FEMALE GENITAL TRACT TUMORS
Female genital tract tumors will be treated in each of the known anatomical segments: ovarian tumors; oviductal tumors; uterine tumors; cervical tumors; and vaginal and vulvar tumors. Ovarian tumors are relatively frequent in animals, especially in bitches, cows and mares, while the tumors of the other anatomical segments of the female genital system (oviduct, uterus, cervix, vagina and vulva) have a significantly lower incidence.

Histological Classification of Tumors of the Genital System of Domestic Animals (Kennedy et al. 1998)

Female

1 Tumors of the Ovary

1.1 Sex cord-stromal (gonadostromal) tumors
   1.1.1 Granulosa cell tumor (granulose-theca cell tumor)
   1.1.2 Thecoma (theca cell tumor)
   1.1.3 Interstitial cell tumor (luteoma, lipid cell tumor, steroid cell tumor)

1.2 Germ cell tumors
   1.2.1 Dysgerminoma
   1.2.2 Teratoma
   1.2.3 Embryonal carcinoma

1.3 Epithelial tumors
   1.3.1 Papillary adenoma, papillary cystadenoma
   1.3.2 Papillary adenocarcinoma
   1.3.3 Rete adenoma

1.4 Mesenchymal tumors
   1.4.1 Hemangioma
   1.4.2 Leiomyoma

2 Tumors Metastatic to the Ovary

3 Tumorlike Lesions of the Ovary

3.1 Adenomatous hyperplasia of the rete ovarii
3.2 Papillary hyperplasia of the surface epithelium
3.3 Stromal hyperplasia
3.4 Vascular hamartoma

4 Cysts in and around the Ovary
   4.1 Cysts in the ovary
      4.1.1 Graafian follicle cysts
      4.1.2 Luteinized cysts
      4.1.3 Epithelial inclusion cysts in the mare (fossa cysts)
      4.1.4 Cysts of the subsurface epithelial structures in the bitch
      4.1.5 Cystic rete ovarii
   4.2 Cysts around the ovary
      4.2.1 Cysts of wolffian (mesonephric) tubules and ducts
      4.2.2 Cysts of müllerian (paramesonephric) duct

5 Tumors of the Uterine Tube (Oviduct)
   5.1 Epithelial tumors
      5.1.1 Adenoma
      5.1.2 Adenocarcinoma
   5.2 Mesenchymal tumors
      5.2.1 Lipoma

6 Tumors of the Uterus
   6.1 Epithelial tumors
      6.1.1 Adenoma of the endometrium
      6.1.2 Adenocarcinoma of the endometrium
   6.2 Mesenchymal tumors
      6.2.1 Fibroma
      6.2.2 Leiomyoma
      6.2.3 Leiomyosarcoma

7 Gestational Trophoblastic Disease
   7.1 Subinvolution of placental sites in the bitch

8 Tumorlike Lesions of the Uterus
   8.1 Adenomyosis of the uterus
   8.2 Cystic endometrial hyperplasia
   8.3 Endometrial cysts
   8.4 Endometrial polyp
10.1. TUMORS OF THE OVARY

Ovarian tumors have a higher incidence in bitches, then in cows, mares and ewes. Tumors are bilateral in bitches, appearing in particular on the epithelial surface and in subepithelial structures. In cows, ewes and mares, ovarian tumors are usually bilateral and are derived from the gonadal stroma, being of granular cell type. There are few cases, reported by the literature, of ovarian tumors in felines and swine. Ovarian tumors in cats are similar to those in dogs [3].

The majority of authors have adopted a simple, practical classification, correlated with the tumor evolution based on the histological structure of the ovary, taking into consideration the pluripotency of cell components and their histogenesis.

Classification of ovarian tumors:
1 epithelial tumors: papillary adenoma; papillary adenocarcinoma; cystadenoma; undifferentiated carcinoma;
2 germ cell tumors: dysgerminoma; teratoma;
3 sex cord-stromal tumors: granular cell tumors; thecoma; luteoma;  
4 connective tissue tumors;  
5 secondary (metastatic) tumors;  
6 unclassified tumors;  
7 tumor-like lesions: adenomatous hyperplasia of the rete ovarii; papillary hyperplasia of the ovarian serosae; vascular hamartoma; ovarian cysts.

10.1.1. Epithelial tumors
Epithelial tumors develop from the surface epithelium of the ovary, which is coelomic mesothelium. In domestic animals, these tumors have a predominantly serous character and present a uniformity regarding location, invasiveness, the mitotic index and morphology. Benign and malignant forms are difficult to differentiate in most cases.

Epithelial tumors are frequent in dogs, less in other species, being similar to serous tumors in humans [1]. In bitches, epithelial tumors represent 40–50% of all ovarian neoplasms [8]. Adenocarcinomas represent 64%, of which almost half metastasize [9].

Papillary adenoma, papillary cystadenoma, is a frequently bilateral tumor, usually on the surface of the ovary, developing from the surface epithelium, infiltrating as a tubular invagination in subepithelial structures.

