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PART I

The Foal

Section (a): Prepartum Assessment of the Foal

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Chapter 1

Identification of the High-Risk Pregnancy

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Introduction

Very few sights are simultaneously as placid and potentially unnerving to an equine clinician as contemplating a group of valuable broodmares in late-term pregnancy. While the majority of pregnancies end with a viable mare and foal, a small but very real percentage of pregnancies end in death or disability for dam or neonate. These high-risk pregnancies often do not show premonitory signs before real trouble begins, and are a challenge for horse owners, animal care personnel and veterinarians.

Considerable time and money are spent manipulating the mare's reproductive cycle to ensure conception and early foaling dates. Numerous sonographic examinations are performed early in the reproductive process to detect ovulation, coordinate insemination or breeding, implant embryos, confirm pregnancy, and rule out twinning. But after the first 45 to 60 days the typical broodmare does not receive close, routine scrutiny again until the last 4–8 weeks of gestation. Consequently many causes of abortion and fetal/neonatal morbidity and mortality during the latter two-thirds of pregnancy remain poorly understood.

Several large retrospective necropsy studies[1,2] have examined the causes of abortion, stillbirth, and perinatal death in horses. Placentitis, due to bacterial, viral and fungal causes, and delivery complications associated with dystocia, birth trauma, and asphyxia represented the most common causes of fetal and neonatal foal mortality.

Conditions that cause high-risk pregnancy can originate in the mare, fetus or placenta. While some situations defy identification before crisis, many can be detected, and intervention can be instituted. As we learn more, treatment is improving the outcomes of equine high-risk pregnancies. Successful intervention in high-risk pregnancy will require identification of risk at the earliest possible time, and is the goal of the equine perinatologist.

Conditions that cause risk to the mare and foal can be subdivided into conditions of the mare, the foal, and the placenta (including umbilical cord) (Tables 1.1–1.3). While these categorizations are not absolute, analyzing them in this way can demonstrate trends in diagnosis and prognosis. In general, maternal conditions are discovered by the clinical signs a mare exhibits and by physical examination. Pain, whether abdominal or lameness, is a frequent component. Assuming appropriate therapy, the risk to the mares' health for maternal conditions is largely determined by the severity of the disease. The fetus is affected in parallel by the maternal systemic condition and potentially by the drugs and therapies administered to the dam. For lameness, unless it is debilitating, the impact is usually minimal, but for conditions with a systemic maternal component, the risk to the foal is roughly an order of magnitude greater for the foal than the mare. Our experience is that most preterm deliveries are the result of fetal death, and the fatal insult usually involves interference with the transfer of nutrients and oxygen and the removal of waste at the placenta.

Placental and umbilical conditions range from clinically silent to those easily detected by an experienced clinician. The most common premonitory signs of placentitis are premature lactation and vulvar discharge, but pregnancies affected with hydrops allantois will present with an abnormally enlarged abdomen, a small fetus, and some degree of abdominal or respiratory distress. Most placental conditions pose little risk to the mare (hydrops being the notable exception) but all pose significant risk to the fetus.

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Table 1.1 Maternal conditions causing high-risk pregnancy, most common clinical signs, and risk estimate to mare and foal

Maternal condition	Premonitory clues	Risk to mare	Risk to foal
Visceral colic	Abdominal pain	Varies with severity of disease	Mild to moderate
Uterine torsion	Abdominal pain, rectal palpation of torsion	Mild to moderate	Moderate to severe
Endotoxemia	Fever, elevated heart rate, dehydration	Varies with severity of disease	Moderate to severe
Laminitis	Lameness	Varies with severity of disease	Mild
Other severe lameness	Lameness	Varies with severity of disease	Usually mild
Abdominal wall injury	Pain, swelling of ventral or lateral abdomen	Varies with severity of disease	Moderate to severe
Infectious disease	Fever, renal, respiratory signs	Usually minimal	Moderate to severe
Misshapen pelvis	Rectal exam reveals compromise to pelvic inlet	Minimal, but can be severe from dystocia	Moderate to severe
Poor quality endometrium	None	None	Moderate to severe

The detection or prediction of fetal conditions causing high-risk pregnancy fall into two categories, those predictable by historical information about the previous pregnancy or suspicious signs during the current pregnancy and those rarely detected or not detectable at this stage of our knowledge. Maternal risk from these conditions is either none or very serious, and the risk to the foal is often severe.

Any mare at risk for a complicated pregnancy or delivery should have a minimum data base established (Table 1.4) that includes a thorough history, general physical examination, and reproductive tract evaluation. Sonographic evaluation and serial monitoring of the fetus, uterus, and placenta is also recommended. Additional tests are performed as indicated by the primary underlying condition.

