



## CASE REPORT

### Induction of Fertile Estrus in Bitch (Pug) With Cabergolin - A Case Report

S Shinde\*, B Krishnappa<sup>1</sup>, Brijesh Kumar<sup>1</sup>, P Perumal<sup>1</sup>, HK Gupta<sup>2</sup> and SK Srivastava<sup>2</sup>

<sup>1</sup>Ph.D scholars; <sup>2</sup>Pr. Scientist, Division of Animal Reproduction, Indian Veterinary Research Institute, Izatnagar, (U.P.) India

#### ARTICLE INFO

Received: November 20, 2013  
Revised: December 23, 2013  
Accepted: January 03, 2014

#### Key words:

Cabergoline  
Estrus  
Proestrus  
Pug bitch  
Vaginal cytology

#### \*Corresponding Author

S Shinde  
sshinde639vet@gmail.com

#### ABSTRACT

A 3-year old pug bitch was presented to the Referral Veterinary Polyclinic, I.V.R.I., Bareilly, with history of anestrus since last one year despite having normal body condition and appetite. Vaginal examination revealed normal genitalia without any abnormalities. For induction of estrus, bitch was treated with cabergoline orally till the bitch shows proestrous bleeding. After 10 days of treatment, bitch showed proestrous bleeding and on 12th days of proestrus, the vaginal cytology revealed presence of more than 90% of cornified cells and advised for breeding the bitch on alternative days until bitch rejects the male. After 45 days of mating the bitch was again presented to clinics for pregnancy diagnosis. Ultrasonographic examination revealed, 45 day old pregnancy. Cabergoline can be used as master drug to induce fertile estrus in any breed of dogs without much side effect.

**Cite This Article as:** Shinde S, B Krishnappa, Brijesh Kumar, P Perumal, HK Gupta and SK Srivastava, 2014. Induction of fertile estrus in bitch (Pug) with cabergolin- a case report. *Inter J Vet Sci*, 3(1): 1-3. www.ijvets.com

#### INTRODUCTION

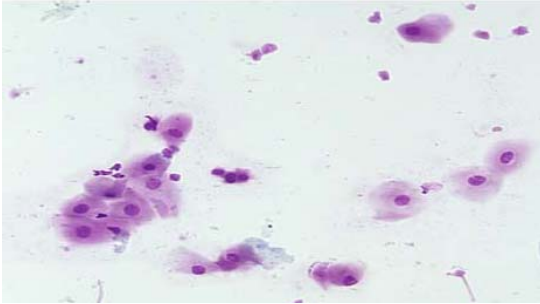
Domestic bitches are non-seasonally monoestrous animals. As a result of this unique reproductive physiology, bitches spontaneously ovulate only once or twice per year and ovulation can occur at any time of the year. Reliable fertile estrus induction (EI) protocols have been difficult to devise in the bitch because of the insufficient understanding of the hormonal events necessary for folliculogenesis in this species (Concannon, 1993). The natural cause of the termination of the long obligatory anestrus and onset of a new cycle is not clearly understood in the bitch. Neither the canine ovary, nor pituitary, is quiescent during anestrus; either luteinizing hormone (LH) or follicle stimulating hormone (FSH) has been reported as "the main hormone" for initiation of folliculogenesis in the dog (Kooistra *et al.*, 1998). Estrus induction is also useful for breeders and owners of pure-bred bitches with normally long interestrous intervals often request to shorten interestrous intervals, so the number of litters per year can be increased. Perusal of literature revealed the use of a variety of exogenous hormones and their combinations viz., GnRH, FSH/LH, eCG/hCG and oestrogens for induction of oestrus in bitches with varying results (Vanderlip *et al.*, 1987, Shille *et al.*, 1984 and Bouchard *et al.*, 1993). Administration protocols of most of these drugs involved daily to weekly injections and the results were not encouraging.

