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Advances in the management of pseudocyesis in bitch: A review

Sachin Kalaswa, Ravindra Jadav and HC Nakhashi

Abstract
Clinical indicators of pseudopregnancy include weight gain, lactation, growth of the mammary glands and nesting behaviour in non-pregnant Bitches (dogs). It usually happens six to twelve weeks after estrus in non-pregnant bitches. Based on the owner's history, clinical symptoms, hematology, vaginal cytology, hormonal changes and a thorough radiographic and ultrasonographic examination, an early and highly advanced diagnosis is made. The exact cause of clinical pseudopregnancy remains unclear, despite prolactin's pivotal involvement in its symptomology. According to some research, bitches that are openly pseudopregnant see an increase in circulating prolactin concentrations during diestrus, relative to bitches that are not affected. The variance in the prevalence and severity of pseudopregnancy within and across breeds may possibly be due to individual variability in peripheral sensitivity to prolactin, or even the existence of molecular variants of canine prolactin with varying bioactivities. Based on the effects of exogenous progesterone and the frequent induction of pseudopregnancy by spaying during the luteal phase in the metestrus stage of the cycle, exposure to progesterone and subsequent removal of progesterone appear to be involved. Since overt pseudopregnancy is typically a self-limiting and perhaps quasi-physiological state, modest cases are typically either deemed not requiring treatment or are not brought forward for therapy. both with non-surgical or surgical management and homoeopathic treatment. The side effects of sex steroids, especially oestrogens, androgens and progestins, which are typically used to treat pseudopregnancy, outweigh any benefits. However, when available, oestrogens like diethylstilbestrol, oestradiol benzoate and oetsradiolcypionate, androgens like mibolerone and progestins like megestrol acetate and medroxyprogesterone may be helpful. It has been demonstrated that the injection of an ergot derivative, such as bromocriptine, cabergoline or metergoline, effectively inhibits the release of prolactin and is a more suitable treatment for canine pseudopregnancy than the use of steroids. Although many ergot derivatives may have undesirable side effects, these are usually mild and easily tolerated or controlled. Very good, side-effect-free homoeopathic therapies for pseudopregnant bitches with *Thuja occidentalis* and *Urtica urens*. Because ovariectomy is the sole long-term preventative strategy, predisposed bitches who are not meant for breeding should be spayed. The aim of this study is to promote awareness on the benefits of early diagnosis and excellent medical, homoeopathic, and surgical/non-surgical care for pseudo-pregnant patients without complications.

Keywords: Bitch, pseudopregnancy, haematology, vaginal cytology, spaying, radiography, ultrasonography

Introduction
A condition known as pseudocyesis, which resembles pregnancy and affects certain domestic mammals, is characterised by the persistence of the corpus luteum and typically follows sterile copulation (Marusic *et al*., 2005) [60]. Or pseudocyesis is a syndrome in which the patient exhibits every indication of pregnancy, with the exception of a fetus's presence being confirmed (Gobello *et al*., 2002) [25]. In order to suggest neuroendocrine or endocrine mechanisms contributing to the establishment of pseudocyetic phenotype Or Pseudocyesis or False Pregnancy aims to identify epidemiological, Psychiatric or Psychologic, gynaecological and endocrine traits related with this disorder (Juan *et al*., 2013) [53]. Pseudocyesis is an uncommon mental illness.It is also known as phantom (false) pregnancy, specious pregnancy, imaginary pregnancy, hysterical pregnancy, nervous lactation, fake pregnancy, pseudopregnancy, and couvade syndrome in literature. Greek terms pseudes, which means pseudo (false), and kyesis, which means pregnancy, were the basis for John Mason Good's 1823 coining of the phrase "pseudocyesis."

When a bitch who isn't pregnant has a strong belief that she is, it's called pseudocyesis. She almost exhibits every pregnancy sign and symptom at the same time. Pseudocyesis and the concept of "couvade" are closely related. The phrase comes from the French term "Couver," which means "to sit" or more figuratively, "to sit on eggs," like a bird.

Research on the endocrinologic conditions that underlie the phenomena as well as the management of sadness and unresolved grief, which are closely related to the genesis of pseudopregnancy, has dominated current efforts. Coined the term "pseudopregnancy" to characterise the unusually prolonged luteal phase of the estrural cycle in rabbits. The phrase was originally used to describe a situation in which ovarian and uterine alterations akin to those observed during pregnancy would occur after copulation but no conception would occur. It is now recognised that among virgin bitches that have not undergone copulation, pseudopregnancy can develop after estrum. It should be kept in mind that, in contrast to rabbits, ferrets and other animal's dogs ovulate spontaneously meaning they don't require a copulation stimulus to cause the follicle to rupture and the ovum to be released. A physiological phenomenon known as pseudocyesis (PSC), pseudopregnancy, false pregnancy or nervous lactation is typified by symptoms like those seen in the postpartum phase (Allen, 1986; Jochle *et al*., 1987; Feldman and Nelson, 1987; Arbeiter *et al*., 1988) [3, 47, 18, 4]. Prolactin (PRL) is widely acknowledged to have a key function in the pathophysiology of PSC formation, although its precise aetiophysiology is still unknown (Grunau *et al*., 1996) [37]. The occurrence of clinical pseudopregnancy may be impacted by age, breed, parity, hormone, stage of the estrous cycle and environmental factors, according to a considerable body of anecdotal and unpublished information. Additionally, it has been proposed that dietary habits could potentially impact the incidence of pseudopregnancy. The idea that dietary habits may have an impact on PSC is explained in a recent paper (Lawler *et al*., 1999) [57].

Prevalence

There have been roughly 600 reports of pseudopregnancy in the previous 200 years. In his autobiographical research, Freud discussed a case of pseudopregnancy. In 1937, Bivin and Klinger collected and reported 444 cases of pseudopregnancy, whereas Cohen reported 100 cases in the same year. These and other similar situations were then presented one at a time. In domestic dogs, pseudocyesis is now often observed; its precise prevalence is unknown, although estimates put it as high as 50±75% (Johnston, 1980) [51].

Aetiology

Probable and proposed causes of clinical pseudopregnancy in female dogs
1. An idiopathic, more widespread rise in prolactin than is seen in a typical diestrual cycle.
2. Idiopathic hypersensitivity to the endocrine shifts that typically take place in late diestrus, including as the progesterone that normally declines naturally and the modestly elevated prolactin.
3. Pseudo-luteal phase brought on by exogenous progestin treatment.
4. Progesterone withdrawal brought on by: a. Ovariectomy during diestrus; b. Abrupt termination of long- or short-term progestin therapy; c. Abrupt luteolysis triggered by prostaglandins or idiopathic causes; and d. Contraceptive medication.
5. Pituitary microadenomas may be linked to idiopathic hyperprolactinemia.
6. Reflexive or physchogenic hyperprolactinemia, which arises from stimulation by other visual, tactile, or social stimuli or from surrogate neonates.

