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CASE I – EPL 3-25-05 (AFIP 2986960)

Signalment: One-year-old, golden retriever, canine (*Canis familiaris*), phenotypic female.

History: Canine presented for a routine ovariohysterectomy.

Gross Pathology: An enlarged clitoris was noted on physical exam. Two intraabdominal gonads were present and situated in the correct anatomical location expected for normal ovaries. One gonad appeared normal. The other gonad is smaller and has a firm cord of tissue on one edge resembling an epididymis. The uterine horn adjacent to the abnormal gonad exhibited segmental hypoplasia/aplasia. The remaining uterus appeared normal.

Histopathologic Description: Histologically the abnormal gonad contained both male and female characteristics. On one edge of the gonad, was a thick cord of fibromuscular tissue containing several tubular structures lined by cuboidal to low columnar epithelium with stereocilia. This structure appeared consistent with an epididymis. The majority of the gonad consisted of sheets or small aggregates of large polygonal cells containing eosinophilic vacuolated cytoplasm (consistent with interstitial cells) interrupted by occasional tubular structures that did not resemble normal ovarian follicles or seminiferous tubules. These tubules were lined by polygonal to spindle shaped cells containing vacuolated basophilic cytoplasm and exhibited a mild degree of anisokaryosis (atypical sex cord stromal cells). In several tubules, these cells appeared consistent with Sertoli cells looking similar to atrophied seminiferous tubules. A single layer of flattened cuboidal epithelium lined

the external surface of this gonad (ovarian surface epithelium) with numerous tubular infoldings into the underlying superficial stroma (subsurface epithelial structures). The contralateral gonad was histologically unremarkable appearing consistent with a normal canine ovary (not present on slide).

Contributor's Morphologic Diagnosis: Ovotestis, unilateral

AFIP Diagnoses: 1. Gonad: Ovotestis, Golden Retriever, canine.
2. Uterus: Essentially normal tissue.

Conference Comment: The gonad contains both ovarian and testicular tissue. Ovarian features include the subsurface epithelial structures (SES) and surrounding ovarian bursa (not present in all slides). Testicular features include an epididymis, tubular structures resembling seminiferous tubules lined by Sertoli-like cells and abundant eosinophilic polygonal cells resembling interstitial or Leydig cells. In some sections of the gonad there is an expansile focus of sex cord germinal cells which may represent the early development of an interstitial cell tumor. Additionally, some slides contain a region of highly convoluted veins suggestive of pampiniform plexus, which is further evidence of testicular development.

Normal sexual differentiation in mammals requires successful completion of a series of consecutive steps under genetic control. These steps are marked by the establishment of chromosomal sex, gonadal sex, and phenotypic sex. Intersexuality is a general term currently used to describe ambiguity among any of these levels of development.

Chromosomal sex is normally determined at fertilization by the formation of either an XY or XX zygote. Studies in mice indicate that expression of the *Sry* (sex-determining region Y) gene located on the Y chromosome is responsible for initiating the cascade of events that are responsible for testicular differentiation. *Sry* also directs the differentiation of germ cells to form Sertoli cells in the developing testis. Sertoli cells are responsible for the secretion of antimüllerian hormone (AMH) which results in regression of the Müllerian duct, which normally develops into the oviduct, uterus and upper part of the vagina in female embryos. Cells in the interstitial space surrounding the developing testis cords differentiate into testosterone-producing Leydig cells. Testosterone, converted to the biologically active form dihydrotestosterone by the enzyme 5-alpha reductase, allows development of the vas deferens and epididymides from the Wolffian ducts and induces the development of the prostate gland and penis. (5) In the absence of the Y chromosome and *Sry* gene, the default pathway to female gonadal sexual

differentiation is initiated. Clitorimegaly, as seen in this case, is a characteristic feature of hermaphroditism and develops under the influence of testosterone.

