

Recent Advances in Equine Obstetrics

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Introduction:

Obstetrics is a branch of veterinary medicine that is concerned not only with the birth process, but also with treatment of the mother before and after the delivery. That is certainly the role ascribed to our obstetrical colleagues in the human field. Veterinary obstetrics encompasses far more than merely resolving difficult dystocias. In order to successfully manage complications that may develop in late gestation it is essential that the practitioner have a thorough appreciation of the complex fetoplacental environment. The horse is unique in so many respects, not the least of which is the hormonal support of pregnancy, and the changes that ultimately trigger parturition. Over the past several decades many distinguished colleagues have focused their research endeavors on unlocking the mare's reproductive secrets. However, in the interest of brevity, this paper will review only the most recent literature (1995 to present) pertaining to the equine periparturient period. Where there is no relevant material from the past decade, some earlier citations are provided.

Placentation:

The morphology of **blood vessels** in the uterine wall can vary considerably, depending on the age and reproductive status of the mare. In a recent study, inflammatory vascular alterations were observed in 20.5% of the endometrial specimens examined¹. Smaller and larger arterial and venous vessels demonstrated mild to severe degenerative lesions. Unaltered vessels were detected only in maiden mares. The incidence and severity of angiosis increases with the number of previous pregnancies and with advancing age¹⁻³. It has been proposed that haemodynamic and hormonal alterations during pregnancy and the puerperium may induce active vascular remodeling, and the ageing processes, chronic inflammation and short foaling intervals may be additional detrimental factors^{1,2}. Severe angiosis is frequently combined with phlebotectasia and lymphangiectasia, with a decrease of uterine perfusion and lymph drainage. Angiosis in older, multiparous mares might therefore be intimately related to infertility, possibly due to detrimental effects on early embryo nourishment and subsequent placentation^{1,2,4}.

Epidermal growth factor (maternal endometrial glands) and insulin-like growth factor II (fetal tissues) appear to play fundamental roles in the hyperplasia and architectural re-modelling of the diffuse, epitheliochorial placenta⁵. By day 40 of pregnancy the **microcotyledonary tufts** are starting to develop under the influence of mitogenic factors secreted by the endometrium, and although the microcotyledons continue to grow during the second half of gestation, most of the mitotic activity is confined to their periphery⁵⁻⁷. In fact, there is evidence that the tips of the microcotyledonary villi continue to branch in the last few days prior to delivery⁷. Degenerative changes (endometrosis) in the maternal endometrium can adversely affect the ability of the microcotyledonary placenta to facilitate optimal hemotrophic nutrition and exchange of waste products^{1,2,8}. If the pregnancy is maintained, dysfunction in the diffuse, non-invasive

epitheliochorial placenta can lead to the birth of small, weak foals (intra-uterine growth retardation)^{8,9}. Although the histotrophic form of nutrition is likely to remain important throughout gestation, adequate hemotrophic nutrition is essential to support the rapid fetal growth that occurs during the latter part of gestation^{5,7,8,10,11}. A so-called 'body pregnancy' occurs when the conceptus fails to expand into one of the uterine horns. These are rare, and usually result in abortion in the last trimester when the nutrient demands of the fetus are no longer being met by the inadequate placental surface area¹².

Mean placental parameters and foal birth weights are lower in primigravid mares, and there is a significant increase in the 'microscopic area of the microcotyledons per unit volume of chorion' (Sv) between the 1st and 2nd parity. The degree of branching, and length of the microcotyledonary villi, increase in the 2nd parity^{13,14}. Although the Sv of the microcotyledons is lowest in aged mares - most likely due to degenerative changes in the endometrium - foal birth weight is maintained by a compensatory increase in chorionic volume. Irrespective of the age and parity of the mare, the total area of feto-maternal contact ultimately governs **foal birth weight**. The kilograms of foal produced per square meter of functional microscopic contact appears to be constant^{13,14}. Some interesting embryo transfer experiments have demonstrated the impact that uterine capacity – and placental area – can have on the size and birth weight of the foal^{11,15-19}. In a Thoroughbred-in-Pony (Tb-in-P) versus Pony-in-Thoroughbred (P-Tb) comparison the TB fetuses matured in a cramped and nutritionally deprived environment whereas the pony fetuses developed in a uterus that surpassed their genetic requirements^{13,19}. Comparison of placental measurements (weight, volume, and surface area) confirmed the impact of nutrient supply on birth weight. Ponies gestated in Thoroughbreds were heavier than Thoroughbreds gestated in ponies^{13,15,16,19}. The growth and development of three pairs of gender matched pony foals were compared from birth to maturity. One foal from each pair had been gestated in a larger, heavier type recipient mare. During the fetal stage the body weight gain and growth were faster in the foals that had been transferred into a larger uterus. The accelerated growth continued during the suckling period, but after weaning the weight gain and growth rate were comparable with the foals that had been gestated in the genetic dams. At maturity the transferred horses were only 2-5% taller (longer cannon bones), indicating that the genetic potential compensated for any gestational influence over the long term¹⁷.

Endocrinology:

At the start of an endocrinology discussion it is perhaps appropriate to remind the reader that the words '**progestogens**', '**progestagens**' or '**progestins**' are terms used to inclusively describe the group of pregnenelone (P₅) or progesterone (P₄) metabolites that appear to be necessary to ensure maintenance of pregnancy in the mare. The unsaturated steroids are called '**pregnenes**' whereas the saturated steroids are referred to as '**pregnanes**'²⁰. Our knowledge about the endocrinology of late gestation, and the initiation of parturition, has evolved tremendously in the past decade. One of the pioneers in the field - Marian Silver - would be well pleased. In the second half of gestation the fetoplacental unit possesses a unique steroid hormone metabolic activity^{5,20,21}. Experimental inhibition of 3 β -hydroxysteroid dehydrogenase (3 β -HSD) in pregnant mares blocks placental conversion of pregnenelone into progesterone, but alternate pathways maintain progestin levels sufficiently to prevent abortion^{20,22}. In fact, there is no significant uteroplacental uptake or outputs of either pregnenelone or progesterone *from* or *to* the maternal circulation from 6 months to term^{23,24}. However, there is significant uteroplacental

uptake of P₅ from the umbilical circulation during the same period, and a significant uteroplacental *output* of P₄ to the fetus occurs from about 8.5 months to term^{23,24}. Since there is no *ductus venosus* in the equine fetus, all the umbilical venous blood is delivered to the liver sinusoids where further steroid metabolism may occur^{20,21}. The gravid endometrium has 5 α -reductase and 20 α -hydroxylase activity^{20,21}. Most of the placental-derived P₄ is further metabolized into 5 α -reduced pregnanes (5 α -pregnane-3,20-dione and 20 α -dihydroxy-5-pregnan-3-one, together with other 5 α -reduced metabolites of P₄ and P₅)^{5,20-22,24,25}. The majority of the total uteroplacental 20 α -hydroxy-5 α -pregnan-3-one (20 α 5P) is distributed into the uterine circulation²⁴. Since P₄ is undetectable (<1 ng/ml) in peripheral plasma of mares in the later half of gestation, plasma 'progesterone-specific' assays are of limited clinical value^{24,26-28}. The circulating P₄ concentration is no longer indicative of what is happening at the uterine level^{21,24}. It has been suggested that a P₄/P₅ metabolite, perhaps 5 α -pregnane-3,20-dione (5 α -DHP; dihydroprogesterone) is the important steroid that maintains myometrial quiescence^{22,28}. Significant 5 α -DHP uteroplacental *outputs* to both the maternal (70%) and umbilical circulations occur from 6 months, and total 5 α -DHP production rises progressively with increasing gestational age. The 5 α -DHP switches from preferential delivery into the maternal (uterine) circulation before 220 days, to release predominantly into the umbilical circulation after day 260²⁴. The *output to the fetus* increases towards term and reaches 70-80% of the total 5 α -DHP production by 10 months^{20,23,24}. While the current focus with respect to uterine quiescence appears to be on 5 α -pregnane-3,20-dione, inhibition of this important progestagen did not result in premature deliveries in all treated late pregnant mares²⁹.

The enlarging **fetal adrenal** at term secretes the extra pregnenelone that is required for this additional placental progestagen production^{5,20,21,24,30,31}. Even at this late stage in equine gestation there is insufficient adrenal 17 α -hydroxylase (P450_{C17}) activity to convert the pregnenelone into fetal cortisol, and thus it passes out in the umbilical vessels and is converted to 5 α -reduced pregnanes in the placenta^{9,20,24,30-32}. Fetal and maternal progestagen concentrations increase gradually in the last month of gestation, and then fall just prior to parturition²⁰. The precise mechanism that couples the **fetal hypothalamic-pituitary-adrenal axis** in the term foal is not known at this time, but it is invariably triggered when the fetus becomes fully mature^{20,31-35}. **Fetal ACTH** concentrations increase significantly over the last 2 days before parturition^{34,35}. When pony mares were subjected to intrafetal injections of ACTH at Day 300 of gestation maternal plasma progestagen concentrations increased significantly³¹. It is not until the maturing **adrenal gland** attains 17 α -hydroxylase (P450_{C17}) capacity that the high levels of pregnenelone are metabolized into fetal cortisol^{20,30-32,34}. Disruption of the final fetal maturational processes appears to play an integral part in the pathophysiology of fescue toxicosis²⁵. The horse has an unusually wide gestational window in which a normal full-term foal may be delivered, but the critical period for fetal maturation occurs within the last 2 to 3 days prior to spontaneous delivery. A recent study reported a range of 315-388 days in Thoroughbred mares that produced a viable foal, and a 320 to 360 day gestational period is not unusual^{20,36,37}. Studies with intrafetal injections of ACTH have indicated that both precocious maturation of the equine fetus and a significant reduction in gestational length is likely to be mediated via adrenal regulation of fetal maturation and production of maternal progestagens³¹. Follow up work by Ousey demonstrated that maternal ACTH administration (high doses) appears to accelerate fetal maturation and delivery in pony mares³⁸. This likely mimics the precocious adrenocortical function that may be present as early as 280 days in a chronically stressed fetus (eg. placental pathology)^{39,40}. Further

work is required to establish the optimal gestational age and dosage for maternal ACTH administration before clinical recommendations can be given for this therapy³⁸.

Fetal cortisol level remains basal until the last couple of days of gestation, when a marked rise culminates in parturition^{9,32,34}. Enhanced adrenocortical activity in the fetus is related to the onset of parturition in many species, but the short period for final fetal maturation makes the foal less likely to survive if it is delivered prematurely^{30-32,34,35,37,41}. The elevated glucocorticoid is associated with increased tri-iodothyronine (T3) concentrations, and facilitates the vital lung maturational changes, glucogenic processes, and the characteristic rise in the fetal N/L ratio⁴². Recent Thoroughbred-Pony embryo transfer experiments have shown that Thoroughbred fetus may have larger gonads than the Pony fetus, and thereby secrete more C-19 precursor steroids (dehydroandrosterone and dehydroepiandrosterone) for aromatization to estrogens by the placenta¹⁶. In the final weeks of pregnancy mean plasma progestagen concentrations rose much earlier, and to significantly higher levels, in the Tb-in-P than in the P-in-Tb pregnancies. An interesting thought is that this may reflect increasing fetal stress in the Tb-in-P fetuses, and thus a compensatory premature maturation of the fetal adrenal gland. The end result was an increased secretion of pregnenolone by the adrenal cortex for conversion to progestagens by the placenta¹⁶.

Detailed investigations into all aspects of **myometrial activity** in the pregnant mare are desperately needed. Many of our current assumptions are extrapolated from what is known about other species^{20,26,43}. LeBlanc et al demonstrated that myoelectrical activity increases at night in late gestation mares, and that this is reversible and progressive as the day of parturition approaches. The frequency and duration of myoelectrical bursts are similar during the night and day until the last week of gestation. Frequency increases steadily over the last 6 days of gestation, with a reversible switch between daytime contractures and nighttime contractions as parturition approaches^{44,45}. The classic theory on uterine motility in most species is that progesterone prevents development of oxytocin receptors, whereas a relative increase in the estrogen:progesterone ratio promotes an increase in the number of oxytocin receptors^{46,47}. However the mare appears to be unique in that parturition can be induced with exogenous oxytocin in the presence of high progestagen levels. In the mare, it is believed that metabolites of pregnenolone and progesterone (progestagens) are responsible for myometrial quiescence^{20,23}. The concentration of progestagens (eg. 5 α -DHP) increase in maternal plasma during the last 3 to 4 weeks of gestation, and then plummets in the last 48 hours prior to the onset of parturition^{20,44}. Since 5 α -DHP binds more readily to uterine P4 receptors than progesterone itself, or any of the other progestagens, it is thought to play a major role in maintaining myometrial quiescence^{20,23,47}.

Administration of P₄-in-oil or the altrenogest progestagen will prevent **prostaglandin-induced abortion** in the 3 to 5 months of pregnancy⁴⁸. However, other progestagenic compounds are less effective in preventing abortion⁴⁹. Prostaglandin dehydrogenase (PGDH) is the critical enzyme that determines metabolism of primary prostaglandins. PGDH is present in maternal epithelial and interstitial cells in the microcotyledons, and has been detected in the trophoblast cells after Day 300. Its expression is determined in part by steroid hormones, particularly the 3 β -hydroxysteroid dehydrogenase (3 β -HSD) derived progesterone at the uterine level^{20,50}. Since cholesterol side chain cleavage enzyme (P450_{scc}) and 3 β -HSD are present in the trophoblast

cells it may be that PGDH is regulated in a paracrine fashion by local diffusion and action of the P450_{SCC} and 3 β -HSD metabolites^{32,50}. Altrenogest may positively impact on 5 α -DHP production, and if this progestagen promotes myometrial quiescence then the product's apparent efficacy in high risk pregnancies would be substantiated²⁸. While it is assumed that progesterone and progestagens are necessary for myometrial quiescence in the mare, recent *in vitro* studies suggest that other factors may also be involved^{46,51}. Progestagens were ineffective at controlling myometrial contractility *in vitro*, and did not inhibit the effects of oxytocin⁴⁶. An oncofetal protein has been shown to reduce oxytocin-induced myometrial contractions *in vitro*, and it has been suggested that this protein may play a role in controlling myometrial quiescence in mares as well⁴⁶. Placental production of **relaxin** may also play a role in myometrial quiescence. It may take a significant rise in uterotonin concentrations (PGF_{2 α} and oxytocin) before its inhibitory effect can be overcome⁵².