Conditions that can cause high-risk pregnancy

Maternal conditions

Gastrointestinal causes of colic

Most colic episodes that occur during pregnancy are mild and resolve with no or minimal treatment. These episodes pose little danger to either the mare or her pregnancy, although frequent episodes, even if mild, can be a cause for concern. Pregnancy can complicate the determination of the best course of therapy for a mare with colic in late pregnancy, as the large uterus and fetus make effective rectal palpation impossible. The pregnant uterus can similarly make obtaining a diagnostic abdominal fluid sample difficult. Transabdominal ultrasonography can be helpful in location of a site for abdominocentesis and for the diagnosis of a cause for colic, but the large uterus also complicates this diagnostic test, and in a late pregnant mare the decision for surgery is often made based on pain and the response to analgesics, presence of reflux, and lack of fecal passage.

Colic that requires surgery but is swiftly resolved is likely to have minimal impact on fetal outcome during most of gestation.[3,4] An exception is a mare with colic in late-term pregnancy, when placental oxygenation is both critical and vulnerable.[3] Hypoxia in the last 60 days of pregnancy results in poorer fetal outcomes for those dams than mares without hypoxia.[3] Short surgical times, appropriate ventilation, and oxygen insufflation can help to promote delivery of oxygen to the fetus; however, in some cases, maintaining appropriate oxygenation is not possible.

Table 1.2 Placental or umbilical conditions causing high-risk pregnancy, most common clinical signs, and risk estimate to mare and foal

Conditions of placenta or umbilicus	Premonitory clues	Risk to mare	Risk to foal
Infectious placentitis	None, premature lactation, uterine discharge	No direct risk. Indirect risk from dystocia	Moderate to severe
Premature placental separation	Occasionally premature lactation, rarely hemorrhage	No direct risk. Indirect risk from dystocia	Moderate to severe
Fescue toxicosis	Prolonged gestation, failure of lactation	No direct risk. Indirect risk from dystocia	Severe
Umbilical abnormalities	None	No direct risk. Indirect risk from dystocia	Severe
Hydrops allantois	Severe abdominal enlargement due to uterus	Severe	Severe
Placental insufficiency	Possibly prolonged gestation	None	Moderate to severe

Table 1.3 Fetal conditions causing high-risk pregnancy, most common clinical signs, and risk estimate to mare and foal

Conditions of the foal	Premonitory clues	Risk to mare	Risk to foal
Neonatal isoerythrolysis	Historical production of NI foal; testing for antibodies	None	Moderate to severe
Twins	Twins detected post breeding	Moderate to severe	Moderate to severe
Fetal malformation	None	Moderate to severe	Severe
Arthrogryposis	None	Moderate to severe	Severe
Fetal malpresentation	None	Moderate to severe	Moderate to severe
Mare reproductive loss syndrome	None	Minimal	Severe

Pregnancies continuing after any surgery should be considered as at-risk and should receive extra scrutiny, but those in which intraoperative oxygenation was poor should be considered at 'high risk.' This determination necessitates more aggressive antepartum evaluation of the fetus and placenta in the postoperative treatment period, which is discussed in detail in Chapters 2 and 4.

Table 1.4 Data base for high-risk pregnancies

Signalment of mare
Age
Breed
Parity

Past reproductive history
Outcome of past pregnancies; if abnormal, was the cause prepartum, intrapartum, or postpartum in origin
Length of gestation(s)
Description of periparturient behavior
Results of last uterine biopsy/culture

Current general health and reproductive history
Vaccination history, deworming regimen, diet
Description of current medical/surgical conditions
List of medications administered during pregnancy
Date last bred; 340-day due date
Presence of vulvar discharge, premature udder development or lactation

Prepartum evaluation and monitoring
Physical examination with vital signs
Bodyweight
Rectal palpation to assess cervix, gravid uterus
Vaginal examination (only if clinically indicated)
Transrectal ultrasonography to evaluate pericervical utero-placental integrity, fetal fluid clarity, fetal activity
Transabdominal ultrasonography to evaluate fetal heart rate (range and reactivity), breathing movements, tone, position and size, fetal fluid clarity and volumes, utero-placental integrity
Maternal complete blood count/serum biochemistries
Serial monitoring of progestagen (progesterone) concentrations
Mammary secretion electrolyte concentrations
Frequent evaluation of pelvic ligament relaxation, udder development, vulva elongation
Regular observation for signs of parturition

Endotoxemia

Endotoxemia resulting from colic is a separate but very important concern. Pregnant mares that show clinical or laboratory signs of endotoxemia such as fever, tachycardia, dehydration, leukopenia, and peripheral vasodilatation/hypotension or cyanosis are at great risk of fetal compromise. Quick resolution of the primary condition is paramount and, when that is not possible, mares should be closely monitored for fetal distress or death. Clinical signs of endotoxemia in pregnant mares with colic are associated with poor fetal outcomes[3,4] and all pregnant mares, after treatment of colic, should undergo fetal ultrasonography periodically while hospitalized. Similarly, endotoxemia resulting from other conditions such as pleuritis, pneumonia, colitis, and peritonitis will have a negative impact on the fetus and should engender similar concern and scrutiny.

