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PREGNANCY COMPLICATIONS AND EVALUATION FOR FETAL WELL-BEING

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Introduction

Any medical event or complaint occurring during pregnancy raises two major questions; 1) Is the problem genital in origin or directly related to the pregnancy?, 2) what will the effects be on the viability of the fetus?. During the last 25 years the authors have examined 434 mares presented for medical complications during pregnancy. The most common complaints were colic (61%), premature lactation (33%), abnormal vaginal discharge (3%), abnormal abdominal development (2%) and abnormal ventral abdominal wall (1%).

In addition to thorough clinical evaluation of the mare, monitoring fetal health during pregnancy is necessary in order to give an accurate prognosis. Recent clinical research has focused on establishing norms for various indicators of the fetal well-being. Evaluation of mares in mid to late pregnancy is indicated in presence of vaginal discharge, premature mammary gland development and lactation, following medical or surgical emergencies, suspicion of fetal fluid hydrops, overdue mares, and following correction of uterine torsion.

The aim of the present paper is to review the techniques used to monitor fetal health and the major complications of pregnancy in the mare.

Evaluation of the high risk pregnancy

Assessment of fetal health requires measurement of heart rate, size, movements and tone of the fetus, thickness of the fetal membranes, echogenicity and quantity of the allantoic and amniotic fluids [74]. Fetal heart evaluation requires the use of 2.5 or 3.5 MHz transducers for a penetration of up to 30 cm [42, 48]. A 7.5 MHz linear transducers is used to evaluate the uteroplacental unit [48]. Sector scanners are preferred in the evaluation of large fetuses. Sedation of the mare should be avoided if possible so that fetal movements and activity would not be affected. In the last trimester of pregnancy, the fetus is generally in cranial presentation lying in the sagittal plane or dorso-pubic position [42, 48].

Fetal and placental evaluation

Fetal heart rate (FHR)

FHR can be monitored by ultrasonography (preferred method) or by electrocardiography when ultrasound is difficult. M-mode ultrasound is more accurate[9]. Fetal heart rate is usually at 1.6 to 1.8 times that of the dam. In early pregnancy FHR is 120 bpm, peaks to 196 minutes by 100 days and decreases slowly to about 60 bpm in the last couple of weeks [1, 76]. Fetal heart rate should be monitored for at least 10 seconds and taken both at rest and during fetal activity. Spontaneous fetal activity results in transient tachycardia (+ 25 to 40 bpm) for approximately 30 seconds [49]. Fetal activity and exacerbated heart responses occur 48 to 72 hours before parturition [1].

Fetal activity

Fetal activity is appreciated by the tone and quality of movements displayed by the fetus during examination [42, 47, 48]. Breathing, a normal activity in the fetus, can be observed if the diaphragm can be visualized [49].

Fetal Measurements

Biometric evaluation of the fetus provides information on growth pattern and health. There is a linear relationships between day of gestation and aortic systolic diameter, biparietal diameter, eye volume, and
kidney cross sectional area from day 100 until parturition [50]. The systolic aorta diameter at the caudal border of the heart is a good estimator of fetal size and birth weight [48]. Fetal gender can be determined with high accuracy was determined to be between 100 to 220 days of pregnancy [51]. A 3.5 MHz transducer is necessary after 160 days of pregnancy. Visualized organs include penis and prepuce in males and mammary glands and teats and fetal gonads in females. Diagnosis of twins in mid to late pregnancy can be made by ultrasonography or suspected during electrocardiographic studies based on a perceived persistent tachycardia without other fetal or placental complications.

**Evaluation of the placenta and fetal fluids**

The amniotic membrane is recognized as a thin hyperechoic undulating membrane. Cysts may be seen in the amniotic membrane [47]. Maximum vertical depth of amniotic and allantoic fluid are 7.9 ± 3.5 cm and 13.4 ± 4.4 cm respectively, between 321 and 360 days of pregnancy [57]. The largest depths are located around the fetal thorax in the region of the elbow [57].

