Blackwell’s Five-Minute Veterinary Consult
Clinical Companion

Equine Theriogenology
Mare
DEFINITION/OVERVIEW

Estrus is the period of sexual receptivity by the mare for the stallion. Estrus is abnormal when overt sexual behavior is displayed for longer or shorter periods than is considered normal for the species or the individual. Abnormal interestrus intervals can result from short or long estrus or diestrus intervals.

ETIOLOGY/PATHOPHYSIOLOGY

The mare is seasonally polyestrous, with estrous cycles in spring and summer months. The length of the average estrous cycle is 21 days (range: 19–22 days), which is defined as the period of time between ovulations that coincides with progesterone levels of less than 1 ng/mL. Estrus and estrous cycle lengths are quite repeatable in individual mares from cycle to cycle.

Key Hormonal Events in the Equine Estrous Cycle

- FSH (pituitary origin) causes ovarian follicular growth.
- Estradiol (follicular origin) stimulates increased GnRH (hypothalamic origin) pulse frequency to increase LH (pituitary origin) secretion.
- The surge of LH causes ovulation; estradiol returns to basal levels 1 to 2 days post-ovulation.
- Progesterone (CL origin) rises from basal levels (less than 1 ng/mL) at ovulation to greater than 4 ng/mL by 4 to 7 days post-ovulation.
- Progesterone causes a decrease in GnRH pulse frequency that results in an increase in FSH secretion to stimulate a new wave of ovarian follicles to develop during diestrus.
- Natural prostaglandin (PGF₂α) of endometrial origin is released 14 to 15 days post-ovulation causing luteolysis and a concurrent decline in progesterone levels.

Length of Estrus

Averages from 5 to 7 days in normal, cycling mares, but it can range from 2 to 12 days.
**Length of Diestrus**

It averages $15 \pm 2$ days, with diestral length exhibiting less variation than estrus in normal, cycling mares.

**Sexual Behavior**

- The absence of progesterone allows the onset of estrus behavior even if estrogens are present in only small quantities.
- Conditions that eliminate progesterone or increase estrogen concentrations are likely to induce estrus behavior. Persistence of these conditions results in abnormal estrus periods or interestrus intervals. The converse is also true.

**Systems Affected**

- Reproductive
- Endocrine

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**SIGNALMENT/HISTORY**

- Mares of any breed may be affected.
- Geriatric mares (older than 20 years) tend to have prolonged transition periods, longer estrus duration, and fewer estrous cycles per year.
- Ponies may regularly have longer estrous cycles than horses (an average of 25 days).

**Historical Findings**

- Chief complaint: Infertility, failure to show estrus, prolonged estrus, split estrus, or frequent estrus behavior may be reported.
- Teasing records: The teasing methods used should be critically reviewed, to include: frequency, teaser type (e.g., pony, horse, or gelding), stallion behavior (e.g., aggressive/passive, vocalization, proximity), and handler experience.
- Seasonal influences: Normal individual variation in the onset, duration, and termination of cyclicity can be mistaken for estrus irregularity.
- Individual reproductive history: Estrous cycle length, response to teasing, foaling data, and previous injuries or infections of the genital tract may be related to current clinical abnormalities.
- Pharmaceuticals: Current and historical drug administration may be related to current clinical abnormalities.

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**CLINICAL FEATURES**

- Body condition: Poor body condition or malnutrition may contribute to abnormal estrous cycles.
Perineal conformation: Poor perineal conformation can result in pneumovagina, ascending infection, or urine pooling, which may result in symptoms consistent with behavioral estrus.

Clitoral size: Clitoral enlargement may be related to prior treatment with anabolic steroids, progestational steroids, or intersex conditions.

TRP: Essential when evaluating mares with abnormal cycles. To be meaningful and allow full assessment of a mare, all three of the primary anatomical components of the mare's genital tract must be described: uterine size and tone; ovarian size, shape, and location; and degree of cervical relaxation. Serial examination three times per week over the course of several weeks may be necessary to completely define the patient's estrous cycle.

U/S: Useful to define normal or abnormal features of the uterus or ovaries.