Microscopically, the tumor develops under a papillary and cystadenomatous form, having small polygonal, cuboid or cylindrical cells, sometimes with cilia. The stroma is discrete but well vascularized, being distributed around the cells ranged in a single layer, under a pseudoglandular form, delimiting small spaces, irregular cavities, having a fluid protein content (Fig. 10.1). Cystadenoma has been diagnosed in dogs, being frequently found in association with cystic endometrial hyperplasia. Papillary cystadenomas in bitches may contribute to the appearance of ascites, by the secretion of tumor cells. Tumor formations develop bilaterally, with variable sizes: they can be small, difficult to detect, or they may appear as irregular masses more than 10 mm in
Cystadenoma located in the ovarian bursa has a cauliflower-like aspect and frequently disseminates by implantation in the peritoneum. The cystic aspect of the tumor is also maintained in section (Fig. 10.2, 10.3).

Papillary adenocarcinoma is a tumor frequently found in the canine ovary, usually bilateral, being histologically similar to the benign form, papillary adenoma. The characteristics that differentiate the malignant and benign forms are: tumor size; the mitotic index; invasion of ovarian stroma and extension in the ovarian bursa, in the peritoneum, frequently with metastases by implantation. Cells have a cuboid shape, lying on fine stromal septa, frequently with digital projections in the cystic microcavities, having a clear or slightly pink protein content. More rarely, tumor cells contain mucin or a squamous change (adenoacanthoma) [7] (Fig. 10.4, 10.5).

Undifferentiated carcinoma is a form of carcinoma composed of poorly differentiated cells whose type is difficult to establish.

10.1.2. Germ cell tumors

Germ cell tumors originate from primordial ovarian germ cells, similar to testicular germ cells. Embryonic carcinomas have not been described in animals. Dysgerminomas and teratomas have an equal incidence in female dogs, and together they account for 20% of all ovarian tumors in this species. Metastases represent 20–30%, with locations in abdominal viscera, lymph nodes, bones and lungs [1].

Dysgerminoma, which is also known as embryonic carcinoma, large cell carcinoma and ovarian seminoma, is relatively frequent in dogs and cats, but much rarer compared to testicular seminoma, being also diagnosed in cows and sows. It may have a uni- or bilateral location, it has a smooth surface and soft consistency, and in section it is white-gray, with hemorrhagic or necrotic foci. Metastases are found in 10–20% of cases, and hormone secretory activity is absent, generally appearing in old bitches. Microscopically, the tumor is formed by a uniform cell population,
large round or polygonal cells, with poorly colored cytoplasm, similarly to seminoma. Nuclei are of variable sizes, vesicular, with 1–3 nucleoli, similar to spermatogonia. Giant cells and mitotic forms are frequently identified. Cells are diffuse or arranged in islands or layers. The connective stroma is variable, but is frequently in a low amount. Lymph node or perivascular formations are frequently noted, and large histiocytes, with clear cytoplasm, occasionally appear (Fig. 10.6, 10.7.) [9, 10, 11]. Teratoma has been rarely found in domestic animals, being reported in bitches, sows and mares. These tumors are well differentiated and benign. A tumor thought to arise from totipotential germ cells that have undergone somatic differentiation and given rise to two or more of the embryonic layers with a variety of tissues being present [10] (Fig. 10.8).

Embryonal carcinoma, a germ cell tumor composed of embryonic multipotential cells that are capable of further differentiation, producing a varied histologic pattern [10]. Normal tissues can be structurally identified along with neoplastic tissues, with solid and cystic areas, containing sebaceous material and hair, sometimes skin, cartilage, bone, teeth and muscles, at other times neural, adipose tissue or respiratory epithelium. A reasonable explanation for the appearance of teratoma could be heterozygosity, as a result of meiotic division. Evidence for this is provided by a number of biochemical and cytogenetic studies showing that ovarian teratoma tissues are unique, in the sense that they are formed by XX diploid cells, but are homozygous in chromosomal loci for which the host is heterozygous [3].

10.1.3. Sex cord-stromal (gonadostromal) tumors

Sex cord-stromal tumors are formed from the gonadal, medullary or cortical stroma, from granulosa cells and theca interna cells. These neoplasms have the capacity to secrete hormonally active steroids (estrogen and/or progesterone). The classification of sex cord-stromal tumors depends on the type predominance and cell origin.

Sex cord-stromal tumors are common in cows and mares, and less
frequent in bitches and ewes. Incidence is higher in old cows and in cows under 4 years of age, or even calves. In mares, the mean age is 9 years, between 7 and 16 years. No breed predilection has been found in any species.

Clinically, cows and mares with sex cord-stromal tumors may have an unchanged behavior or they can present the signs of an oversecretion of estrogens and androgens. The manifestation of abnormal signs can last for several months, one year or more. Mares manifest nymphomania or behave like stallions, and cows have the same behavior. The behavior of animals with ovarian sex cord-stromal tumors is deeply changed. Estrus in these cows and mares is usually irregular, prolonged or absent, and animals are infertile. Bitches show signs of hyperestrogenism, manifesting by cystic endometrial hyperplasia, prolonged estrus, enlarged vulva and vaginal secretions. These clinical signs occur in approximately 50% of bitches with sex cord-stromal tumors. In cats, the following have been noted: prolonged estrus, hair loss and thinned pilose covering [6].

