

# When it comes to estrus suppression, is mare a four-letter word?



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## Abstract

Perceived misconduct in mares is often suspected of being associated with estrous behaviors and may or may not be directly connected to the estrous cycle. Mares are seasonally polyestrous and based on the presence or absence of reproductive hormones, specifically estrogen and progesterone, their behavior can vary throughout the year. Concerns pertaining to mares' behavior are often attributed to their estrous cycle; however, undesirable behaviors need to be differentiated from other abnormal behaviors from nonreproductive causes. Although multiple treatments have been utilized by veterinarians for estrus suppression and manipulation, some of them are poorly effective whereas others may actually promote estrous behavior. Treatments can be categorized as progestogen supplementation, prolonging the luteal phase, suppression of ovarian follicular activity, and ovariectomy. This review details the individual therapies available for the potential treatment of estrous behavior and each therapy's associated efficacy.

**Keywords:** Mare, estrus suppression, ovariectomy, contraception

## Introduction

A challenge for the horse industry is that of 'difficult' or 'misbehaving' performance of mares when in behavioral estrus. Mares are frequently presented by owners and trainers for undesirable behavior perceived to correlate with cyclicity. However, a variety of other issues may result in mare's declining performance, including musculoskeletal, gastrointestinal, behavioral, and urinary tract disorders. Furthermore, perceived misbehavior should be considered as a welfare concern for those mares ridden by misinformed and frustrated owners or trainers deeming them as simply uncooperative. In cases where mares appear to be refractory to behavioral modification efforts, uninformed owners may persist in seeking an ovariectomy and insist that veterinarians perform this surgical procedure before documenting that the undesired behavior is due to estrus. This occurs despite evidence that estrous behaviors increase in mares after ovarian removal.<sup>1</sup> For veterinarians, it can be extremely frustrating in attempting to differentiate a lack of 'chemistry' between horse and rider, a deficiency of targeted horse training, or a true change in mare behavioral physiology over the course of the mare's estrous cycle. Therefore, it is important to combine baseline knowledge of normal mare's estrous cycle and associated reproductive behaviors with a complete physical examination and potential ancillary tests (e.g., endoscopy of the reproductive tract, lameness examination, etc.) before attributing behaviors to specific stages within the reproductive cycle. Briefly the normal estrous cycle and associated behaviors in the mare will be reviewed followed by various treatment options while focusing on their

individual level of empirical evidence of success, advantages, and disadvantages.

## Equine estrous cycle

Mares are long-day, seasonally polyestrous breeders. Mare's reproductive seasonality (regulated by photoperiod) has 4 phases in a year: anestrus, spring transitional period, ovulatory season (include estrus and diestrus), and autumn transitional period. However, a small percentage of mares will ovulate year-round and never enter the other 3 phases.<sup>2,3</sup>

Ovulatory season begins by the first ovulation that may be detected via regular transrectal ultrasonographic examinations or by determination of serial serum progesterone concentrations. As stated above, estrous cycle has 2 stages: estrus and diestrus. Estrus averages 6.5 days and is characterized by sexual receptivity, dominant follicle emergence, basal concentrations of plasma progesterone (< 1 ng/ml), and ovulation. Estrogen begins to increase 6 - 8 days prior to ovulation and its presence is due to increased follicular growth and activity. Higher concentrations of estrogen with baseline progesterone concentrations are positively correlated with estrous behavior expression. Length of this estrus period becomes abbreviated as day length increases and summer solstice approaches. Ovulation marks the end of estrus (day 0); however, mares can still exhibit estrous behavior up to 24 - 48 hours after ovulation. Diestrus averages 15 -16 days, is initiated after ovulation, and continues through luteolysis. This stage is characterized by the presence of a corpus luteum (CL), higher concentrations of

plasma progesterone, and mare's nonreceptive behavior toward stallion.