It is the author's (EMS) observation that pregnancies in mid-gestation are the least susceptible to the effects of endotoxin. An explanation may be that endogenous prostaglandin release as a result of experimental endotoxemia can cause luteolysis and abortion in early pregnancy,[5] and in late pregnancy may compromise uterine perfusion by initiating excessive uterine contractions.

Uterine torsions

Uterine torsions occur in mid to late gestation and the primary clinical sign is abdominal pain. Mares with uterine torsions usually exhibit mild to moderate pain, and some will continue to pass feces despite discomfort.[6,7] Diagnosis of uterine torsion is made by rectal palpation. On rectal palpation, affected mares will have a tight broad ligament that runs vertically on the side that the uterus is twisted towards, and a tight broad ligament dorsal to the uterus on the side from which the uterus is twisted away. Vaginal palpation is of minimal diagnostic value since the cervix and vagina are rarely involved in uterine torsion in mares.

When the diagnosis of uterine torsion is made, a high-risk pregnancy is identified. Survival rates for mares (97%) and foals (72%) are better if the torsion occurs at less than 320 days of gestation, and worse (mares 65%, foals 32%) when the torsion occurs at 320 or more days of gestation.[7] Torsions greater than 180° increase the risk of compromised utero-placental blood flow and subsequently fetal oxygenation. If torsion occurs at term, it is usually associated with dystocia. Uterine rupture with subsequent septic peritonitis is the leading cause of maternal fatality.[8]

Lameness

Laminitis and other lamenesses are fairly common in broodmares, and the impact of the musculoskeletal problem on the pregnancy is thought to be relatively minimal. However, some indirect factors associated with the management and treatment of severe lameness may have an effect. The administration of medications is often implicated in the delivery of small or weak foals, but the effect of drugs is largely speculative. Less tangible factors such as poor appetite, a lack of exercise and social herd interaction, and the stress of disability probably contribute to poor fetal outcomes.

Abdominal wall injuries

Disruptions of the abdominal tunic most commonly occur in late pregnancy, and presumably are at least partially the result of the expanding uterine mass and volume. Tears occur in the prepubic tendon and the muscular portions of the abdomen[9,10] and are more common in older, multiparous mares. The condition is more prevalent in draft and heavier breeds and unfit horses, although prepubic tendon rupture and/or defects in the rectus abdominis musculature have been reported in lighter breeds including Arabians and ponies. Conditions that cause severe distention of the body wall such as hydrops, twinning, severe ventral edema or body wall trauma may result in rupture of the prepubic tendon or abdominal wall hernia.

This is a serious injury to the mare that results in pain, difficulty moving, and warm, painful edema and swelling of the affected portion of the ventral abdomen. Severe cases are depressed, tachycardic, tachypneic, and off-feed. Affected mares frequently assume a 'sawhorse' stance and are reluctant to move. Signs of shock and colic may develop if peritonitis and/or internal hemorrhage develop. If injury to the prepubic tendon is severe, the iliosacral joint dorsiflexes, resulting in an elevated tail head and tuber ischii, and lordosis of the thoracolumbar spine. The ventral aspect of the abdomen extends more ventrally, the mammary gland flattens, and the teats tip caudally. There can be hemorrhage from the teats.

The diagnosis of hernias and thinned areas of the abdominal wall can be appreciated by external and rectal palpation. Transabdominal ultrasound can confirm rents in the abdominal wall. Abdominal tunic injuries result in a high-risk pregnancy largely because of the risk to the mare. The abdominal disruption itself is painful, and further colic can result from viscera becoming entrapped in the abdominal wall hernia with the development of intra-abdominal adhesions and peritonitis. Direct risk to the fetus is moderate, and can be evaluated by ultrasonic examination of the fetus and placenta.

All mares with abdominal wall tears should be evaluated for hydrops of the fetal membranes, a condition that worsens the fetal prognosis. A small retrospective study reported a 75% short-term survival rate for mares and about a 50% survival rate for foals.[10] This is impressive, and is superior to the authors' experience. Successful treatment is directly related to the amount of abdominal wall damage and internal abdominal trauma; when damage is extensive the risk for both mare and foal is significant.

Miscellaneous infectious agents

Several infectious agents have been shown to cause equine abortion and include equine herpesvirus 1 (EHV-1), leptospirosis,[1,11] and equine viral arteritis (EVA). Selected causes of infectious equine abortion are listed in Table 1.5.

