TO BREED OR NOT TO BREED? THAT IS THE QUESTION. PRE-BREEDING AND GENETIC EVALUATION

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The recent sequencing of the canine genome has opened up a whole new frontier in veterinary medicine. In the last century, veterinary medicine has made major advances in treating and eliminating many diseases through vaccination, parasite control and proper nutrition. A whole new realm of possibilities for diagnosis, prevention and treatment of disease is on the horizon with genetic modalities. Over 200 genes and their function have been identified in the canine genome—genes specific for phenotype (such as coat color and hair pattern) or breed specific diseases (such as retinal atrophy, and von Willebrand’s disease).

Genetic disease often results from a single mutation in an individual’s DNA. The mutation may be a point mutation, translocation, repeat or insertion affecting a gene or its promoter. Subsequently, the gene’s encoded protein is malformed or eliminated; altering its activity, transport function, or receptor function. If these genetic changes result in favorable characteristic changes, we preferentially select for them. If the mutations results in an unfavorable characteristic changes, we call it disease. Mammals are diploid and carry two genes for each function. The corresponding gene on the alternate chromosome may produce the normal protein and completely or partially compensate for the mutation’s effect. This is known as a recessive trait mutation. In the homozygous state, both genes are affected and the mutation will be expressed. If the mutation alters a dominant gene, the effect will be expressed even if only a single gene is mutated. When disease occurs from a dominant trait mutation, it is readily identified and eliminated through selective breeding.

The artificial establishment and maintenance of pure-bred dogs is a double-edged sword. On the one hand, it guarantees consistency in body type, temperament, instinct and function. On the other hand, inbreeding and line-breeding for selection of phenotypic characteristics creates a bottleneck, or founder effect, decreasing the gene pool. This loss of genetic diversity leads to increased genetic disease and decreased adaptability. The prevalence of genetic defects in pure-bred dogs is a simple matter of statistical probability. As the gene pool becomes smaller, it becomes statistically more probable that two recessive genes will align to form a homozygote, thus expressing the mutation. Even now with most breeds and breed standards being established, we witness further narrowing of the gene pool by the “popular sire” effect. Overuse of a single popular individual over represents his genetics in a breed population, increasing the possibility for expression of a recessive genetic disease for which he was an unknown carrier.

The canine genome project determined that the canine DNA sequence encodes 40,000 genes. Use of the canine genome and development of a complete gene map will ideally lead to elimination of mutant genes from the population by identification and sequestration of carrier animals from the breeding stock. Elimination of carriers, however, could detrimentally decrease the gene pool even further—especially in rare breeds with very small populations. It is thus preferable, in some cases, to allow breeding of identified carriers to non-carriers. The affected gene would remain in the genome in a heterozygous state, the incidence of disease would be eliminated, and genetic diversity maintained.

Unfortunately, the elimination of all genetic diseases cannot be accomplished by gene mapping alone, because epigenetics complicates genetic management. Simply put, epigenetics is the effect of environmental influence or pressure which alters gene expression without altering the genomic sequence. One way this is done is through methylation of the cytosine nucleic acid which contributes to the folding and unfolding of the DNA double helix and its association with histones. Heat damage, toxins, nutritional deficits, or excesses may alter the degree of methylation; activating quiescent genes or deactivating functional genes. The deregulation of genes can lead to diseases such as cancer, immune dysfunction or heart defects. Hypomethylation has been shown to be associated with numerous cancers including lymphoma, leukemia, and hemangiosarcoma. It is hypothesized that deregulation of growth factor genes result in unregulated cell division. If deregulation of genes by epigenetics affects the germ cells, sperm or oocytes, the condition may be propagated to the offspring. Such
epigenetic disease cannot be diagnosed by gene mapping, as the DNA sequence is unaltered.

Epigenetics, and the fact that many diseases are the result of interaction of multiple genes (e.g. hip dysplasia), mean pre-breeding evaluations (such as OFA tests) continue to be necessary. The combination of such an evaluation, in conjunction with DNA testing, is destined to improve the genotype and phenotype of our best friend.