Estrogen is not the main dictator for reproductive behavior but it is rather regulated by progesterone concentrations. Basal concentrations of progesterone will allow for varying degrees of behavior consistent with estrus. It should be noted that the ovulatory season is the only period of the year during which there is endogenous progesterone production by the CL as a result of ovulation of 1 or more follicles. This concept needs to be understood to determine whether or not a behavior is associated with a cyclical pattern, and if it is, what is the dominant hormone dictating behavior expression. Furthermore, in most mares, these phases are differentiated by the distinct behaviors when mares are 'teased' under controlled conditions to a stallion. It is only when a stallion is used to tease a mare that a particular behavior can be attributed to a particular stage of the estrous cycle. Additionally, transrectal ultrasonographic examinations and estimation of serum progesterone concentrations can aid in determining the phase of mare's estrous cycle.

Anestrus occurs when shortened day length increases pineal gland melatonin production and a subsequent decrease in hypothalamic gonadotropin releasing hormone (GnRH) production. During this period of lower GnRH production, most mares are anovulatory and generally reproductively quiescent. Although ovulation does not occur during this phase, some follicular growth is sustained. There is no luteal source of progesterone during this phase and as a result, mares may exhibit varying degrees of estrous behavior and stallion receptivity.

Spring transition occurs during increasing daylength, whereas autumn transition occurs during decreasing daylength and both are characterized by estrus without ovulation. It is during these periods that owners get frustrated with unpredictable estrous behavior since mares produce follicular waves without ovulation that may extend to several days and weeks. During spring transition there is a progressive increase in follicular activity with development of up to 3 anovulatory follicular waves prior to the ovulatory wave.<sup>4</sup> It has been hypothesized that failure of ovulation during spring transition is due to insufficient stores of pituitary luteinizing hormone (LH) or lack of steroidogenic competence of ovarian follicles.<sup>5,6</sup> During autumn transition there is a progressive decline in luteal and follicular activity marked by decreased steroidogenesis contributing to either a long anovulatory follicular phase or a shortened luteal phase. Lastly, anovulatory hemorrhagic follicles are more common in autumn transition. These occur when a dominant follicle fails to ovulate and subsequently, the follicular lumen fills with blood. Some anovulatory hemorrhagic follicles appear to luteinize and synthesize progesterone; however, they do not appear to be responsive to prostaglandin  $F_{2\alpha}$  and the average interovulatory interval is  $38.5 \pm 15$  days.<sup>7</sup> In summary, autumn transition is accompanied by erratic estrous cycles characterized by long follicular phase/short luteal phase or anovulatory hemorrhagic cycles. This transition can be  $\geq 60$  days.

## Estrous behavior

It is important to understand the range of behavior in normal mares during estrus (i.e., the follicular phase) in order to assess whether or not a behavior is attributable to ovarian hormone production (or lack thereof). These behaviors can only be objectively evaluated in the presence of a stallion under controlled teasing conditions. Such estrous behaviors include increased frequency of approaching the stallion, leaning hindquarters toward the stallion, relaxed facial muscles, slightly lowered head, ears turned toward the side, posturing, clitoral eversion, bent forelimb, vulvar winking, and urination. Posturing is the most significant sign of receptivity and is characterized by a full body response: arched tail, flexed stifles and hocks, tipped pelvis, and weight distribution to the front limbs; this posture allows the mare to support the weight of a stallion during breeding.<sup>1</sup> In the absence of a stallion, estrous behavior may be directed towards inanimate objects or other animals including geldings, mares, and even cattle; however one cannot truly conclude if a mare is in 'heat' based on her behavior in the absence of a stallion. In contrast, during diestrus, and thus under the influence of luteal progesterone, mares are nonreceptive to stallion advances and may squeal, bite or kick. Other nonreceptive behaviors include pinned ears, tail swishing, and walking or running away from the stallion.

Given that the absence of progesterone is a prerequisite for displaying estrous behavior in mares, behaviors consistent with estrus are observed in anestrus mares and even ovariectomized mares.<sup>1</sup> In fact, the adrenal gland serves as a small source of sex steroid production (estradiol, progesterone, and testosterone) and it is believed to have a role in facilitating paradoxical estrous behavior by some.<sup>8</sup> Paradoxical estrous behavior is unique to the mare and is thought to be important for maintaining a bond between a stallion and his harem of mares in the wild, as they band year-round. This phenomenon is of vital importance clinically because bilateral ovariectomy may not improve estrous behavior and may exacerbate the objectionable behavior. In fact, bilateral ovariectomy may be performed to make a 'jump' or 'teaser' mare for use in situations for semen collection from stallions.