Vaginal examination: Inflammation, urine pooling, cervical competency, or conformational abnormalities may be identified. May also be used to help identify the stage of the estrous cycle (e.g., appearance, degree of external cervical os relaxation).

When determining the cause of abnormal estrus intervals, it is helpful first to classify the abnormality in one of four categories and then to consider the common causes in each category as outlined here.

**Shortened Estrus Duration**

- Seasonality: Estrus duration tends to decrease in the height of the breeding season. This change may relate to more efficient folliculogenesis later in the breeding season (a normal physiologic shift).
- Silent estrus: Normal cyclic ovarian activity is occurring, but minimal or no overt signs of sexual receptivity are displayed. This is often a behavior-based problem associated with nervousness, a foal-at-side, or a maiden mare. Silent estrus has also been associated with previous anabolic steroid use.

**Lengthened Estrus Duration**

- Seasonality: Erratic estrus behavior associated with the transition period is common. Sexual receptivity can be short or long during vernal transition, but protracted estrus behavior is most common.
- Ovarian neoplasia (GCT, GTCT): Affected mares may chronically be in anestrus, exhibit persistent or frequent estrus behavior, or develop stallion-like behavior.
- Congenital disorders: Gonadal dysgenesis due to chromosomal defects (e.g., XO [Turner's syndrome], XXX) may be the underlying cause of anestrus, erratic estrus, or prolonged estrus.
- Hormone imbalance: Older mares may fail to ovulate and exhibit prolonged estrus, presumably due to ineffective LH release.

**Shortened Interestrus Interval**

- Uterine disease: Uterine inflammation (e.g., endometritis, pyometra) can result in atypical endometrial PGF$_2$α release, luteolysis, and an early return to estrus.
Systemic illness: Endotoxin-induced PGF$_2\alpha$ release can lead to premature luteolysis and a shortened interestrus period.

Iatrogenic/Pharmaceutical: PGF$_2\alpha$ administration, intrauterine infusions, and uterine biopsy procedures can also result in early regression of the CL and premature return to estrus.

Lengthened Interestrus Interval

Prolonged luteal activity: Can occur with a normal, but diestrual, ovulation that results in the formation of a CL insufficiently mature to respond to endogenous PGF$_2\alpha$ release during a cycle that would otherwise be of normal length; severe uterine disease (pyometra) that prevents release of uterine PGF$_2\alpha$; EED after maternal recognition of pregnancy has already occurred; a CL that is persistent (i.e., its function is prolonged beyond the normal range); or subsequent to an ovarian hematoma, a prolonged period may be necessary to achieve luteinization that it may respond to PGF$_2\alpha$.

Persistent CLs have also been associated with consumption of fescue forages.

Pregnancy: Luteal function persists in the presence of a conceptus. Estrus behavior during pregnancy is a normal occurrence and can be confused with abnormal interestrus intervals.

Iatrogenic/Pharmaceutical:

- Administration of progestin compounds to suppress behavioral estrus.
- NSAIDs can potentially interfere with endometrial PGF$_2\alpha$ release and result in prolonged luteal activity. There is no evidence that chronic administration at recommended therapeutic dosages inhibits the spontaneous formation and release of PGF$_2\alpha$ from the endometrium.
- GnRH agonist (deslorelin) implants used to stimulate ovulation have been associated with prolonged interovulatory intervals. At this time, deslorelin implants are unavailable in the United States but are still on the market in Canada and other countries. Their effect is more profound if PGF$_2\alpha$ is used during the diestrus period in an attempt to “short-cycle” the mare.

