

Induced Termination of Pregnancy in Domestic Farm Animals

Review Article

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ABSTRACT

Induced abortion may be desired during a normal or abnormal pregnancy. The methods of induced abortion differ between species mainly because of different sources for progesterone production during pregnancy between species and within a species according to different stages of gestation. In cows and buffaloes, pregnancy can be effectively terminated from 5 to 150 days by administration of luteolytic doses of prostaglandin F₂ alpha (PG). From 150 days onwards and till term bovine and bubaline pregnancies can be safely terminated by administration of a combination of PG and dexamethasone. During the last month of pregnancy in these two species, pregnancy can be successfully terminated by using either a PG or dexamethasone. In goats pregnancy can be terminated during the entire gestation by administration of luteolytic doses of prostaglandins. In sheep pregnancies up to 55 days can be terminated by administration of 100 µg cloprostenol or 10-12 mg of dinoprost. From day 55 onward the termination of sheep pregnancies requires the administration of single or multiple injections of dexamethasone. Early pregnancy (day 5-34) termination in the mare can be achieved by physical methods or administration of PG. The same treatment is effective in terminating pregnancies between day 35-120 but repeated injections are required and because the endometrial cups continue to exist for a couple of days after pregnancy termination, mares do not return to estrus for prolonged periods. The termination of equine pregnancy after 4 months is difficult till term. The results of administration of PG or corticosteroids is suboptimal and manual disruption of the fetus after dilation of the cervix with PGE₂ creams is more reliable method of pregnancy termination.

KEY WORDS abortion, cow, goat, induction of parturition, mare, pregnancy termination, sheep.

INTRODUCTION

Induced abortion can be described as the elective termination of an undesirable pregnancy for safety of the mother. It may also apply to induced parturition at the end of gestation. Indications for inducing abortion during a normal pregnancy include accidental breeding of very young animals (Barth *et al.* 1981; Thomas, 1997), unwanted pregnancies in animals intended for sale as food animals (Henricks *et al.* 1977; Echterkamp *et al.* 1987), clinical disease in the mother (Purohit *et al.* 2006), change in use of the animal (Card, 2010) or age of the animal (Ragon, 1997). An abnormal pregnancy (hydroallantois, hydroamnion, ventral

hernia, rupture of the prepubic tendon, fetal mummification, pregnancy toxemia) is an additional indication for termination of pregnancy (Memon *et al.* 1981; Momont, 2005; Drost, 2007; Macpherson, 2007; Pycoc, 2008; Brozos *et al.* 2011). Elective termination of pregnancy near completion of gestation is largely used as a management tool in species like cattle, horses and goats (Currie, 1975; Kask *et al.* 2001; Mansell *et al.* 2006; Compton and Mc Dougall, 2010) and as a procedure to reduce the time to progeny test carpet wool rams by evaluating the birth coat of their lambs (Edey *et al.* 1982).

In most domestic animal species, early gestation is maintained by the progesterone produced by the primary corpus

luteum, although in sheep and mare the major source of progesterone during most part of pregnancy is the placenta (Stellflug *et al.* 1997). Due to the species particularities, the methods of pregnancy termination would depend upon the stage of gestation and the species. The aim of this study was to review the methods for termination of pregnancy in cattle, buffaloes, goat, sheep and mare.

Physiology of pregnancy maintenance in farm animals

The maintenance of pregnancy in most domestic animals is dependent on the secretion of progesterone. The primary corpus luteum (CL) formed on the ovary acts as a progesterone secreting endocrine gland and persists throughout pregnancy in most domestic animals except for the horse and sheep (Jainudeen and Hafez, 2000). The source of progesterone during the latter half of pregnancy is from the placenta in mare and ewes (Stellflug *et al.* 1997). The CL is necessary to secrete progesterone and maintain pregnancy through days 55 to 60 in sheep after which the placenta becomes competent to secrete sufficient progesterone to maintain pregnancy in the absence of the ovaries (Denamur and Martinet, 1955; Weems *et al.* 1992).