Equine herpesvirus 1 (EHV-1) is capable of causing abortion during the last 4 months of pregnancy, as well as respiratory disease and meningoencephalomyelitis. EHV-1 produces a latent infection in at least 80% of the horses it infects. Latency is established in circulating lymphocytes and the trigeminal ganglion. Broodmares may become infected from new arrivals shedding virus in their respiratory secretions, or from stress-induced reactivation of their own latent herpesvirus within the blood vessels of the uterus or placenta, resulting in endothelial cell infection and thrombo-ischemia in those organs.[12–14] This cell-associated viremia has an affinity for endothelial cells and has been shown to cause abortion in one of two ways: (i) infection of the placental vasculature, resulting in ischemic insult and placental insufficiency, premature placental detachment, and abortion of a virus-negative fetus; and (ii) infection of the fetus resulting in fetal demise and abortion of a virus-positive fetus. Mares affected by EHV-1 can abort during late pregnancy or deliver weak, compromised foals prematurely or at term.[15] Stress from shipping or overcrowding is considered to be a contributory factor to the occurrence of abortion.

Table 1.5 Selected infectious causes of equine abortions

Infectious agent	Clinical signs	Diagnostics
EHV-1	No premonitory signs; abortion during last trimester; aborted fetus is fresh with minimal autolysis; hydrothorax, hydroperitoneum; multifocal hepatic necrosis	Fetal tissues (liver, lung, thymus): histopathological findings of intranuclear inclusions; fluorescent antibody test (FAT) positive; virus isolation
Leptospirosis	Mild disease in mares; uveitis; abortion follows mild illness by 1–3 weeks; abortions usually occur ≥ 6 months of gestation	Leptospires in fetal fluid or blood; dark-field or phase-contrast microscopy; FAT; PCR; MAT; paired sera titers; *L. pomona kennewicki* is the most prominent pathogenic serovar in horses
Potomac horse fever	Mare experiences varying degrees of illness due to PHF (fever, colitis, laminitis) 2–4 months prior to abortion	Fetuses have increased volume of feces within small and large intestines; liver discoloration; histopathological findings: lymphohistiocytic enterocolitis, myocarditis, periportal hepatitis; *N. risticii* recovered by cell culture from fetal bone marrow, spleen, colon, liver; PCR
Nocardioform	Sporadic abortions usually during late gestation (8–11 months); premature lactation; gross changes in portions of placenta occupying base of uterine horns or cranial uterine body	Culture placenta, fetus and uterine discharge; bacteria grow slowly on blood agar
Equine viral arteritis	Rare outbreaks of respiratory disease with subsequent abortion; abortion can occur with no visible illness in mare	Fetus often autolytic; necrosis in media of small arteries; fetal tissues – FAT, virus isolation; rising VN titers in mares obtained 1–2 weeks apart

Aborting mares often do not show any premonitory signs, although the EHV-1 strain responsible for abortion is also implicated in herpesviral myelitis outbreaks. The fetus and placenta are usually grossly normal. High levels of virus can be found in fetal tissues and placenta, and infected mares can shed EHV-1 virus in their reproductive tract secretions for as long as 3 weeks following abortion. Confirmation of EHV-1 as the abortigenic agent often is by demonstration of the virus by culture or polymerase chain reaction (PCR) and immunohistochemical identification of intranuclear inclusion bodies in fetal and placental tissues.

Leptospirosis can be a significant cause of equine abortion, with recent studies claiming 1.5–5.9% of equine abortions are related to leptospirosis.[11,16] Although multiple serovars have been associated with abortion, among the most common serovar is Pomona type kennewicki.[17] Horses are considered incidental hosts for most serovars of *Leptospira*, but may act as maintenance hosts for *L. interrogans* serovar *Bratislava*.[18–22] Leptospiremia, resulting in vasculitis, precedes infection of the reproductive organs, and in pregnant mares can cause fetal resorption, abortion, stillbirth or full-term delivery of weak neonates. Leptospiral abortions typically occur in middle to late gestation. Placentas are frequently thickened, edematous, and hemorrhagic with the chorionic surface appearing brown and mucoid.[16] Aborting mares may not show any premonitory signs of disease and yet still mount a high antibody titer. When present, systemic signs in the dam can include fever, anorexia, listlessness, icterus and laboratory evidence of renal disease.[11] Uveitis may develop a variable period of time post-exposure.