Perhaps the number of oxytocin receptors and myometrial gap junctions do not increase until just prior to parturition in the mare⁴⁶. Gap junctions provide low resistance pathways that increase the electrical conductivity in the myometrium, thereby permitting the development of spontaneous, well co-ordinated labor contractions. The myometrial gap junction protein, Connexin-43, is modulated by steroids and prostaglandin⁵². Research in several species has shown that there is a complex interaction between **oxytocin and PGF_{2 α}** . Prostaglandin is integrally involved in a feedback loop with oxytocin, even though the molecules have different receptors on the myometrium, and different second messengers within the cells⁵³. The oxytocin-neurophysin I (OT-NP I) gene is transcribed into mRNA in the endometrium of mares, and mRNA levels are negatively correlated with serum progesterone concentrations⁵³. In a recent study the oxytocin mediated response of the myometrium in cycling mares was negatively correlated with increasing plasma progesterone concentrations, but there was no correlation between the uterine response and plasma estradiol-17 β concentration⁵⁴. There is a positive correlation between PGF_{2 α} release, endometrial oxytocin receptor density, and plasma oxytocin concentrations in nonpregnant mares^{55,56}. The fact that oxytocin injections can induce myometrial contractions before term is consistent with the findings of Ousey et al in that 5 α -DHP doesn't prevent oxytocin-induced myometrial contractions in myometrial strips *in vitro*⁴⁶. Progestagen inhibition and oxytocin stimulation may be a dose dependent mechanism *in vivo*. The amount of oxytocin required to induce delivery, and the time until fetal expulsion decreases as gestation progresses. High and repeated doses are required to induce expulsion when the fetus is immature, whereas a single small dose is effective when the fetus is mature and the time for spontaneous delivery is close^{37,46}. Exogenous oxytocin causes a rapid release PGF_{2 α} which then enhances the action of oxytocin on the myometrium by stimulating oxytocin receptors and gap junction formation^{31,37}.

As parturition approaches the myometrium appears to become more responsive to oxytocin and prostaglandin, and eventually the high concentrations of oxytocin and prostaglandins may overcome the inhibitory effects of **relaxin**^{33,46,52,57}. When periodic pituitary blood samples were collected from the intercavernous sinus of mares from at least 6 h before rupture of the chorioallantois, a significant increase in PGF_{2 α} concentration was detected before a significant increase in **oxytocin** concentration⁵⁸. There was a significant correlation between PGF_{2 α} and oxytocin concentrations after a 6 min lag period, indicating that in the 2 h before delivery of the foal, an increase in prostaglandin was followed 6 min later by an increase in oxytocin. Thus,

although oxytocin secretion from the maternal posterior pituitary gland appears to begin before, or in association with, the onset of the second stage of labor, PGF_{2α} levels increase in the peripheral circulation before a rise in oxytocin occurs⁵⁸. This complex hormonal interaction is not yet completely understood. In an oxytocin induced parturition study flunixin meglumine (a potent cyclooxygenase inhibitor) significantly lowers PGF_{2α} - metabolite levels but didn't affect the time to rupture of the chorioallantois or to delivery of the foal⁵⁹. Oxytocin levels reach peak concentrations during the expulsive (stage II) phase of parturition^{58,59}. Maternal straining (contraction of the abdominal muscles) is almost always associated with large sustained uterine contractions.

Serum **estrogens** in the pregnant mare include estradiol, estrone, and the equine-specific steroid ring-B unsaturated estrogens – equilin and equilenin⁶⁰. The C-19 estrogen precursors, dehydroandrosterone (DHA) and dehydroepiandrosterone (DHEA), are produced in large quantities by the enlarged fetal gonads during mid-gestation, and are aromatized into estrogens by the placenta. Levels of conjugated estrogens peak at 300-400 ng/ml by approximately day 240 of gestation, and then decline towards term^{9,16}. It is noteworthy that the maternal total estrogen concentration at delivery is still higher than that in non-pregnant mares, and the rapidly falling progestagen levels cause a relative increase in the estrogen:progestagen ratio^{9,34,61}. The fact that labor is weak and ineffective in mares carrying gonadectomized fetuses suggests that the baseline estrogen levels are detrimental to the normal parturient process^{9,37,51}. There are nocturnal elevations in the concentration of estradiol 17β in late gestation - especially during the last 6 days prior to parturition. Estradiol 17β has a high affinity for the uterine estrogen receptors in late gestation^{47,62}. This increasing estrogen is likely to be associated with the increasing nocturnal myoelectrical activity at this time⁴⁵. The adrenergic and peptidergic **innervation of the equine uterus and cervix** has recently been studied⁶³. Neuronal factors are thought to play an important role in the regulation of uterine motility, endometrial secretion, and uterine blood flow. The high density of innervation in the cervix indicates a role in regulating cervical closure and relaxation. Some neuropeptides have a contractile effect while others promote relaxation⁶³. The contracting myometrium forces the chorioallantoic sac against the softening cervix and Stage I of parturition ensues.

Conditions associated with 'High-Risk' Pregnancy:

In North America the incidence of **twin abortions** has dropped significantly due to early intervention after ultrasonographic diagnosis of a multiple pregnancy^{64,65}. However, diagnostic errors still occur. This author consults on 2-3 pending abortion cases each year that are confirmed to be due to a twin diagnostic error. Twin abortions in the last few months of gestation often cause a dystocia. Bicornuate twins are more likely to survive because each membrane can attach to an entire horn and one side of the uterine body, but the resulting foals are likely to be stunted due to intra-uterine growth retardation (IUGR)⁶⁶. **Umbilical cord torsion** is an uncommon cause of abortion, but must also be considered when presented with a mare that has premature mammary development. A recent report reviewed 168 cases from the University of Kentucky Livestock Disease Diagnostic Center over a 5-year period⁶⁷. These twisted cord abortions represented 6.0% of the equine fetus submissions during that 5-year period. The gestational age of the fetuses ranged from 5-10 months, with a mean of 7.5 months. It is interesting that the peak incidence of abortions due to umbilical torsions occurs at the time that the hindlimbs can become permanently enclosed in the uterine horn⁶⁶. Perhaps in some instances

this prevents the unraveling of those critical few rotations that can lead to circulatory compromise? There is no doubt that a longer umbilical cord predisposes the fetus to this condition. The mean umbilical cord length for full-term Thoroughbred foals is reported to be 55 cm, but in the Kentucky torsion study the cords varied from 62 to 125 cm⁶⁷. The average length of the affected cords (96cm) exceeded that described in another abortion study by almost 10.0 cm⁶⁸. The cords tended to be highly twisted with areas of constriction, edema, hemorrhage and/or thrombosis, and fluid-filled sacculations. The fetuses were slightly-to-moderately autolyzed. This is consistent with fetal death prior to abortion. Urinary bladder dilation was noted in some cases, presumable due to obstruction of urachal outflow⁶⁷. A long cord/cervical pole ischemia disorder was diagnosed in 3.1% of 1252 fetuses studied in a recent English report⁶⁹. The fetuses were fresh and expulsion was attributed to abrupt placental separation subsequent to perforation of the necrotic cervical pole. An opportunistic secondary ascending placentitis was noted in some of these cases⁶⁹.

Placentitis, vasculitis, or any condition that limits the fetus's glucose or oxygen supply (eg. surgical colic), or delays clearance of metabolic wastes can cause abortion^{33,51}. It would appear that aberrations in the cardiovascular and metabolic status of the mare and fetus are more detrimental to pregnancy maintenance than the actual **medical or/or surgical condition** that causes colic in a pregnant mare^{70,71}. Anesthesia that is maintained on halothane alone can cause marked cardiovascular depression in horses. This may compromise umbilical circulation, and cause lower PO₂ umbilical venous blood gas values compared with a 'triple drip' protocol⁷¹. Maternal hypoxemia increases the risk of abortion because it causes an immediate decrease in umbilical venous oxygen tension⁷¹. Horses positioned in dorsal recumbency are more likely to have a low Pao₂, and the weight of a gravid uterus invariably results in aortocaval compression. Any reduction in uterine blood flow negatively impacts on placental perfusion, and leads to fetal stress⁷¹⁻⁷³. Stage of gestation and duration of anesthesia are less critical factors provided that maternal oxygenation is adequate⁷⁴. Dorsal recumbency (with a 'gaping' vulva) may predispose late pregnant mares to ascending placentitis. While **placentitis** accounts for approximately one third of fetal/neonatal losses in the mare, it tends to be a sporadic, individual mare problem that seldom has any lasting effect on mare fertility⁷⁵. The incidence of placentitis abortions in England is reported to be only 10%, apparently because in that country much more significance is attributed to umbilical cord pathology (39%)⁶⁹. Both bacterial (beta-hemolytic streptococci, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*) and fungal (*Aspergillus* spp.) organisms may be incriminated^{76,77}. Ascending infections predominate, resulting in a suppurative, necrotizing inflammation and detachment of the placenta in the region surrounding the cervical star^{77,78}. However, obvious vaginal discharge is not a consistent feature of the condition. Bacteria appear to move up the umbilical cord into the amniotic cavity, and then are swallowed/aspirated by the fetus. The lung is the organ of predilection⁷⁹. The result may be premature delivery of a dead, sick or precociously mature, viable foal^{33,78}.

Leptospira spp. [*L.interrogans* serovar *pomona* (type *kennewicki*) and serovar *grippotyphosa*] induce a diffuse placentitis with large numbers of spirochetes in the placental tissues^{80,81}. Leptospirosis has been incriminated as a sporadic - but significant - cause of placentitis, abortion, and premature births in central Kentucky⁸²⁻⁸⁴. Abortions generally occur from 6 months to term, with no premonitory clinical signs. The placenta is edematous, with a necrotic chorion covered with a mucoid exudate^{80,82}. The spirochetes tend to be numerous and are readily demonstrated in

the stroma and villi of the placenta. Therapy is aimed at preventing urinary shedding, and possibly prophylactic treatment of pregnant in-contact mares that have high titers⁸⁰. High doses of potassium penicillin G (20 million units IV, q 12 hr) may be effective in preventing infection of a fetus if the mare has a high titer. Oxytetracycline has also been used^{84,85}. A unique **nocardioform placentitis** has been reported as a sporadic cause of abortion and weak foals in central Kentucky over the past decade⁸⁶. The initial lesion is localized in the cranio-ventral aspect of the uterine body, extending cranially onto the base of the horns, and circumferentially around the placenta. Outcomes vary from abortion to birth of a normal foal. Some foals are premature, while others are delivered at term but are either stillborn, or weak and compromised with a malnourished appearance^{77,80}. This latter finding is indicative of the chronic nature of this condition. Most affected mares appear normal, although many will display signs of placentitis (premature mammary development and lactation)^{75,77,80,87}. Vaginal discharge is not a feature of this condition since the area around the cervical star is not involved⁸⁶. The causative organism was recently identified as *Crossiella equi*^{88,89}. In vitro testing has demonstrated that the nocardioform bacteria is susceptible to sulfonamides and trimethoprim⁸⁰. This combination is an ideal choice for systemic medication of a pregnant mare when placentitis is suspected since these antimicrobial agents are known to gain acceptable levels in the fetal fluids. A recent report from England suggests that PCR and immunohistochemistry of the fetal membranes should become a routine part of abortion investigations⁹⁰. In a highly virulent **EHV-1** abortion, fetal infection may not be necessary. Virus-related thromboses and endometrial infarction may cause complete detachment of the chorioallantois from the necrotic endometrial epithelium, and expulsion of the fresh fetus still enclosed within the intact fetal membranes⁹⁰.

A detailed review of the following conditions has recently been published⁹¹. The composition of amniotic fluid changes very little during gestation, with most changes occurring in the allantoic fluid⁹². The amniotic fluid originates from the amniotic epithelium, salivary glands and secretions of the nasopharynx. In late gestation the fetal skin releases the vernix, and this likely contributes to the cloudiness of the amniotic fluid⁹³. By mid- to late gestation the biochemical profile of allantoic fluid is similar to that of urine. Fetal urine passes exclusively into the allantoic sac via the urachus until the patency of the urethra is established. Some fetal urine can then enter the amniotic cavity as well, and creatinine concentration in that compartment increases⁹². The allantoic cavity is not only a reservoir for fetal urine, but also is lined by the chorioallantoic membrane. This membrane lies in close apposition to the mare's endometrium⁹⁴. Dysfunctional placentation may cause an increased production of transudate, or disruption of transplacental fluid absorption. There does not appear to be any consistent abnormality of the fetus or fetal membranes that is characteristic of the **hydrops condition in the mare**⁹⁵. Bain and Wolfsdorf have incriminated a mild diffuse placentitis or endometrial vasculitis in some cases⁹⁶. They have used a partial drainage technique in an attempt to manage some cases that were diagnosed within 2 to 4 weeks of term. The mares receive abdominal support (belly band), intravenous fluids, broad spectrum antibiotics, and anti-inflammatory medication. The technique of slow, repeated drainage involves a major time commitment and would not be cost effective for many cases. Fetal death may occur due to placental separation. There also appears to be a considerable risk for iatrogenic fetal infection following contamination of the fetal fluids, despite attempts to perform the drainage technique in an aseptic manner. Thus, despite heroic attempts in valuable mares, the fetus is likely to be lost in cases of hydrallantois⁹⁶.