In the mare, progesterone concentration up to day 35-40 reflects secretion by the primary CL (Jainudeen and Hafez, 2000). The progesterone level then rises with the development of secondary corpora lutea, under the influence of equine chorionic gonadotropin (eCG) and reach their maximum between days 60 and 100 of the gestation (10-20 ng/mL) and plateau until days 120 to 150.

From mid gestation, other progestagens assume greater quantitative significance typically reaching concentrations in the maternal plasma between 5 and 50 ng/mL (Ousey, 2006). The fetus (gonads and adrenal gland) synthesizes large quantities of pregnenolone which is converted into 5α pregnanes in the endometrium (Hamon *et al.* 1991; Han *et al.* 1995).

The fetal production of progestagens increase in late gestation and consequently, progestagen concentration also increase in maternal plasma, typically peaking a few days before parturition and declining on the last day or even hours before birth (Ousey, 2006). In the cow, peripheral progesterone levels fluctuate between 6 and 15 ng/mL throughout gestation (Randel and Erb, 1971) with a gradual decline in the 2-4 weeks preceding parturition (Hunter *et al.* 1970). The progesterone is luteal in origin for the first 150 days of gestation (Gross and Williams, 1988). Between 150 and 250 days of gestation the placenta acts as an additional source of progesterone (Amin and El-Sheikh, 1973; Ullmann and Reimers, 1989; Schuler *et al.* 1999). The exact functions of placental steroids in the bovine species continue to be poorly defined (Schuler *et al.* 2008). In the final month of gestation, placental progesterone declines

and pregnancy is again dependent upon luteal progesterone (Thomas, 1997; Shenavai *et al.* 2010). Although, subtle differences do exist in the physiology of gestation and parturition between cattle and buffaloes they behave similarly in some aspects (Dobson and Kamonpatana, 1986). Nearly similar to cows the increase in progesterone in placental tissue in the buffalo is highest between days 97 and 250 (Amin and El-Sheikh, 1973).

Progesterone receptors have been observed in the binucleate trophoblastic cells of buffalo placenta (Carvalho, 2007). Prepartal decrease in the progesterone starts from days 276-278 (Arora and Pandey, 1982). Rapid decline in the plasma progesterone 3 days prepartum has been observed (EL-Beley *et al.* 1988). The maintenance of pregnancy in the goats is dependent for the entire gestation upon the secretion of progesterone by the CL of pregnancy (Van Rensburg, 1971; Buttle, 1978; Braun, 2007). The caprine placenta produces little or no progesterone at all (Irving *et al.* 1972; Braun, 2007).

Cattle and buffaloes

Pregnancy can be terminated in cattle and buffaloes by physical and hormonal methods. Little data is available on induction of abortion or parturition in buffaloes and as such, based on clinical experience and a few reports the techniques used for cattle are presumed to be similarly applicable in the buffalo.

Physical methods

Physical methods described to terminate pregnancy include the physical enucleation of the CL (Roberts, 1986), manual rupture of the amniotic vesicle before 65 days of gestation and decapitation of fetus between days 65 to 90, (Parmigiani *et al.* 1978). Abortion usually occurs within days 10-14. However, the CL may be maintained for prolonged periods of days 18-35 and some fetuses may mummify instead of being expelled (Kassam *et al.* 1987). Because of the damage that can be inflicted on the uterus due to physical methods of pregnancy termination, the longer time taken and the unpredictability of resumption of estrus cyclicity, physical methods are no longer advised for pregnancy termination in cattle and buffaloes (Thomas, 2007; Purohit, 2010).

