

MEDICAL MANAGEMENT OF ADRENAL DISEASE

Angela M. Lennox, DVM, DABVP-Avian
Avian and Exotic Animal Clinic, Indianapolis, IN
Purdue University, Indianapolis, IN

Adrenocortical disease is well described in ferrets. Presentation can include symmetrical alopecia, pruritus, vulval swelling in females, prostatic enlargement in males, and increased aggression and odor. Diagnosis is commonly assumed based on clinical presentation. Other aids to diagnosis include ultrasonography of the adrenal glands, and measurement of sex hormones, including estradiol, 17-hydroxyprogesterone and/or androstenedione.

Treatment options can be roughly divided into surgical and medical; however, in some cases treatment modalities can be combined. Surgical treatment is described in detail in other presentations. Medical therapy is aimed toward reduction of sex hormone production. There is no current compelling evidence that this type of therapy will slow tumor growth or reduce tumor size.

Most medical therapy focuses primarily on one class of drugs: gonadotropin-releasing hormone (GnRH) agonists. These drugs suppress production and/or release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) by down-regulating GnRH pituitary receptors

Leuprolide acetate (Lupron Depot, TAP Pharmaceuticals) is a long-acting GnRH agonist used to treat prostate and testicular cancer in men and endometriosis in women, and has been shown to reduce hormone production and alleviate symptoms of adrenal disease in ferrets. Currently recommended dosages are 100 to 150 µg/kg/month; however, in clinical practice dosages are often increased, and some report administration every 4 to 8 weeks depending on clinical response. The 1-month formulation appears to suppress hormone secretion for about 30 days and the 3-month formulation for 60 to 90 days. Studies in ferrets with naturally occurring adrenal disease demonstrated reduction of sex hormone production for about 1 to 3 months without untoward effects. Lupron is available from compounding pharmacies; however, the clinician must be certain the product offered is indeed the depot formulation, and not the simple leuprolide acetate in non-depot form. In clinics where Lupron is used frequently, the drug is purchased, reconstituted and diluted, and then drawn up into 100 to 200 µg dosages, then frozen until used. Anecdotal and unpublished information suggests retained potency for many months in frozen form. In some cases, owners can be instructed on how to safely store and inject at home.

Deslorelin acetate (Suprelorin, Peptech Animal Health) is another GnRH analog in implant form designed for slower release. Deslorelin implants are not available within the United States, and are ordered from Australia from Peptech directly, or from a distributor (see notes below).

Studies of deslorelin acetate have mostly focused on blockage of hormone production in intact ferrets. Dr.

Nico Schoemaker and colleagues updated their findings at the Association of Exotic Mammal Veterinarian's annual meeting in August 2010; single 4.7-mg deslorelin implants demonstrated effective blockage of sex hormones in male ferrets for 301 to 1249 days and in female ferrets for 637 to 872 days. These findings were based on phone surveys of pet owners who had elected implantation for their pets; therefore, observations may be somewhat subjective. In two ferrets where owners claimed the implants were no longer functional, measured adrenal hormones were below the detection limit of the assay. In summary, duration of action likely exceeds two years in both sexes. A 2010 study comparing various drugs for elimination of fertility in intact jills demonstrated superior length of action and safety for deslorelin implants.

Wagner published on the effects of deslorelin on ferrets with adrenal disease in 2009. Thirty ferrets with naturally occurring disease were implanted with 4.7 mg deslorelin acetate. In all ferrets, clinical signs were monitored, and ultrasonography of the adrenal glands performed; in 18 ferrets, adrenal hormone levels were measured before and after treatment. All ferrets demonstrated reduction in clinical symptoms, which included enlarged vulva, hair loss, pruritus, and enlarged prostate, with the exception of four who experienced incomplete regrowth of tail hair. In general, most ferrets demonstrated decrease in one or more adrenal hormones. While not all ferrets were available for multiple ultrasonographic evaluations, in general, there was no significant reduction in adrenal gland size after treatment. Two ferrets developed large adrenal masses just prior to clinical relapse.

Twenty-five of 30 ferrets ultimately experienced relapse of clinical symptoms post implantation, which occurred on average 17.6 months +/- 5 months, with a range of 8 to 30 months.

Implants are relatively large, as is needle size. Some clinicians recommend anesthesia for implantation. However, the author and many others routinely implant the conscious ferret while scruffing and offering a treat. Bleeding rarely occurs.

There is currently not enough information to recommend a specific GnRH analog over another based on efficacy. For practical purposes, however, deslorelin appears to have some distinct advantages. While initial cost is high, the cost of monthly Lupron injections rapidly exceeds that of a single deslorelin implant. Owners unwilling to inject Lupron at home must factor in travel time and costs related to monthly veterinary visits. A similar related issue is owner compliance, which is improved with the implant.

Melatonin has been reported to be useful for control of symptoms related to adrenal disease. One study showed decrease in serum estradiol and prolactin with oral administration for 4 to 8 months. Androsterone and 17-hydroxyprogesterone were also decreased, but not as significantly. Clinical signs generally returned within 12 months. There was no evidence melatonin impacted tumor growth or size. No adverse signs were reported in this study; however, melatonin is not used in human patients with hepatic insufficiency, and contraindicated in humans with renal disease. Melatonin is available in oral

formulation and 5.4-mg implants (Ferretonin; Melatek LLC).

A number of drugs have been proposed and used anecdotally for the treatment of secondary prostatic enlargement and include androgen receptor blockers such as bicalutamide (Casodes, AstraZeneca) and flutamide (Eulexin, Intervet/Schering-Plough). It is unclear if these medications provide additional benefit over administration of GnRH analogs alone.

REFERENCES

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APPENDIX – IMPORTATION OF FOREIGN DRUGS INTO THE UNITED STATES

Current US law permits importation of legal foreign drugs into the United States as long as the quantity does not exceed that representing a 30-day supply, and the drug is intended for personal use, eg, within the veterinarian's hospital, and not intended for redistribution. These rules are reflected in FDA's Regulatory Procedures Manual, Chapter 9-Import Operations and Actions, Section 9-2, Coverage of Personal Importations, updated March 2009.

If a shipment is intercepted at the US border by FDA personnel, the recipient will likely receive a phone call requesting more information. Explain the shipment is a 30-day quantity of a legal foreign drug for personal use, and refer to section C of the personal drug importation guidelines as listed above. In nearly every case of which the author is aware, the shipment is released to the recipient. The worse consequence is return of the shipment to the country of origin. As long as the shipment does not contain an illegal or prohibited substance, there will be no legal action taken against the recipient.

To order contact Vetafarm in Australia: www.vetafarm.com.au. This drug is not listed on the company website, and must be requested by direct e-mail.