

## How to recognize and manage the high-risk pregnancy mare

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### Introduction

The early diagnosis of a pregnancy that is in jeopardy could be a challenging issue for veterinarians. There are many conditions that could put the pregnancy of the mare at risk, particularly during the last trimester of pregnancy.

Mares could become high risk of carrying a foal to term either because they have medical/reproductive issues at the time of breeding that can be exacerbated during the pregnancy, or because they develop medical conditions during the gestation. Examples of pre-existing conditions include metabolic syndrome, osteo-arthritis, metabolic syndrome and poor perineal conformation/uterine health. Examples of conditions that may develop as gestation advances include Undiagnosed twins, placental infection, excessive abdominal distention, abdominal or Musculo-skeletal pain. Some of these although not directly related to the reproductive tract can put the mare and/or the fetus at risk.

### Conditions causing the risk of the mare or the fetus

It is important particularly for mares with a history of reproductive problems to monitor the pregnancy on a regular basis. Things that should be evaluated include the placental thickness, the nature of the allantoic and of amniotic fluid and the viability of the fetus gauge through the fetal heart rate. It is not uncommon for mares with history of previous pregnancy losses to be maintained on a progestagen such as altrenogest for prolonged period of periods of time. Failure to monitor mirrors that are on prolonged therapies can result in the death of the fetus with a consequent mummification or maceration.

Poor perineal confirmation coupled with poor breeding management could result in seeding the vagina or the cervix with bacteria that could colonize the pregnant uterus and the placenta provoking a placental infection jeopardizing the viability of the fetus.

Hydropic conditions such as hydro-allantois or hydro amnion Our conditions that have a sudden onset of large abdominal distension with the mere slightly painful and on the rectal exam it is difficult to identify the foal due to the large volume of fluid and the tightness of the uterus. Depending on the length of gestation it is often recommended to induce abortion.

Colic in the late term pregnant mare could be challenging because of the size of the uterus occupying a large portion of the abdominal cavity. Clinical signs become a critical part of making a diagnosis. Colleague of gastrointestinal origin we'll have a mayor with moderate to severe pain. Oftentimes the rectal exam could be difficult and other signs such as fecal production and gastrointestinal motility become hallmarks for the diagnosis. Uterine torsion is another important differential in colic. However, these mares often will present with low grade pain of prolonged duration That most of the time is refractory to painkillers. Rectal exam is the most important procedure for diagnosis.

Musculoskeletal problems include weakening of the ventral abdominal musculature With the development of herniation or pre pubic tendon rupture. Treatment for these conditions include pain management

and support of the ventral abdominal musculature. In addition these mares should be considered candidates for following induction. Depending on the situation the reproductive future of these mares is likely to be limited to assisted reproductive technologies such as embryo transfer.

Osteoarthritic conditions, or soft tissue problems of the feet and legs could also represent a problem for late term pregnant mares. As the fetus increases in size and the mare becomes heavier, chronic pain could become an issue. Orthopedic management as well as pain management become an important part for a good prognosis.

Often owners as well as veterinarians are concerned because of excessively prolonged gestations in mares. In the southern United States it is common that mares that have been fed fescue grass contaminated with the fungus *Acremonium Coenophialum* will have a low prolactin level particularly in the last trimester of pregnancy making these mares delay the readiness for birth. As a consequence, these mares often will have a thickened placenta and weak foals that often ha foals are weak. Other reasons why mares could have prolonged gestations include uterine fibrosis reducing utero-placental contact, time of breeding and a sire effect.

### Summary

In summary, there are several conditions that can put the health of the mare and or the fetus at risk. Consequently the veterinarian must be vigilant to the sudden and subtle changes that could indicate possible problems. Early detection becomes paramount in order to be able to support both mare and fetus in order to carry a pregnancy to term. Veterinarians attending high risk mares must always keep in mind that high risk mares may have a higher incidence or be prone to dystocia. In addition foals born from high risk mares even though they might appear healthy in the first few hours of life, need to be observed closely to insure that they normal.

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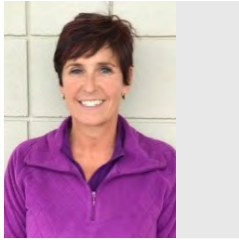
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## Update on Placentitis

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A recent report estimated that the proportion of annual lost pregnancies in Thoroughbred mares ranges from 7.9% to 15.2% in the UK, Ireland, and Kentucky. MaCleay et al, showed that the most common causes of pregnancy loss world-wide from 1960-2020 include EHV-1, placentitis, leptospirosis, twinning, congenital abnormalities, EHV-4, umbilical cord torsion and equine amnionitis/mare reproductive loss syndrome. Therefore, if reproductive problems that arise during gestation, especially placentitis are diagnosed early, and treated appropriately fetal viability may increase, producing a live foal.

Placentitis accounts for 20% of reproductive failures in Kentucky verses 9.8% in the United Kingdom. There are three different categories by which placentitis can be defined depending on where bacteria gain access to the fetus: ascending, focal mucoid, and hematogenous. Although bacteria such as *S. Zooepidemicus*, *E. Coli*, *Pseudomonas Pasteurella*, *Crosiella Equi*, *Amycolatopsis* and *Aspergillus* spp. have been the norm, new bacteria are being identified such as *Mycobacterium* spp. *Cellulosimicrobium cellulans*, *Pantoea agglomerans*, *Stenotrophomonas maltophilia*.