Prolactin appears to play a role in canine interoestrus interval, possibly by affecting gonadotrophin secretion and/or ovarian responsiveness to gonadotrophins. Suppression of prolactin secretion by administration of dopamine agonists (DA) shortened the duration of anoestrus (Van Haften *et al.*, 1989) or induced oestrus in cases of prolonged anoestrus (Jochle *et al.*, 1987; Arbeiter *et al.*, 1988 and Kutzler, 2007). The precise mechanism by which DA shortens anestrus is not yet known. Whether the action causes a decrease in PRL concentration by their dopaminergic effect or by a direct dopaminergic action on either the gonadotrophic axis or on ovarian gonadotrophin receptors remains to be determined. Some studies have shown that bromocriptine increases FSH concentration that results in enhancement of follicle development. The role of the dopaminergic paths in the control of gonadotrophin secretion is still unknown in the bitch. It has also been postulated that DA have a direct effect on the ovaries (Jeffcoate, 1993). It is possible that cabergoline might mature gonadotropin ovarian receptors by its DA action (Harvey *et al.*, 1997). In this report, induction of fertile estrus with cabergoline without side effect in pug breed of dog is presented.

#### History and clinical diagnosis

A 3-year old bitch (pug) with second parity was presented to the Referral Veterinary Polyclinic, I.V.R.I., Izatnagar, Bareilly, with history of infertile mating in

previous year, since then the bitch didn't exhibit estrus symptoms despite of having normal body condition and appetite. Abdominal palpation and vaginal examination revealed apparently normal uterus external genitalia respectively. To rule out uterine pathology ultrasonography was performed which shown hypoechoic regions indicating small quantity of fluid in uterus. Furthermore, vaginal aspirate was taken for exfoliative vaginal cytology. In cytological finding, parabasal and intermediate cells with few neutrophils noticed (Figure 1). On integrating all the above findings it was confirmed that the bitch was in anestrus without any abnormalities.



**Fig. 1:** Parabasal and intermediate cells with few neutrophils during anoestrus phase.

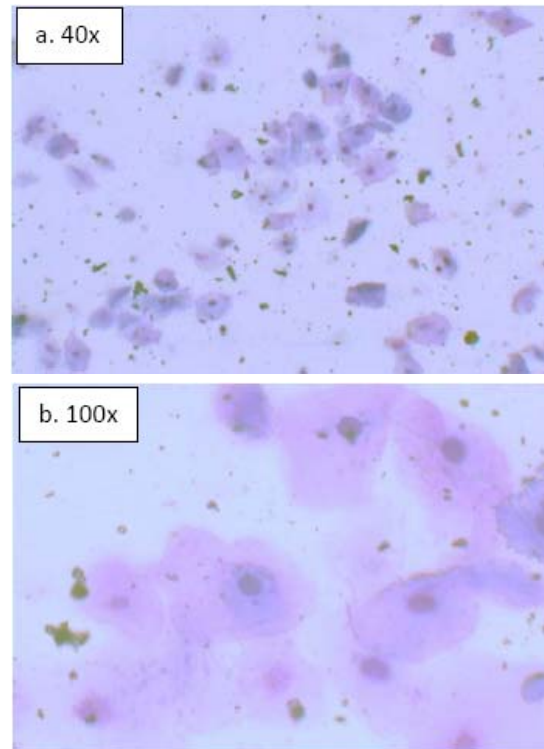
#### Treatment

To induce estrus, the bitch was treated with cabergoline (Prolactin inhibitor) at dose rate of 5 µg/kg body weight orally till the bitch showed proestrus bleeding. However, within 10 day of treatment bitch exhibited proestrus bleeding and treatment was discontinued thereafter. Importantly, pet was apparently normal during the course of treatment without side effects. Exfoliative vaginal cytology was performed as per standard procedure with Giemsa's stain from 4<sup>th</sup> day of proestrus to determine the optimum breeding time (Figure 2:a,b). The cytology was repeated at 2 days interval till 90% of exfoliated cells get cornified. On 12<sup>th</sup> day of proestrus vaginal cytology examination revealed presence of more than 90% of superficial cornified cells (Figure 3:a,b) indicating optimum breeding time. Owner was advised to breed the bitch on same day and to repeat mating on alternative days until bitch rejects the male (three successful mating done).

