

Oxytocin use in the mare during breeding

By Jos Mottershead

Oxytocin acts on smooth muscle in the body, causing it to contract. One such area of tissue, which is of tremendous importance relative to breeding, is the mare's uterus.

It has been recognized for some time that fluid build up in the uterus can be detrimental to establishing or maintaining pregnancy, and with a view to removal of such fluid there has been research into the use of oxytocin.



Uterine fluid is most commonly seen by ultrasound post-breeding, and is usually present as a result of a natural response to a foreign object in the uterus - semen. In most mares, this fluid poses no problem to the establishment or maintenance of pregnancy, and is cleared within 24 - 48 hours by the mare herself. In some mares however, especially older multiparous mares, or mares with poor reproductive conformation, a condition known as "delayed uterine clearance" may occur. This results in the fluid *not* being cleared, and will typically result in low-grade endometritis, causing the conceptus to encounter an inhospitable environment when it enters the uterus about 5½ days post-ovulation, with subsequent pregnancy loss.

Uterine fluid encountered in estrus mares during an ultrasonic evaluation prior to breeding (often during an examination of the follicular status of the ovaries) has been established to be detrimental to establishing or maintaining pregnancy¹. Generally amounts in excess of one-half inch depth are considered excessive, and suitable for treatment with oxytocin. Amounts in excess of one inch are considered to be more likely to respond favourably to lavage with subsequent oxytocin treatment, and the resulting

exudate should also be evaluated for inflammatory cells and bacteria, as a bacterial uterine infection may be the cause. If the fluid is seen to be a clear black colour *per ultrasound*, it is most commonly sterile. If however it appears cloudy, the presence of infectious material should be considered a distinct possibility.

The post-breeding treatment that we have seen to be most effective has been intramuscular oxytocin, combined with an intra-uterine infusion of a broad-spectrum antibiotic. Experimental work by others has also found this to be effective². As the half-life of oxytocin in the mare is only 6.8 minutes³, we have noted that multiple treatments with oxytocin are required. The first intramuscular or intravenous injection of oxytocin (see below for dosage discussion) should be at 4 hours after breeding, which allows adequate time for all sufficiently progressively motile sperm to make their way to the oviducts (which are not affected by the oxytocin treatment). This is then followed by an intra-uterine infusion of antibiotic at least 2 hours later, and then three more intramuscular or intravenous injections at six hourly intervals (the first of which takes place 6 hours after the uterine infusion). Note that this treatment commences *post-breeding* and not post-ovulation. In highly susceptible mares, we have found it beneficial to continue oxytocin treatment on a six-hourly treatment schedule through to 3½ days post-ovulation. Treatment after that time will not be beneficial, as the cervix will have closed sufficiently to prevent clearance of fluid. We prefer not to use the aminoglycoside antibiotics (Amikacin or Gentamycin) post-breeding as we consider them to be more irritating to the uterus, which we want to keep as "calm" as possible while awaiting the arrival of the conceptus.

Pre-breeding, it is considered to be more important to solely remove the fluid, rather than infusing antibiotic (as long as no uterine bacteria have been found to be present) hence repeated (4 times daily) oxytocin treatment alone is recommended.

In the past the suitable dosage level of oxytocin was commonly considered to be 40 international units (i.u.) or more in some cases. Recent research⁴ has suggested a lower dose - 10 i.u. intravenously or 20 i.u. intramuscularly - to be more suitable prior to ovulation. The research indicated that the higher dosages results in a universal constriction of the smooth muscle, whereas the lower dosage results in methodical contractions starting at the distal portion of the horns working caudally, which results in a more complete and systematic evacuation of the fluid. Injections can be either intramuscular or intravenous, and after treatment with 20 IU, it has been shown⁵ that >90% of intrauterine content is eliminated within 15 to 30 minutes. Once ovulation has occurred, the effect of oxytocin is reduced⁶, so increasing the dosage to 20 i.u. intravenously or 30 i.u. intramuscularly may be appropriate.

Some users of this treatment protocol are favouring the use of the synthetic prostaglandin analogue Cloprostenol (Estrumate[®], Intervet), rather than oxytocin, as it is felt to have a longer active period than does the oxytocin. Additionally, intramuscular use rather than intravenous has been favoured as allowing a slower, longer passage. Recent research^{7,8} on the use of prostaglandin analogues at the post-ovulatory stage however has indicated that there may be an interference with the development of a fully functional Corpus Luteum, and may therefore be not recommended. It is a reasonable extrapolation of that finding to believe that similar use of prostaglandin as well as a prostaglandin analogue would yield the same results. Other researchers⁸ have suggested that progesterone secretion of the CL is only temporarily affected and rebounds by day-7 post ovulation if the synthetic prostaglandin treatment is carried out over only the first 48 hours post-ovulation and at a lower dosage (250 micrograms IM). As a matter of convenience, up to 24 hours post-ovulation, we will use Cloprostenol for the evening treatment, as it provides a 12 hour coverage, thereby preventing the need for middle-of-the-night treatments. We feel that this is a happy compromise between practicality and not risking compromise of CL function. As both prostaglandin and Cloprostenol are produced in thin liquids and a low volume is being injected, insulin syringes may be used, which causes minimal distress to the mare or the person performing the injection.

Mares that are likely to benefit from the use of an oxytocin protocol such as one outlined above include those mares with known delayed uterine clearance problems, mares with uterine fluid presence pre- and/or post-breeding, older mares that may have uterine lymphatic issues, mares post-breeding with frozen semen, and - in our experience - some other "problem mares" that have defied pregnancy establishment for no apparent reason. It should be noted that we will use oxytocin prophylactically in mares that we consider may present breeding problems even in the absence of identified problems, and have seen good - if inexplicable - success. The treatment is cheap, easy and carries minimal risks.

A point possibly worthy of serious consideration has recently been raised. From the above research we have established that the presence of systemic low levels of prostaglandin post-ovulation interfere with CL formation and related progesterone release. There is an increasing belief among some researchers that low progesterone levels in the mare may be present because of low-grade endometritis causing low levels of prostaglandin to be released. This endometritis may be as a result of either undetected uterine pathogenic presence (that should have been identified in a pre-breeding uterine culture and cytology evaluation), or delayed uterine clearance issues causing failure of clearance of normal post-breeding inflammatory response fluids. It may well be that money would be better spent on pre- peri- and post-breeding evaluations and suitable treatments rather than the excessive progestin supplementation commonly seen.

If during the pre- or post-breeding evaluations the cervix is found to be excessively tight, treating the mare with Estradiol Cypionate (ECP) or a topically applied cream made with the synthetic prostaglandin Misoprostol may also be indicated. This may be done either pre- or post-breeding, depending upon the need. It should be noted that higher dosage rates of estradiol prior to ovulation should be carried out with caution, as this may delay ovulation.

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