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MANAGEMENT OF THE INFERTILE/SUBFERTILE MARE

Sidney Ricketts, Professor, LVO, BSc, BVSc, DESM, DipECCEIM, FRCPath, FRCVS
Rossdale & Partners, Newmarket, UK.

The commercial horse breeder aims for a live foal every year from their brood mares. While small family bands of feral horses and native ponies may sometimes achieve this, most populations of commercial brood mares suffer conception and pregnancy failures which result in some mares entering the next breeding season not pregnant, i.e. ‘barren’. Assuming normal stallion fertility and adequate management, in most cases this is a matter of sporadic mare subfertility, most commonly associated with obstetric injuries, uterine infections, age-related genital tract disease or managerial problems. True infertility and epidemic subfertility, e.g. epidemic venereal infections or viral pregnancy failures, are uncommon in mares.

It is the responsibility of the equine gynaecologist to:-
1. Maximise the reproductive health and efficiency of all mares under his/her care, so that conception and pregnancy failures are kept to a minimum.
2. Specifically aid individual mares with reproductive problems to overcome or compensate for their problems in order that they may conceive, undergo normal pregnancy and produce a healthy live foal at normal term.

Fertility Expectations
Historically, it has been suggested that the equine species inherently achieves relatively low fertility figures and that domestication makes matters worse. With good management, this is not the case. Mare fertility results vary between populations. Data from the 2006 Weatherbys’ Statistical Review records that 653 registered Thoroughbred stallions at stud in UK and Ireland mated 23,415 Thoroughbred mares. After excluding those mares for which no returns were made and those that were exported or who died, the conception rate was 97.1%, the gestational failure rate was 8.3%, the live foal rate was 88.8% and the barren mare rate was 11.1%. Therefore, normally fertile and well-managed populations of Thoroughbred horses expect conception rates in excess of 90% and live foal rates in excess of 80% and these are now the targets for both equine studfarm clinicians and stud managers.

However, population statistics help little when considering aspirations for individual mares. Weatherbys’ data demonstrates a linear decline in the fertility potential of mares with age with a 75% live foal rate for 4-year-old mares as compared to a 50% live foal rate for 20-year-old mares. It is vital that clinicians, stud managers and owners understand that age has a major and irrevocable limiting effect on a mare’s fertility potential.

By definition, an infertile mare is incapable of conceiving when mated by a fertile stallion and is thus, by true definition, a sterile mare. The latter is uncommon for horses and is often associated with congenital defects of the reproductive tract or gonadal dysgenesis, often manifesting in demonstrable karyotype abnormality. In contrast, temporary breeding failures are relatively common and these mares are more correctly termed subfertile. A barren mare is one who is not pregnant at the end of the breeding season, for whatever reason.

Preparing barren mares for next season
In order to achieve maximal breeding efficiency, all barren mares should receive a thorough examination after the end of the breeding season and before they go into winter anoestrus, e.g. in September (northern hemisphere), with the aim of:-
1. Making a diagnosis of genital abnormality, if one is present.
2. Making a provisional breeding prognosis based on the abnormalities diagnosed.
3. Formulating and carrying out a logical treatment programme, if indicated.
4. Assessing the response to treatment after a period of rest.
5. Making a more accurate breeding prognosis based on the abnormalities diagnosed and their response to treatment.
6. Repeating or substituting alternative treatment if their response to treatment is unsatisfactory, until improvement occurs or retirement is recommended.
7. Allowing an extended period of rest before the next breeding season.
Without this preparation, mares may enter the next breeding season with persistent genital abnormalities that then require diagnosis, treatment, re-assessment and recovery, delaying mating and wasting valuable time.

**The autumn barren mare examinations and treatments**

An accurate diagnosis is, as always in veterinary medicine, a pre-requisite to prognosis, treatment and successful management. This requires a detailed logical investigatory approach, which, after taking a detailed reproductive history, may include a variety of tests to examine the mare's perineum, vulva, vagina, cervix, uterus and ovaries. Diagnoses are then made and specific treatments are performed.

**Reproductive history**

The mare's age and breeding history are vital pieces of information with which to start the diagnostic process and are essential data with which to allow meaningful interpretations of gynaecological abnormalities to be made. A young barren maiden mare (not pregnant after her first season at stud with no history of conception) may be immature or even have gonadal dysgenesis (e.g. X0 or XY sex reversal, manifesting with very small and persistently inactive ovaries), whereas an 18 year-old mare who has produced 10 foals, suffered an early foetal death, an abortion and two barren years, will not have gonadal dysgenesis but is most likely to have chronic/progressive perineal conformational and/or uterine degenerative problems. A mare that has failed to conceive or maintain a pregnancy following dystocia should be examined carefully for cervical injury and/or incompetence.