Mares that may be considered high risk for pregnancy loss or placentitis can undergo, monitoring of the utero-placental and fetal units by screening monthly with transrectal and transabdominal ultrasonography, with measurement of hormone and inflammatory biomarkers so early detection of abnormalities is possible. Trans-rectal ultrasonographic evaluation of the caudal reproductive allows determination of fetal presentation, combined utero-placental thickness at the cervical star, orbital diameter, umbilical chord and blood flow of the fetus. Integrity of the utero-placental unit at the cervical star region helps to identify opening and measurements of the cervix, placental separation, placental or uterine edema or the presence of exudate. Qualitative and quantitative assessment of fetal fluids can be monitored by trans-rectal ultrasonography. Fluids that have increased echodensity may have increased cellularity from infection or inflammation and therefore should be re-evaluated. Bucca determined that measurement of the intra-cranial blood flow impedance of the middle cerebral artery can also help identify a compromised fetus.

Trans-abdominal ultrasonography is useful in evaluating multiple fetuses, fetal growth, activity, mobility, presentation, viability as well as placental abnormalities, fetal fluid volume and echogenicity. A rapid examination protocol (fetal heart rate, aortic diameter and CTUP) can be used or a more indepth evaluation of heart rate and rhythm, fetal activity, size, stomach measurements, cervical pole and fetal fluid depth can be done. Although placental thickening is difficult to interpret trans-abdominally, due to the stretching and contracture of the different regions of the pregnant uterus and fetal positioning, separation of the chorioallantois from the endometrium and the presence of exudate as seen with mucoid or hematogenous placentitis can be identified.

In the normal physiology of pregnancy, progesterone (P4) is synthesized by the ovaries until about 150 days of gestation. During the second half of pregnancy little if any P4 is present because it is rapidly metabolized into progestagens. These progestagens increase gradually during the last few weeks prior to parturition (>300 days) but decline within a few days or even hours of delivery. In the first trimester impending abortion is preceded by declining or low P4 levels. However, fetal losses or premature deliveries in late gestation, particularly those caused by placentitis are associated with high concentrations of total progestagens in the maternal plasma. Ousey et al further demonstrated using gas chromatography-mass

spectrometry that progestagen profiles for mares with placentitis had increased P5 and/or P4 production by the fetus, probably caused by chronic fetal stress, leading to increased metabolism and elevation of several other progestagens. In mares with avillous placenta, placental edema, fetal distress (colic, uterine torsion) production of progestagens was dramatically reduced indicating the importance of a healthy fetoplacental unit for progestagen formation and suggesting lack of functional placental. Care must be taken when evaluating progestagen levels that it is known which progestagens cross-react with the particular laboratory assay and what the normal reference ranges are for that specific laboratory.

Although commercially only total serum estrogens from the mare can be assessed at this time, recent studies have looked at circulating concentrations of steroid hormones and AFP during ascending and mucoid placentitis. Comparing serum concentrations of progestagens, estradiol-17 $\beta$ , the ratio of estradiol-17 $\beta$  to progestagens, and AFP of mares with ascending placentitis to gestationally age-matched control mares, there is a significant increase in progestagen and AFP noted in ascending placentitis in the weeks preceding parturition. Additionally, a significant decrease in both estradiol-17 $\beta$  and the ratio of estradiol-17 $\beta$  to progesterone was noted in the diseased group when compared to controls. (Fedorka et al 2020/2021) Serum Amyloid A (SAA) an acute phase protein has also been identified to be elevated in experimental placentitis compared to normal pregnancies. (Canisso 2014, Russolillo 2023). It is important however to remember that natural placentitis is potentially a slow progressive process versus experimental. A recent study in which there were normal matched gestational aged mares, in pre-onset and early onset of ascending placentitis found no differences between groups and timepoints for immunological and inflammatory parameters including SAA and AFP. In hormonal assays no difference was found in plasma progestogen levels and estradiol 17B/progestogen ratio. Plasma estradiol-17B concentrations approached significance. (Feijo 2023)

In an effort to identify the mechanisms by which to treat placentitis, Fedorka et al, identified pro and anti-inflammatory cytokines within the different compartments of the fetal placental unit and serum of the mare. Tissues in contact with the cervical migration of bacteria (endometrium and chorioallantois) experience a pro-inflammatory response (IL-1 $\beta$ , IL-8). The fetus then produces pro- (IL-1 $\beta$ , GRO), anti- (IL-10), and inflammatory-modulating (IL-6) cytokines that are excreted into the amniotic fluid. These cytokines then signal to the mare that the fetus is active and return through either diffusion across the fetal membranes (amnioallantois) and allantoic fluid, or via umbilical blood. Using this work further studies from the University of Kentucky Gluck Equine Research Center (UKGRC) have assessed genomics, transcriptomics and proteomics in normal pregnancy as well as in pregnancies affected by placentitis. They have determined that three primary events occur in equine placentitis that prompt preterm delivery of the neonate: Myometrial activation – induced by inflammation, cervical ripening and placental separation and rupture (El-Sheikh 2021). Therefore, while control of bacterial infection is a primary approach to treatment of placentitis, inflammatory modulation is essential to disease management.