Hormonal methods

Various hormones have been suggested to terminate bovine and bubaline pregnancies including prostaglandin $F_{2\alpha}$ (PG), glucocorticoids, estrogen and oxytocin (Barth *et al.* 1978; Prakash and Madan, 1985; Nasser *et al.* 1994; Henricks *et al.* 1977; Nasser *et al.* 2008; Shukla *et al.* 2008; Compton and Mc Dougall, 2010) according to the stage of gestation when pregnancy termination is desired.

Pregnancy up to 150 days

Since the maintenance of bovine and bubaline pregnancy up to 150 days is dependent on the luteal progesterone, administration of a PGF₂ α or its analogs (Table 1) is the most suitable drug to terminate the pregnancy. Cows do not respond until 5 to 7 days after ovulation. After that time majority of cows respond by abortion and return to estrus within 3 to 5 days of treatment (Day, 1977; Copeland *et al.* 1978). Cows not in estrus within 5 days of treatment should be given a second injection of the PG.

Estrogens administered within 72 hours of ovulation impair oviductal transit of the embryos thus preventing the establishment of pregnancy. Beyond this period, estrogens are luteolytic and thus induce abortion. Estrogens cause luteolysis by inducing the endogenous luteolytic cascade from the endometrium and also do have effects on the fetoplacental unit (Thomas, 2007). Up to 5 months of gestation a single or repeated injection of estrogen valerate (10-20 mg IM) and other estrogen preparations result in abortion in 60-80% of the treated heifers (Barth, 1986). Estrogens are associated with potential dangers of reduction in the milk production, vaginal prolapse and ovarian cysts in cattle and buffaloes thus their use in lactating buffaloes and cows is not suggested as PG is much safer option as a luteolytic agent.

Pregnancy between 150 to 180 days

Between 5-8 months of gestation, a combination of PGF₂ α and dexamethasone is necessary to remove both luteal and extra ovarian sources of progesterone. Prostaglandins cause luteolysis whereas, dexamethasone alter the fetal placental steroidogenesis by activating the C-17, 20-lyase enzyme complex (Gross and Williams, 1988), thus increasing the levels of estrogens instead of progesterone and the pregnancy is lost. Glucocorticoids function only in the presence of a functional fetoplacental unit; hence their administration is more useful when the fetus is alive. This combination is preferable to all other treatments. Abortion will occur within a mean time of 5 days (Barth *et al.* 1981). This treatment (500 μ g cloprostenol and 25 mg dexamethasone) is 95 percent effective and known to induce abortion at all stages of gestation in heifers (Barth *et al.* 1981). Similar treatments of buffaloes in gestation of less than 300 days with 20 mg dexamethasone and 25 mg PG F₂ α resulted in parturition within 37.83 \pm 2.6 hours (Shukla *et al.* 2008).

Pregnancy termination at term

In the last month of pregnancy, either dexamethasone or prostaglandin alone induces parturition within 2 to 3 days of administration both in cattle and buffaloes (Le Voie and Moody, 1973; Kordts and Jochle, 1975; Henricks *et al.* 1977; Sioan, 1977; Memon *et al.* 1981; Peters and Poole,

1992; Phogat *et al.* 1994; Kornmatitsuk *et al.* 2000; Nasser *et al.* 2008; Shukla *et al.* 2008; Villaroel and Lane, 2010). However, a combination of dexamethasone and PG are suggested when parturition is to be induced more than 15 days ahead of term. This assures more precise termination and better fetal viability (Lewing *et al.* 1985; Echternkamp *et al.* 1987; Kask *et al.* 2001).

To reduce complications associated with parturition induction, like reduced milk production (Morton and Butler, 1995), retained placenta or poor calf survival (Garcia *et al.* 1992), a long acting corticosteroid triamcinolone at the dose rate of 1 mg/60 kg has been proposed to be administered 7 days before injection of 20 mg of dexamethasone and 500 μ g cloprostenol (Nasser *et al.* 1994; Nasser *et al.* 2008). The demerits of parturition induction in dairy cows are offset by the benefits of subsequent improved reproductive performance and more efficient management of the herd (Mansell *et al.* 2006).