Macroscopically, in most cases in mares and cows, these tumors are unilateral, 10–23 cm in diameter. They have an ovoid or spherical shape, they are lobulated, with a flaccid to dense consistency, usually being encapsulated and limited to the ovary. Color is yellow-gray, with red bands and cysts that have a watery, red-brown or yellow content. Necrotic and/or hemorrhagic foci frequently appear in section [4, 6].

Metastases have been found in mares, cats and cows, less in bitches. Granulosa cell tumors have a higher malignancy compared to Sertoli cell tumors. Metastases in the peritoneum, large ligaments, spleen, liver and lungs, lumbosacral, retroperitoneal and abdominal parenchymatous organ lymph nodes have been found. Granulosa-theca cell tumors or granulosa cell tumors have a benign character, they are unilateral, incidence increases with age, but they have also been diagnosed in young animals.

Macroscopically, the tumor ranges between 4 and 16 cm in diameter, it has a soft to dense nodular consistency. In section,
dense areas, cysts and frequent hemorrhages and/or necroses are found, of white-gray or yellow color. Some tumor forms produce steroids, which determines the appearance of characteristic clinical signs, especially in cows and mares. Microscopically, cells are similar to normal granulosa cells, appearing as a uniform population, with poorly colored cytoplasm, poorly delimited, with round or ovoid eccentric nuclei, few or no mitoses (Fig. 10.12 and 10.13). Tumor cells can be arranged under the form of: diffuse sarcoma; long cords; islands delimited by connective septa; follicles, in which cells may group forming spaces or foci with protein material, similar to Call-Exner bodies from granulosa cells in humans [7].

In mares, these tumors are relatively frequent, and clinical manifestations consist of anestrus, continuous and intermittent estrus, and male behavior. Affected animals have high plasma testosterone levels. The ovary without tumor is atrophied. The microscopic tumor is characterized by microcysts and prominent tubes, lined by double cell layers, with basal ovoid nuclei. In some microscopic fields, structure is of follicular type. Some cells have abundant, poorly colored cytoplasm, similar to testicular Sertoli cells, the connective stroma being well represented in the tumor mass [3].

In cows, tumors formed by granulosa cells and Sertoli tumors are described. The incidence of these tumors is lower in this species. Neoplasms formed by granulosa cells have a microfollicular structure, with follicles of variable sizes, lined by cells similar to follicular epithelium, to normal de Graaf follicle [6]. Cells are arranged in one, two or more layers. The lumen of microfollicles contains acidophilic homogeneous or granular material. Follicular cells can appear in the lumen, suggesting a cumulus oophorour aspect (Fig. 10.9), or proliferations can be of papillary type, similar to a cystic papillary carcinoma. Tumor cells under the form of solid masses or small rosettes have been noted, suggesting embryonic follicles. Neoplastic cells are round or ovoid, fusiform,
similar to normal follicular cells. Sizes are variable, with round or ovoid hyperchromatic nuclei, the cytoplasm is vacuolated. Mitoses are present, sometimes in a high number.

Microscopically, **neoplasms formed by Sertoli cells** show a tubular or fascicular growth, with connective septa. The cell cytoplasm is vacuolated, amphophilic staining. Cells have elongated shapes, frequently with sharp tips, fusiform cells being exceptional. Nuclei are small, uniform, vesicular, nucleoli are inapparent, mitoses are rare. Sertoli cell tumors, in animals, are not identical to those in women, in which Leydig cells and immature mesenchymal structure also appear.

The origin of Sertoli cells in the ovary is explained by the common origin of female and male gonads, from the same primordia.

In bitches, stromal ovarian neoplasms microscopically appear composed of three cell types: granulosa cell tumors; Sertoli cell tumors; and non-specific gonadal tumors. In this species, these tumors coexist with cystic endometrial hyperplasia and pyometra. **Granulosa cell tumors** are composed of cells similar to developing follicles. Cells are round, with small hyperchromatic nuclei, of variable sizes, and mitoses are numerous. Some cells are similar to Sertoli cells, with foamy and poorly colored cytoplasm. **Sertoli cell tumors** are formed by elongated cells, frequently with sharp tips, with foamy or clear cytoplasm, with small uniform nuclei. Mitoses are in a low number. Cells are arranged in tubular columns, bundles or clusters, separated by fine connective tissue septa (Fig. 10.10, 10.11).

**Non-specific gonadal tumors** are formed by cells similar to granulosa cells. Mitoses are rare and anaplastic foci appear. In cats, granulosa cell tumors are predominant. Cells are small, with eccentric hyperchromatic nuclei; cells form microfollicles or Call Exner bodies with tumor cells arranged radially around eosinophilic material. Mitoses and cellular atypias are obvious. In this species, a tumor with lipid, round, uniform and well delimited cells can appear, some of which are similar to Leydig cells [6].
Thecoma or theca cell tumor is exclusively composed of theca cells, which are fusiform or stellate, well delimited, arranged in bundles. Nuclei are ovoid, elongated or fusiform, the cytoplasm is pale, with lipid drops. Usually, thecoma is a benign tumor with expansive growth, without metastases [7] (Fig. 10.14). Luteoma is a rare tumor that has been reported in cows, female dogs and cats. Some authors consider it to be similar to thecoma [3].