Behavior problems in the performance mare: etiology and clinical evaluation

Often mares are presented to veterinarians for complaints of estrous behavior affecting performance. Common complaints from owners that are not associated with estrous behavior include kicking, biting, squealing, stomping in the trailer, tail swishing, and poor attitude. Not all owners can rightfully discriminate actual estrous behavior from other behavioral issues associated with poor discipline or medical problems. Described behaviors by some owners will be the result of inadequate training e.g., the inability of an owner to catch a mare in a pasture is likely not estrus related. However, some mares do fail to perform at their best due to strong estrous behavior and may become difficult to manage, perform erratically, or appear lame.<sup>9</sup> Estrogen has also been associated with laxity in ligaments so lameness may be exacerbated during estrus.<sup>9</sup> Common complaints associated with estrus include elevating tail or winking during performance; leaning on fences toward other horses or stimuli; slowing or stopping at other horses

while riding; wet stall/legs/tail due to excessive urination; posturing in the arena and/or intermittent colic. Therefore, 'problem' mares should be examined by a veterinarian when owner perceives that the behavior is occurring and examination procedures need to include, not only evaluation of the reproductive tract, but must also include a complete lameness evaluation to identify issues that may or may not be estrogen related and exclude other causes of poor performance and undesirable behavior before assigning a diagnosis.

A complete reproductive examination should include transrectal palpation and ultrasonography, external examination, vaginal speculum examination, estimation of serum progesterone concentrations, and teasing behavior to a stallion. Granulosa-theca cell tumors can be characterized by variable unwanted behavior, depending on the predominant hormone. Undesirable behavior can also occur with actual ovarian pain manifested in the region of the epaxial muscles during the periovulation period, termed 'mittelschmerz' in women, should be considered as a potential reason for lameness or lack of performance in 'misbehaving' mares expressing behavioral estrus.

Confusion between contraception and suppression of behavioral estrus in mares, especially by laypeople, may exist in part due to 'mittelschmerz'. Mares that exhibit pain at ovulation can be painful on palpation of the ovary, painful when touching their flanks, or painful while riding. These mares may resist saddling occurs near the period of ovulation. Mares may require serial reproductive examinations to determine the frequency of the behavior and the relationship to the estrous cycle. If the behavior is deemed not related to the estrous cycle, it is important to systematically evaluate other organ systems to determine other medical problems that may be occurring. Musculoskeletal conditions such as joint and/or back pain should be ruled out as a primary cause of poor performance. Gastrointestinal abnormalities such as enteroliths or gastric ulcers must be considered as a cause for intermittent pain. Although urogenital conditions (e.g., uroliths, vaginitis, and pneumovagina) can be confused as causes of estrus-associated behaviors due to increased frequency of urination or vulvar winking, these conditions can be ruled out during a thorough urogenital examination.

Treatment for estrus suppression can be pursued once other causes of poor performance and undesirable behavior are ruled out and it is determined that the mare is free from ovarian pathology. It is important to emphasize to owners that estrous behavior is a normal behavior, some mares exhibit it more intensely than others and that there are several treatment options available to suppress estrous behavior with varying efficacy. Depending on the owner's goals, mares with overt estrous behavior may need to be treated either for a prolonged period or only short term (i.e., to get through a show). Some treatment options are superior to others, with each having both advantages and disadvantages. Not all treatments may be suitable for all mares given that behavioral problems may occur at different stages of the estrous cycle.

## Progestogen therapy

Progesterone has a strong negative feedback effect on LH secretion by the adenohypophysis<sup>10,11</sup> and can be implemented throughout the year as a therapy for estrus suppression. Progestogens bind and activate progesterone receptors thereby suppressing estrous behavior. Plasma progesterone concentrations > 1 ng/ml must be maintained to block estrous behavior.<sup>12</sup> Progesterone has a stronger negative impact on LH secretion than it does on follicle stimulating hormone (FSH) secretion, therefore, follicular activity is present due to incomplete FSH suppression, and 'silent' diestrus ovulations (i.e., not associated with estrus) are still possible.<sup>13</sup> Mares that demonstrate misbehavior associated with 'mittelschmerz' pain may not benefit from exogenous progestogens as ovulation, and thus ovulatory pain, is still possible. In humans, progesterone has a tranquilizing effect on the central nervous system,<sup>14</sup> thus it can be argued that progestogen treatment may not be ideal for mares that are high-performance athletes.

