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The periparturient period can be associated with high morbidity and even mortality for the dam and neonates. The periparturient period is defined here as the immediate prepartum period (1-2 weeks before parturition) and the 30-45 day post partum period before weaning. The diagnosis of periparturient problems first requires their recognition and differentiation from normal situations; effective treatment depends on both a timely diagnosis and therapeutic intervention.

Premature labor

Late term gestational loss attributed to pre term or premature labor is a controversial topic in small animal reproduction. Both hypoluteoidism and inappropriate uterine activity accompanied by cervical changes have been implicated in the pathophysiology of preterm birth in veterinary medicine, but the syndrome is not well understood or even researched. While the human literature is abundant on the topic, publications on the topic are few in veterinary medicine.

Premature labor is defined here as uterine activity and cervical changes leading to the loss of pregnancy via resorption or abortion before term, for which no metabolic, infectious, congenital, traumatic or toxic cause is identified. Premature labor is associated with progesterone levels that are <2 ng/ml. Premature labor is often a retrospective diagnosis, achieved after thorough evaluation of the dam and fetuses has been performed because of loss of pregnancy. This evaluation should include metabolic screening of the dam for systemic disease, infectious disease evaluation, histopathology of expelled fetuses and placentae, and review of kennel/cattery husbandry including nutrition, medications and environmental factors. All results are normal or negative. Dams experiencing premature myometrial activity in one pregnancy may or may not exhibit it during subsequent pregnancies, but the syndrome can be a chronic cause of failure to reproduce.

In human medicine, preterm birth complicates 10-12% of human pregnancies, but it accounts for 80% of fetal morbidity and mortality. The diagnosis of preterm labor placing the fetus at risk of premature delivery is dependent upon evaluation of uterine contractility by tocodynamometry, and fetal fibronectin and transvaginal cervical length measurement determined via ultrasonography, which together have high negative predictive value. Amniocentesis is also advocated as a method of evaluating fetal lung maturation and microbial invasion of the amniotic cavity. The presence of contractions alone does not warrant intervention. Tocodynamometry identifies labor onset earlier than subjective maternal perceptions, and home uterine monitoring is advocated in high risk groups as an initial screening test. Multifetal gestations (i.e. litters) are associated with exaggerated physiologic changes which promote premature labor and complicate tocolytic therapy. Women with histories of preterm deliveries do appear to be at risk for such in subsequent pregnancies.

If intervention is indicated, tocolytics agents have been commonly advocated. Antibiotics, bed and pelvic rest and hydration do not appear to have benefit. Contraindications to tocolytics therapy include severe preeclampsia, placental abruption, intrauterine infection, lethal congenital or chromosomal abnormalities, advanced cervical dilation, and evidence of fetal compromise or placental insufficiency. Tocolytic agents inhibit myometrial contractions, and include beta mimetics (terbutaline, ritodrine), magnesium sulfate, calcium channel blockers and prostaglandin synthetase inhibitors (indomethacin, ketorolac, sulindac). Contraindications to beta mimetics include maternal cardiac arrhythmias, poorly controlled diabetes mellitus and hyperthyroidism; fetal and maternal tachycardia and myocardial ischemia, maternal pulmonary edema and hypotension and fetal myocardial hypertrophy, hyperglycemia and hyperinsulinemia are potential side effects. A contraindication to magnesium sulfate is maternal myasthenia gravis; side effects include maternal lethargy, muscle weakness, headache, pulmonary edema and cardiac arrest, and fetal respiratory depression, hypotonia, lethargy and demineralization. Contraindications to calcium channel blockers include maternal cardiac disease, renal diseased and hypotension; side effects include maternal nausea, hypotension and headache. Contraindications to prostaglandin synthetase inhibitors include maternal renal or hepatic impairment; side effects include maternal acute renal insufficiency, neurological dysfunction and hypotension. Contraindications to indomethacin and ketorolac include placenta previa and placental abruption. Contraindications to ritodrine include maternal severe hypertension, and maternal atrial or ventricular arrhythmias. Contraindications to terbutaline include maternal or fetal tachycardia and myocardial ischemia. Contraindications to thes agents are many, and often develop in tandem with maternal hypertension, proteinuria, uterine contractions and fetal distress. If intervention is indicated, tocolytic agents have been commonly advocated. Antenatal corticosteroids and magnesium sulfate appear to have benefit. Antenatal corticosteroids inhibit fetal lung maturation; benefits include improved fetal survival and decreased need for mechanical ventilation. Magnesium sulfate inhibits uterine contractility and decreases fetal excitability; benefits include improved fetal survival and decreased need for mechanical ventilation. Premature labor must be prevented or controlled to achieve such benefit, and should be considered with the goals of improving maternal health and decreasing fetal morbidity and mortality.
Physicians hope to intervene in the future with anticytokine (interleukin-10) and antiprostaglandin therapy to more completely suppress the pathogenic process at multiple sites along the pathway rather than just treating the processes at the end of preterm labor.

Small human trials based on prophylactic treatment with progestational compounds have been reported. Not all reported positive results with meta analysis, the prevention of preterm delivery or the prevention of recurrent miscarriage appears to be based on the use of only the natural metabolite of progesterone, 17 alpha-hydroxyprogesterone caproate (17P). In one study, no increase in the rate of congenital anomalies in the progesterone group was noted over the control group. The benefit of 17P in preventing preterm delivery appears to be best in a cohort of women at very high risk, and the cohort still exhibited a high rate of preterm delivery (36%) despite significant reduction as compared to untreated control (54%), indicating that other causes of preterm delivery were at play. Tocolytic therapy was added in 17% of the treated group and 16% of the untreated control group. Interestingly, serum progesterone levels were not reported.

The maintenance of canine and feline pregnancy requires serum progesterone levels of >1-2 ng/ml. Serum progesterone levels during pregnancy normally range from 15 to 90 ng/ml, declining gradually during the latter half of gestation, and falling abruptly at term (usually the day before or the day of parturition). Progesterone promotes the development of endometrial glandular tissue, inhibits myometrial contractility (causes relaxation of myometrial smooth muscle), blocks the action of oxytocin, inhibits the formation of gap junctions and inhibits leukocyte function in the uterus. In several species, local changes in the progesterone level or the ratio of progesterone to estrogen in the placenta, decidua or fetal membranes is important in the initiation of labor. Progesterone antagonists administered at term can result in an increased rate of spontaneous abortion. In the bitch, the corpora lutea are the sole source of progesterone, while in the queen, placental progesterone production occurs in the latter half of gestation. Canine luteal function is autonomous early in pregnancy but supported by luteotrophic hormones (LH and prolactin) after the second week of gestation.

Hypoluteiodism, primary luteal failure occurring before term gestation, is a potential but not yet documented cause of late term abortion in otherwise normal bitches. It has been documented that the induction of abortion in a normal but undesired pregnancy requires a reduction of plasma progesterone levels <2 ng/ml. The diagnosis of gestational loss caused by premature luteolysis is difficult, requiring documentation of inadequate plasma progesterone levels prior to abortion for which no other cause is found. Measurement of precise progesterone levels, especially in the critical 1-3 ng/ml range, is not accurate using currently available rapid in house Elisa kits, necessitating the use of commercial laboratories in most practice situations. A few academic and human private laboratories provide more rapid (< 8h) turnaround, facilitating the diagnosis.