Pathologic pregnancies

The ability to effectively obtain the termination of bovine pregnancies with dropsical condition of the fetal membranes (hydroallantois and hydroamnion) is extremely poor (Momont, 2005; Drost, 2007). Pregnancy can be terminated within 48 hours with simultaneous administration of PG F₂ α and dexamethasone using doses recommended for terminating a normal pregnancy; however, supportive treatment is necessary to compensate for sudden fluid loss (Momont, 2005). Nevertheless, the risk for decompensation and hypovolaemic shock is huge. In spite of rigorous treatment, 4 of 5 cows with hydroallantois treated with prostaglandin and dexamethasone died at the time of fetal delivery at our centre (Purohit, 2006). Fetal mummification and fetal maceration can be treated with prostaglandin administration (Drost, 2007). However, some cows may require repeated treatments.

Mummified fetuses may sometimes be retained in the uterus for prolonged periods and such cases may not respond to treatments and necessitate surgical removal. In the authors experience attempts to dilate the cervix by using isoxsuprine HCl (50 mg IM or IV) or ritodrine (150 mg IV) were unsuccessful in dilating the cervix of cows with mummified fetuses and allow manual extraction. The prognosis of induced abortion in the case of macerated fetuses is always poor because of the severe endometrial damage (Drost, 2007).

Goats

Pregnancy day 5 to term

Since the caprine pregnancy maintenance is dependent on the luteal (CL) progesterone for the entire pregnancy, PGF₂ α or its analogs are the drug of choice for induction of

Table 1 Dosage of currently used medicaments for induced abortion in farm animals

		Cattle and buffaloes	Sheep	Goat	Mare
Prostaglandin	Window of administration	5-150 Days at term	Upto day 55	Day 5-term	Day 5-120
Fenprostalene		1 mg	-	-	-
Dinoprost tromethamine		25 mg IM	10-12.5 mg	5-10 mg	10 mg
Cloprostenol		500 µg IM	100-250 µg	62.5-100 µg	250 µg
Fluoprostenol		-	-	-	250 µg
Prostalene		-	-	-	2 mg
Carboprost tromethamine		500 µg	125 µg	125 µg	-
Corticosteroids	Window of administration	275-283 days	60 days to term	-	-
Dexamethasone		20-25 mg	15-20 mg	-	-
Flumethasone		5-10 mg	2 mg	-	-
Prednisolone		100 mg	20 mg	-	-
Betamethasone		20 mg	8-10 mg	-	-
Cortisol acetate		-	-	100 mg	-
Triamcinolone		20-30 mg	6 mg	-	-
Corticosteroid + PG	Window of administration	150-283 days	-	-	-
Dexamethasone + Cloprostenol		20 mg + 500 µg	--	-	-
Oxytocin	Window of administration	-	-	-	Term

abortion in goat, resulting in more number of live births when parturition is near. Also, it is more effective in pregnancy termination at all other stages of pregnancy. Treatments are followed by a dramatic decrease in plasma progesterone concentration within 24 hours of injection (Bretzlaff and Ott, 1983). Prostaglandins can be given at the dose rate 5 mg (Bretzlaff and Ott, 1983), 7.5 mg (Purohit *et al.* 2006) or 15 mg (Bosu *et al.* 1979). Other prostaglandins suggested for the goat include carboprost trometamine (125 µg IM) (Purohit, 2006) or cloprostenol (100 µg IM) followed by 50 µg IM ten hours later) (Maule-Walker, 1983). If pregnancy is not terminated within 48 hours the treatment should be repeated (Purohit *et al.* 2006). In goats administration of synthetic prostaglandins (125 µg cloprostenol or 5-10 mg dinoprost) will usually cause luteolysis and termination of a pregnancy (within 30-36 h) from day 5-7 of gestation till term (Braun, 1997; Day and Southwell, 1976). Hormonal methods can be used to induce abortion in goats. Both ACTH (Currie and Thorburn, 1977) and corticosteroids (Van Rensburg, 1971) have been used for early termination of pregnancy in goats. Infusion of 10 µg ACTH/hour into the fetus on day 126 of gestation resulted in live births on day 131 (Thorburn *et al.* 1972).