Pathophysiology

Pseudocyesis was first thought to be brought on by either aberrant persistence of CL or an excess of P4 (Marshal and Halnan, 1917) [59]. Subsequent research revealed that the sudden drop in P4 levels in late LP was responsible for the elevated concentrations of PRL that were linked to clinical symptoms of PSC (Smith and McDonald, 1974; Graff *et al*., 1977; Gerre *et al*., 1988; Concannon and Lein, 1989) [79, 35,, 24 9]. It is challenging to explain, though, why not all unmated animals exhibit overt PSP, given that this hormonal shift happens in both pregnant and non-pregnant bitches (De Coster*et al*., 1983 and Fernandes *et al*., 1987) [19]. Studies where the condition was successfully treated by administration of PRL secretion inhibitors (Mialot *et al*., 1981; Janssens, 1986; Jochle *et al*., 1989) [49, 64] provided more evidence for a connection between PRL and PSC. PRL's primary function in mammals is to stimulate the mammary gland at every stage of development, from the end of lactation until mammogenesis (Brugere, 1998) [5]. Despite species-specific variations in the hormone requirements for lactogenesis (Forsyth, 1986) [22]. PRL appears to play a role in maintaining maternal conduct in the bitch, including getting ready for delivery and taking care of the litter afterward. How PRL and oxytocin share these effects is unclear (McCarthy *et al*., 1992) [61]. While PRL seems to be the primary endocrine element regulating PSC, other hormones may possibly contribute to the process' continuation (Brugere, 1998) [5]. The discovery that some bitches have a positive connection between PRL and oestrogens is noteworthy in this context (Hadley, 1975) [39].

There is little information available about the secretory patterns of PRL in dogs over a 24-hour period (Grunau, 1994 and Gobello *et al*., 2001) [29, 36]. Furthermore, because different research utilise different PRL assay techniques and because it is not usually considered if PSC is clinically overt, data on circulating PRL concentrations in PSPT bitches are unclear. Therefore, while an early study (Reimers *et al*., 1978) [74] found no significant differences in PRL concentrations between pregnant and covertly PSPT beagle bitches, two more recent studies that attempted to differentiate between patients with overt and covert PSC did find differences in PRL levels. These latter papers dealt with several breeds' clinical cases. Up until day 80 following the LH surge, the first of these investigations revealed an overlap in PRL values between covertly and overtly PSPT bitches, with 55% of the PSPT animals' PRL levels falling within the mean SD of control covert bitches. PRL levels were subsequently greater in openly PSPT bitches in the same sample (Olchewiski, 1987). At day 60 of the oestrous cycle, bitches who were overtly PSPT had considerably greater PRL levels than those who were secretly PSPT (Grunau, 1994) [36]. According to a more recent study (Okkens *et al*., 1997) [68], PSPT Afghan hound bitches had greater PRL levels than Afghan hounds in an earlier stage of the LP or non-PSPT Beagles in the same stage. While the majority of the aforementioned findings point to elevated PRL concentrations as the cause of overt

PSC, a recent study in 28 Labrador Retrievers did not find any statistically significant variations in mean blood PRL levels between PSPT and non-PSPT bitches over the course of 13 weeks (Lawler *et al*., 1999) [57].

There has also been evidence of an overlap in PRL serum levels between PSPT and non-PSPT bitches after spaying (Harvey *et al*., 1999) [43] and no discernible difference in PRL levels between surgery-induced PSPT and non-PSPT animals (Hoffmann *et al*., 1992; Gobello *et al*., 2001) [44, 29]. A finding of low PRL levels in two spayed PSPT bitches suggests that high PRL levels are not required for PSP maintenance (Harvey *et al*., 1997) [42]. As a result, it is doubtful that there is a single serum PRL level that causes PSC in bitches. Although no significant changes in the proportion of each PRL variant were detected in this initial investigation, it was recently reported that 22 PSPT bitches had molecular heterogeneity for PRL, likely due to varying bioactivity.

Table 1: Clinical symptoms

Signs	Clinical symptoms observed during pseudopregnancy in dogs
Behavioural signs	Maternal behaviour (nestling, mothering inanimate objects, adopting other bitches' puppies) and prepartum behaviour (restlessness, anxiety, excitement, sluggishness, digging, over-affection, over-protectiveness, over-defensiveness, anorexia, decreased activity, aggression, and abdominal licking)
Physical Signs	Gaining weight, expanding the abdomen, distension and expansion of the breasts, Breastfeeding unrelated neonates or self-nursing can often induce lactation and milk secretion, as well as occasionally resemble parturition-like abdominal contractions.
Clinical signs	Anorexia, indigestion, itchiness, headache, insomnia, muscular tremor, irritability, vomiting, gastric symptoms, and colonic hypochondria, Depersonalisation, Deconstructiveness, bleeding from the nose, diarrhoea, polyuria, polydipsia, and polyphagia

(Mialot *et al.*, 1984; Feldman and Nelson, 1996 and Gobello *et al.*, 2001) [29, 18, 64]

Diagnosis

Based on (I) Clinical symptoms (II) Haematology (III) Vaginal Cytology (V) Hormonal changes (VI) Radiography and Ultrasonography.

(I) Clinical symptoms: (A) Behavioural Findings (B) Clinical findings and (C) Physical Findings: (i) Mammarygland enlargement and (ii) Galactorrhea and nesting behaviour (Johnston, 1980; Mialot *et al.*, 1984; Feldman and Nelson., 1996 and Gobello *et al.*, 2001) [51, 29, 64, 18].

Table 2: Quantitative measurement of dimension of mammary glands

Groups (n: 10)	Mammary dimension (cm)				Mean and standard deviation (X±SD)	
	Minimum		Maximum		Longitudinal (cm)	Transversal (cm)
	Longitudinal	Transversal	Longitudinal	Transversal		
	2.8	2.5	8.8	6.6	4.92±1.81	4.19±1.32
Overt psp	2.3	1.6	8.4	5.3	4.86±1.86	3.50±1.28
Covert psp	1.2	1.0	4.2	3.5	2.59±1.15	2.23±0.74

Results of measurements were significantly different between pregnant/overt pseudopregnant and covert pseudopregnant bitches ($p< 0.001$), X = mean, SD = standard deviation, (Nihat *et al.*, 2005) [67].

(II) Haematology

Erythrocytic parameters as indicators for differentiating between the pregnant and pseudopregnant bitches

In eight bitches, weighing between 10 and 12 kg and aged between two and three years, the erythrocytic parameters during pregnancy and pseudopregnancy were examined and compared. Prior to mating, during the three trimesters of pregnancy, and after giving birth, blood samples were taken from the bitches. Standard techniques were used to calculate the red blood cell count (x106/µl), packed cell volume (PCV %), and haemoglobin concentration (Hb gm/dl). Next, calculations were made to determine the mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC). There were two pseudopregnant bitches and six pregnant bitches. According to the findings, during the third trimester of pregnancy, pregnant bitches' PCV drastically dropped from premating values of 51.37+0.94% to 34.00+8.04% ($P<0.05$). Additionally, there was a noteworthy drop in Hb levels ($P<0.05$) from 16.30±0.20gm/dl during the premating period to 11.25±1.80gm/dl during the third trimester of pregnancy. During the premating period (12.70+3.15), the red blood cell (RBCx106/µl) values did not exhibit a significant difference from those recorded during the first, second, and third trimesters (11.13+3.87, 10.38+4.54 and 12.24+3.15, respectively). In the bitches with pseudopregnancy, there was no pattern of declining PCV and Hb values. This indicates that as early as the first 20 days following mating, bitches can be detected and the difference between pregnancy and pseudopregnancy can be made using these erythrocytic characteristics. (Ajala and others, 2011) [2].