Hermaphrodites are classified according to the morphology of the gonads present. A true hermaphrodite has at least one gonad containing ovarian and testicular tissue (i.e. an ovotestis) or has one male and one female gonad. A pseudohermaphrodite has gonads of one sex and accessory reproductive organs of the opposite sex. A male pseudohermaphrodite has testes and female accessory sex organs; a female pseudohermaphrodite has ovaries and male accessory reproductive organs.

Another well-described anomaly of development is freemartinism. Freemartinism is an abnormality of chromosomal sex, in contrast to true hermaphrodism and pseudohermaphrodism which are abnormalities of gonadal sex and phenotypic sex, respectively. (3)

Freemartinism is primarily described in cattle and, although rare, it also occurs in sheep, goats, and swine. A freemartin is a female born as a co-twin to a male and is an XX/XY chimera. The freemartin is sterile because anastomoses between the placental circulations allow AMH from the male fetus to influence the female fetus. This suppresses female genital development and allows male structures to develop. Common gross findings in freemartins are vestigial seminal vesicles (always present), stunted ovaries, a hypoplastic vagina, lack of communication between the vagina and uterus, and an enlarged clitoris. (1,2)

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CASE II – 05-1467 (AFIP 2984137)

Signalment: 16 months old, intact female, Golden Retriever, canine (*Canis familiaris*)

History: During routine spaying, the submitting veterinarian noticed a mass in one uterine horn (side not specified). This was sent to the surgical biopsy service of the University of Tennessee for histological evaluation.

Gross Pathology: The submission consisted of a segment of uterine horn which was focally thickened by a firm swelling measuring 2.5cm long and 2cm in diameter. This was flanked by grossly normal uterine horn. On cut section through the swelling, the uterine lumen was much narrower than normal (ranged from 2-5mm) and the surrounding uterine wall was circumferentially and uniformly expanded by an inner pale tan/white layer which was 2mm thick and an outer homogeneous, tan layer up to 6mm thick (Fig 1. Bar = 1cm)

Histopathologic Description: The slide contains a transverse section of uterus (taken through the uterine horn) in which there is circumferential expansion of the endometrium by two distinct layers. The layer adjacent to the myometrium consists of fairly uniformly dilated glandular structures, corresponding to cystic hyperplasia of the basal zone of the endometrium. These glands are lined by a single layer of cuboidal to attenuated epithelial cells. Most are empty but some contain sparse eosinophilic, proteinaceous material, erythrocytes and necrotic leukocytes. This glandular layer surrounds a much thicker layer composed of thin, anastomosing trabeculae and papillary projections of fibrovascular connective tissue covered by a single layer of cuboidal to columnar epithelial cells. The trabeculae form a meshwork which narrows the uterine horn lumen and corresponds to hyperplasia of the crypt (glandular) epithelium. The epithelial cells have moderate amounts of sometimes highly vacuolated, bright pink cytoplasm with prominent apical blebbing and basally located nuclei. The crypts contain basophilic, mucinous material (mucus). The meshwork immediately surrounding the lumen is largely necrotic, with multifocal mineralization, correlating with lesion regression.

Contributor's Morphologic Diagnoses: Uterine horn: Pseudocyesis (pseudopregnancy) site

Contributor's Comment: Pseudocyesis (pseudopregnancy; false pregnancy) is still a fairly poorly understood physiological condition. At least historically the term pseudopregnancy is confusing, especially in the bitch. This is because, in other

species, “pseudopregnancy” has been traditionally used to describe lengthening of a normally short luteal phase following a sterile mating; the corpora lutea (CL) then persist for a length of time similar to pregnancy. The bitch is different because the luteal phase is the same length whether pregnant or not. The confusion is also partially due to some authors specifically using the term to describe the normal luteal phase which occurs in the bitch (1). It is now generally agreed that it should be reserved for those times when signs of late pregnancy/early lactation occur in the absence of a conceptus (2).