Daily doses of cortisol acetate (100 mg IM) to goats before day 112 and after day 136 resulted in delivery at normal term (Van Rensburg, 1971). Administration of 16 mg dexamethasone IM to goats on day 144 resulted in delivery of live kids but fetal membranes were retained (Ott *et al.* 1980). Administration of estradiol benzoate (12-25 mg IM) to goats resulted in abortion at 126-147 of pregnancy (Currie *et al.* 1976; Bosc *et al.* 1977). A major disadvantage of such a therapy was the delivery of nonviable kids.

Recently, aglepristone has been demonstrated to induce parturition in full term pregnant goats. Doses of 2.5 mg, 3.3 mg and 5.0 mg of aglepristone given SC once induced parturition in 97.2% of treated goats within 30-34 h without any effect on fetal viability or the incidence of retained placenta (Batista *et al.* 2011).

Pathological pregnancies

In goats, abnormal pregnancies needing pregnancy termination include hydrometra (Wittek *et al.* 1998; Purohit *et al.* 2006), hydroallantois (Morin *et al.* 1994; Jones and Fecteau, 1995; Purohit *et al.* 2006), rupture of prepubic tendon (Mobini *et al.* 2002; Purohit *et al.* 2006) and pregnancy toxemia (Tontis and Zwahlen, 1987; Brozos *et al.* 2011).

Pregnancy termination in these cases is simple, as a single dose of PG is sufficient in most cases.

If without response within 48 h, the injection should be repeated. Cesarean section is required in some does with hydroallantois or pregnancy toxemia (Purohit *et al.* 2006; Brozos *et al.* 2011).

Sheep

Pregnancy up to 55-60 days

In ewes, pregnancy up to 55-60 days can be terminated by IM injections of PG. Ewes injected at 20-60 days of pregnancy with 125 or 250 µg of cloprostenol aborted and 83% exhibited estrus within 7 days (Tyrrell *et al.* 1981). Cloprostenol at the dose rate of 100 µg (Nancarrow *et al.* 1982) to 250 µg (Audicana and Harvey, 1993) or dinoprost at the dose rate of 10-12 mg administered IM are suggested for termination of early pregnancy in ewes.

The injection may be repeated after 7 days if the ewes do not respond (Nancarrow *et al.* 1982; Audicana and Harvey, 1993).

Pregnancy beyond day 60

Pregnancy beyond 60 days can be terminated by intramuscular injections of 15-20 mg of dexamethasone given once or more times. Premature parturition in sheep following administration of synthetic corticoids is well documented (Skinner *et al.* 1970; Fylling, 1971). Administration of 10 mg of dexamethasone daily for 5 consecutive days starting on day 88 of pregnancy resulted in abortion in a great majority of ewes (Fylling *et al.* 1973). Higher doses are needed to induce midterm abortion than to induce premature parturition (Fylling *et al.* 1973).

The administration of PG to ewes near term would not induce labor (Liggins, 1973) and a combination of dexamethasone and PG did not lower the lambing interval (Kastelic *et al.* 1996). The CL of sheep at 90-100 days of gestation is functional and responsive to prostaglandins but luteolysis is not sufficient to induce abortion (Weems *et al.* 1992). The intramuscular administration of 10 or 20 mg of dexamethasone to ewes on day 133-142 of gestation induced parturition within 72 h (Adams and Wagner, 1970). Intra fetal infusion of a synthetic adrenocorticotropin at 120-130 days of gestation resulted in abortion in most treated ewes (Carbalum *et al.* 1982) but such an administration is only of experimental significance. Congenital abnormalities like cyclopia can result into a prolonged gestation (Binns *et al.* 1962) because of malfunctioning of the fetal pituitary adrenal system (Holm, 1966) and lack of the parturition induction signals.