**Examination of the Vulva and Perineum**

The conformation of the mare's perineum and the integrity, shape and angle of slope of her vulva, in relation to her anus is first evaluated, to determine if she is likely to suffer from pneumovagina, i.e. she requires Caslick's vulvoplasty surgery to be performed. Sometimes, small fistulas are found in the vulval scar following previous surgery, and these need to be repaired. If the mare's perineal shape is very poor to the extent that Caslick's operation is insufficient to prevent pneumovagina, Pouret's perineal reconstruction operation may be recommended. The vulval lips are examined for signs of accidental injury, leading to incompetent closure. For broodmares, all vulval injuries need careful repair and successful reconstruction to avoid incompetent closure, leading to pneumovagina. The vulval lips should be manually separated while the examiner pays attention to aspiration of air into the vagina. In mares with a dysfunctional or weak vestibulo-vaginal fold, separation of the vulval lips creates a characteristic sound when air is aspirated into the vagina. These mares, and those where the upper commissure of the vulva is above the level of the pelvis, should be considered prone to pneumovagina.

In the UK, Ireland, France, Germany and Italy swabs are routinely collected from the urethral opening, clitoral fossa and sinuses for annual screening for the potential equine venereal disease organisms *Taylorella equigenitalis*, *Klebsiella pneumoniae* (capsule types 1, 2 and 5) and *Pseudomonas aeruginosa*, as recommended by the Horserace Betting Levy Board's (HBLB) Code of Practice for the Control of Equine Venereal Diseases. These pathogens may exist in all of these sites and, if found, constitute carrier status. Carrier mares are excluded from mating until they have been successfully treated and proven so by repeated follow-up swabbing. *T. equigenitalis* is sensitive to environmental conditions and swabs should be placed into Amies charcoal transport medium immediately following collection to preserve the organism during transportation to the diagnostic laboratory. The swabs should not be subjected to extremes of temperature during transportation.

**Vaginoscopic (speculum) examination**

The cervix and vagina are examined, via a sterile vaginascope (speculum), for their appearance in relation to cyclic state (moist, pink and relaxed in oestrus, dry, pale and tight in dioestrus), and for signs of injury, incompetence, discharge and/or vaginal urine pooling. Cervical lacerations that impair normal function, particularly closure, always carry a poor prognosis for future breeding. Some require attempts at surgical repair but such mares often remain 'high risk' for ascending placentitis, which often results in abortion or the birth of an impoverished foal. Other cases heal sufficiently to allow functional closure without surgical interference. In such cases some clinicians recommend that the mare is supplemented with oral progestagens (altrenogest), to aid tight cervical closure, on empirical grounds.
If the mare is in oestrus, swabs are collected from the endometrium, through the open cervix, via a sterile speculum for cytological screening for inflammation (the presence of polymorphonuclear leucocytes, i.e. PMNs in a smear test), for the equine venereal disease organisms *T. equigenitalis*, *K. pneumoniae* (capsule types 1, 2 and 5) and *P. aeruginosa*, and for any of the multitude of opportunistic pathogens (most commonly b-haemolytic streptococci, i.e. *Streptococcus zooepidemicus*, *Escherichia coli* and *Staphylococcus aureus* and the anaerobe *Bacteroides fragilis*). These opportunistic organisms are only considered to be of significance, i.e. causing endometritis, if there is cytological evidence of inflammation in the smear sample.

If the mare is not in oestrus, swab samples are taken from the endometrial biopsy sample after it has been collected.

**Rectal palpation and ultrasound scan examination**

During oestrus, the uterus has minimal palpable tone and, especially in early oestrus, endometrial oedema delineates the endometrial folds on scan examination. During dioestrus, the normal uterus should have uniformly palpable tone and no palpable enlargements. Ventral dilatations (areas of fold atrophy and myometrial stretching) may contain lumenal fluid accumulations that may be either hypoechoic or hyperechoic on scan, the former indicating clear fluid and the latter indicating haemorrhage or, more commonly, inflammatory fluids. In pyometra, which is less commonly seen in mares than some other species, the uterus is uniformly enlarged, palpably distended or ‘doughy’ and contains particulate fluid, giving a ‘scintillating’ hyperechoic ultrasound scan appearance.

Equine ovaries are highly variable in size and activity depending on cyclic state. During oestrus they may be large and contain follicles in varying stages of development, in addition to old, non-functional corpora lutea. During dioestrus there will be at least one functional corpus luteum in addition to follicles in varying stages of development. During anoestrus they will be small and inactive, containing neither active follicles nor corpora lutea.