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Dystocias may be classified into two categories: Passive and Obstructive. Passive Dystocia is failure to engage or cessation of abdominal and uterine contractions—Uterine Inertia (UI). UI is the most common cause of dystocia. It can sometimes be managed medically, but often requires emergency C-section. Two types of UI are recognized. Primary UI is failure of the dam to progress to second stage labor (rupture of chorio-allantoic membranes). Secondary UI is cessation of uterine contractions after the delivery of part of the litter. The physiologic explanation for UI is incompletely understood but is likely a combination of effects related to hormones and electrolyte concentrations. Calcium and magnesium, as evidenced in dairy cattle, play an active role in uterine contraction and hence in UI. The positive response and return to labor after calcium supplementation in dogs further supports the role calcium plays in UI. It has been demonstrated that ionized calcium and total serum calcium concentrations, although within physiologically normal ranges, are significantly decreased in bitches in dystocia compared to eutocia. Similarly, prostaglandin and vasopressin are decreased in bitches diagnosed with uterine inertia, while oxytocin levels remain insignificantly different from eutocia bitches. Obstructive Dystocia is a physical impairment interfering with normal delivery (e.g. fetal oversize or fetal malposition). Prolonged obstructive dystocia may result in secondary UI.

Primary uterine inertia often presents the greatest diagnostic challenge as it is difficult to ascertain if the dam has entered first stage labor. Serum progesterone levels less than 2 ng/ml are consistent with term pregnancy and indicative that labor should have begun or will soon commence. In-house testing may not be available or sensitive enough to safely determine progesterone levels <2 ng/ml and delays of send out testing make it impractical. Tocodynamometry or electrohysterography are extremely valuable tools in diagnosing UI and monitoring progression of labor, but are not readily available in most clinical settings. Therefore, diagnosis of primary UI is commonly made based on breeding history, clinical signs of first stage labor (panting, restlessness), and failure to progress to second stage labor 24 hours after onset of clinical signs or the progesterone-associated temperature drop. Secondary UI, too, is best diagnosed using a uterine monitoring device. If unavailable, a history of active dystocia, or a prolonged interval between delivery of puppies supports a diagnosis of secondary UI.

The incidence of canine dystocia is difficult to assess as most normal deliveries go unrecorded; however, dystocia has been estimated to occur in 5-16% of whelpings. Incidence appears to be related to breed and litter size. Singleton or very large litters are more likely to be problematic. Brachycephalic breeds have a higher incidence as a result of physical attributes—large, blunt heads in relation to fetal body size and maternal pelvic diameter. Small and Toy breeds have an increased rate of dystocia because of body size, predisposition to eclampsia (hypocalcemia), and a propensity for small litters resulting in fetal oversize. Dystocia also has familial tendencies and nutritional associations.

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Management of dystocia is a continuous assessment and re-assessment of fetal and maternal wellbeing, diagnosis of cause, and response to treatment. On presentation a physical examination of the dam should include a vaginal exam (digital or speculum) to assess patency of the cervix or presence of fetus in the birth canal. Fetal heart rates indicate the urgency for immediate surgical intervention or the potential to pharmacologically intervene. C-section should be initiated immediately if fetal heart rates (FHR), measured with ultrasound or fetal Doppler, drop below 150 bpm (in response to intrauterine stress, FHR decrease). If dam and fetal vitals are stable, abdominal radiographs should be taken to rule out obstructive dystocia (eg. transverse presentation, fetal monsters or oversize) and determine number of fetuses remaining in utero.

If obstructive dystocia is diagnosed and cannot be corrected, C-section is indicated. If puppies partially delivered into the birth canal can be manipulated and delivered vaginally, subsequent puppies may be whelped without further intervention or the bitch may require treatment of secondary UI. Attempts to increase uterine tone and contractions in face of an obstructive dystocia may result in uterine rupture or hemorrhage and fetal hypoxia and increased neonatal losses.