Macroscopically, the tumor is large, of yellow-brown color. Microscopically, it is formed by a population of large, uniform lutein cells, similar to those of the corpus luteum. Lipid cell tumors and Leydig cell tumors have been identified. Lipid cell tumors are known in cats. Histologically, they are formed by large cells, loaded with lipids, similar to those of the adrenal cortex, with small nuclei and well delimited margins. Leydig cell tumors have a low incidence in domestic animals. Cells are uniform in shape and size, polygonal, well delimited, with dark, granular cytoplasm, with numerous lipid vacuoles. Nuclei are small, ovoid and hyperchromatic, with small nuclei and numerous mitoses. The connective stroma is fine, with numerous capillaries, delimiting in some tumors pseudolobular forms.

10.1.4. Connective tissue tumors

Connective tissue tumors of the ovary are classified and have the characteristics known from the chapter concerned. Hemangiomas and leiomyomas have a higher incidence. Ovarian hemangioma is rare in domestic animals, except for swine. The tumor appears in adult and old sows. Macroscopically, it has a globular, well circumscribed form, red-brown color, smooth surface, with obvious superficial vascularization. The tumor develops in the ovarian cortex and occasionally it can be bilateral. Microscopically, the tumor is composed of well differentiated endothelial cells, forming capillaries with erythrocytes in the lumen. The connective tissue delimits vascular areas. No malignant forms of these tumors have been reported. Leiomyoma develops from the smooth muscle fibers of the
mesovarium and has been reported in bitches and sows. Rats treated with beta-adrenergic receptor stimulants have developed mesovarian leiomyomas [3].

**10.1.5. Metastatic tumors**

Ovarian metastases of neoplasms from other tissues or organs are rare in domestic animals. Ovarian metastases from breast carcinomas have been found in bitches, and uterine and intestinal carcinomas in cows can metastasize in the ovaries. In female dogs and cats, metastases of pancreatic carcinomas are reported in the ovaries [7].

**10.1.6. Tumorlike lesions**

Adenomatous hyperplasia of the rete ovarii is a rare lesion, which has been described in dogs. The peripheral epithelium forms gland-like structures, located in the ovarian capsule. These lesions could be considered preneoplastic, and their functional potential is not known.

Papillary hyperplasia of the ovarian serosa occurs as a result of prolonged estrogen stimulation. The lesion appears bilaterally, with papillary proliferations on the ovarian serosa; it occurs in the bitch.

Stromal hyperplasia, the nonneoplastic proliferation of ovarian stroma; it is usually bilateral and occurs in older animals [10].

Vascular hamartoma is a congenital abnormality that is rare in cows, sows and bitches. The lesion appears as a vascular, arterial or venous malformation, in a connective tissue mass. Macroscopically, it has large sizes, weighing several kilograms. Due to vascular thrombosis, edema, hemorrhage and necrosis occur, followed by connective tissue proliferation. Small hamartomas are clearly delimited from the ovarian tissue, but the ovarian mass is gradually incorporated. Differential diagnosis between hemangioma and vascular hamartoma is difficult [3].

Cysts in and around the ovary. Cyst formation in and around the ovary in domestic animals is common. In many cases, the lining cells degenerate and determining the origin of the cyst may be difficult.
Ovarian cysts frequently occur in domestic animals, especially in bitches, sows and cows. The anatomical and histological structure of ovarian cysts is difficult to determine, requiring a thorough examination and multiple sections in various areas, for microscopic examination.

*Graafian follicle cysts* can be solitary or multiple and are frequent in all species. They have a special importance for cows and sows, in which they manifest by nymphomania. Cysts have a clear liquid, with the presence of granulosa cells in the wall of small formations, and a single cuboid or flat cell layer in large formations, sometimes granulosa cells being absent.

*Luteinized cysts* occur in mature follicles that have undergone the luteinization of the theca interna and the total cysting of the luteal tissue line. These cysts have a spherical cavity, without projecting on the ovarian surface, and are common only in the cow and sow. *Corpus luteum cysts* appear after ovulation, but the follicle rupture surface closes prematurely and blocks the fluid in the center of the corpus luteum. The ovular cavity is present and the cyst has an irregular outline (Fig. 10.15).

*Rete tubules cysts* are found in the majority of domestic animal species, frequently in dogs and cats. The tubular network is located in the ovarian hilar region. Cyst growth induces the compression of the ovarian cortex (Fig. 10.16 and 10.17).

