Adrenal Disease in Ferrets
Drs. Foster & Smith Educational Staff

In the ferret, adrenal disease - or hyperadrenocorticism - most commonly occurs when a tumor or lesion on the adrenal glands causes an overproduction of the hormones produced by the adrenal glands. Adrenal disease is most common in ferrets over the age of three years, but it can affect ferrets as young as a year old. Adrenal disease is one of the most prevalent ferret diseases, and there is no definitive test for it. Ferret owners need to know as much as possible about it to be able to recognize it and help the ferret after the condition is diagnosed by the veterinarian.

CAUSES
While we don't know for sure what exactly causes adrenal disease in ferrets, most theories point to two possible causes:

Spaying and neutering at a young age
Many large ferret breeders spay or neuter ferrets at the age of 5 or 6 weeks, which may cause the ferret's body to overcompensate for the lack of normal sex hormones. Adrenal disease has occurred in ferrets that are spayed or neutered after they have reached sexual maturity, but it is not nearly as common.

Extended photoperiods
Most ferrets have been forced to adapt to their owner's lifestyle and are exposed to at least four or five hours of artificial light in the evening in addition to the natural light during the day. This limits the time they spend in darkness, which decreases melatonin production. Too little melatonin results in overstimulation of the adrenal glands. Ferrets should have no less than 12 hours of complete darkness throughout a 24 hour period.

When a ferret develops adrenal disease, it is most likely the combination of a variety of factors. In addition to environmental factors, some ferrets are probably genetically predisposed to developing adrenal gland cancer.

SIGNS
Hair loss or hair thinning - at the base of the tail, on his feet, on his belly, in an obvious pattern, or in a patchy appearance - are classic signs of adrenal disease. There are multiple causes for hair loss in ferrets, but a ferret owner should always suspect adrenal disease and report this to his or her veterinarian, especially if the ferret is 3 years of age or older. However, while hair loss is the classic sign of adrenal disease, not all ferrets will have this sign.

Unlike other diseases, there is not a standard set of signs that a ferret with adrenal disease will always display. The range of signs that your ferret shows will depend on where the tumor is on his adrenal glands. The adrenal glands produce many hormones, so the location of the tumor will affect which hormones are overproduced. The types of hormones that are
overproduced determines which signs you will see.

Here are the various signs of adrenal disease:

- Hair loss, either in a symmetrical pattern or patchy with no apparent pattern *
- Thinning hair
- Loss of appetite
- Lethargy
- Papery thin or translucent looking skin, sometimes with sores from scratching
- Excessive scratching and itchiness
- 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
- 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

* It is important to note that you may see partial or complete hair regrowth without treatment. This does not mean that your ferret is fine, it just means that the hormonal imbalances have balanced out again, probably due to a season change. The hormones will become unbalanced again, and hair loss will occur, usually more severe than before.

Always remember that you can see any combination of these signs - there is no set group of signs! Keep an eye on your ferrets as they grow older, watching for any symptoms or odd behavior. Something as seemingly innocuous as your ferret running from litter box to litter box trying to go to the bathroom should result in a trip to the veterinarian.

**DIAGNOSING ADRENAL DISEASE**

If your veterinarian has a lot of experience with ferrets or if your ferret has the traditional hair loss, he or she may be able to diagnose your ferret through clinical signs (symptoms).

Your veterinarian may decide to use the Adrenal Panel run by the University of Tennessee, often referred to as the "Tennessee Panel," in cases where adrenal disease is suspected. This is a blood test that evaluates the levels of hormones and steroid production. The test is not always 100% correct, and has been known to result in false positives and false negatives, but it is the only blood test available to test for adrenal disease.

Radiographs (x-rays) and ultrasounds help determine whether or not adrenal disease is present, but can be misleading. Diseased adrenal glands can be normal in size and shape and, therefore, an x-ray or ultrasound may not raise any concerns. However, ultrasounds can be helpful in showing prostate enlargement (a complication of adrenal disease in male ferrets).

When it comes to diagnosis, if your ferret is displaying any of the obvious signs, your veterinarian will probably suggest beginning treatment rather than spending money on expensive tests and other diagnostic measures. Ferrets can suffer from adrenal disease for a long time before actually showing symptoms, so no matter how your veterinarian arrives at the diagnosis, it's important to commence treatment immediately after the diagnosis has been made.

**TREATMENT**

Your veterinarian may opt to use any of the following options to treat your ferret's adrenal disease:

**Surgery**

This is the most common treatment for adrenal disease, and is the only way to completely remove the tumor. It is also the most recommended treatment by most veterinarians. If your veterinarian seems at all hesitant about the surgery or does not perform surgeries, ask for a recommendation to a more experienced ferret veterinarian.

If your ferret has already had surgery to remove one gland and adrenal tumors develop in the remaining gland, your veterinarian may decide that surgery is not the best choice. Ferrets that have both glands removed may develop Addison's disease, which is a severe or complete deficiency of the hormones made in the adrenal glands. Your veterinarian will probably want to check your ferret's cortisol (a hormone produced by the adrenal glands) levels within three days of the surgery.

Though surgery is the only option that could completely rid your ferret of adrenal disease, it is important for you to know that there are risks involved with surgery:

- If the tumor is on the right adrenal gland, your veterinarian may choose not to remove it. The right adrenal gland is directly adjacent to the vena cava, the largest vein in the body, and there could be serious complications.
- If any microscopic piece of affected adrenal tissue remains, the tumor can grow back either on the same side, or the opposite side.
- There is always a chance that the ferret may not make it through the surgery or through the recovery period in the first few days after the procedure is done.
IN SUMMARY

Darkness each day. It is thought that this will allow your ferret to produce the most melatonin possible.