Progesterone levels diminish in response to fetal death, thus documentation of a low progesterone level after an abortion does not establish the diagnosis of hypoluteiodism as the primary cause for reproductive failure. Administration of progesterone to maintain pregnancy in dams with primary fetal abnormalities, placenta, or intrauterine infection can cause continued fetal growth with the possibility of dystocia and sepsis. Administration of excessive progesterone to maintain pregnancy in a dam not actually requiring therapy can delay parturition and impact lactation, endangering the life of the bitch and her fetuses, and can masculinize female fetuses.

Dams with documented low progesterone levels and historical late term loss of pregnancy with no apparent pathology can also be also evaluated for premature myometrial activity mid gestation, using uterine monitoring. Elaboration of prostaglandins from the endometrium and placenta associated with premature myometrial activity can result secondarily in luteolysis. Premature uterine activity endangering fetal survival can be identified before significant luteolysis occurs, and intervention indicated if the pregnancy is normal otherwise. Pharmacologic intervention to decrease myometrial activity is indicated, using progestational compounds and tocolytic agents alone or in combination.

Therapeutic intervention in primary hypoluteiodism can be accomplished with the administration of injectable natural progesterone or oral synthetic progestagens. Total serum levels of progesterone can be monitored only when supplemented with the natural product. Progesterone in oil is given intramuscularly at 2 mg/kg q 72h. Altreonogest (Regumate, Hoechst-Roussel), a synthetic progestagen manufactured for use in the mare,
is dosed orally at 0.088 mg/kg q 24h. Both forms of supplementation must be discontinued in a timely fashion so as not to interfere with normal parturition, within 24h of the due date with the oral synthetic product, and within 72 h with the natural, injectable depot form. This requires accurate identification of gestational length via prior ovulation timing (parturition expected to occur 64-66 days from the LH surge or initial rise in progesterone, or 56-58 days from the first day of cytologic diestrus). Less accurate identification of gestational length can be made from breeding dates (58-72 days from the first breeding), radiography, or ultrasound.

Terbutaline (Brethine, Ciba Geigy) .03 mg/kg PO q 8h has been used to suppress uterine contractility in bitches and queens with historical loss of otherwise normal pregnancies preterm. The dose is ideally titrated to effect using tocodynamometry. Therapy is discontinued 24h before term.

Further work evaluating the pathophysiology of premature labor and preterm delivery in the bitch and queen is needed, including evaluation of the ovary, placenta, myometrium and fetus for contributing factors. Multicenter studies including identification of the criteria for diagnosis of significant premature labor, specific therapy, outcome and follow up (dam and neonatal health, subsequent pregnancies) is encouraged.

Metabolic conditions
Gestational diabetes occurs infrequently in the bitch and queen, and is attributed to the anti-insulin effect of progesterone (mediated by increased levels of growth hormone) during the luteal phase. Polydipsia, polyuria and polyphagia with weight loss occur. Higher protein lower carbohydrate diets may be helpful in the queen, while high fiber diets promote euglycemia in the bitch. Insulin may be indicated. Oversized fetuses can result from their increased production of insulin in response to maternal hyperglycemia, and may cause dystocia due to fetal-maternal mismatch.

Pregnancy toxemia in the bitch occurs as a result of altered carbohydrate metabolism in late gestation resulting in ketonuria without glycosuria or hyperglycemia. The most common cause is poor nutrition or anorexia during the last half of gestation. Hepatic lipodosis can occur. An improved plane of nutrition can resolve the condition in most cases, but termination of the pregnancy may be indicated in severe cases.

Puerperal tetany or eclampsia occurs most commonly during the first 4 weeks postpartum, but can occur in the last few weeks of gestation. The condition occurs in bitches more frequently than queens. Puerperal tetany can be life threatening, caused by a depletion of ionized calcium in the extracellular compartment. Predisposing factors include improper perinatal nutrition, inappropriate calcium supplementation and heavy lactational demands. Small dams with large litters are at increased risk. Excessive prenatal calcium supplementation can lead to the development of puerperal tetany by promoting parathyroid gland atrophy and inhibiting parathyroid hormone release, thus interfering with the normal physiologic mechanisms to mobilize adequate calcium stores and utilize dietary calcium sources. Thyrocalcitonin secretion is stimulated. The use of a balanced growth (puppy/kitten) formula commercial feed without additional vitamin or mineral supplementation is optimal during the second half of gestation and throughout lactation. Supplementation with cottage cheese should also be avoided as it disrupts normal calcium-phosphorus-magnesium balance in the diet.

Metabolic conditions favoring protein binding of serum calcium can promote or exacerbate hypocalcemia, such as alkalosis resulting from prolonged hyperpnea during labor or dystocia. Hypoglycemia and hyperthermia can occur concurrently. Therapeutic intervention should be initiated immediately upon recognition of the clinical signs of tetany, without waiting for biochemical confirmation. The signs preceding the development of tonic clonic muscle contractions (progressing to seizures) include behavioral changes, salivation, facial pruritus, stiffness/limb pain, ataxia, hyperthermia and tachycardia. Immediate therapeutic intervention should be instituted with a slow intravenous infusion of 10% calcium gluconate (1-20 ml) given to effect. Cardiac monitoring for bradycardia and arrhythmias should accompany administration, their occurrence warrants temporary discontinuation of the infusion and a slower subsequent rate. Because cerebral edema can occur from uncontrolled seizures, diazepam (1-5 mg intravenously) or barbiturates can be used to control persistent seizures once eucalcemia is attained. Mannitol may be indicated for cerebral inflammation and swelling. Corticosteroids are undesirable because they promote calciuria, decrease intestinal calcium absorption and impair osteoclasia. Hypoglycemia should be corrected if present, and exogenous treatment for hyperthermia given if necessary. Once the immediate neurologic signs are controlled, a subcutaneous infusion of an equal volume of calcium
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Chapter 2

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Canine Herpes Virus

Adequate exposure of a non-immune bitch to canine herpes virus (CHV) during the last three weeks of gestation can result in infection of the dam and subsequently her neonates. Venereal transmission is believed to be rare and community (respiratory) transmission more common. Signs in the bitch are usually limited to a mild, clear upper respiratory discharge and soft sneezing. Late term abortion or neonatal death within the first few weeks of life commonly results. The recently infected bitch generally has minimal clinical signs, but has inadequate time to form protective maternal antibodies and allow passive immunity (placental or transmammary) to be acquired by the neonates. Incompletely developed immune systems and inadequate thermoregulation during the first days of life make neonates vulnerable to systemic infection (bacterial and viral). Adequate ingestion of colostrum must occur promptly post partum for puppies to acquire passive immunity. The transmission of protective immunity (placental or colostral antibodies) between a bitch and her puppies depends upon the prior existence of adequate serum maternal antibodies.

Transmission of CHV from an infected, viremic dam to neonates occurs subsequent to contact with infectious vaginal fluids or oronasal secretions. Signs in the neonate are progressive and severe, and include anorexia (poor weight gain), dyspnea, abdominal pain, incoordination, diarrhea, serous to hemorrhagic nasal discharge and petechiation of the mucous membranes. The mortality rate in untreated litters infected in utero or during birth is commonly 100%, with deaths occurring during the first few days to 3 weeks of life. Infection in neonates born to a non-immune bitch may also result from contact with CHV from another dog shedding the organism in the vicinity. Older naive (> three to four weeks of age) puppies exposed to herpes virus may have an in apparent infection but later central nervous signs including blindness and deafness have been observed. Subsequent litters of the bitch infected during a pregnancy are usually resistant to infection, having acquired circulating maternal antibodies.