Systemic treatment can include antimicrobials, exogenous progestagens, estradiol 17B/Estradiol cypionate, anti-inflammatories, and rheostatic agents. Specific antibiotics have been documented as crossing the placenta and achieving therapeutic values in the fetus and fetal fluids. These include; Penicillin, Gentocin, Trimethoprim Sulfadiazine, most recently Doxycycline, and Enrofloxacin. (Canisso 2023) Further long-term studies using Enrofloxacin need to be performed to determine the long-term effects in foals past 30 days of age. Monthly antibiotic treatment has been suggested for the prevention of focal mucoid placentitis, however in a retrospective study Fedorka et al concluded that administration of prophylactic antimicrobials or altrenogest throughout gestation did NOT decrease the risk of disease or improve neonatal outcomes.

Anti-inflammatories used consists of Flunixin Meglumine and Firocoxib. A combination of Firocoxib, trimethoprim sulfamethoxazole and altrenogest improved foal survival after administration to mares with experimentally induced placentitis. (Burden 2023) Pentoxifylline was identified in fetal fluids of normal treated mares and mares with placentitis and has been used with antimicrobials and progestins to successfully treat clinical disease. Acetylsalicylic acid improves uterine and ovarian perfusion and increases plasma progesterone concentration in nonpregnant mares and results indicate increased uterine blood flow in mares during late pregnancy. (Sielhorst 2022) Therefore, it may be a good adjunct therapy for perfusion and inflammation in placentitis. Finally adding estrogen (estradiol 17b or estradiol cypionate), for short periods of time in clinically induced placentitis, showed foals to have increased birth weights. (Curcio 2017) Further studies need to assess the feasibility of continued long term use in chronic placentitis and foaling rate.

New discoveries, such as the components of the normal placental microbiome, modifications of steroid's pathways such as DHEA and cortisol, options to interrupt the inflammatory pathways, combined with modern technology available and affordable to the equine practitioner will hopefully aid in early diagnosis and more successful treatment of placentitis.

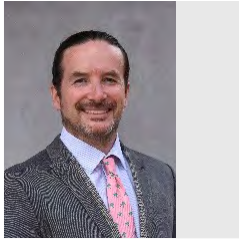
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## Field solutions for dystocia management

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Dystocia is encountered in approximately 10 % of births (McCue and Ferris 2012).. The approach to dystocia in the field setting is governed by the level of experience of the attending clinician and assistance provided by mare owner or stud manager. If manipulation of the fetus (rotation) does not rapidly correct the malposture one has to decide if delivery is to be attempted via a controlled vaginal delivery under general anaesthesia, fetotomy, or refer for caesarean section. Many referral centres will have a dystocia management protocol (Lynch Norton et al. 2007), designed to minimise the time from admission to foal delivery or surgical incision, to maximise foal survival rates. In some cases economic and geographic considerations mean that there is not an opportunity to refer and clients look to the attending clinician to resolve the situation one way or another.

One needs to quickly take control of the situation. A brief physical examination of the mare should be performed to determine her physical status, followed by evaluation of the reproductive tract to identify the problem and determine if the fetus is alive. Fetal viability is determined using limb withdrawal, ocular reflex, swallowing reflex, heart beat, and anal reflex, however it is not always easy to determine conclusively that a foal is dead. History should be taken from the attendees; when was she due, when was she last observed, how long has she been foaling for, what actions have been taken, has the mare had any previous problems? In order to restrain the mare intravenous sedation may be indicated, the author prefers romifidine (without butorphanol) for initial sedation and this is advantageous if the situation progresses to anaesthesia however. Alpha2 agonist can be used in combination with butorphanol and/or acetylpromazine.

### Assisted vaginal delivery

Any abnormal combination of the extremities, single limb, fore and hind limbs, three limbs, absence or presence only of the head indicates a maldisposition. The duration of the dystocia, state of the reproductive tract and fetal viability will dictate what happens next. The ability to deal with these cases quickly lies not only in experience with techniques but in the decision making process. It is important for the attending clinician to ask themselves have they got the equipment and the expertise to deal with this within the next 15 minutes, if not, does one need to have an alternate plan?

In order to even start the following obstetrical equipment should be available: Clean obstetrical chains (or ropes) with handles: 2 x leg @ 1100mm; 1 x head @ 1400 to 2000mm, obstetrical lubricant and buckets, clean stomach tube and pump, tail bandage.

Liberal application of lubrication around the fetus and within the uterus will greatly aid in fetal repositioning and subsequent extraction. Once the fetus has been correctly aligned traction can be applied, as a general rule the force applied to should not exceed that which can be applied by two people; excess force inevitably leads to damage to the reproductive tract of the mare and potentially to the foetus. Traction is best applied along with straining of the mare, alternate-limb traction (up to 10 cm) applied until both forelimbs extended and then simultaneous traction applied to extract the chest, minimises the force required. The use of a head rope will spread the tractional forces between the extremities and offers a significant advantage in tight situations. Ideally two assistants will apply traction under direction of the clinician allowing them to have hands free to monitor progress of the delivery. Traction should be applied in a downward direction and if the mare is recumbent this can be applied towards or between the mare's hind legs resulting in flexion of

the fetal spine which is advantageous when the fetal hindquarters engage. Rocking of the fetus from side to side can aid extraction.

