Hormonal Induction of Fertile Oestrus in Bitches

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Dogs are non-seasonal breeders and can exhibit ovarian cycles throughout the year. Usually they attain puberty a few months after the attainment of the adult height and body weight. It is a general finding that small breeds attain puberty by 6 to 10 months of age and large breeds by 12 to 18 months. Generally first breeding is recommended during the second or third oestrus.

Compared to other species of animals they have prolonged follicular and luteal phases. The lifespan of the corpora lutea in non-pregnant bitches is the same as that in pregnant bitches, creating problems in pregnancy diagnosis and efficient breeding programme formulation. The inter-oestrus interval usually varies from 3.5 to 13 months depending on the breed. For example, a German Shepherd cycles in every 4 to 4.5 months with good fertility, but Basenji exhibits ovarian cycles only once in a year.

The basic aim of commercial dog breeding is to obtain maximum number of pups during the breeding life of a female dog. Delayed puberty, anoestrus and prolonged inter-oestrus interval create problems in formulating an efficient breeding programme for canines. Reliable and rapid methods of induction of fertile oestrus can be used in bitches, which are slow in attaining puberty, to shorten the naturally long anoestrous phase, to reduce an unusually long inter-oestrous interval, to tackle soboestrus and split oestrus and to treat a variety of infertility conditions.

Body will perform reproduction maximally only when all the other systems are functioning optimally. Before starting any treatment for inducing oestrus, the reproductive and general health status of the bitch has to be assessed. It should have attained the breedable age and size and should be well fed and supplemented to avoid any nutritional deficiencies. The bitch should not be obese, if so treat for obesity before starting the treatment for inducing oestrus. Animal has to be vaccinated and dewormed two weeks prior to treatment. Even though oestrus can be induced during any phase of the oestrous cycle optimum fertility should be expected only if induction and mating occur approximately three months or more after the previous oestrus. Animals treated for inducing oestrus during early dioestrus often develop cystic follicles as the existing progesterone blocks the LH release from the pituitary. A detailed vaginal cytological examination has to be performed to assess the stage of the oestrous cycle before starting the treatment. Anoestrous animals can be selected either by vaginal cytological examination two times at weekly intervals or by assessing the progesterone profile.

Several exogenous, natural and synthetic hormones have been employed to induce oestrus in bitches. Administration of thyroxine tablets (Eltroxin- 50 ug for small breeds and 100 ug for large breeds) daily for 10 consecutive days is found to be effective in reducing obesity and inducing oestrus in bitches. Serial administration of gonadotrophins (PMSG or FSH) or

gonadotrophin releasing hormones (GnRH) or its analogues can be used for inducing oestrus in bitches. Administration of PMSG at a dose rate of 20 IU/kg body weight intramuscularly for five consecutive days is an efficient treatment regimen. It can be combined with a terminal injection of an ovulating dose of hCG also (500-1000 IU, i/m). The animal under treatment should be monitored for behavioural and cytological changes of oestrus to avoid over stimulation and hyperoestrogenism. An oestrogen priming regimen using diethylstilbesterol (DES) (DES administered orally at a dose rate of 5 mg / dog for 7 to 9 days consecutively to induce proestrus) followed by the administration of FSH-P at a dose rate of 10 mg / dog intramuscularly on day 5, 9 and 11 after the start of induced proestrus is also very effective.

Administration of gonadotrophin releasing hormone (GnRH) is another method of induction of oestrus in bitches. It produces follicular growth and spontaneous ovulation as a result of gonadotrophin surge triggered by the oestrogen produced endogenously. The drawback of this regimen is the requirement of continuous pulsatile administration for a prolonged period. To avoid this single depot preparations can be used to effect sustained release. Depot preparation of leuprolide acetate (Lupron depot), a synthetic GnRH analogue at a dose rate of 100 ug / kg body weight intramuscularly can be used for induction of oestrus. It is usually combined with a single dose of GnRH (Gonadorelin 3 ug / kg body weight, i/m) at the onset of the induced oestrus for ensuring ovulation.