Canine herpesvirus is a commonly blamed cause for fading puppy syndrome resulting in neonatal death. Premortem diagnosis of CHV infection in neonates can be challenging. Postmortem diagnostics include appropriate histopathology and virus isolation. Pathognomonic changes occurring in the kidneys include multifocal petechial hemorrhages, although this can be seen with bacterial septicemia and associated thromboembolic disorders as well. Intraneural inclusion bodies can be difficult to find. Diagnosis by virus isolation or CHV-specific PCR is confirmatory and desirable, especially before litter mortality reaches 100%.

Until recently, treatment of CHV infection in neonates has been reported to be unrewarding and rare, with recovery suspected to be associated with residual cardiac and neurologic damage. Treatment with immune serum from affected dams is reported to be ineffective in infected puppies. Vaccine development is hampered by the poor immunogenicity of the herpes virus, as evidenced by other herpesviral vaccines developed for different species, such as feline and bovine rhinotracheitis. Successful treatment with the antiviral agent acyclovir has recently been reported.

Acyclovir is an antiviral agent with activity against a variety of viruses including herpes simplex. Acyclovir is preferentially taken up by susceptible viruses and converted into the active triphosphate form, inhibiting viral DNA replication. Acyclovir is poorly absorbed after oral administration and is primarily hepatically metabolized. Acyclovir can increase the toxicity of nephrotoxic drugs. The half-life in humans is approximately three hours. Its use in veterinary medicine is not well established and it should be used with caution and only in situations where indicated. The safety and effectiveness in humans less than two weeks of age is not established. The dose was extrapolated from that for humans (20 mg/kg po q 6h x 7 days).
Canine Brucellosis

Brucellosis is the primary contagious infectious venereal disease of concern in canine reproduction. Canine brucellosis is caused by B. canis, a small, gram-negative, non spore forming aerobic cocobacilli. B. canis was first isolated by Leland Carmichael in 1966. Brucella abortus, B. melitensis and B. suis, have occasionally caused canine infections but are comparatively rare. Transmission occurs through direct exposure to bodily fluids containing an infectious dose of organism (semen, lochia, aborted fetuses/placentas, milk and urine). There are 2 X 106 colony forming units in an infective dose. Transmission is therefore primarily oral, nasal, conjunctival and secondarily venereal (i.e. through the mucous membranes), the former associated with the ingestion or aerosolization of infectious materials. The aerosol route is especially important if kennel conditions are crowded. Transplacental transmission and direct cutaneous inoculation can occur.

Canine brucellosis has high morbidity but low mortality in the adult dog. The clinical systemic signs are often subtle (suboptimal athletic performance, lumbar pain, lameness, weight loss, lethargy). The primary clinical sign of canine brucellosis in the breeding bitch is pregnancy loss, which can occur early (day 20) in gestation resulting in fetal resorption, or more commonly (75%) later in gestation (generally 45-59 days) resulting in abortion. Bitches with pregnancy loss early in gestation can appear to be infertile (failed to conceive) unless early ultrasonographic pregnancy evaluation is performed. Non gravid bitches can be asymptomatic, or can show regional lymphadenopathy (pharyngeal if orally acquired, inguinal and pelvic if venereally acquired).

Infected dogs and bitches should be removed from breeding programs and quarantined. Eradication of the disease in kennel situations has not been successful without removal (culling) of all infected (current or historically) dogs. Because of the zoonotic potential of the disease and difficulty in actually eradicating the infection, euthanasia of affected dogs has been advised. Infection in household or small hobby kennel dogs often results in client requests for alternatives to euthanasia. Neutering decreases the amount of organism shed in semen and uterine discharge, but does not eradicate the infection. Urine shedding can persist, and the organism can be found in internal organs and the bloodstream.

Antibiotic therapy has not been historically rewarding, likely due to the fact that the organism is intracellular and bacteremia periodic. Antibiotic therapy may reduce antibody titers without clearing the infection. Relapses are common. Combination therapy with tetracyclines (doxycycline or minocycline 25 mg/kg bid PO for 4 weeks) and dihydrostreptomycin (10-20 mg/kg bid IM or SC for 2 weeks, week 1 and 4) or an aminoglycoside (gentamicin 2.5 mg/kg bid IM or SC for 2 weeks, week 1 and 4) has been advocated as being the most successful, but unavailability, nephrotoxicity, parenteral therapy requirements and expense remain problematic. Recently one study reported a slightly encouraging outcome of therapy with enrofloxacin (5.0 mg/kg bid PO for 4 weeks, often for multiple courses) in a small group of infected dogs and bitches. Enrofloxacin was not completely efficacious in eliminating B. canis, but it maintained fertility and avoided the recurrence of abortions, transmission of the disease to subsequently whelped puppies, and dissemination of microorganisms during parturition. Ultimately, however, most treated individuals remained culture positive.

Private breeders should require screening testing of all bitches presented for breeding and confirmatory negative testing if positive results occur during screening before accepting a bitch into their kennel. Stud dogs should be screened appropriately at least annually. Because of the potential for non venereal transmission, screening of maiden dogs and bitches before breeding is also recommended.

OBSTETRICAL EMERGENCIES II
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The periparturient period can be associated with high morbidity and even mortality for the dam and neonates. The periparturient period is defined here as the immediate prepartum period (1-2 weeks before parturition) and the 30-45 day postpartum period before weaning. The diagnosis of periparturient problems first requires their recognition and differentiation from normal situations; effective treatment depends on both a timely diagnosis and therapeutic intervention.
Dystocia

Although many bitches and queens deliver in the home or kennel/cattery setting without difficulty, requests for veterinary obstetrical assistance are becoming more common. The increased financial and emotional value of stud dogs, brood bitches, toms, queens and their offspring to the pet fancy makes the preventable loss of even one neonate undesirable. Breeding colonies in academic, scientific and industrial facilities need to maximize neonatal survival for financial and ethical reasons. Veterinary involvement in canine and feline obstetrics has several goals: to increase live births (minimizing stillbirths resulting from the difficulties in the birth process), to minimize morbidity and mortality in the dam, and to promote increased survival of neonates during the first week of life. Neonatal survival is directly related to the quality of labor. Optimal management of whelping/queening requires an understanding of normal labor and delivery in the bitch and queen, as well as the clinical ability to detect abnormalities in the birthing process.

Dystocia is defined as difficulty in the normal vaginal delivery of a neonate from the uterus. Dystocia must be diagnosed in a timely fashion for medical or surgical intervention to improve outcome. Additionally, the etiology of dystocia must be identified for the best therapeutic decisions to be made.

Normal parturition

Gestation

Clinicians are commonly asked to ascertain if a bitch or queen is at term pregnancy, ready chronologically to deliver a litter, and then to intervene if labor has not begun. An accurate determination of gestational length can be difficult, especially if numerous copulations occurred and no ovulation timing was performed. Prolonged gestation is a form of dystocia. Gestation in the bitch is more challenging to calculate than in the cat, because bitches are spontaneous ovulators. Normal gestation in the bitch is 56 to 58 days from the first day of diestrus (detected by serial vaginal cytologies, defined as the first day that cytology returns to <50% cornified/superficial cells), 64 to 66 days from the initial rise in progesterone from baseline (generally >2ng/ml), or 58 to 72 days from the first instance that the bitch permitted breeding. Predicting gestational length without prior ovulation timing is difficult because of the disparity between estrual behavior and the actual time of conception in the bitch, and the length of time semen can remain viable in the bitch reproductive tract (often up to >7 days). Breeding dates and conception dates do not correlate closely enough to permit very accurate prediction of whelping dates. Additionally, clinical signs of term pregnancy are not specific: radiographic appearance of fetal skeletal mineralization varies at term, fetal size varies with breed and litter size, and the characteristic drop in body temperature (typically less than 99 degrees Fahrenheit) may not be detected in all bitches and varies in many. Breed, parity and litter size can also influence gestational length. Because the queen is an induced ovulator (ovulation follows coitus by 24-36 hours), gestational length can be predicted more accurately from breeding dates, assuming copulation provided adequate coital stimulation for the LH surge and subsequent ovulation, and a limited number of copulations were permitted. The gestational length of queens ranges from 52-74 days from the first to last breeding. The mean gestational length is 65-66 days. Because of the poor outcome with the delivery of premature puppies and kittens, elective intervention is best delayed until stage I labor has begun, or prolonged gestation confirmed.