The most commonly diagnosed ovarian abnormality is the granulosa cell tumour. This benign tumour causes one ovary to enlarge, sometimes enormously, and appear full of cysts on scan examination, whilst the other ovary is characteristically inhibited and becomes small, hard and inactive. Granulosa cell tumours are hormonally active and measuring the mares’ blood hormone profile can support a clinical diagnosis. Diagnostic assays to detect granulosa cell tumours include inhibin, testosterone, and progesterone. In a single blood sample of a mare with a granulosa cell tumour, a-inhibin is elevated in approximately 90%, serum testosterone in approximately 50%, and progesterone concentrations should be below 1 ng/ml since these mares are not cycling. The cancerous ovary is removed surgically (often now via laparoscopic surgery), allowing the inhibited ovary to regain normal function within 2-12 months. Other, much less common ovarian tumours are cystadenomas, dysgerminomas, teratomas and malignant adenocarcinomas.

True cystic ovarian disease is rarely confirmed in mares. Occasionally mares haemorrhage excessively into an ovary after ovulation, causing enlargement and pain. A typical homogeneous hyperechoic ultrasound scan appearance of the blood clot allows the diagnosis to be confirmed. Most cases resolve with time but occasionally pain cannot be controlled without removing the affected ovary surgically. Rarely, large ovarian haematomas are at risk of rupture, with fatal peritoneal exsanguinations, so persistent or uncontrollably painful ovarian haematomas should be treated by unilateral ovariolectomy. Ovulation failure is a normal physiologic event for the mare during the spring and autumn transition periods, but it may also occur occasionally in the cycling mare. Persistent anovulatory follicles (PAF) are large (5-15 cm in diameter), and may result in prolonged interovulatory intervals. The cause of ovulation failure is not fully understood, but has been suggested to be endocrine in nature. PAF has been reported to occur in approximately 8.2% of oestrous cycles, and the incidence was found to increase with age. PAF may contain blood, which can be detected ultrasonically as scattered free-floating echogenic spots within the follicular fluid. Eventually the haemorrhage will organize into echoic fibrous bands traversing the follicular lumen. The majority of PAF develop into luteal tissue, which can be confirmed by elevated plasma progesterone concentrations. Luteinised PAF can be treated with prostaglandins, and non-luteinised PAF will regress spontaneously in 1-4 weeks. Pregnancy will not occur if the follicle becomes hemorrhagic or luteinised without ovulating.
**Endometrial biopsy**

Special long (55 cm) basket-jawed forceps are essential to provide interpretable endometrial biopsy specimens. Unfortunately, specimens obtained via endoscopic biopsy instruments are inadequate for histopathological appraisal. Non-pregnancy must be confirmed prior to biopsy. One biopsy taken from a mid-horn region is diagnostically representative unless there are palpable uterine abnormalities, when more than one sample should be taken. A mid-dioestral biopsy is recommended as a routine. The sample is retrieved carefully from the instrument with fine forceps or a needle to avoid artefactual damage and then placed into fixative without delay. If the mare is not in oestrus and a swab for bacteriological examination was not collected via the cervix then the inside of the biopsy forceps should be swabbed immediately after removal of the tissue specimen. On some occasions, additional tissue (usually an adjacent endometrial fold) is retrieved, not required for fixation for histopathological examination and this can be used for bacteriological examinations. Bouin’s fluid is preferred as histopathological fixative for reproductive tissues in general and endometrial samples in particular because their high water content leads to excessive artefactual shrinkage in more conventional fixatives, i.e. formol saline. The fixed tissues should be processed for microscopic examination and interpreted at a laboratory that has specific experience with equine endometrial biopsy samples and with equine gynaecology.

**Cyclic histology:** the microscopic architecture of the endometrium reflects the hormonal status of the mare so changes that occur during oestrus, dioestrus and anoestrus can be classified accordingly.

**Histopathology:** microscopic pathological abnormalities are usually mixed so specific changes are classified and their significance is assessed in terms of the mare’s age and gynaecological history. They can be conveniently classified as inflammatory (acute and chronic endometritis) and non-inflammatory conditions, including endometrial hypoplasia, hyperplasia and chronic degenerative conditions.

**Acute endometritis** is diagnosed by the presence of PMNs and, in severe cases, luminal epithelial degenerative changes, in endometrial biopsy samples taken at any stage of the non-pregnant mare’s cycle. It is recognised that as mares age and suffer the gynaecological and obstetric effects of a busy breeding career, their natural uterine defence mechanisms become less competent and they become more susceptible to recurrent/persistent acute endometritis. These defence mechanisms involve local endometrial factors and myometrial function.

