ABSTRACTS
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Endocrine responses following Gonadotropin releasing hormone (GnRH) immunization in intact male dogs

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INTRODUCTION: GnRH is responsible for the release of luteinizing hormone (LH) and follicle stimulating hormone (FSH) from the pituitary, which regulates reproductive steroid hormone synthesis. When vaccinated against GnRH, endogenous GnRH will be prevented from binding to its receptor in the pituitary, halting LH and FSH production. As a result, steroid hormones will not be synthesized. The objective of this study was to measure the endocrine responses to GnRH immunization in intact male dogs. Based upon the manufacturer’s label, we hypothesized that vaccinating against GnRH would elicit a GnRH antibody titer and decrease LH and testosterone concentrations in intact male dogs for six months.

METHODS: Four privately-owned intact male dogs were used for this study. All were vaccinated with Canine Gonadotrophin Releasing Factor Immunotheraputic® (Pfizer Animal Health, Exton PA) and boostered again four weeks later. Venous blood samples were collected at 0, 4, 12, and 20 weeks. Sera were separated, aliquoted, and frozen at -20°C until analyzed.

GnRH antibody titers were determined using an enzyme-linked immunosorbent assay (ELISA) using 1 µg/mL LH-RH as the antigen (71447-49-9, Sigma, St. Louis, MO, USA). LH samples were run in duplicate using a canine-specific ELISA (LH-Detect® for canines, ReproPharm, Nouzilly, France) and performed according to the manufacturer’s instructions. The sensitivity of the assay was 0.01 ng/mL and a value greater than 0.80 ng/mL was determined to be a positive result. Testosterone concentrations were determined using a double antibody radioimmunoassay (Diagnostic Products Corporation, Los Angeles, CA). The detection limit of the assay was 0.04 ng/mL. Mean±SEM were determined for LH concentrations and compared between animals at the four time points using ANOVA with Bonferroni corrections. Mean±SD were determined for testosterone and GnRH antibody concentrations and compared between animals using ANOVA with Bonferroni corrections. Analysis was performed using Stata statistical software (Version 12; StataCorp. 2011, College Station, TX). Significance was defined as p<0.05.

RESULTS: GnRH titers peaked 12 weeks following initial vaccination, which differed significantly from weeks 0 and 20 (Figure 1). Although LH and testosterone concentrations appeared to lower at week 4 and week 12, respectively, these changes were not significant.

DISCUSSION: GnRH immunization is an ideal candidate for nonsurgical contraception in dogs and cats because a single product should be effective in both males and females. However, GnRH is a weak immunogen and must be coupled to a large protein and combined with an adjuvant to enhance its antigenicity (1). The vaccine used in the current study was prepared commercially and our laboratory has previously used this vaccine to suppress estrus in female horses (2). It is not clear why these four male dogs responded weakly to vaccination. However, using a different GnRH vaccine construct, Levy and coworkers (2004) reported that one-third of the male cats vaccinated against GnRH had a partial response with low positive GnRH antibody titers accompanied by equivocal serum testosterone concentrations (3). The small sample size in the current study is a limitation. Although assuming the differences observed in this study would be similar in a large population, 19 dogs would have needed to be studied to demonstrate significance.

Figure 1: Serum GnRH antibody titer as compared to testosterone and LH concentration (ng/mL) at weeks 0, 4, 12, and 20 of four intact male dogs vaccinated with Canine Gonadotrophin Releasing Factor Immunotherapeutic®.