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Reproductive problems are encountered frequently over the course of a breeding season. A problem mare may be defined as 1) a mare that is not pregnant after being bred to a fertile stallion over 3 estrous cycles, 2) a mare that cannot successfully carry a foal to term, 3) a mare with known reproductive pathology, or 4) a mare with behavioral issues related to reproduction.

Occurrence of many problems can be predicted based on mare age, breed, parity, or additional factors. A list of the common and less common reproductive problems in broodmares are presented in the table below.

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Anovulatory Follicles

Ovulation failure is a normal physiologic event for the mare during the spring and fall transition periods. The development of anovulatory follicles may occasionally occur during the physiologic breeding season. The cause of ovulation failure has been suggested to be either a) endocrine in nature, due to a lack of sufficient pituitary gonadotropin stimulation to induce ovulation or from insufficient estrogen production from the follicle itself b) due to insufficient gonadotropin receptors in the ovary to respond to endocrine signals or c) due to alterations in follicular blood flow. One recent report suggests that the incidence of anovulatory follicles increases following the use of prostaglandins.

Types of Anovulatory Follicles

There are two subtypes of anovulatory follicles. Approximately 85% of anovulatory follicles are associated with hemorrhage and eventual luteinization. Hemorrhagic anovulatory follicles (HAF) occur when significant bleeding occurs into the lumen of the dominant follicle during estrus. Initially the blood does not clot due to anticoagulant factors present in equine follicular fluid. Eventually the blood clots and the fibrin scaffolding within the blood clot allow granulosa and theca cells to invade and luteinize. The now luteinized anovulatory follicle produces a large amount of progesterone. Approximately 15% of anovulatory follicles remain as non-viable persistent anovulatory follicle (PAF). As the follicle becomes non-viable, estrogen levels decrease, uterine edema goes away and the mare goes out of heat. A PAF does not luteinize and therefore does not produce progesterone.

In addition to the two primary subtypes of anovulatory follicles, a low percentage of mares may exhibit partial collapse of a follicle. An initial presumption may be that the mare was examined while in the process of ovulating, but in reality the partially follicle will remain in this state for many days. Pregnancy rates associated with a partially collapsed follicle are low, possibly due to failure of the oocyte to be discharged from the follicle or possibly a deficiency in follicular or oocyte quality.

Diagnosis

Hemorrhagic anovulatory follicles contain blood which can be detected ultrasonically as scattered free-floating echogenic spots within the follicular fluid. Ballottement of the follicle will cause the echogenic particles to swirl within the non-clotted hemorrhagic follicular fluid. The follicular fluid will eventually form a gelatinous, hemorrhagic mass within the follicular lumen which may be viewed as echogenic fibrous bands traversing the follicular lumen. A thickening of the follicular wall may be observed in association with luteinization of the follicular wall. Plasma progesterone concentrations are often markedly elevated. In contrast, a PAF will retain a similar ultrasound appearance as a large viable pre-ovulatory follicle. Occasionally a small amount of echogenic particles may be visible in the follicular lumen. A PAF may remain present for several weeks and eventually be replaced by a new dominant follicle.
**Treatment**

Luteinized HAF and PAF will both eventually regress spontaneously. A luteinized HAF can be eliminated with a single dose of prostaglandins (i.e. Estrumate®; cloprostenol; 250 µg, im) administered 9 to 10 days after the initial recognition of echogenic particles within the follicular lumen. A PAF will not respond to prostaglandin administration as there is no luteinized tissue present. In addition, attempts to induce luteinization or ovulation of a PAF by administration of human chorionic gonadotropin or deslorelin is generally not effective.

**Ovarian Hematomas**

Ovarian hematomas were historically noted to be a result of excessive hemorrhage into the follicular lumen following ovulation, or essentially greatly enlarged corpora hemorrhagica. The contralateral ovary was reported to be normal in size and function, and mares with this condition continued to cycle normally. No specific behavioral abnormalities were noted and endocrine patterns of the mare were normal.

