

Ovarian Remnant Syndrome (ORS) in the bitch and queen and the use of Anti-Müllerian Hormone (AMH)

Steven Metcalfe BSc BVMS(Hons) MSc MANZCVSc^a

Jenny Hill BVSc(Hons) DipACVP^b

^aApplecross Veterinary Hospital, PO Box 891 Canning Bridge WA 6153

08 93647666 steve@applecrossvet.com.au

^bVetpath Laboratory Services

PO Box 18, Belmont WA 6984

08 92593666 jenny@vetpath.com.au

ORS is a well documented phenomenon in the bitch and queen and occurs when an animal returns to oestrus following an ovariohysterectomy(OVH)/ovariectomy(OE). ORS is also recognised in women. Excellent reviews and reports have been published recently^{1,2,3}. Pearson (1973), in a review of complications of bitch ovariohysterectomy, stated

“Twelve animals in this series were presented for investigation of post-operative heat periods with vulval swelling, pro-oestrous bleeding, the characteristic odour, and often lactation during false pregnancy. In one animal, regular periodic milk secretion was the only indication of a preceding oestrus. In all cases, functional residual ovarian tissue was found at exploratory laparotomy and it is significant that the right side was more frequently affected than the left. It is probable that any gonadal tissue inadvertently left at ovariohysterectomy will prove functional and at subsequent laparotomy, such remnants are often very small indeed and may not be macroscopically recognizable in the fat of the surrounding bursa and mesosalpinx. At surgery, if residual ovarian tissue cannot be seen or palpated, its presence is often manifest by increased vascularity of the ovarian pedicle on the affected side. In cases of post-operative oestrus, the correct treatment is excision of the ovarian remnant as advocated by Brodey & Harvey (1971), and this is best performed during metoestrus.”^{4,5}

The causes of ORS have been attributable to a number of factors;

- 1) Poor surgical technique when stretching/breaking the ovarian pedicle ligament prior to ligation leading to inappropriate location of pedicle clamps and incomplete excision of the ovary^{2,4}.
- 2) Dropped ovarian tissue into the abdomen that revascularises^{6,7}.
- 3) Presence of aberrant ovarian tissue within the ovarian pedicle or elsewhere in the abdomen (rare)⁸.
- 4) There is mention of the possibility of post OVH oestrus occurring due to adrenal dysfunction but this has not been documented in the bitch or queen.

Miller (1995) documented 46 ORS cases (29 queens and 17 bitches) that showed no significant effect of age, breed, surgeon experience or tendency to the presence of right, left or both sided ovarian remnants. Histological assessment showed follicles and/or corpora lutea were present in 59/65 (91%) of specimens examined. All remnants in this report had been surgically located in the vicinity of their original ovariectomy site. The time between initial OVH and clinical evidence of ORS is weeks to months in queens and months to years in bitches⁸.

There are no published reports indicating whether the incidence of ORS is more frequent in animals undergoing OVH by flank versus midline approach although there is one

anecdotal report suggesting that ORS may be less likely in animals undergoing OVH/OE by laparoscopy because of the better visualisation and magnification provided by this technique.

The undesirable clinical issues recognised with ORS are return to oestrus and its behavioural ramifications, uterine disease – stump pyometra, ovarian disease – cyst formation, neoplasia and possibility of unwanted pregnancies^{2,9,10,11,12,13}. There are also medico-legal considerations.

A strong clinical suspicion is present for ORS in any bitch or queen that clinical records document previous OVH, they present for return to oestrus with or without vaginal discharge and have no history of exposure to exogenous oestrogens.

Investigation involves reviewing the history and clinical investigation. Vaginal cytology for epithelial cornification confirms oestrogen effect. Any detectable serum progesterone level above baseline confirms the presence of active luteal tissue in bitch or queen. This may not be present in the queen so stimulatory testing using 500 IU hCG IM and assessing for a rise in serum progesterone 7 days after injection has been shown to indicate ORS¹⁴.

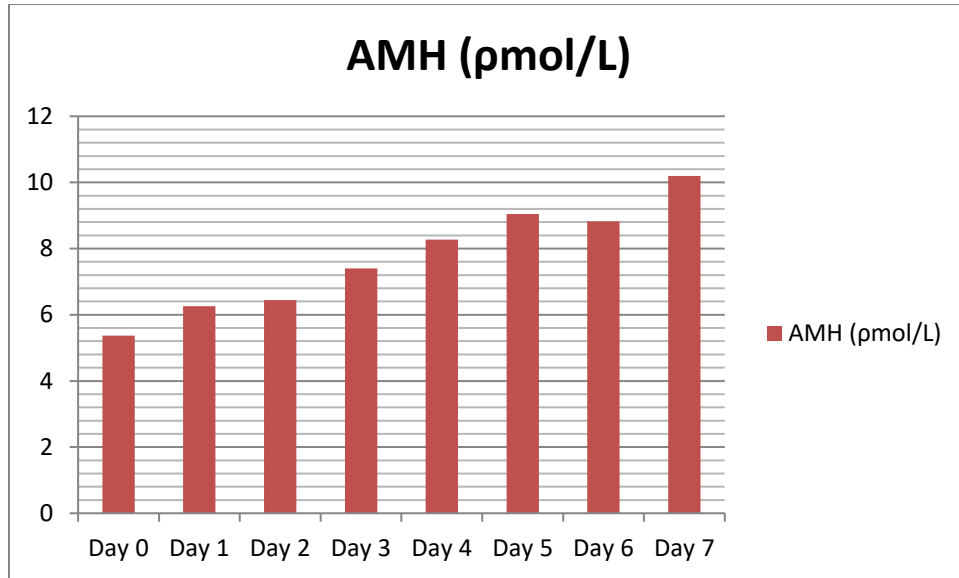
Detection of residual ovarian tissue in the bitch or queen when not displaying signs of oestrus may be accomplished by measuring serum Anti-Müllerian Hormone (AMH).