In most cases induction of parturition may be advisable before the mare's condition deteriorates further. Continued abdominal enlargement will predispose the mare to prepubic tendon rupture. Induction is not without risk (shock, dystocia), but the prognosis for survival of the mare is good provided that appropriate supportive therapy is instituted⁹⁵. The prognosis for the mare's reproductive future may also be favorable provided that there are no untoward sequelae (cervical lacerations, retained fetal membranes, metritis). Although oxytocin is widely considered to be the most efficacious method for routine induction of parturition, in hydrops cases the distended uterine musculature may not be able to contract effectively⁹⁷. This uterine inertia is common and gentle manual dilation of the cervix – or perhaps prior application of prostaglandin E – may be warranted^{95,98}. Bain and Wolfsdorf have reported a smooth induction following two doses of cloprostenol (500 µg) administered 30 minutes apart⁹⁶.

Apart from pronounced ventral edema, the classic presentation for a mare with a **ruptured prepubic tendon** is reluctance to walk, lordosis, and hemorrhagic mammary secretions⁹⁹. Palpation of the defect is often not possible due to pain and edema. The discontinuity in the body wall can be verified by transcutaneous ultrasonography. A padded canvas sling will provide support if the mare is to be nursed until the fetus is mature. If induction of parturition is elected to prevent further tearing then assisted vaginal delivery is usually necessary since the mare will have difficulty mounting a normal abdominal press. Herniation of bowel into the rent in the body wall can cause colic⁹⁹.

The cause - or causes - of **uterine torsion** in the mare are not well defined. The condition is much more common in cattle, and in that species a large term fetus has been implicated as a major risk factor. The majority of uterine torsions in cows occur at term and most are thought to be a direct result of fetal positional changes during late first stage and early second stage labor¹⁰⁰. In the author's clinical experience the vast majority of equine cases occur prior to term, and may be seen as early as 8 months of gestation. In fact, one report documented a case as early as 126 days of gestation. In that instance the mare experienced colic due to incarceration of the distal jejunum in a 360° uterine torsion. The condition was resolved at surgery and the mare subsequently delivered a healthy term foal at 354 days of gestation¹⁰¹. Although Ginther and co-workers have shown that the fetus is locked into a dorsopubic position during the final months of gestation, it is still possible for the entire pregnancy (uterus and fetus) to rotate approximately 90° on the lower maternal abdominal wall⁶⁶. This occurs because any rotational movement of the caudal half of the fetus (pelvis and hindlimbs) by necessity will involve the close-fitting uterus. It seems likely that in extreme cases this rotating action can lead to a clinical uterine torsion. In a recent study, 80% of term fetuses were in dorsosacral position when the uterine torsion was corrected. This suggests that fetal righting reflexes may have played a role in creating the torsion^{102,103}.

The clinical signs that will attract the owner's attention are the result of abdominal pain^{91,104}. Occasionally the condition may remain undiagnosed for several weeks¹⁰⁵. In these instances an owner may have attempted treatment with analgesics that they have used for previous mild colic episodes^{91,104}. Sometimes the veterinarian may incorrectly diagnose the condition as being a mild gastro-intestinal colic, and initially treat the mare medically with analgesics and mineral oil¹⁰³. Palpation per rectum is essential to determine whether a uterine torsion is present^{91,104}. Although vaginal involvement in the torsion is very common in the cow, uterine torsions in the

mare seldom cause detectable changes in the vagina^{91,100,103,105}. Severe torsions, or mis-diagnosed cases that are more chronic, may develop significant uterine compromise that results in changes in the composition of the peritoneal fluid. Any alterations in the composition of the peritoneal fluid may indicate the presence of a compromised, or ruptured, uterine wall¹⁰⁶. A flank laparoscopic examination can confirm the condition of the uterine wall¹⁰⁷. This information will facilitate an informed choice of surgical approach, or perhaps support a decision for euthanasia if economic considerations preclude surgical intervention.

Anecdotal reports suggest that rolling the anesthetized mare provides a simple and economical method of correction. Unfortunately there is limited documentation of the outcome of this approach in the literature. A retrospective study of a meaningful number of cases would provide valuable information on the safety of this technique for both the mare (uterine rupture, hemorrhage) and the fetus (abortion). In the standing flank approach a grid incision is made on the same side as the direction of the torsion. More difficulty may be experienced in mares that are close to term. In these cases an incision in the opposite flank will permit a second surgeon to assist by gently pulling across the top of the uterus as it is elevated from below¹⁰³. The prognosis for cases of equine uterine torsion depends on the degree of vascular compromise. Severity and duration of the condition will affect placental circulation and subsequent fetal viability. In chronic cases where there is significant uterine compromise it is feasible to perform an ovariectomy to salvage the mare for non-breeding purposes^{104,105,108,109}. It has been this author's experience that if the fetus is alive, and the uterine wall is not severely congested and edematous, then the prognosis for both the mare's survival and for the birth of a live foal at term is good^{91,101}. There is controversy surrounding the prolonged use of progestins in late gestation¹¹⁰. However, progestin supplementation for 3 to 5 days after the manipulations involved in correcting a uterine torsion may be indicated to ensure myometrial quiescence, and thus maintenance of the placental attachment²⁶. Although supplementation after a uterine torsion would be in the last 2-3 months of gestation, there are reports of mares retaining a nonviable (died at 3 to 5 mths gestation) fetus while being administered progestins¹¹¹. Thus, if progestin supplementation is administered to a mare after correction of a uterine torsion, it is prudent to monitor fetal viability at regular intervals.

Monitoring Fetal Well-being:

Mammary development normally starts about 3 weeks from parturition coincident with the late gestation rise in progestagen concentration^{20{Rossdale, 1997 #85,38}}. Mares that develop premature mammary enlargement (with or without lactation) should be suspected of having placentitis or a compromised fetoplacental unit⁷⁷. Not all cases of placentitis will have obvious vulvar discharge. Recent studies suggest that measurement of relaxin levels may serve as a useful means of monitoring placental function and treatment efficacy in the mare¹¹². Since **relaxin** is produced by the equine placenta, a reduction in plasma relaxin levels may be indicative of placental compromise^{57,112-114}. Low relaxin levels in late pregnancy have been associated with various causes of placental dysfunction, including fescue toxicosis, oligohydramnios, and placentitis^{113,115}. **Estrogen** levels in maternal plasma reflect the activity of the fetal gonads (DHEA), and may provide a useful assessment of fetoplacental well-being between 150 to 300 days of gestation¹¹⁶. The hypertrophied gonads regress in size towards term. It is recommended that serial samples be obtained from a suspect mare. This may help to identify a clinically useful trend in hormone concentrations^{42,51,117}. If there is disruption of the fetoplacental unit (in this

case the enlarged fetal gonads and placenta) then estrogen production may be affected. A sudden fall in estrogen levels mimics the classic work of Pashen and Allen in which the estrogen level in the peripheral plasma of mares plummeted to baseline when the fetuses were gonadectomized approximately 3 months prior to term. If noted during serial monitoring, a sudden decline may signal imminent demise of the fetus^{42,48}. It is important to be sure of what the laboratory is actually reporting. Fetal estrogens are present in both conjugated (Bound; ng/ml) and unconjugated forms (Free; pg/ml). Estrone and equilin (E₁) may be in a conjugated (to sulfates) or unconjugated form whereas estradiol (E₂) is unconjugated⁶¹. High concentrations of estrone and equilin are found in the maternal plasma during the second half of pregnancy, peaking at approximately day 240, then decreasing towards term as the hypertrophied fetal gonads regress in size. The estrogen lab data may be useful in providing a prognosis for the owner¹¹⁶.

Optimal biosynthesis of the **progestagens** involves close interaction between a viable fetus and a healthy fetal membrane-endometrial (placental) unit²⁰. The RIA levels are maintained at 5 to 10 ng/ml until the last 3-4 weeks of gestation, when they start to increase to a peak of 20 to 25 ng/ml²⁰. A sudden decline occurs a few days prior to delivery. When monitoring “progesterone” levels in late pregnancy it should be remembered that what is being measured is the level of progestagens in the peripheral plasma. Little, if any, progesterone is found in the maternal circulation during late gestation²⁴. The RIAs and ELISAs used to detect progesterone in endocrine labs also cross-react with the mare’s fetoplacental derived progestagens. While ‘total progestagen’ levels may be measured by an immunoassay, specific progestagens are measured quantitatively by gas chromatography-mass spectrometry technology that can accurately differentiate minor differences in steroid structure^{21,22,28}. Clinicians should be aware that while total progestagen levels may be increased significantly by the administration of P₄-in-oil, they will remain unchanged in mares receiving altrenogest per os. The detectable increase in the former likely reflects the presence of exogenous P₄ in maternal plasma²⁸. Measuring progestagen levels every couple of days during a ‘high risk’ period may provide helpful prognostic information, but a single assay is of little use. By comparing relative changes over time the clinician can more accurately plan therapeutic intervention¹¹⁶. If the progestagen level remains below 2ng/ml for several days then the prognosis is poor and abortion is likely to occur⁴². In mares that have developed some placental or fetal pathology in late gestation there may be a premature rise in progestagen concentrations associated with a fetal stress response that causes precocious adrenal gland maturation. In some cases this may lead to birth of a surprisingly mature foal at 290 to 310 days of gestation^{31,33,42,51,118}. Since an increase in the last month is characteristic of normal maturation, the dilemma is in not knowing exactly what was to be the last biologically programmed month for this particular fetus: day 300-330? ; day 315-345? ; or perhaps even later. A sudden fall in progestagen levels may be associated with an acute fetal crisis, and often heralds that abortion is imminent^{20,51,116}.

Fetal **palpation per rectum** is a notoriously insensitive method for assessing fetal well-being since a normal fetus may have periods when it is unresponsive to ballottement⁴². Likewise, it is impossible to predict the likelihood of dystocia based on fetal posture prior to the onset of parturition. Vigorous hindlimb thrusts, in association with elevation of the fetal rump, can result in the hooves being pushed well past the cervix into the recto-genital pouch {Ginther, 1998 #431}. Thus, the fetal hooves being palpated *per rectum* may sometimes be attached to the hindlimbs. While the primary use of **ultrasound** in broodmare practice is undoubtedly early

confirmation of pregnancy, transabdominal and transrectal ultrasound can provide valuable information in late gestation as well ^{117,119-125}. Either a 3.5- or 2.5-MHz curved linear-array or sector-scanner transducer is best for transabdominal examinations since these can penetrate to a depth of 20 or 30 cm respectively ^{123,126}. Fetal gender determination (penis/prepuce; mammary gland/teats) can be performed accurately up to the end of the 7th month of gestation ¹²⁷. After that time the fetus is typically lying on its back making imaging of the ventral aspect of the larger abdomen difficult. During an attempt at gender determination the growth and well-being of the fetus can also be assessed ¹²⁸. The late gestation gravid uterus extends along the ventral abdomen to the xiphoid ^{119,120,123,129}. By the ninth month of gestation the fetus should be in anterior (cranial) presentation, and dorso-pubic or dorsolateral position ^{66,122}. Thus, in late gestation the fetal head should be positioned near the mare's pelvis. An abnormal presentation, or the presence of twins, is possible if a fetal head is detected along the ventral abdomen during late gestation ¹²³. Identification of the non-gravid horn can be useful to help rule-out the possibility of twins. The posture of the extremities will vary with fetal movement ^{66,122}.

Transabdominal examination of the ventral uterus may reveal separation of the chorioallantoic membrane from the uterine wall, and often with evidence of inflammatory exudate accumulation between the two surfaces. Placentitis and associated placental edema will result in a thickened uteroplacental image ⁸⁶. The average **uteroplacental thickness** on a normal transabdominal ultrasound image should be between 9 to 14 mm ¹¹⁹. While transabdominal placental assessment has proven useful in cases of Nocardioform placentitis, and in studying fescue toxicosis, the main advantage of transabdominal ultrasonography is the ability to evaluate the fetus itself ⁸⁶. In a normal pregnancy the majority of the fetal fluids are within the allantoic cavity ^{92,94}. The **amniotic membrane** divides the imaged fetal fluid into two distinct cavities and is most easily seen around the fetal neck, shoulder, thorax, and foreleg. Typically the largest pocket of amniotic fluid is imaged where the forelimb and neck meet the thorax ¹²³. The maximum vertical depth of amniotic and allantoic fluid, and the quality of amniotic and allantoic fluid are useful guides to fetal well-being ¹²³. Any measurements of fluid depth should be made as perpendicular to the uteroplacental surface as possible ^{120,123}. In the normal equine pregnancy the mean maximum ventral fetal fluid pocket depth for amniotic fluid is 8 cm, and 13.4 cm for allantoic fluid ^{119,123}. Extremes in either direction are not normal. Obviously deficient amounts of fetal fluid are indicative of placental dysfunction, and excessive amounts are suggestive of a hydrops condition ¹¹⁹. Reef suggests that fetal fluid quantities should be considered excessive if the maximal vertical amniotic fluid depth exceeds 14.9 cm, or the maximum vertical allantoic fluid depth exceeds 22.1 cm ¹²³. The **quality of the fetal fluid** is scored from 0 (anechoic) to 3 (echogenic fluid with numerous particles) ^{120,123}. It is not unusual for echogenic particles to be noted in the fetal fluids, especially during periods of fetal activity. These represent sloughed cells and proteinaceous debris. An increase in the number of echogenic particles in late gestation may not be abnormal ¹²⁰. However, if a high risk pregnancy is being regularly monitored, and a sudden increase in fluid turbidity (grade 3) is observed, the prognosis is not good ¹²⁰. The clinician should consider the possibility of inflammatory exudates, meconium passage by a compromised fetus, or even hemorrhage. It should be remembered that hippomanes (allantoic calculi) are a normal feature of the equine pregnancy, and may be observed on the ventral aspect of the allantoic cavity ¹²³.