**Cysts around the ovary**

Cysts of wolffian (mesonephric) tubules and ducts or paraovarian cysts are single or multiple, having sizes that range from several millimeters to several centimeters in diameter. Locations are in the mesovarian tissue or in the mesosalpinx. Cysts originating from the mesonephric ducts contain a clear liquid and are lined by cuboid cells. Smooth muscle fibers surround the cysts. The anterior mesonephric ducts have mesonephric remnants that frequently become cysts. These structures are located in the lateral pole of the ovary adjacent to the fimbrial oviductal area. In mares, cysts are 6–8 cm in diameter [7] (Fig. 10.18). Cysts of müllerian (paramesonephric) duct, most are located near
the fimbria of the uterine tube. Surgical treatment is indicated in all ovarian tumors, ovariohysterectomy being recommended, since it prevents the dissemination of neoplastic cells in the abdominal cavity. For malignant tumors, especially when metastases have developed after excision and hormone treatment, prognosis, even reserved, is difficult to predict [8]. In the case of cystadenocarcinomas, cyclophosphamide, chlorambucil and intracavitary bleomycin treatment may be attempted. Good results can be obtained in the case of granulosa cell tumors, even with metastases, by immunotherapy using mixed bacterial toxin [2].

10.2. TUMORS OF THE UTERINE TUBE (OVIDUCT)
Tumors of the uterine tube are rare in domestic mammals, but are not rare in chickens [10]. Oviductal tumors are extremely rare in all domestic mammalians; a moderate frequency is found in chickens. Oviductal tumors have been reported in dogs, horses, cats, sheep, swine and cattle [5]. A classification of oviductal tumors includes the following forms:
1 epithelial tumors: adenoma and adenocarcinoma;
2 mesenchymal tumors: lipoma;
3 tumor-like lesions.

10.2.1. Epithelial tumors
Adenoma has been described in bitches, as a formation adjacent to the ovary; microscopically, papillary proliferation with mature epithelium is detected, and in other areas, fibrous connective tissue with smooth muscle fiber elements appears. Adenocarcinoma has been reported in dogs, as an epithelial tumor with implantations in the abdominal cavity. Histologically, the tumor is similar to adenoma.

10.2.2. Mesenchymal tumors
Lipoma is a rare oviductal tumor that is located in the ovarian bursa of dogs. The lipomatous mass has the characteristics of mature adipose tissue.

10.2.3. Tumorlike lesions
The majority of domestic mammals can have paramesonephric cysts, attached to the fimbriated end of the salpinx. In large species, these formations can be several centimeters in diameter.

**10.3. TUMORS OF THE UTERUS**

Uterine tumors in domestic animals are uncommon, leiomyoma in cows and bitches, as well as uterine carcinoma in cows being more frequent. The incidence of uterine tumors in domestic animals could be higher, but systematic follow-up and the thorough examination of the uterus in the slaughter house and on necropsy leaves to be desired. The classification of uterine tumors takes into consideration the histological structure of this segment:

1. epithelial tumors: adenoma and adenocarcinoma;
2. mesenchymal tumors: fibroma; fibrosarcoma; leiomyoma;
   - leiomyosarcoma; lipoma and lymphoma;
3. unclassified tumors;
4. tumor-like lesions: adenomatosis, cystic endometrial hyperplasia; endometrial polyp; lymphangiectasia; mesonephric duct cysts; serous cysts; subinvolutioned placental sites and squamous metaplasia [5].

**10.3.1. Epithelial tumors**

Adenoma is a rare tumor that consists of discrete nodules, being a well differentiated endometrial glandular tissue. The stromal and adenomatous component may exist in extremely various ratios, from one subject to another. Sometimes, it may have a polyploid aspect, with proliferations in the uterine lumen.

Adenocarcinoma of the endometrium is a neoplasm found in cattle and rabbits, being exceptionally reported in other species (cats and dogs). It occurs in old cows, usually after the age of 7 years, being difficult to diagnose clinically, except for cases in which the subject presents extensive metastases in the lymph nodes and lungs.

Macroscopically, uterine carcinoma appears as single or multiple nodules, with a dense structure and uneven distribution in the uterine wall, more frequently in the uterine horns, more rarely in the cervical uterine corpus. The tumor infiltrates deep in the
myometrium, without being in relation to endometrial epithelium. The uterine wall is significantly thickened, sometimes it can reach 10 cm, having an annular arrangement, which determines the significant narrowing of the lumen. The umbilication of the serosa is mentioned, with an aspect characteristic of this neoplasm. Microscopically, uterine carcinoma in cows has a scirrhous character, with infiltrative growth in the myometrium, being intensely vascularized and with frequent muscle bundles. The tumor develops from the deep uterine glands and is clearly distinguished from normal structures. The neoplasm is formed by glands with irregular shapes and sizes, and cells are stratified and without polarity. Cells are large, pleomorphic, with abundant cytoplasm, large, vesicular nuclei and numerous mitoses. The gland lumen contains amorphous eosinophilic material. The stromal connective tissue has an aspect of intense proliferation. The rate of metastases in lymph nodes and lungs is high. Lymph nodes, especially iliac ones, are enlarged in volume, sometimes 10-fold larger than normal, having a bosselated surface with numerous nodules. Lung metastases are usually bilateral, affecting all lobes; more rarely, metastases are reported in the liver, visceral peritoneum or other viscera [6]. In dogs and cats, adenocarcinoma is non-sclerotic, having a typical character of distinct proliferation in the endometrium. The tumor is frequently well differentiated, with a glandular structure, formations with a distinct lumen, lined by cylindrical cells, multinucleated cells also being noted. Fibrosis is present (Fig. 10.19 and 10.20). The factors that determine uterine carcinoma in domestic animals are little defined, and the comparison to what is known in women proves the presence of special conditions in the latter case. Prolonged estrogenicity, with cystic endometrial hyperplasia, represents precancerous lesions in women, which induce the development of this neoplasm [8].