Pregnancy at term

When parturition induction is desired in sheep, doses of 15 mg dexamethasone are suggested to be given IM on day

144 and this treatment induces lambing within 33.8±2.7 hours of injection (Shevah, 1974; Webster and Haresign, 1981; Harrison, 1982; Owens *et al.* 1985; Rubianes *et al.* 1991; Ingoldby and Jackson, 2001). Sheep treated with 2 mg flumethasone IM at 141 days of gestation lambed within 72 h post treatment. Poor lamb survival commonly seen with induction of parturition can be reduced if exact breeding dates are known (Ingoldby and Jackson, 2001). The results of betamethasone were found to be more promising when given in the fetal jugular vein to 125 days pregnant sheep (Derks *et al.* 1996). However, such a procedure does not seem to be of clinical significance. When glucocorticoids administered to ewes stimulated increased secretion of estrogen due to increased release of 17 α -hydroxylase by fetal placental tissue (Anderson *et al.* 1975) and a subsequent increase in prostaglandin F $_{2\alpha}$ (Wimsatt and Nathaneilsz, 1995), thus resulting into parturition like changes and fetal expulsion. A combination of dexamethasone (12 mg) and estradiol benzoate (20 mg) administered IM to ewes for parturition induction at 120 days of gestation offered no advantage as most lambs were either born dead or died within 2 hours of birth (Edey *et al.* 1982).

Pathological pregnancies

The most common pathological pregnancy observed in ewes is pregnancy toxemia (Tontis and Zwahlen, 1987; Pastor *et al.* 2001). The use of glucocorticoids to terminate such pregnancies does not offer good results (Pastor *et al.* 2001). Administration of high and long acting doses of corticosteroids to animals under stress may cause uremia as a result of increased protein catabolism (Koenig and Contreras, 1984). Emergency cesarean section is suggested with extreme care for removal of fetuses (Pastor *et al.* 2001).

Other less frequent pathological pregnancies recorded in ewes include hydroallantois (Milton *et al.* 1989) rupture of prepubic tendon (Mobini *et al.* 2002) and hydrometra (Yotov *et al.* 2009). The termination of these types of pregnancies can be achieved by administration of corticosteroids and estradiol but the outcome is not promising.

Mares

Pregnancy days 5 to 34

Two methods of pregnancy termination suggested during this period of gestation are physical and hormonal.

Physical methods

Intrauterine infusion or uterine lavage after day 6 terminates pregnancy in mare (Ragon, 2007). The technique can sometimes be used up to day 70 of pregnancy but is usually successful up to day 35 (Lofstedt, 1986). Abortion is probably caused by embryo toxic effects or release of endogenous PGF $_{2\alpha}$ as a result of cervical and uterine manipu-

lations (Paccamonti, 1991). Uterine lavage can be performed by placement of a long Foley catheter (30 French, 80 cm) in the uterus and infusion of sterile saline (2 to 3 liters in increments of 500-1000 mL) or lactated Ringer solution (Pycock, 2007). Infusion of dilute povidone iodine, weak Lugol's solution or nitrofurazone have been used successfully (Pycock, 2007), however, the potential dangers of damage to the endometrium preclude the frequent use of these infusions. Manual crushing of conceptus can be performed easily between day 16 and 25 after ovulation. After day 25, this technique is more difficult and less efficacious (Ragon, 2007).

Hormonal methods

The simplest method of terminating early equine pregnancy is the intramuscular injection of PGF₂α or its analogs (Paccamonti, 1991; Squires and Bosu, 1993). The transient side effects that may follow administration of PG to mares include profuse sweating, mild colic, hypothermia and diarrhea (Klem *et al.* 1982) and must be brought to the notice of owners before administration. Commonly used PG includes dinoprost tromethamine and fluprostenol. Before day 12-14 a single injection of either product has been shown to cause lysis of the CL and effectively terminate pregnancy. After this period, two or more consecutive injections may be necessary to lyse diestrus or secondary corpora lutea (Ginther, 1992). Mares can be expected to return to estrus within 3 to 5 days (Ragon, 1997).