With the common use of ultrasound to closely monitor ovarian function, the occurrence of an ovarian hematoma as a post-ovulatory structure is now considered to be uncommon. It is likely that most structures previously reported to be ovarian hematomas were hemorrhagic anovulatory follicles and that the hemorrhage occurred within the dominant follicle.

**Persistent Corpus Luteum**

The corpus luteum that forms after ovulation is usually functional for 14-15 days in the nonpregnant mare. Corpora lutea that fail to regress at the normal time postovulation are considered to be pathologically persistent. Luteolysis, or destruction of the corpus luteum, occurs as a result of prostaglandin release from the endometrium. Occasionally, a mare may fail to regress her corpus luteum spontaneously at the normal time. The most common causes of a persistent corpus luteum are (1) ovulations late in diestrus, resulting in corpora lutea that are immature (<5 days old) at the time of prostaglandin release; (2) embryonic loss after the time of maternal recognition of pregnancy; (3) chronic uterine infections, resulting in destruction of the endometrium and therefore diminished prostaglandin release, and (4) inadequate prostaglandin release at days 13-15.

If untreated, the corpus luteum may persist for 2-3 months. This syndrome may be suspected clinically in mares that are not expressing normal estrous behavior during the physiologic breeding season, and it must be differentiated from the syndrome of mares with silent heat. In addition, mares that have been bred and do not return to heat and are later diagnosed as not pregnant may also have a persistent corpus luteum.

**Diagnosis**

Diagnosis of a persistent corpus luteum is made by an analysis of plasma progesterone concentrations or a clinical response to prostaglandin administration. Progesterone concentrations >1.0 ng/ml are indicative of the presence of luteal activity. Mares with a persistent corpus luteum will have good tone in the cervix and uterus on palpation, and the cervix will appear tight and dry on vaginal speculum examination because of the influence of progesterone.

**Treatment**

A persistent corpus luteum will usually be eliminated by the administration of a single intramuscular dose of prostaglandins (PGF₂α, 10 mg; or cloprostenol, 250 mg).

**Shortened Luteal Phase (Premature Luteolysis)**

Diestrus in the normal mare lasts approximately 15 days. Premature destruction of the corpus luteum (luteolysis) may be associated with an early onset of estrus and a decrease in the interovulatory interval. The most common cause of premature luteolysis in the mare is endometritis. Inflammation of the endometrium can result in sufficient synthesis and release of prostaglandins to cause luteal regression.

**Diagnosis**

Clinical diagnosis of short-cycling is made by evaluation of the interestrus or interovulatory intervals of a mare. A mare that exhibits a shortened diestrus should be examined for endometritis. A culture, biopsy and cytologic examination of the uterus may be indicated.

**Luteal Insufficiency**

Primary luteal insufficiency implies a deficiency in progesterone production. Luteal insufficiency has been suggested to be a cause of subfertility in mares, although data is limited. Maintenance of pregnancy in some habitually aborting mares following administration of exogenous progestogens offers circumstantial evidence that progesterone insufficiency may be responsible for some cases of pregnancy loss.

**Diagnosis**

Documentation of progesterone insufficiency as a cause of pregnancy loss would necessitate 1) an accurate initial pregnancy diagnosis, 2) ruling out other potential causes of pregnancy loss, and 3) measurement of low progesterone concentrations in a series of daily blood samples. Minimum concentrations of progesterone required to maintain pregnancy in the mare has been suggested to be 4.0 ng/ml.
**Treatment**

The most common treatment for luteal insufficiency is supplementation with the synthetic progestogen altrenogest (Regu-Mate®) at a dose of 0.044 mg/kg (1 ml/110 lbs of body weight), orally once daily. Options for duration of altrenogest supplementation include 1) treatment until day 60 of pregnancy or greater (a time when secondary corpora lutea should be present and active in most mares) and measurement of endogenous progesterone level of > 4.0 ng/ml, 2) treatment until day 120 of pregnancy, or 3) treatment until the end of pregnancy. The latter is the least common option.