AMH is a 140-kDa dimeric glycoprotein hormone belonging to the transforming growth factor β family (TGF- β). It is secreted by precursor and mature Sertoli cells in males and granulosa cells from small primary and secondary follicles in females. In embryonic development the Müllerian ducts transform into the cervix, uterus and oviducts in females. In males AMH induces regression by a cascade of reactions acting via the AMH I and AMH II receptors on the ducts and surrounding mesenchymal cells. In females, AMH has an inhibitory effect on the recruitment of primordial follicles and the responsiveness of growing follicles to follicle stimulating hormone (FSH). AMH assays are currently used in women to assess for functional ovarian reserve and prediction of excessive response to ovarian hyperstimulation.^{15,16}

Place *et al.* demonstrated in bitches older than 6 months of age, the sensitivity (probability of correctly identifying intact dogs) of the AMH test was 93.9% (95% CI: 82.1-98.4%), and the specificity (probability of correctly identifying OVH dogs) was 93.8% (95% CI: 69.8-99.7%).¹⁷

Our current investigations have been performed using the AMH Gen II ELISA (Beckman Coulter, Inc. 250 S. Kraemer Blvd, Brea CA 92821, USA).

AMH stability testing was performed on whole blood from a mature intact greyhound bitch. Blood was collected into a plain clot tube and allowed to sit at room temperature. Every 24 hours an aliquot was taken, frozen and all samples were batch assayed after the last sample was collected. AMH values increased from 5.37 to 10.2 pmol/L between day 0 to 7. Correlation coefficient is 0.98. The most probable explanation for the increase is the AMH dimer is splitting and the immunoassay is detecting both peptide chains. These results suggest that delays between collection and assay when whole blood is shipped should be considered when interpreting the result.



Whole blood samples from 36 client owned bitches and 16 client owned queens were submitted by general practitioners with information regarding presence or absence of ovaries to determine reference ranges as given below.

Reference AMH Concentrations (pmol/L)		
Bitch Category	Known OVH (n=12)	Known Intact (n=24)
Range	0.00 – 0.38	1.63 – 9.49
Median	0.00	2.82
Mean ± SD	0.11 ± 0.15	3.37 ± 1.47
Queen Category	Known OVH (n=9)	Known Intact (n=7)
Range	0.00	5.92 – 32.7
Median	0.00	14.30
Mean ± SD	0.00	16.25 ± 8.28

Whole blood samples were then submitted from 7 bitches and 2 queens with suspected ORS based on behavioural and clinical signs. The two queens were 10 and 12 months old, had both undergone juvenile ovario-hysterectomy and had serum AMH concentrations of 24.6 and 10.8 pmol/L, respectively. Based on the comparison to reference range these levels were consistent with ORS. These findings are consistent with the previously reported study that showed AMH levels clearly demarcated between intact and OVH queens.¹⁷

The bitch results are given in the table below. In the two bitches younger than 9 months, the AMH concentration was low. However, bitch 3 had elevated serum progesterone indicative of active follicular tissue. Bitch 1 also had elevated progesterone despite low AMH and was confirmed to have a sex chord stromal cell tumour on histopathology following mass removal at surgery. The AMH concentrations in bitches 5 to 7 were consistent with expected reference ranges and presentation. Our data is consistent with the previously reported study showing that AMH concentration may be used to detect the presence of ovarian tissue in mature bitches that do not have neoplastic disease.

Ultrasound examination of the abdomen, particularly for the presence of uterine stump enlargement as well as focal changes in the region of the ovarian pedicle may provide additional information.

Ultimately, surgical exploration of the cranial abdomen, resection of all suspicious tissue around the pedicle and histological examination of these tissues is required to confirm and cure ORS.

AMH Concentrations (pmol/L) in bitches with suspected ORS					
No.	Breed	Age (months)	AMH (pmol/L)	Progesterone (nmol/L)	Clinical findings
1.	Jack Russell	72	0.14	3.1	Sex chord stromal cell tumour
2.	Golden Retriever	8	0.21		Unknown
3.	Husky	9	0.29	25.8	ORS
4.	Kelpie	51	0.4		Mammary hyperplasia
5.	West Highland White Terrier	12	2.5		OVH at 5 months. Vulval swelling at 7 and 12 months
6.	Border Collie	228	2.6		Two oestrus episodes seen despite two previous OVH surgeries
7.	Groodle	57	2.9		ORS. Bilateral complete ovaries present at surgery

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