### Controlled vaginal delivery

If the foal is viable and assisted vaginal delivery is not possible one could consider a controlled vaginal delivery under GA, however beware maldispositions such as anterior ventro-vertical with bilateral hip flexion (dog-sitter), posterior bilateral hip flexion (breech) and transverse presentations (ventro- or dorso-transverse), as they can be extremely difficult if not impossible to correct even with the benefits of anaesthesia. The author induces anaesthesia using ketamine and diazepam and has top-ups of ketamine and romifidine available as required. Skilled assistance in such situations is extremely valuable so if professional assistance is available, it should be called for. Elevation of the hind limbs during anaesthesia can be advantageous to increase the space available in the caudal abdominal cavity enabling the clinician to repel fetal parts to correct a maldisposition and align the fetus.

### Fetotomy

Fetotomy can be an extremely valuable procedure that can avoid the need for prolonged manipulations or caesarean section. In the hands of a clinician experienced in the technique, mare survival and future fertility can be better than cesarean section. However in inexperienced hands it has the potential to damage a mare, compromising future fertility or put the mare's life at risk. Although one may find oneself requiring the technique as a last resort, for the best outcome for the mare the decision to perform a fetotomy should be made as early as possible. If fetotomy is to be in the clinicians 'toolkit' one should make a plan in advance as specialised equipment is essential for anything but the simplest of cuts.

I would like to take this opportunity to thank my sponsors, without whose support I would not have been able to present at the conference. With many thanks to BOVA Specials UK Ltd, MSD Animal Health UK & Equine Reproductive Services (UK) Limited.

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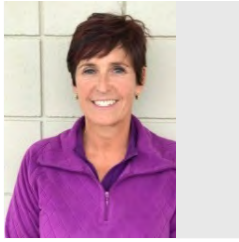
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*James has published work on many topics relevant to clinical practitioners including material on breeding soundness evaluation, infectious disease, peri-partum problems, ovarian abnormalities, oestrus suppression, persistent endometrial cups, management of spring transition and twin pregnancy. James continues to perform and publish practice based research and collaborates widely. In 2013, he became director of Equine Reproductive Services (UK) Limited growing and developing a busy first opinion and referral equine practice in Yorkshire. James is recognised as an Advanced Practitioner in Equine Stud Medicine, he is a current BEVA council member and trustee of the International Equine Reproduction Trust.*

*James has made a sustained and significant contribution to veterinary professional development with formal and informal teaching and assessment of post graduates. James has organised and delivered many CPD courses and congresses in the UK and Europe and has delivered presentations on material ranging from basic to advanced topics around the World. In 2022, his efforts were recognised by the Royal College of Veterinary Surgeons who awarded James with a Fellowship for meritorious contributions to clinical practice.*

*If you require a different style of biography or photograph please do not hesitate to let me know.*



## Retained placenta in the mare: An Up-Date

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In the mare placental separation from the endometrium occurs during third stage of labor. Postpartum uterine contractions along with the decreased blood supply from the fetal placental vessels and endometrium allow maternal crypts to relax and the chorionic villi to shrink. The progression of the chorioallantois into the vaginal vault through the cervix stimulates continued release of oxytocin and placental delivery. The cause of a retained placenta is unclear. However, it is the most common postpartum complication with an incidence of 2-10.5%. A higher incidence has been reported in draft mares, increased age, prolonged gestation, hydrops, abortion, stillbirth, twinning, dystocia, placentitis and cesarean sections. A placenta is generally considered "retained" if it is still attached to the endometrium 3 hours after parturition. The non-pregnant horn is more commonly retained than the edematous pregnant horn, however the amount retained can be variable from a small piece to the entire membrane. Devitalized and autolyzed tissue, together with delayed uterine involution, provide a suitable environment for bacterial growth. Increased nitric oxide production during the inflammatory process decreases uterine contractility so debris, bacteria, endotoxins and inflammatory byproducts are not expelled, allowing translocation of bacteria or endotoxin into the systemic circulation resulting in life-threatening endotoxemia, septicemia, laminitis and death. Early identification and treatment are therefore essential.

### Clinical signs:

The fetal membranes may be either visible and partly expelled, or completely contained in the uterus. Commonly, the mare becomes pyretic, depressed, and anorexic with an exudative discharge from her vulva lips if the retained placenta is not identified promptly. With continued uterine contractions or invagination of a uterine horn, signs of mild colic may also ensue.

### Diagnosis:

Examination of the placenta soon after expulsion is imperative to determine if the placenta is complete and initiation of therapy is needed. Examination of the chorionic and allantoic surface by placing the placenta in a "F" shaped pattern allows for the body and both horns including the tips (identified by the avillus area of the oviductal opening) to be examined in the entirety. One of the most common types of retention is when a small piece of the chorio-allantois remains attached within the non-pregnant horn after tearing and expulsion of the detached portion. If gross examination of the placenta lacks a horn or is shredded examination of the uterus is imperative.