Growth charts have been established for a variety of biometric measurements. Some variables have a strong linear relationship with the day of gestation (aortic systolic diameter, biparietal diameter, approximate eye volume, and femur length)¹²⁵. An equine **biophysical profile** has been proposed as a guide to assessing fetal well-being, and predicting perinatal morbidity and mortality^{120,129}. While a low score is definitely indicative of a negative outcome, higher scores do not guarantee the birth of a viable neonate¹²³. This limits the value of this information. Fetal breathing, heart rate and rhythm, fetal tone, and general activity are useful guides when evaluating fetal health and well-being. Thus, chemical sedation of the mare should be avoided since commonly used drugs (eg. detomidine or butorphanol) will reduce fetal heart rate variability and may suppress normal fetal activity¹³⁰. Beat-to-beat variations and observation of periodic accelerations are important. It is normal for the heart rate accelerations to occur in association with fetal activity. Reef recommends that multiple measurements of **fetal heart rate** and assessments of fetal heart rhythm be made over a 30-minute period while evaluating the fetus, fetal fluids, and placenta¹²³. The fetal heart beat is normally regular, and will decrease from >120 bpm in mid-gestation to between 60-90 bpm in late gestation^{119,120}. Transient low heart rates of less than 60 bpm are not uncommon. Cardiac accelerations (20-40 bpm above baseline) are normal if they are associated with fetal movement^{119,123}. However, persistent tachycardia in the absence of fetal activity is indicative of fetal stress. A resting heart rate in excess of 104 bpm is indicative of fetal stress in a late gestation fetus^{120,123}. A heart rate of < 57 bpm in a fetus in that is less than 330 days of gestation, and a rate of < 50 bpm in a fetus older than 329 days gestation, should be considered abnormal^{120,123}. A fetus suffering from hypoxemia will have a slow heart rate, with minimal limb activity or fetal breathing, indicative of CNS depression^{120,122,123}. However, if the condition is chronic, and ischemic conditions are developing, the fetus will become tachycardic despite a lack of fetal activity. This is a prelude to fetal demise. In terminal cases, extreme bradycardia ensues just prior to fetal death^{120,131}. If the Doppler ultrasound equipment is available, the Doppler transducer is placed directly over the site where the best image was detected by the ultrasound scan. Tracings of fetal heart rate and rhythm can be recorded. The fetus is noted to have **tone** if it is observed to flex and extend the limbs, torso, or neck. Tone is poor or absent if the fetus appears flaccid^{120,123}. Fetal movements include partial to full rotation around the long axis of the fetus, as well as less marked activity such as extension and flexion of the extremities^{120,123}. Fetal activity is rated on a scale from 0 to 3, with 3 being a very active fetus. A score of 0 indicates that no fetal movement was noted during the examination period^{120,123}. Long periods without noticeable fetal activity are cause for concern, and should be evaluated in conjunction with information about the fetal heart rate and rhythm. The fetus may be distressed, suffering from advanced hypoxia and CNS depression¹²⁰.

Measurements such as **fetal aortic diameter** are a reflection of fetal size^{120,122,125}. They can be used to estimate the age a fetus, or to evaluate fetal growth when breeding dates are known. If fetal size is not consistent with the stage of gestation then intrauterine growth retardation (IUGR) should be suspected. Decreased blood flow to the placental unit will inhibit growth of the fetus, and some form of chronic placental insufficiency should be suspected¹²³. Fetal aortic diameter is correlated with the weight of the pregnant mare, as well as the final neonatal foal weight^{119,120,125}. Thus, the pregnant mare's weight can be used to estimate what the fetal aortic diameter should be, using the regression equation ($Y = 0.00912 \times \text{Pregnant mare's weight in pounds} + 12.46$) where "Y" is the predicted fetal aortic diameter (mm)^{120,123}. The actual diameter of the fetal aorta should then be measured in the thoracic cavity, as close to the fetal heart as possible

^{119,120,125}. A smaller than predicted aortic diameter may be an indication of a dysmature or growth-retarded fetus – or twins. The maximal **thoracic diameter** is measured from the spine to the sternum over the caudal part of the thorax, and in a late gestation fetus it should be 18.4 ± 1.2 cm ^{120,123}. It has been correlated with fetal aortic diameter and neonatal foal weight in high risk pregnancies ^{120,123}. Foal girth measurements and hip height have also been correlated with fetal aortic diameter measurements. **Biparietal measurements** and **orbital diameters** have also been used to estimate fetal size ^{123,125}.

Transrectal ultrasonography provides an excellent assessment of the current status of the caudal allantochorion, and as such, it is an invaluable aid when examining a late pregnant mare that is presenting with signs of placentitis. Normal values for the **combined thickness of the uterus and placenta** (CTUP) have been established ⁹³. The area cranial and ventral to the cervix provides the most consistent measurement in normal mares, and this is the recommended site for any measurements ¹³². The echogenicity of the allantoic and amniotic fluids may be graded from I (strongly echogenic; hyperechoic) to IV (black; anechoic). In late gestation the more echogenic amniotic fluid is consistently graded II, whereas the allantoic fluid tends to be graded as III ⁹³. More free floating particles (FFPs) are in suspension during periods of active fetal movement. In late gestation the fetal skin releases the vernix, and this likely contributes to the cloudiness of the amniotic fluid. A sudden increase in fluid turbidity may be associated with hemorrhage, inflammatory debris, or the fetal diarrhea/meconium passage that often follows hypoxic stress ⁹³. It has been established that an increased CTUP any time from mid-gestation through until term is indicative of placental disruption and pending abortion ^{124,128,133}. CTUP values that are suggested as being indicative of placental failure and impending abortion are >8 mm (between days 271-300), >10 mm (between days 301-330), and >12mm after day 330 ^{117,134}.

It is important to monitor **fetal viability** if a high-risk pregnancy is being maintained on altrenogest supplementation. Mummification of an equine fetus is uncommon. However, while most non-viable fetuses will be aborted, there are reports of a mummified fetus being retained when the mare was maintained on long-term progestagen supplementation, and in at least one case the mummified fetus was retained even after the supplementation was discontinued ^{111,135}. This is not unlike the natural scenario when a mummified twin is retained due to the viable fetoplacental unit's production of enough progestagens to prevent abortion.

High Risk Pregnancies - THERAPEUTICS:

Separation from the endometrium is a consistent feature in many abortions. The uteroplacental tissues include the fetal membranes, the endometrium, and the myometrium. This metabolically active site facilitates exchange between the maternal and fetal blood streams, and also synthesizes nutrients, hormones and growth factors ⁷⁴. The exact cause of premature fetal expulsion is not known. Placentitis may cause an acute loss associated with bacteremia, or abortion of an IUGR (intra-uterine growth retardation) fetus may follow a more focal, chronic thickening of the fetal membranes. However, if therapeutic intervention can postpone delivery for even a few weeks, the stressed fetus may undergo precocious development that permits survival of the foal with limited neonatal care. Current therapeutic regimens for managing placentitis are based primarily on clinical experience, rather than detailed scientific investigations. Data is limited on the success rate of these treatments, and none are guaranteed to prevent premature delivery. Objectives should be to prevent or reduce the synthesis, release, or

effect of inflammatory mediators; inhibit bacterial replication; maintain a quiescent myometrium; and enhance oxygenation of the fetoplacental unit.

Placentitis is detrimental to the pregnancy not only because it disrupts nutrient exchange, but also because of the pro-inflammatory cytokines and other inflammatory mediators that are released by the diseased placenta. Both PGE₂ and PGF_{2a} concentrations in the allantoic fluid of mares with induced placentitis increase markedly by 4 days prior to fetal expulsion⁷⁸. Thus, **anti-inflammatory medication** (flunixin meglumine, 1.1 mg/kg) is indicated to suppress the prostaglandin cascade. Although Deals' endotoxemia studies have demonstrated that this is difficult to stop once it is initiated, there appears to be no detrimental effects from short term non-steroidal anti-inflammatory medication when used in a well hydrated mare¹¹⁷. The diffuse, microcotyledonary equine placenta continues to grow and increase in weight throughout gestation⁷. The uteroplacental tissues are especially sensitive to nutrient deprivation, and this is a major consideration in mares that are anorectic, or are muzzled due to some medical/surgical condition⁷⁴. These tissues receive a larger share of the uterine glucose uptake at both mid- (73%) and late gestation (61%), although fetal uptake of glucose rises with increasing gestational age, and is significantly higher near term than at mid-gestation⁷⁴. Lipids are synthesized by the equine uteroplacental tissues, and can be mobilized readily in response to nutritional cues¹³⁶. A reduction in uteroplacental glucose supply in late gestation may permit the rate of prostaglandin production to exceed the rate of prostaglandin metabolism. The rising prostaglandin levels may then initiate increasing uterine contractions which could negatively impact on placental blood flow. The end result is often initiation of premature delivery¹³⁷. Thus, 'at-risk' mares should receive intravenous dextrose saline fluid therapy to decrease the possibility of prostaglandin production by the uteroplacental tissues⁴². If the localized production of high concentrations of prostaglandins stimulates the formation of gap-junctions, then the subsequent hypermotility may impede placental blood flow as the uterus contracts^{26,42}. This will reduce fetal oxygenation and increase fetal stress. Abortion cases later in gestation tend to be associated with chronic placentitis and severe tissue reaction that results in utero-placental insufficiency^{87,138}. Foals from more chronic placentitis cases tend to suffer from malnourishment and intra-uterine growth retardation (IUGR).

Placentitis associated with early abortions tends to be acute, with the fetus succumbing to bacteremia. **Broad spectrum antibiotics** that have been recommended, somewhat empirically, include Trimethoprim-sulfadiazine (15-30 mg/kg p.o., BID), Procaine penicillin (30,000 IU/kg, SID) and Gentamicin (6 mg/kg, SID), and Ceftiofur (1-5 mg/kg, BID)^{42,117}. Trimethoprim-sulfonamide drugs have been the treatment of choice for placentitis because of their reported ability to gain access to the fetal fluids. Gentamicin was undetectable in the plasma of new born foals after the mares had been treated with the antibiotic (6.6 mg/kg) an hour prior to parturition¹³⁹. However, a new microdialysis model was able to detect significant levels of both Penicillin G potassium and gentamicin in the allantoic fluid following intravenous administration to mares in late pregnancy¹⁴⁰. The penicillin G levels were comparable to the concentration in the systemic circulation. Concentrations of gentamicin were lower than in the serum, but still appeared to be adequate for the treatment of placental infections caused by *E.coli* and *Klebsiella spp*¹⁴⁰. Obviously further work is needed to reconcile these conflicting studies. Although flunixin meglumine was undetectable in the allantoic microdialysates, its beneficial action would be principally at the level of the placental tissues. Furthermore, if flunixin meglumine did reach

the allantoic fluid it would be protein bound, and thus unable to penetrate the microdialysis membrane ¹⁴⁰.

Since it is known that progesterone inhibits gap junction formation, it is clinically valid to conclude that **progestin supplementation** may be beneficial when utero-placental inflammation is suspected. Recent *in vitro* studies have demonstrated that neither progesterone nor progestagens prevent oxytocin-stimulated contractions in myometrial strips ⁴⁶. Thus, it was proposed that progestagens may not be the primary regulator of myometrial quiescence and, hence, the onset of contractions that lead to fetal expulsion in mares ⁴⁶. However, extrapolation from these *in vitro* studies may not be appropriate since the complex hormonal milieu in the parturient mare may be impossible to replicate in laboratory studies ⁴⁶. Daels et al have demonstrated that progesterone or altrenogest can prevent abortions induced by exogenous prostaglandin between 3 and 5 months of gestation ⁴⁸. It was concluded that circulating progestagen concentrations may play a role in the outcome of pregnancy during prostaglandin-induced abortion. This is the rationale behind the current recommendation to treat suspected placentitis cases, and mares in the acute phase of a medical or surgical condition when prostaglandin levels are likely to be elevated, with a double dose of **altrenogest** (0.088 mg/kg sid) ^{42,51,117,118}. If the condition warrants muzzling (nil per os) then short-term use of **progesterone-in-oil** (up to 300 mg SID) injections are warranted. A recent study has demonstrated that neither medroxyprogesterone acetate, hydroxyprogesterone hexanoate, norgestomet, nor megestrol acetate (when dosed as per manufacturer's recommendations) will prevent prostaglandin induced pregnancy loss between 18 to 30 days after ovulation. It is therefore unlikely that any of these synthetic progestagens will be effective for pregnancy maintenance later in gestation ⁴⁹. Long term progestagen therapy, once the medical crisis has passed, does not appear to be justified ¹¹⁰. It is possible that exogenous P₄ or altrenogest may affect enzymes in the progestagen biosynthetic pathway ²⁸. High concentrations of progestagens can inhibit 3 β -hydroxysteroid dehydrogenase metabolism of pregnenolone *in vitro* ²⁰.

