Pathology of the mare reproductive system

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Anomalies of phenotypic and genotypic sex

Pseudohermaphrodites are rare in the equine species. In these animals the chromosome constitution and gonadal sex are in agreement, yet the internal or external genitalia are ambiguous. There is one type of gonad, by which the individual is classified, and ducts modified toward those of the other gender. In animals, male pseudohermaphrodites are more common than female pseudohermaphrodites which are rare; for many of these abnormalities the mechanisms are not understood.

Hermaphrodites are also very rare. Both types of gonadal tissue are present; male and female cells coexist in the same individual. The chromosomal make-up is a chimera, mosaic, XX with or without SRY gene, or unknown. In unilateral hermaphrodites an ovotestis is on one side while bilateral hermaphrodites have an ovotestis on both sides. Lateral hermaphrodites have an ovary on one side and a testis on the other and the ducts are abnormal. One or both testes may or may not be palpable, but are undescended. The diagnosis can be confirmed via karyotyping and histopathology. In species other than the horse possible causes include congenital adrenal gland hyperplasia, fetal exposure to sex hormones, testicular feminization syndrome, XY gonadal dysgenesis, XY gonadal agenesis, and chromosomal abnormalities. SRY is present in many but not all cases in humans.

Ovarian lesions

Agenesis is the complete absence of the ovary and its associated primordium. It is very rare in horses.

Hypoplasia is the incomplete development or underdevelopment of the ovary with decreased numbers of cells. Follicles are usually absent. Aggressive testosterone treatment in racing mares can mimic this condition. In these cases the ovaries are both smaller than normal with minimal gross evidence of follicular activity, though histologically follicles are evident. Treated mares may present clitoral hypertrophy.

Turner syndrome is characterized by partial or complete absence of one X chromosome (XO gonadal dysgenesis). The Turner mare is affected by hypogonadism (small fibrotic ovaries). They may also have short stature, a broad-based neck, and narrowing of the aorta. External genitalia tend to be small and the tubular tract is small and flaccid. Mares with this disease lack one of the pair of sex chromosomes resulting in a 63,X karyotype. The origin of the defect may be an accident in development, not an inherited problem. The syndrome has been diagnosed in various horse breeds throughout the world including Thoroughbred, Arabian, Welsh Pony, Tennessee Walking Horse, Standardbred, American Saddlebred, Paso Fino, Belgian, Quarter Horse, Appaloosa, as well as in grade horses.

Cysts may arise from both mesonephric and paramesonephric embryonic duct systems. There are cysts adjacent to the ovary and cysts within the ovary. Cysts within the ovary include non-gonadal stromal cysts (inclusion cysts, cystic rete ovarii), gonadal stromal cysts (from corpora lutea and follicles), anovulatory luteinized cysts, cystic corpora lutea, and neoplastic cysts. It is debated if cystic Graafian follicles occur in mares.

Oophoritis is the inflammation of the ovary. It is a rare event.

Follicle atresia is a degenerative breakdown of follicles. Excessive atresia can ultimately result in infertility. The selective loss of ovarian follicles by atresia occurs via apoptosis and this process is most evident within the granulosa cell layer.

Hemorrhage is secondary to trauma, vasculitis and neoplasia. Hematomas may develop near ovulation.

Ovarian neoplasms are comprised of germ cell tumors (teratoma, dysgerminoma), gonadal stromal tumors and surface tumors (cystadenoma, carcinoma, mesothelioma).

Teratoma is rare, usually well-differentiated, and benign, exhibiting at least two of the three embryonic germ layers. It is generally comprised of nonproliferating somatic tissues.

Dysgerminoma is even more rare than teratoma, analogous to seminoma and generally as malignant as this sporadic tumor in stallions. The neoplastic parenchyma is pale brown. The gross and microscopic appearance is essentially the same as that of a seminoma.

Granulosa cell tumor is a very common tumor in mares. It is rarely malignant in large animals. The gross appearance may be multicystic, unilocular cystic, or solid. Forty to fifty percent produce androgens resulting in stallion-like behavior and ninety percent produce inhibin causing regression of the contralateral ovary. The nymphomania reported in mares seems to be due to lack of progesterone (not elevated estrogens) caused by increased inhibin production by the neoplastic granulosa cells (80-90 % of the cases). Anestrus due to failure to cycle occurs. Granulosa cell tumors can also occur in pregnant mares.

