## **Adrenal Gland Disease**

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Adrenal gland disease is common in ferrets over 4 years old, affecting up to 25% of these ferrets. The normal adrenal gland contains several types of cells that produce different hormones, such as cortisone and some male and female sex hormones. Excessive amounts of female hormones are often produced by adrenal gland tumors in ferrets, whereas cortisone is overproduced in adrenal gland tumors in dogs. Palpation, <u>radiography</u>, and <u>ultrasonography</u> are used to identify an enlarged adrenal gland. The enlargement may be caused by hyperplasia (normal cells proliferating at an unusual rate), or by a benign or malignant tumor.

Possible cause of adrenal gland disease in ferrets

It is likely that more than one factor determines any ferret's susceptibility to adrenal gland disease.

#### Early spaying or neutering

It has been suggested that <u>spaying and neutering</u> 6- to 7-week-old ferrets induces adrenal gland disease. The theory is that the adrenal glands of animals spayed or neutered at a very young age might try to compensate for the lack of normal sex hormones by proliferation of cells in the adrenal gland that produce sex hormones. However, many ferrets spayed or neutered when much older have developed adrenal gland tumors, and occasionally animals that have not been spayed or neutered also have adrenal gland tumors.

Even if there is also some association with removal of gonads, the risk of not spaying is far greater than the chance that a spayed jill will develop adrenal tumors at a young age. About 50% of unspayed jills left in heat too long will develop bone marrow hypoplasia and die, but under natural light conditions, a very small percentage of ferrets spayed at any age develop adrenal tumors.

#### Extended photoperiod

Early spaying or neutering is certainly not the whole answer. The disease was uncommon in the hunting ferrets that were their ancestors, and is still rare in animals that live outside, as they tend to do in the United Kingdom and in Australia. The incidence of adrenal gland disease is increasing in the United Kingdom as pet ferrets begin to share their owners' homes instead of living in the back garden.

It is possible that the incidence of adrenal gland disease has increased because we have forced our ferrets to adapt to our life style. Ferrets are strongly affected by photoperiod. Under natural conditions, there are only about 8 hours of strong light a day in the winter months, and the proportions of light and dark gradually change during the spring and fall. We have removed all these stimuli when we keep the ferret in a house where electric lights extend day length to at least 12 hours, all year round.

Changing photoperiod causes the ferret to lose weight and hair in the spring, and come into breeding condition. In the fall, as the hours of light decrease, ferrets stop breeding, grow a heavy winter coat, and put on extra fat to prepare for the cold weather. A primitive part of the brain called the pineal gland governs the ferret's response to light. The pineal gland produces a hormone called melatonin only during hours of darkness. Melatonin reduces the output of hormones called gonadotrophins from the pituitary gland. Gonadotrophins bind to cells in the ovary or testicle, inducing production of sex hormones. The same gonadotrophins also bind to cells in the adrenal gland. When ovaries and testicles are removed, these gonadotrophins can bind only to adrenal cortical cells.

It is possible that constant stimulation of the adrenal glands because of the long hours of light eventually causes first benign hyperplasia (enlargement), and then benign tumors to develop in the adrenal cortex. In some animals, the tumors become malignant or are malignant from the outset. Whether the condition is hypertrophy, a benign tumor, or cancer, excessive levels of adrenal cortical hormones are produced.

Hyperplasia, in some instances, may be corrected if the ferret is put in a place where the light can be limited to 8 hours a day. The ferret's hair may start to regrow 3 to 6 weeks after the change. By definition, tumor cells are out of control, and modifying photoperiod cannot reverse hair loss when any type of tumor is producing sex hormones.

People want their ferrets to be awake and playing in the evening when they come home from work, so the ferret is exposed to natural light all day, and artificial light in the evening. The obvious way to limit the ferret's exposure to 8 hours of light a day, without preventing him from interacting with his family, is to give him a dark place to sleep during the day. It has to be really dark, excluding all light, like a moonless night.

This might be arranged by putting the ferret's cage inside a well-ventilated closet, or using light-excluding drapes on the windows in the ferret's room. Reducing the ferret's exposure to light usually results in an improvement in coat condition and an increase in body weight a few weeks after the new arrangement - these responses show that the original photoperiod was too long. Providing short days only during the winter months is sufficient, as this mimics the natural seasonal variation in day length.

In a survey of about 300 ferrets performed in the Chicago area in the early '90's, the lowest incidence of adrenal gland tumors was found in ferrets used for breeding, and these animals must have been housed under short photoperiod at least part of the year or they would not have been productive. The association between adrenal gland tumors and artificial light conditions cannot be ignored.