'Tocolysis' is derived from the Greek words 'tokos' (birth) and 'lysis' (dissolution). Agents that inhibit labor are known as 'tocolytic drugs' - or tocolytics ¹⁴¹. Adrenergic α and β receptors are found in organs with sympathetic innervation. There are two types of β receptors - β_1 occur in the heart and small intestine, while β_2 are found in the vascular smooth muscle, myometrium and bronchial tree. **Isoxuprine** may cause some undesirable side-effects (tachycardia, hypotension) due to nonspecific β -receptor stimulation. The newer β -adrenergics (eg. clenbuterol, terbutaline, ritodrine) are more β_2 selective ¹⁴¹. Veterinary tocolytics are widely used in Europe as injectable formulations for ruminants, but the literature is not readily accessible. Isoxsuprine's tocolytic effect reportedly develops within 10-15 min after i.m. injection (0.4-2.0 mg/kg). Isoxsuprine is used in human medicine as a uterine relaxant to prevent premature labor. It is widely used by North American equine practitioners to treat navicular disease based on its peripheral vasodilator activity ^{142,143}. However, recent studies have demonstrated that while it can relax digital arteries constricted by noradrenaline, it was not effective on those constricted with PGF_{2 α} . Clenbuterol, on the other hand, proved capable of relaxing PGF_{2 α} -induced tone ¹⁴⁴. Apparently isoxsuprine requires a very high density of β_2 - adrenoceptors to exert a direct relaxant effect. Isoxsuprine has been shown to increase red cell deformability and reduce platelet adherence to artery subendothelium ¹⁴². Thus, this drug warrants scientific investigation in high risk pregnancies - especially those with placentitis. Unfortunately the bioavailability of orally administered

isoxsuprine (1.2 mg/kg po. q. 12 h for 8 days) is questionable, and plasma concentrations may not be sufficient to produce pharmacological effects ¹⁴³.

Clenbuterol has been used both intravenously and i.m., with a 10-15 min onset after an i.v. injection (0.3 mg total dose). We should remain cognizant of the fact that a drug's efficacy can be highly dependent on the route of administration. Many equine clinicians have advocated the use of an oral β_2 -sympathomimetic drug (clenbuterol) to suppress uterine motility and improve blood supply to the fetoplacental unit ^{117,145}. In the United States the product is marketed as an oral formulation (0.8 μ g/kg bid) to treat chronic obstructive pulmonary disease. Research is needed to determine what oral dose of this bronchodilatory compound – if any – is actually effective on the β_2 adrenergic receptors of the gravid equine uterus. It is apparently well absorbed from the intestinal tract ¹⁴⁶. In a study involving early pregnancy, a 600 μ g i.v. dose of clenbuterol decreased both tone and contractility when given to mares on the day of embryonic vesicle fixation, yet it decreased tone but not contractility when given on day 19 ¹⁴⁷. The effect occurred within 20 to 30 min, and it took over 2 h to return to baseline values. Similarly, a 300 μ g i.v. dose of clenbuterol reduced palpable uterine tone for approximately 2 hours, but the effects were most pronounced in early pregnancy. Later in pregnancy the effects were more subtle, and in some cases no effect was palpable ¹⁴⁸. This decreased effect in later pregnancy is supported by the fact that when intravenous clenbuterol (0.6 mg; 1.0mg; 1.5 mg) was administered each evening (10:00pm) once milk calcium exceeded 13mM, there was no difference between groups (and saline controls) for length of gestation, number of treatments prior to foaling, or the time to foaling after the last dose ¹⁴⁹. Thus, the β_2 - adrenergic agonist properties of clenbuterol do not appear to be effective in preventing the onset of myometrial contractions that begin in response to the normal hormonal parturient cascade in the mare. It is possible that in clinical situations, where uterine hypermotility is of concern, that a different myometrial response may occur. The injectable formulation is reported to facilitate successful resolution of equine dystocia ¹⁵⁰. Further scientific investigation in this area is desperately needed to verify anecdotal claims of efficacy ¹⁴⁹.

The rate of **oxygen** uptake by the gravid uterus, fetus and uteroplacental tissues are 2- to 3-fold higher in late gestation compared with mid-gestation. The uteroplacental tissues account for approximately 50% of this oxygen uptake, perhaps a reflection on their high metabolic rate ⁷⁴. Thus, intranasal oxygen insufflation to a compromised mare may improve oxygen delivery to the fetoplacental unit ¹⁵¹. The rationale for other treatment regimens is based on extrapolations from the human literature, and application of sound reasoning for the potential efficacy of a particular drug. Some clinicians advocate the use of oral tocopherol (**Vit E**) because of its potential antioxidant effect in a hypoxic fetus. Mean umbilical and uterine blood flows in a healthy, late gestation mare are significantly higher than the corresponding values in mid-gestation ⁷⁴. The administration of **pentoxyfylline** has been recommended in 'at risk' mares, based on its use for treating tissue ischemia in humans, and on its ability to modulate the inflammatory process ^{117,152-154}. Pentoxyfylline's hemorrheologic properties include increased erythrocyte flexibility, reduced blood viscosity, and decreased potential for platelet aggregation and microvascular thrombosis. The net effect is to increase oxygenation of tissues in diseases that are characterized by reduced blood flow through capillary beds ¹⁵⁴. Inflammation driven uterine hypermotility may impede circulation in the placental capillary bed, and it is thought that this drug may increase fetal oxygenation by improving microvascular blood flow ^{155,156}. It may be that any beneficial

effect of pentoxifylline in these cases comes from its modulation of the inflammatory process in placental tissues. While the beneficial effects of pentoxifylline were limited when administered i.v. to horses after *in vivo* challenge exposure with endotoxin, a pentoxifylline/flunixin meglumine combination may help to offset the deleterious hemodynamic effects of endotoxin^{153,157}. Pentoxifylline (7.5 mg/kg, p.o. BID) has been recommended, but the dose, dosage interval, and dose formulation may not be appropriate since the absorption of pentoxifylline from the equine gastrointestinal tract is poor and erratic, and varies considerably between individual animals^{117,152-154,158}. It has been suggested that there may be a prior food consumption effect on pentoxifylline absorption.

Fescue Toxicity and Agalactia:

A wide range of reproductive problems (thickened placenta, abortion, prolonged gestation, dystocia, dead or weak foals, agalactia) have been attributed to the effects of the fungal endophyte (*Acremonium coenophialum* – now known as *Neothyphodium coenophialum*)^{159,160}. The endophyte produces a dopaminergic, vasoactive, ergopeptine alkaloid (ergovaline)¹⁵⁹. This alkaloid disrupts the feto-placental production of progestagens, but the precise mechanism has not been established^{25,161}. Umbilical vein progestagen levels suggest that the disruption is not at the level of placental steroidogenesis – a remarkable observation when the fetal membranes are so edematous²⁵. Premature chorioallantoic separation, and the failure of the membrane to rupture (“red bag”), are attributable to the edematous splanchnic mesoderm¹⁵⁹. Ryan and co-workers have demonstrated that an effect of fescue toxicosis in pregnant mares is a lowering of the circulating relaxin levels¹¹². Clinical observations suggest that a one-time injection with fluphenazine improved pregnancy outcome by reducing the adverse effects of fescue toxicosis concomitant with a stabilization of plasma relaxin concentrations. These data support the hypothesis that systemic relaxin may be a useful biochemical means of monitoring placental function and treatment efficacy in the mare¹¹². ACTH, tri-iodothyronine (T₃), progestagen and cortisol concentrations are lower in foals born to endophyte-exposed mares suggesting that the effects are actually at the level of the fetal hypothalamo-pituitary axis, thyroid, and adrenal cortex^{25,162}. This is likely to be the basis for the prolonged gestation and fetal dysmaturity that are associated with fescue toxicosis^{25,161}.

The ergovaline also inhibits prolactin secretion in affected mares by acting as a dopamine agonist at the maternal pituitary level. Since late pregnant mares are so susceptible to the toxic effects of ergopeptine alkaloids they should not be permitted to graze endophyte-infected Tall Fescue pasture, or hay derived from such pasture. Short-term exposure by mares at 300 days of gestation results in a significant decline in both prolactin and total progestagen concentrations within 48 hours. Fortunately, removal of pregnant mares (300 days gestation) from infected pasture results in a significant increase in prolactin and progestagen levels within 3 days. This will prevent the development of the typical symptoms associated with fescue toxicosis^{25,161}. Even when alternate feed sources are limited, every attempt should be made to remove pregnant mares from endophyte infected fescue by 30-60 days prior to the expected foaling date. When this is not possible, prophylactic administration of the dopamine receptor antagonist, **domperidone** (EquidoneTM) can prevent the development of fescue toxicosis^{160,163-169}.

Spontaneous and Induced Parturition:

Vital fetal maturational changes do not occur until the last 24-48 hours prior to birth, and thus the equine fetus is at a substantially increased risk of dysmaturity/prematurity if an induction is not carefully planned^{33,37,170}. **Gestation length** is notoriously unpredictable in mares, with Thoroughbred mares typically foaling between 330 and 345 days after ovulation^{20,36,171,172}. Although the frequently recommended minimum gestation length for successful induction is 330 days, it must be remembered that many mares will carry a foal past 340 days, and occasionally to 360 days and beyond^{20,36,37,61,172,173}. In a retrospective study of standardbred mares the mean duration of gestation was 343.3 days and was significantly greater for colt fetuses (344.4 days) than for filly fetuses (342.2 days)¹⁷⁴. In a recent Thoroughbred study the gestation length ranged from 315 to 388 days (mean 344 d) - all resulting in viable foals - and colt pregnancies were significantly longer than fillies (approx. 4 d)³⁶. This gender difference holds true for draft breed mares as well¹⁷⁵. In another Thoroughbred study, foals less than age 320 gestational days at birth had a greater risk of mortality than did those foals carried for 320 days or longer¹⁷⁶. This finding is consistent with earlier reports. Sire has been associated with duration of gestation; gestation after mating with certain sires was consistently less than 340 days in duration, whereas duration after mating with other sires was consistently more than 350 days¹⁷⁴. The time of year must be considered when evaluating gestation length. Although reports vary, mares tend to carry foals longer if they are due to foal early in the season (shorter day length), whereas gestation length may be shorter if the foal isn't due until longer summer days have arrived^{36,172,174,175,177,178}. Exposure to artificial lighting may cause some shorter gestation lengths (7-10 days) early in the season^{36,116}.

Monitoring changes in **mammary secretion electrolyte concentrations** is the most reliable guide to imminent parturition in healthy mares^{37,179,180}. The characteristic changes in milk electrolyte composition coincide with the sudden decline in progesterone concentration from its late gestation peak^{20,38}. An inversion in the sodium:potassium ratio, followed by a rapid rise in calcium concentrations in the last 24-48 hours has been correlated with fetal maturity. It has been well established that 10 mmol/L (40 mg/dL; 400 ppm) calcium in mammary secretions is a reliable indicator of fetal "readiness for birth"^{37,171,180}. Several stall-side tests are available that can measure the calcium ion (Ca^{++}) concentration in mammary secretions based on a colorimetric change of pads on a test strip. Water hardness kits are also useful for determining the concentration of calcium in mammary secretions¹⁷⁰. However, it is important to ensure that the water hardness kit is only measuring calcium levels if using it to decide when to safely induce parturition. Many kits merely test for divalent cations, which includes magnesium as well as calcium¹⁷¹. Since magnesium levels peak earlier than calcium, misleading information about fetal maturity may be obtained¹⁸⁰.

Although the fetus likely initiates parturition, the mare appears to be able to regulate the actual timing of delivery^{33,181}. The natural 'fright and flight' reaction causes catecholamine release from sympathetic nerves such that heart rate increases, blood flow to the skeletal muscles is accentuated, and the uterus relaxes. This evolutionary mechanism permits the mare to foal when perceived threats are minimal. Thus, any untoward changes in the mare's environment may cause her to "postpone" the delivery. This can create disagreement with predictions based on mammary secretion electrolyte concentrations. Calcium levels can change rapidly during a single day. Thus, testing secretions morning and evening may be useful. If a single test is to be performed, it is preferable to check the calcium levels late in the day¹⁷¹. Primiparous mares can

be especially difficult to monitor since no change in mammary secretion electrolyte composition may be detected until immediately prior to foaling^{37,170}. Placentitis and other placental pathology are often associated with precocious mammary gland development and premature changes in mammary secretion electrolyte concentrations. Thus, milk electrolyte changes may be unreliable for assessing fetal readiness for birth in abnormal pregnancies (eg. placentitis, impending twin abortion). In these cases electrolyte patterns may change in concert with hormonal changes in the mare, even though the fetus is not fully mature^{37,42}.

Monitoring milk electrolyte changes, and planned **induction of parturition**, ensures that obstetrical assistance is readily available. A compromised foal can receive immediate supportive care^{37,97,171}. Reimer has reported on a case with fetal omphalocele that was diagnosed by transabdominal ultrasonography. Parturition was induced in the hospital when the fetus was determined to be 'ready for birth', and the foal taken to surgery immediately upon delivery. The extra-abdominal intestines were successfully replaced, and the foal recovered uneventfully¹⁸². However premature placental separation, dystocias, fetal hypoxia, and dysmaturity are not uncommon sequelae of the induction procedure, and thus induction should not be practiced for convenience alone. Owners should be informed that delivery is only indicated if the probability of extrauterine survival exceeds that for continued maternal support. Experience suggests that an abnormal uterine environment will often be more successful at maintaining a fetal foal's life than a neonatal intensive care unit^{37,42}. A fetus that has been exposed to an adverse uterine environment for some time may be more tolerant of premature delivery^{33,51}. Some clinicians will administer a dose of corticosteroids to the mare if premature delivery appears to be unavoidable, in the expectation that it may stimulate surfactant production and promote accelerated maturation of the fetal lung^{33,37}. The actual benefit remains to be studied since the placental enzyme 11 β -HSD converts active cortisol to inactive cortisone in the mare, and appears to be an effective barrier to cortisol transfer between the mare and fetus^{33,38,39,183}. Massive doses of dexamethasone (100mg daily for 5 days) may induce delivery, but this causes deleterious effects in the mare (eg. laminitis)⁴².

The presence of cervical softening has traditionally been suggested as a prerequisite for optimal induction of parturition in the mare, and in a recent study mares with a relaxed cervix prior to induction had a more rapid delivery⁹⁷. This study found that foals delivered from mares with a pre-induction, relaxed cervix stood and nursed sooner, and had fewer signs of intrapartum asphyxia (hypercapnia, maladjustment) than foals delivered from mares with a non-dilated cervix. Those mares that developed parturient complications (premature placental separation, dystocia) all had a closed cervix prior to induction^{97,170}. A recent innovation has been the administration of intracervical **PGE₂** (2.5 mg) prior to induction, but there was no apparent difference in the mean interval from initial oxytocin treatment to rupture of the chorioallantois, or to the delivery of the foal⁹⁸. However, the impact on foal viability was positive in that foals delivered from PG E₂ treated mares suckled sooner. Any induced mare should be closely monitored for complications. An unruptured chorioallantois can be opened, and abnormal fetal position or posture corrected before the foal becomes impacted in the vaginal canal.

