Clinical techniques that may be used in the diagnosis and differentiation of ovarian abnormalities include behavioral observations, physical examination of the mare, palpation of the ovary per rectum, ultrasonography of the ovary per rectum, hormone analysis, ovarian biopsy and karyotyping. A majority of ovarian abnormalities can be diagnosed with a minimum of equipment or diagnostic tests. However, some abnormalities require a more extensive evaluation. Disorders of ovulation or luteal function usually resolve spontaneously over time. In contrast, disorders such as ovarian tumors will not resolve spontaneously and may require surgical intervention. If a clear diagnosis cannot be determined utilizing the techniques noted above, it might be prudent to postpone surgery until it is certain that the ovary will not return to normal function. Pathological conditions of the equine ovary can be divided into abnormalities of follicular development, ovulation, or luteal function, ovarian tumors and miscellaneous other abnormalities.

**Abnormalities of Follicular Development**

**Chromosomal Abnormalities**

Chromosomal abnormalities, especially of the sex chromosomes, have been associated with infertility in the horse. The prevalence of sex chromosome abnormalities in the mare has been reported to be less than 3% [1]. A chromosomal abnormality may be suspected in a mare of breeding age with primary infertility and gonadal hypoplasia. The most commonly reported chromosomal abnormality of the horse is 63, X gonadal dysgenesis, in which only a single sex chromosome is present [2]. The condition may occur when the sex chromosome pair fails to separate during meiosis, producing one gamete without a sex chromosome and another with two sex chromosomes. The equine condition is analogous to Turner’s syndrome in humans. The 63, X (or XO) condition has been detected in most domestic horse breeds, including draft and miniature breeds.

Horses with gonadal dysgenesis develop as phenotypic females because of the absence of a Y sex chromosome. Affected horses are often small in size for their age and breed, have small ovaries lacking follicular development, and have endometrial gland hypoplasia. The uterus and cervix are generally small and flaccid (Fig. 1).

![Figure 1. Reproductive tract of a mare with 63, XO gonadal dysgenesis (Turner's Syndrome). Note the small inactive ovaries and the underdeveloped uterus. - To view this image in full size go to the IVIS website at www.ivis.org.](image)

The external genitalia are female, but the vulva may be smaller than normal and there is no clitoral hypertrophy. XO mares may exhibit anestrous or irregular estrous behavior and occasionally stand to be mated. True XO mares are considered to be sterile. However, mares with a mosaic or chimeric karyotype (63, XO/64, XX) are not always small in stature and some have been reported to produce a foal. Mosaic mares account for approximately 15 - 30% of all cases of gonadal dysgenesis. Numerous other chromosomal abnormalities have also been reported in the mare [3]. Diagnosis of a chromosomal abnormality is based on chromosome analysis or karyotyping. Karyotyping can be performed on any tissue with actively dividing cells. A fresh blood sample collected into acid citrate dextrose or heparin may be sent by overnight courier to a laboratory specializing in animal karyotyping. An examination of peripheral blood smears for sex chromosome appendages, or drumsticks, on polymorphonuclear neutrophils (PMN’s) can be used as a screening procedure to
detect a reduced number of chromosomes. Drumsticks appear as a lobe on the nucleus of PMN’s and are present in approximately 10% of PMN’s from normal mares and are absent in stallions and geldings. An examination of peripheral blood smears will reveal an absence of drumsticks in XO mares.

**Age-Related Ovarian Dysfunction**

Ovulatory dysfunction has been identified as a cause of subfertility in mares approximately 20 years of age or older. No effective treatments are currently available in the mare for promoting follicular growth in senescent ovaries. Other factors associated with decreased fertility in older mares such as poor perineal conformation and ineffective uterine clearance should be addressed. Older mares may also have decreased oocyte viability and a higher incidence of early embryonic loss and abortion.

The interovulatory interval of older mares may be longer than that of younger mares because of a longer follicular phase [4,5]. A lengthening of the follicular phase in association with elevated gonadotropin concentrations may indicate impending reproductive senescence in older mares [6]. Complete ovulation failure or ovarian senescence has been observed in aged mares and may be due to an insufficient number of primordial follicles. In addition, older mares may experience a delay in their initial ovulation of the year by an average of 2 weeks.

**Exogenous Hormone Treatment**

Anabolic steroid administration may affect both estrous behavior and ovarian function. The treatment of mares with low doses of anabolic steroids may cause aggressive or stallion-like behavior, while high doses may inhibit ovarian activity and result in failure of follicular development and ovulation [7]. The administration of anabolic steroids to prepubertal fillies may result in clitoral hypertrophy. The use of anabolic steroids should be avoided in fillies and mares intended to be used for breeding.