#### Genetics

Individual people and animals are more susceptible to some types of cancer than others. Some ferret families may be especially susceptible to adrenal gland cancer.

Signs that a ferret has an adrenal tumor

Weight loss, hair loss - especially at the base of the tail, feet and abdomen, and scratching for no apparent reason, are often the only early signs of adrenal disease in either a male or female ferret. Intact hobs with adrenal tumors might have permanently enlarged testicles but will be sterile. They may also have difficulty urinating because of an enlarged prostate. The first sign noticed by the owner of a spayed female with an adrenal gland tumor is often the sudden appearance of a swollen vulva, as if she were in heat.

# Signs of adrenal disease in ferrets:

- Hair loss, either in a symmetrical pattern or patchy with no apparent patten. This may come and go depending upon the season.
- Hair which pulls out easily.
- Loss of appetite.
- Lethargy
- Papery thin or translucent looking skin, sometimes with sores from scratching.
- Excessive scratching and itchiness, especially between the shoulder blades.
- Increase in musky body odor.
- Excessive grooming of self or other ferrets, including ear sucking.
- Sexual aggression and mating behavior in neutered males with other ferrets, inanimate objects, etc.
- Swollen vulva in spayed females, with or without a mucous discharge.
- Difficulty urinating for males this is a sign of an enlarged prostate, a condition usually associated with adrenal disease.
- Weakness in back legs usually seen in advanced or extreme cases.
- Increased thirst, increased urination.
- Weight loss due to a decrease in muscle mass, but with a pot bellied appearance.

### Diagnosis of adrenal gland disease

The diagnosis of adrenal gland disease in ferrets is generally made as a result of the symptoms and results of routine blood testing and tests for elevated adrenal hormones. An ultrasound examination may reveal enlarged adrenal glands. The definitive way to determine the actual nature of the disease (hyperplasia, benign tumor, or malignant tumor) is through surgical removal and microscopic examination of the affected gland.

#### Treatment of adrenal gland disease

#### Surgery

The most effective treatment is to surgically remove the abnormal adrenal gland. If the left adrenal gland is the one affected, it is generally easier to remove than the right. If the right gland is affected, surgery is more difficult because the right adrenal gland lies very close to the vena cava, the large blood vessel that returns blood from the body to the heart. Sometimes it is not possible to remove the entire right adrenal gland because of this. Surgery will greatly benefit an animal that has itching, whereas some of the medical treatments may not.

### Medical Treatment

The goal of medical treatment is to decrease the signs of adrenal gland disease. Medical treatment will not cure the condition, and must be given for the life of the animal. Most of the therapies are quite expensive.

Leuprolide acetate (Lupron Depot) can be given as an injection, and is usually given every 4 weeks. Resistance to this medication can occur.

Arimidex is an oral medication that blocks the effects of estrogen. Like leuprolide, resistance may occur, and it may take over a month to see results. It may have a slightly better effect against itching than the other medical therapies.

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Flutamide is an oral medication that blocks the effects of some of the male sex hormones. It may help reduce the size of the prostate, and can also be used to help reduce some of the other signs of ferret adrenal disease.

Melatonin has shown some success alleviating the symptoms of adrenal gland disease in ferrets. It is given orally or as an implant. It may be used alone, but often has to be used in conjunction with other therapies. Caution must be used if this melatonin is used in ferrets who also have an insulinoma.

Mitotane (Lysodren) is a drug that reduces the amount of hormone being produced by a benign inoperable tumor, extending the quality life time of the ferret. Unfortunately it has side effects, and is no longer commonly used.

Prognosis for ferrets with adrenal gland tumors

If left untreated, ferrets with adrenal gland tumors usually lose all but the hair on their heads and a tuft on the tail tip. Their skin gets very thin, they have a pot-bellied appearance, and they sleep most of the time. Fortunately, although they have an odd appearance with almost no fur on their bodies, ferrets with benign adrenal gland tumors can live a reasonably normal life, if they do not become anemic due to high levels of estrogen. Jills often appear to be in heat, and because this is associated with a swollen and open vulva, they are susceptible to urinary tract infections. Neutered or intact male ferrets may develop life-threatening urinary obstruction because high hormone levels cause the prostate gland to hypertrophy (enlarge) and constrict the neck of the bladder.

Some tumors are malignant and do not respond to medical treatments. They metastasize to other organs or recur after removal. Ferrets with malignant tumors have a short life expectancy after diagnosis.

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