Table 3: The Hematological Parameters of the Bitches during pregnancy:

Haematological Parameter	Premating	1st Trimester	2nd Trimester	3rd Trimester	2 Weeks Post-Partum
PCV (%)	51.37 ±0.94	42.33±7.51*	40.75±4.99*	34.00±8.04*	30.75 ± 8.302*
Haemoglobin(gm/dl)	16.30 ± 0.20	12.80±1.34*	12.08±1.06*	11.25±1.80*	9.75±2.783*
RBC (x106/µl)	12.70 ±3.15	11.13 ± 3.87	10.38 ± 4.54	12.24 ± 3.15	9.34±3.953*
MCV (fl)	40.45 ±1.72	40.10±10.54	43 ± 13.41	29.00±5.71*	32.92±0.30*
MCHC(gm/dl)	31.73 ± 0.67	30.67±13.50	31.25 +±1.71	32.25 +±1.71	31.71±0.70

(Ajala *et al.*, 2011) [2]

Values are expressed as means ± S.E.M, * $P<0.05$ significantly different from the premating value, 1st trimester = 1st – 20th day after mating, 2nd trimester= 21st -42nd day after mating, 3rd trimester – 43rd – 63rd day after mating.

Table 4: Haematological Parameters of Pseudopregnant Bitches:

Parameter	Premating	0–20 days Postmating	21–42 days Postmating	42–63 days Postmating
PCV (%)	51.37±0.94	50.92±0.45	50.75±0.75	50.75±0.75
Haemoglobin (gm/dl)	16.30±0.20	16.48±0.18	16.95±0.45	16.95±0.46
RBC (x106/µl)	8.33±0.10	8.42±0.08	8.51±0.21	8.51±0.21
MCV(fl)	61.77±1.72	60.45±0.72	59.77+1.76	59.77±1.77
MCHC(gm/dl)	31.81±0.67	31.37±0.18	33.39±0.55	33.39±0.55

(Ajala *et al.*, 2011) [2]

The values are presented as means± S.E.M. From the premating phase through the three trimesters and the conclusion of gestation, there was no discernible variation in the parameters assessed (Table 1). The RBC value before mating and the values during the first, second, and third trimesters of pregnancy did not differ significantly ($P<0.05$). Prior to mating, the MCV value was not statistically different from the values during the first and second trimesters, but it was significantly greater than the values during the third trimester and two weeks post-partum ($P<0.05$) (Ajala *et al.*, 2011) [2].

(III) Vaginal Cytology

Evaluation of vaginal smears in pregnant, overt and covert pseudopregnant bitches: Analysis of the groups 2 and 3's vaginal smears showed that there were more basal, parabasal, and intermediate epithelial cells than superficial cells. Groups 2 and 3's vaginal smear results were statistically comparable. Furthermore, there was a statistically significant difference between group 1 and the other groups. Although groups 2 and 3 had identical mean progesterone values, group 1's progesterone level was statistically greater than that of groups 2 and 3 ($p< 0.01$) (Nihat *et al.*, 2005) [67].

Table 5: Shows in basal (%) group

Groups	Basal (%) (X±SE)	Parabasal (%) (X±SE)	Intermediate (%)(X±SE)	Superficial (%)(X±SE)
Preg.1 (n: 10)	3.60a±2.10	17.60a±2.75	56.00a±4.77	22.80a±5.13
Overt psp (n: 10)	30.90b±5.98	29.80b±2.06	30.50b±4.08	8.20b±1.87
Covert psp (n:10)	30.00b±1.91	32.40b±1.63	29.20b±1.20	8.80b±1.77
P	<0.001	<0.001	<0.001	<0.01

(Nihat *et al.*, 2005) [67].

(IV) Hormonal changes

(i) Plasma concentrations of P_4 (ng/mL) and PRL (ng/mL) before and during the appearance of overt signs of pseudo pregnant bitches: Plasma concentrations of progesterone (ng/mL) and prolactin (ng/mL) in four bitches examined before and during the appearance of overt signs of pseudopregnancy.

Table 6: Shows in bitch days sampled

Bitch	Days sampled	Progesterone (ng/mL)		Prolactin (ng/mL)	
		Before	During	Before	During
A3	62 and 76	2.3	2.2	2.0	14.1
A24	44 and 57	13.1	1.8	1.5	11.8
A26	30 and 85	16.0	0.2	3.2	41.4
A29	42 and 71	4.6	0.5	0.9	7.6

In the four bitches studied prospectively, prolactin concentrations when they were showing signs of PSP were higher ($P<0.05$) than in the previously collected samples (Tsutsui *et al.*, 2006) [83].

(ii) Mean serum progesterone concentrations in the Pregnant, overt and covert pseudo pregnant bitches: Minimum, maximum, and mean serum progesterone concentrations in the study groups.

Table 6: Serum progesterone concentration (ng/ml)

Groups (n: 10)	Minimum	Maximum	Mean and standard deviation (X±SD)
Pregnant (10)	4.38	32.28	17.05^{a}±10.05
Ovetpsp (10)	1.18	11.31	5.07^{b}±3.00
Covert psp (10)	0.56	26.54	9.66^{b}±8.92

a, b: Difference is statistically significant in groups with different letters in the same column ($p< 0.01$), Pregnant bitches in the serum progesterone hormone level is statistically significant ($p<0.01$)) higher than overt and covert pseudo pregnant bitches, so the higher level of progesterone hormone in those bitches its indicate that bitches positive for pregnancy test (Nihat *et al.*, 2005 and Lee *et al.*, 2006) [67, 58].

(iii) Levels of prolactin, GH, and IGF-I in ovariectomized bitches during luteal phase

Table 7: Shows in hormone before OVX

Hormone	Before OVX	1st day after OVX	7th day after OVX	P
P_4 (nmol1 1^{-1})	4.1±9*	2.9±0.7	0.9±0.3	=0.009
GH (µg1^{-1})	1.4±0.9	1.0±0.4	4.6±0.9*	= 0.01
PRL (µg1^{-1})	1.3±0.3	3.6±1.8	7.4±5.0*	=0.03
IGF-I (µg1^{-1})	180±15*	117±7	54±1	=0.02

(Lee *et al.*, 2006) [58]

Ovariectomy performed during the mild luteal phase if progesterone (P4) and insulin-like growth factor (IGF-I) levels were statistically substantially higher prior to the procedure than they were on the first and seventh days following it. On the other hand, after the seventh day of ovariectomy, the levels of prolactin (PRL) and growth hormone (GH) were statistically considerably greater than they were before the procedure.