In the absence of obstruction, and if dam and fetal vitals are stable (FHR > 150 bpm), delivery of remaining fetuses may be attempted using medical therapies including calcium supplementation (5-10 mg/kg slowly IV) and low dose oxytocin (1-5 IU SQ q30 min) given 30 minutes after administration of calcium if no progress is observed. The response to medical therapy and re-evaluation of dam and fetal wellbeing will determine the need to repeat medical intervention or to proceed to C-section. A minimum data base, including a CBC and Serum Chemistry Panel, provides information on the condition of the dam, and is useful if the bitch requires anesthesia or surgery. Serum total calcium and ionized calcium levels may be within normal range, but the bitch may still respond to calcium supplementation. Serum glucose levels should be monitored to avoid hypoglycemia.

Puppy survival is directly correlated with the degree of fetal stress which correlates to the duration of labor. It is therefore essential for the veterinarian to effectively and accurately determine the cause of dystocia, the potential for correcting the problem non-surgically or the need to proceed to emergency C-section. The decision to proceed to C-section is based on maternal and fetal well being, financial constraints of the owner, number of puppies remaining in utero, and the cause of dystocia.

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Vaginal cytology consistent with estrus or a negative lutenizing hormone (LH) test should confirm the presence of ovarian tissue. Normally, ovarian negative feedback suppresses LH release from the anterior pituitary (except during the LH surge of estrus). In ovarioctomized animals, LH release is not suppressed and can be measured in sufficiently high concentrations in serum. Therefore, a positive LH test indicates either ovarioectomy or a physiologic surge of LH during estrus. A vaginal cytology at the time of LH testing will differentiate the positive test.

Alternatively, a serum progesterone greater than 2 ng/ml would indicate the presence of luteal tissue which must be ruled out. If progesterone testing is done between luteal phases, baseline progesterone levels will not differentiate an anestrus bitch from a spayed bitch, and a diagnosis will be inconclusive.

Once diagnosed, surgical removal of the ovarian remnant is required. Surgery is best undertaken while the bitch is in diestrus as the active corpus luteum (CL) will make the ovarian remnant more evident.

Stump Pyometra is actually the sequel of an ovarian remnant. It is purulent inflammation of the remaining uterine tissue post-hysterectomy under the influence of progesterone. Affected bitches may or may not present with vaginal discharge, anorexia, polyuria, polyp Dysia, or hyperthermia. Stump pyometra should always be a consideration in a spayed bitch with fever of unknown origin. Diagnosis should be made by demonstrating the presence of ovarian tissue with elevated serum progesterone or a positive LH test. Ultrasonography can be done to demonstrate enlargement or fluid within the uterine stump. Treatment is to remove the uterine stump AND the ovarian remnant.

Vaginitis or Vestibulitis is perhaps the most common reproductive pathology of spayed bitches. Chronic licking of the vulva is the usual presenting complaint. It is usually diagnosed simply on the presence of purulent vulvar discharge but must be distinguished from stump pyometra. A speculum or vaginoscopic exam should differentiate vaginitis from vestibulitis. Cytology commonly demonstrates mature, hypersegmented, non-degenerate polymorphonuclear leukocytes (PMN); and culture often results in no significant or mixed bacterial growth.

Vestibulitis commonly results from conformational abnormalities of the vulva, such as inverted vulvar folds or perivulvar fat pads. Perivulvar dermatitis or clitoral hypertrophy may also cause vestibulitis or may be sequela from chronic licking. Common etiologies for vaginitis include primary infection (Brucella canis, herpes virus) and infection secondary to a foreign body, urinary incontinence or urine pooling, tumors, or vaginal abnormalities such as strictures or bands. Most adult onset vaginitis is idiopathic. Juvenile/puppy vaginitis occurs in young bitches as a symbiotic relationship is established between bacteria and the naïve vaginal mucosa.

Successful treatment requires resolving the inciting cause and may require long term antibiotics (4-6 weeks) to completely resolve any associated dermatitis. Treatment with antibiotics alone is discouraged as symptoms are likely to reoccur. Some chronic vaginitis in spayed bitches respond to estrogen therapy (DES)—probably as a direct result of increased urethral sphincter tone resolving urinary incontinence, more than estrogen’s immunologic effects on the mucosa at such low doses. Conservative treatment and the tincture of time often resolve idiopathic and juvenile vaginitis.