Pregnancy between days 35-120

Repeated administration of prostaglandin is the treatment of choice for termination of pregnancy in mares more than 40 days pregnant (Daels *et al.* 1995). It is well documented that PGF₂α or its analogues need to be administered every 12-24 h (3-5 days) for successful induction of abortion (Douglas *et al.* 1974; Squires *et al.* 1980; Rathwell *et al.* 1987; Card, 2010).

Suggested preparations include dinoprost tromethamine (10 mg IM) (Rathwell *et al.* 1987), fluprostenol 250 µg IM (Squires *et al.* 1980) and cloprostenol 250 µg IM (Daels *et al.* 1995). Fluprostenol appears to present minimum side effects (Ragon, 2007). Mares abort within 2-5 days of treatment. A problem with termination of pregnancy at this time is the continued existence of endometrial cups that secrete eCG for prolonged periods. This delays estrus and ovulation after abortion and thus breeding of the mare in the same breeding season is seldom possible (Douglas *et al.* 1974; Squires *et al.* 1980; Rathwell *et al.* 1987; Lange, 1989).

A relatively new technique, frequently used for reduction of twin pregnancy in mares, is transvaginal or transcutaneous ultrasound guided allantocentesis, aspiration of allan-

toic fluid followed by injection of potassium penicillin or potassium chloride (Macpherson and Reimer, 2000), a technique that can also be used for termination of single pregnancies (Squires and Tarr, 1994; Macpherson *et al.* 1995). The technique involves a 5 or 7.5 MHz transvaginal ultrasound transducer for use in large animals. The technique can be used for pregnancy termination between days 20-65 but need sufficient expertise and is better when performed early (days 20-35) (Macpherson and Reimer, 2000). A less common procedure for pregnancy termination is the intra-allantoic infusion of dexamethasone solution. Abortion occurred within 72 h in the mares at pregnancy days 167-172 (Wichtel *et al.* 1988). However, intra-allantoic administration is difficult under most clinical settings.

Pregnancy termination after 4 months

Termination of equine pregnancy beyond 4 months appears to be difficult. The results of pregnancy termination by the use of prostaglandins are suboptimal. While some studies revealed that they are ineffective for inducing abortion when administered during mid gestation (days 140-150) (Bosu and Mc Kinnon, 1982; Van Leeuwen *et al.* 1983; Paccamonti, 1991), others report that 150 days pregnant mares aborted within 37-61 h of treatment when administered a prostaglandin twice daily for 3 to 5 days (Madej *et al.* 1987). Mares at the same gestation period also aborted when administered a combination treatment with estradiol benzoate and oxytocin within 13-27 h of PG injections (Madej *et al.* 1987).

A reliable technique for termination of late pregnancies is the manual disruption of fetal membranes and removal of the fetus (Ragon, 2007). The dilation of the cervix can be accomplished by administration of 6-10 mg of estradiol 24 h before induction of abortion (Lofstedt, 1986) or intracervical application of PGE₂ tablets or creams (Card, 2010).

Pregnancy termination at term

Termination of full term pregnancies should not be attempted unless the fetus is mature because pregnancies can extend up to 390 days without any abnormality. A reliable test to evaluate the fetal maturity is the assay of electrolytes in the colostrum (Ousey *et al.* 1984; Ley *et al.* 1998; Macpherson, 2000). If pregnancy is terminated before fetal maturity is achieved, immature foals may be born that may succumb easily.