The uteroplacental unit is examined either by trans-abdominal (5 MHz) or by transrectal (7.5 MHz) ultrasonography to determined the combined utero-placental thickness (CUPT)[1, 48, 49, 52, 76]. In normal pregnancies, CUPT should be between 7.1 ± 1.6 mm and 11.5 ± 2.4 mm.[49] Transrectal evaluation is preferred because it helps detect early stages of ascendant placentitis at the cervical star region (3 to 5 cm cranial to the cervix). CUPT does not change between 4 and 8 months of pregnancy and should be <8 mm, <10 mm, and <12 mm respectively for mares at 271 to 300 days, 301 to 330 days and more than 330 days of pregnancy [1, 48, 49, 52, 76].

**Endocrinological evaluation**

Hormones reflecting placental activity are: progestins, oestrogens and relaxin. Progestins inhibit myometrial contractility,[10, 23, 26, 70] The main source of progestins beyond 80 days of pregnancy is the feto-placental unit.[22] Concentration of progesterone decreases and remains low in the second half of pregnancy then increases near term to peak 24 to 48 hours prior to parturition.[21, 23]

Estrone and equiline, a steroid unique to the pregnant mare, may play a role in the preparation of the uterus for delivery by potentiating production of PGF 2alpha and increasing the contractions of the uterus. Estrone sulfate was considered to be an indicator of fetal well being but proved to be unreliable. Estrone sulfate concentration decreases before abortion following medical or surgical colics or uterine torsion [37, 55].

Relaxin is produced by the placenta. Relaxin levels are lower in mares with clinical signs of placentitis and fescue toxicosis [54].

In the normal fetus, production of cortisol precedes the peak of maternal plasma concentration of progestins by 24 to 72 hours.[61],[60] Cortisol concentration of mares with colic that subsequently aborted was higher at presentation but not statistically different from mares that did not abort [55]. Equine alpha-fetoprotein, and alpha-globulin produced by the fetal liver may be found in high concentration in maternal serum in cases of placentitis, placental separation, uterine trauma and fetal death.[63] This test is however not readily available.

**Feature of placental pathology**

Placental pathology, particularly placentitis, is the most common finding in abortion[20, 24] and birth of dysmature or weak foals [29]. Increased CUPT (>13 mm) is associated with placental edema, impending premature placental separation, placentitis and delivery of abnormal foal. Placental pathology is also associated with fetal tachycardia. An increase in plasma progesterone concentration before 310 days of pregnancy has been associated with fetal stress and cortisol production due to placental abnormalities or placental separation [53]. Increased release of prostaglandins is also seen in compromised pregnancies. Pockets of hyperechoic fluids have been associated with nocardia form of placentitis.

**Features of fetal stress**

Persistent fetal tachycardia or brachycardia are signs of fetal asphyxia [1]. Fetal stress is usually concomitant with presence of progressively enlarging areas of placental detachment, and rapid drop of
progestins and impeding abortion [26, 53]. This is found in rhinopneumonia, maternal or fetal hypoxia, endotoxemia or starvation.[37, 55]

**Features of Fescue toxicosis**

This condition is characterized by increased utero-placental thickness, low plasma progesterone concentration, prolonged pregnancy, altered adrenal and thyroid function[5, 6] and decreased relaxin level.[54]

**Other fetal anomalies**

Fetal biometrics may be a valuable tool for the diagnosis of fetal abnormalities. Excessive amount of amniotic fluid, edematous and enlarged umbilical cord, reduced fetal activity and bradycardia have been reported in a case of hydrops amnii [58]

**Management of compromised pregnancies**

Progestin, NSAID (flunixin meglumine or Phenylbutazone) and broad spectrum antibiotics (Trimethoprim-sulfadiazine, Procain penicillin + Gentamicin, Ceftiofur) are administered to limit the effects of endotoxemia, placentitis, prostaglandin release and ensure myometrial quiescence and provide adequate nutrition and gas exchange to the fetus.

