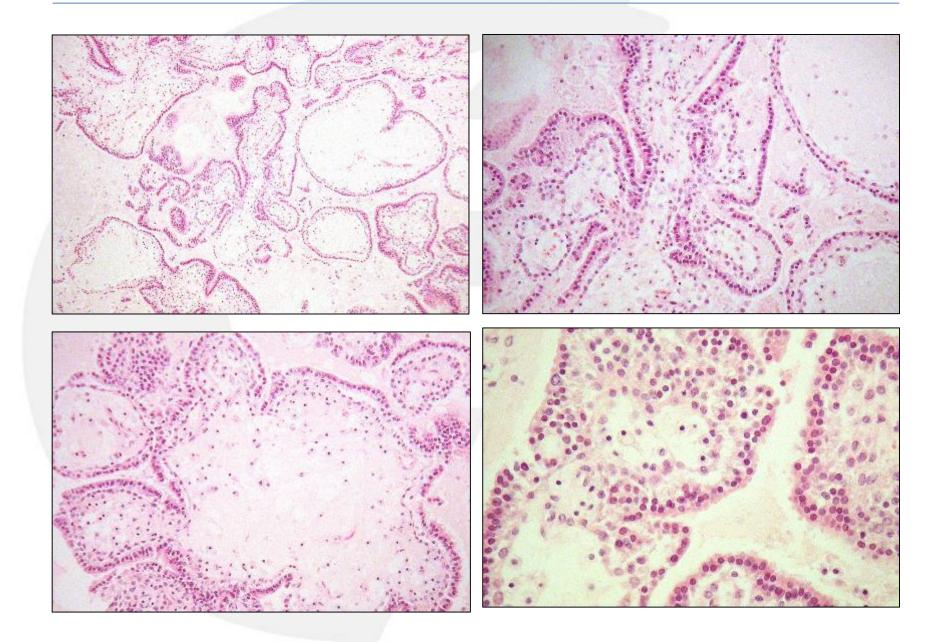
Mammary Gland-Epithelial Neoplasms: Adenoma

- Well demarcated with preserved regular structure
- Cells well differentiated
- Mitosis may be present
- Differential Diagnose: Adenocarcinoma