Adrenal glands leading to adrenal disease. A ferret’s optimal light cycle is about eight hours of light and sixteen hours of total darkness, thereby decreasing the production of melatonin. Less melatonin means more GnRH is released, which then overstimulates the pituitary gland, which stops the production of the hormones that are overstimulating the adrenal glands. So if the Lupron shots are stopped, the pituitary gland resumes its normal function, and all of the problems start again.

If your veterinarian recommends doing surgery, but you can't do it right away for whatever reason, some veterinarians may recommend that the ferret receive Lupron in the meantime. This may prevent the disease from progressing any further and, at the very least, may make your ferret more comfortable by alleviating some of the symptoms.

Melatonin implants alone cannot be used to treat adrenal disease for the long term, and the best results are seen if Melatonin implants are used in conjunction with Lupron Depot.

Medical

Your veterinarian may suggest medical treatment options in cases where surgery cannot be performed, either due to the health of the ferret or other issues. These options include:

- **Lupron Depot Injections**
  
  Lupron Depot may be prescribed at 1 month, 3 month, or 4 month intervals. "Depot" refers to the fact that the entire dosage is released over the given time period. This means that your ferret will need to get this shot at the appropriate time for the rest of his life. Lupron may shrink the tumor, but in most cases, it only affects the symptoms.

  Even if all symptoms cease, Lupron must continue to be administered. Lupron works by desensitizing the pituitary gland, which stops the production of the hormones that are overstimulating the adrenal glands. So if the Lupron shots are stopped, the pituitary gland resumes its normal function, and all of the problems start again.

  If your veterinarian recommends doing surgery, but you can't do it right away for whatever reason, some veterinarians may recommend that the ferret receive Lupron in the meantime. This may prevent the disease from progressing any further and, at the very least, may make your ferret more comfortable by alleviating some of the symptoms.

- **Melatonin Implants**
  
  Melatonin is a natural hormone that serves many functions in your ferret's body, one of which is to inhibit the release of GnRH (gonadotropin releasing hormone). Less GnRH means that the pituitary gland releases fewer hormones, which means that the adrenal glands are stimulated less.

  Melatonin can be used in oral (liquid or pill) or implant form. While you can use oral melatonin, the success or failure of it depends on the time of day it is given. It needs to be administered exactly 7 - 9 hours after sunrise to mimic the natural release of melatonin. If given at this time every single day, oral melatonin is extremely effective. Unfortunately many ferret owners are not home during this time. A more convenient way to administer melatonin effectively is to use Ferretonin, a melatonin implant. Implants last about 3 - 4 months, and provide a steady level of melatonin over that time period.

  Melatonin implants alone cannot be used to treat adrenal disease for the long term, and the best results are seen if Melatonin implants are used in conjunction with Lupron Depot.

- **Medications to avoid**
  
  **Lysodren (mitotane)** was formerly used as a common treatment for adrenal disease, but studies have shown that Lysodren doesn't stop the stimulation of the adrenal glands and causes low blood sugar. This is a concern, as insulinoma and adrenal disease are often seen together, and ferrets with insulinoma struggle with low blood sugar already. Overdosages or incorrect dosages of Lysodren were also known to cause Addison's Disease.

  **Nizoral (Ketoconazole)** is used to treat Cushing's disease (hyperadrenocorticism) in dogs, which is completely different from adrenal disease (also hyperadrenocorticism) in ferrets. Though they are the same disease, the same drugs cannot be used to treat both.

  **Vetoryl (Trilostane)** is also used in dogs with Cushing's Disease, and increases the level of a hormone that is already quite high in ferrets with adrenal disease. Giving this to a ferret with adrenal disease would make the problem worse.

  **Nolvadex (Tamoxifen)** is an anti-estrogen medicine in humans. However, it actually has estrogen-like effects in ferrets, which would have a negative effect on many ferrets with adrenal disease.

**PREVENTING ADRENAL DISEASE**

Unfortunately, there are no proven ways to prevent adrenal disease. It is currently thought that the early neutering/spaying that is done by large scale breeders directly contributes to adrenal disease, and in most cases, the ferrets that you get will already have had this surgery. If they are intact, it is recommended that you wait until they are at least 6 months of age before getting them spayed or neutered. Adrenal disease is still seen in ferrets who are spayed or neutered after reaching sexual maturity, but it is not as prevalent.

Recent studies have shown that light cycles also contribute to the development of adrenal disease. Melatonin, as mentioned above, regulates the release of GnRH. GnRH affects how much the adrenal glands are stimulated. Melatonin is produced when the ferret is in total darkness. Most of our ferrets live in the same environment we do - natural daylight during the day, and several hours of artificial light in the evenings. This obviously shortens the amount of time the ferret is in darkness, thereby decreasing the production of melatonin. Less melatonin means more GnRH is released, which then overstimulates the adrenal glands leading to adrenal disease. A ferret's optimal light cycle is about eight hours of light and sixteen hours of total darkness each day. It is thought that this will allow your ferret to produce the most melatonin possible.

**IN SUMMARY**
It's important to add one more thought here - adrenal disease is very treatable in most cases. Not treating adrenal disease is condemning your ferret to die, when this doesn't have to be the case. If you see signs of adrenal disease in your ferret, please get him checked out as soon as possible. Ferrets can live long and happy lives after they are treated for adrenal disease, and we all want that for our fuzzies!