Transrectal ultrasound examination after delivery or abortion, can sometimes aid in the visualization of the placenta as a mass of tissue within the uterus. However, this can be difficult if uterine involution leaves little or no fluid outlining the tissue within the lumen. Most retained placentas are best felt and identified during manual uterine examination. If the tip however is retained and the uterus is still very big, this may not be possible as it can be difficult to traverse the entire horn and palpation only possible to the bifurcation of the uterus. Fetid thick fluid or exudate may be an indicator that placenta is still present. If there is any uncertainty in the completeness of the placenta, a uterine lavage should be performed, as the retained piece may become lodged in the tip of the tube. Culture of the uterine contents prior to lavage allows for specific bacteria to be isolated and sensitivity patterns assessed. Trans-abdominal ultrasonography can also aid in detecting the presence of retained placenta, again more easily if intra-luminal fluid is present.



**Treatment:**

The uterus during parturition is naturally contaminated with bacteria, therefore after eight hours of retention with autolyzing retained fetal membranes an environment is produced that is conducive to exponential bacterial growth. The increased number of bacteria and inflammatory products can produce a metritis allowing absorption of bacteria and toxins causing septicemia, endotoxemia and laminitis. Initial therapy should focus on removing the nidus of bacteria (the retained placenta) as well as the endotoxin-producing bacteria. In the author's opinion a good initial therapy is to use Oxytocin, 10-20 IU every 15 minutes until placental release or for a maximum of three treatments, if treated within the first 3-8 hours. Most placentas will release after the first two doses, and minimal additional treatment may be necessary. Different regimens of oxytocin may be used including addition to 1-5 liters of saline + / - calcium borogluconate as a drip (care must be taken because oxytocin seems to accumulate at the bottom and signs of colic may be evident as the fluids are finished). Pulling on the membranes is not recommended if they are firmly attached, due to the potential of endometrial hemorrhage, tear, contamination, retention of the tip of a placental horn, uterine tip invagination, permanent endometrial damage and delayed uterine involution.

If a piece of placenta is felt in a horn, the author will start by culturing the endometrial contents, then perform a large volume lavage using a bucket of warm water +/- salt and dilute betadine (1% solution), or if there is concern about the integrity of the uterus, sterile fluids may be used. It is imperative whichever method is used to use large volume in and out so that dilution of bacteria and endotoxins occurs. In addition, as the uterus is distended a twisting motion of the retained piece of tissue at the base of attachment can help peel the placenta gently from the endometrium. Infusion with the appropriate broad-spectrum antibiotic such as Ticarcillin plus clavulanic acid, nitrofurantoin, ceftiofur, Trimethoprim Sulfamethoxazole tablets can combat the variety of endotoxin-producing bacteria. After lavage and infusion N-butylscopolammonium bromide systemically can be given to relax the uterus which will be alternated with oxytocin. The author has found that the dynamic relaxation and contraction of the uterus aids in placental release.

Another recent technique described by Burden et al allows for gentle manual separation of the placenta from the endometrium with the tips of the fingers and a circumferential hand motion towards the tip of the horn. This allows for complete removal while on the farm if the ability to perform lavage twice daily or return to the farm is not feasible. If the chorioallantois is still completely intact, infusion of the sac with saline allows distention of the uterus with subsequent placental release. This technique was first described by Burns et al in 1977. The fluid needs to be kept in the allantoic space by holding the membranes tightly around the nasogastric tube. Membrane expulsion usually occurs in 5-30 minutes. An old technique initially described by Zeddum has been revisited by Dr. Meijer from Holland and subsequently others. The procedure incorporates introduction of a 9mm diameter nasogastric tube into the umbilical vessel toward the root of the umbilical attachment on the placenta. The nasogastric tube is attached to a garden hose and water is continuously infused into the umbilical vessel under low pressure for approximately 5 minutes. As the umbilical vessel distends the umbilical cord and nasogastric tube are held tightly by hand to prevent retrograde leakage of water from the umbilical vessels. It appears that the infusion of water induces edema and swelling of the tissue causing separation of the chorioallantois from the endometrium. In most cases the placenta has been released completely as the procedure is completed. This technique unfortunately does not seem to work after an abortion or after cesarean section. If the placenta remains fixed firmly or after initial removal of the placenta, further treatment should focus on removal of inflammatory debris and bacteria by intrauterine lavage with large volumes of fluid as described above. Flushing should continue until the solution is the same color going in as coming out. This procedure may need to be done twice a day depending on the amount, consistency, and smell of the intrauterine fluid. If the placenta remains retained after oxytocin, manipulation and lavage, supplemental systemic broad-spectrum antibiotics such as Procaine Penicillin or sulfamethoxazole and Gentocin as well as anti-endotoxemia/laminitis therapy consisting of Flunixin Meglumine, and Pentoxifylline are essential and should be initiated to help prevent complications such as laminitis. Icing the mares' feet can be a precautionary procedure. Administration of intrauterine antibiotics is controversial due to their potential irritation to the uterus and inactivation by autolyzed tissue and bacteria. Suggested antibiotics include Ampicillin, Ticarcillin, Gentamicin, polymyxin B, metronidazole, Nitrofurazone-urea boluses, or Trimethoprim Sulfa tablets. This author prefers to administer Ticarcillin and clavulanic acid diluted in 60cc saline intrauterine.