DIFFERENTIAL DIAGNOSIS

Differentiating Conditions with Similar Symptoms

- Frequent urination caused by cystitis or urethritis, bladder atony, urine pooling, vaginitis, or pneumovagina may mimic submissive urination and thus be confused with behavioral estrus.
- Defensive or aggressive behavior can be confused with anestrus. Teasing methodologies should be reviewed or altered to clarify.
Differentiating Causes

- Minimum database: Complete medical and reproductive history (including teasing records), general physical examination, and reproductive examination (TRP and U/S [to distinguish pregnancy and pyometra], vaginal examination). Additional diagnostic samples that may aid in establishing a diagnosis include uterine cytology, culture, and endometrial biopsy.
- Silent estrus is often due to poor estrus detection (teasing). Diagnosis: TRP at least three times per week combined with frequent serum progesterone assays to allow detection of a short or inapparent estrus period.
- The transition period in the northern hemisphere typically extends from February through April, the period in which anestrus mares begin to develop follicles but have irregular estrous cycles. Mares may exhibit persistent estrus behavior, irregular estrus periods, or irregular diestrus intervals. Diagnosis: season, combined with results of serial TRP and U/S confirming the presence of numerous small to large follicles on both ovaries that fail to progress to ovulatory size.
- GCT/GTCT can occur at any age, but it is more typically is seen in the middle-age or older mare. The affected ovary is usually enlarged and often the ovulation fossa is obliterated. The contralateral ovary is usually small and inactive. U/S of the affected ovary often reveals a multilocular *honeycomb* appearance. Diagnosis: TRP and U/S; endocrine assays are also useful (see Large Ovary Syndrome).
- Gonadal dysgenesis may not be recognized until a mare enters the breeding herd and fails to have normal estrous cycles. Diagnosis: TRP and U/S confirm the absence of normal ovarian tissue and a juvenile reproductive tract. Karyotyping provides a definitive diagnosis.
- Ovulations can occur in diestrus. The CL that forms from a diestrus ovulation may not be sufficiently mature (responsiveness requires a minimum of 5 days post-ovulation) to be lysed by endogenous PGF$_2$α at the end of diestrus. Therefore, diestral ovulations after day 10 of the estrous cycle result in persistent CL activity. Diagnosis: demonstration of a normal reproductive tract with failure of clinical estrus for more than 2 weeks post-ovulation and progesterone levels of greater than 4 ng/mL that last more than 2 weeks.
- The diagnosis of pregnancy, pyometra, endometritis, abortion, large ovary syndrome (including ovarian hematoma), and EED are discussed elsewhere.

**DIAGNOSTICS**

- Serum progesterone concentrations: basal levels of less than 1 ng/mL indicate the absence of ovarian luteal tissue. Active CL function is associated with progesterone levels of more than 4 ng/mL.
- Serum testosterone and inhibin concentrations: mares typically have testosterone values less than 50 to 60 pg/mL and inhibin values less than 0.7 ng/mL. Hormone
levels suggestive of a GCT/GTCT (in a nonpregnant mare) are: testosterone greater than 50 to 100 pg/mL (produced if thecal cells are a significant tumor component) or inhibin greater than 0.7 ng/mL, with a progesterone level less than 1 ng/mL.

- Transrectal U/S is routinely used to evaluate the equine reproductive tract. The reader is referred to other texts for a comprehensive discussion on this technique.
- Uterine endoscopy is useful to diagnose intrauterine adhesions, glandular or lymphatic cysts, and polyps.
- Uterine cytology, culture, and endometrial biopsy techniques are discussed elsewhere.

**THERAPEUTICS**

- Evaluate teasing methods: silent estrus may be a reflection of poor teasing management.
- Monitor the problem mare, including TRP or U/S, three times weekly to better define the reproductive cycle.
- The treatment of pregnancy, pyometra, endometritis, abortion, large ovary syndrome (including ovarian hematoma), and EED are discussed elsewhere in this text.
- Artificial lighting (photo stimulation) is a management tool used to initiate ovarian activity earlier in the year. When successful, mares bred earlier in the season foal earlier the next year, to accommodate breed registries that use the January 1 equine “universal birth date.” Photo stimulation does not eliminate vernal transition, but it merely shifts it to an earlier time of onset. Photo stimulation should begin no less than 90 days prior to the onset of early season breeding.