**Pregnancy complications**

**Placenta**

Causes of abortions have been reviewed extensively in several countries (UK[43, 62, 80], USA [20, 24, 25, 66-69], New Zealand and Australia [2], France [17, 77], Egypt [11], India [19]). Infections represent one third to one half of all causes of abortions [62]. Numerous organisms have been associated with infectious abortion including viruses, bacteria and fungi [62]. In England, Equine herpes viral abortion predominates [62]. In France, 79% of infectious abortions are caused by bacteria and 21% are cause by viruses [17]. In Morocco, most abortion storms are due to EHV-1 infection.

Placentitis is a significant cause of equine late term abortion, premature delivery and neonatal deaths [71]. Retrospective studies show that placenta is found in up to 50% of all abortion diagnosis work up [20, 24, 25, 45, 62, 81, 82]. Placentitis is caused by a variety of bacteria, fungi, viruses and protozoa [43, 44, 46]. Bacterial placenta is the majority of chronic bacterial infection whereas fungal placenta is reported in less than 10% of all cases of placenta [24, 25, 62].

Placentitis is generally classified in three types: ascending, diffuse, and focal mucoid [82]. With the expectation of Leptospira spp. most cases of bacterial or mycotic placenta are ascending infections [34, 69].

**Ascending placenta**

Ascending placenta is the most predominant type of placenta [71] [82]. In a retrospective study on 954 cases of equine abortion, placenta was diagnosed in 24.7% of all submission [25]. A bacteria or fungi was isolated in 68.6% of the placenta cases and 57.4% of all cases yielded bacteria both from the placenta and fetal organs. The most common microorganisms isolated include Strept. zooepidimicus, E. coli, Leptospira spp, Nocardioform actinomyces, Pseudomonas aeruginosa, S. equisimilis, Enterobacter agglomeran, Klebsiella pneumonia, alpha-hemolytic streptococci; Staphylococcus aureus, and Actinobacillus spp There is a wide geographic variation in the frequency of the bacteria and fungi isolated due to differences in climate and other environmental factors [71]

Bacterial placentitis induce abortion mostly between the 6 and 9 month of pregnancy. Fetoplacental infection occurs generally following opportunistic infection by organisms from the lower genital tract or immediate environment gain due to abnormal perineal conformation. Placentitis due to E. coli tends to cause later abortion and more stillbirths. Placentitis due to Strept. equi zooepidemicus, tends to be acute and focal or diffuse. In acute bacterial placentitis, the fetus is generally expelled before 8 months of pregnancy. Acute or diffuse placenta may not be easy to determine on gross examination of the placenta. Histological evaluation of the allantochorion may reveal bacterial emboli with necrosis of chorionic villi or infiltration of neutrophils in the intervillous space.
Chronic and/or focal placentitis causes mainly premature births of weak foals or late term abortions with varying degrees of severity. Lesions tend to be located at the cervical star where discoloration and thickening is observed.

E. coli placentitis tends to be acute in abortions before 7 months and more chronic and focally extensive and involved the cervical start after 9 months. Pseudomonas aeroginosa placentitis causes abortion between 6 and 9 months. This placentitis is mostly acute and either focal or diffuse. Thickened and discolored cervical star.

Lesions seen with infection due to S. Equisimilis are similar to those of S. equi Zooepidimicus and abortion occurs between 6 and 8 months of pregnancy.

Mycotic placentitis and abortion are observed mostly in the late gestational period. The most common isolates are Aspergillus, Mucorceous fungi, Histoplasma capsulatum, Candida spp, Mucor and Coccidioideoides (see review by Tibary and Fite [71]). Cryptococcus neoformans has been identified in cases of endometritis, ascendant placentitis and aborted 9 month old fetus.