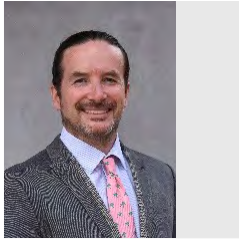
One of the most important aspects of treating retained fetal membranes is recognition of their presence. Not all retained placentas are visible and unless a placenta has been examined for completion it may not be discovered until the mare presents depressed, febrile, anorexic, tachypneic, toxic with bounding digital pulses. Therefore, it is imperative to stress the importance of placental evaluation by whomever is present at delivery. Examination of the fetal membranes ascertains completeness, in addition to being able to identify any other abnormalities such as placentitis, which can allow the veterinarian to gain time and insight into the treatment of potential problems in the mare and foal.

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## Beyond retained fetal membranes: Managing conditions affecting the postpartum mare

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Complications in the early postpartum period are a common and challenging problem for the equine clinician. This presentation reviews some of the specific problems encountered in the postpartum mare.

### Periparturient haemorrhage

The most frequent cause of haemorrhage during parturition is rupture of the middle uterine artery and the risks of rupture are greater in older mares especially those that have had multiple foals. The majority of bleeds are contained within the broad ligament resulting in a haematoma however the bleed can occur directly into the abdominal cavity or into the uterus. Broad ligament, uterine or pelvic wall haematomas often result in colic due to the stretching of the tissues. If an artery ruptures directly into the peritoneal cavity the mare may not be painful but the haemorrhage may be more profuse and rapidly fatal.

In the acute phase of haemorrhage haematology may show an increase, decrease, or no change in packed cell volume (PCV) due to splenic contraction, hypoproteinemia and hyperlactatemia would be suggestive of blood loss in a horse. If the mare survives the acute phase, a drop in PCV is usually observed over the following days before a regenerative red cell response can be made. Transabdominal ultrasound can be performed to detect free fluid in the abdomen and abdominocentesis can be obtained to confirm an elevated red cell count indicative of haemoabdomen. In cases with broad ligament haematoma the peritoneal fluid protein levels can be significantly elevated (up to 50 g/l) with normal white cell count.

Treatment is challenging and often controversial. If the mare survives the initial haemorrhage, it is likely that a clot has formed. In all cases, keeping the mare quiet is paramount to her survival. If the mare is actively haemorrhaging the approach is governed by the facilities available and the economics of the particular case. In some instances, an extreme hypotensive state may actually offer the best chance for survival, whereas in others an attempt to restore intravascular pressures and circulatory volume with iv fluid therapy could be indicated. The need to support cardiac output and ensure oxygen delivery must be balanced against the prospect of the increased arterial pressure promoting further haemorrhage. Conservatively mild sedation (alpha-2 agonist), pain relief with butorphanol and/or flunixin meglumine are recommended. Prophylactic broad-spectrum antibiotic coverage is warranted and low dose (10 iu) oxytocin therapy may be useful to promote uterine involution.

Aminocaproic or tranexamic acid may be beneficial; in horses an extrapolated dose of 10mg/kg tranexamic acid is given by slow i/v injection up to three times in the first 24 hours depending on the severity of bleeding. Fletcher and co-workers (2013) showed that the minimum concentrations of aminocaproic and tranexamic acid required to inhibit fibrinolysis in horses were approximately 1/20 those required in humans. Although controversial, formalin (16 ml of 10% buffered formalin diluted in 45 ml of 0.9% saline solution and administered by slow i/v injection has also been used to treat uncontrolled haemorrhage in horses and appears to have short term safety (Moreno et al. 2021).

### Metritis

Incidence of metritis is low but increases with birth trauma and retained fetal membranes. It usually presents within 2-4 days postpartum and is often associated with a pronounced neutropenia. Inflammation

of the uterine wall permits bacteria and toxins to enter the systemic circulation, resulting in bacteraemia and endotoxaemia. Any postpartum mare with fever and anorexia should be suspected of having metritis. A large volume of toxic, red-brown, watery fluid may accumulate within the postpartum uterus before any obvious vaginal discharge becomes apparent.

Treatment should include broad-spectrum antibiotics, anti-inflammatory drugs and intravenous fluids if indicated. A combination of procaine penicillin and gentamicin are widely used to provide broad-spectrum systemic coverage. Anti-endotoxic doses of flunixin meglumine (0.25 mg/kg bodyweight three times a day) should be considered as a minimum; 10-20 iu oxytocin every 4-6 hours will promote uterine clearance and involution. Daily or twice daily large volume uterine lavages with 0.9 per cent saline solution are a routine part of managing mares with metritis. Homemade (non-sterile) saline can be used in the post-foaling mare by mixing 90 g of table salt with 10 litres of tap water. The lavage is repeated until the recovered fluids are free from gross contamination.