(V) Radiography and Ultrasonography

(I) Ultrasonography of pregnant bitch (II) Radiography of pseudo pregnant bitch

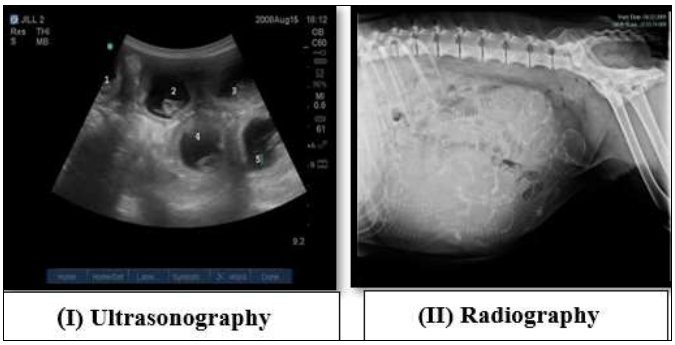

Fig 1: Ultrasonography and Radiography give definitive diagnosis.

(I) Ultrasonography: A fluid-filled, anechogenic black area of varying size, divided by thin, double layers of tissue that represent sections through the opposing walls of the inflated, bent uterine horn, is the characteristic that ultrasonography uses to diagnosis pseudopregnancy. Days 17 and 30 of pregnancy were marked by the detection of the anechogenic gestational sac, the heartbeat (cardiac activity) on day 22, and the presence of foetal movement in the echogenic linner layers surrounding the gestational sac (Aissi, 2012) [1].

(II) Radiography: When in doubt, abdominal radiography should be used to get a conclusive diagnosis. Radiographs can be done 45–47 days into pregnancy to see the pups in utero and count the number of foetuses (Gobello *et al*., 2002) [25]. On day 35, the skeleton was found to be a hyperechoic structure (Aissi, 2012) [1].

Complications

Clinical PSC problems including mastitis and breast dermatitis are rare; until these issues manifest, PSC symptoms often go away after two to four weeks (Johnston, 1986) [52]. In subsequent oestrous cycles, susceptible bitches have a high recurrence rate (Johnston, 1986; Feldman and Nelson, 1987) [18, 52]. Additionally, during LP, overt PSC has been noted during progestin therapy and three or four days following ovariectomy (Johnston, 1980, 1986 and Gobello *et al*., 2001) [29, 51, 52]. This is not shocking because luteolysis prior to parturition is very similar to these two P4 deficiency scenarios. According to some research, there may be a connection between the incidence of pseudopregnancy episodes and subsequent reproductive illnesses or issues with fertility (Findler *et al*., 1966; Johnston, 1980) [51, 1]. It is uncertain if prolactin contributes to the development of breast tumours. Prolactin (PRL) receptors are present in just 30% of malignant tumours, and the quantity of prolactin receptors in benign mammary tumours is no greater than that of normal tissue (Rutteman and Misdorp, 1989) [76]. However, prolactin and pseudopregnancy have been linked to the development of breast tumours (Verstegen, 1999) [95]. The buildup of carcinogenic materials within the mammary acini, the neoplasia formation, and the retention of milk may account for the increased risk of mammary neoplasia linked to pseudopregnancy (Goya *et al*., 2001) [33].

Treatments

Since PSC is a physiological state that self-limits, small cases typically don't require therapy. Therefore, it is advised to discourage maternal activity and occasionally wear Elizabethan collars to stop self-nursing or licking the mammary glands; yet, simply stroking the collar against the mammary glands may be enough to extend lactation, the production of milk. Avoiding key lactation triggers such as licking, milking, or packing the glands hot or cold is necessary. Water removal for five to seven nights promotes normal renal function, helps end lactation, and drives fluid conservation (Mialot and Bohnert, 1980; Mialot *et al*., 1984; Feldman and Nelson, 1996) [62, 18]. Phenotiazines are not advised since they enhance PRL secretion; nevertheless, mild tranquilization with non-phenotiazine medications is helpful when behavioural indications are significant (Voith, 1983) [89].

Sex Steroid Therapy: Although sex steroids have historically been used to treat PSC, these drugs typically have more negative effects than positive ones. Although the growth of mammaries depends on sex steroids, large dosages of these hormones negatively affect the hypothalamic-pituitary axis, perhaps preventing the pituitary from releasing PRL (Johnston, 1980 and Allen, 1986) [3]. The most frequent sex steroids used historically for the treatment of PSP are: **(I) Estrogens:** Oestrogens such as

(A) Diethylstilboestrol (DES): Its synthetic nonsteroidal estrogenic Stilbene®, reduced physiological and social / behavioural disorders; Brand names were available in the form of Gauze® 5 mg, Distilbene® 1 mg, Comprimesstilbesterol® 1 mg, and Lilly® 5 mg; Diethyl-stilbestrol concentration was taken orally, with a dose rate of 1.55 to 5 mg/kg total dose for 3 to 7 days. The side effects included cancer (Johnston, 1980 and Allen, 1986) [3, 51], nausea, vomiting, and benign and malignant tumours of the cervix and vagina.

(B) Oestradiol benzoate: It is an estrogenic steroidal sex hormone that is also accessible as estradiol and benzyl ester. Brand names such as Oestrogen® inj. 5 mg, Phenokinon® F5 mg inj, Estradiol® inj. 2 mg, and PREGHEAT® inj. 2 mg were available. Foster and Smith (2007) [78] include vaginal discharge, bloody discharge, decreased urine volume,

elevated heart rate, fever, redness, and itching as side effects.

(c) Oetsradiolcypionate: Estrogene is a steroidal sex hormone that is also available in the form of Estrtadiol and 3-Cyclopentylpropanoyl synthetic ester. Brand names of Depo®-Estradiol 5mg (Pfizer) (Pharmaca) and Roodriddle 5mg were available in concentrations like 5mg/ml estradiol cypionate route in intramuscular/subcutaneous with dose rate at 2 mg/kg body with repeat 1 month later (if necessary) with side effects including vaginal discharge, burning, irritation, headache, nausea, pain, swelling, or redness at the injection site, stomach bloating and upset, swelling, vaginal infection, and changes in weight (Foster & Smith, 2007) [78]. They may also result in uterine illnesses such pyometra and bone marrow depression (Hypoplasia), which causes anaemia, or they may cause pro-oestrus or oestrus symptoms. Nevertheless, it is not advised to utilise oestrogen.

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(II) Androgens: Lactation suppression is a function of androgens, such as testosterone and synthetic androgens. Clitoral enlargement, other types of virilization, and epiphora are among the side effects of androgens, such as testosterone. Previously, the synthetic androgen mibolerone was sold as a daily liquid added to dog food, called Cheque Drops®, for use as an oral contraceptive. But it's no longer easy to find this product.