Mammary Neoplasia: Mammary tumors (MT) are the most common neoplasia seen in dogs. Slightly over 50% of MT in dogs are benign and non-metastatic. Ovariohysterectomy (OHE) prior to the first estrus nearly eliminates the risk of MT. OHE following the second heat showed no benefit in decreasing the incidence of MT. Tumors which have progesterone or estrogen receptors are more likely benign, and tumor growth is retarded by elimination of estrogens and progesterone. However, OHE in conjunction with mastectomy or nodulectomy does not improve survival or decrease incidence of subsequent tumor development. As would be expected, prognosis is worse for large tumors, multiple tumors, older dogs and higher grade tumors.

Prostatic Neoplasia (PN) has a significantly higher incidence in castrated dogs. Castration eliminates the risk of benign prostatic hypertrophy (BPH). However, unlike prostate cancer in humans, BPH has no effect on the incidence of prostatic cancer in dogs. In addition, canine PN is non-androgen dependent. Clinical signs...
of PN are similar to BPH, including hematuria and hemospermia. However, unlike BPH which generally has eccentric enlargement away from the urethra, PN often invades the urethra and causes stranguria. Diagnosis is primarily made based on clinical signs, evidence of asymmetric enlargement of the prostate on ultrasonography and cytology of prostatic fluid or fine needle aspirate, and histology. There are no reliable prostate specific markers which distinguish BPH from PN. There is no effective treatment for PN, neither surgical, chemotherapeutic nor radiation. Further, PN is highly metastatic and metastasis is likely to have occurred by the time of diagnosis.

**Paraphimosis** is protrusion of the penis from the prepuce without an erection. It is primarily a preputial disease. A small preputial opening may constrict venous blood flow from the exposed penis resulting in swelling and edema which further prevents retrogression. Weakness of the preputial muscles preventing it from pulling the prepuce cranially over the penis, or an unnaturally short prepuce, or behavior may also be implicated. Manual replacement is usually possible. Chronic paraphimosis and excoriation or trauma to the penis necessitates surgical correction. One dog developed squamous cell carcinoma from chronic exposure and irritation (personal observation, unpublished). Cranial advancement of the prepuce is the preferred treatment. Enlargement of the preputial opening must be done in such a way to avoid strictures. Purse string suturing is ill advised, as the penis may penetrate the purse string and become strangulated.

**Priapism** is persistent erection of the penis. The etiology and pathophysiology of priapism is uncertain. The mechanism for penile erection has both a psychogenic and a neurogenic component. Parasympathetic stimulation from sacral nerves 1-3 release Nitric Oxide (NO) which causes relaxation of smooth muscle of the corpus cavernosum and spongiosum, increases arterial pressure blood to the penis, and decreases venous outflow by mechanical constriction of excurrent veins. Detumescence is facilitated by increased sympathetic tone (norepinephrine), contraction of smooth muscle of corpus cavernosum and ejection of blood from the penis.

Medical resolution has had mixed efficacy but may be improved if treatment is initiated within three hours of onset. Persistent erection causes stasis and sludging of blood, coagulation and fibrosis, low oxygen saturation and increased carbon dioxide concentrations resulting in cell death and permanent, irreversible damage.

