Corticosteroids (Steroids, Predisone, etc.)

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Corticosteroids comprise one of the most beneficial groups of medications used in dogs, cats, and other pets. These medications have one of the widest ranges of use of any class of drugs. If misused, however, problematic side effects can be seen.

Types of corticosteroids

All mammals constantly produce their own supply of corticosteroids within their bodies. One of the first corticosteroids discovered was cortisol, which is naturally produced by the adrenal glands of all animals. The adrenal glands are small, paired structures, one lying in front of each kidney. They produce three different types of steroids: mineralocorticoids, sex steroids, and the glucocorticoids.

Mineralocorticoids: Mineralocorticoids get their name from the fact that they have the responsibility of maintaining the levels of the minerals sodium and potassium in the body, and because they are produced by the cortex of the adrenal glands. Through their effect on sodium and potassium, as well as other actions, they conserve or maintain the body’s concentration of water at a near constant level. Mineralocorticoids exert most of their effect on the kidneys, causing parts of these organs to selectively excrete excess potassium in the urine and at the same time conserve or retain sodium. These actions maintain the concentrations of these electrolytes within a very narrow range that is compatible with life. The use of the mineralocorticoids or their synthetically produced imitations in veterinary medicine is much less common than the other two forms of steroids. Therefore, they will not be covered in this text.

Sex Hormones: The second steroid type produced by these glands is the sex steroids. Examples of these are the female hormones estrogen and progesterone and the male androgens such as testosterone. These same substances are also produced in much greater quantities by the ovaries in the female and the testicles in the male. The androgens are the group that are sometimes referred to as the anabolic steroids. Although they have accepted uses in medicine today, they often get considerable publicity when they are abused by athletes to increase their strength and abilities unethically. They are totally different in activity and usage from the glucocorticoids or mineralocorticoids.

Glucocorticoids: The previously mentioned cortisol belongs to the glucocorticoid group. The members of this group get their name because they affect glucose metabolism and are produced by the cortex section of the adrenal glands. The glucocorticoids are the predominant steroids used in veterinary medicine. These naturally occurring steroids cause proteins (e.g., muscles) and lipids (e.g., body fats) to be chemically broken down and converted into glucose. This is why the glucocorticoids are also referred to as the “catabolic” steroids. Catabolism means to break down large molecules into smaller ones. Additionally, the glucocorticoids also cause carbohydrates stored in the form of glycogen to be converted back to glucose and deposited into the circulating blood. There it is available to all the body’s tissues. To break down the proteins or fats of the body may seem harmful to the animal, but remember that glucose is the main energy source for all of the body’s activities. The vast majority of the glucose that the body utilizes comes directly from the diet or stored glycogen, but in emergency situations it can be derived from its own protein and lipids. It is generally thought that the glucocorticoids only cause this to occur to a significant degree during periods of exceptional need.

Glucocorticoids also suppress inflammatory processes within the body. A bruise, bee sting, bacterial infection, or arthritis are just a few examples of inflammation within a pet’s body. Inflammation is specifically defined as an area of the body characterized by redness, swelling, heat, and pain, often with impaired function. The warmth and redness seen in these affected tissues comes from an increase in the number and size of blood vessels within the area. The swelling (edema) is caused by free fluid within the tissues and also the engorged blood vessels. All of these changes are brought on by physical trauma and/or irritants within the tissues. The pain is caused by the swelling, by harmful substances putting pressure on, or by stimulating the local nerve fibers. The loss of function can be caused by pain or the simple inability of the body to move or act correctly.

Indications for using glucocorticoids in veterinary medicine

When corticosteroids are mentioned in the treatment of animal disorders, they are almost always of the glucocorticoid type. Naturally occurring cortisol is not used, but is replaced by others that can be produced more economically. Their use is generally intended to directly or indirectly reduce inflammation and irritation or to decrease the body’s natural response against itself or outside stimuli. Examples of these products would be hydrocortisone, prednisone, prednisolone, dexamethasone (Azium), betamethasone (Betasone), triamcinolone (Vetalog), methylprednisolone (Cortisate-20, Depo-Medrol, and Medrol), and others. Generic formulations are very common and are available in topical or systemic forms.

For patient information sheets on a variety of medications containing corticosteroids, click on the appropriate class of drugs listed below.

