

Role of LH in the Pathophysiology of Urinary Incontinence in Ovariectomized Bitches



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INTRODUCTION

‣The incidence of urinary incontinence in ovariectomized (OVX) bitches is prevalent compared to intact bitches¹

‣Ovariectomy results in permanently elevated gonadotropin concentrations, which may contribute to the development of incontinence¹

‣Reducing gonadotropin concentrations through the use of GnRH agonists restores continence in ~50% of incontinent bitches^{2,3}

‣Decreasing gonadotropin concentrations by immunizing against GnRH may therefore also restore continence (Figure 1)

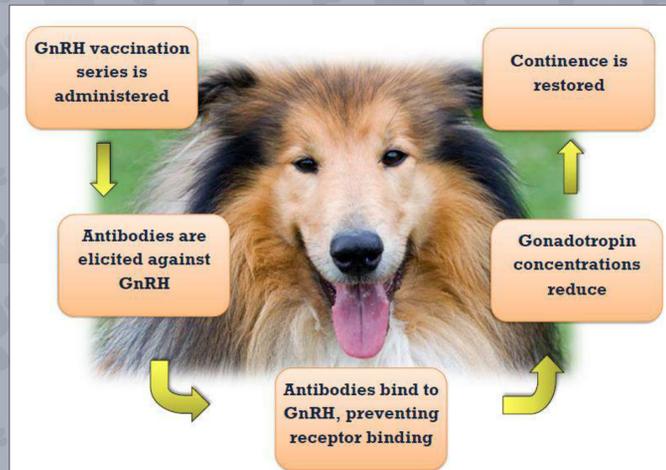


Figure 1. GnRH immunization mechanism of action

MATERIALS AND METHODS

EXPERIMENT 1

‣27 continent and 16 incontinent bitches of medium (30-49 lbs) and large (50-100 lbs) breeds recruited

‣Venous blood samples were collected to measure plasma LH using a canine-specific ELISA (LH-Detect®, Repropharm)

‣Comparisons between bitches analyzed using PROC TTEST in SAS® (V. 9.2, SAS Institute Inc.)

EXPERIMENT 2

‣14 incontinent bitches taking phenylpropanolamine (PPA; Proin®, PRN Pharmacal) recruited

‣9 bitches were vaccinated against GnRH (Canine Gonadotropin Releasing Factor Immunotherapeutic®, Pfizer Animal Health) twice at four week intervals (Figure 2)

‣5 bitches received placebo injection

‣Venous blood samples were collected over a 6 month period and treated dogs discontinued PPA after vaccination (Figure 3)

‣Plasma LH measured as in experiment 1

‣Comparisons between groups analyzed using PROC MIXED in SAS® (V.9.2, SAS Institute Inc.)



Figure 2. GnRH vaccine for Experiment 2

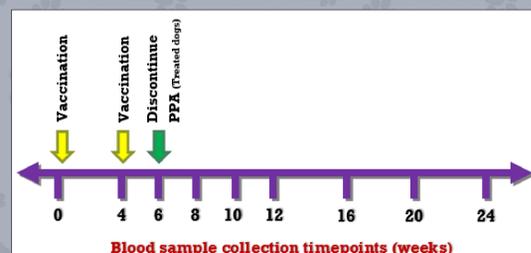


Figure 3. Time line for Experiment 2

RESULTS

EXPERIMENT 1

‣Continent bitches had significantly higher LH concentrations than incontinent bitches (Table 1)

‣Medium bitches had significantly higher LH concentrations than larger bitches (Table 1)

VARIABLE	N	MEAN LH CONCENTRATION (ng/mL)	SEM	P
Continent bitches	27	7.85	1.05	0.04
Incontinent bitches	16	4.78	0.51	
SIZE				
Medium bitches	23	8.56	1.07	0.004
Large bitches	20	4.56	0.69	
Medium continent bitches	15	10.34	1.40	0.02
Medium incontinent bitches	8	5.22	0.72	
Large continent bitches	12	4.71	1.07	0.79
Large incontinent bitches	8	4.32	0.73	
Medium continent bitches	15	10.34	1.40	0.005
Large continent bitches	12	4.71	1.07	
Medium incontinent bitches	8	5.22	0.72	0.39
Large incontinent bitches	8	4.32	0.73	
TIME OF SPAY				
Bitches ovariectomized ≤ 1 year	30	7.12	0.90	0.37
Bitches ovariectomized > 1 year	13	5.72	1.12	
Continent bitches ovariectomized ≤ 1 year	17	8.57	1.47	0.06
Incontinent bitches ovariectomized ≤ 1 year	13	5.22	0.54	
Continent bitches ovariectomized > 1 year	10	6.59	1.34	0.17
Incontinent bitches ovariectomized > 1 year	3	2.86	0.71	
Continent bitches ovariectomized ≤ 1 year	17	8.57	1.47	0.37
Continent bitches ovariectomized > 1 year	10	6.59	1.34	
Incontinent bitches ovariectomized ≤ 1 year	13	5.22	0.54	0.07
Incontinent bitches ovariectomized > 1 year	3	2.86	0.71	

Table 1. LH concentration comparisons (mean ± SEM) between continent and incontinent bitches

EXPERIMENT 2

‣All bitches immunized against GnRH experienced a decrease in LH concentrations to basal levels (Figure 4)

‣There was an overall significant effect of the vaccine on LH ($p=0.0004$)

‣4/9 vaccinated dogs remained continent after PPA was discontinued

‣One dog became incontinent again 14 weeks after PPA was discontinued; the other three dogs remained continent through the end of the study

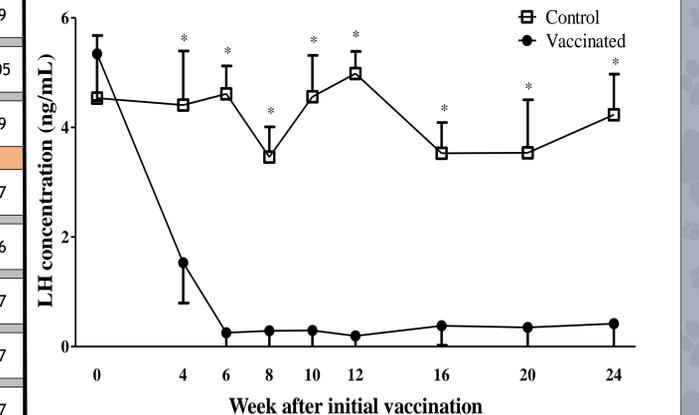


Figure 4. LH concentrations (mean ± SEM) in vaccinated and control bitches. * $p<0.05$ compared to controls

DISCUSSION

‣Continent bitches had higher LH than incontinent bitches, in agreement with findings by Reichler and coworkers⁴

‣Also in agreement was the effect of size, specifically that larger bitches had lower LH concentrations

‣Despite these observations, decreasing LH concentrations restored continence in some, but not all, bitches indicating a role for LH in the pathophysiology of urinary incontinence

‣However, this role remains unclear

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OBJECTIVE AND HYPOTHESES

‣Overall objective was to evaluate the role of LH in the pathophysiology of urinary incontinence in OVX bitches

‣Hypothesis 1: OVX continent bitches would have lower LH than OVX incontinent bitches

‣Hypothesis 2: Decreasing LH via GnRH immunization would restore continence in bitches with incontinence