Labor and delivery

Bitches typically enter stage I labor within 24 hours of a decline in serum progesterone to below 2-5 ng/mL, which occurs in conjunction with elevated circulating prostaglandins and is commonly associated with a transient drop in body temperature, usually to <100 degrees Fahrenheit (33.7 C). Queens typically enter stage I labor 24 hours after serum progesterone levels fall to less than 2 ng/mL. Monitoring serial progesterone levels for impending labor is problematic due to the fact that in house canine kits enabling rapid results are inherently less accurate between 2-5 ng/mL, and a rapid decline in progesterone levels can occur over a period of a few hours. Commercial laboratories offering quantitative progesterone by chemiluminescence typically have a 12 to 24 hour turn around time, which is not rapid enough to enable decisions about an immediate indication for obstetrical intervention.

Stage I labor in the bitch normally lasts from 12 to 24 hours, during which time the uterus has myometrial contractions of increasing frequency and strength, associated with cervical dilation. No abdominal effort (visible external contractions) is evident during stage I labor. Bitches may exhibit changes in disposition and behavior during stage I labor, becoming reclusive, restless, and nesting intermittently, often refusing to eat and...
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Dystocia results from maternal factors (uterine inertia, pelvic canal anomalies, intrapartum compromise), fetal factors (oversize, malposition, malposture, anatomic anomalies) or a combination of both. For effective management, the recognition of dystocia must be made in a timely manner, and identification of etiologic factors made correctly.

Uterine inertia is the most common cause of dystocia. Primary uterine inertia results in the failure of delivery of any neonates at term, and is thought to be multifactorial, including metabolic defects at the cellular level. An intrinsic failure to establish a functional, progressive level of myometrial contractility occurs. A genetic component may be present. Secondary uterine inertia results in the cessation of labor once initiated, and consequential failure to deliver the entire litter. Secondary inertia can result from metabolic or anatomic (obstructive) causes, and is also thought to have a genetic component. Birth canal abnormalities such as vaginal strictures, stenosis from previous pelvic trauma or particular breed conformation, and intravaginal or intrauterine masses can cause obstructive dystocia. In most cases, canal abnormalities can be detected in the pre breeding examination, and resolved or avoided by elective cesarean section. Causes of intrapartum compromise rendering the dam unable to complete delivery include metabolic abnormalities such as hypocalcemia and hypoglycemia, systemic inflammatory reaction, sepsis, and hypotension (due to hemorrhage or shock).

Fetal factors contributing to dystocia most commonly involve mismatch of fetal and maternal size, fetal anomalies and fetal malposition and/or malposture. Prolonged gestation with small litter size can cause dystocia due to an oversized fetus(es). Fetal anomalies such as hydrocephalus and anasarca similarly can cause dystocia. Fetal malposition (ventrum of fetus proximal to the dam’s dorsum) and fetal malposture (flexed neck and scapulohumeral joints most commonly) promote dystocia as the fetus cannot transverse the birth canal smoothly.

An efficient diagnosis of dystocia is dependent upon taking an accurate history and performing a thorough physical examination in a timely manner. The clinician must quickly obtain a careful reproductive history detailing breeding dates, any ovulation timing performed, historical and recent labor, as well as a general medical history. The physical examination should address the general status of the patient, as well as include a digital and/or vaginoscopic pelvic exam for patency of the birth canal, evaluation of litter and fetal size (radiography most useful), assessment of fetal viability (doppler or real time ultrasound ideally) and uterine activity (tokodynamometry most useful).

A novel approach to veterinary obstetrical monitoring in use in the United States involves the use of external monitoring devices using tokodynamometry (Healthdyne Inc., Marietta, GA, USA) and a hand held doppler (Sonicaid, Oxford Instruments, England) to detect and record uterine activity and fetal heart rates. These devices can be used either in the home setting or at the veterinary clinic. Their use requires that the hair coat be lightly clipped caudal to the ribcage, over the gravid area of the lateral flanks, to allow proper contact of the uterine sensor and fetal doppler. The uterine sensor detects changes in intrauterine and intra amniotic pressures. The sensor is strapped over the lightly clipped area of the bitch’s/queen’s caudolateral abdomen using an elasticized strap.

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The sensor’s recorder is worn in a small backpack placed over the caudal shoulder area. Bitches/queens are at rest in the whelping/queening box or in a crate or cage during the monitoring sessions. The monitoring equipment is well tolerated. Subsequent to each recording session, data is transferred from the recorder via a modem using standard telephones. Fetal doppler monitoring is performed bilaterally with a hand held unit with bitches/queens in lateral recumbency, using acoustic coupling gel. Directing the doppler perpendicularly over a fetus results in a characteristic amplification of the fetal heart sounds, distinct from maternal arterial or cardiac sounds, which enables determination of fetal heart rates.

Interpretation of the contractile pattern in strips produced by the uterine monitor requires training and experience. Data is transferred by modem to obstetrical personnel capable of interpretation, who subsequently consult with the attending veterinary clinician and client. Recordings are made on a twice daily, hour long basis when home monitoring is performed, then intermittently on bitches or queens at home as indicated during active labor, or on site in the veterinary clinic for shorter periods of time (minimally 20 minutes) when patients are being evaluated for suspected dystocia.

The canine and feline uterus each have characteristic patterns of contractility, varying in frequency and strength before and during different stages of labor.

Serial tocodynamometry in the bitch and queen permits evaluation of the progression of labor. During late term, the uterus may contract once or twice an hour before actual stage I labor is initiated. During stage I and II labor, uterine contractions vary in frequency from 0 to 12 per hour, and in strength from 15 to 40 mm Hg, with spikes up to 60 mm Hg. Contractions during active labor can last 2 to 5 minutes in duration. Recognizable patterns exist during pre labor and active (stages 1-3) labor. Aberrations in uterine contractility can be detected during monitoring. Abnormal, dysfunctional labor patterns can be weak or prolonged, and often are associated with fetal distress. Additionally, the completion of labor (or lack there of) can be evaluated via tocodynamometry.
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Treatment
The use of uterine and fetal monitors allows the veterinary clinician to detect and monitor labor, as well as manage labor medically or surgically with insight instead of guesswork. At Guide Dogs for the Blind, inc., the overall stillbirth rate declined from 9.2% to 2.5% with incorporation of uterine and fetal monitoring into the whelping process. Medical therapy for dystocia, based on the administration of oxytocin and calcium gluconate, can be directed and tailored based on the results of monitoring. Generally, the administration of oxytocin increases the frequency of uterine contractions, while the administration of calcium increases their strength. Oxytocin, 10 USP u/ml (American Pharmaceutical Partners Inc., Los Angeles, California, USA) is effective at mini doses, starting with 0.25 units SC or IM to a maximum dose of 4 units per bitch or queen. Higher doses of oxytocin or intravenous boluses can cause tetanic, ineffective uterine contractions that can further compromise fetal oxygen supply by placental compression. The frequency of oxytocin administration is dictated by the labor pattern, and it is generally not given more frequently than hourly. Calcium gluconate 10% solution with 0.465 mEq Ca++/ml (Fujisawa Inc., USA) is given SC at 1 ml/5.5 kg BW as indicated by the strength of uterine contractions, generally no more frequently than every 4-6 hours. Calcium is given before oxytocin in most cases, improving contraction strength before increasing frequency. Additionally, the action of oxytocin appears to be improved when given 15 minutes subsequent to calcium. Most bitches/queens are eucalcemic, suggesting that the benefit of calcium administration is at a cellular or subcellular level.