Mibolerone: Its properties include selective blocking of LH, antigonadotrophic action, anabolic and androgenic steroid, and prevention of estrural activity. Brand names were Cheque® Drops and GP. Miboleronepropyleneglycol, 100 mg tablets, and Cheque® Drops 100 mg/tab were available in concentrations of 100µg/ml and 1 mg/ml. The tablets were to be taken orally, with a dose rate of 0.5 to 1.o mg/kg per day for 32 days. The side effects included clitoral hypertrophy, virilization, epiphora, eaginal discharge, mounting other dogs, aggression, change in voice, increase in oily skin and body odour, reproductive tract lesions, tearing or urinary incontinence, and liver diseases (Foster and Smith, 2007) [78].

(III) Progestins: Oral progestins, such megestrol acetate and medroxyprogesterone acetate, have been used to suppress overt pseudopregnancy symptoms. Although the exact process is unknown, it most likely entails lowering tissue sensitivity to prolactin or suppressing prolactin release. When therapy is stopped, there is sometimes a resurgence in symptoms, including lactation, with the progestin withdrawal replicating the typical endocrine changes at parturition. Some of the most common side effects of progestin therapy are mammary gland nodules, breast tumours (Neopasia), acromegaly, and cystic endometrial hyperplasia-pyometra complex and insulin resistance (Feldman and Nelson, 1996) [18]. Therefore, progestin administration is not advised.

(A) Megestrol acetate:- Megestrol acetate tablets are administered orally with a dose rate of 2.5 mg/kg/day given orally for 8 days. They are also used in the treatment of advanced breast or endometrial carcinoma, but side effects include weight gain, nausea, vomiting, and edoema (Jochle *et al*., 1987 and Romatowski, 1989) [47]. It is a synthetic derivative of the naturally occurring sex steroid hormone and antineoplastic progestational; brand names were available in the form of UNISTROL®4 40 mg, IUAX ® 40 mg, TEVA ® 20 mg, and ENDACE ® 40 mg.

(B) Medroxyprogesterone: Progestogen and a progesterone derivative, it is a synthetic steroidal progestin acetate. It has no androgenic, oestrogenic, or anti-cancer properties. It was marketed under several brands, including Provera® 5 mg tab, Modus® 10 mg tab, Depo-provera ® inj, and SicorTM / Greenstone ® 150 mg/ml inj. Some side effects include breakthrough bleeding, spotting, amenorrhoea, galactorrhea, thrombophlebitis, pulmonary embolism, nausea, cholestatic jaundice, mental depression, and insomnia. Medroxyprogesterone acetate injection, available in concentrations of 150 mg/mL, and 2.5, 5 mg, or 10 mg MPA tablets, are administered orally, I.M./S.C.

Prolactin-Suppression Therapy: Dopamine Agonists: An important advancement in the treatment of canine PSC has resulted from the inhibition of PRL secretion by ergot derivatives, or ergot alkaloid medicines. The hypothalamus controls the tonic inhibitory control of PRL secretion by the pituitary, mostly by the direct inhibitory effect of dopamine, the primary prolactin inhibiting factor (PIF), or Serotonin, which inhibits dopamine release (Releases) and raises prolactin, can indirectly affect this inhibition (Thorner *et al*., 1998). Furthermore, prolactin and thyroid stimulating hormone (TSH) are released by the hypothalamus tri-peptide, thyrotropin releasing hormone (TRH). The most often used drugs to block PRL secretion are metergoline, another ergot alkaloid that is a serotonin antagonist with a dopaminergic effect at high doses and thus lowers prolactin secretion (Hamon *et al*., 1981; Janssen, 1986 and Jochle *et al*., 1989) [49]. Bromocriptine and cabergoline act directly on D2 dopamine receptors of the lactotroph cells of the anterior pituitary gland.

(A) Bromocriptine: In veterinary medicine, bromocriptine (Parlodel®, Perrigo ®/ Proctinal ®/ Bromocriptin ®) 2.5mg Tab. has been used since 1980. Numerous treatment plans have been put up that call for doses between 10 and 100 µg/kg daily for a period of 10±14 days (Mialot *et al*., 1981; Verstegen and De Coster, 1985; Janssen 1989) [64, 86]. Bromocriptine frequently causes side effects that are dose-related. They include anorexia, sadness, vomiting, and behavioural abnormalities (Peterson and Drucker, 1981). Antiemetic medication delivery is one way to treat vomiting. Use of metoclopramide or other central dopamine blockers of synaptic transmission should be avoided since they have an opposite effect to bromocriptine's. According to Mialot *et al*. (1981, 1984) [64-65], bromocriptine should be taken with food or in escalating amounts to avoid this side effect. Since most nations only provide 2.5 mg tablets of bromocriptine for human use, fractioning is required to provide the recommended dosage of 20 µg/kg each day for PSPY bitches (Mialot and Bohnert, 1980; Purswel, 1998) [62].

(B) Cabergoline: Compared to bromocriptine, cabergoline (Galastop®, DOSTINEX® 0.5, CABGOLIN® 0.5, and TEVA® 0.5) has a (Greater) higher level of bioactivity, superior D2-Receptor specificity, and a longer duration of action. Additionally, cabergoline remains bound to pituitary receptors and retains some efficacy for two or more days after therapy termination. For PSP bitches, 5 µg/kg per day for 5±10 days is recommended. Due to its limited ability to pass the blood-brain barrier, cabergoline has less adverse effects related to central emesis (Jochle *et al*., 1987; Arbeiter *et al*., 1988; Dumon *et al*., 1993 and Harvey *et al*., 1997) [41, 47, 4]. Gastrointestinal symptoms are uncommon and the ED50 for

emesis is four times the therapeutic dose.

(C) Metergoline: A daily dosage of 0.2 mg/kg of metformin (Contralac®; Vibrac Laboratories, Carros, France) is administered for 8±10 days. Methyroline's central antisertoninergic impact causes behavioural changes, which are the most common side effects (Hamon *et al*., 1981; Mialot and Dumon, 1986; Arbeiter *et al*., 1998) [5, 63]. These changes include anxiety, aggression, hyperexcitation, and fussiness. Methyridine should thus not be administered to bitches who are agitated or nervous or who already exhibit significant behavioural abnormalities as a result of PSC. However, while having a brief serum half-life and a negligible emetic action, it also has a mild antiprolactinic activity (Fieni *et al*. 1995).

Homeopathy

(A) *Thuja occidentalis*: The plant known by various names in English, including Northen White Cedar, Arborvitaes, Eastern White Cedar, Swamp Cedar, Thujas, and White Cedarn, is native to North America, Eastern Asia, and Canada. It contains terpenethujone, which has various actions on the body, including antibacterial, antiviral, and anti-fungal, internal analgesic, and effects on the central nervous system. It is also effective in reversing mammary gland and endometerial edoema by affecting renal function and inhibiting milk secretion. The dosage of *Thuja occidentalis* is 8 globules, taken three times a day, per o.s., and can be used safely and effectively without causing any side effects. (Aslan *et al*., 2008 and Nihat, 2008) [6]. Both Aslan *et al*. (2008) [6] and Nihat (2008) [6] noted that the Batches fully recovered from the physical changes in their mammary glands and the behaviours of pseudopregnant bitches within 30 days after considering its benefits; thus, homoeopathy has the potential to be used in pseudopregnant bitches when using *Thuja occidentalis* globules. As a homoeopathic agent, 8 globules of *Thuja occidentalis* were given orally, three times a day.