### Uterine laceration

Uterine lacerations occur most frequently after dystocia but can occur in mares that foal normally. The most common sites of laceration are the ventral and dorsal uterine body and the tip of the pregnant horn. In the early stages there may be no obvious outward clinical signs. Subsequent signs are dependent upon the degree of contamination of the uterus and abdominal cavity. If peritonitis develops the mare becomes increasingly ill over 24-72 hours with fever, inappetence, reduced gut motility and abdominal pain. Abdominocentesis will reveal signs consistent with septic peritonitis and changes in haematological and biochemical parameters may also be present. One should be aware that peritonitis due to traumatised and devitalised bowel is a major differential.

### Uterine horn tip inversion

Inversion of the tip of the uterine horn may result in mild to severe colic symptoms. A short and thickened uterine horn with a tense mesovarium may be identified on rectal palpation. Manual reduction can be performed from within the uterine lumen; infusion of several litres of saline into the uterus will aid replacement; 10-20 iu oxytocin every 4-6 hours will promote uterine involution.

I would like to take this opportunity to thank my sponsors, without whose support I would not have been able to present at the conference. With many thanks to BOVA Specials UK Ltd, MSD Animal Health UK & Equine Reproductive Services (UK) Limited.

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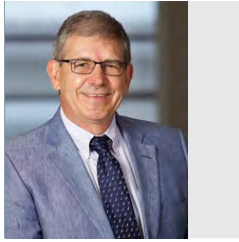
**James** graduated from the Royal (Dick) School of Veterinary Studies, Edinburgh in 2001. After four years in mixed practice he travelled between the hemispheres working for a number of years in specialist stud practice in the UK, Australia and New Zealand. In 2010 he was awarded the RCVS certificate in Equine Stud Medicine and in 2011 became a lecturer at Liverpool University examining the stud medicine certificate since 2012.

James has published work on many topics relevant to clinical practitioners including material on breeding soundness evaluation, infectious disease, peri-partum problems, ovarian abnormalities, oestrus suppression, persistent endometrial cups, management of spring transition and twin pregnancy. James continues to perform and publish practice based research and collaborates widely. In 2013, he became director of Equine Reproductive Services (UK) Limited growing and developing a busy first opinion and referral equine practice in Yorkshire. James is recognised as an Advanced Practitioner in Equine Stud Medicine, he is a current BEVA council member and trustee of the International Equine Reproduction Trust.

*James has made a sustained and significant contribution to veterinary professional development with formal and informal teaching and assessment of post graduates. James has organised and delivered many CPD courses and congresses in the UK and Europe and has delivered presentations on material ranging from basic to advanced topics around the World. In 2022, his efforts were recognised by the Royal College of Veterinary Surgeons who awarded James with a Fellowship for meritorious contributions to clinical practice.*

*If you require a different style of biography or photograph please do not hesitate to let me know.*





## How to manage the anovulatory mare during breeding season

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### Introduction

The female of the equine species is stimulated to cycle with increasing exposure to day length. Consequently, mares are considered seasonally polyestrous which means that they have a long period of regular cyclicity also known as the breeding season where mares have inter-estrus intervals of 15-16 days and inter-ovulatory intervals of 20-21 days. In the northern hemisphere the breeding season extends from late March or early April until early October. In the majority of the mares this period of regular cyclicity is marked by a variable transitional phase on both the early (spring) and late (fall) in which mares might show behavioral estrus but fail to have regular ovulatory cycles. The start of the ovulatory season in mares is determined by the first ovulation of the year, except in mares that foal early in the year (January, February) and have not been exposed to artificial light. These mares often will have an initial ovulation and revert to anestrus for another few weeks. In between the late fall transition and the early spring transition most mares have a period of anestrus where follicular activity is suppressed. Since the breeding season is limited in the northern and southern hemispheres, mares that fail to cycle during this period pose an economic burden to the breeding operation.

### Conditions that interfere with regular cyclicity

a) Inter-estrus and inter-ovulatory intervals for mares that are bred to carry their own pregnancies inter-estrus intervals (16 days) and inter-ovulatory intervals (19-22 days) are key indices for brood mare management. Prolonged luteal phases are presumably caused by a block of the endometrial release of prostaglandin at around 15 days. On the other hand, short luteal phases are likely caused by an early release of uterine prostaglandin causing a premature lysis of the CL. Both of these conditions are not normal and should be investigated further either with a culture and/or preferably by evaluating a uterine biopsy to insure that the uterine health is normal. It is imperative that veterinarians have an exact day of ovulation from the previous cycle in order to accurately evaluate those indices. Pregnancy and possible early embryonic death after day 14 must also be ruled out in cases of prolonged luteal phases.

b) Anovulatory follicles- Follicles that fail to ovulate are a frustrating condition for veterinarians especially when mares are being bred by artificial insemination. Anovulatory follicles either bleed into the antrum creating a localized hemorrhage or keep growing after the expected day of ovulation. In either case these follicles fail to release an oocyte and consequently the mare is not able to become pregnant. It is important that veterinarians recognize the failure to evacuate follicular fluid and ovulation since often the organized anovulatory hemorrhagic follicle (AHF) could be similar to a corpus luteum or a hemorrhagic CL. Unfortunately there are no markers or indicators that would reliably help predict the formation of an AHF. However, in the author's experience there are certain mare conditions that increase the risk of developing AHF. Some of these conditions include:

1- Failure to ovulate within 48 hrs after an ovulatory agent is administered- Timely administration of ovulatory inducing agents is imperative for good mare breeding management and efficient stallion use. However mares that are treated with the appropriate dose when a dominant follicle(s) is present and the mare has marked uterine edema and fail to ovulate within 48 hrs of administration are at a high risk of developing AHF's.