**Ovarian Tumors**

The most common ovarian tumor in the mare is the granulosa cell tumor (GCT). Granulosa cell tumors are almost always unilateral, slow growing, and benign. An examination of the affected ovary by using transrectal ultrasonography often reveals a multicystic or honeycombed structure, but the tumor may also present as a solid mass or as a single large cyst. The contralateral ovary is usually small and inactive, although mares with a GCT on one ovary and a functional contralateral ovary have been reported. Behavioral abnormalities such as prolonged anestrus, aggressive or stallion-like behavior, and persistent estrus or nymphomania may be expressed in affected mares.

**Diagnosis**

Granulosa cell tumors are hormonally active, and clinical diagnostic assays for the detection of a GCT include the measurement of anti-Müllerian hormone (AMH), inhibin, testosterone, and progesterone. AMH has recently been described as the most sensitive indicator of the presence of a granulosa cell tumor, and is elevated in approximately 95% of mares with histologically confirmed GCT. Inhibin is elevated in approximately 90% of the mares with a GCT. It has been hypothesized that inhibin produced by the GCT is responsible for the inactivity of the contralateral ovary through the suppression of pituitary follicle-stimulating hormone release. Serum testosterone levels may be elevated if a significant theca cell component is present in the tumor (i.e., a granulosa-theca cell tumor, or GTCT). Testosterone is elevated in approximately 50-60% of affected mares and is usually associated with stallion-like behavior. Progesterone concentrations in mares with a GCT are almost always below 1 ng/ml, since normal follicular development, ovulation, and corpus luteum formation do not occur.

Measurements of AMH level above 4 ng/ml, inhibin levels >0.7 ng/ml, testosterone levels >50-100 pg/ml, and progesterone levels of <1 ng/ml are suggestive of a granulosa cell tumor in a nonpregnant mare (Table 1).

**Treatment.**

Granulosa cell tumors are usually surgically removed if the tumor affects follicular development on the contralateral ovary, causes behavioral abnormalities, or is a source of colic. Surgical approaches for tumor removal include colpotomy, flank and ventral midline laparotomy, and laparoscopy.

Ovulation from the remaining ovary will occur approximately 6-8 months after tumor removal. Attempts at inducing follicular development and ovulation in the remaining ovary within 1 month after tumor removal by the administration of gonadotropin-releasing hormone (GnRH) has not been successful. However, the administration of equine follicle-stimulating hormone, in the form of equine pituitary extract, has been successful in inducing an ovulation from the contralateral ovary after the surgical removal of a GTC that resulted in a pregnancy.

Other ovarian tumors include the cystadenoma (a tumor of the surface epithelium of the ovary) and the teratoma or dysgerminoma (germ cell tumors). These tumors are not considered to be hormonally active and do not cause regression of the contralateral ovary.

**Fossa Cysts and Parovarian Cysts**

Cysts within the region of the ovulation fossa and cysts adjacent to and within the oviductal tissue may be found in a high percentage of mares as incidental findings. These cysts are generally not associated with reduced fertility unless they obstruct the process of ovulation or oocyte transport into and through the oviduct. No treatment is necessary for fossa cysts or parovarian (fimbrial) cysts that are not interfering with ovulation or oocyte transport.

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**Table 1. Hormone Concentrations in the Normal Nonpregnant Mare**

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Normal Range</th>
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<tbody>
<tr>
<td>AMH</td>
<td>&lt; 4.0 ng/ml</td>
</tr>
<tr>
<td>Inhibin</td>
<td>0.1-0.7 ng/ml</td>
</tr>
<tr>
<td>Testosterone</td>
<td>20-45 pg/ml</td>
</tr>
<tr>
<td>Progesterone</td>
<td>&lt;1 ng/ml</td>
</tr>
<tr>
<td>Estrus</td>
<td>&gt;1 ng/ml</td>
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<td>Diestrous</td>
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