Most aborting mares have titers to multiple leptospiral serovars and these titers do not necessarily correspond with the cause of the abortion.[23] Many mares will have titers indicating exposure to these infectious agents and not abort, but rising titers or extremely high titers ($\geq 1:100\,000$) to *L. interrogans*[18] indicates infection. Confirmation of the etiologic agent is made on examination of aborted fetal tissues, and in the case of *Leptospira*, can be made by detecting the agent in mare urine. Culture, dark-field microscopy, immunohistochemical staining, PCR, and fluorescent antibody testing (FAT) are some of the techniques used to identify *Leptospira* in fetal tissues and fluids.[11]

Equine viral arteritis (EVA), another potentially abortigenic virus, is transmitted between horses primarily through either respiratory or venereal routes.[24] Abortion, when it occurs, is usually not preceded by any premonitory signs in the broodmare and may occur any time from 3 months to over 10 months of gestation.[24,25] Clinical signs, when they occur, include pyrexia, depression, anorexia, conjunctivitis and rhinitis, periorbital edema, edema of the ventrum, mammary gland and hindlimbs, and urticaria.[24,25] Diagnosis is based on virus isolation, indirect immunohistochemistry, and PCR performed on

fetal and placental tissues or nasopharyngeal swabs from the affected dam.[24,26]

Another pathogen that may not be thought of as an abortigenic agent is *Neorickettsia risticii*, the causative agent of Potomac horse fever (PHF). PHF can cause colitis and laminitis in horses, and occasionally causes abortion in mares around 7 months of gestation.[27] In experimentally infected mares, abortion occurred 65–111 days after inoculation,[28] which might allow this pathogen to be forgotten as a possible cause of pregnancy loss by the time a mare aborts following initial infection. Transplacental transmission of *N. risticii* has been reported in natural infections, and the organism can induce fetal resorption, abortion, or cause the delivery of weak foals.[29]

Any pregnancies exposed (airspace for the viruses, water, feed and urine for leptospirosis) to horses affected by these conditions should be considered at high risk. Risk to the mare infected with these agents is variable. Mares affected with EHV-1 and EVA experience mild risk, but systemic effects of leptospirosis raise the risk to moderate levels due to possibility of renal insult.

Pelvic abnormalities

Mares that have had pelvic injuries that result in a diminution of the pelvic inlet can have serious difficulty in delivery. The diagnosis of the condition is made during rectal palpation, and risk is assessed by the amount of encroachment on the pelvic inlet. Dystocia would result in severe risk to the foal and moderate to severe risk to the mare.

Endometrial insufficiency

A poor-quality endometrium can result in a high-risk pregnancy because of poor delivery of nutrients and disposal of fetal waste. This can result from uterine scarring, endometrial atrophy, or surgical removal of portions of the uterus. Foals gestating in this environment can be poorly nourished, and grow poorly, and often have prolonged gestations. In severe cases, abortion can result if a fetus outgrows its nutrition. Premonitory signs are most commonly a previous history of small foals and prolonged gestation, but could include treatment of uterine infection and severe dystocia. There is little risk to the mare, but fetal risk with a poor-quality endometrium is moderate to severe.

Miscellaneous

The most serious insults to the fetus are those that interfere with perfusion of the placenta or the delivery of nutrients and oxygen and removal of waste products. A healthy placenta is critical to delivery of a healthy foal.[30] Conditions that result in hypoxemia, hypovolemia, hypotension or toxemia (including endotoxemia) can all have a negative effect on the fetus. Examples of uncommon conditions that would affect the pregnancy include heart failure, severe chronic obstructive pulmonary disease, upper respiratory obstructions, severe hemorrhage, and renal failure. Diagnosis of these conditions in a pregnant mare should increase scrutiny of the fetus. Risk to both mare and foal will depend on the severity of the underlying disease.

Placental conditions

Placentitis

Infection of the placenta is a common condition, and can be caused by bacteria, viruses or fungal elements.[1] Bacteria are the most common cause of placentitis with *Streptococcus equi* subspecies *zooepidemicus*, *Escherichia coli*, *Klebsiella* spp, *Pseudomonas* spp, and *Staphylococcus aureus* most often implicated in disease. Mares rarely show clinical or laboratory evidence of systemic infection. The condition is usually well-established before diagnosis, and can be clinically silent until abortion. More frequently, mares will show premature mammary gland development, lactation, and vulvar discharge.[31–33] Most infections are ascending,[34] although hematogenous infection can occur. Mares are typically affected during the last trimester of pregnancy. Infecting pathogens disrupt the contact between allantochorion and endometrium, resulting in placental separation that begins at the cervical star and dissects cranially along the body of the uterus. A speculum examination of the caudal reproductive tract will often reveal loss of the cervical plug and uterine discharge, which will sometimes be apparent at the vulva. Transrectal or transabdominal ultrasound of the uterus and conceptus will often reveal thickening of the caudal segment of the placenta and uterus, separation of the placenta from the endometrium, and pus between uterus and placenta.[35,36] Gram stains and culture of uterine discharge can establish the infectious agent.