10.3.2. Mesenchymal tumors

Fibroma is a benign tumor, of hard consistency, white color, spherical or ovoid shape, located in the uterine wall. Incidence is
sporadic in bitches and cows, the tumor being frequently single, and more rarely multiple. Microscopically, the tumor is formed by fibrous connective tissue. Fibrosarcoma is a rare neoplasm in all domestic animal species, several cases have been reported in cows, mares and bitches. The microscopic structure is that characteristic of fibrosarcoma described in the chapter on connective tissue tumors. Leiomyoma is a nodular tumor, of firm consistency, brown color, being reported in cattle and cats, more frequently in dogs. In dogs and cats, 85–90% of uterine cases are estimated to be leiomyomas [8]. In bitches, the tumor appears at middle and old age, being frequently associated with ovarian follicular cysts and also with endometrial hyperplasia, mammary hyperplasia and mammary neoplasm. Bitches castrated at a young age do not develop leiomyoma, and in subjects with leiomyomas, the disease regresses after castration. The administration of low estrogen amounts in female Guinea pigs induces leiomyoma. In general, clinical evolution is asymptotic, sometimes it can be associated with vaginal secretion or pyometra, and in the case of large tumors, it compresses the neighboring organs (intestines or urinary tract) [3]. Macroscopically, leiomyoma can reach 10–12 cm in diameter, without being invasive. Initially, when the tumor is small, it has a fleshy consistency, which becomes firm or even hard as it develops, hence the term fibroid, due to stromal connective tissue. The section surface is wet, shiny, pink or white. The tumor is not encapsulated, but is well delimited. In most cases, the tumor projects like a nodular tumor into the uterine, vaginal or cervical lumen. The tumor may develop in two directions: the progressive development of muscle tissue in a mass of fibrous connective tissue, or the appearance of edema and liquefying and cysting of the tumor. In the first case, fibrosis progresses by hyalinization and mineralization. In the second case, leiomyoma, especially vaginal leiomyoma, which is pedunculated and poorly vascularized, degenerates. Histologically, the tumor is formed by smooth muscle fibers,
anarchically arranged in a mass of stromal connective tissue. Muscle fibers can have a vortex arrangement, under the form of nests, being covered with normal epithelium at the surface [3] (Fig. 10.22, 10.23).

Leiomyosarcoma is a rare neoplasm, being sporadically reported in cats, cattle, dogs and horses. The macro- and microscopic characteristics are those known for leiomyosarcoma, but it is cellularized, with large hyperchromatic nuclei and moderate mitotic index [5] (Fig. 10.24).

Lipoma is a rarely diagnosed tumor, being located at the site of insertion of large ligaments, in dogs. Histologically, adipose cells are found. The transformation into liposarcoma has not been reported.

Malignant lymphoma is common in cows, more rarely in bitches, sows, mares and cats. The microscopic structure is similar to lymphomas of other organs.

10.3.3. Tumorlike lesions of the uterus

Adenomyosis of the uterus refers to the presence of the endometrium in the myometrium. Endometrial glands have a stromal support with large numerous blood vessels. The disease should not be confused with endometriosis. This disorder has been noted in numerous laboratory monkey species. Sporadic adenomyosis has been found in most species, but more frequently in cats, cattle and dogs. In the bitch, it is often associated with cystic endometrial hyperplasia [10,11].

Cystic endometrial hyperplasia is the result of estrogen or progesterone stimulation. In sheep and cattle, cystic endometrial hyperplasia is associated with estrogen stimulation, either from the ovary, or by estrogen injections or accidental clover ingestion.

In bitches, three morphological types of endometrial hyperplasia are distinguished: the cystic hyperplasia-pyometra complex, mainly induced by progesterone; cystic hyperplasia caused by certain estrogenic compounds; false gestation (Fig. 10.21).

Diffuse patterns of cystic endometrial hyperplasia are produced in the cow, bitch and ewe by hyperestrogenism. In the dog and cat,
focal forms of endometrial hyperplasia are more common than diffuse. The cells that line the cysts with papillary infolding and the nondistended glands as well as the luminal surface are cuboidal to low columnar and have scant cytoplasm. There is only modest stromal proliferation and usually no inflammation.

In sows and mares, cystic endometrial hyperplasia does not have a well established etiology [10,11]. Endometrial cysts may be the result of endometritis or hormonal stimulation, but the resultant cysts may persist long after the initial cause has been removed. Small cysts are common adjacent to caruncles in ruminants. Cystic endometrial glands are lined by flattened epithelium and surrounded by varying amounts of fibrous connective tissue [10].