Mammary Gland, Rat: Adenoma



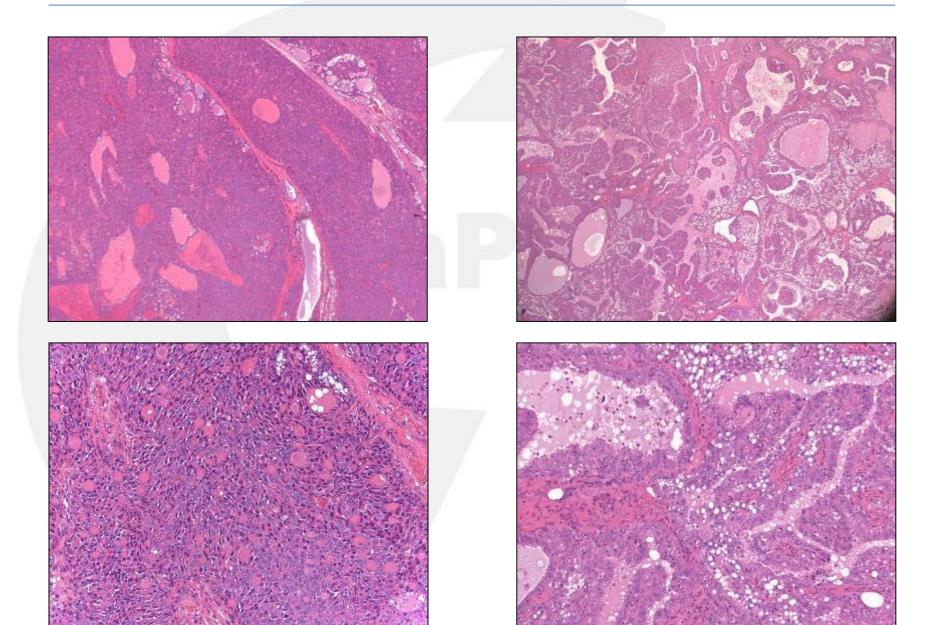
Mammary Gland, Rat: Cystadenoma



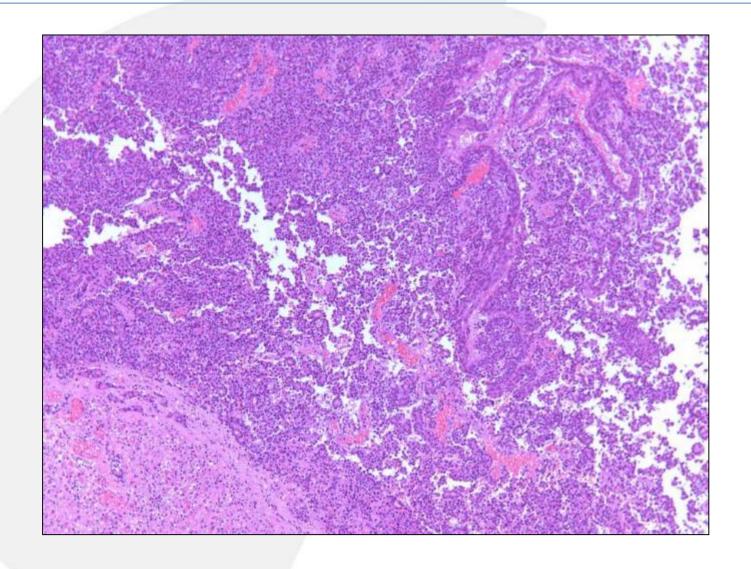
Mammary Gland-Epithelial Neoplasms: Adenocarcinoma

- Occasionally well demarcated
- Do preserved regular structure
- Often different growth patterns in single neoplasm
- Necrosis, hemorrhage, stromal reaction
- Intracystic papillary patterns
- Multilayered cell sheets
- Intraductal type: Attention!
- Differential Diagnose: Adenoacanthoma, Adenoma

Mammary Gland, Rat: Adenocarcinoma



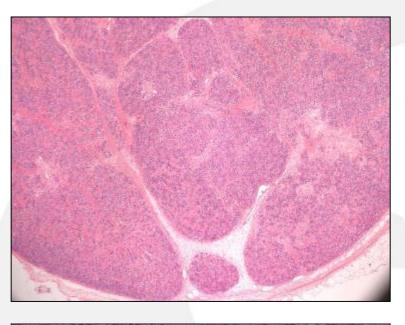
Mammary Gland, Mouse: Adenocarcinoma

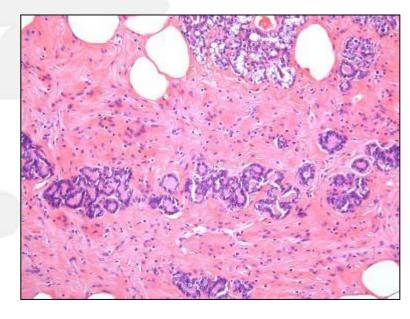


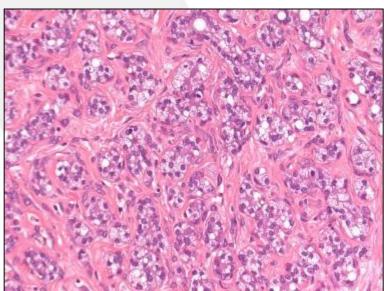
Mammary Gland-Epithelial Neoplasms: Adenofibroma

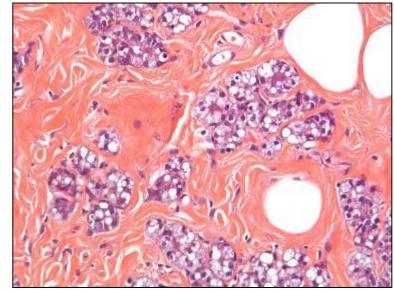
- Glandular epithelium and fibrous connective tissue (amounts may be very variable between single neoplasms)
- Epithelium often forms ducts, nests, sheets, alveoli or small cysts
- Mitosis may be present
- Focal areas of atypia or pleomorphism may be present
- Differential Diagnose: Adenoma, Adenocarcinoma