Surgical intervention (cesarean section) is indicated if a bitch or queen fails to respond to medical management, or if fetal distress is evidenced despite adequate to increased uterine contractility (suggesting mismatch of maternal birth canal to fetal size, or fetal malposition or malposture incompatible with vaginal delivery), or if aberrant contractile patterns are noted by uterine monitoring. Well orchestrated cesarean sections result when anesthetic and neonatal resuscitative protocols are established and coordinated, and the preoperative preparation of the dam optimized. It should always be remembered that the dam may be debilitated and require careful anesthetic management, there may be little time for routine pre-anesthetic preparation, and the dam may have been fed recently. Minimally, the hematocrit, total solids, serum calcium and glucose levels should be

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**Figure 5:** Empty post partum uterus.

**Figure 6:** Uterine hyperstimulation, obstructed puppy, ecblolis contraindicated. Fetal distress was evident (persistent fetal bradycardia).

The presence of fetal distress is reflected by sustained deceleration of the heart rates. Normal canine and feline fetal heart rates at term are from 170 to 230 beats per minute (bpm), or at least 4X the maternal heart rate. In the periparturient period the cardiac output of the fetus/neonate is mainly dependent on heart rate as the right ventricle is relatively stiff (low compliance) and the autonomic nervous system is immature (minimal inotropic response to catecholamines). Decelerations associated with uterine contractions suggest mismatch in size between the fetus and dam, or fetal malposition or malposture. Transient accelerations occur with normal fetal movement. Fetal heart rates of <150 to 160 bpm indicate stress. Fetuses with heart rates <130 bpm have poor survival if not delivered within 2 to 3 hours, and fetuses with heart rates <100 bpm are an indication for immediate intervention to hasten delivery (medical or surgical) before their demise.

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evaluated pre operatively. Intravenous fluid support at an operative rate minimally is indicated (10 ml/kg/h).

For premedication, atropine is best not given routinely, because it crosses the placenta and blocks the normal, adaptive bradycardic response of the fetus to hypoxia and causes relaxation of the lower esophageal sphincter, making maternal aspiration more likely. However, the use of an anticholinergic is indicated for the dam because of the anticipated vagal stimulation during manipulation of the gravid uterus. Glycopyrrolate (0.01-0.02 mg/kg SC) does not cross the placenta and is preferred. Most dams are tractable and do not need preanesthetic tranquilization, which has a depressant effect on the fetuses. Phenothiazine tranquilizers are transported rapidly across the placenta and are depressants. Alpha2-adrenoceptor agonists such as dexmedetomidine and xylazine are contraindicated because of their severe cardiorespiratory depressant effects. Similarly, the respiratory depressant effect of opioids makes them unpopular prior to removal of the fetuses. If tranquilization is necessary with an intractable dam, narcotic sedatives are preferable as their effects can be reversed (naloxone 1-10 µg/kg IV or IM) during neonatal resuscitation. Metoclopramide (0.10-0.20 mg/kg) can be administered subcutaneously or intramuscularly prior to the induction of anesthesia to reduce the risk of vomiting during the procedure.

Pre-oxygenation by mask (5-10 minutes) is always indicated. Initial preparation of the abdomen (clipping and first scrubbing) can be undertaken during this time. For induction of anesthesia, dissociative agents such as ketamine and the barbiturates are best avoided because they produce profound depression of the fetuses. Propofol (6 mg/kg IV to effect) appears to be most useful; because of its rapid redistribution therefore have a limited effect upon the fetuses after delivery. Mask induction actually produces more maternal and fetal hypoxemia than propofol induction. For maintenance of anesthesia, volatile agents are preferable, especially those with low partition coefficients such as isoflurane and sevofoxyzine. These agents show rapid uptake and elimination by the animal, and it may have a better cardiovascular margin of safety than the more soluble agents such as halothane. Nitrous oxide may be used to reduce the dose of other anesthetic agents, it is transferred rapidly across the placenta and, although it has minimal effects upon the fetus in utero, it may result in a significant diffusion hypoxia after delivery. Using a local anesthetic (Bupivicaine 2 mg/kg) line block in the skin and subcutaneous tissues prior to incising permits a more rapid entry to the abdomen while the dam is making transition from Propofol induction to inhalant maintenance, and helps with post operative discomfort.

Operative speed is important because surgical delay and prolonged anesthetic time are associated with fetal asphyxia and depression. However, care should be taken during incision of the linea alba to ensure that the gravid uterus is not also incised. Ideally the uterus should be exteriorized and packed off with moistened laparotomy sponges to prevent abdominal contamination with uterine fluid. This process should be undertaken carefully to ensure that the uterus and its broad ligament do not tear; it may be easier in some cases to exteriorize one horn at a time. The uterus should be penetrated in a relatively avascular area, and it is best to elevate the uterine wall from the fetus and to extend the incision with scissors to ensure that the fetus is not lacerated. The fetuses may be brought to the incision by gently ‘milking’ them along the uterus, although in some cases or in large dams it may be necessary to make more than one incision. As the fetal fluid is released it is best to remove this by suction, and then to clamp the umbilicus (twice, incising between clamps) before passing the fetus to an assistant for immediate resuscitation. After each fetus is removed the associated placenta should be detached by gentle traction, but the placenta may be left in situ if they are firmly attached and their removal causes significant hemorrhage. Placentas can be spontaneously passed post operatively, or managed medically. It is essential that the uterine horns, the uterine body and the vagina are inspected thoroughly to ensure that all fetuses have been removed. Finally, after closure the uterus, its broad ligament and the vascular supply should be inspected carefully to ensure that any previously unnoticed tears have been identified before closure of the abdomen. Ovariohysterectomy at the time of cesarean section is again the option of the surgeon and owner, but results in longer anesthetic time for the dam, delayed nursing for the neonates, and increased loss of blood in the dam, so should be postponed if reasonable. There is some belief that estrogen acts in a permissive fashion for prolactin receptors in the mammary glands, making ovary removal at cesarean section undesirable. If uterine viability is questionable an ovariohysterectomy should be performed. In the normal dam the uterus will begin to involute shortly after removal of the fetuses, but if this is not the case oxytocin may be administered (0.25-1.0 u per dam) to facilitate involution and arrest any hemorrhage; this also promotes milk let down.

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Post surgical discomfort should be acknowledged in the dam. Once the fetuses are removed, narcotic analgesia can be administered parenterally to the dam. Post operatively, non steroidal antinflammatories are not advisable due to their uncertain metabolism by the nursing neonates with immature renal and hepatic metabolism. Narcotic analgesia is preferable. Oral narcotics such as Tramadol, 10 mg/kg/day in divided doses provide excellent post operative analgesia for nursing bitches with minimal sedation of the neonates. In all cases, clients should be advised to closely monitor bitches post operatively until normal maternal behavior emerges. Post cesarean section, bitches can be clumsy and inattentive to the neonates, and can even become aggressive, as the normal mechanisms of maternal bonding have been bypassed. Nursing should be supervised and neonatal care ensured.