Endometrial polyps are focal endometrial proliferations with stromal elements of the endometrium, found in dogs and cats. The stroma is frequently edematous.

Lymphangiectasia is a dilation of lymphatic vessels, in the ventral portion of the uterine corpus of old mares; it also occurs in sows; focal areas of lymphangiectasia in the myometrium occur in the bitch and cow.

Mesonephric duct cysts, which are remnants of these mesonephric ducts, can persist in the endometrium and the myometrium, in almost all domestic animals. In dogs and cows, large cysts occur in the uterine wall. Usually, epithelium is cuboid, with clear cytoplasm, the ducts being surrounded by two muscle layers. Serosal cysts are delimited from the peritoneum and appear on the uterine serosa in mature or old cows and bitches. In bitches, they appear as prominent formations at antimesometrial uterine level, while in cows they develop on the intercornual ligament.

Subinvolutioned placental sites. These lesions are more common in dogs, most of them around the age of three years. Macroscopically, large placental adherence sites occur. Microscopy shows large cells with eosinophilic cytoplasm in a connective mass, infiltration of plasmacytes, lymphocytes and macrophages with hemosiderin. Numerous eosinophils invade the myometrium.
Squamous metaplasia appears on the surface of the endometrium, occasionally in pyometra cases, in most domestic species. Sometimes, the endometrium can change into squamous type epithelium. Tumors metastatic to the uterus are common in lymphoma in cattle, less so in horses; they are rare in other species; serosal implantations do occur in peritoneal carcinomatosis [10].

10.4. CERVICAL TUMORS
In general, cervical tumors are identical to uterine neoplasms. These are: *fibroma, leiomyoma, sarcoma* and *unclassified tumors*. Tumor-like lesions at the level of the cervix mainly include: *epithelial cysts; fibrosis* and *squamous metaplasia*.

10.5. TUMORS OF THE VAGINA AND VULVA
Vaginal and vulvar tumors are morphologically similar to penile and uterine tumors. The classification of vaginal and vulvar tumors includes the following types:

1 epithelial tumors: papilloma (transmissible genital papilloma in pigs);
2 fibropapilloma;
3 leiomyoma;
4 canine transmissible venereal tumors;
5 malignant lymphoma;
6 fibrosarcoma;
7 vascular tumors;
8 malignant melanoma;
9 unclassified tumors;
10 tumor-like lesions; Gartner duct cysts; Bartholin gland cysts; granular vaginitis; herniated adipose tissue; estrous vulvar edema.

10.5.1. Epithelial tumors
Papilloma is a rare benign tumor, with a papilliform proliferation aspect, having the connective stroma covered by keratinized epithelium. It is usually small, but sometimes it may have large sizes. The papilloma implantation base is infiltrated with
lymphoplasmacytes. The tumor is induced by a venereally transmitted virus that appears in swine. Transmissible genital papilloma in pigs appears in the preputial diverticulum of the boar. The lesion can be experimentally reproduced by the scarification of the vulvar mucosa. The lesion can be transmitted by the sexual act to sows and it has sizes between 1 and 3 cm, a papular aspect; sometimes, lesions are larger, being of papillary type. Clinical evolution may last for several weeks, after which the lesion starts to regress or desquamate. The animal is immune to reinfection. Microscopically, it has a typical papillomatous character, with extensive uneven acanthosis of the covering epithelium, with a weak mesodermal reaction. The thickened malpighian layer contains dispersed cells with intracytoplasmic inclusions. Inclusions are large, spherical, homogeneously acidophilic, surrounded by a halo. An infiltration with mononuclear cells is found at the base of the tumor in the dermis [3]. Squamous cell carcinoma is almost exclusively found in cows, but it has also been described in sheep exposed for a longer time to solar radiation, also in mares and bitches. Macroscopically, the neoplasm is identified on the vaginal mucosa or at the junction of the vulvar mucosa with the skin, appearing almost exclusively in the unpigmented vulva or vulvar areas. In section, nodules or firm bundles of homogeneous tissue are detected, of yellow or gray color, with necrotic and/or hemorrhagic foci, separated by fibrous white-gray bands of stromal connective tissue. Depending on the intensity of keratinization, the neoplasm can have a soft, firm, dry or wet consistency. Histological structure is different depending on the carcinoma stage. In the early stage, the horny layer shows a thickening under the form of foci, the granular layer is non-uniform, and the spinous layer cells become more elongated and sharp. The dermal connective tissue is less dense and slightly edematous, being intensely vascularized, with slight eosinophilic and lymphocytic infiltration. Sebaceous glands are large and more active, compared
to normal areas. In the acanthotic stage, hyperkeratosis is moderate; the spinous cell layer is hyperplastic, with large irregular cells, hyperchromatic nuclei and pale cytoplasm. Basal cells have an irregular palisade arrangement, and are round. Dermal papillae are intensely vascularized, with eosinophilic and lymphocytic infiltration. Sebaceous glands are large and active, some of them being cystic. The tumor grows similarly to papilloma, with marked acanthosis. The early carcinoma develops in acanthotic and papillomatous areas, under the form of foci formed by round or oval cells, with pale cytoplasm, poorly evidenced outline, large nuclei of various sizes. The general aspect is of malignization, with a spiral cell arrangement. A penetration of the significantly elongated spinous cells gradually appears, and the basal layer cells are irregularly arranged in palisades. Epithelial buds develop from cells that no longer resemble the cells of origin. Keratinized cells appear under the form of epithelial pearls, and peripheral cells from these epithelial buds proliferate and infiltrate in all directions. Vaginal squamous cell carcinoma finally has all the growth and structural characteristics of squamous cell carcinoma developed in other skin areas. In the depth and around carcinomatous cells, a fibrous stroma with lymphocytic infiltration develops. Vulvar squamous cell carcinoma metastasizes in regional lymph nodes and lungs [6].