(B) *Urtica urens*: The European native nettle, also known by other names such as annual nettle, dwarf nettle, small nettle, dog nettle, burning nettle, annual nettle and stinging nettle, is higher in alkaloids, saponins, and phytates. Its actions include reducing galactopoiesis and lactation, promoting hormonal balance, and acting as an antioxidant, antibacterial, antiviral, and antifungal. Aslan *et al*. (2008) [6] and Nihat (2008) [6] reported that the effective and safe dosage of PSP bitch was 8 globules taken three times a day for a period of six days. There were no negative effects reported. According to Aslan *et al*. (2008) [6] and Nihat (2008) [6], after 6 days of therapy with Urticaurens, the percentage of bitches experiencing behavioural issues dropped dramatically from 33.3% to 6.7% in just 3-5 days, and after 10 days, all bitches' behavioural symptoms vanished.

Ovariectomy or spaying

The only long-term prophylactic approach is ovariectomy, so bitches who are not meant for breeding should be spayed (Johnston, 1980, 1986) [51-52]. While lactation may cause PSC to continue, this should ideally be done during anoestrus (Allen, 1986 and Mialot *et al*., 1984) [3, 64]. Following surgery, spaying late metaoestrous bitches with a history of overt PSC may cause additional episodes (Gobello *et al*., 2001) [29]. Spaying during the diestrus or metestrus can cause a pseudopregnancy episode three to seven days following the

procedure. Castration-related long-term problems, such as obesity and urine incontinence, can be controlled with diet and substitute oestrogen therapy (Stubbs *et al*., 1995) [80].

Conclusion

Pseudocyesis is the Luteal Phase of non- fertile induced ovulatory cycles, A short LP with an abrupt decline in P_4 levels which stimulate PRL release and provoke PSC- Bromocriptine, Cabergoline, Metergoline and sex Steroids are used in Pseudopregnancy bitch at time of treatment encounter side effects more than the homeopathic treatment, Homeopathy is very effective and safe and alternatively usable pharmacological agent (*Thuja occidentalis*). Pseudopregnancy predisposes the occurrence of Mammary glands Neoplasia or Tumours, Ovariectomy of bitches in the midluteal phase stops progesterone-induced GH release and lowering of the circulating IGF-I concentration and also increases plasma PRL concentration- Leading to proliferation of mammary gland epithelium and promoting lobulo alveolar development & facilitate the development of pseudopregnancy and Ovariectomy must be performed during anoestrus only as a permanent preventive measure for Pseudocyesis and ovariectomy.

References

1. Aissi A. Monitoring of Pregnancy by Ultrasonography in Bitches Depending on the First Mating. Abstracts, July 26-29, 7th International Symposium on Canine And Feline Reproduction, Whistler, Canada.
2. Ajala OO, Fayemi OO, Kolawole TO. Erythrocytic parameters as indicators for differentiating between the pregnant and pseudopregnant bitches in Nigeria. The Journal of Physiological Sciences. 2011;26:019–022.
3. Allen WE. Pseudopregnancy in the bitch. The current view on aetiology and treatment. The Journal of Small Animal Practice. 1986;27:419-424.
4. Arbeiter K, Brass W, Ballabio R. Treatment of pseudopregnancy in the bitch with cabergoline, an ergoline derivative. The Journal of Small Animal Practice. 1988;29:781-788.
5. Arbeiter K, Hofman E, Russe M. Metergoline zurbehandlung von Pseudograviditatundzu Brugere H. The role of prolactin in the genital function of the female dog. Rhode Island Medical Journal. 1998;174:7-15.
6. Aslan S, Beceriklisoy HB, Nihat O, Handler J. Effectiveness of *Thuja occidentalis* and *Urtica urens* in pseudopregnant bitches. Veterinary Medical Austria / Wien. Tierärztl. Mschr. 2008;95:263–268.
7. Concannon PW. Biology of gonadotrophin secretion in adult female dogs. Journal of Reproduction Fertility Suppl. 1993;47:3-27.
8. Concannon PW. Canine physiology of reproduction. In: Burke T, ed. Small Animal Reproduction and Infertility. Philadelphia: Lea and Febiger; 1986:23-77.
9. Concannon PW, Lein DH. Hormonal and clinical correlates of ovarian cycles, ovulation, pseudopregnancy and pregnancy in dogs. In: Kirk R, ed. Current Veterinary Therapy, Small. Animal. Practice, Vol. X. Philadelphia: WB Saunders Co; c1989. p. 1269-1282.
10. Concannon PW, Gimpel T, Newton L, Castracane VD. Postimplantation increase in plasma ®brinogen concentration with increase in relaxin concentration in pregnant dog. American Journal of Veterinary Research. 1996;57:1382-1385.
11. Concannon PW, Hansel W, McEntee K. Changes in luteinizing hormone, progesterone and sexual behavior associated with periovulatoryluteinization in the bitch. Biology of Reproduction. 1977;17:604-619.
12. Concannon PW, Westein R, Whaley S, Frank D. Suppression of luteal function in dogs by luteinizing hormone antiserum and bromocriptine. The Journal of Reproduction & Infertility. 1987;81:175-180.
13. Cortese G, Oliva G, Verstegen J. Hyperprolactinemia and galatorrhea associated with primary hypothyroidism in a bitch. Journal of Small Animal Practice. 1997;38:572-575.
14. Decoster R, Beckers JF, Beerens D. A homologous radioimmunoassay for canine prolactin: Plasma levels during the reproductive cycle. Acta Endocrinology. 1983;103:473-478.
15. Donnay I, Rauis J, Verstegen J. Influence des antécédentshormonauxsurl' apparitioncliniques des tumeursmammaires chez la chienne. Etude épidémiologique. Animal Science Research Indian Journal veterinary Medicine. 1994;138:109-117.
16. Dumon C, Dumoulin PY, Collet JP. Traitement de la lactation de pseudogestation chez la chiennepar la cabergoline. Prat Med Chir Anim Comp. 1993;28:573-577.
17. Elvira K, Snježana V, Molnar S, Mužinić L, Đorđević V. Pseudocyesis and Couvade syndrome. durs. istraz. zagreb god"BR. 2002;6(62)STR:1031-1047.
18. Feldman EC, Nelson RW. Canine and Feline Endocrinology and Reproduction. Philadelphia: WB Saunders Co; c1987.
19. Fernandes PA, Bowen R, Kostas AC, Sawyer HR, Nett T. Luteal function in the bitch: changes during diestrus in pituitary concentrations of and number of luteal receptors for luteinizing hormones and prolactin. Biology of Reproduction. 1987;37:804-811.
20. Fieni F, Verstegen J, Heraud V. Physiologie de la prolactine, pharmacologie des antiprolactiniqueset applications chez la chienne. Prat Med ChirAnim Comp. 1992;34:187-199.
21. Findler IJ, Brodley RS, Howson AE. Relationship of anestrus irregularity, pseudopregnancy and pregnancy to canine pyometra. Journal of the American Veterinary Medical Association. 1966;149:1043-1044.
22. Forsyth IA. Variation among species in the endocrine control of mammary growth and function: The roles of prolactin, growth hormone, and placental lactogen. Journal of Dairy Science. 1969;3:886-903.
23. Gerres S. Investigations on the importance of progesterone as a regulatory factor for the occurrence of pseudopregnancy in bitches. Thesis; c1991. p. 183.
24. Gerres S, Hoeveler B, Hoffman B. Canine pseudopregnancy. Veterinary Journal Fuerden Veterinaer. 1988;5:29-31.
25. Gervasio C, Yanina CY, Gobello C. A clinical trial of the prolactin inhibitor metergoline in the treatment of canine pseudopregnancy. Revistacientífica, fcv-luz / vol. xii, nº. 6. 2002:712-714.
26. Gobello C, Delasota RL, Goya RG. Review of Canine Pseudocyesis. Journal of Reproduction Domestic Animal. 2001;36:283-288.
27. Gobello C, Bolognani F, Delasota RL, Goya RG. Twenty four hour pro®les of serum prolactin and luteinizing hormone in anestrous crossbred bitches. The Journal of Reproduction Domestic Animal. 2001;36:41-45.
28. Gobello C, Concannon PW, Verstegen J. Canine