In this case, the uterine lesion was grossly and microscopically characteristic of that described in the literature for pseudopregnancy (3). Similar histological features were described in a subgroup of 24 bitches with a history of false pregnancy (2). This subgroup was composed of animals at the peak of their clinical signs. All had large CLs. We had no specific description of the ovaries (ovarian tissue was not submitted) and no pertinent clinical signs were mentioned by the referring veterinarian. However, it is recognized that the intensity of signs can be variable. While signs may be conspicuous in some bitches, others may have no symptoms at all, the latter known as covert pseudopregnancy (4). The histological features of pseudopregnancy recapitulate the placental zone in the canine gravid uterus but there are some important differences. In the pseudopregnant state the fetal membranes are absent and, since there is no chorion, the endometrium remains intact. The crypt zone visible in this case would have been completely lost in the truly gravid state since the canine placenta is endotheliochorial (2). Moreover, this particular animal had never been bred.
The original hypothesis proposed that pseudopregnancy was caused by overproduction of progesterone or abnormal persistence of the CL. This premise was challenged by one study which found no difference between circulating progesterone levels in non-pregnant bitches, regardless of whether or not they had symptoms consistent with pseudopregnancy (1). The advent of a canine prolactin assay in the 1970s confirmed that, during late pregnancy and in lactation, prolactin levels rose in conjunction with a sharp drop in progesterone levels. Since inhibitors of prolactin are therapeutically successful, it is generally now accepted that increased prolactin levels are key to the development of pseudopregnancy (3). Sex steroids (estrogens, androgens and progestins), which inhibit pituitary release of prolactin, also suppress the condition (1), indicating pituitary dysfunction.
However, some propose other additional underlying factors to explain why the condition only occurs in some bitches, despite fairly similar hormonal patterns. For instance, it seems likely there are genuinely predisposed breeds, although this is poorly documented in the literature (4). Furthermore, susceptible bitches tend to have a high recurrence rate in succeeding estrus cycles which may involve increased peripheral sensitivity to prolactin (4). It is also notable that, in humans, there is variation in the molecular composition of prolactin, with different forms having different degrees of hormonal potency. Since this heterogeneity has also

now been demonstrated in the dog, it may ultimately help to clarify the exact role of prolactin in canine pseudopregnancy.

AFIP Diagnosis: Uterus, endometrium: Hyperplasia, labyrinthine, segmental, marked, with mucometra, periluminal necrosis and mineralization, Golden Retriever, canine.

Conference Comment: The contributor provides an excellent review of false pregnancy in the bitch. Conference attendees discussed the presence of the uterine gland cystic hyperplasia within the lamina-propria-submucosa and the marked, labyrinthine hyperplasia of the endometrial mucosa as the physiologic response of the uterus to pregnancy. In this case; however, there is no placental chorion and; therefore, no loss of the placenta-like zone of the endometrium, resulting in accumulation and persistence of the hyperplastic mucosa. Coagulative necrosis of the tips of the endometrial fold is a consistent feature of segmental endometrial hyperplasia.

During false pregnancy, bitches may exhibit behavioral changes such as restlessness, anorexia, decreased activity, aggression, licking of the abdomen and maternal behavior (nesting, mothering inanimate objects, adopting other bitches' puppies). Physical signs include weight gain, mammary enlargement, lactation and even abdominal contractions. (2,4)

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CASE III – Case 1 (AFIP 2957438)

Signalment: Female, cynomolgus monkey (*Macaca fascicularis*), approximately 1 year 5 months of age.

History: An abdominal mass was found during a routine physical exam. Exploratory abdominal surgery was performed to determine the location of the mass and attempt resection. The mass was large and involved the uterus and left ovary. After excision of the mass the tissues were submitted for microscopic examination. The monkey was not pregnant and to our best knowledge had never been mated.