A variety of agents and methods have been used to induce parturition in the mare, including glucocorticoids, prostaglandins and oxytocin. Glucocorticoids have limited efficacy for inducing parturition in the mare (Alm *et al.* 1974; Alm *et al.* 1975; First and Alm, 1977). The fetal cortisol increases only in the last 48 hours before delivery and maternally administered glucocorticoid does not induce labor

in the horse (Silver and Fowden, 1991). Prostaglandins have been successful in initiating parturition in the mare (Macpherson, 2000). The prostaglandin analogs fluprostenol (Jeffcott and Rossdale, 1977; Rossdale *et al.* 1979; Leadon *et al.* 1982), fenprostalene and prostalene (Ley *et al.* 1989) are successful on pregnancy termination, while natural prostaglandin is not a reliable induction agent (Alm *et al.* 1974).

The injection to parturition interval with fenprostalene (Ley *et al.* 1989) and fluprostenol (Ousey *et al.* 1984) is more variable (1-6 hours) and may take a longer time than spontaneously foaling mares or those induced with oxytocin (Rossdale *et al.* 1979). Neonatal adaptative abnormalities, neonatal weakness and fractured ribs have resulted from prostaglandin induced parturition (Jeffcott and Rossdale, 1977). Moreover, side effects of PG's in the mare, like sweating, hypothermia, increased respiration rate and diarrhea (Klem *et al.* 1982), render the use of PG less rewarding.

Oxytocin is generally considered the drug of choice for induction of parturition in the mare (Hilman, 1975; Jeffcott and Rossdale, 1977; Hillman and Ganjam, 1979; Pashen, 1982; Terblanche, 1983; Bennet, 1988; Pycock, 2008; Card, 2010). In the last month or so of gestation the relatively high levels of circulating estrogen and low concentrations of progesterone together with high levels of progesterone metabolites (Pashen, 1984; Ousey *et al.* 1987) may well create a hormonal environment in which oxytocin receptors are present well before term and consequently endogenous myometrial activity is high (Haluska *et al.* 1987). High doses of oxytocin (20 IU–120 IU) have been suggested as a bolus injection, within an IV infusion or in increments of 15 IU every 15 minutes (Purvis, 1977; Hillman and Lesser, 1980; Pashen, 1980; Macpherson *et al.* 1997). However, since higher doses are associated with more complications like premature placental separation, colic and dystocia, repeated low doses are advisable (Card, 2010). The increase in myometrial contractility that occurs following oxytocin administration is dose related (Ousey *et al.* 1998) and high doses without the foals readiness for birth may compromise foal viability. Thus, currently low daily dosage after assuring foal maturity is suggested (Pashen, 1980; Camillo *et al.* 2000; Duggan *et al.* 2007; Villani and Romano, 2008). A high proportion of mares (50-60%) foal with the first injection (Camillo *et al.* 2000; Duggan *et al.* 2007) of oxytocin (2.5-5.0 U): with delivery occurring within 120 min of injection.

Pathological pregnancies

Pathological pregnancies in mares include hydroptic conditions (hydroamnios, hydroallantois) and prepubic tendon rupture (Tibary *et al.* 2006; Macpherson, 2007; Pycock,

2008; Card, 2010; Macpherson, 2010). In these and other problems, like laminitis, chronic colic or ventrolateral abdominal muscle disease, the mares' condition may deteriorate quickly (Card, 2010) and consideration should be given to induction of abortion, induced preterm delivery, terminal cesarean section or euthanasia (Honnas *et al.* 1988; Ross *et al.* 2008).

CONCLUSION

Different approaches exist for termination of pregnancy in domestic farm animals. The major determinant for selecting a drug to terminate a pregnancy depends on the species and the stage of gestation. In ruminants, prostaglandins can terminate pregnancy at stages of gestation when only luteal progesterone is operative in pregnancy maintenance whereas when placental progesterone maintains pregnancy corticoids would be helpful. In mares the mechanism of pregnancy maintenance are different from ruminants and consequently different approaches are needed at different stages of gestation.

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