Several experimental protocols have been reported for induction of parturition in the term mare, including glucocorticoids, prostaglandins, and oxytocin^{37,97,98,184}. **Oxytocin** is the preferred drug for induction of parturition in the mare. A wide range of protocols have been suggested over the

years, including a bolus dose (up to 100 units), low doses (2.5-20 units) repeated every 15 minutes to effect, and as a slow intravenous drip of 60-120 units total (1.0 unit/minute)³⁷. Recent work suggests that the choice of oxytocin regimen is less important for foal viability than appropriate case selection and adherence to criteria for induction^{97,170}. A low dose protocol has been recommended since it appears to only work in those mares that have a mature fetus¹⁸⁴. As little as 1.0 IU i.v. in pony mares (250-350 kg) will induce delivery within 45 min if they are ready for birth³⁷. In another study pony mares were diagnosed as being ready for birth by mammary secretion calcium strip test measurements. A single injection of 2.5 IU oxytocin i.v. was given between 1700 and 1900 h, and resulted in the delivery of a normal foal within 120 min in 95% of mares. It was concluded that the major advantage of injecting a daily low dose of oxytocin appears to be that such a low dose only induces delivery in mares that are carrying a mature fetus and which are ready to foal. It has been proposed that this 'low dose, early evening, oxytocin protocol' could be used as a reliable method to induce parturition, and/or to predict that the mare would not foal that night, if parturition did not occur within 2 h of treatment¹⁸⁴. When 30 light or draft horse mares were treated with oxytocin (0.1, 0.5, 1.0, 2.0 IU) at 5:00pm once mammary secretion calcium exceeded 13 mM/l, the 2.0 IU group required significantly less repeated daily treatments, with 61% foaling within 2 hours of treatment¹⁸⁵. A slightly larger dose (3-5 IU) may be required in these larger breeds. Interestingly, there was a significant increase in PGF_{2a} metabolite concentrations after all treatments, irrespective of whether the mare foaled in response to the treatment¹⁸⁵. The reader is cautioned that even these promising low-dose protocols have limitations since it is still possible to occasionally induce a mare to deliver a premature foal - especially with repeated treatments³⁷.

Obstetrics:

Fetal death and **maceration** is uncommon in the mare. The condition has been successfully treated by ovariohysterectomy, but the uterine contents must be small enough to permit access to the uterine vessels¹⁰⁸. The author has managed a case of macerated twins in a draft breed mare that suffered no ill effects systemically. The mare was only presented for evaluation when the owner noticed a foul smelling vaginal discharge. The cervix was manually dilated after application of crushed PGE tablets in a lubricating jelly. Densely calcified mandibles, ribs and long bones were then able to be extracted without inciting cervical trauma. In another maceration case, the mare presented for bloody vaginal discharge after being bred!! There had been no prior history of vaginal discharge or systemic illness in this mare either¹⁸⁶. A detailed review of equine obstetrics has recently been published^{102,187-189}. This section will discuss current thinking on the management of obstetrical complications in the mare.

By late gestation the fetus should be in cranial presentation and in a dorsopubic position. A complex mechanism involving entrapment of the fetal hindlimbs within the gravid uterine horn may explain the fact that 98.9% of foals are delivered in cranial presentation. It has been proposed that neurologic signals in the maturing inner ear may prompt the fetus to lie with its cranial aspect elevated towards the cervix, thus orient the dorsum of the fetus with the concave slope of the ventral uterine wall. The acute angle between the uterine horn and body by seven months of gestation means that the fetus must be in dorsal recumbency before the hindlimbs can gain entry. After nine months the hindlimbs remain enclosed within the gravid horn, and the hooves reach the tip by the tenth month⁶⁶. Ultrasonographic studies in Dr. Ginther's lab have verified the classic study by Jeffcott and Rossdale which demonstrated the fetal postural changes

during parturition. It has been proposed that the increasing uterine tone during **stage I** of parturition somehow stimulates the fetus to extend its head and forelimbs ⁶⁶. Dystocia cases that involve a dorso-pubic position with flexed extremities suggest that the fetus was compromised prior to the start of the parturient process. In some cases this may be indicative of advanced placentitis or fetal infection, and thus submission of tissue from a stillborn fetus is recommended. The neck and forelimbs will not normally be returned to a flexed posture once a viable fetus in stage I of delivery has actively extended them. The onset of stage II is heralded by rupture of the chorioallantois and discharge of the watery allantoic fluid. This occurs when the fetlocks - and sometimes the knees - are at the level of the external cervical opening ⁶⁶.

While the cranial aspect of the foal is passing through the birth canal the hindlimbs remain locked within the uterine horn. The **second stage of labor** is characterized by strong abdominal contractions that provide the expulsive force necessary to expel the fetus. Appearance of one hoof within the translucent fluid-filled amnion at the vulva lips can be expected to occur within 5 min of rupture of the chorioallantois ¹⁹⁰. One forelimb should precede the other by several inches, such that the shoulders enter the pelvis successively. By the time the nose reaches the vulva the cranial half of the torso has already rotated from a dorso-pubic to a dorso-ilial position. The foal's withers continue to rotate into a dorso-sacral position as the head appears through the vulvar lips ⁶⁶. At this time the foal's shoulders have entered the pelvic canal. Second stage labour in the mare is rapid, with the most forceful contractions occurring as the fetal thorax passes through the pelvic cavity. The amniotic sac may rupture during these expulsive efforts. However, the foal can be delivered with a portion of the sac wrapped around its head ¹⁹⁰. The fetal pelvis rotates through a dorso-ilial position into a dorso-sacral position, and the hindlimbs become extended as the fetal abdomen begins to pass through the vulvar lips. This occurs because at this point the stifles impinge upon the pelvic brim. The foal's rump remains closely apposed to the cranial dome of the uterine body as the contracting uterus and abdominal press combine to expel the foal. Thus, at the time of the foal's delivery the cranial aspect of the uterine body is only about twelve inches from the cervix ⁶⁶.

Most foals are delivered within 20–30 min after the chorioallantoic membrane ruptures. Primiparous dams generally require longer to expel the fetus than multiparous dams ^{190,191}. Delayed delivery (**prolonged foaling time**) increases the likelihood of fetal asphyxia, or neonatal problems associated with hypoxia due to placental separation ¹⁹². A number of foaling monitors and video camera systems are available for this purpose ¹⁹³. Attendants should suspect that the mare is experiencing obstetrical problems if either the first or second stage of parturition is prolonged, or not progressive. Occasionally, the chorioallantois fails to rupture and the velvety, red membrane ('red bag') appears at the vulva lips. This is a common complication of induced parturition, and placental edema is a major problem in mares that have been exposed to endophyte-infected fescue hay or pasture ^{97,159}. In the latter scenario the pregnancy may be prolonged, and the mare is also likely to be agalactic. Signs that a mare may be experiencing difficulties include failure of any fetal parts, or of the amniotic membrane, to appear at the vulval lips within 5 minutes after rupture of the chorioallantois. Other causes for concern are hooves upside-down, or any abnormal combination of extremities appearing at the vulva (only one limb; hooves and nose in abnormal relationship; nose but not hooves; both forelimbs protruding but no head visible at the level of the carpi) ¹⁹⁰. The most common impediments to delivery are malpostures of the long fetal extremities (head and neck, or limbs) ¹⁰². Failure to quickly identify

a dystocia often results in the fetus becoming impacted in the birth canal by the mare's uterine contractions, and strong abdominal straining. The secret to foal survival is a combination of experience and expediency. In one study, mares that had 'difficult deliveries requiring veterinary assistance' were 24 times more likely to deliver a dead foal. The risk for neonatal disease was 23 times greater among foals that survived such assisted deliveries, and the risk of subsequent death within 2 weeks of delivery was 6 times greater than in normal foalings^{176,192}. If farm personnel are experienced, and referring veterinarians are well trained in dystocia management, prompt referral to a hospital in close proximity may permit delivery of a viable foal - even after an hour has elapsed since the chorioallantois ruptured¹⁹⁴. It is probable that limited intervention causes less disruption of the fetal membranes, and thus permits longer placental support of the fetus.

Assessment of a dystocia case: Time is the critical factor when managing an equine obstetrical case¹⁹⁴. Although fetopelvic disproportion is uncommon in the mare, it can be a factor in some equine dystocias - especially those in primiparous mares^{195,196}. Once the cause of the dystocia has been determined, the obstetrician should ensure that the owner understands the various treatment options and costs, and the inherent risks that may be associated with each approach. The prognosis for survival of both the mare and foal, and the impact of the treatment options on the mare's future fertility should also be discussed. Sometimes the owner will place more value on the mare's non-reproductive attributes, while in other cases the mare's future fertility is of paramount importance. The economics of the case, the expertise of the clinician, and the proximity of hospital facilities are all factors to be considered when planning the best course of action to resolve a dystocia case^{187-189,194,197,198}. In prolonged dystocias the severity of the foal's impaction, amount of contraction of the uterus around the foal, and the presence of vaginal swelling, mucosal tearing, hematoma formation, and drying of the mucosa will influence the clinician's approach - especially in referral hospitals. In many of these cases caesarean section may be preferable to further vaginal intervention¹⁹⁷.

Four options are available to resolve dystocias in a mare: **assisted vaginal delivery** where the mare is conscious and variable manipulation and traction is used to deliver the foal vaginally; **controlled vaginal delivery** where the mare is anesthetized and the obstetrician is in complete control of the vaginal delivery; **fetotomy**; and **caesarean section**¹⁹⁸. Each of these approaches has its place in veterinary obstetrics. One should keep an open mind when managing a dystocia, and be prepared to employ "a continuum of potentially changing strategies" as the clock ticks¹⁹⁸. If a well equipped veterinary hospital is close by then immediate referral for general anesthesia, controlled vaginal delivery, or caesarean section may offer the best prospect for *foal survival* and the mare's subsequent fertility^{194,197}. Unfortunately fetotomy is frequently used as a last resort when prolonged manipulations have failed to correct the problem, and extensive soft tissue trauma has already been inflicted. In these cases it is often the prolonged manipulations, and not the fetotomy procedure itself, that causes the most trauma and adverse impact on fertility. If the foal is dead it is a mistake to prolong unrewarding vaginal manipulations in the belief that the urgency of rapid delivery no longer applies¹⁹⁷. Prompt use of fetotomy by experienced clinicians can markedly reduce intervention time when the foal is dead. When dystocias are managed under optimal hospital conditions the subsequent foaling rate is similar for both caesarean section and controlled vaginal delivery mares¹⁹⁴. Studies are lacking with respect to fertility after appropriate use of fetotomy by experienced operators.

Chemical Restraint: Sedation of a mare with acepromazine does not appear to affect the fetus⁷¹. Acepromazine suppresses myometrial activity in cycling mares, whereas the α_2 -adrenoceptor agonists (detomidine and xylazine) cause increased myometrial activity¹⁹⁹. However, when a similar dose of detomidine was used in mares in the last trimester of pregnancy the myometrial activity was decreased⁷¹. In another late-gestation detomidine (0.015 mg/kg i.v.) study the fetal heart rate declined initially, but rhythm remained regular. Fetal activity was decreased within 5 min, but had returned to baseline levels by 90 min. Repeated sedation, at 3 week intervals, had no measurable detrimental effects on the outcome of pregnancy in 11 healthy mares. There were no signs of intra-uterine growth retardation (IUGR), dysmaturity, or peripartum asphyxia¹³⁰. Since opioid analgesics can cause some gastrointestinal stasis and impaction, it is especially important to administer mineral oil once the dystocia has been resolved if these agents have been used¹³⁰. Although intravenous or intramuscular administration of tocolytic agents will cause rapid uterine relaxation, it is not known whether the oral formulations will achieve sufficient blood levels to provide the same effect on the parturient uterus¹⁴⁸.

In referral hospitals it is common practice to immediately anaesthetise these mares, and to maintain them with controlled ventilation and intravenous fluids^{71,194}. Fluid therapy, and provision of oxygen with intermittent positive pressure ventilation, will minimize any disturbance of maternal and fetal wellbeing⁷¹. By using the hind end elevation technique, almost three-quarters of such cases can be resolved by controlled vaginal delivery. However, if the fetus is still alive and has not been delivered within 15 min, a caesarean section is performed. Under these optimal circumstances a 29% foal survival rate has been reported^{194,200}. Anesthesia that is maintained on halothane alone can cause marked cardiovascular depression in horses. This may compromise umbilical circulation, and cause lower PO₂ umbilical venous blood gas values compared with a 'triple drip' protocol⁷¹. In the field, total intravenous anaesthesia (TIVA) may combine an alpha-2 agonist, with a central nervous system acting muscle relaxant, and a dissociative anesthetic. Detomidine, ketamine and guaifenesin is reported to provide good placental perfusion, and a quiet but relatively prolonged recovery⁷¹. The so-called 'triple drip' in North America contains xylazine, guaifenesin, and ketamine produces a relatively rapid and uneventful induction, a stable maintenance phase, and a quiet uncomplicated recovery from anesthesia²⁰¹. This type of anesthesia is best suited to short periods of time, and clinicians should be cognizant of potential post-anaesthetic myopathy, especially in heavy draft breeds. Thus, even if the fetus is dead, an eye must be kept on the clock so that a mare is not kept hoisted for prolonged periods. Arterial hypoxemia, hypercarbia and hypotension can produce skeletal muscle ischemia and hypoxia that may complicate the recovery process²⁰². Creatine Kinase is released following even minor muscle damage and is elevated at 4-12 and 24-36 hours post-partum in normal foaling mares. Elevation of AST and LDH may also reflect muscle trauma; although neither enzyme is muscle specific. In normal post-partum mares both enzymes are elevated at 24-36 hr and 42-60 hr. CK will decline rapidly after transient muscle damage whereas AST and LDH may take days to decline²⁰³. An advantage of the 'triple drip' protocol is that, when combined with inhalation anesthetic (eg. halothane, isoflurane) for maintenance, there is less indication for drugs (eg. dobutamine) to support hemodynamics (cardiac output, arterial blood pressure). This may be due to the ability to decrease the maintenance inhalant anesthetic concentration, and thus reduce its cardiovascular depressant effects²⁰¹. "Triple Drip" anesthesia should not be used for long procedures (max. 1 hr) unless oxygen supplementation and respiratory support are provided.