Ultrasound scan may help to demonstrate the severity of inflammation by the degree of endometrial oedema and the volume and scan appearance of retained luminal fluid. Persistent endometritis indicates an inflammatory response to semen and/or a contaminating microorganism or microorganisms. Spermatozoa induce a physiological inflammatory reaction in the uterus, which is an important part of normal sperm elimination. However, normal mares resolve the inflammation within 24-36 and a failure to do this results in persistent endometritis. If the endometritis is of bacterial origin, the associated organism(s) can be determined by bacteriological examinations.

Persistent breeding-induced endometritis may resolve spontaneously with sexual rest. Waiting for this to happen is often not practical during a short breeding season, and treatment options include the intravenous administration of 10-25 iu oxytocin and/or uterine lavage with large volume (1-2 L) of a buffered saline solution at 6-12 hours after breeding. The mare should be considered susceptible to recurrent endometritis each time she is mated and appropriate prophylactic measures should be taken. Infectious endometritis is treated with local infusions of appropriate non-irritant, water-soluble antibiotics (e.g. 1 g ceftiofur sodium is recommended as a useful ‘first choice’, although choice of antibiotics vary between clinicians, on grounds of availability, experience and cost). Where there are signs of uterine fluid accumulation or pyometritis/pyometra, large volume (3 litres) sterile saline irrigation, (sometimes including 3% hydrogen peroxide) is recommended to remove uterine lumenal inflammatory fluids and debris prior to starting antibiotic treatment. Irrigation is best performed via a uterine flushing catheter. Uterine fluid clearance can be stimulated by transrectal massage of the uterus, or by the intravenous administration of 10-25 iu oxytocin. Large volume uterine flushing, antibiotic therapy and oxytocin treatment may be repeated daily or, if indicated, twice daily until ultrasound scan examinations suggest resolution. In addition to local treatment with antibiotics, systemic treatment.
may, on occasions, be indicated. Experience suggests that systemic antibiotic treatment alone is of little value in the treatment of equine uterine infections. In most cases the infecting organism is in the uterine lumen and the most superficial part of the endometrium rather than in the deeper parts of the endometrial tissue. Thus local uterine lumenal treatments are likely to be the most successful. The suitability of the preparation used for intra-uterine irrigation is very important (irritant and incompletely dissolvable materials should be avoided) and 1 g ceftiofur sodium in 20 ml sterile water for injection has been found to be an excellent ‘first choice’ pending identification of the pathogen(s) and specific antibiotic sensitivity test results.

Fungal infections of the uterus may produce clinical signs that vary from none, in which the infection is luminal and there is no tissue invasion, to severe purulent endometritis, demonstrable by ultrasound scan. If persistent, these infections lead to conception failure or, if infection occurs during pregnancy, to ascending placentitis and abortion. Treatment of mares with fungal infections is generally more challenging than for bacterial infections. Common treatment strategies include initial large volume (3 l daily or twice daily) uterine irrigations with sterile saline solution (sometimes with added 3% hydrogen peroxide solution). Irrigation with dilute (0.5%) povidone iodine solutions has been used but care must be taken to avoid severe genital inflammation in individual mares. Culture and sensitivity will determine the choice of antifungal drugs. Daily intrauterine infusions for 7-10 days may be required to effectively resolve the infection. A single dose of a benzoylphenyl urea (Lufenuron) has been suggested to be effective in treating mares with fungal endometritis. Additional systemic (oral) treatment with ketoconazole may help resolution in some cases.

The success or failure of treatment for acute endometritis is monitored by ‘follow-up’ endometrial smear/swab, ultrasound scan and/or biopsy examinations, taken 3–4 weeks after the end of the course of treatment.

**Chronic infiltrative endometritis** is diagnosed by the presence of mononuclear cells (histiocytes/lymphocytes and plasma cells) in biopsy specimens. The presence of these cells indicates a local immune response and therefore previous or on-going challenge by semen or infectious agents. If uncomplicated by other abnormalities, this natural immune response is considered normal and no specific treatment is indicated. Occasionally, the immune response appears excessive, occasionally to granulomatous proportions, when treatment with a prolonged course of appropriate intrauterine antibiotics followed by a prolonged period of sexual rest may be indicated to help remove chronic deep-seated foci of infection.

**Chronic degenerative endometrial disease (endometrosis)** is diagnosed by the presence of glandular degenerative changes in biopsy specimens in the form of gland ‘nests’, surrounded by lamellae of fibrous tissue or, less commonly, gland ‘cysts’, lined by glandular epithelial cells. Peri-glandular, peri-vascular or, less commonly, diffuse stromal fibrosis and angiopathy are seen. These degenerate glands are malfunctional. Diffuse stromal fibrosis is considered to be a poor prognostic sign for the maintenance of future pregnancies. Pools of tissue fluid lined by lymphatic endothelial cells (lymphatic ‘lacunae’) may be seen scattered in the stroma. As these develop they become larger and migrate into the uterine lumen, attached to the endometrium by a ‘stalk’ of lymphatic duct and connective tissue. These endometrial cysts, when large enough, can be seen by ultrasound scan. It is unusual to sample a lymphatic cyst, using conventional biopsy techniques.