### Natural progesterone

Natural progesterone can be compounded in an intramuscular injectable oil-based form, with 100 mg of progesterone per day sufficient to block estrous behavior in mares.<sup>15</sup> Anecdotally, this is the quickest acting therapy available and achieves adequate suppression within 1 - 2 days after treatment. A long-acting intramuscular formulation is available and is given every 7 - 10 days for suppression of estrous behavior by maintaining concentrations of serum progesterone > 2 ng/ml.<sup>16</sup>

Advantages of natural progesterone include its high efficacy at suppression of estrous behavior, its rapid onset, and ease of treatment year-round for estrus suppression. Disadvantages of natural progesterone include associated injection site swelling and pain that is not ideal for performance mares, the need for multiple injections, and the associated human safety issues due to liposolubility and ease of transdermal absorption.

### Altrenogest

Altrenogest (Altren®, Aurora Pharmaceutical, Inc., Northfield, MN; Regumate®, Merck Animal Health, Summit, NJ) is a progestin considered to be the 'gold-standard' therapy for the suppression of unwanted estrous behavior. It has been FDA approved for the use in horses and is given orally once a day. Estrus suppression is accomplished within 3 days after treatment initiation. Because of its high efficacy, treatment of altrenogest and observation for behavioral improvement may be used as a diagnostic trial when it is unclear whether a particular behavior is due to reproductive cyclicity.

Altrenogest has also been compounded into an intramuscular injectable form.<sup>17</sup> There are 2 formulations available: a 12-day formulation (Altrenogest BioRelease LA150, BETPharm, Lexington, KY) and a 30-day formulation (MP500, BETPharm, Lexington KY). However, these injectable forms are not FDA approved and available studies have only been completed by the compounding drug company.<sup>17</sup>

Advantages of oral use of altrenogest include its high efficacy, ability to be implemented as therapy year-round, absence of reported long-term adverse consequences on mare fertility and body condition, and oral treatment.<sup>18</sup> Disadvantages include the associated human safety issues with ease of transdermal absorption, the daily dosing regimen, and the cost of the product. The advantages of formulated, intramuscular altrenogest preparation include its reduced frequency of treatment compared to its oral formulation, its progestogenic effect to successfully block return to estrus, and its ability to implement year-round. Disadvantages of injectable altrenogest include injection site soreness, cost, and lack of long-term fertility studies.

### Synthetic progestin implants

Various hormone implants are available in other species and have been unsuccessfully used in mares for estrus suppression.<sup>19-21</sup> Although implants may be requested by owners, they do not provide the minimum amount of progesterone required to prevent estrous behavior in the mare and therefore are not effective.

### Other injectable progestins

Numerous sustained-release injectable progestins, including synthetic progestins formulated for human use, have been used off-label in mares to suppress estrous behavior. The perceived advantage of these preparations is that they may be given periodically instead of daily. However, use of these products does not ensure that the compound will bind to mare's progesterone receptors and result in suppression of estrous behavior. The most common progestins available are the human contraceptive medroxyprogesterone acetate (Depo-Provera® Pfizer Injectables; New York, NY), hydroxyprogesterone caproate (Makena®, AMAG Pharmaceuticals, Inc; Waltham, MA), and megestrol acetate (MGA 200 Premix®, Zoetis; Parsippany, NJ). All 3 of these progestins have been examined with regard to their ability to maintain pregnancy in the mare as an indicator of maintaining adequate blood progesterone concentrations<sup>22</sup> and all 3 failed to maintain early pregnancy. Medroxyprogesterone acetate is the only 1 that has been studied for its ability to suppress estrous behavior in mares and failed to do so.<sup>23</sup> Therefore, none of these progestins can suppress estrous behavior in mares. However, many owners and veterinarians continue to use these products with the perception that they are effective. This further indicates that many perceived misbehaviors are likely unrelated to reproductive hormones or cyclicity. Currently, the only effective synthetic progestogen in mares is altrenogest.