Cystadenoma, carcinoma and mesothelioma are rare. Cystadenoma is unilateral.

Uterine (Fallopian) tube lesions

Hydrosalpinx is the distention of the uterine tube by clear fluid.

Salpingitis is the inflammation of the uterine tube due to bacterial and viral infections.

Pyosalpinx is characterized by gathering of pus within the oviductal lumen predisposed by bacterial infection.

All these salpingeal lesions are rare in mares.

Uterine lesions

Segmental aplasia is rare and characterized by the failure of Müllerian ducts to fuse with the urogenital sinus. Prostaglandin produced in the blind uterine horn can cause luteolysis in the contralateral ovary during pregnancy. Long-term distention can cause inability to produce endometrial prostaglandin with failure of regression of the corpus luteum.

Imperfect fusion of primordial ducts may lead to the formation of a double uterine fundus. The normal sequence of fusion of the paired ducts is from posterior to anterior.

Uterine torsion is predisposed by pyometra, mucometra, and pregnancy and leads to hypoxia, infarction, and shock.

Prolapse may involve pregnant uterine horn, body, urinary bladder and intestine, also leading to hypoxia, infarction, and shock.

Endometrial atrophy follows loss of ovarian function in cases of inhibin secreting neoplasia or very old age.

Adenomyosis is characterized by ectopic endometrial glands within the myometrium; it is very rare in horses.

Endometritis is the inflammation of the mucosal uterine layer and is related to introduction of semen, pregnancy, parturition and postpartum involution. Most infections start within the endometrium. Several factors may play a role.

Progesterone may make the uterus more susceptible to infection. Estrogens increase leukocytic phagocytosis and induce cervical opening with consequent drainage and/or exposure. Prostaglandins trigger uterine motility. Usually, in mares with endometritis, after a short diestrus due to early prostaglandin F2alpha release there is an early return to estrus. In cases of chronic endometritis there is decreased capability to produce prostaglandin and a corpus luteum and progesterone production may persist. The etiologic agents inducing endometritis can also cause abortion (e.g. *Streptococcus equi equi* and *S. equi zooepidemicus*). Occasionally the process can spread to the wall, leading to metritis. Pyometra is the acute to chronic suppurative inflammation of the uterus with pus accumulation within the uterine lumen. Endometritis is followed by fibrosis (transluminal fibrous adhesions may occasionally occur), which can impair the uterine gland functions and predispose to the formation of cystic glands. Glandular cysts are frequent microscopic findings and lymphatic cysts are the most common macroscopic cyst observed in mares. Lymphatic cysts occur in multiparous mares over 14 years of age and can be single or multiloculated. Persistent endometritis can be induced by mating. Breeding is followed by inflammation, decrease of mechanical clearance, increase of intraluminal fluid, increase of inflammation,

interstitial edema and fibrosis and cyclic endometrial irritation. Poor conformation and perhaps abnormal hormonal release may decrease the mechanical clearance.

Perimetrial adhesions and abscesses are associated with trauma.

Uterine foreign bodies may include marbles, placental remnants, and cotton from swab tips.

Uterine primary and metastatic neoplasms are rare in the mare. In cases of lymphoma often the pregnant horn is less involved. Endometrial carcinoma is very rare. Leiomyomas and fibroleiomyomas are likewise rarely observed.

Cervical lesions

Double cervix is very rare and caused by the failure of fusion of the Müllerian ducts. Other malformations of the cervix are also very rare, including hypertrophy, hypoplasia, and diverticula. All these changes can create problems for artificial insemination.

Cervicitis is caused by trauma and infectious agents.

Vulvar and vaginal lesions

Vulvo-vaginitis is caused by viruses, bacteria, fungi, chemicals and trauma. Pneumovagina and urovagina can be associated with conformation anomalies.

Melanoma, lymphoma and squamous cell carcinoma are the most common vulvar neoplasms. Solar radiation and papillomavirus may be triggering factors of vulvar squamous cell carcinomas.

Complications arising from parturition are numerous. Rectal prolapse, rupture of small colon mesentery, bladder eversion, prolapse and rupture, and cervical, vaginal and perineal lacerations may occur. Postpartum hemorrhage in the broodmare is a common problem. Vessel rupture usually involves the uterine artery, but the ovarian and iliac arteries may also be affected. Retained fetal membranes can be associated with fescue toxicity, abortion, dystocia, placentitis, uterine inertia, and twin pregnancy, but can also be seen following an otherwise normal delivery.