Chronic endometrial degenerative changes are progressive and are associated most importantly with the normal ageing process and cyclic hormonal effects. The repeated stimulatory challenges of semen, micro-organisms, external genital and environmental debris, and the physical challenges of obstetric difficulties may accelerate the progression of these changes and it is possible that they may, to a large extent, account for the linear decline in fertility seen in the Thoroughbred mare population with age (see above). These degenerative changes are frequently seen in mares that suffer repeated pregnancy failure or prolonged gestation with foetal dysmaturity. Degenerative changes are inevitable to a degree and thus each biopsy specimen must be assessed in terms of the mare’s age and parity. The severity of these changes has been shown to be correlated with age to an extent which suggests that, in general terms, mares up to 9 years of age should have no signs, mares up to 13 years of age should have no more than mild signs, mares up to 15 years of age should have no more than moderate signs and mares of 17 years and older are likely to have advanced signs of chronic degenerative changes. Conversely,
successful normal reproductive activity also appears to slow the development of these changes, suggesting that repeated successive normal pregnancy, without obstetric difficulty, helps maintain a healthy endometrium. It is well recognised that older maiden mares, e.g. performance mares who retire later in life than Thoroughbred mares, frequently have degenerative changes in their biopsy specimens to degrees that are markedly in excess of what would be considered acceptable for their age. These mares often find difficulty in achieving a successful first pregnancy. Conversely, old Thoroughbred mares that have produced foals year after year since 4 years of age, without failures and while managing to avoid obstetrical difficulties, have chronic endometrial degenerative changes that suggest a much younger age. It is probably that the periodic interruptions to ovarian steroid hormone cyclicity that pregnancies afford have a ‘protective’ effect on endometrial gland integrity. The ‘moral’ of the story for mare management is therefore good gynaecological and obstetric management and avoiding years of reproductive rest.

Where the degree of degenerative change is considered excessive for age, treatment with mechanical endometrial curettage may be attempted. Improvements in histopathological appearance and fertility can be expected in some mares, more reliably in those who are less than 17 years old. If this technique is of value, it must be by mild stimulation of endometrial blood supply. Attempts at chemical curettage are best avoided because the severity and complications of its effects in individual mares are unpredictable and uncontrollable. If such treatments result in trans-lumenal adhesions or cervical damage, these may end the mare’s reproductive career.

**Endometrial atrophy** is diagnosed by loss of normal glands from the endometrium. Temporary diffuse glandular atrophy is seen following prolonged ovarian inactivity and is therefore a normal temporary feature during winter anoestrus. This is seen in some mares with ovarian functional depression associated with ovarian granulosa cell tumours. True endometrial atrophy, with lumenal and glandular atrophy, may be seen in aged mares, usually in association with senile ovarian malfunction and is an ‘end-stage’ process. Rarely, true endometrial atrophy has been seen in younger mares following severe recurrent acute endometritis with *P. aeruginosa* infection. No treatment is successful for true endometrial atrophy and retirement is the most practical option.

**Endometrial hypoplasia** is diagnosed by signs of diffuse glandular under-development and has been seen in young barren maiden mares, sometimes in association with ovarian cyclic irregularities. It appears to be a feature of relative genital immaturity and usually resolves, without treatment, in time. In a young maiden mare, where the degree of hypoplasia is marked and ovarian size is minimal, or where the condition persists, the possibility that fundamental ovarian abnormality (gonadal dysgenesis) is involved should be considered and chromosome analysis (karyotype) should be performed.

**Endometrial hyperplasia** is diagnosed by signs of endometrial glandular over-activity. Glandular hyperplasia with hypersecretion is a normal feature of the post-partum or post-pregnancy failure period and normal glandular architecture and secretory activity is usually achieved by 10 to 12 days but occasionally may persist for weeks if not months, when it is considered pathological. In such cases, acute endometritis is often a complicating feature. Treatment with the intravenous administration of 10-25 iu oxytocin often gives good results. It is believed that oxytocin may reduce endometrial hyperplasia via its endometrial vasoconstrictive effect, as reported in other species. Acute endometritis, where involved, should be treated as discussed above.

In some cases, recurrent acute endometritis appears to produce diffuse glandular hyperplasia, probably associated with short cycling and hyperoestrogenism. Successful treatment of the acute endometritis will reduce the signs of diffuse glandular hyperplasia and treatment with oxytocin appears to aid resolution.