### Prolongation of luteal phase

Extending the function of CL will prolong the luteal phase (diestrus) and the production of endogenous progesterone. Because estrus suppression methods based on this mechanism of action rely on ovulation and subsequent CL formation, they can only be used in cycling mares.

### Pregnancy and pseudopregnancy

Prior to pharmacological methods of estrus suppression becoming available, pregnancy was used as a method for suppressing estrous behavior. Duration of pregnancy is quite variable and can range from 320 - 380 days. During the early period, the primary CL is responsible for endogenous progesterone production and subsequent pregnancy maintenance and suppression of estrus. By day 35, endometrial cups begin forming and produce equine chorionic gonadotrophin that is responsible for luteinization of ovarian follicles. Equine chorionic gonadotropin is continually secreted, and progesterone reaches maximal concentrations at 90 - 120 days of pregnancy when the placenta begins to maintain pregnancy via placental progestogen production. Pregnancy is currently not recommended as a method of estrus suppression. In addition, an important disadvantage to pregnancy is the regulations by differing sports' governing bodies regarding the stage of pregnancy during which a mare can compete.

Pseudopregnancy, or false pregnancy, is accomplished when an embryo is manually reduced after the period of maternal recognition of pregnancy. Embryos can be reduced via the transrectal pinching technique after day 16. Manual reduction of embryos between days 16 - 22 resulted in prolonged interestrus interval (mean 82 days) in 10 of 11 mares.<sup>24</sup> This method is effective at suppressing estrous behavior due to maintenance of endogenous progesterone production for at least 60 days. However, this method may present ethical issues by termination of a viable pregnancy and includes the accumulated costs accompanying breeding and cycle management. Similar to the above recommendations pertaining to pregnancy and estrus suppression, this is also not a currently recommended method to suppress estrus.

### Intrauterine devices

There have been similar results reported in mares with marbles and other intrauterine devices.<sup>25-28</sup> From these results, it was ascertained that behavioral estrus suppression should not be expected to occur following insertion of an IUD. Further, noted disadvantages in addition to the difficulty of retrieval is that there is a high probability of failure and with marbles well-documented cases of diffuse endometrial damage induced from glass shards embedded into the endometrium, in addition to cases of pyometra.<sup>29</sup> Therefore intrauterine devices have been shown to be unreliable by several studies, with numerous substantial complications reported. There are other superior methods available to suppress estrus.

### Exogenous oxytocin

Serial oxytocin treatment has become a method of increased practicality and efficacy to prolong CL function (i.e., luteostasis) in the mare; not often discussed is the path taken, and discoveries made, prior to arriving where we are today. In an attempt to induce luteolysis with exogenous oxytocin to stimulate an endogenous PGF<sub>2α</sub> release, it was reported<sup>30</sup> that 10 IU of intravenous oxytocin treatment in the mid to latter half of the luteal phase, prevented 4 mares from returning to physiological estrus, as none of the mares' serum progesterone concentrations reached below 4 ng/ml. Also, mare's recognition



of pregnancy occurs between days 11 and 13, a period when uterine responsiveness (i.e., secretion of  $\text{PGF}_{2\alpha}$ ) to oxytocin is noticeably different between pregnant and nonpregnant mares.<sup>30</sup>

Endometrial biopsy tissue collected from nonpregnant mares exposed to exogenous oxytocin released  $\text{PGF}_{2\alpha}$ .<sup>31</sup> Additionally, biopsies collected 14 days after ovulation from nonpregnant mares had higher concentrations of endometrial oxytocin receptors compared to day 14 pregnant mares. When uterine biopsies were obtained at points when oxytocin receptors were described to be at their lowest (i.e., estrus, day 8 postovulation), no  $\text{PGF}_{2\alpha}$  release was identified.