Progestins are commonly given to cycling mares for the suppression of estrus or synchronization of ovulation. Mares may continue to ovulate during progestin administration, especially if treatment is started late in the luteal phase. A high incidence of persistent corpus luteum formation has been noted for mares ovulating during progestin treatment [8]. Administration of the potent GnRH agonist deslorelin acetate (Ovuplant®, Ft. Dodge) to induce ovulation has been associated with delayed follicular development and a prolonged interovulatory interval [9,10]. Deslorelin acetate is very effective in inducing ovulation, but treatment also causes a prolonged period of depressed follicle stimulating hormone (FSH) secretion. Low FSH levels are associated with decreased follicular populations. Administration of prostaglandins 7 - 8 days after ovulation to cause premature luteolysis appears to increase the risk of delayed follicular development. Prostaglandin administration ‘resets’ the timing of the estrous cycle in a period when limited follicular activity is present.

**Equine Cushing’s Disease**

Mares with hypertrophy, hyperplasia, or adenoma formation in the *pars intermedia* of the pituitary (Equine Cushing’s Disease, or ECD) have been reported to have abnormal estrous cycles, infertility, or both [11,12]. The mechanisms by which ECD cause reproductive abnormalities have not been determined. A majority of horses diagnosed with ECD are older, with the average age being approximately 20 years. Consequently, the decrease in reproductive efficiency in mares with ECD may be partly due to advanced age. Possible causes of reproductive abnormalities in mares with ECD include an increased production of androgens from the adrenal gland and compression of the hypothalamus or anterior pituitary by the enlarged *pars intermedia*. Both factors may lead to a decrease in gonadotropin secretion and consequently a reduction in ovarian follicular development. In addition, mares with ECD may be predisposed to uterine infections. Documentation of the effects of ECD on reproductive performance in the mare is limited.

Clinical signs of ECD include hirsutism (Fig. 2) and abnormal hair-coat shedding patterns, polyuria, polydipsia, and hyperhidrosis [13]. Diagnostic tests for ECD include measurements of serum glucose, insulin, adrenocorticotropic hormone (ACTH) and cortisol levels and dexamethasone suppression, ACTH stimulation, and thyrotropin-releasing hormone response tests. The measurement of single samples for basal cortisol or ACTH concentrations are of limited value in the diagnosis of ECD.

Figure 2. Mare with Equine Cushing’s Disease exhibiting hirsutism. This mare did not shed her long hair coat, even during the summer months. - To view this image in full size go to the IVIS website at www.ivis.org . -
Abnormalities of Ovulation

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 [14]. Anovulatory follicles may be quite large (5 - 15 cm in diameter), persist for up to 2 months, and result in abnormal estrus behavior and prolonged interovulatory intervals [15]. The cause of ovulation failure has been suggested to be endocrine in nature, either from a lack of sufficient pituitary gonadotropin stimulation to induce ovulation or from insufficient estrogen production from the follicle itself. Persistent anovulatory follicles (PAF) may contain blood and have been termed hemorrhagic anovulatory follicles. The hemorrhage can be detected ultrasonically as scattered free-floating echogenic spots within the follicular fluid (Fig. 3). The follicular fluid may form a gelatinous, hemorrhagic mass within the follicular lumen (Fig. 4).

Figure 3. Ultrasound photo of a large follicle with multiple echogenic particles within the follicular fluid. The echogenic spots may represent blood or rafts of granulosa cells floating within the follicular lumen. - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 4. Ultrasound photo of a persistent anovulatory follicle with echogenic strands traversing the follicular lumen. The strands may be fibrin tags scattered throughout the follicular lumen. - To view this image in full size go to the IVIS website at www.ivis.org . -

Ultrasonographically, these structures may contain echogenic fibrous bands traversing the follicular lumen. A thickening of the follicular wall may be observed in some anovulatory follicles. This thickening may be associated with luteinization of the follicular wall. In many mares, plasma progesterone concentrations are elevated over baseline levels because of the presence of luteal tissue. Pregnancy does not usually occur if a persistent follicle eventually spontaneously ovulates or is induced to ovulate. This is likely a result of degeneration of the oocyte over time. Pregnancy obviously will not occur if the follicle becomes hemorrhagic or luteinized without ovulating.

Ovarian Hematomas
In the older literature, ovarian hematomas were reported to be one of the most common causes of unilateral ovarian enlargement [15,16]. Hematomas were noted to be a result of excessive hemorrhage into the follicular lumen following ovulation, or essentially greatly enlarged corpora hemorrhagica (Fig. 5). 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.