Natural and synthetic oestrogens can also be used for inducing oestrus. Diethylstilbesterol at a dose rate of 0.2 mg / kg body weight orally (one 5 mg tab for large breeds and half a tab for small breeds) for 7 to 9 consecutive days or up to the third day of induced proestrus can be used. It is economic, easy and reliable method of induction of oestrus in prepubertal bitches and those with delayed puberty. Care should be taken to avoid potential risk of oestrogen toxicity when oestrogen preparations are used for inducing oestrus.

It has been observed that the luteotrophic action of prolactin in dioestrus can be inhibited by the use of prolactin inhibiting substances. As a result they can be used for inducing oestrus, treating pseudopregnancy and reducing the inter-oestrus intervals. Twice daily administration of 250 ug of bromocriptine, a potent anti-prolactin drug until proestrus occurs can be tried. The duration of the treatment varies from 45 to 55 days. Bromocryptine may induce vomiting initially and if so reduce the dose to half initially and then gradually increase. Administration of cabergoline daily at a dose rate of 5 mg / kg body weight orally until three to eight days of induced proestrus is another regimen. The duration of this treatment varies from 4 to 30 days.

Bitches in deeper stages of anoestrus require increased dosages and / or longer period of therapy for induction of oestrus. Since over dosage of drugs may produce either multiple follicular development or a refractory stage in which the ovaries fail to develop follicles. Care should be taken not to over treat the individual animals.

Usually in case of induced oestrous cycle, the proestrus is shortened (5 to 6 days only) and oestrus is of normal duration (about 9 to 10 days). So vaginal cytological examination and / or hormonal profile may be employed to assess the exact time of ovulation thereby timing of mating effectively. Clomiphene citrate can be given orally (25-50 mg daily for five days) for inducing ovulation during the periods of mating.

Commonly used products

PMSG	: Folligon, Trophovet
FSH	: Foltrophin-V, Super-OV
hCG	: Chorulon, Life, Choragon, Pregnyl
GnRH	: Fertagyl
GnRH depot	: Lupron depot
Clomiphene	: Clome, Clofert, Fertomid, Rejun
DES	: Nemestrol, Vetoestrol
Bromocriptine	: Brom, Proctinal, B-crip

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methemoglobin formation in groups receiving and not receiving bioflavonoid antioxidants; however, Heinz body concentrations were significantly less in the group that received antioxidant protection. The investigators concluded that oral administration of bioflavonoid antioxidants to cats at risk for oxidative stress may have a beneficial effect on their ability to resist oxidative injury to red blood cells.

Liver Disease

Optimal management of chronic liver disease requires an understanding of etiologic factors and conditions that initiate and sustain tissue damage. Accumulation of transition metals (copper or iron retention) and depletion of natural antioxidants play pivotal roles. Membrane lipid peroxidation is one result. ROS production is increased in hepatic mitochondria in fatty livers, possibily making viable hepatocytes more vulnerable to necrosis.

Pulmonary Disease

Lung injury is a frequent side effect of anticancer therapy. In people, simultaneous administration of high doses of ionizing radiation and cytotoxic drugs is thought to cause pneumonitis and pulmonary fibrosis. Growing evidence indicates that ROS play a key role in the development of these disorders.

Conclusion

Reactive oxygen and nitrogen species are produced in health and disease. The antioxidant defense system- a complex system that includes intracellular enzymes, nonenzymatic scavengers, and dietary components such as vitamin E-normally controls the production of ROS. Oxidative stress occurs when there is a marked imbalance between the production and removal of reactive oxygen and nitrogen species. This imbalance arises when antioxidant defenses are depleted or free radicals are overproduced. There is much evidence suggesting that ROS play a significant role in the aging process and contribute to the development and/or exacerbation of a wide variety of degenerative diseases. A growing body of evidence also exists showing that enhancing the antioxidant defense system can reduce markers of oxidative stress prolong the lifespan of some invertebrates, and serve as therapy for some chronic diseases. The role of dietary antioxidants in preventing the effects of aging and reducing the risk of major disease states is a promising area of current and future investigation.

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