Laboratory Results: Immunohistochemistry findings:
AE1/AE3 – Strong positivity in all tumor cells
Wide spectrum cytokeratin antibodies – all tumor cells positive
Inhibin – large pleomorphic tumor cells were strongly positive, smaller tumor cells negative
Placental alkaline phosphatase – all tumor cells weakly positive
Human chorionic gonadotropin (hCG) – Very rare large multinucleated tumor cells were positive
Human placental lactogen – Diffusely positive, stronger signal in larger, more pleomorphic tumor cells.
Vimentin, CAE, AFP, EMA – tumor cells are negative

Histopathologic Description: [Submitted tissues: ovary and uterus] The mass consisted primarily of infiltrative sheets and cohesive clusters of neoplastic cells distorting and replacing uterine and ovarian tissue. Eosinophilic extracellular hyaline material surrounded some individual tumor cells and tumor cell aggregates in H&E slides. In PAS-stained slides (slides not provided) many aggregates of neoplastic cells and many individual cells were separated by eosinophilic, hyaline extracellular material. In the uterus the mass was located primarily in the muscle wall. The ovary was nearly effaced. Most tumor cells were round to polygonal with moderate amounts of eosinophilic cytoplasm, round to oval to irregularly-shaped coarsely stippled nuclei and single to multiple nucleoli. Lower numbers of neoplastic cells were of increased size, had marked amounts of cytoplasm, and had increased pleomorphism, karyomegaly and bizarre nuclear shapes. The degree of pleomorphism was moderate to marked. The neoplastic cells were morphologically consistent with neoplastic intermediate trophoblasts. Rare cells had multinucleation and were consistent with neoplastic syncytiotrophoblasts (hCG +). The morphology of the cells in the ovary and the uterus locations was similar; however, in the ovary most cells were of the larger more pleomorphic morphology. There were 2-10 mitoses per high power field. There were large areas of necrosis

with hemorrhage, variable amounts of fibrosis, and minimal to mild multifocal lymphoplasmacytic infiltrates in both the uterus and the ovary.

Contributor's Morphologic Diagnosis: Uterus and ovary: Malignant trophoblastic neoplasia consistent with malignant placental site trophoblastic tumor.

Contributor's Comment: The monkey recovered uneventfully from the surgical procedure; however, it was later euthanized due to a poor prognosis. A limited necropsy was performed after euthanasia. Metastatic foci were in the lungs. No other lesions were noted at the time. The microscopic appearance of the lung metastases was similar to that of the ovarian/uterine tumor.

Trophoblastic diseases in humans include hydatiform moles, invasive mole, choriocarcinoma, placental site trophoblastic tumor (PSTT), epithelioid trophoblastic tumor (ETT), exaggerated placental site, and placental site nodules.[1] The current case was most consistent with trophoblastic neoplasia, specifically PSTT, based on the histomorphologic features and immunohistochemical pattern of immunoreactivity. The primary differential diagnosis was ETT. Other differential diagnoses included choriocarcinoma and ovarian or uterine carcinoma. PSTT and ETT are both tumors of the intermediate trophoblast. The intermediate trophoblast is one of 3 types of trophoblastic cells found in the placenta: cytotrophoblast, syncytiotrophoblast, and the intermediate trophoblast. The cell morphology and immunohistochemical pattern of staining of PSTT are consistent with intermediate trophoblasts of the implantation site while the cells of ETT are consistent with intermediate trophoblasts of the chorion laeve.[2-3] PSTT and ETT can be differentiated based on morphologic features, immunohistochemical expression patterns, and gene expression profiles.[4] The cells of PSTT are typically larger and more pleomorphic than those in ETT. PSTT grows in a more infiltrative pattern frequently invading the myometrium. ETT has a nodular expansile growth pattern. Deposition of eosinophilic extracellular material is a common finding in PSTT and ETT; however, in human PSTT the material is more homogeneous and in ETT it is reportedly more fibrillar and may resemble keratin.[5] Although PSTT and ETT share immunohistochemical features, there are differences that can be used to differentiate between the two tumors. For example, cells of PSTT have greater numbers of cells positive for MelCAM (CD146) consistent with their reported origin from the implantation site of the placenta.[3]