**Other uterine abnormalities**

**Endometrial lymphatic cysts**: The development of these cysts has been discussed above. They are commonly seen during ultrasound scan examinations in multiparous mares over 14 years old. They can be seen during ultrasound scan examination because the lymphatic fluid that they contain is anechoic. The cysts may be unilocular or multilocular. They are frequently inconvenient in that they may confuse pregnancy examinations, but otherwise, unless very large where they may prevent the normal intrauterine mobility of the pre-fixed embryo, essential for early recognition of pregnancy and/or they are widespread throughout the uterus, they appear to have no specific
effect on fertility. They can, if considered necessary, be visualised and removed with laser ablation or loop-wire thermocautery via a videoendoscope.

**Trans-lumenal fibrous adhesions:** These may follow obstetrical injuries or the injudicious intrauterine use of irritant chemicals. If widespread and diffuse, these are untreatable and the mare is most sensibly retired. If focal and discrete, they may be removed with laser ablation, thermocautery or removal by biopsy attachment, via a videoendoscope, with variable success in terms of future fertility.

**Intra-uterine foreign bodies:** Use of the videoendoscope in mares with recurrent non-responsive endometritis has revealed, in some cases, lumenal foreign bodies consisting of placental remnants, cotton wool (presumably swab tip fragments) and amorphous debris with a central core of multiplying bacteria or unidentifiable degenerate debris. Once removed with a biopsy attachment, via a videoendoscope, these cases responded to treatment for acute endometritis.

**Endometrial neoplasia:** Leiomyomas and fibroleiomyomas are uncommon but are the most frequently diagnosed equine endometrial tumours. They are usually small and benign and have no primary effect on fertility. They may be obstructive and may bleed. Treatment, by laser surgery, via a videoendoscope or surgical removal via hysterotomy, via laparotomy or laparoscopy, is only indicated where the tumour is large, when it may be pedunculated, and may cause persistent endometrial haemorrhage and secondary endometritis. Malignant endometrial adenocarcinoma has been only rarely recorded. One such case had respiratory signs and necropsy examination confirmed pulmonary metastases.

**Videohysteroscopic examinations**
Examinations are best made with the videoendoscope, which gives better visualisation than is possible with conventional fibreoptic technology endoscopes. Endometrial lymphatic cysts, fluid accumulations, fibrous adhesions, foreign bodies and endometrial tumours may be visualised and sometimes removed, using laser or thermocautery instruments. Biopsy specimens obtained with instruments supplied for passage through the endoscope are too small to be diagnostically useful. Conventional basket-jawed endometrial biopsy forceps can be passed alongside the endoscope and visually directed samples can be obtained.

**Laparoscopic examinations**
This technique has been used to study ovulation in mares and to treat blocked fallopian tubes with external applications of prostaglandins. Fallopian tube blockage is a rare condition in mares.

Expertise and experience with equine laparoscopic surgery has improved markedly during recent years and neoplastic ovaries and intractable ovarian haematomas are now most commonly removed by this technique, with the mare standing under sedation and local analgesia. The technique may be used for intra-pelvic exploration of the genitalia in specific cases.

**Exploratory Laparotomy**
Rarely, mid-line or flank laparotomy, with the mare under general anaesthesia, may be indicated for the investigation and/or treatment of uterine abnormality.

**Extra-uterine abnormalities**
Organising broad ligament haematomas or pelvic adhesions may be detected by their palpably hard consistency and their homogeneous appearance on ultrasound scan examination. Peri-uterine abscesses sometimes follow obstetric injuries and these require intensive medical treatment with systemic antibiotic therapy.

**Prognosis for future breeding**
Some mare owners request a prognosis for the chances for successful future breeding to help with mating plans or to help with the decision to retire the mare. While this is an understandable request, prognoses should be made with great caution. Prognoses are most usefully and more accurately made, in 2 stages, on the following basis:-

1. Following the first examination and biopsy, aged mares with true (not seasonally-induced) endometrial atrophy, i.e. in effect, senility, and young maiden mares with fundamental chromosome abnormalities (gonadal dysgenesis) are appropriately retired at this stage. Mares with recurrent acute endometritis and those with severe chronic
endometrial degenerative disease invariably demonstrate increased clinical ‘susceptibility’ to uterine infection.

2. Following the second, i.e. follow-up examination and biopsy, failure to improve, or deterioration after specific uterine treatments and, where necessary, further examinations and further specific treatments have been performed are considered very poor prognostic signs.