Fetal Manipulation (Mutation): Overzealous intervention is a major cause of uterine rupture, and it may not be possible to achieve meaningful - yet safe - repulsion if the uterus is contracted down around the fetus^{106,204}. Most iatrogenic lacerations occur in the uterine body, whereas a rupture at the tip of the gravid horn is more likely to be caused by the thrusting activity of the fetal hindlimbs^{66,204}. The cervix and vagina can easily be lacerated, and extreme pressures created by extraction attempts with an uncorrected malposture can cause **fetal rib fractures** and severe internal trauma. It should be noted that rib fractures and contusions can also occur during an unassisted delivery^{195,196}. Excessive use of force may injure a viable foal and inflict maternal soft tissue trauma. Neonatal thoracic trauma is more common in primiparous mares¹⁹⁵. Serious birth-related injuries in a foal may include fractured ribs, bruised costochondral junction of ribs, hemoarthrosis of shoulder joints, as well as internal hemorrhage and/or a ruptured viscus^{192,195,196}. Dystocia due to elbow retention may cause increased pressure on the thoracic cage. In some cases thoracic trauma may go unnoticed because the foal does not exhibit any clinical signs. A depression associated with rib fracture may be noted at or near the costochondral junction of the cranial ribs (#3 to #8)^{195,196}. Serious complications following rib fracture include pericardiac and cardiac lacerations, pneumothorax and lung lacerations, and diaphragmatic hernia. Obviously hemothorax is a compounding problem^{195,196}. If the fetus is dead, many malposture cases can be rapidly resolved by one or two fetotomy cuts - provided that the clinician has the appropriate skills and equipment. Poor technique and inappropriate fetotomy cuts often lead to infertility. The alternative is cesarean section^{194,197}.

Cranial (anterior) Presentation: *Absolute* feto-pelvic disproportion (**fetal oversize**), is not as common in mares as it is in cattle^{102,194}. The shape of the mare's pelvis, and the more elongated equine fetus, tend to facilitate ease of delivery in most cases. The size of the uterus (breed variation) plays a much greater role in determining ultimate fetal size than does the stature of the stallion^{15,19}. Allen's studies have indicated that maternal uterine size modulates the fetal genotypic growth potential *in utero* by influencing both the gross area of the diffuse chorioallantois as well as the density, branching and depth of the microcotyledons that develop on it¹⁹. Despite this, owners will often express concern about fetal oversize if the foal has been carried several weeks past the expected due date. *Relative* feto-pelvic disproportion may be a significant factor in primiparous mares, and obstetrical assistance (traction) is required much more often in these younger animals¹⁹⁵. Foals from primiparous mares are more likely to sustain thoracic trauma compared to foals from pluriparous mares¹⁹⁵. Approximately 30% of referral hospital dystocia cases are in primiparous mares, and these younger mares were disproportionately represented in reports on dystocia and neonatal asphyxia^{102,190,195}. Apart from fetal issues (malposition, malposture), dystocia in primiparous mares may be further complicated by a tight vaginovestibular sphincter. This will predispose such cases to lacerations and rectovaginal tears¹⁹⁵.

If a **foot-nape posture** is present, one or both of the forelimbs will be displaced over the foal's head and pushed against the vaginal roof. The abnormal posture increases the diameter across the fetal chest, and the elbows may be lodged against the pubis. The mare's straining can cause the fetal hoof to lacerate the vaginal roof, and in extreme cases it may perforate completely through into the rectum. This recto-vaginal fistula may be all that occurs if the foal withdraws its hoof

from the rectum prior to delivery. However, if the mare's strong expulsive efforts force the trapped limb caudally it will dissect through the rectovaginal shelf - and may even rupture through the anal sphincter. The resulting cloaca-like opening is known as a 3rd degree perineal laceration^{205,206}. Since most **carpal flexions** are relatively easy to correct manually, the obstetrician should be cognizant of the possibility of contracted tendons when difficulties are encountered. Flexural deformities are considered to be the most common congenital anomaly of foals. Limb contractures are generally bilateral, with the forelimbs being affected more often than the hindlimbs - although it is not uncommon for all four limbs to be involved¹⁹⁴. Severely affected limbs can not be straightened, and needless trauma can be inflicted on the genital tract by prolonged attempts to manually correct this malposture. Malpostures involving the **head and neck** often occur when a viable foal pulls back from vaginal manipulations that are intended to correct a minor postural problem. Head and neck malpostures are very difficult to correct because the long neck often makes it impossible to reach the foal's head once this type of dystocia has occurred. Prolonged, unrewarding manipulations can easily jeopardize the mare's future fertility. Inexperienced clinicians should consider referral as soon as a head and neck malposture is diagnosed¹⁸⁹. In fact, reflection of the fetal head and neck is the most common reason for referring a dystocia case to a veterinary hospital^{102,194,197}.

Caudal (posterior) Presentation predisposes the mare to dystocia because the synchronized rotation of the fetal body - and extension of the extremities - that has been described for cranial presentation often doesn't occur⁶⁶. In many cases the abnormally presented fetus will be in a dorso-ilial position¹⁰². Although only about 1% of foals are presented caudally, this malpresentation may account for 14-16% of referral hospital dystocia cases since any postural abnormalities of the long limbs create a major complication^{102,194}. Typically both hindlimbs are involved in the malposture suggesting that the etiology is associated with a failure of the normal extension mechanism¹⁰². Both bilateral hock and hip flexion cases are extremely difficult to correct under field conditions due to space limitations within the birth canal. **Hock flexion** malposture accounts for about one quarter of referred caudal presentation cases¹⁰². The flexed hocks are palpable either at the pelvic inlet, or impacted more caudally in the vaginal canal. If the foal is dead, and the obstetrician is experienced, it may be safer to correct a flexed hock dystocia by fetotomy. Approximately half of referred caudal presentation cases are breech (bilateral hip flexion posture). Cesarean section will usually provide the best prognosis for fetal viability and future fertility in these cases.

Cesarean Section: Hemorrhage into the uterus can be a serious complication following cesarean section. Recently the merit of placing sutures along the uterine incision edge (hemostatic suture) prior to hysterotomy closure (two inverting layers) has been questioned. One study found that use of the hemostatic suture did not appear to reduce the occurrence of severe uterine hemorrhage, and it had the disadvantage of prolonging surgery time. This can be especially problematic in the heavy draft breeds that are susceptible to post-anesthetic myopathy²⁰⁷. While other surgeons still advocate its use, they also take the precaution of ligating any easily identified large vessels before placement of the hemostatic suture¹⁹⁸. When the hemostatic suture is not placed it is important to close the hysterotomy with a full thickness suture pattern (eg. modified Lembert) that is sufficiently tight to compress vessels in the uterine wall. A Cushing pattern is not suitable for this purpose, but is useful to support and bury the Lembert suture, thereby reducing the risk of post-operative adhesions²⁰⁷. When dystocias are managed under optimal

hospital conditions the subsequent foaling rate is similar for both caesarean section and controlled vaginal delivery mares¹⁹⁴. A minimum of a 6 week post-caesarean section interval is recommended before breeding a mare by natural mating. Since the ventral midline closure is not being tested by artificial breeding it may be feasible to attempt earlier inseminations in those breeds that condone AI¹⁹⁴.

Complications in the Postpartum Mare:

A detailed review of these conditions has recently been published^{208,209}. Abdominal discomfort in the peripartum mare may be due to uterine contractions, especially if the mare has been treated with oxytocin to promote passage of the fetal membranes. However, other causes of abdominal pain should not be discounted¹⁰⁶. Transabdominal ultrasound is a useful diagnostic tool when evaluating a mare exhibiting signs of colic²¹⁰. When a postpartum mare displays abdominal discomfort, and/or fever with signs of depression, this author believes that **abdominocentesis** is indicated²¹¹. The normal foaling process does not alter the composition of the peritoneal fluid from within the normal range^{106,212}. Even a dystocia will not necessarily cause significant changes in the peritoneal fluid. If an experienced obstetrician performs the vaginal manipulations and/or fetotomy, the fluid should remain normal¹⁰⁶. If the peritoneal fluid is normal then the mare should be monitored closely for signs of clinical deterioration. Repeated abdominocentesis may be indicated in cases where clinical signs suggest that a parturient related abdominal lesion may be present, since the peritoneal fluid constituents can change within hours¹⁰⁶. A single, elevated peritoneal fluid value (total protein, white cell count, or percent neutrophils) may be an incidental finding. Elevation of two or more values often signals the onset of clinical abnormalities. It has been the author's experience that if a postpartum peritoneal fluid sample has TPr > 3.0 g/dl, in conjunction with WBC count >15,000 cells/μl, and WBC differential count of >80% neutrophils (especially if degenerative changes are present) then the presence of a potentially life-threatening lesion is likely¹⁰⁶. The peritoneal fluid analysis should not be viewed in isolation, and must be considered in conjunction with the history and clinical signs being exhibited by the mare. In this author's experience, detection of changes in the peritoneal fluid almost invariably indicates the presence of foaling related trauma in either the reproductive or gastrointestinal tract. An early diagnosis followed by appropriate medical and/or surgical intervention will often result in a favorable outcome. If treatment is not implemented until the affected mare has become depressed and febrile, with accompanying signs of shock and toxemia, the prognosis may be more guarded.

Periparturient hemorrhage: While rupture of the uterine artery is the most common cause of death in post-partum mares, a ruptured artery can occur prior to foaling, or several weeks after delivery. In the later group this may be due to rupture of a hematoma that had previously formed in the broad ligament. Uterine artery rupture tends to be a problem in older mares due to weakening of the arterial wall subsequent to repeated enlargement and shrinkage with multiple pregnancies²¹³. The changes in the extrauterine vessels (ovarian and uterine arteries) in aged mares are classified as being primarily fibroses and fibroelastoses^{3,214}. The uterine vessels develop an elastosis predominantly increasing with the number of foals - the so-called "pregnancy sclerosis"^{1,214}. In doppler ultrasonographic studies of uterine blood flow it was reported that mares with moderate to severe endometrial angiopathies have a significantly higher vascular resistance in the uterine artery. This likely causes higher hemodynamic stress^{3,215,216}. An association with low serum copper levels has been proposed as a reason for vessel fragility in

aged mares, but recent work has not demonstrated any beneficial effect of supplementation. The plasma copper concentration declined during the third trimester in all pregnant mares that were studied, and this was not affected by copper supplementation - even though liver copper levels did tend to increase²¹⁷. The rupture (2 to 3 cm) can occur anywhere along the length of the vessel, without evidence of an aneurysm. The tear tends to be oriented parallel to the long axis of the vessel and will have ragged margins²¹³. Affected mares typically exhibit signs of severe pain if a hematoma is forming in the broad ligament, and this may be confused with the contractions of uterine involution - especially if the mare has been treated with oxytocin to expedite expulsion of the fetal membranes. If there is rupture into the peritoneal cavity the mare may be found dead, or in a state of hemorrhagic shock²¹³.

Depending on the economics of the case, and the severity of the clinical signs, treatment may range from keeping the mare quiet through to aggressive fluid therapy¹⁵². The primary objective is to maintain an effective circulating intravascular volume, and to provide an oxygen supply to avoid tissue hypoxia²¹⁸. There is some debate in the human trauma literature about the use of aggressive fluid resuscitation to increase intravascular fluid volume and elevate blood pressure while there is uncontrolled hemorrhage. Anything that counters the tamponade effect exerted by the hematoma may promote further hemorrhage. Some clinicians advocate the use of agents such as aminocaproic or tranexamic acid (to stabilize the clot) and naloxone an opioid antagonist), but controlled studies on their efficacy in hemorrhaging mares are lacking. One such study was not able to demonstrate an effect "formalin therapy" on coagulation parameters or template bleeding times in normal horses²¹⁹. If hemorrhage is contained within the wall of the uterus then the intramural hematoma may be an incidental finding at the foal heat examination. However, some mares may exhibit variable signs of abdominal discomfort, even to the extent of warranting an exploratory celiotomy²²⁰. Abscessation of a retroperitoneal hematoma can become a life-threatening complication following a dystocia, and thus prophylactic broad-spectrum antibiotic coverage is warranted. Mares with an infected retroperitoneal hematoma develop signs of toxemia. In these cases the peritoneal fluid has an increased TPr content (3.0 to 5.0 g/dl) with a massive increase in the WBC count (often exceeding 100,000 cells/ μ l)¹⁰⁶. Partial ovariohysterectomy has been performed to remove a uterine horn that was compromised by a hematoma. The mare was subsequently used for embryo transfer¹⁰⁹.

