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## Ovarian remnant syndrome: A review

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**Abstract**

Ovarian remnant syndrome (ORS) is a condition that occurs when ovarian tissue remains inside the body after a female dog is spayed. This is the result of failure to remove some or all of an ovary during ovario-hysterectomy (OHE). Suggested reasons include surgical error, failure to remove ectopic extra ovarian tissue at the time of OHE and auto transplantation of ovarian tissue. This tissue can produce estrogen, triggering signs of heat in the bitch. Second cause of ORS was suggested as dropping of some ovarian tissue into the abdomen during the surgery. Most common clinical sign of ovarian remnant surgery is when a previously spayed bitch goes into heat. This can happen at any time after spay surgery, with interval of months to years. The affected animals might show typical proestral or estral signs such as vulvar swelling, sero-sanguineous discharge, attractiveness to male dogs, copulation and/or signs of false pregnancy. Diagnosis of ORS is not an easy case, by use of vaginal cytology, baseline hormone profile and ultrasound tool, it can be judged significantly. Only recommended treatment for ORS is surgical removal of the remnant tissue. Lifelong usage of megestrol acetate or mibolerone has been mentioned in the medical treatment of ORS.

**Keywords:** ORS, bitch, ovario-hysterectomy, vaginal cytology, sterilization

**Introduction**

Sterilization of domestic animals by surgical operation has been performed for many centuries and it is the most common, reliable, effective and the least controversial contraception method (Concannon and Meyers-Wallen, 1991; Salmeri *et al.*, 1991) [4, 20]. Ovario-hysterectomy and ovariectomy are the surgical techniques routinely performed for surgical sterilization of female animals. Although, this method also have some untoward consequences i.e. Ovarian remnant syndrome (ORS) (Concannon, 1995) [5].

Ovarian remnant syndrome (ORS) is a condition that occurs when ovarian tissue remains inside the body after a bitch is spayed. This is the result of failure to remove some part of tissue or all of an ovary during ovario-hysterectomy (OHE). Suggested reasons include surgical error, failure to remove ectopic extra ovarian tissue at the time of OHE and auto transplantation of ovarian tissue (Wallace, 1991) [26]. In humans with ORS, primary risk factors are pre-existing intra-abdominal abnormalities (which include endometriosis, pelvic inflammatory disease and previous abdominal surgery) that obscure identification of the ovaries at the time of surgical removal (Fleischer *et al.*, 1998, Magtibay, 2006). These risk factors have not been identified in reports of ORS in domestic animals (Miller *et al.*, 1995) [14]. Ovarian remnant syndrome predispose to show clinical signs indicating as the presence of functional ovarian tissue in a previously ovario-hysterectomized or ovariectomy bitch or queen. Ovarian remnant syndrome (ORS) is a specific long term complication of ovario-hysterectomy and ovariectomy when the ovarian cortex is not fully removed. It is not considered as pathological condition but it is a complication of ovariohysterectomy. It develops when a retained piece of ovarian tissue becomes functional and revascularizes. The most common observation is recurrent estrus in after ovario-hysterectomized or ovariectomy *i.e.*, vulvar swelling, flagging, standing to be mounted (Wallace, 1991) [26].

When bitch or queen is ovario-hysterectomized or ovariectomy, spayed bitch or queen no longer has ovaries, cannot produces estrogen, or goes into heat. If recently spayed bitch shows the signs of heat, indicates that functioning ovarian tissue (known as an ovarian remnant) is still present and that continuous producing estrogen. Ovarian remnants may be left behind during ovario-hysterectomized or Ovariectomy, or may be the presence of accessory ovarian tissue.

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## Etiology

The mechanism was first described by Shemwell and Weed (1970) [23], who investigated that the ovarian cortex could be functional if implanted elsewhere in the abdomen rather than in its anatomical origin.

Wallace (1991) [26] shows that the factors such as obesity, pyometra and being deep chested bitch, that may cause difficulty in the ovario-hysterectomized or ovariectomy were not related with ORS. Three basic causes have been suggested for the development of ORS in companion animals (Feldman and Nelson 2004) [7].

The first and the most accepted explanation is incomplete surgical removal of one or both ovaries as a surgical error. This occur due to a small abdominal incision, makes difficult to visualize, reach and carry out the ligation of the ovary or ovaries, or to incorrect ligating of ovarian tissues or due to anatomical location of the right ovary (Wallace, 1991; Miller, 1995; Johnston *et al.*, 2001a, Prats, 2001) [26, 14, 11, 18].

Anatomically, the right ovary and uterine horn are located in a more cranial position than the left ovary and uterine horn which makes difficult to locate it by the surgeon due to it leave the ovary or ovarian tissue during the surgery (Evans and Christensen, 1993) [6].