Pseudopregnancy: A Review. In: Concannon PW, England G, Verstegen J, eds. Recent Advances in Small Animal Reproduction. Ithaca, New York, USA: International Veterinary Information Service (www.ivis.org); c2001.
29. Gobello C, de la Sota L, Castex G, Baschar H, Goya RG. Dioestrousovariectomy: A model to study the role of progesterone in the onset of canine pseudopregnancy. The Journal of Reproduction & Infertility. 2001;57:55±60.
30. Gobello C, delasota L, Castex G, Baschar H, Goya R. Diestrousovariectomy: A model to study the role of progesterone in the onset of canine pseudopregnancy. Journal of Animal Reproduction & Fertility. 2001;57(Suppl):55-60.
31. Gobello C, Delasota RL, Goya RG. Study of the change of prolactin and progesterone during dopaminergic agonist treatments in pseudopregnant bitches. Animal Reproduction Science. 2001;66:257–267.
32. Gobello C, Scaglia H, Colombani M, delasota L, Goya RG. Characterization of prolactin molecular variants in pseudopregnant bitches. In: Forsberg M, Greve T, Gustafsson H, Katila T, Kinqahl H, Ropstad E, eds. Proc. 14th Int. Congr. Anim. Reprod. Stockholm, Sweden. Elsevier, Stockholm, suppl; c2001. p. 117 (Abstr).
33. Gobello C, de la Sota RL, Goya RG. Study of the changes of prolactin and progesterone during dopaminergic agonist and placebo treatments in pseudopregnant bitches. Animal Reproduction Science. 2001;66:257-267.
34. Graff K, Entrebay K. Endocrinology of reproduction in the female beagle dog and its significance in mammary gland tumorogenesis. Acta Endocrinology. 1979;90(Suppl. 222):1-33.
35. Graff K, Friendreich E, Matthews S. Homologous immunoassay for canine prolactin and its application in several physiological states. The Journal of Endocrinology. 1977;75:93-103.
36. Grunau B. Zurbehandlung von Prolaktinbei Pseudograviditat der Hundin. Inaugural Dissertation. Tierarztliche Hochschule. Hannover, Germany; c1994.
37. Grunau B, Nolte I, Hoppen HO. Investigation on the treatment of pseudopregnancy in the bitch with the prolactin inhibitors metergoline and bromocryptine. Tierarztl. Prax. 1996;24:149-155.
38. Grunau B, Nolte I, Hoppen HO. Investigation on the treatment of pseudopregnancy in the bitch with the prolactin inhibitors metergoline and bromocryptine. Tierarztl. Prax. 1996;24:149-55.
39. Hadley JC. Unconjugated estrogen and progesterone concentrations in the blood of bitches with false pregnancy and pyometra. Journal of Veterinary Research. 1975;96:545-547.
40. Hamon M, Mallat M, Herbet A. H3 Metergoline, a new ligand of serotonin receptor in the rat brain. Journal of Neurochemistry. 1981;36:613-626.
41. Harvey MA, Cauvin A, Dale M, Lindley S, Ballabio R. Effect and mechanism of the antiprolactin drug cabergoline on pseudopregnancy in the bitch. Journal of Small Animal Practice. 1997;38:336-339.
42. Harvey MA, Cauvin A, Dale M. Effect and mechanism of the antiprolactin drug cabergoline on pseudopregnancy in the bitch. Journal of Small Animal Practice. 1997;38:336-339.
43. Harvey MA, Dale MJ, Lindley S. A study of the aetiology of pseudopregnancy in the bitch and the effect of cabergoline therapy. Journal of Veterinary Research. 1999;17:433-436.
44. Hoffmann B, Hoveler R, Hasan SH. Ovarian and pituitary function in dogs after hysterectomy. Journal of Reproduction and Fertility. 1992;96(2):837-845.
45. Jackson RD, Worstman J, Malarkey WB. Characterization of large molecular weight prolactin in women with idiopathic hyperprolactinemia and normal menses. Journal of Clinical Endocrinology and Metabolism. 1985;61:258-264.
46. Janssens LA. Treatment of pseudopregnancy with bromocriptine, an ergot alkaloid. Journal of Veterinary Research. 1986;119:172-174.
47. Jochle W. The sexual cycle in the bitch: recent insights and impact on therapy and reproduction. Tierarztl. Prax. 1987;15:295-300.
48. Jochle W. Prolactin in canine and feline reproduction. Reproduction in Domestic Animals. 1997;32:183-193.
49. Jochle W, Arbeiter K, Post K. Effects on pseudopregnancy, pregnancy and interoestrous intervals of pharmacological suppression of prolactin secretion in female dogs and cats. Journal of Reproduction and Fertility. 1989;39:199-207.
50. Jochle W, Ballabio R, DiSalle E. Inhibition of lactation in the beagle bitch with the prolactin inhibitor cabergoline: Dose response and aspects of long term safety. Theriogenology. 1987;27:799-810.
51. Johnston SD. False pregnancy in the bitch. In: Morrow DA, ed. Current Veterinary Theriogenology. Philadelphia: WB. Saunders; c1980. p. 623-624.
52. Johnston SD. Pseudopregnancy in the bitch. In: Morrow DA, ed. Current Veterinary Theriogenology. 2nd ed. Philadelphia: WB. Saunders; c1986. p. v490-491.
53. Juan J, Tarin C, Hermenegildo MA, Antonio C. Endocrinology and physiology of pseudocyesis. Tarin Reproductive biology and Endocrinology. 1950;11:39.
54. Konig MP, Kopp P. Hyperprolactinemia. Schweiz Med Wochenschr. 1986;116:265-270.
55. Larrea F, Villanueva C, Cravioto MC. Further evidence that big, big prolactin is preferentially secreted in women with hyperprolactinemia and normal ovarian function. Journal of Fertility and Sterility. 1985;44:25-30.
56. Larsen PR, Inbar SH. The thyroid gland. In: Wilson J, Foster D, eds. Williams Textbook of Endocrinology. 8th ed. Philadelphia: W.B. Saunders; c1992. p. 357-487.
57. Lawler DF, Johnston SD, Keltner DG. Influence of restricted food intake on estrous cycle and pseudopregnancy in dogs. Animal Journal of Veterinary Research. 1999;60:820-825.
58. Lee WM, Kooistra HS, Mol JA, Dieleman SJ, Okken AC. Ovariectomy during the luteal phase influences secretion of prolactin, growth hormone, and insulin-like growth factor-I in the bitch. Theriogenology. 2006;66:484–490.
59. Marshall FH, Halnan ET. On the post oestrus changes occurring in the generative organs and mammary glands of the non-pregnant dog. In: Proceedings of the Royal Society of London. 1917;89:546-559.
60. Marusic S, Karlovic V, Zoricic Z, Martinac M. Pseudocyesis: A case report. Journal of Acta Clinical Croat. 2005;44:291-295.
61. McCarthy MM, Know LM, Pfaff DW. Speculation concerning the physiological significance of central oxytocin in maternal behavior. In: Pedersen CA,

