Causes and cures for repeated early pregnancy failure in the mare

Twink Allen
The Paul Mellon Laboratory of Equine Reproduction, 'Brunswick', Newmarket, Suffolk, UK

Abstract

Some 14% of Thoroughbred mares lose their pregnancy between initial diagnosis at 12-14 days post-ovulation and term and around 60% of these losses occur during the first 42 days of gestation, with a further 25% between days 42 and 150. Discounting infective endometritis as a possible cause of this high early stage loss (pathogenic bacteria or fungi would usually kill the embryo well before initial diagnosis of pregnancy at day 12), and from karyotyping studies in other species, notably women and pigs, it may be reasonably assumed that as many as 50-60% of the early losses stem from chromosomal aberrations occurring at fertilization. They are a matter of 'good riddance to bad rubbish' at a sufficiently early stage to generate a second normal pregnancy and they are often seen ultrasonographically as an anembryonic conceptus that simply 'fades away' between 20 and 30 days after ovulation.

Repeated failure to conceive in the face of normal ovulation and an absence of uterine/cervical pathology may be caused by accumulations of spirals of inspisated follicular fluid at the ampullary-isthmus constriction in both oviducts which inhibit the downward passage of the embryo to the uterus. The condition is successfully overcome by laparoscopic application of a human preparation of prostaglandin E_2 gel to both oviducts but the question remains as to how many mares in the population have one blocked oviduct thereby reducing their fecundity rather than causing full infertility.

As demonstrated convincingly by the late Cliff Irvine in New Zealand, progesterone deficiency is not a significant cause of early pregnancy loss in the mare in spite of the huge quantities of altrenogest and other progestagens shovelled into mares during this period. On the contrary, exogenous progestagen administration is likely to downregulate luteal function and, thereby, endogenous progesterone production, especially if given prior to the luteotrophic support provided by the commencing secretion of equine chorionic gonadotropin (eCG) around day 38-40. Likewise, an injection of human chorionic gonadotrophin (hCG) given prior to eCG secretion will also induce luteolysis and pregnancy loss.

The horse conceptus must imbibe appreciable amounts of endometrial gland secretions (histotroph) if it is to survive during its first 40 days of 'free living' in the mare's uterus. And even after microvillous attachment and allantochorion-endometrium interdigitation commences around day 40, histotroph imbibition via the highly absorptive areolae situated between the microcotyledons on the allantochorion remains a vital source of nutrients for the growing fetus. Hence, severe deprivation of histotroph uptake, such as occurs frequently in the misaligned member of unicornuate twin conceptuses, or as a result of significant scarring of, or excessive cyst formation in, the endometrium at the base of the uterine horn where the conceptus will initially become 'fixed' and try to implant, can be lethal to it as a consequence of the resultant starvation.

The precise role of the considerable quantities of estrogen secreted during early pregnancy, initially by the conceptus itself up to day 40, and by the primary and secondary corpora lutea (CL) thereafter in response to the luteotrophic stimulus of commencing eCG secretion, has not been determined. It is likely to play an important, and perhaps vital, part in stimulating histotroph secretion, especially in those glands in direct contact with the expanding trophoblast, and to act in concert with vascular endothelial growth factor (VEGF) to develop the extensive capillary networks required on both the maternal and fetal sides of the placental interface. Whether any deficiency in estrogen production may occur during early pregnancy, from the conceptus membranes or the accessory CL, perhaps caused by a lack of steroid precursor availability occasioned by restricted dietary intake, has yet to be determined.

Finally, it is clearly important that the horse embryo signals its presence correctly to the maternal organism early in gestation to gain immunological acceptance in the uterus. As in women who suffer repeated early pregnancy failure, active immunization of mares that do likewise against lymphocytes extracted from the peripheral blood of the sire of the conceptus results in live births from a significant proportion of the treated animals. The mechanism of action and true value of such therapy is still hotly debated in human gynaecology circles but it is clear that it can protect the immunologically threatened conceptus in some persistently aborting mares.