**Hematogenous multifocal or diffuse placentitis**

Multifocal or diffuse placentitis is less commonly diagnosed and is associated with hematogenous spread of microorganisms to the uterus. This type of lesions is generally associated with leptospirosis, salmonellosis, histoplasmosis and candidiasis [25]. A special focal mucoid form of placentitis, Nocardioform placentitis, is emerging as a common type of placentitis in several regions of the USA [25].

Leprosyplana placentitis is characterized by its diffuse lesions due to hematogenous spread. Leptospirosis as a cause of placentitis seems to be more diagnosed in Kentucky reports [12, 13, 25, 82], than in other regions of the world [78, 80]. This is probably due to specific regional characteristics and the difficulty in isolating or detecting the pathogen. An outbreak of leptospirosis abortions has been described in a thoroughbred farm in California following a flood [28]. Most abortions occur between 6 and 9 months of gestation. The affected placenta is thick, heavy, edematous, hemorrhagic and occasionally covered with a brown mucoid material on the chorionic surface or lacked detectable gross lesions [71].

Nocardioform placentitis is a distinct type of equine placentitis that was first described in the USA in the late 1980s. Over the past decade and a half an increasing number of cases of nocardioform placentitis have been diagnosed in Kentucky, USA [14, 20, 24, 82].

Nocardioform actinomycete induces a typical chronic placentitis that causes late term abortion, stillbirth or premature birth. The lesion is characterized by an extensive and severe exudative, mucopurulent and necrotizing placentitis centered upon the junction of the placental body and horns rather than the cervical pole [25]. Infection of the placenta is generally thought to be a sequel of the hematogenous spread of the microorganisms from a primary port of entry [14, 79]. The fetus is generally severely underdeveloped with no remarkable gross or histological lesions. The lesion is focally extensive (15 to 30 cm) and frequently located at the base of the uterine horns or at the junction between the body and horns of the placenta. The affected area is thickened and its chorionic surface is covered with brown, necrotic mucopurulent exudate and dotted with white/yellow granular structures. Various groups of Gram-positive, filamentous, branching bacteria have been isolated in other cases and include Nocardia species, Rhodococcus rubropertinctus and Amycolatopsis species [4, 16, 24]. However, most of the severe infections were caused by the actinomycete Crossiella equi [15]. Nocardioform placentitis has been reported in south Africa in a case associated with Amycolatopsis species infection[79] and in Italy due to Crossiella equi [8]. The case in Italy was associated with, placental separation and hemorrhagic vaginal discharge for 4 days before abortion. The mare presented also with bilateral laminitis, which was speculated to have helped in the hematogenous spread of the organism.

**Pathogenesis and diagnosis of placentitis**

Because of the importance of placentitis in the pathogenesis of bacterial abortion, researchers at the University of Florida have developed models for the study of ascendant placentitis which allowed to gain some insight on the pathogenesis and to the development of clinical methods for its recognition [31-33, 35, 64]. Bacterial infection of the chorioallantois induced and increase in expression of pro-inflammatory cytokines (IL-6 and IL-8) in placental tissue which results in the release of PGE2 and
PGF2α in the allantoic fluid leading to premature delivery [30, 32, 35]. The premature delivery of the fetus is most likely due to acceleration of the fetal maturation process induced by changes in placental function. The resulting endocrine changes lead to increased uterine contractures and intrauterine pressure causing dilation and induction of labor. Data from experimentally induced ascendant placentitis show that a premature rise in maternal plasma progestins may be an indication of accelerated fetal maturation or fetal stress. Foal may survive if they are near term (>305 days) [31, 38, 39].

Clinically, placentitis is suspected in mares with premature udder development or lactation and/or vaginal discharge. However, most mares with placentitis do not show any outward signs of infection [31, 82].