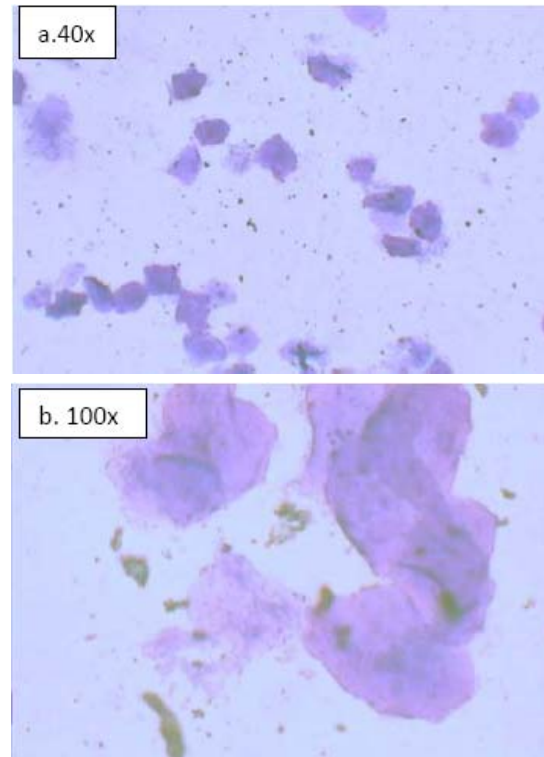
After one and half month, pug was presented to clinics for confirmation of pregnancy. Visual examination revealed edematous teats and distended abdomen (Figure 4) and abdominal palpation revealed presence fetus and fetal swelling. For confirmation, ultrasonography (B-mode) performed and revealed presence of fetal skeleton with fetal movement and fetal heart beat. To assess the gestational age, fetal head diameter was measured (Figure 5) and age of fetus found to be 45 days. After completion full term, pug delivered six healthy pups without assistance.

#### DISCUSSION

Many methods of estrus induction exist for both canids and felids, success (induction of estrus, ovulation,



**Fig. 2 (a,b):** Exfoliative cytology after 4<sup>th</sup> day proestrus bleeding.



**Fig. 3(a,b):** Exfoliative cytology after 12<sup>th</sup> day of proestrus bleeding (90% cornified cells).

pregnancy and delivery of offspring) rates vary between and within various protocols. Long-acting preparations (placental gonadotropins, GnRH analogue implants) are convenient for the owner and less stressful for the patient



**Fig. 4:** Bitch showing edematous teats and distended abdomen after 45 days of mating.



**Fig. 5:** Ultrasonography showing skull of 2-3 fetuses.

but are associated with premature luteal failure and subsequent reduced pregnancy rates. Based on studies by Jochle *et al.* 1987 and Jeukenne *et al.* 1997, DA such as bromocriptine and cabergoline have been recently included in the available methods of EI with success in some European countries. Cabergoline (5µg/kg/day) was used orally for 5 to 18 days in 28 bitches with prolonged anestrus, and all the animals had estrus cycles after treatment and became pregnant. However the duration of treatment and proestrus varies within the breed of same species. Verstegen *et al.*, (1999) showed animals responding to the treatment, the mean time taken from treatment onset to proestrus was found to be 13 days but in present case the duration was 10 days. Care should be taken not to administer cabergoline too early in anestrus as the insufficient uterine involution of the previous cycle could prevent implantation. The findings of the present trial revealed that the anti-prolactin drug, cabergoline @ 5 µg/kg body weight once daily orally for a period of two weeks could be used for the successful

induction of oestrus with satisfactory conception rate in anoestrus bitches of different breeds and age groups.

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