**Immediate post partum period**

Normally, dams stay very close to their offspring during the first 2 weeks postpartum, leaving the whelping/queening box briefly if at all to eat and eliminate. They are alert and content to remain with their offspring. Some protective dams may show aggression to housemate animals or even people with whom they are normally tolerant, such behavior tends to dissipate after 1-2 weeks of lactation. Lactation typically presents the greatest nutritional and caloric demand of the female’s life. Weight loss and dehydration may occur and impact lactation if food and water are not made readily available, sometimes this entails leaving both in the nest box with a nervous dam. Partial anorexia can be exhibited during the last weeks of gestation and in the immediate postpartum period, but the appetite should return and increase as lactation progresses. Poor appetite during the last weeks of gestation can be due to displacement of the gastrointestinal tract by the gravid uterus. Partial anorexia early in the postpartum period can occur secondary to digestive upset following the consumption of numerous placenta. Diarrhea can occur secondary to increased rations and rich food (bacterial overgrowth secondary to carbohydrate malassimilation). Marked postpartum effluvium is normal in the bitch, usually occurring at 4-6 weeks after whelping, and sparing only the head. This is usually more marked than that which occurs in conjunction with the typical estrous cycle, and can be interpreted as pathologic by an owner, especially in conjunction with the weight loss typically associated with lactation.

The body temperature of the dam may be mildly elevated (<103.0 degrees F) in the immediate postpartum period, reflecting anticipated normal inflammation associated with parturition, but should return to normal levels within 24-48 hours. If a cesarean section took place, differentiating normal post surgical inflammation from fever associated with pathology may be difficult. The physical examination and a complete hemogram help the clinician differentiate between the two. Normal postpartum lochia is brick red in color, non odorous, and diminishes over several days to weeks (uterine involution and repair occur for up to 16 weeks in the bitch). The mammary glands should not be painful; rather they are symmetric and moderately firm without heat, erythema, or palpable firm masses. If expressed, normal milk is grey to white in color and of watery consistency.

**Clinical problems**

**Inappropriate maternal behavior**

Appropriate maternal behavior is critical to neonatal survival and includes attentiveness, facilitation of nursing, retrieving neonates, grooming and protecting neonates. Although maternal behavior is instinctual, it can be negatively influenced by anesthetic drugs, pain, stress, and excessive human interference. Maternal bonding is a pheromone mediated event initiated at parturition. Whelping and queening should take place in quiet, familial surroundings, with minimal human interference, yet adequate supervision. Dams with good maternal instincts exhibit caution when entering or moving about the nest box so as not to traumatize neonates by stepping or lying on them. A guardrail along the inside of the whelping box prevents inadvertent smothering of canine neonates.

The neuroendocrine reflex regulating mammary gland myoepithelial cell contraction and subsequent milk ejection is mediated by oxytocin and activated by neonatal suckling. During stress, epinephrine induces vasoconstriction, blocking the entry of oxytocin into the mammary gland and preventing milk ejection. A nervous, agitated dam will likely have poor milk availability. Dopamine antagonist tranquilizers, with minimal prolactin interference (ace promazine 0.01-0.02 mg/kg) administered at the lowest effective dose to minimize neonatal sedation, can improve maternal behavior and mild ejection in nervous dams. Piling of littermates near their dam facilitates the maintenance of their adequate body temperature (neonates cannot thermoregulate/shiver for up to 4 weeks of age) and makes nursing readily

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available. Normal maternal behavior includes gentle retrieval of neonates who have become dispersed and isolated across the nest box. Grooming of the neonates immediately following parturition stimulates their cardiovascular and pulmonary function and removes amniotic fluids. Dams demonstrating little interest in resuscitating neonates can have poor maternal behavior throughout the postnatal period. Later, maternal grooming stimulates reflex neonatal urination and defecation and maintains the neonatal coat in a clean, dry state. Occasionally, excessive protective behavior or fear-induced maternal aggression can occur. Mild tranquilization of the dam with an anti-anxiety agent can help, but neonatal drug administration via the milk can be problematic. Benzodiazepines, GABA synergists, are reportedly superior to phenothiazines for fear-induced aggression (diazepam 0.55-2.2 mg/kg). The role of newer anti-anxiety pharmaceuticals in maternal aggression has not been described in a controlled setting.

**Uterine disorders**

Complete or partial prolapse of the uterus is an uncommon postpartum condition in the bitch, occurring rarely in the queen. The diagnosis is based on palpation of a firm, tubular mass protruding from the vulva postpartum, and inability to identify the uterus with abdominal ultrasonography. Vaginal hyperplasia and prolapse, secondary to a hypersensitivity of focal (periurethral) vaginal mucosa to estrogen, can recur near parturition and should be ruled out by physical examination, vaginoscopy, or contrast radiography. The prolapsed uterine tissues are at risk for maceration and infection from exposure and contamination. The size of most bitches and queens precludes manual replacement; laparotomy and ovariohysterectomy are usually indicated.

Rupture of the uterus occurs most commonly with very large litters causing marked stretching and thinning of the uterine wall, especially in multiparous dams with dystocia. Immediate laparotomy for retrieval of fetuses and repair or removal of the uterus, as well as culture and lavage of the abdominal cavity, is indicated. The uterus should be carefully examined at any cesarean section for any areas with or prone to rupture. Peritonitis can result from an undetected uterine tear. Unilateral hysterectomy can be considered if the damaged area is limited and the dam valuable to a breeding program.

The persistence of serosanguinous to hemorrhagic vaginal discharge beyond 16 weeks post partum can indicate subinvolution of the placental sites of attachment (SIPS) in the bitch. Histologically, fetal trophoblastic cells have persisted in the myometrium instead of degenerating, endometrial vessel thrombosis is lacking, and normal involution of the uterus is prevented. Normal interplacental regions exist. Eosinophilic masses of collagen and dilated endometrial glands protrude into the uterine lumen, oozing blood. The cause is unknown, blood loss is usually minimal, intrauterine infection not present, and fertility is unaffected. Treatment is generally not necessary, as recovery is spontaneous and symptoms mild. In the uncommon situation where vaginal bleeding from SIPS is copious enough to cause serious anemia, coagulopathies (likely defects in the intrinsic pathway or thrombocytopenia/thrombocytopenias), trauma, neoplasia of the genitourinary tract, metritis and proestrus should be ruled out. Vaginal cytology, vaginoscopy, coagulation testing and abdominal ultrasound assist in the diagnosis. Treatment in these cases can be attempted with ergonovine (0.2 mg/15kg IM) administered once or twice. The benefit of therapeutic prostaglandins and/or oxytocin is questionable and not proven in any controlled study. The preventative value of oxytocin given in the immediate postpartum period is also unproven. Laparotomy and ovariohysterectomy are curative. Histologic examination of the uterus is indicated to confirm the diagnosis.