**Drug(s) of Choice**

- PGF₂α (Lutalyse® [Pfizer], 10 mg, IM) or its analogs, to lyse persistent CL tissue.
- Ovulation can be stimulated if a follicle is at least 30 mm by deslorelin, or equal to or greater than 35 mm by hCG (2,500 IU, IV).
- Altrenogest (Regu-Mate® [Intervet], 0.044 mg/kg, PO, SID, minimum 15 days) can be used to shorten the duration of vernal transition, providing follicles larger than 20 mm diameter are present and the mare is demonstrating behavioral estrus. PGF₂α on day 15 of the altrenogest treatment increases the reliability of this transition management regimen by lysing any late-to-luteinize (during the Regu-Mate treatment) transitional follicles.

**Precautions/Interactions**

**Horses**

- PGF₂α and its analogs are contraindicated in mares with asthma, COPD, or other bronchoconstrictive disease.
- Prostaglandin administration to pregnant mares can cause CL lysis and abortion. Carefully rule out pregnancy before administering this drug or its analogs.
- PGF$_2\alpha$ causes sweating and colic-like symptoms due to its stimulatory effect on smooth muscle cells. If cramping has not subsided within 1 to 2 hours, symptomatic treatment should be instituted.

- Antibodies to hCG can develop after treatment. It is desirable to limit its use to no more than two or three times during one breeding season, if possible. The half-life of these antibodies ranges from 30 days to several months; they typically do not persist from one breeding season to the next.

- Deslorelin implants have been associated with suppressed FSH secretion and decreased follicular development in the diestrus period immediately following its use, leading to a prolonged interovulatory period in nonpregnant mares. Implant removal within 1 to 2 days post-ovulation may decrease this possibility.

- Altrenogest, deslorelin, and PGF$_2\alpha$ should not be used in horses intended for food purposes.

**Humans**

- PGF$_2\alpha$ or its analogs should not be handled by pregnant women or people with asthma or bronchial disease. Any accidental exposure to skin should immediately be washed off.

- Altrenogest should not be handled by pregnant women or people with thrombophlebitis or thromboembolic disorders, cerebrovascular disease, coronary artery disease, breast cancer, estrogen-dependent neoplasia, undiagnosed vaginal bleeding or tumors that developed during the use of oral contraceptives, or estrogen-containing products. Any accidental exposure to skin should immediately be washed off.

**Alternative Drugs**

Cloprostenol sodium (Estrumate® [Schering-Plough Animal Health], 250μg, IM), is a prostaglandin analog. This product is used in similar fashion as the natural prostaglandin, but it has been associated with fewer side effects. It is not currently approved but is widely used in horses.

**Surgical Considerations**

- Poor vulvar conformation should be addressed by performing a Caslick's vulvoplasty (e.g., episioplasty) of a portion of the dorsal vulvar commissure to control pneumovagina.

- GCT/GTCT ovarian tumors should be removed surgically (ovariectomy).

- Urine pooling, rectovaginal fistulas, or cervical tears should be corrected surgically.

**Comments**

**Patient Monitoring**

Until normal cyclicity is established or pregnancy has been confirmed, regular reproductive examinations are recommended.
Possible Complications

Unless corrected, abnormalities in estrus behavior frequently result in infertility.

Abbreviations

CL      corpus luteum
COPD    chronic obstructive pulmonary disease
EED     early embryonic death
FSH     follicle stimulating hormone
GCT     granulosa cell tumor
GnRH    gonadotropin releasing hormone
GTCT    granulosa theca cell tumor
hCG     human chorionic gonadotropin
IM      intramuscular
IV      intravenous
LH      luteinizing hormone
NSAID   nonsteroidal anti-inflammatory drug
PGFα    natural prostaglandin
PO      per os (by mouth)
SID     once a day
TRP     transrectal palpation
U/S     ultrasound

See Also

- Aggression
- Anestrus
- Clitoral enlargement
- Disorders of sexual development
- Early embryonic death
- Endometritis
- Large ovary syndrome
- Ovulation failure
- Pneumovagina/Pneumouterus
- Prolonged diestrus
- Pseudopregnancy
- Pyometra
- Urine pooling/Urovagina
- Vaginitis and vaginal discharge
- Vulvar conformation

Suggested Reading


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