2- Mares with insulin resistance or other endocrinological issues- These mares although not completely acyclic, characteristically will have multiple small to medium follicles for several weeks and fail to ovulate on a regular basis. For these mares it is recommended to place them on constant pergolide therapy.

3- Delayed follicular growth due to endometritis- As discussed above mares with uterine infections can have a long period of poor follicular growth and in extreme cases anestrus. This can be often seen in post-partum mares that have foaled under poor hygienic conditions.

4- Chronic stress/pain- Social stress in a herd situation or the stress from pain due to osteoarthritic conditions, laminitis or social stress have the potential to interfere with follicular growth and ovulation and consequently the development of AHF's.

### **Conditions that result in acyclicity**

Permanent lack of cyclicity although not common in general is due to either permanent conditions such as chromosomal or genetic or to acquired conditions that have conditions that have been failed to be diagnosed.

A clinician evaluating a mare for lack of regular cycles or anestrus must insure that there is no iatrogenic cause for the condition such as exogenous use of progesterone, progestogens, estrogens or anabolic steroids.

Chromosomal problems most commonly the 63 XO condition also known as Turners syndrome. These mares will have a smaller body, small genitalia and underdeveloped uterus and ovaries. However with more recent techniques and the sequencing of the equine genome, new conditions of permanent acyclicity have been surfacing in the face of a normal 64 XX karyotype. These mares in contrast to the 63XO mares, have normal body size, and genitalia but have very small ovaries with follicles that do not grow past 5-10 mm and have an inability to respond to exogenous gonadotropin stimulation.

Breeds such as Arabians and ponies are well known for their longevity. In addition with mares from other breeds with proper husbandry and veterinary care can also reach advanced age. In addition mares that are in regular and prolonged Transvaginal Oocyte Aspiration programs are likely to go through "menopause" due to lack of follicles for recruitment.

As described above, mares that foal under poor hygienic conditions are at high risk of having uterine contaminants that could affect cyclicity. In some of these mares one could argue that they have a period of lactational anestrus. However in my experience primary lactational anestrus as seen in other species is a rare condition in the horse, unless the mares are under a severe malnutrition and with very low body condition scores while nursing a foal. Mares without a foal at foot but under a constant plane of poor nutrition are also at a high risk of falling into a prolonged period of acyclicity.

The endometrial cups which result from the invasion of the embryonic chorionic girdle/trophoblast into the endometrium are an important phenomenon for the development of secondary follicles and the consequent formation of accessory or secondary CL's. The endometrial cups that start to form at around 35 days of gestation and reach maximum maturity by 60 days produce equine chorionic gonadotropin (eCG). These structures have a finite life span and ~ 120 days they have regressed and eCG returns to undetectable levels. Although not very common the condition of retained or persistent endometrial cups has been described in mares. They can occur in mares that lose the gestation after 60 days and in other occasions persist through out gestation and post-foaling. Mares with this condition characteristically will have medium size follicles that regularly become luteinized. Diagnosis is done by clinical signs, ultrasonography, endoscopic visualization of the structures and by detectable levels of eCG in serum. Therapy consists on scraping the retained cups from the uterus.

Endocrinologically active ovarian tumors will cause prolonged periods of acyclicity. The most common ones are Granulosa or Granulosa Thecal Cell tumors (GCT or GCTC) depending on the type of cell involved. Although behavioral signs can vary from permanent estrus to aggressive stallion-like behavior initial diagnosis is made by identifying the enlarged ovary with the concomitant atrophy of the contralateral ovary. Endocrinological diagnosis is done by obtaining no progesterone, and high inhibin with variable

levels of testosterone in serum. Final and definitive diagnosis is done by finding high levels of Anti-Müllerian Hormone (AMH) in serum. Therapy consists of the removal of the affected ovary and return to cyclicity on the remaining ovary is expected in 6-9 months post surgery.

### Summary

Lack of regular cyclicity or acyclicity in mares is a problem that can severely impact the results of a breeding operation, particularly in temperate climates where breeding seasons are finite. There are many causes for these problems and consequently the diagnosis requires of evaluation of adequate husbandry practices, proper history, fine attention to clinical signs and diagnostic procedures.

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*He has published several peer-reviewed manuscripts on numerous topics related to equine reproduction and is the author of two editions of Equine Breeding Management and Artificial Insemination and a co-author of Current Therapy in Equine Reproduction. He was recently appointed as a specialty chief editor for the Animal Science – Theriogenology section of Frontiers in Veterinary Science.*

*Dr. Samper's current research focuses on the implementation of sexed stallion semen in the equine industry.*