ETT and PSTT have been rarely reported to occur in non-human primates.[6-7] Interestingly, both reported cases and the current case occurred in non-gravid, female cynomolgus monkeys.[6-8] The reported case of ETT originated in the left ovary and metastasized to the lungs, and the reported case of PSTT originated in the left ovary but did not metastasize. The exact origin of the tumor in this case (ovary vs. uterus) could not be determined; however, the tumor involved the left ovary and the uterus. It is unknown if the involvement of the left ovary in all three

cases is a coincidental finding. Similar to the reported cases of non-human primate PSTT and ETT, the monkey in the present report was not pregnant, was born in captivity, and to the best of our knowledge had never been mated. In humans PSTT and ETT are reportedly rare, typically occur after gestation, and may occur in sites other than the uterus.[4,6]

AFIP Diagnosis: Uterus; ovary, left (per contributor): Placental site trophoblastic tumor, Cynomolgus macaque (*Macaca fascicularis*), nonhuman primate.

Conference Comment: Trophoblasts are the ectodermal cells that cover the blastocyst, erode the uterine mucosa and transfer nutrients from the mother. There are three types: cytotrophoblasts, intermediate trophoblasts and syncytiotrophoblasts. Cytotrophoblasts are small, undifferentiated stem cells with a high nuclear:cytoplasmic ratio. Syncytiotrophoblasts are the terminally differentiated cells that produce the majority of the placental hormones, and regulate gas and nutrient exchange. Syncytiotrophoblasts are multinucleated, with abundant cytoplasm. Intermediate trophoblasts share some of the morphological and functional features of the other two types. They are usually mononucleate, and larger and more polygonal than cytotrophoblasts, but smaller than the multinucleated syncytiotrophoblast. Cytotrophoblasts are immunopositive for cytokeratin, and are negative for inhibin. Since they do not produce hormones, they are also negative for hPL and hCG. Syncytiotrophoblasts can produce both hCG and hPL, depending on the stage of gestation and trophoblastic maturation. Therefore, staining for hPL and hCG is variable, although staining for hCG usually predominates. Syncytiotrophoblasts also typically express cytokeratin and inhibin. Intermediate trophoblasts are positive primarily for cytokeratin, hPL and inhibin. As trophoblasts mature, the focus of their hormone synthesis changes from hCG to hPL. This change is reflected in the hormone profile seen during a normal gestation. (9,10)

PSTT is a neoplastic proliferation of intermediate trophoblasts that resembles the non-neoplastic infiltration of intermediate trophoblasts that occurs at the endometrial implantation site during pregnancy. It is a rare neoplasm that typically occurs in the postpartum uterus. There are rare reports of extrauterine locations, including the ovary, oviduct and testicle. (11,12) Like normal intermediate trophoblasts of the implantation site, neoplastic cells characteristically invade blood vessels and myometrium. Clinical signs include amenorrhea or abnormal vaginal bleeding. Grossly, the tumors are usually well demarcated and tan, with areas of hemorrhage and necrosis. Histologically, PSTT are primarily composed of intermediate trophoblasts, with rare cytotrophoblasts and syncytiotrophoblasts. Extensive deposition of fibrinoid matrix and vascular invasion is common. By immunohistochemistry, neoplastic cells are positive for cytokeratin, inhibin and hPL,

with few cells positive for hCG. PSTT's are usually benign. However, extensive necrosis, large clusters of neoplastic cells, and a mitotic rate >5/10 HPF, as in this case, are suggestive of malignancy. (10) Rare cases of metastasis to the lungs, liver, abdominal cavity and brain have occurred in humans. (10)

The tumor cells were diffusely and strongly positive for keratin and inhibin. Approximately 50% of the cells were positive for hPL, and less than 2% of the cells were positive for hCG. PSTT's consist primarily of intermediate trophoblasts with a few widely scattered syncytiotrophoblasts. By immunohistochemistry, intermediate trophoblasts and syncytiotrophoblasts are positive for hPL and hCG, respectively. Therefore, PSTT's have predominant staining for hPL, with rare cells positive for hCG, as in this case. (10)

The differential diagnosis included epithelioid trophoblastic tumor, choriocarcinoma, anaplastic carcinoma, juvenile granulosa cell tumor and yolk sac tumor.