Mammary Gland, Rat: Adenofibroma

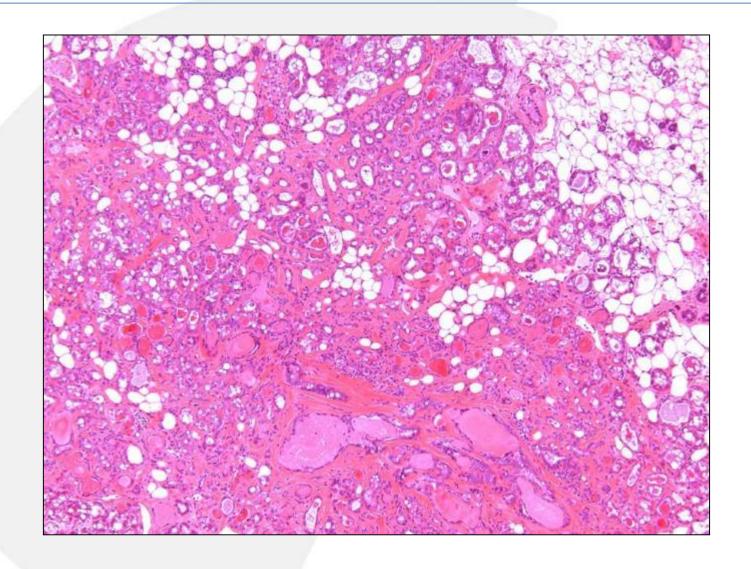








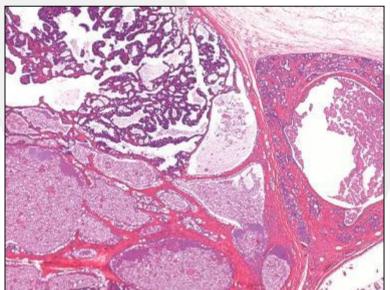
Mammary Gland, Mouse: Adenofibroma

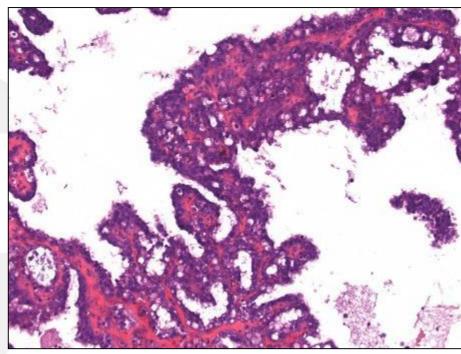


- Two distinct tumor types
- Differential Diagnose: Adenoacanthoma, Adenoma
 Fibroadenoma, Adenocarcinoma

Mammary Gland, Rat: Carcinoma in Adenofibroma



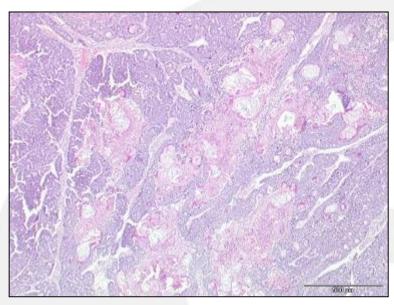


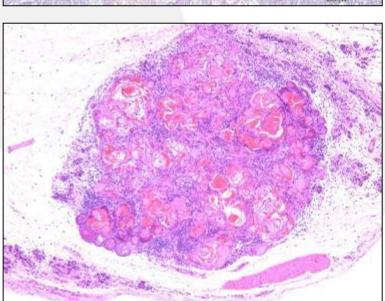


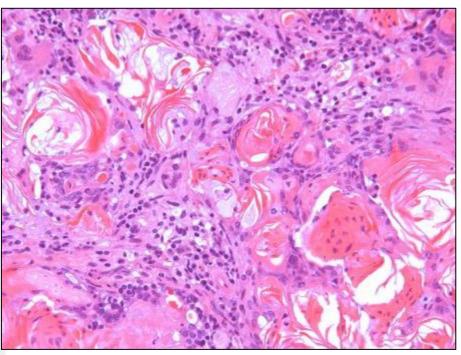
Mammary Gland-Epithelial Neoplasms: Adenoacanthoma

- May be well circumscribed
- Glandular and squamous differentiation
- Squamous areas cover more than 25% of area
- Differential Diagnose: Adenocarcinoma, Squamous carcinoma

Mammary Gland, Mouse: Adenoacanthoma







Mammary Gland-Epithelial Neoplasms: Carcinosarcoma

- Malignant mixed tumor
- Epithelial and mesenchymal components

Differential Diagnose: Adenocarcinoma

Mammary Gland, Rat: Carcinosarcoma