Subsequent management

After a satisfactory follow-up examination, a management plan is formulated to help the individual mare compensate for her residual abnormalities. The aim is to limit uterine exposure to semen and bacteria, and to assist the uterus to physically clear contaminants and inflammatory products after breeding. This can be achieved, in populations of horses where registration authorities allow, by the use of artificial insemination (AI) with antibiotic-extended semen:

1. Satisfactory endometrial swab and smear test results are obtained at the current oestrous period, i.e. no signs of acute endometritis.
2. An apparently normal, developing, mature ovarian follicle is palpable.
3. Insemination is arranged as close as possible to the estimated time of likely ovulation. Ovulation may be aided by the administration of hCG or a GnRH analogue.
4. AI using a semen extender that contains antibiotics is performed.

4. Physical clearance following breeding can be assisted by the use of oxytocin and/or uterine lavage:
   a. Oxytocin or PGF$_{2\alpha}$ treatment at 4-8 hours after breeding will effectively aid in uterine clearance, resulting in improved pregnancy rates in susceptible mares. Data suggest that a lower dose of oxytocin (5-10 IU) may be more effective than higher doses, in promoting uterine clearance. Care must be taken with regards to the timing of PGF$_{2\alpha}$ treatment. PGF$_{2\alpha}$ can cause a delay in the formation of a functional CL when administered within 2 days after ovulation, potentially causing pregnancy failure.
   b. Large-volume uterine lavage at 6-12 hours after breeding will also effectively assist in clearing the uterus from fluid and inflammatory products. Because sperm transport to the oviduct is completed within 4 hours after breeding, uterine lavage between 6-12 hours after breeding will have no adverse effect on fertility.
   c. Manual dilation of the cervix in mares with poor cervical dilation may help these mares to more effectively clear their uteri of fluid.

5. AI should be limited to once per oestrous period, since each exposure to semen induces an inflammatory response.

Where AI is not applicable, i.e. in Thoroughbred horses, ‘minimal contamination breeding techniques’ may be used with natural mating. These consist of:-

1. Satisfactory endometrial swab and smear test results are obtained at the current oestrous period.
2. An apparently normal, mature, developing ovarian follicle is palpable.
3. Mating is arranged as close as possible to the estimated time of likely ovulation.
4. Pre-breeding semen extender, containing low-fat skimmed milk powder (2.5 g), gelatine (0.5 g), glucose (5.0 g), crystalline penicillin (300 mg), crystalline streptomycin (300 mg) dissolved in 100 ml sterile water for injection, may be instilled into the mare’s uterus as soon as possible prior to mating, if considered appropriate. The powdered mixture may be stored at -4°C in sealed plastic sachets, prior to use following reconstitution at 37°C in 100 ml sterile water for injection.
5. LH in the form of hCG or a GnRH analogue is used to hasten ovulation.
6. The uterus is flushed with 1-3 l sterile saline (depending on size of mare/uterus) and then treated with a water-soluble, non-irritant, broad-spectrum antibiotic solution to which the common equine uterine aerobic and anaerobic pathogens are sensitive (e.g. 1 g. ceftiofur sodium in 20 ml sterile water for injection), 12–24 h after mating, followed by 10-25 iu oxytocin administered iv to aid uterine clearance. This may be repeated 24 hours and occasionally 48 hours later, depending on the circumstances of the individual case.
7. A second mating during that oestrous period is not recommended.
Management for ‘high risk’ during achieved pregnancies

Pregnancies achieved from mares with compromised uteri should be identified as ‘high risk’ and should be monitored by watching the mare’s udder and in appropriate cases by serial ultrasound scan examinations. Unnecessary maternal stress should be avoided throughout pregnancy. Prolonged gestation sometimes occurs in mares with advanced chronic endometrial degenerative disease and this identifies the foetus as ‘high risk’ and neonatal critical care facilities should be prepared for use, when required.

Ultrasoundographic examinations of the placenta in mares that are considered to be at risk for abortion during late gestation can be performed by transabdominal and transrectal approaches.

Transabdominal Ultrasonographic examinations

Using a 3.5 or 5 MHz sector scanner, four quadrants of the placenta (right cranial, right caudal, left cranial, and left caudal) should be examined by the transabdominal approach. Mares with normal pregnancies should have a minimal combined thickness of the uterus and the placenta (CTUP) of 7.1±1.6 mm, and a maximal CTUP of 11.5±2.4 mm. Pregnancies with an increased CTUP have been associated with the delivery of abnormal foals. The caudal portion of the allantochorion cannot be imaged by this approach, preventing the clinician from diagnosing ascending placentitis in its early stages. However, placental thickening and partial separation of the allantochorion from the endometrium may be observed in mares with placentitis originating from a haematogenous infection.