Acute infection of the postpartum endometrium should be suspected if lethargy, anorexia, decreased lactation and poor mothering occur accompanied by fever and malodorous vaginal discharge. Metritis is serious and sometimes preceded by dystocia, contaminated obstetrical manipulations, or retained fetuses and/or placentae. Hematologic and biochemical changes often suggest septicemia, systemic inflammation reaction and endotoxemia. Vaginal cytology shows a hemorrhagic to purulent septic discharge. Ultrasound of the abdomen allows evaluation of intrauterine contents and the uterine wall. Retained fetuses and placentae can also be identified with ultrasound. A guarded cranial vaginal culture is likely representative of intrauterine flora and should be submitted for both aerobic and anaerobic culture and sensitivities, and permits retrospective assessment of empirically selected antibiotic therapy. Bacterial ascension from the lower genitourinary tract is more common than hematogenous spread, and Escherichia coli the most common causative organism in both bitches and queens. Therapy consists of intravenous fluid and electrolyte support, appropriate bactericidal antibiotic administration and pharmacologic uterine evacuation.
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usually with prostaglandin F2 alpha (in the United States) at a dose of 0.10-0.20 mg/kg q 12-24h for 3-5 days. An ovariohysterectomy may be indicated if the bitch’s condition permits, and she is poorly responsive to medical management. Ergonovine (0.2 mg/kg given once IM) is also an effective ecbolic agent, but may cause rupture of a friable uterine wall. Synthetic prostaglandins offer more uterine specific therapy where available. Oxytocin is unlikely to promote effective uterine evacuation when administered >24-48 hours postpartum. Nurslings should be hand reared if the dam is seriously sick. Metritis can become chronic and cause infertility.

Mammary disorders

agalactia is defined as a failure to provide milk to neonates. Primary agalactia, a lack of mammary development during gestation, results from a failure of milk production and is uncommon. A defect in the pituitary ovarian mammary gland axis is suspected. The use of progesterone compounds late in gestation can interfere with lactation. Secondary agalactia, a lack of milk availability due to a failure of ejection, is more common. Mammary development is marked, but milk cannot be readily expressed through the teat sphincter. The normal production of colostrum in the immediate post partum period should not be confused with agalactia. Agalactia can occur secondary to premature parturition, severe stress, malnutrition, debility, metritis, or mastitis. Treatment includes providing supplementation to the neonates while encouraging suckling to promote milk ejection, providing optimal levels of nutrition and adequate water to the dam, and resolution of any underlying disease. If detected early, milk let down can often be induced pharmacologically. Mini dose oxytocin, 0.25-1.0 units per injection, is given subcutaneously every 2 hours. Neonates are removed for 30 minutes post injection, and then encouraged to suckle, or gentle stripping of the glands performed. Metoclopramide, 0.1-0.2 mg/kg.sc is given q 12h (dopamine antagonist) to promote milk production. Therapy is usually rewarding within 24 hours. Some authors advise a much higher dose of metoclopramide, but neurologic side effects become possible.

Galactostasis can cause engorgement and edema of the mammary gland with associated discomfort making further nursing unlikely, and becoming self perpetuating. Galactostasis occurs secondary to inverted or imperforate teats, failure to rotate nurslings, litter loss, an unusually small litter, or rarely with pseudocyesis.

Mastitis, septic inflammation of the mammary gland, can be acute and fulminate, or chronic and low grade, involving a single or multiple mammary glands. Coliforms, staphylococci, and streptococci are most commonly isolated in both bitches and queens. The source of bacteria is cutaneous, exogenous or hematogenous. Mild mammary discomfort and heat, galactostasis, cutaneous inflammation, and the presence of an intramammary mass are the earliest signs. Milk is commonly discolored red or brown due to the presence of red and white blood cells. Moderate cases exhibit pain, reluctance to nurse or lie down, anorexia and lethargy. Fever can be marked and may precede other clinical signs. Advanced cases can present in septic shock, with abscessed or necrotic glands. The diagnosis is based upon physical examination. Milk cell counts in bitches are not predictive of mastitis. Culture and sensitivity of milk collected aseptically from affected glands allows retrospective evaluation of antibiotic selection. Therapy should begin immediately, consisting of broad spectrum, bactericidal antimicrobials and gentle physical therapy. Analgesics may be indicated; neonates tolerate opioid analgesia in the dam. First generation cephalosporins (cephalexin 10-20 mg/kg q8-12 h) and beta lactamase resistant penicillins (Clavamox 14 mg/kg q 12 h) are advised and safe for the neonates. Antibiotic therapy may be warranted until weaning, and can preclude further nursing if sensitivities force the choice of a drug potentially toxic to neonates. Warm compresses or whirlpool therapy of the affected gland with gentle stripping of milk can potentially avert abscessation and rupture of the gland. Severe necrosis warrants mastectomy when the dam is stabilized, and aggressive wound management. Antiprolactin therapy (cabergoline 1.5-5.0 ug/kg/day divided bid) may be indicated in severe cases, to reduce lactation. There is no evidence that nursing from affected glands is problematic for neonates, but they tend to avoid glands which are difficult to obtain milk from. The affected gland should be protected from trauma from nest box edges and neonatal claws. Mastitis can recur in subsequent lactations regardless of preventative measures taken. Early detection and treatment is optimal, rather than prophylactic antibiotics, which tend to favor resistant organisms.

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Use of progestogens for oestrus prevention may lead to the following side-effects:

- Development of cystic endometrial hyperplasia (CEH)-endometritis
- Prolonged gestation if conception occurs after a progestogen is administered subcutaneously at the onset of the follicular phase; Caesarean section may be needed.
- Hypersecretion of growth hormone, which may lead to diabetes mellitus.
- Increased risk of neoplastic transformation of mammary tissue; in young cats fibroadenomatous hyperplasia.

With the exception of prolonged pregnancy, these side-effects are largely dependent upon the total progestogen exposure. Using the recommended doses the exposure may be greater with MPA and MA than with proligestone, the latter being a rather weak progestogen.

Because of the mentioned side-effects it is clear that an alternative to progestogens is desirable. This alternative would have to be a highly targeted strategy that ideally only suppresses oestrous, thus without systemic side-effects and with complete reversibility.

The hypothalamic-pituitary-gonadal axis (figure 1) shows that targeting GnRH would theoretically be an elegant way of interfering with reproductive function, as GnRH mainly targets the gonadotrophic cells of the pituitary.

The progestogens most frequently used for oestrus prevention in the dog are proligestone and MPA. These drugs should be administered during anoestrus, approximately 1 month before onset of the expected follicular phase. After the administration of proligestone oestrus is usually suppressed for 9-12 months and after MPA it may be up to 2-3 years. For that reason the manufacturer does not recommend using MPA in animals intended for breeding at a later date.
GnRH agonists or GnRH antagonists have been identified as interesting targets. As yet, GnRH antagonists are unsuitable for clinical use, because of cost, inconvenience for long-term use, and side-effects (first-generation GnRH antagonists). However, a single dose of the third-generation GnRH antagonist acyline has recently been shown to be safe in bitches and highly effective in preventing ovulation (6). However, simultaneous administration of acyline and a GnRH agonist implant did not prevent oestrus in nine of twelve bitches, five of which also ovulated (6). More research on the effects and mode of delivery is needed before this can be used as an alternative to progestogens.

GnRH agonists administered in high doses over a long period of time prevent oestrus by pituitary down-regulation. However, initially the gonadotrophin secretion is stimulated which may cause oestrus to be induced (7). A more recent discovery is the key role of the kiss1/gpr-54 system in the regulation of reproduction (8). For example, these kisspeptin neurons, which are located in the arcuate nucleus in the hypothalamus, express the sex steroid receptors that the GnRH neurons lack (9). Future research could be aimed at manipulating the function of this system to suppress reproduction.

References:

GnRH agonists administered continuously in high doses over a long period of time prevent oestrus by pituitary down-regulation. However, in female animals, the initial stimulatory effect of GnRH analogues may cause signs of oestrus.