This accumulated information was later applied clinically for the purposes of behavioral estrus suppression, wherein it was reported that 60 IU of oxytocin treatment in the muscle, twice daily, on days 7 - 14 postovulation, prolonged CL function in 6 out of 6 mares through day 30.<sup>32</sup> Later it was reported that decreasing the injection frequency to once daily was equally effective; it has since been concluded that the critical threshold for oxytocin to promote luteostasis is somewhere between 10 - 60 IU and it should be noted that 10 IU intravenous or intramuscular treatment once daily failed to induce CL luteostasis.<sup>33,34</sup>

A behavior study utilizing 60 IU intramuscular once daily treatment protocol prolonged CL function (i.e., serum progesterone concentrations maintained  $> 1.0$  ng/ml) for  $68.8 \pm 4.1$  days in 67% of treated mares; interestingly, 'weak' expression of estrous behavior was noted in 5 of 6 treated mares with prolonged CL function.<sup>35</sup> Also of interest, is that 2/9 saline-treated control mares with spontaneous luteostasis maintained CL function for  $77.5 \pm 0.2$  days.<sup>35</sup>

Disadvantages of this method, as described above, includes the requirement of reproductive cyclicity, multiple daily injections, and veterinary fees associated with cycle management needed to accurately identify the day of ovulation and time oxytocin injections appropriately. However, if the owner wants to forgo cycle management costs, 60 IU of oxytocin in the muscle, once daily, for 29 consecutive days has also proven effective (i.e., 7/9 oxytocin treated mares experienced luteostasis compared to 1/7 saline-treated control mares).<sup>36,37</sup> One notable caveat to this protocol that owners should be made aware of is that initiating injections on a random day within a mare's estrous cycle will ensure that a certain percentage of these mares will enter estrus within a short time frame. Oxytocin-induced luteostasis was observed in 3 of 7 treated mares only after they entered estrus and completing ovulation; these events were reported to occur within 1 week after initiating injections.<sup>37</sup>

Advantages associated with oxytocin-induced luteostasis for estrus suppression includes its efficacy, low cost, and reversibility with exogenous  $\text{PGF}_{2\alpha}$  treatment. It has yet to be reported that the use of 60 IU (3 ml) of oxytocin has resulted in adverse effects even though 60 IU is higher than doses typically utilized for management of abnormal uterine fluid accumulation during breeding cycle management or treatment of endometritis (i.e., 0.5 - 1 ml). Concerns of unyielding uterine contractions and subsequent colic behaviors can be attenuat-

ed when one recalls that, not only is there an increase in the amount of uterine-relaxing progesterone concentrations, but there also appears to be a relatively low number of oxytocin receptors within the diestrous uterus when oxytocin injections are initiated.<sup>31</sup>

## Diestrual ovulation

In contrast to other species, mares can ovulate during diestrus in the presence of high circulating progesterone concentrations. The frequency of diestrous ovulations varies according to breed. Thoroughbreds and Quarter Horses having as many as 20% of ovulations occurring during diestrus whereas the frequency is very low in ponies.<sup>38,39</sup> Diestrual ovulations that occur 1 - 4 days prior to luteolysis may cause a prolonged luteal phase, as the immature CL does not undergo luteolysis following release of endogenous prostaglandin. Induction of a diestrual ovulation using 3000 IU of human chorionic gonadotropin (hCG) intravenously successfully resulted in a prolonged luteal phase (2 - 3 months) in 4 of 5 treated mares that developed a follicle  $> 30$  mm in size.<sup>40</sup> However, not all mares developed a large enough follicle to induce ovulation on their first cycle. Advantages of this option for treatment of estrus suppression include its effectiveness if conditions are met (30 mm late diestrual follicle that responds to hCG treatment). However, a major disadvantage is that only a small percentage of mares will present with a diestrual follicle large enough to respond to treatment, and they may or may not respond to hCG treatment. Another limitation that hinders its use in practice includes the necessity of multiple transrectal ultrasonography to identify an appropriately sized diestrual follicle that is capable of responding to an ovulation induction agent.