Placentitis may be diagnosed by transrectal and/or transabdominal ultrasound examinations [7, 75, 82]. Measurement of the Combined Thickness of the Uterus and Placenta (CTUP) by transrectal ultrasonography is particularly helpful in the diagnosis and monitoring of ascendant placentitis [27, 50-52, 72-74]. The measurements are taken 2.5 to 5 cm cranial to the cervical-placental junction using a 5 or 7.5 mHz linear transducer. The area measured should be on the ventral aspect of the uterine body just above the middle branch of the uterine artery (Figure 10). Normal CTUP for light horses is < 8mm between 271 and 300 days of gestation, <10mm between 301 and 330 days of gestation and < 12 mm from 330 days of gestation to term [3, 27, 50, 51, 73]. These measurements are slightly higher in warmblood and heavy horses and lower in ponies [3, 7, 27]. Placental malfunctions has been associated with CTUP of more than 15 mm in horses and more than 12 mm in ponies after 310 days of gestation [7, 31].

During ultrasonographic evaluation other features of infectious placentitis may be identified. These include placental separation and accumulation of purulent hyperechoic heterogeneous fluid between the endometrium and the placenta and increased echogenicity of fetal fluid. Increased echogenicity of fetal fluid is due to presence of meconium, inflammatory debris and hemorrhage[31].

Endocrinological evaluation may also help in determining placental pathology and risk for abortion. The most important hormones evaluated are progestins which in a normal pregnancy are relatively stable during. A change (rise or fall) by more than 50% or a value that is constantly out of reference lab range signals placental pathology or fetal stress [31, 40].

Following abortion or premature birth, the majority of chronic placentitis can easily be recognized on gross examination but microscopic histological examination is important to determine presence of acute placentitis (Figure 11) [62]. In acute placentitis, the infection may be contained within the placenta and the fetuses are usually sterile. Some foals may be born alive with neonatal septicemia [62].

**Treatment of placentitis**

The ultimate goal of treatment is to maintain gestation for as long as possible to enhance foal viability [33, 82]. This can be accomplished by the combined use of tocolytic drugs to reduce uterine contraction, anti-inflammatory drugs to block the production of cytokines and prostaglandins and antimicrobials to control growth of bacteria [31, 33].

Antimicrobial therapy should be based on culture and sensitivity from vaginal discharge or cervical swabs. Pharmacological studies have shown that trimethoprim sulfadiazine, gentamicin, potassium penicillin and cephalothin can all cross the placenta and reach MIC sufficient to control S. equi for penicillin G (22,000 IU/kg q 6 h, IV) and E. coli or K. pneumonia for gentamycin (6.6 mg/kg q 24 h, IV) (43, 44, 47). Trimethoprim sulfadiazine (30 mg/kg, q 12 h) presents an excellent choice for the treatment of placentitis because of its good uterine penetration [31, 56, 59].

Reduction of the effects of inflammation and pro-inflammatory cytokine can be achieved by administration of NSAID (flunixin meglumine) and pentoxyfilline (8.5 mg/kg, q 12 h) [30, 31, 33, 36].

Induction of uterine quiescence is obtained by administration of progestins in order to interfere with up-regulation of prostaglandin and oxytocin and reduce myometrial activity (56). The oral synthetic progestin, altronegest, is used at normal (0.044 mg/kg, q 24 or q 12 h) or double (0.088 mg/kg, q 24 hr) dose [82]. Alternatively, progesterone in oil can be used at 300 mg, q 24 hr, IM [31, 33].
Colic in the pregnant mare

Colic in the pregnant mare may have a gastrointestinal or a genital origin. Large colon impaction may occur during pregnancy. Large colon torsion may also occur in late pregnancy. Mares with recurrent signs of colic during pregnancy should be examined for uterine torsion and abdominal wall hernias. Per rectum examination may be difficult because of the displacement of the gastrointestinal tract caused by the pregnant uterus [65]. Hydrops of the fetal membranes may cause severe distension of the abdominal wall, colic and respiratory distress.