Several strategies have been proposed to prevent initial induction of oestrus. First, administering the implant during the luteal phase, when the plasma progesterone concentration is high. However, in bitches, oestrus may even be induced if the implant is administered during the luteal phase, when plasma progesterone concentrations are high, although information on this topic is contradictory. Alternatively, induction of oestrus by implantation of a GnRH agonist during anoestrus may be prevented by the prior administration of a progestogen. However, the efficacy of this approach appears to depend on the interval between the onset of progestogen treatment and administration of the implant, the stage of anoestrus, the dose of progestogen, and the type of GnRH analogue (6,9). Furthermore, adding progestogens to prevent the initial stimulation of GnRH...
agonists cancels the advantage of not administering progestogens for oestrus prevention. Secondly, it is possible to prevent the induction of oestrus by administering a GnRH agonist to pre-pubertal bitches at 4 months of age but not at 7 months, although in the latter dogs oestrus is delayed for a long time. However, Rubion et al. (2006) reported that GnRH agonist implants administered to bitches before puberty prevented reproductive function for 1 year. Following removal of the implant oestrous occurred naturally in 7 of 10 bitches and was induced in the other three after 1.2-14.3 months.

Another potential disadvantage of the use of GnRH agonist implants for oestrus prevention, is the occurrence of complications, such as persistent oestrus or uterine pathology. A thorough gynaecological examination, which rules out pre-existing ovarian or uterine pathology might reduce the chance on these complications to occur, but more research regarding the risk factors for these complications to occur is warranted.

In cats, several studies have showed that oestrus prevention can be achieved with GnRH agonist implants. Similar to bitches, oestrus may be induced after implant administration in adult cats. Depending on the GnRH agonist and the dose used, the GnRH agonist implant may be effective for periods up to three years in cats, which might be inappropriately long for queens that are destined to be bred. Limited data are available on implantation before puberty to avoid oestrus.

When long-term oestrus prevention is desired, owner compliance, eg. presenting the animal for timely re-implantation, is of importance and an aspect that deserves attention. Timely re-implantation is necessary to prevent spontaneous oestrus to occur or oestrous induction upon re-implantation.

References:

REGULATION OF CORPUS LUTEUM FUNCTION IN THE DOG AND INDUCTION OF PARTURITION

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Introduction
In cases of dystocia, a caesarean section is often the last option for delivering live puppies. If performed timely and lege artis with a good anaesthetic protocol, caesarean section is safe for both puppies and bitch. However, in cases of prolonged pregnancy, an elective caesarean section is performed to prevent prenatal mortality due to placental insufficiency. Prolonged gestation is most often seen in bitches carrying small litters of only 1 or 2 puppies. In these cases the caesarean section is usually performed on day 66 or 67 after mating, which might be an over- or underestimation if ovulation timing was not performed.

Performing a caesarean section when parturition is not initiated spontaneously means that several endocrine changes that normally occur around parturition are not...
well synchronized. This can have several consequences that need to be addressed. For example: induction of maternal behaviour may be impaired, especially in primiparous bitches. This might necessitate tube feeding of the puppies because of inadequate maternal care by the bitch. Additionally, perioperative complications that otherwise form minor problems, can be more severe, e.g. blood loss from placental sites while the cervix is still closed.

**Induction of parturition**

Although the triggering mechanism for parturition in the bitch is not yet fully understood, it is clear that progesterone, of which the corpora lutea are the sole source in the bitch, is necessary for maintaining pregnancy in the bitch (1,2). For this reason several protocols that have been evaluated for induction of parturition in the bitch have targeted the influence of progesterone.

Successful induction of parturition with progesterone-receptor blockers (antiprogestins), such as mifepristone (RU38486) and aglépristone (RU46534), has been examined, using different protocols. Fieni and others (2001) administered 15 mg/kg b.w. (s.c.) aglépristone on day 58 of gestation, with alfaprostol (n=5) or oxytocin (n=5) given 24 h later and every 2 h afterwards as a standard treatment until the expulsion of the last pup. All bitches whelped within 27 to 38 h after treatment. Baan and others (2005 and 2008) administered 30 mg/kg b.w. (s.c.) aglépristone on day 58 of gestation (n=6) (3,4). Six dogs served as controls. In this study the first pup was expelled within 32 to 56 h after the first treatment, on day 59.5 ± 0.2 (sem). All parturitions in this study were managed using a standard intervention protocol in order to diminish variation in the course of parturition induced by random treatments. Applying this protocol, the number of interventions was not significantly different, but vaginal explorations and oxytocin injections were needed twice as often in the induced group compared to the spontaneously whelping group. Number of stillborn puppies and weight at birth were similar in both groups. In conclusion, successful induction of premature parturition can be achieved by treatment with aglépristone. The lower plasma PGFM concentrations in the induced group may explain why parturition in this group required more interventions than in the control group, although the difference was not statistically significant. Therefore, close monitoring of the induced parturition by the clinician is advisable.

In most studies concerning induction of parturition in the bitch using a protocol with aglépristone, parturition was induced around day 58 of gestation in order to show that parturition occurred as a result of the treatment. The situation is different when dealing with cases of prolonged gestation. These cases usually involve litters with smaller numbers of puppies than the litters that are described in literature. Treatment may be indicated after the owners have waited for spontaneous parturition to occur on the expected date. In our experience, using aglépristone as the only treatment in 1 and 2 puppy litters starting with treatment from day 65 of gestation onwards, parturition did not progress beyond stage I of labor and a caesarean section was indicated. However, a successful induction of parturition in one bitch with a prolonged pregnancy by treatment with aglépristone followed by PGF2α, 12 and 24 h later, has been described (5).

An alternative method to decrease the plasma progesterone concentration is inhibition of progesterone synthesis. Keister and others (1989) showed that epostane, a 3β-hydroxysteroid dehydrogenase-inhibitor, can be used to induce parturition in Beagle bitches (6). A preliminary study on the effects it has on luteal progesterone secretion showed that trilostane is probably not a good candidate for induction of abortion and parturition in the dog (7).

**Conclusion**

Prolonged gestation as an indication for medical induction of parturition using aglépristone based protocols needs more study. Primarily because it is unclear if the treatment is efficient and safe in this type of patient. Furthermore, it is not known on which day of gestation treatment with aglépristone should be started to prevent unnecessary treatment and if oxytocin or PGF2α should be added to the protocol.

References:


Reproductive tract pathology is diverse, with many different possible diagnoses. However, the symptoms that your patients are presented with are limited, eg. infertility or vaginal discharge. Therefore, a thorough history and complete physical examination are required in order to achieve an accurate differential diagnosis and to limit the number of necessary further examinations (1,2).

History
To be able to interpret the findings during the following physical examination in intact queens and bitches, it is important to take into account information regarding the oestrous cycle. In cases of vaginal discharge, for example, knowledge on the oestrous cycle stage can help to interpret the discharge as either physiological or pathological.

Physical examination
Besides the external examination, in bitches, an internal examination often is a necessary part of a complete physical examination. In cats, however, due to the small dimensions, an internal examination is difficult to perform and therefore only indicated in selected cases. If necessary, cats are sedated in order to be able to perform the examination properly.

As observation of the entire vagina is important, a rigid tubular speculum with a minimal length of 20 cm and a diameter of 12 mm, in conjunction with a light source, can be used to perform vaginoscopy. Human paediatric proctoscopes (eg. cat. no. 8834.08, R. Wolf, Germany), that can be connected to a light source, are a practical alternative for use in bitches of most sizes. Another option is the use of a cysto-urethroscope, which are longer and have a smaller diameter (eg. cat. no. 027KL/027NL/325B, K. Storz, Germany).

Depending on the resulting differential diagnosis, further examination can range from diagnostic imaging to provocation tests of the pituitary-gonadal axis and establishing the karyotype.

In several clinical cases, the diagnostic steps taken will be discussed and examples will be given of the expected findings.

References: