Can single administration of a high dose GnRH agonist persistently suppress the canid reproductive axis? The coyote (*Canis latrans*) as a model

[1]MacGregor, M. J., [3]Asa, C., and [1, 2]Skinner, D. C.
[1]Department of Zoology and Physiology and [2]Neurobiology Program, University of Wyoming, Laramie, WY 82071; [3]Wildlife Contraception Center, St. Louis Zoo, St. Louis, MO 63110

GnRH agonists to contracept male dogs are now routinely used in Australia and Europe. These agonist implants initially ensured suppression of the reproductive axis for 6 months but, more recently, have been developed to contracept for at least 1 year. A primary difference between these differences in duration was the starting amount of GnRH agonist, *deslorelin*, within each implant. A preliminary study in dogs indicated that increasing the agonist amount, to 12mg, could suppress the reproductive axis for 1.7 years. Evidence from human studies, where men are routinely treated with the GnRH agonist, *leuprorelin*, suggests that after a certain period (for men, 3 years) of uninterrupted exposure to a GnRH agonist, may render the reproductive axis permanently suppressed. We hypothesized, therefore, that if a canid was exposed to a high enough dose of *deslorelin* in a constant release implant that, if suppression lasted for long enough, it may be possible to induce permanent contraception. Specifically, we hypothesized that if *deslorelin*-mediated suppression followed a linear dose-response relationship, then a 47mg *deslorelin* dose would suppress the canid reproductive axis for at least 4 years. Although our initial studies in rats indicated no harmful unintended consequences, testing this hypothesis in the dog was not feasible as such a high dose had never been tried. There was also a compelling need to develop an alternative approach to managing coyotes, which currently is through lethal control, with an estimated 80,000 killed annually in the USA. Specific objectives are to establish (1) the effect of GnRH agonist dose on duration of suppression of coyote reproduction; (2) the effect, if any, of a high-dose *deslorelin* on body composition (in the male rat we had evidence of increased adiposity); and (3), as GnRH receptors are detected in tissues outside the pituitary gland (e.g. gonads, heart, brain), to note any pathology associated with high dose GnRH agonist exposure. Preliminary data show full suppression of the reproductive axis for over 24 months as indicated by complete absence of sperm, almost unpalpable testes and suppressed testosterone. Analysis of blood chemistry parameters and body composition found no difference between *deslorelin*-treated and control coyotes. Our study shows that a single high dose GnRH agonist contracepts the male coyote with no evident pathophysiological effects for at least two years.