Uterine Rupture: In any dystocia case there is a risk for iatrogenic tears, and the uterus should always be checked for any obvious lacerations immediately after extraction of the fetus. However, obstetrical intervention is not always the cause of uterine tears. Although the fetal hooves are covered with hard gel-like pads that presumably protect the placenta and uterine wall, the vigorous piston-like thrusts of the hindlimbs may occasionally cause a rupture^{66,204,211}. Affected mares generally experience bouts of colic, and become depressed, febrile and anorectic as peritonitis develops. The interval from occurrence of the tear to diagnosis and initiation of therapy has a marked impact on the prognosis for survival^{106,204}. Recent research has proven that even a fetotomy procedure does not alter the composition of the postpartum peritoneal fluid if it is performed correctly, and thus abnormalities noted in a 'belly tap' generally indicate the presence of a life-threatening complication¹⁰⁶.

Retained Fetal Membranes and Toxic Metritis: The fetal membranes will normally be expelled within 3 hours postpartum¹⁷⁵. The incidence of retention has been reported to range

from 2 to 10% of foalings, and draft breeds appear to be especially prone to membranes retention¹⁷⁵. Retention rates for 116 mares that experienced a dystocia (vaginal correction or cesarean section) were 65% for >3hr; 12% for >72hr; 10% for >96hr; and 2% for 120hr¹⁹⁷. In a study where mares received two treatments with flunixin meglumine at 8 and 1 hours prior to oxytocin-induced parturition, there was a significant delay in fetal membrane expulsion - possibly associated with a significant suppression in PGF_{2a} concentrations⁵⁹. This warrants further study because anti-inflammatory medication is frequently used to prevent the onset of laminitis in mares with fetal membrane retention. The precise mechanism involved in detachment of the chorioallantoic membrane must be investigated before the underlying causes of retention can be fully understood and managed therapeutically. Certainly inadequate postpartum **myometrial contractions** seem to play a role in the etiology of this condition. In a study of heavy draft breed mares there was a significant negative correlation between placental retention time and the oxytocin concentration immediately after foaling²²¹. Oxytocin is an overdosed - but not over-utilized drug. There is tremendous biological variability in the clinical response of the postpartum mare to oxytocin therapy, and this appears to be unrelated to the size of the mare²²². A dose that may have one mare sweating, pawing the ground and rolling, may have no overt effect in another mare of comparable stature. Thus, this author believes that a low initial dose (10-20 IU) is prudent until the response of the mare can be gauged. Although the work was performed in non-pregnant mares, Madill et al showed that there was a significant dose-response relationship between intramuscular administration of oxytocin and increased uterine motility²²². A dose of only 20 IU (typically 1.0 ml) oxytocin provided 90 minutes of increased activity, with an average latent period of 12 minutes after the i.m. injection. Doubling the dose did not increase the duration of response or the amount of time that the uterus was in a state of contraction.

The **calcium ion** plays a vital role in myometrial contractility, and it is important to ensure that calcium levels are within the normal range^{180,223,224}. Supplemental calcium can markedly expedite the rate of passage, suggesting that uterine hypomotility is a component in some of these cases. Inadequate serum calcium levels will reduce the efficacy of oxytocin therapy²²⁴. A recent study noted that the number of endometrial mast cells observed during the puerperal period is significantly lower in the endometrium of mares with retained fetal membranes²²⁵. It has been demonstrated that immediately after birth more white blood cells enter the fetal membranes than subsequently leave through the umbilical vein²²⁶. It was proposed that trapped leukocytes degranulate rapidly after leaving the vascular bed, releasing inflammatory products into the tissues. Whether this finding has any relevance to fetal membrane passage remains to be determined. It is widely accepted that excessive traction on the fetal membranes is contraindicated. However, a recent study suggests that cautious **manual removal** of the membranes may not be as deleterious to future fertility as previously thought²²⁷. When the membranes are extracted by force there is inevitably disruption of the epithelial barrier, making the traumatized uterine lining more susceptible to bacterial invasion and the development of metritis. Recent studies suggest that a safe, and potentially effective, treatment for retained fetal membranes in mares may be intraplacental injections of collagenase^{228,229}. The normal rapid uterine involution process is delayed in mares that have experienced dystocias or retention of fetal membranes. Asymmetry on D9 is palpable more frequently in mares with dystocia (57.1%) and delayed expulsion of the fetal membranes (42.9%)²³⁰. The normal desquamation of the microcaruncular

epithelia into the uterine lumen is delayed in mares that experience dystocia and retention of the fetal membranes²³⁰.

Therapy for mares that are at risk for - or suffering from - **toxic metritis** is generally based on clinical experience, and the collective wisdom of peers. While the WBC count is decreased at 24-36 hr and 42-60 post-partum in normal foaling mares, these values should remain within the normal reference range²⁰³. This compares with Blanchard's documentation of a marked leukopenia and neutropenia in mares that have experienced a dystocia. A survey of Diplomates of the American Colleges of Veterinary Internal Medicine and Veterinary Surgeons reported on treatments for endotoxemia²³¹. **Laminitis** is by far the most common complication, and 77% of respondents prophylactically treat horses that are considered to be at risk for the development of **endotoxemia**^{231,232}. Early intervention is important. The enzymatic (matrix metalloproteinases) separation of the basement membrane from hoof lamellar epidermal cells has progressed significantly before any clinical signs are apparent. Preventive strategies must be implemented when endotoxemia is considered to be risk so that significant lamellar damage does not ensue²³³. Measures most commonly used to prevent endotoxemia included IV fluid treatment (usually Lactated Ringer's), flunixin meglumine (0.25 mg/kg, IV, q 8 h rather than the higher 1.1 mg/kg q 12 h dose), and administration of antimicrobials - the most common choices being penicillin and gentamicin²³¹. Antibiotic treatment is especially important in mares with toxic metritis because of the concurrent septicemia, and those antimicrobials with a gram-negative spectrum would be most appropriate. When aminoglycosides are used, mares should be well hydrated to reduce the risk of nephrotoxicosis. A low dose (1,000 to 5,000 U/kg) of Polymixin B may have potential due to this drug's ability to bind the lipid A component of the endotoxin molecule, and reduce generation of cytokines (tumor necrosis factor)^{234,235}. However, a single dosage is suggested due to concerns about nephrotoxicity²³². While only 11% of respondents used amikacin, the author's lab has identified this drug as being especially useful for organisms isolated from metritis fluid²³⁶. Hyperimmune antiendotoxin plasma or serum (1 to 2 L diluted at least two-fold in balanced i.v. fluids) was used by 65% of respondents, but almost half were uncertain of its effectiveness. It must be used early in the disease process to be effective. Only 35% indicated that they used heparin (40 IU/kg SC or IV, q 8 h) prophylactically, and guidelines for dosage vary²³¹. Some clinicians will use pentoxifylline in an attempt to prevent development of acute laminitis. Obviously treatment of endotoxemia must include correction of the primary disorder - retention of the fetal membranes and metritis. There has been a movement away from the use of intra-uterine antibiotics in recent years, but most clinicians still advocate lavaging the uterus as often as is necessary to remove the fetid fluid - the source of the endotoxin.

Gastro-intestinal Complications: Prolonged straining during dystocia can lead to variable amounts of rectal mucosa being forced out through the anal sphincter (Type I rectal prolapse). In a type III prolapse there is a full thickness rectal prolapse plus an intussusception of the peritoneal rectum or small colon; in a type IV prolapse the intussuscepted bowel protrudes through the anus such that there is a palpable trench that may extend several meters into the rectum, depending on the length of the intussusception¹⁰⁷. If **avulsion of the mesocolon** has occurred there will be a reduction or absence of fecal passage leading to signs of impaction colic. Since early intervention is essential, sequential abdominocentesis is indicated when a type III or IV rectal prolapse is being conservatively managed. Initially there may be negligible changes in the composition of the peritoneal fluid. However, if an avulsion has occurred then the

compromised segment of bowel will soon lose its integrity, and a massively increased WBC count, with protein leakage, can occur within 24-48 hours as peritonitis ensues¹⁰⁶. Standing flank laparoscopic evaluation of the abdomen can provide an immediate assessment of bowel integrity, and permit an accurate prognosis to be given to the owner¹⁰⁷. Owners should be advised that surgical correction is only feasible if the segment of devitalized bowel is accessible. Postpartum mares appear to be at an increased risk for development of **large colon torsion**. This condition presents as an especially violent colic with readily discernable abdominal distension. Extensive ischemic damage affects the prognosis, but early surgical intervention can increase the survival rate²³⁷. The tip of the **cecum** is the most likely site of a foaling related rupture in the alimentary tract, and affected mares exhibit signs of acute abdominal pain and soon develop septic shock. On palpation per rectum the inflamed serosal surfaces will feel roughened with a discernable crepitus. Abdominocentesis will reveal dark green-brown gastro-intestinal fluid that contains plant material and massively increased neutrophil numbers. Humane euthanasia is indicated since the condition is invariably fatal²³⁸. Cecal perforation is the 2nd most common cause of death in postpartum mares - after rupture of the uterine artery.

Eversion of the urinary bladder: The mare's urethra has a large diameter and occasionally the bladder may be everted up into the vagina following severe straining²³⁹. However, edematous swelling may preclude replacement without an incision being made through the urethral sphincter. In rare instances correction of the eversion may be complicated by prolapse of abdominal viscera into the everted bladder. This can be verified by ultrasound.

Rupture of the urinary bladder or ureter: Occasionally the bladder may rupture as a consequence of increased intra-abdominal pressure in the foaling mare, or due to direct trauma during parturition^{240,241}. The onset of clinical signs is delayed, and a presumptive diagnosis can be confirmed by the characteristic serum electrolyte imbalances (hyponatremia, hyperkalemia), and the elevated creatinine and BUN concentrations. Affected mares may be depressed and inappetent, with failure to void urine. Clinical examination will reveal tachycardia, tachypnea, and decreased gastro-intestinal activity. Evaluation of a peritoneal fluid sample will help to confirm the diagnosis. The fluid will contain elevated urea and creatinine levels, and calcium carbonate crystals^{241,242}. Cystoscopy is useful to evaluate the size and extent of the bladder injury. Once the mare's medical condition has been stabilized, surgical repair is indicated²⁴⁰⁻²⁴². A standing vaginal approach eliminates the need for general anesthesia and allows excellent observation and repair of bladder tears in adult mares^{240,242}. **Rupture of the ureter** has been associated with parturient trauma. It may be repaired surgically, but the large amount of urine accumulation in surrounding tissues may preclude this approach. A temporary indwelling ureteral stent catheter may be used to restore continuity of the urinary tract, and facilitate healing²⁴³.

Recto-vaginal fistulas and Perineal lacerations: Third degree perineal lacerations generally occur during unassisted foalings when the fetal hoof catches on the vaginal roof at the vestibulovaginal junction, especially in primiparous mares²⁴⁴. Forceful straining by the mare can drive the hoof through the rectovaginal shelf such that the fetal hoof comes to lie within the rectum. If the fetus is viable it may remove the affected limb and delivery will proceed unimpeded - a rectovaginal fistula results. If the limb remains within the rectum then continued passage of the fetus causes the trapped limb to tear out the perineal body and anal sphincter. The

resulting defect is called a third degree perineal laceration. These injuries do not respond well to immediate surgical intervention and the general recommendation is to wait 4 to 8 weeks before attempting reconstructive surgery^{239,244}. In the interim the mare should be treated with broad-spectrum antibiotics, anti-inflammatory medication, tetanus prophylaxis, and fecal softeners. Rectovaginal fistulae may be converted to third degree perineal lacerations and repaired accordingly, or may be approached without transection of the intact perineal body. Both two-stage and one-stage methods of third degree perineal laceration repair have been described^{244,245}.

Lactation:

During the latter part of gestation the mammary gland is exposed to high levels of estrogen and progestagens, and this prior hormonal stimulation seems to be necessary for prolactin to initiate lactation^{246,247}. **Prolactin** is produced by lactotrophic cells in the anterior pituitary, and is regulated by the 'prolactin inhibiting factor - dopamine'²⁴⁸. Naloxone-induced prolactin release is most pronounced towards term. It has been suggested that this is indicative of an increase in the naloxone-releasable pool and/or the absence of other prolactin-release inhibitory mechanisms²⁴⁷. Plasma prolactin concentrations increase in the last two weeks of gestation, reach a maximum in the week of foaling, and then decrease rapidly thereafter²⁴⁹. Treatment with a dopamine D₂ antagonist i.m. (sulpiride 0.5 mg/kg bid) at the beginning of the breeding season (after light therapy) can induce lactation. Prolactin secretion increases immediately, and milking should start 6 days after the sulpiride treatment is started²⁴⁶. Another approach has been to prime mares with an altrenogest/estradiol benzoate impregnated vaginal sponge, and then treat with sulpiride (1mg/kg i.m., bid from day 8)²⁵⁰. The minimum effective induction protocol involved a week of treatment, with manual milking starting at the end of the week. Although elevated prolactin levels aren't necessary for ongoing lactation in foaling mares, continuation of the sulpiride treatment beyond 2 weeks may further increase milk production when lactation has been induced^{249,250}. Mares with an induced lactation are able to adopt and nurse a foal to weaning age²⁵⁰.

Oxytocin is synthesized in the supraoptic and paraventricular nuclei of the hypothalamus and stored in the posterior pituitary. Milk is secreted in the alveoli and expelled into the lactiferous ducts and teat cisterns when oxytocin causes contraction of the myoepithelial cells. Although it is assumed that nursing by the foal stimulates the release of oxytocin from the neurohypophysis, recent research has revealed that the process is more complicated than that in the mare^{58,221}. A significant effect of suckling on oxytocin release by the mare was detected in only two of nine mares, and two of eight mares in two independent studies^{58,221}. When foals were prevented from sucking for 1 h, by being either muzzled (n = 2) or separated from the mare (n = 2), there was no significant association between resumption of suckling and oxytocin release by the mare. The results of these studies show that suckling is not significantly related to oxytocin release in mares^{58,221}. This is an interesting finding when one considers the process of uterine involution in mares with a stillborn or non-vital foal.

References:

A detailed list of citations (250 references) is available from the author (frazier.6@osu.edu).