

Adrenal Disease in the Ferret

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Introduction

When we refer to adrenal disease in the ferret, we almost always mean HYPER adrenal disease, where adrenal hormone levels are increased, as opposed to HYPO adrenal disease, where hormone levels are decreased. This is one of the most common problems of the domestic ferret. There are numerous proposed possible reasons including genetic predisposition, early neutering, nutrition and seasonal light cycle variations. A large study conducted in Holland demonstrated that ferrets neutered later in life still had nearly as high an incidence of adrenal disease as American ferrets, but it occurred an average of about one year later. It's most likely this problem is the result of a combination of factors and not a single simple one.

Mammals have two adrenal glands, which are typically located near the kidneys. The normal size of the ferret adrenal gland is about one-thirtieth the size of the kidney. In ferrets, the left one lies in an easily accessible area between the kidney and the vena cava, which is the largest blood vessel in the rear half of the body. The right adrenal lies in a much more difficult spot. It is usually attached to the vena cava itself and is hidden under the central lobe of the liver. It has traditionally been very difficult to remove surgically.

The adrenal glands produce many hormones (steroids), which are essential to life. To date, more than 50 different steroids have been isolated from the adrenal cortex, the outer 2/3 portion of the gland. These can be divided into three main groups: the glucocorticoids (cortisones), the sex hormones (androstenedione, estradiol, testosterone), and mineralocorticoids (aldosterone). The inner 1/3 of the gland, the medulla, produces adrenaline (epinephrine).

Diagnosis

In the ferret, most adrenal tumors involve the area of the adrenal gland that produces sex hormones, although tumors that produce cortisol or epinephrine do occasionally occur. For this reason, most of the clinical signs of adrenal disease are related to either estrogen or testosterone overproduction. Either of these can occur in either sex. In most cases, adrenal disease is relatively easy to diagnose, since the signs are so characteristic.

The most common sign of adrenal disease is hair loss. The most serious sign in female ferrets is an enlargement of the vaginal labia, which results from too much estrogen production. The result, if untreated, can be anemia and death. High estrogen levels can cause the bone marrow to stop production of red blood cells. In ferrets, this can be seen as early as three months from the beginning of labial

enlargement. The most serious sign in male ferrets is difficulty urinating. This results from enlargement of the prostate gland due to high hormone levels. If untreated, the swollen prostate can completely block the flow of urine and death will result from uremia.

Treatment may be either medical or surgical. While surgical removal of the affected gland is still the treatment of choice, a new medical treatment is showing a lot of promise.

Treatment/Surgery

Removal of the left adrenal gland is a fairly straightforward and uncomplicated process and may be performed by anyone with a little ferret surgery experience. Removal of the right adrenal gland demands a great deal of confidence and experience on the part of the surgeon, since the right adrenal is intimately attached to the largest blood vessel in the body (vena cava). In our experience, freezing, scraping or any form of "subtotal" removal of the right gland does not yield satisfactory results, as the gland usually grows back within three to six months. The only sure method of removing the entire gland is to remove the portion of the vena cava to which the gland is attached, and then suture the remaining portion of the vessel back together. This is a procedure with a high degree of difficulty and should only be attempted by surgeons with a lot of experience. It is nearly impossible to determine which gland (possibly both) is involved prior to surgery. The glands are so small that ultrasound may not give accurate results.

Although there is always some degree of risk associated with general surgery, we have performed hundreds of adrenal surgeries, both right and left, with very few complications. Adding a melatonin implant at the time of surgery when one adrenal gland is removed may help prevent the remaining gland from becoming diseased.

Treatment/Medical

Medical options are available for ferrets who cannot undergo surgery. Medical treatment usually consists of a melatonin implant, Lupron injection, or a combination of the two.

Melatonin is a hormone that influences the entire endocrine system. It is thought that this hormone may play a role in preventing adrenal disease or reversing early adrenal disease in the same way that manipulation of light cycles may play a role.

The use of artificial lights to stimulate hair growth is not a new concept. During the 1930's several studies were done using artificial light to induce estrus cycles (heat). During the 1950's the neuropathways of light-induced estrus were studied. During the 1960's, 70's, and 80's the hormones and neuropathways involved in reproductive neuroendocrinology in ferrets were studied. The amount of light per day (photoperiods) regulates the amount of melatonin. During the spring/summer months the photoperiod increases (13-15 hours of light per day) and the melatonin levels decrease. During the fall/winter months the photoperiod decreases (8-12 hours of light per day) and the melatonin levels increase. Melatonin directly and indirectly controls the hypothalamus-pituitary-adrenal/gonadal axis. Thus the increased melatonin levels (8-12 hours of light) cause the seasonal weight increase, end the estrus cycles, and stimulate the hair follicles to grow hair (i.e. putting on their winter coat). Conversely the decreased melatonin levels (13-15 hours of light)

cause the seasonal weight loss, start the estrus cycles, and cause the hair follicles to shed.

Early studies showed that continuous, long-term dosing of oral melatonin did work in many cases, but only for a period of eight to ten months. After initial improvement, ferrets taking oral melatonin had a rebound effect and adrenal symptoms returned.

We are now using time-release melatonin implants injected under the skin to mimic natural hormonal cycles. These implants are administered every three to six months, and are showing extremely good results treating adrenal disease that is not too far advanced. The implants are inexpensive.

Lupron is an estrogen blocker that is used mainly in treatment of breast cancer in women. It has proved effective in treating a high percentage of adrenal tumors. It appears to be as effective against testosterone-producing tumors as it is against estrogen-producing ones. It is very safe and has about an 80% efficacy rate. Its main disadvantage is expense, costing approximately \$50 a month and continuing for the life of the ferret.

Combining the effects of Lupron and melatonin seem to offer the best possible medical option. In my experience, adding melatonin to Lupron therapy improves Lupron's effectiveness significantly.

Conclusions

There is still much to be learned about ferrets and adrenal disease. There are currently ongoing studies by practicing veterinarians all over the U.S. who are combining their information to produce useful data on surgical techniques and promising medical treatments. It is an exciting possibility that the use of melatonin as a preventive in healthy ferrets will reduce the incidence of adrenal disease as well. It is of the utmost importance that you seek experienced veterinary help in deciding on a preventive or a treatment plan for your ferret.