Caldwell JD, eds. Oxytocin in Maternal Sexual and Social Behaviors. New York: Academy of Sciences; 1992:652:70-82.
62. Mialot JP, Bohnert M. Lactation de pseudogestation chez la chienne. Le Point Vétérinarian. 1980;11:33-35.
63. Mialot JP, Dumon CH. Utilisation de la metergoline pour le tarissement de la lactation chez les carnivores domestiques. Prat Med Chir Journal of Comparative Animal Physiology. 1986;21:177-181.
64. Mialot JP, Begon D, Guerin C. Pathologie de la mamelle. In: Anonymous, ed. Pathologie de la reproduction chez les carnivores domestiques. Alfort: Editions Du Point Vétérinarian; c1984. p. 143-158.
65. Mialot JP, Lagneau F, Chaffaux S. Inhibition de la lactation de la pseudogestation chez la chienne par la bromocryptine. Journal of Medical Veterinary Research. 1981;157:351-365.
66. Murrel TCG. Epidemiological and biochemical support for the theory and the cause and prevention of breast cancer. Medical Hypotheses. 1991;36:389-396.
67. Nihat O. Effectiveness of homeopathy for the treatment of Pseudopregnancy in bitches. Turkish Journal of Veterinary & Animal Sciences. 2005;29:903-907.
68. Okkens AC, Dieleman S, Kooistra H. Plasma concentrations of prolactin in overtly pseudopregnant Afghan hounds and the effect of metergoline. Journal of Reproduction Fertility supp. 1997;51:295-301.
69. Olschewski C. Die lactatiofalsa de Hunden: Klinische und hormonanalystiche Untersuchungen unter besonderer Berucksichtigung einiger Therapieverfahren [The false lactation of dogs: Clinical and hormone analytical investigations with particular consideration of some therapeutic methods]. Inaugural Dissertation, Justus-Liebig University Giessen, Giessen, Germany; c1987.
70. Olson PN, Bowen RA, Behrendt MD. Concentrations of progesterone and luteinizing hormone in the serum of diestrous bitches before and after hysterectomy. Am J Vet Res. 1984;45:14-153.
71. Onclin K, Verstegen JP. Secretion patterns of plasma prolactin and progesterone in pregnant compared with nonpregnant dioestrous beagle bitches. J Reprod. 1997;51:203-208.
72. Peterson ME, Drucker WD. Advances in the diagnosis and management of canine cushing syndrome. In: Proceedings of the 31st Gaines Veterinary Symposium. 1981;8:12-17.
73. Purswell BJ. Pharmaceuticals used in canine theriogenology. In: Proceeding of the Annual Meeting Society for Theriogenology. 1998;9:92-7.
74. Reimers TJ, Phemister RD, Niswender GD. Radioimmunological measurement of FSH and prolactin in the dog. Biol Reprod. 1978;19:673-679.
75. Rodolfo L, Delasota RG, Gobello C. Heterogeneity of circulating prolactin in the bitch. Reprod Nutr Dev. 2001;41:505–511.
76. Rutteman GR, Misdorp W. Canine mammary tumor disease: Role of hormones in pathogenesis and treatment. Tijdschr Diergeneeskd. 1989;11:345-455.
77. Sinha YN. Structural variants of prolactin: Occurrence and physiological significance. Endocr Rev. 1995;6:354-369.
78. Smith D, Foster K. Elizabeth Stormshak, Patricia Chamberlain, and Rachel Bridges. “Placement disruption in treatment foster care.” J Emot Behav Disord. 2007;9(3):200–05.
79. Smith MS, McDonald LE. Serum levels of luteinizing hormone and progesterone during the estrous cycle, pseudopregnancy and pregnancy in the dog. Endocrinology. 1974;94:404-412.
80. Stubbs WP, Salmeri KR, Bloomeberg MS. Early neutering of the dog and cat. In: Kirk RW (ed.), Curr Vet Ther XII. WB Saunders, Philadelphia, USA. 1995;5:1037-1040.
81. Thorner MO, Vance ML, Laws RE. The anterior pituitary. In: Wilson JD, Foster DW, Kronenberg HM, eds. Williams Textbook of Endocrinology. 9th ed. Philadelphia: WB Saunders Co. 1998;45:249-340.
82. Thorner MO, Vance ML, Laws RE, Horvath E, Kovath K. The anterior pituitary. In: Wilson JD, Foster DW, Kronenberg HM, Larsen PR (eds), Williams Textbook of Endocrinology, 9th edn. WB Saunders, Philadelphia, USA. 1998;5:249-340.
83. Tsutsui T, Kirihara N, Hori T, Concannon PW. Plasma progesterone and prolactin concentrations in overtly Pseudopregnant Bitches: A clinical study. Theriogenology. 2007;67:1032–1038.
84. Tucker HA. Endocrine and neural control of mammary gland. In: Larson BL, ed. Lactation. Ames, IA: Iowa State University Press. 1985;3:39-79.
85. Verstegen J. Intérêt et applications des antiprolactiques en la cancérologie chez la chienne [Interest and applications of antiprolactics in oncology in the bitch]. In: Proceedings of the 24th World Small Animal Veterinary Congress Paris, France; c1999.
86. Verstegen J, Decoster R. Lactation nerveuse de la chienne et bromocryptine [Nervous lactation in the bitch and bromocriptine]. J Vet Med Sci. 1985;125:375-377.
87. Verstegen JP, Onclin K, Silv LD, Concannon PW. Effect of stage of anestrus on the induction of estrus by the dopamine agonist cabergoline in dogs. Theriogenology. 1999;51(3):597-611.
88. Voith VL. Functional significance of pseudocyesis. Mod Vet Pract. 1980;61:75-79.
89. Voith VL. Behavioral disorders. In: Ettinger SJ, ed. Textbook of Veterinary Internal Medicine. 2nd ed. Philadelphia: W.B.Saunders Co. 1983;21:513-522.