**Parasympathetic** antagonists could decrease erectile stimulation; however, as the penile receptors are NO induced (rather than muscarinic or nicotinic) there is no specific acting parasympathetic inhibitor. Anti-cholinergic drugs block both parasympathetic and sympathetic innervation non-preferentially and have been used with mixed results in treating priapism. Benztropine (0.015 mg/kg IV) has been effective in people and in horses. Sympathetic stimulation could facilitate detumescence by increasing smooth muscle tone in the cavernosum, forcing blood out of the penis. Phenylepherine, an alpha 1 agonist, has been used locally to facilitate resolution of priapism with equivocal results.
Artificial insemination (AI) in dogs has become wildly popular over the last decades—partly due to advances in canine reproduction and partly due to the lucrative pet industry. Some dog owners opt for AI to avoid complications of natural breeding such as injury or transmission of venereal diseases. Others prefer to improve their genetic line by use of a sire some distance away; it is easier and cheaper to ship semen than either dog. Other owners have no choice but to use AI for problem breeders including subfertile bitches or studs, geriatric or young, inexperienced studs which cannot achieve a tie, aggressive bitches, or conformationally challenged breeds (e.g. English Bulldog). Recently, many owners have elected AI to improve pregnancy rates and litter size.

Pregnancy rates (# of bitches pregnant/# of bitches bred) and conception rates (# of fetuses/# of ovulated oocytes) achieved using AI can equal or exceed rates achieved by natural breeding.2 This is in large part due to accurate timing of insemination in relation to ovulation and improved semen extenders when cooled shipped semen is used. Perhaps the greatest contributing factor is the wide spread use of trans-cervical insemination (TCI): non-surgical deposition of semen directly into the uterus by catheterization of the cervix. TCI can be achieved using a “Norwegian catheter” or rigid cystoscope. It has major advantages over surgical AI (“implant”) in that it avoids anesthesia, surgical complications, and most importantly, can be easily repeated. Pregnancy rates and litter size are significantly improved with multiple breedings.2

Direct deposit of semen into the uterus eliminates the greatest barrier sperm encounter from natural breeding or vaginal AI: the cervix. Studies have shown that the cervix may prevent >50% of the sperm from entering the uterus.1 Once past the cervix, the sperm’s quest for the oocyte is still fraught with many obstacles. Sperm must traverse the length of the uterus (which may exceed 10 inches in giant breed or multiparous dams), pass through the uterotubal junction, attach to the wall of the uterine tube (oviduct), wait for the oocyte to arrive and mature, capacitate, hyper-activate, bind and penetrate the zona pellucida, and incorporate its haploid DNA. It is suggested that only 1 in a million sperm ever reach the ovum.3 Direct deposit of sperm into the uterus dramatically decreases the minimum number of sperm necessary to reliably achieve pregnancy. The standard recommendation has been ~200 million progressively forward motile (pfm) sperm per breeding dose. With TCI, that number can be decreased by at least half. 100 million pfm sperm has become a standard breeding dose using frozen semen. One study using sex-sorted chilled semen achieved pregnancy and a normal sized litter using 40 million pfm sperm divided between three breedings.4

The minimum number of sperm, however, is a somewhat arbitrary number. It has become evident to me working with other veterinarians who commonly ship or freeze semen—some Theriogenologists, some General Practitioners—that semen counting methods vary greatly between individuals and the results may differ by as much as twofold. The gold standard for sperm counting is the Neubauer hemocytometer hand count. Semen is diluted 1:100 (commonly 20 microliters : 1.98 ml diluent) and a controlled volume fills the sample well by capillary action. Sperm are allowed to settle into one focal plane and are then counted using 100X magnification light microscopy. All the sperm in one of the 3 by 3 squares in the Neubauer grid are counted (see figure). The count is repeated on the grid on the opposite side of the slide and the two numbers are averaged together. For quality control, the two numbers should ideally agree within 10% of each other. The averaged number is the concentration in millions of sperm/ml. Total sperm count is therefore the concentration times the total volume of semen. An alternative method is to count any 3 of the 3 by 3 squares, add them together, multiply by 3 and add 10% of the product, then divide by 10. The result is still concentration of sperm in millions/ml. The availability of automated sperm counters (spectrophotometry, CASA, etc.) could standardize sperm counts and doses; however, validation of those devices with hemocytometer counts show significant variability at low concentrations and high concentrations.5,6

Standard semen evaluation—count, motility, and morphology—has been met with justifiable criticism for its short comings: subjectivity and inability to diagnose...
One must grasp an understanding of the normal reproductive cycle in the bitch to efficiently breed, manage pregnancy and parturition, and diagnose urogenital diseases. Estrus designates the entire reproductive cycle of the bitch from standing heat (breeding) through 3 non-breeding stages back to standing heat. The entire estrous cycle averages about 7 months.