## Intrauterine plant oil

An intrauterine infusion of 1 ml of either coconut or peanut oil on day 10 after ovulation prolonged the luteal phase in 11 of 12 treated mares as assessed by concentrations of progesterone above baseline for 30 days.<sup>41</sup> However, estrous behavior was not documented. In a follow-up study,<sup>42</sup> return of mares to estrus was observed on days 10; 12 of 12 mares returned with a normal decline in progesterone at luteolysis. Based on the conflicting data, more work is needed to determine whether intrauterine plant oil treatment is an effective method for estrus suppression in mares and whether there are any associated side effects. If effective, it would require some cycle management to identify the day of ovulation with resultant prolongation of endogenous progesterone production. As with other methods of prolongation of luteal function, reproductive cyclicity must be present.

## Suppression of ovarian follicular activity

There is a difference between suppression of behavioral estrus and contraception. The focus in this section is on suppressing ovarian function. This is by targeting and subduing the hypothalamic-adenohypophyseal-ovarian axis. By downregulating the hypothalamic production of GnRH, there is a subsequent reduction in pituitary gonadotropin production and a resultant suppression of ovarian activity. Methods used in this effort include GnRH agonists wherein the adenohypophysis is

initially hyperstimulated and eventually desensitized.<sup>43</sup> However, the duration of estrus suppression is short-lived (until follicular growth resumes) and dose dependent. Another strategy is GnRH antagonists that act by inhibiting the action of GnRH and thereby inhibiting gonadotrophin secretion and subsequent ovarian activity.<sup>44-47</sup> Although ovarian activity can be suppressed herewith, behavioral estrus can be inconsistent with this treatment; additionally, frequent treatment, short-term effects, and highly variable responses among mares also reduce the indications for clinical application of this treatment option.

By employing these methods, the reduction in follicular growth and subsequent lack of ovulation decrease endogenous production of estrogen and progesterone. Typically, mares that undergo these therapies exhibit behavior similar to their anestrus behavior; therefore, it may not suppress or solve behavior problems if mares are reported to exhibit estrous behavior in the winter months. The therapies listed below may be a useful test of the likelihood of the efficacy of ovariectomy for behavioral modification. Finally, antiGnRH immunization, where a GnRH carrier protein and adjuvant can induce neutralization of the deca-peptide via production of anti-GnRH antibodies. There is a decrease in gonadotropin production and a subsequent reduction in ovarian activity. However, mare response, as indicated by antiGnRH antibody titers, is variable and estrus related behavior may or may not correlate with the achieved level of ovarian suppression.<sup>47</sup>

### Bilateral ovariectomy

Regarding bilateral ovariectomy, confusion between contraception and suppression of behavioral estrus in mares, especially by laypeople, may exist in part due to public experience with spayed bitches and the dogma that 'ovarian removal results in removal of natural breeding behavior'.<sup>48</sup> In contrast to the bitch, however, as noted above, mares that have been ovariectomized express paradoxical behavioral estrus. Also, there is often an increase in the frequency compared to ovary-intact mares since there are cyclical phases of diestrus in the latter.<sup>8,48-50</sup>

In that bilateral ovariectomy will result in abolishment of luteal potential and abolishment of ovulation and its associated discomfort, it may be an effective therapy for behavioral modification in mares that exhibit adverse behavior during diestrus or mares that exhibit adverse behavior due to 'mittelschmerz'. Bilateral ovariectomy may also be effective in mares that have estrous behavior problems only during the ovulatory season and do not exhibit estrous behavior problems during anestrus. However, bilateral ovariectomy may not be effective in mares that exhibit overt estrous behavior during the ovulatory season and also overt estrous behavior during anestrus as bilateral ovariectomy will result in the same endogenous hormonal environment as is present during anestrus or even times of ovarian suppression. Therefore, when considering ovariectomy as a treatment option for overt estrus behavior, it would be useful to observe response to therapy aimed at suppression of ovarian activity (see above) or anestrus behavior. In general, client satisfaction with bilateral ovariectomy is relatively high with 78% (18/23) of owners being satisfied or very satisfied with the procedure.<sup>51</sup> Veterinarians must keep in mind that an

ovariectomy may be classified as successful by an owner even if a behavior was not reproductively related. The advantage of this treatment option is that potential long-term success.

However, due to mare variability, bilateral ovariectomy may not be effective in eliminating unwanted behavior. Additionally, ovariectomy poses surgical risk as well as irreversible loss of breeding potential. Case selection is therefore extremely important if considering this option.

### Conflict of interest

None to declare.

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