Second cause of ORS was reported as dropping of some ovarian tissue into the abdomen during the surgery (Wallace, 1991; Feldman and Nelson, 2004; Romagnoli, 2004) [26, 7, 19]. If a piece of ovarian tissue is dropped accidentally into the abdomen during the ovario-hysterectomized or ovariectomy, this tissue get revascularizes with omentum or the serosa of abdominal viscera and behaves like a normal ovary (Prats, 2001) [18].

Third one is presence of an accessory ovary or part of ectopic ovarian tissue that is localized in the broad ligament may also cause ORS (McEntee, 1990; Miller, 1995; Feldman and Nelson, 2004) [13, 14, 7]. Ectopic ovarian tissue has been identified within the ovarian ligament at its junction with abdominal wall in the bitch, (Johnston *et al.*, 2001a) [11].

## Clinical signs

The most common clinical sign of ovarian remnant syndrome is when a previously spayed bitch comes into heat. This can happen at any time after spay surgery, with a delay of months to years.

Signs of heat in the bitch include swelling of the vulva and blood-tinged vaginal discharge. A bitch or queen that is in heat may show behavioral changes, such as being more receptive to males, and will often be more attractive to male dogs. bitch or queen having functioning ovarian tissue, go into heat at every six to eight months (Pearson, 1973) [16].

Affected bitch or queen shows the typical proestrus or estrus signs like as vulvar swelling, sero-sanguinous discharge, and attractiveness to male dogs, copulation or signs of false pregnancy (Pearson, 1973; Wallace, 1991; Johnston *et al.*, 2001a; Feldman and Nelson, 2004; Romagnoli, 2004; Sangster, 2005) [16, 26, 11, 7, 19]. Interval between previous ovario-hysterectomy or Ovariectomy and the onset of signs of oestrus in bitches had a range from three months to five years (Miller, 1995) [14].

Additional clinical signs that are recorded in the medical records Included mammary gland enlargement or masses, pollakiuria and stranguria, dermal hyperpigmentation and alopecia, postural behavior indicative of estrus (i.e., lordosis, vulvar or vaginal masses, vaginal mucosal enlargement, polyuria and polydipsia, polyphagia, a poor coat, weight loss,

and recurrent urinary tract infections (Ball *et al.*, 2010) [1].

## Diagnosis

Diagnosing ORS is not an easy task. Diagnosis is based on anamnesis, clinical symptoms, vaginal cytology, hormonal analysis, and exploratory laparotomy (Wallace, 1991; Miller, 1995; Johnston *et al.*, 2001a; Feldman and Nelson, 2004; Romagnoli, 2004) [26, 14, 11, 7, 19]. Clinical history and symptoms are very important in leading a clinician to suspect ORS (Prats, 2001) [18].

This makes history and clinical assessment of the patient prior to blood sampling essential to optimizing the chance of a correct diagnosis

**1. Vaginal Cytology:** This test involves taking a sample swab from vagina while animal showing signs of heat. Changes in circulating levels of oestradiol affect the vaginal epithelial cells and they can be monitored by vaginal cytology to assessment of the sample under the microscope for the presence of a specific type of cell such as cornified cells (Olson *et al* 1987.). If these cornified cells are found, this indicates that bitch is under the influence of estrogen. Vaginal Cytology is often used as a preliminary screening test for the presence of an ovarian remnant, though it is not specific for an ovarian remnant. The presence of cornified anucleate or pyknotic vaginal epithelial cells confirms ovarian activity to be present (Wright 1990).

It is the cheapest, easiest and most reliable tool in the diagnosis of ORS. In the presence of a functional ovarian remnant, oestrogen secretion will cause a progressive cornification of the vaginal epithelial cells (Wallace, 1991) [26].

**2. Baseline Hormone Levels:** A variety of studies have examined the use of baseline hormone testing in diagnosing ovarian remnant syndrome. However, these tests are not frequently recommended, due to low reliability and costly too or not available easily. Abnormal hormone levels can indicate the presence of an ovarian remnant,

Key to performing the correct test is deciding whether the patient is exhibiting the actual signs of oestrus. hCG stimulation tests are performed if the patient does show signs of oestrus, while GnRH stimulation tests should be performed if the patient does not show any signs of oestrus.

**3. Ultrasound:** Ultrasound can be used to visualize ovarian tissue, if it is performed while the bitch or queen is in heat. Accuracy of this way of diagnosis, however, is influenced by the size of the ovarian remnant, the stage of the heat cycle during which the test is performed, and the skill power of the ultrasonographer. Again, this test is not frequently used.

**4. Hormone Stimulation Test:** Test is widely used as the most accurate test for diagnosing ovarian remnant syndrome. A synthetic hormone (hCG or GnRH) is administered while bitch or queen is showing signs of heat. A blood sample is taken then five to seven days later. If the test shows an increase in progesterone, this indicates the presence of functioning ovarian tissue.