10.5.2. Fibropapilloma of cattle

Vulvar fibropapilloma is a benign tumor, common in young cattle. Bovine papillomavirus is incriminated in the etiology of the tumor, which causes the appearance of papillomas, with a relative growth of the connective tissue and a marked thickening of the epidermis. The tumor can be transplanted from the vulva to the penis and vice versa. Macroscopically, tumors are usually sessile, initially round, then they gradually become cauliflower-like or fungoid, less than 3 cm in diameter, with a large implantation base. Large tumors are frequently ulcerated or they bleed. Spontaneous regression seems
to be frequent, extending over a period of 1–6 months or more. There are occasional tumor recurrences after excision. Microscopically, the tumor is formed by bundles of fibroblasts and epithelial proliferations that develop in the fibromatous mass. In early tumor growth, numerous mitotic figures are found, which makes difficult the differentiation from fibrosarcoma. There are numerous fusiform cells with large nuclei, bizarre nucleoli, and pale eosinophilic intranuclear inclusions some-times appear. Stromal collagen formations gradually develop into fibrosis. In the case of superficial ulcerations, inflammatory reaction appears [3, 5].

10.5.3. Vulvar leiomyoma
Vulvar leiomyomas are benign nodular, whitish and firm tumors, being common in dogs. These tumors are formed by bands of smooth muscle fibers that alternate with collagen bundles.

10.5.4. Transmissible venereal tumors
Transmissible venereal tumors are formed by diffuse or nest-like submucosal cell masses that extend in the generating layer of the mucosa. The surface epithelium is frequently hyperplastic and sometimes ulcerated. The trabecular connective tissue contains congested blood vessels that traverse the neoplastic mass. Neoplastic cells have a low density, the cytoplasm is poorly delimited, oval or round, eosinophilic, with large round to oval nuclei, mitotic figures are common. Chromatin is fine, dispersed, with visible nucleoli, and mitoses are frequent. In some tumors, lymphocytes and plasmacytes are present, in others they are absent, eosinophilia is found in many neoplasms. Metastases are not a rule, but they can be found in regional lymph nodes (Fig. 12.4. and 12.5.). Spontaneous regression is frequently found 2 months after onset. Transmissible venereal tumors of the vagina are identical to those found in males.

10.5.5. Sporadic vaginal and vulvar tumors
Malignant lymphoma is frequent in cattle, and rare in dogs, swine and cats. Its structure and behavior are identical to those of the
malignant lymphoma of the hematopoietic tissue and lymph nodes. Fibrosarcoma is a rare tumor in the majority of domestic animals, some cases being reported in cows, mares and bitches. Morphologically, the neoplasm has all the characteristics of connective tissue fibrosarcoma presented in the chapter concerned. Vascular tumors, such as hemangioma and hemangiosarcoma, are rare at this level and they morphologically correspond to the types described for connective tissue neoplasms. Melanoma and melanocytoma are tumors that are found in particular in white mares, under the form of large ulcerated nodules, located in the vulva or the perineum. Unclassified tumors are proliferative formations that cannot be included in the categories mentioned and described in the previous chapters.

10.5.6. Tumorlike lesions

Gartner duct cysts are in general extremely rare in virgin females; in contrast, they can be frequently diagnosed in multiparous females, in which vaginal infections are also found. Bartholin gland cysts occur post-inflammation and they can be associated with ovarian cysts in the cow. Granular vaginitis is a common disease in cows, with the involvement of submucosal lymphoid follicles, appearing under a nodular form in the vaginal and vulvar mucosa. Herniated adipose tissue is found in excessively fat cows, at the junction between the vulva and the vagina. It appears as an adipose perineal mass, which projects in the lumen of the genital tract. Estrual edema of the vulva appears in the subepithelial connective tissue of bitches, with a diffuse aspect. Fibrosis develops in chronic evolution. In swine, ingestion of an estrogenic mycotoxin, zearalenone, which is produced by fungi of the genus *Fusarium*, causes congestion and edematous swelling of the vulva and vagina.

BIBLIOGRAPHY


Patnaik AK, Greenlee PG. Canine ovarian neoplasms: A clini-


Fig. 10.1 Papillary adenoma, ovary. *)
Fig. 10.2 Cystadenoma. *)
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Footnotes

*Courtesy of W.H.O.

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Cystadenoma. *)

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Dysgerminoma. *)

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