Epithelioid trophoblastic tumor consists of a monomorphic population of intermediate trophoblasts resembling those lining the chorionic laeve (chorionic-type intermediate trophoblasts), whereas cells of PSTT resemble the intermediate trophoblasts of the placental implantation site (implantation site intermediate trophoblasts). Neoplastic cells in epithelioid trophoblastic tumors are smaller with less nuclear atypia than PSTT. By immunohistochemistry, neoplastic cells are positive for cytokeratin and inhibin, and are focally positive for hCG and hPL. Epithelioid trophoblastic tumors are nodular and expansile and do not typically invade blood vessels, as opposed to the more infiltrative PSTT. (5)

Choriocarcinomas consist of a biphasic population of cytotrophoblasts and syncytiotrophoblasts, as opposed to the largely monomorphic population of intermediate trophoblasts in a PSTT. By immunohistochemistry, choriocarcinomas stain predominantly for hCG, with fewer cells positive for hPL. In contrast to PSTT, choriocarcinomas are often malignant and a fibrinoid matrix is not present. (9,10)

Anaplastic carcinoma was ruled out based on the positive immunostaining for hPL and hCG. (9)

Juvenile granulosa cell tumors are typically solidly cellular, with multifocal follicle formation, and a variable amount of thecomatous differentiation. Cells have more abundant eosinophilic to vacuolated cytoplasm than those of the adult granulosa cell tumor. Although juvenile granulosa cell tumors are more pleomorphic than their adult counterparts, the degree of atypia in this case would be unexpected. Granulosa cell tumors are typically immunoreactive for inhibin, and negative for hPL and hCG. (13)

Yolk sac tumors are malignant germ cell tumors that typically occur in the ovary and testicle, and recapitulate the different developmental stages of the normal yolk sac. The neoplastic polygonal cells form a variety of microscopic patterns, ranging from nests, cords, and papillary structures, to a reticular or microcystic pattern. Cells typically have clear cytoplasm, which contains lipid or glycogen. Other features may include enteric or hepatic differentiation, deposition of an eosinophilic extracellular basement membrane material, and eosinophilic PAS-positive intracellular eosinophilic inclusions. Neoplastic cells are positive for cytokeratin, and are negative for hPL and hCG. (13)

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CASE IV – UK-LDDC 5 4984 (AFIP 2985454)

Signalment: Adult, female, Thoroughbred, *Equus caballus*, Equine.

History: The mare delivered the fetus and placenta 1 month prematurely. The mare had been receiving multiple antibiotics and other medications for a month prior to the abortion. The fetus and placenta were submitted for necropsy.

Gross Pathology: The allantochorion in the region of the cervical star and adjacent body was multifocally discolored light brown and thickened; the chorionic surface was covered by thick, tenacious, brown exudate. No gross lesions were observed in the remainder of the placenta or fetus.

Laboratory Results: Cultures of the placenta yielded numerous *Aspergillus* sp. *Pantoea (Enterobacter) agglomerans* was isolated from the fetal stomach contents. Florescent antibody test for *Leptospira* spp. on placenta and kidney was negative. Polymerase chain reaction tests for *Crossiella equi* and *Amycolatopsis* spp. were negative.

Histopathologic Description: Sections of the allantochorion are characterized by diffuse amorphous eosinophilic material on the chorionic surface containing degenerated cells and fungal hyphae. There is necrosis of the underlying chorionic villi. Additional alterations include a moderate inflammatory infiltrate consisting of degenerate and intact polymorphonuclear cells and macrophages in the chorionic villi and underlying chorionic stroma. The mycelia within the exudate contain dichotomous branching and septate hyphae, often with vesicular swellings.

Contributor's Morphologic Diagnosis: Equine, placenta, mycotic placentitis, focally extensive, chronic, severe.
Etiology: *Aspergillus* sp.