Estrus—standing heat—last a mean of 9 days. Unique to the dog, the hormones responsible for the behavioral signs of estrus are a decreasing level of estrogen and an increasing level of progesterone (P4)—both produced by the follicles. Ovulation occurs in mid-estrus following a 24-48 hour surge in luteinizing hormone (LH).

Estrus is followed by diestrus (or metestrus)—the pregnancy period. The bitch is no longer receptive to the male. The predominant hormone is P4 produced by the corpus luteum (CL). During pregnancy, diestrus lasts 57 days; cut short by fetal induction of parturition. During non-pregnancy, diestrus may last over 75 days as the canine uterus does not produce prostaglandins to induce luteolysis.

Following diestrus, the bitch enters a period of apparent reproductive quiescence termed anestrus. Repro-
Serum hormone levels provide invaluable information in reference to stage of cycle, ovulation timing, determination of whelping date, and monitoring pregnancy. Serum LH can be used to determine ovulation date for managed breedings; or it can be used to determine the sexual status of dogs or cats.\(^2,3\) LH concentrations can be measured using in-house Elisa tests; however, the short duration of the surge necessitates frequent blood tests. More commonly, the LH surge is indirectly diagnosed using serum P4 concentration (and retrospective validation of the LH surge with an ELISA test if necessary). It has been repeatedly demonstrated that the LH surge occurs when the serum P4 concentration rises to 1.5-2.5 ng/ml.\(^4, 5\) Serum P4 is also used to monitor pregnancy. Canine pregnancy relies entirely on CL production of P4 and requires levels to remain above 2 ng/ml. Serum estradiol is rarely measured clinically as levels can be estimated based on vaginal cytology. Serum relaxin is a pregnancy specific hormone produced by the placenta. It can be measured throughout pregnancy starting approximately 25 days post-ovulation.

Ovulation occurs 36-48 hours after the LH surge.\(^4, 5\) Following ovulation, the progesterone levels are extremely variable, probably related to the number of ovulated follicles and subsequent CL.

Reference:

Estrous is the only stage of the estrous cycle which can be definitively identified by evaluation of a single vaginal cytology. Red blood cells may be present; neutrophils (PMN) are absent. Vaginal cell populations are almost entirely cornified (squamous) cells. By convention, cytological estrus is defined as cornification of >80% of the vaginal epithelial cells.

Differentiating proestrus from diestrus can be difficult based on a single cytology. Vaginal epithelial cells during proestrus and diestrus are predominantly a mix of parabasal, intermediate, and (<80%) cornified cells. Serial cytology repeated several days apart may be necessary to determine if cornification is progressing (proestrus) or regressing (dierstrus). The presence or absence of red blood cells or neutrophils in conjunction with the physical exam and history will aid in determining the stage of estrous, a definitive diagnosis cannot be made without further evaluation or serum hormone assays.

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PREGNANCY MONITORING AND MANAGEMENT OF HIGH RISK PREGNANCY IN THE DOG
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All pregnancies are high risk. The well being of both the dam and the fetuses is jeopardized by the process. Pregnancy physiologically and physically stresses the dam’s metabolism and body, affecting every organ system directly or indirectly. Maternal cardiac output and renal tubular perfusion increase. The immune system is mildly suppressed by progesterone (P4) and concomitantly challenged by the presence of foreign proteins on the embryo and placenta. The gastrointestinal system must increase nutritional absorption while being compressed. The skin is stretched. The musculoskeletal system is forced to bear greater weight while having its underlying support system stripped away one calcium atom at a time. The dam’s pulmonary effort is increased, and the hepatic system is working overtime trying to compensate for increase energy demands, alternating glucose excesses and deficiencies, increased toxins and increased hormone metabolism. Given the array of physical challenges, it is truly amazing how rarely we see pregnancy associated disease of the dam.