Figure 5. Ovarian hematoma surgically removed from a mare. This may actually be an enlarged hemorrhagic persistent anovulatory follicle. Surgical removal is not indicated. - To view this image in full size go to the IVIS website at www.ivis.org . -

With the common use of ultrasound to closely monitor ovarian function, the occurrence of the ovarian hematoma as a post-ovulatory structure should be reconsidered. It is the author's hypothesis that most structures previously reported to be ovarian hematomas are most likely persistent anovulatory follicles. Dramatic enlargement of a corpus hemorrhagica following detection of a true ovulation is rare (if it ever happens). In contrast, formation of a blood filled follicular lumen in an anovulatory follicle is relatively common.
**Abnormalities of Luteal Function**

**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 [17]. Luteolysis, or destruction of the corpus luteum, occurs as a result of prostaglandin release from the endometrium. Occasionally, a mare may fail to regress the 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 estrus 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 estrus and are later diagnosed as not pregnant may also have a persistent corpus luteum. 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.

**Shortened Luteal Phase (Premature Luteolysis)**
Diestrus in the normal mare lasts approximately 14 - 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. Consequently, 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 [18], 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. 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 have been suggested to be 4.0 ng/ml.

**Ovarian Tumors**

**Granulosa Cell Tumor**
The most common ovarian tumor in the mare is the granulosa cell tumor (GCT) [19]. Granulosa cell tumors are almost always unilateral, slow growing, and benign. An examination of the affected ovary by transrectal ultrasonography often reveals a multicystic or honeycombed structure (Fig. 6 and Fig. 7), [20,21] but the tumor may also present as a solid mass or as a single large cyst (Fig. 8).
The contralateral ovary is usually small and inactive, although mares with a GCT on one ovary and a functional contralateral ovary have been reported [22]. Behavioral abnormalities such as prolonged anestrus, aggressive or stallion-like behavior, and persistent estrus or nymphomania may be expressed in affected mares. Granulosa cell tumors are hormonally active, and clinical diagnostic assays for the detection of a GCT include the measurement of inhibin, testosterone, and progesterone [23-25]. Inhibin is elevated in approximately 90% of the mares with a GCT [23]. 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 (Fig. 9).

Figure 9. Mare with a granulosa-theca cell tumor exhibiting stallion-like behavior. The affected mare is mounting a mare in estrus. Note that the estrual mare is standing to be mounted by the mare with the tumor. Testosterone levels in mares with granulosa-theca cell tumors showing stallion-like behavior are typically markedly elevated. - To view this image in full size go to the IVIS website at www.ivis.org . -

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. Therefore, measurements of 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).

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Normal Range</th>
</tr>
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<tbody>
<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></td>
</tr>
<tr>
<td>- Estrus</td>
<td>&lt;1 ng/ml</td>
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<tr>
<td>- Diestrus</td>
<td>&gt;1 ng/ml</td>
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**Cystadenoma**

The most common tumor of the surface epithelium of the equine ovary is the cystadenoma. Cystadenomas occur unilaterally, and the contralateral ovary is normal. The ultrasonographic appearance of the affected ovary may include one to many cyst-
like structures (Fig. 10). In general, these tumors are rare and benign and are not considered to be hormonally active, although mares with cystadenomas with elevated plasma testosterone concentrations have been reported [19,26].

Figure 10. Photograph of a cystadenoma surgically removed from a mare. - To view this image in full size go to the IVIS website at www.ivis.org. -

Teratoma and Dysgerminoma
Teratomas and dysgerminomas are rare ovarian tumors of germ cell origin [27,28]. Teratomas are considered to be benign, while dysgerminomas are potentially malignant. Both are unilateral, hormonally inactive, and associated with normal contralateral ovaries. Germ cell tumors may contain hair, bone, muscle, and other tissues (Fig. 11). They do not alter the behavior of the mare and do not interrupt the estrous cycle.

Figure 11. Ovarian teratoma removed from a mare. Note the hair present within the larger cystic area. - To view this image in full size go to the IVIS website at www.ivis.org. -

Miscellaneous Ovarian Abnormalities

Cystic Structures Within the Ovary
A case of bilateral polycystic ovaries was diagnosed in a 6-year-old Andalusian mare presented to Colorado State University. The ovaries were each approximately 15 cm in diameter and had remained enlarged for almost 2 years. Ultrasonographic evaluations and measurements of serum hormone concentrations were performed every 1-3 months. A laparoscopic ovarian biopsy was eventually performed on each ovary, and a histologic diagnosis of polycystic ovaries was made independently by pathologists at two institutions. The ovaries were subsequently removed, and a further histologic evaluation confirmed the previous diagnosis of polycystic ovaries. Cysts within the region of the ovulation fossa (Fig. 12) 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.

Figure 12. Equine ovary with multiple cystic structures in the region of the ovulation fossa - To view this image in full size go to the IVIS website at www.ivis.org. -

References

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