Two tests are generally used to assess whether functional ovarian tissue is present. These are both stimulation tests using either human chorionic gonadotropin (hCG) or a gonadotropin-releasing hormone (GnRH) agonist to measure

changes in progesterone or oestradiol, respectively (Idexx Laboratories, 2015).

Differential diagnoses must be done with vaginitis, uterine stump pyometra, and exogenous estrogen therapy. A commercially available luteinizing hormone test can be used to distinguish ovariectomized and sexually intact bitches. In dogs with a vaginal swelling, vaginal cytology offers a rapid and simple means of assessing whether oestrogen levels are elevated.

### Treatment and Discussion

The only and last recommended treatment for ORS is surgical removal of the remnant tissue (Perkins and Frazer, 1995; Johnston *et al.*, 2001a; Prats, 2001; Feldman and Nelson, 2004; Romagnoli, 2004) [11, 18, 7, 19]. Lifelong usage of megestrol acetate or mibolerone has been prescribed in the medical treatment of ORS (Johnston *et al.*, 2001a; Feldman and Nelson 2004; Romagnoli, 2004) [11, 7, 19]. The side effects of progestagens such as increasing the incidence of mammary gland tumors (Briggs, 1980; Van Os *et al.*, 1981; Bruun, 1997), induction of growth hormone secretion and promotion of acromegaly condition (Scott and Concannon, 1983) [22], and suppression of adreno-cortical function (Van den Broek and O'Farrell, 1994), rule out medical treatment with these compounds. Moreover, medical treatment with mibolerone is also not recommended since it may cause clitoral enlargement, vaginal discharge, or behavioral changes (Evans and Sutton, 1989).

Today, the best way to treat the syndrome is surgical excision of the remnant tissue for the surgical approach; a mid-line ventral laparotomy is preferred instead of a flank incision. A mid-line ventral laparotomy would provide clear visualization of the abdominal cavity which would make the surgery easier. By mid-line approach, it would be possible to remove the remnant uterine tissue if present.

The timing of the exploratory laparotomy is very important. If the animal is under the influence of oestrogen or if the ovulation has occurred, it will be much easier to detect the ovarian tissue. In both cases, the ovary will be enlarged because of the follicles or corpora lutea. However, due to the increased vascularity, intra operative bleeding could be a complication.

Some reports have suggested the surgery should be performed two weeks to four weeks post-estrus as the luteal tissue may be more prominent and hence easier to locate (Hess, 2015).

Laparotomy is not recommended during anestrus, since the remnant tissue might be too small to be detected (Wallace 1991, Perkins and Frazer 1995) [26]. Harvey (1998) [8], suggests that the best timing for the surgery would be two weeks after attractiveness has ceased in which oestrogen and prolactin concentrations would be at basal levels. The abdominal incision should be more cranial than for routine OVH. During the surgery, the caudal poles of both kidneys, the broad ligament, the omentum and the abdominal wall should be examined deeply to identify any ovarian tissue. Miller (1995) [14] demonstrated that in most cases ovarian remnants were located around the ovarian pedicles. In dogs, ovarian tissue is often found in the region of the right or left ovarian pedicles. While the right side has been shown to be the more common site, all areas should be examined – irrespective of preoperative findings or initial assessment (Ball *et al.*, 2010) [1].

### Conclusion

Best way to avoid the development of the ovarian remnant

syndrome is prevention. Sufficient abdominal wall incision to visualize the surgical area, proper ligation of the reproductive organs and total removal of both ovaries without leaving any ovarian tissue has crucial importance in prevention of the syndrome. Early age neutering or prepubertal ovario-hysterectomy can be considered another preventive factor since the syndrome is not detected in animals spayed younger than four months.

Complications of ovarian remnant syndrome include the formation of granulosa cell tumors, uterine stump pyometra, and mammary neoplasia; thus surgical excision of the ovarian remnants should be highly recommended (Johnston, 1991). Granulosa cell tumors can also secrete estrogens and progesterones, resulting in the same clinical signs as ovarian remnant syndrome. Though formation of the tumor may induce the onset of the clinical signs, these tumors will only form if an ovarian remnant or accessory ovarian tissue, which has never been reported in dogs, remains in the animal (Feldman & Nelson, 2004) [7].

Although identified as a syndrome, ovarian remnant syndrome is an iatrogenic condition that can be prevented through careful and proper surgical technique. When presented with a spayed animal showing signs of estrus, a series of diagnostic tests culminating in exploratory laparotomy and excision of the remnant tissue is recommended.

### What happens if ovarian remnant syndrome is not treated?

With an untreated ovarian remnant are subject to the same risks as animal that is not spayed. Continued influence of estrogen predisposes dogs and cats to mammary gland tumors (breast cancer), pyometra (infection of the uterus), and ovarian tumors.

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