Gestational Diabetes Mellitus (GDM), also called Pregnancy-Induced Insulin Resistance, is perhaps the most significant metabolic condition we see in the pregnant bitch; and it can be life threatening. P4 and growth hormone induce insulin resistance, by some as yet unknown mechanism, at the level of the insulin receptors. The resulting decreased cellular uptake of glucose, in the presence of normal or elevated insulin levels, results in hyperglycemia which eventually spills out into the urine, creating the characteristic polyuria/polydypsia of DM. If the condition persists long enough and the cells become deprived of glucose, ketones accumulate in the circulation resulting in diabetic ketoacidosis. Management of GDM requires careful monitoring of the dam and higher than expected insulin doses to control hyperglycemia. Termination of the pregnancy by C-section may be necessary to remove the offending P4. If C-section is done on or after day 62 from the LH surge (d62), fetal survival is possible as some will remain permanently afflicted. Ovariohysterectomy is recommended to prevent GDM from re-occurring in subsequent pregnancy or diestrus (under the influence of P4).

Fetal risk includes the panoply of factors that can trigger fetal loss—infeciton, maternal factors or fetal factors. Fetal factors, failure of embryogenesis or genetic defects, usually result in loss of one or a few individual conceptuses. Rarely, an entire litter may be lost due to fetal factors such as anasarca (fetal hydrops) or, anecdotally, genetic incompatibility between the dam and sire.

Maternal and infectious factors usually result in loss of the entire litter. Maternal factors affecting normal fetal development include uterine or endocrine abnormalities. Cystic endometrial hyperplasia (CEH) predisposes the uterus to infection and may occlude the uterine lumen preventing transuterine migration of the embryos, thus impeding normal placentation. Maternal endocrine insufficiency —functional failure of the corpus luteum (CL)—could be a primary cause of pregnancy loss as canine pregnancy is dependent on the CL for production of P4. More likely, however, failure of the CL is secondary to maternal or fetal stress, systemic infection, inflammation, or exogenous prostaglandin.

Infectious factors commonly result in abortion. The most widely implicated virus is Canine Herpes Virus I. Most dogs have prior exposure to the virus, but during pregnancy, stress or P4-induced immunosuppression may allow the virus to emerge from dormancy. A CHV-1 vaccine (not available in USA) has been shown to effectively increase whelping rates and litter size and decrease neonatal loss when dams are vaccinated prior to breeding and boostered prior to whelping.

Management of canine pregnancy should begin with pre-ovulatory diagnosis of the luteinizing hormone (LH) surge (d0) in order to determine the best breeding dates (d3-d6) and the whelping date (d64-d66). This information is invaluable for maximizing conception rates and predicting or managing problems which may develop later in gestation. Pregnancy should be diagnosed to establish pregnancy dates and to determine pregnancy vesicles evaluated, measured and counted at that time. Prior to whelping (post d45) radiographs should be taken to verify the pregnancy.
establish an accurate fetal count, and evaluate the size and position of the fetuses (see time line).

If fetal resorptions are noted at the time of the ultrasonic exam, or if the bitch has a history of resorption, she should be watched closely throughout pregnancy with repeated ultrasonic exams to monitor fetal viability and measure fetal parameters to assess normal gestational development. Serum P4 concentrations should be evaluated to ascertain they are sufficient to maintain pregnancy (>2 ng/ml, >6 nmol/L). If P4 levels are low and there is no indication of an infectious component, progesterone supplementation may be helpful in maintaining the pregnancy. Resorptions reportedly occur in 10% of canine pregnancies. If available, uterine monitoring (electrohysterography or tocodynamometry) should be included in the management of pregnancy. If premature uterine contractions are noted and progesterone levels are normal, a tocolytic drug may be indicated. Use of tocolytic drugs is inferred from human medicine, but as of yet have no proven efficacy and may be detrimental to the welfare of the dam or the fetuses.

* All references to days of gestation will be from the day of the LH surge, and will be designated as dX where “X” is the number of days from the LH surge (d0).

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