Placentitis that involves more cranial segments of the placenta can be difficult to image. Several fungal elements classified as nocardioform invade the base of the gravid horn,[37] and can be difficult to detect. The limitation of transabdominal ultrasound is that not all of the placenta can be imaged. In these cases, placentitis is suspected, based on the presence of premature lactation. In mares with precocious mammary development, it is important to exclude the presence of twins, using ultrasound. Twin pregnancies will often present similarly, but require different risk

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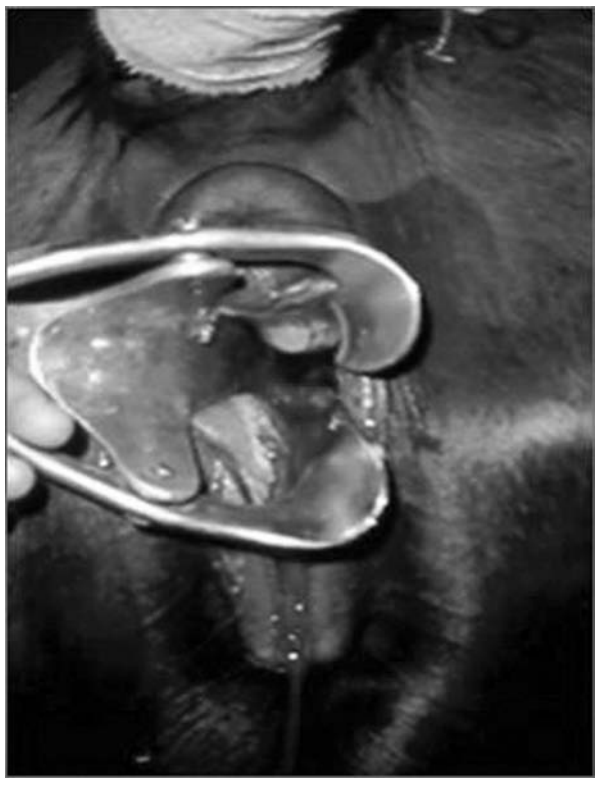

Figure 1.1 Speculum examination of a mare with a hemorrhagic vaginal discharge associated with diffuse premature placental separation.

assessment and therapy. There is little risk to the mare affected with placentitis, and fetal risk is difficult to estimate. Anecdotal evidence suggests that approximately 75% of pregnancies end with delivery of a live foal.[38,39] It is the authors' experience that better outcomes occur when clinical signs occur later in gestation and when there is a quick reversal of mammary development in response to appropriate therapy.

Premature placental separation

Occasionally, premature placental separation can occur without evidence of placental infection. Clinical signs are similar to placentitis, and in addition, occasionally uterine hemorrhage can be seen (see Figure 1.1). The diagnosis is made on clinical signs and ultrasonic examination of the uterus. Risk to the mare is low, and fetal risk is related to the amount of placenta affected.

Prolonged gestation

The mare's reported range of 'normal' gestation lengths is quite elastic, with some references describing normal pregnancies lasting for up to 374 days or longer. Therefore it is difficult to define what constitutes a post-term pregnancy by days of gestation alone. Once human error and miscalculation of the foaling date and/or inaccurate breeding date have been ruled out, other causes of prolonged gestation length include fescue toxicosis, delayed embryonic development, severe maternal malnutrition, and other ill-defined hormonal imbalances including a syndrome described in Western Canada associated with congenital hypothyroidism and dysmaturity.

Duration of gestation is partly controlled by a number of factors. Colts tend to have longer gestation lengths than fillies. Mares due to foal earlier in the year may have longer gestation lengths due to the shorter photoperiod. Older mares tend to have longer gestations.

Fescue toxicosis

Fescue toxicosis, an intriguing model of maternal and fetal disease, is the result of mares eating fescue grass infested with a fungus (*Acremonium coenophialum*) that elaborates a mycotoxin that interacts with dopamine receptors. Dopaminergic stimulation results in decreased prolactin secretion. Prolactin plays an active role in the endocrine regulation of steroidogenesis and lactogenesis.[40] The initiation of parturition in the mare involves proper maturation and function of the fetal hypothalamic–pituitary–adrenal (HPA) axis.[41] Prolonged gestation length associated with fescue toxicosis may be due to hypoprolactinemia-induced changes in utero-feto-placental steroid metabolism or may be due to inhibition of D_2-dopamine receptors on corticotrophs in the fetal anterior pituitary gland.[40,41]

In the mare, fescue toxicosis is characterized by an unreadiness-for-parturition leading to prolonged gestation, abortion, dystocia and agalactia accompanied by placental abnormalities that include premature placental separation, thickening and edema.[42] In the foal an unreadiness-for-birth is associated with an increased incidence of sepsis, peripartum asphyxia syndrome, failure of passive transfer, dysmaturity, and birth of weak foals with failure 'to adapt' following delivery.[42–45] Late-term mares grazing endophyte-infected tall fescue demonstrate decreased concentrations of prolactin and relaxin[43,45–47] and fail to exhibit the normal late gestational surge in progestins.[43,46,48] Some studies report increased levels of estrogens and decreased levels of thyroxine (T_4)[50] in exposed mares. Foals exposed to ergopeptine alkaloids during late gestation have decreased plasma levels of immunoassayable progestins, cortisol, T_4, and tri-iodothyronine (T_3).[43,51]

Mares should not be exposed to fescue infected with the endophyte at all, but at a minimum should be removed from infected pastures for the last 30 to

60 days of gestation. Mares exhibiting toxicity are at great risk from dystocia, as is the fetus. Identification of the condition is made by determining the grass in pasture.

Umbilical cord abnormalities

Approximately 3% of aborted and foals born dead at term are associated with abnormalities of the umbilical cord that include edema, torsion, sacculations, strangulations, and over-long cords.[1] These disorders are virtually impossible to predict before delivery, and risk is assessed in retrospect. Average cord length in Thoroughbreds is between 36 and 83 cm. Unusually long cords (>80 cm) have been associated with hypoperfusion of the allantochorion and may be prone to cord torsion, which may contribute to fetal strangulation, hypoxia, death, and abortion. Excessively short cords place increased traction on the placenta during delivery and may predispose to premature placental separation. Not all abnormalities cause fetal compromise, but should increase scrutiny of an affected live foal so that any necessary intervention can occur without delay.

Hydrops of the fetal membranes

Hydrops refers to the overproduction of fluid into either the amniotic or allantoic cavities (hydrallantois or hydramnion). Both conditions are rare, but hydrallantois is the more common of the two. Clinical signs associated with hydrops typically develop in the last trimester after an otherwise uneventful pregnancy. Although the pathophysiology of this condition is poorly understood, there are multiple causes that can result in either increased production or decreased clearance of fetal fluids, and include fetal defects, placental disease, and umbilical cord abnormalities. The increased volume of fetal fluids results in maternal anorexia, tachycardia and tachypnea, dyspnea, depression, colic, decreased manure production, difficulty walking, and marked ventral edema. Advanced cases may develop ventral abdominal hernia or prepubic tendon rupture. Suspicion of the condition is raised when there is a dramatic increase in abdominal distention in a later-term mare, that results in the mare having difficulty moving, eating or breathing.[31]

Diagnosis is made by rectal palpation of the uterus, which will be grossly fluid-filled, and the fetus will be difficult to palpate. Transabdominal ultrasound of a mare affected by placental hydrops will also reveal a massively fluid-filled uterus. Hydrops when severe can result in damage to the maternal abdominal tunic, causing uterine rupture, abortion, and retained placenta. At delivery, the expulsion of fluid can cause hypovolemic shock. For most patients, severe risk would be assigned to both mare and foal, although two reports of hydrops record live foal deliveries (one long-term survival) and mare survival after treatment of hypovolemic shock after delivery.[52,53]

Clinical signs of hydrops allantois include an enormous increase in abdominal size over 10 to 14 days due to rapid accumulation of allantoic fluid. Mares with hydramnion develop less dramatic abdominal distention over a more prolonged time course of weeks to months.

Palpation per rectum reveals a large, fluid-distended uterus. It is often difficult or impossible to feel the fetus. The condition is confirmed via transabdominal ultrasonography. A large volume of clear fetal fluids is observed. Hydrops allantois tends to be more life-threatening for the mare due to its rapid onset and the excessive volume of fluids that accumulate (sometimes in excess of 100 L). The fetus may be normal in some of these pregnancies, but fetal survival depends on how late in the pregnancy the condition develops and how successfully the mare is supported during labor. Subsequent pregnancies can be normal.

Placental insufficiency

Placental insufficiency is a poorly defined condition and is often a histological diagnosis of exclusion. The result of placental insufficiency is inadequate fetal nutrition, and the cause is believed to be a compromised endometrium that does not allow attachment of a robust placenta. The inability to attach to healthy endometrium results in a small and poorly developed (avillous) placenta. Fetuses can be aborted due to placental insufficiency, but are also born small, underweight even for their small size, and dysmature (fine hair coats, weak musculoskeletal systems, immature cardiovascular and gastrointestinal systems). This diagnosis is often made in retrospect, although historical information can be useful, as mares tend to deliver dysmature foals repeatedly. Risk to the mare from placental insufficiency is minimal, but is moderate to severe for the foal.

Fetal conditions

Neonatal isoerythrolysis

Hemolytic anemia occurs in horse and mule foals that absorb maternal immunoglobulins in colostrum that contains antibodies that bind to the foal's erthrocytes.[54] Mares at greatest risk for producing foals affected by neonatal isoerythrolysis (NI) lack certain red blood cell antigens. Aa and Qa are most commonly implicated alloantigens, but others are also

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sometimes responsible.[55] Mares are exposed to foreign blood types by a previous pregnancy, and those carrying mule foals appear to be at increased risk. The greatest risk exists in mares that have previously produced an NI foal. The diagnosis of NI is made after birth by a positive Coombs test (antibody attached to erythrocytes), but the risk can be determined before birth by testing the mare for the presence of anti-erythrocyte antibodies in the mare serum, and should be performed in all mares that have produced NI foals. In such mares, the condition can be prevented or predicted by screening stallions for blood types that are compatible with the mare's immune status. There is no risk to the mare in this condition, but the risk to the foal is severe.

Twins

Twinning is a common condition in the Thoroughbred mare, and also occurs in other light horse breeds. Twinning results in high-risk pregnancy because the fetuses are often aborted and because, if carried to term, dystocia can occur and result in maternal reproductive tract trauma and even death. The mortality rate for twins is almost 90%.[56] Most twins are diagnosed early in pregnancy and either one or both vesicles are eliminated by veterinarians or naturally by the mare. This early pregnancy loss causes no risk to the mare. Twin pregnancies become a greater issue once past the stage of possible natural reduction (about 40 days of gestation),[57] although natural reductions at a later stage of gestation can occur. The diagnosis of twin pregnancy can be made by detecting a large uterus by rectal palpation, and is confirmed by transrectal or transabdominal ultrasound. At the later stages of gestation, diagnosis can be challenging, because the hearts of both fetuses cannot be obtained in one image, and care must be taken to assure that there truly are two fetuses present. If not aborted when small, twin pregnancies pose a moderate risk to the mare and a severe risk to both foals. The risk is due to the possibility of preterm birth and dystocia.

Fetal malformations, arthrogryposis, and fetal malpresentations

Fetal abnormalities such as schistosomas reflexus, arthrogryposis, and hydrocephalus cause high-risk pregnancy due to risk to the foal because these conditions are inconsistent with life, and to the mare because they cause dystocia. These conditions are almost never diagnosed before delivery. Possibly these conditions could be diagnosed antepartum by transabdominal ultrasound, but that level of scrutiny, routinely given to human fetuses, is rarely afforded to the horse. These conditions are diagnosed during the second stage of parturition when they result in dystocia.

Fetal malpresentations

Malpositioning of the fetus causes high-risk pregnancy to the fetus because of the potential for asphyxia due to a prolonged stage 2 labor, and the potential for damage to the mare's reproductive tract.[58] Most malpositionings occur during delivery, so could not be diagnosed before delivery began. An exception is a breech presentation, which is rare, but can be diagnosed via ultrasound in late pregnancy, by observing a caudal presentation after the time a fetus can no longer turn in the uterus. Malpresentations are diagnosed by direct fetal palpation through an open cervix, although the entire fetus cannot always be palpated. Some malpresentations such as 'dog-sitter's' (dorso-sacral presentation with flexed hindlimbs that cause impingement of the hind fetlocks in or on the pelvis) only become apparent as the fetus is in the process of delivery.

Mare reproductive loss syndrome

During the spring of 2001, veterinarians reported an outbreak of early fetal losses at about 77 days of gestation (approximately 25% of mares),[59] later-term abortions, and birth of weak foals in central Kentucky. The cause of the syndrome was obscure, and is still not totally elucidated, but a risk factor was access to pasture.[59] Pathological examination of aborted fetuses was not pathognomonic and revealed a range of findings, most commonly pulmonary lesions, placentitis, and funisitis (umbilical inflammation).[60] *Actinobacillus* and *Streptococcus* could commonly be cultured from tissues. The syndrome could be reproduced by feeding the Eastern tent caterpillar (ETC) to pregnant mares between 40 and 80 days of gestation, [61] but the specific toxic principle has not been elucidated. A recent review of the syndrome supports the hypothesis that, following ingestion of the ETC, the setae (bristles on the skin) inbed into the submucosa of the horse's alimentary tract and create microgranulomtous lesions that permit translocation of gut bacteria into the bloodstream.[62] The bacteria (most commonly incriminated are *Streptococcus*, *Actinobacillus* and *Enterococcus* spp) establish infections in distant locations, including the fetus and placenta, where the immune surveillance of the mare is reduced.[62] Identification of the syndrome can be made immediately before abortion by observing hyperechoic allantoic fluid (J.P. Morehead, personal communication, 2001). The strongest risk factor is access to the Eastern tent caterpillar,[63] which is not confined to central

Kentucky. Risk to the mare is minimal, but risk to the fetus is severe.

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