Transrectal Ultrasonographic examinations

Imaging the caudal allantochorion in late gestational mares provides an excellent image of the placenta close to the cervical star. A 5 MHz linear transducer should be positioned 1-2 inches cranial of the cervical-placental junction, and then moved laterally until the middle branch of the uterine artery is visible at the ventral aspect of the uterine body. The CTUP should then be measured between the middle branch of the uterine artery and the allantoic fluid. The clinician must make sure that the amnion is not adjacent to the allantochorion, since this may result in a false increased CTUP. It is important to obtain all CTUP measurements from the ventral aspect of the uterine body, since oedema of the dorsal aspect of the allantochorion has been noted in normal pregnant mares during the last month of gestation. Increases in CTUP >8 mm between day 271 and 300, >10 mm between day 301 and 330, and >12 mm after day 330 have been associated with placental failure and impending abortion. In advanced stages of placentitis, hyperechoic fluid may be imaged in the space between the uterus and the placenta.

The equine placenta is part of an endocrine foetoplacental interaction, which synthesizes and metabolizes progestagens. Mares with advanced stages of placentitis or placental separation may have increased plasma concentrations of progestagens as a result of stress to the foetoplacental unit. Since foetoplacental progesterone is rapidly metabolized to 5alpha-pregnanes, its metabolites may not be recognized by all commercial progesterone assays. Therefore, maternal serum progesterone concentrations in late pregnant mares do not always reflect the conditions in the uterus. Mares that develop a chronic form of placentitis respond with increased plasma progesterone concentrations, while mares that developed acute placentitis and abortion soon after infection experienced a drop in plasma progesterone concentrations. Therefore, measurement of repeated samples of plasma progestagen concentrations in mares with placentitis may be a useful method to identify those that may abort or deliver prematurely.

Treatment of mares with placentitis should be aimed toward elimination of the infectious agents, reduction of the inflammatory response, and reduction of the increased myometrial contractility in response to the ongoing inflammation. Poor perineal confirmation, urine pooling, and cervical lesions should be corrected prior to breeding to prevent an ascending route of infection during pregnancy. Mares with clinical signs of placentitis, or abnormal placental findings upon ultrasonographic evaluation may be treated with broad-spectrum antibiotics (e.g. trimethoprim sulphua), anti-inflammatory medication (flunixin meglumine, 1.1 mg/kg BID or phenylbutazone, 4 mg/kg BID), and tocolytics (al trenogest, 0.088 mg/kg SID or clenbuterol, 0.8 µg/kg BID). Pentoxifylline (7.5 mg/kg per os BID) has been suggested to increase oxygenation of the placenta. Bacterial and fungal cultures should be obtained in mares with vaginal discharge for isolation of a causative agent and sensitivity to antibiotics. Following foaling or abortion, the entire placenta (and foal in case of abortion) should be submitted for necropsy examinations. The
endometrium should be cultured and the mare should be treated for endometritis if the placental cultures suggest infection.

Has progress been made?

Weatherbys annual returns made by owners of Thoroughbred mares in the United Kingdom and Ireland report that during the 29 years from 1977 to 2006, the number of mares registered as 'mated by registered Thoroughbred stallions' has increased from 14,556 to 23,415 and the number of live foals from 8,099 to 17,121. When these data are presented in terms of percentage of mares mated (minus 'no returns' and 'mares dead and exported', for whom accurate data is not available), encouraging trends emerge. Conception rate has increased from 77.5% to 97.1%. Similarly, live foal rate has increased from 68.1% to 88.8%. Barren mare rate has decreased from 22.5% to 11.1%. Gestational failure rate has reduced from 9.4% to 8.3%. Closer examination of the latter data shows a downward trend from 1977 to 1989, followed by a rise which is believed to be associated with the widespread use of ultrasound scan examinations making possible the diagnosis of early gestational failure which has since been reflected in mare owners’ returns. Since then it appears that some progress has been made to decrease pregnancy losses.

The progressive fall in the barren mare rate by more than 50% over the last 23 years is particularly encouraging. Although it is only possible to speculate on the probable multifactorial causes of this improvement, one must hope that progress in mare management and equine gynaecology has at least played a useful part.

Conclusions

Few mares are truly infertile and with an accurate diagnosis, rational treatment and careful management, most can be encouraged to breed successfully. Preparing the barren mare for the new breeding season early is essential to maximise chances for an early successful pregnancy and to help prolong the mare’s long-term breeding career. Management ‘teamwork’ is a vital factor and sufficient commitment is required from the owner, in terms of interest and finance, from the studfarm manager, in terms of interest and staff time and facilities, and from the veterinarian, in terms of interest, time, knowledge, expertise, experience and provision of the necessary equipment.

Further reading


Ginther, O.J. (1986) detailed ultrasonic imaging and reproductive events in the mare in a publication from Equiservices, Cross Plains, Wisconsin, USA.