Contributor's Comment: Aspergillosis of the placenta was diagnosed based on the morphological characteristics of the hyphae and the results of the culture. Aspergilli are omnipresent in the soil and derive nutrients from decaying organic material. *Aspergillus* spp. have been found in poor quality hay and compost heaps (1). Aspergilli readily produce numerous spores that are dispersed by wind and dust. *Aspergillus* spp. have been isolated from the nasal passages of normal horses (2). Clinical cases of aspergillosis in horses are relatively uncommon and have been reported to cause nasal granulomas, guttural pouch mycosis, intestinal aspergillosis, keratitis, lower respiratory tract infections, and mycotic placentitis (1,2).

Mycotic placentitis in the horse primarily occurs in late gestation. Fungal infections may reach the placenta via a hematogenous route, but most ascend through a relaxed cervix (3). *Aspergillus* spp. is the most commonly isolated fungus in mycotic placentitis cases (3,4,5). Abortion may result from placental insufficiency due to the infection involving substantial portions of the chorionic surface (6). Also, the infection and resultant inflammation may stimulate cytokine elaboration leading to abortion (7). The route of infection in this mare was not determined, but it is probable that it was through the urogenital tract.

AFIP Diagnosis: Allantochorion: Placentitis, necrohemorrhagic, chronic-active, diffuse, severe, with pseudomembrane, congestion and edema, multifocal trophoblast squamous metaplasia, and many fungal hyphae, etiology consistent with *Aspergillus* sp., Thoroughbred, equine.

Conference Comment: Common causes of equine placentitis and abortion include bacterial, fungal and viral etiologies. Bacterial pathogens include *Streptococcus zooepidemicus*, *E. coli*, *Leptospira* spp., *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*, and nocardioform placentitis caused by *Crossiella equi* and similar unclassified bacteria. *Aspergillus fumigatus* is the most common fungal cause of equine abortion. Other fungal causes include the phycomycetes (*Absidia* spp., *Mucor* spp., *Rhizopus* spp.), *Candida* spp. and *Histoplasma* spp. Viral causes include equine herpesvirus 1 and equine arteritis virus. Poor perineal conformation of the mare may contribute to an ascending infection of bacterial or fungal placentitis. As mentioned by the contributor, ascending infections generally occur through a relaxed cervix. The cervical star or the portion of the placenta overlaying the internal cervical os is generally thickened and covered in plaque-like foci of inflammation in cases of both mycotic and bacterial infection.

The moderator stressed that in cases of mycotic abortion there are five key histologic features which can usually be identified in addition to the fungi:

evidence of placental separation and an accumulation of debris around the chorioallantoic membranes; squamous metaplasia of trophoblastic cells; edema; congestion; and adenomatous dysplasia of the equine allantois. In this case, all five features are identifiable; however, adenomatous dysplasia of the equine allantois is not present in all tissue sections. Adenomatous dysplasia of the equine allantois has been associated with fetal disease, can occur anywhere within the allantois, and is characterized by nodules which may be solid or cystic. The affected allantois is thickened by variably sized glandular structures which are lined by cells that are occasionally continuous with the epithelial cells of the allantoic surface. (3) In this case there are multiple small cysts within the allantois which are lined by attenuated cuboidal to polygonal cells and which are either empty or contain sloughed cells, cellular debris, and/or homogenous, eosinophilic, proteinaceous material.

Aspergillus spp. fungi are an important cause of disease and serve as opportunistic pathogens in immunosuppressed domestic animals and humans. Typical gross findings include multifocal to coalescing pale nodules. Histologically, aspergillosis is characterized by fungal granulomas or pyogranulomas composed of a central area of necrosis containing hyphae that are 3-5 μm wide, with regularly septate parallel walls, and dichotomous acute angle branching, surrounded by variable numbers of neutrophils, lymphocytes, epithelioid macrophages, and fibroblasts. Many cases also demonstrate vasculitis (8).

Readers are encouraged to review WSC cases 3 and 4, conference 15, 2002 for examples of *Candida* sp. and nocardioform placentitis.

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