Uterine torsion

Uterine torsion occurs generally after the 8th months of pregnancy. However, some cases have been reported as early as 110 days. Most uterine torsion cases are reported late during pregnancy because it is then that they may be accompanied by the most alarming clinical signs due to fetal stress and its excessive activity [18]. It is believed that fetal positioning in preparation for birth may be a factor in late term uterine torsion. History may reveal excess activity of the fetus observed at flank, recurrent colicky syndrome, straining and premature lactation.

Abdominal pain is variable and probably depends on the extent of the torsion. The owner may report signs of restlessness, sweating, anorexia or poor appetite, frequent urination, sawhorse stance, stretching, self-auscultation, rolling and kicking at the abdomen. These signs may last several days. The interval between the beginning of this syndrome and the final diagnoses greatly affect the chances of fetal survival.

Per rectum examination is the key to diagnosis of uterine torsion. The broad ligament should be examined carefully for tightness and direction. Each ligament is followed from the corresponding dorsal lumbar and ventrally. A diagnosis of uterine torsion is reached if both ligament meet as they pass under the uterus. The ligament on the side of the torsion tends to be more caudal and is palpable as a thigh vertical band while the opposite ligament is pulled horizontally across the top of the uterus.

Fetal and placental evaluation should be performed by transabdominal ultrasonography. Long standing uterine torsion may show changes in the drainage of the uterine wall, uterine and placental edema and placental detachment. Abdominocentesis is indicated if the mare is severely affected as uterine rupture may be a complication of uterine torsion [41].

Three approaches are described for the correction of uterine torsion: vaginal manipulation, rolling and surgical correction. The choice of the technique to be used depends on the stage of pregnancy, mare condition and fetal compromise. At term, the fetus may be manipulated vaginally to correct the uterine torsion. Manipulations are done in the standing mare after epidural anesthesia. The mare should be placed on a slope so that the hindquarters are slightly elevated in order to facilitate the manipulation.

Rolling under general anesthesia may be performed at any stage. The mare should be positioned on the side of the direction of the torsion and rolled to the opposite side while a aid is maintaining the position of the uterus by exerting pressure using a plank. It may be necessary to roll the mare several times before the torsion is corrected. The mare is checked per rectum after each roll while she is in a sternal position. This technique has been associated with low incidence of uterine rupture or hemorrhage.

Surgical correction of uterine torsion may be accomplished by laparotomy using a standing flank approach on the side of the torsion or a ventral midline approach.

Hydroallantois and hydramnios

Excessive accumulation of allantoic fluid (hydrallantois) or amniotic fluid (hydramnios) is rare. Hydrallantois is the most common of the two hydrops. Mares are generally presented for a sudden abnormal increase of abdominal size. Mares that are not treated will progressively deteriorate and show anorexia, signs of respiratory and other metabolic and circulatory complications. Transrectal palpation is important for the diagnosis and should be performed with extreme care. The distended uterus is pushed against the pelvic canal and prevents the examiners from feeling other organs and even limits passage of the forearm. Ultrasonography may confirm presence of excessive amount of fluid and possible abnormalities of the fetus and umbilical cord. This technique may also be valuable in
differentiating the condition from twin pregnancy although detection of twins is not always possible. Treatment consists of induction of abortion using oxytocin. The allantochorion should be manually ruptured using a uterine biopsy forceps or scissors. Drainage of the fluid should be done slowly to avoid hypovolemic shock. Intravenous administration of fluids is warranted and may help reduce the hypovolemic compromise. Dystocia is often a complication and the practitioner should be prepared for controlled vaginal delivery.

Other complication of pregnancy

Other rare complications of pregnancy in the mare include prepubic tendon rupture

Uterine rupture/hemorrhage, ventral hernia. Mare management during these crises is important. In the case of prepubic tendon rupture or ventral hernia, termination of pregnancy is warranted for the well-being of the dam. Surgical repair has been attempted but is not always without complication.

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