- Oral or injectable glucocorticoids
- Inhalers
- Ophthalmic (eye) preparations
- Ophthalmic (eye) preparations with antibiotics
- Topical (skin) medications
Treat Addison's Disease: Addison's Disease (hypoadrenocorticism) is a result of insufficient mineralocorticoids and glucocorticoids being produced by the adrenal glands. In primary hypoadrenocorticism, mineralocorticoid-like medications must be administered to maintain the life of the animal. Depending upon the severity of the condition, glucocorticoids may need to be given on a regular basis, or if the animal is undergoing stress (e.g., surgery). Animals with secondary hypoadrenocorticism require only glucocorticoid therapy.

Control inflammation: Exactly how glucocorticoids (either those produced naturally or given as a medication) reduce inflammation is not exactly understood at this time. It is believed that they stabilize individual cells and their internal structures so that they do not release the substances which initiate or perpetuate the irritation, pain, and swelling referred to as inflammation. Glucocorticoids probably also inhibit those substances already within the affected area. The ability of glucocorticoid steroids to control or suppress inflammation is the most common reason for their use in medicine.

Inflammation which can be treated with glucocorticoids can occur in many systems including:

- Skin: allergies
- Gastrointestinal system: inflammatory bowel disease
- Neurologic system: intervertebral disc disease
- Eye: acute uveitis
- Respiratory: asthma
- Kidney: glomerulonephritis

An example of the inflammatory action of glucocorticoids is in their use in an animal that has ruptured a disc between the vertebrae in its back. The swollen, herniated disc puts pressure on the spinal cord and other nerve fibers in the area. This is painful and the pressure on the spinal cord prevents nerve impulses from passing between the brain and the rear part of the body. The animal may be unable to walk or control its colon or bladder. Severe damage to the spinal cord can lead to total paralysis or death. Although surgery is required in a small portion of these cases to relieve the pressure on the spinal cord, most of these dogs can be successfully treated with rest and steroids. The steroids, and this case it is often dexamethasone, are able to remove the swelling and fluids within the disc and surrounding tissues, thereby removing the pressure from the spinal cord. This allows the nerve fibers within it to function correctly. Given time, the disc shrinks back down and the steroids are slowly discontinued. Remember, the steroids do not 'heal' the disc; they only reduce the swelling while it slowly returns to its normal size and shape.

Suppress the immune system: Glucocorticoids also decrease the body's response to substances, cells, or organisms that are, or are perceived as, potentially harmful or foreign. In a healthy pet, the immune system correctly recognizes disease-causing bacterial, viral, or fungal organisms as foreign invaders. It attacks them with white blood cells and large protein molecules called antibodies. This is totally beneficial to the individual. However, in an animal affected by an autoimmune disease such as lupus, the immune system mistakenly sees parts of its own body as foreign and tries to destroy them. In the example of lupus, the system specifically attacks its own blood cells, kidneys, and joint surfaces. In the absence of medical treatment, this usually leads to the animal's death. In the treatment of lupus, high levels of glucocorticoids eliminate the immune system's ability to see particles as abnormal, or decreases the response against them. This suppression of the immune system can be either beneficial or an unwanted side effect of glucocorticoids, depending on the situation in which they are used.

The most common usage of steroids in the home is to control or decrease an animal's response to allergies. Some allergies will be seasonal, with the problem coming from exposure to pollen, flea bites, or molds. When pets develop an allergy to something they inhale (e.g., pollen), or something that comes in contact with their skin (e.g., flea bite or particular carpet fiber), or something they eat (e.g., beef by-products in their diet), the disease presents itself as a skin disease. Dogs with allergies scratch their sides, chew on their feet, and may have repeated ear infections. The scratching and chewing is brought on by severe itching sensations. The allergy actually causes an inflammatory reaction within the skin in these areas. Rather than being at a single site, the inflammation associated with allergies is often found over large areas of the body.

Allergies are generally treated with corticosteroids using a higher initial 'loading dose' to immediately 'put the fire out.' The client would then be sent home with prednisone or prednisolone tablets to use over the expected duration of the problem. The dosage would be reduced gradually so the animal is slowly weaned off the medication.

Cancer treatment: Some forms of cancer such as lymphosarcoma and mast cell tumors respond to high doses of glucocorticoids, or glucocorticoids combined with other medications.

Side effects and risks of glucocorticoid therapy

The problems or side effects associated with glucocorticoid usage can occur immediately or long after the drugs have been discontinued. It is important that both owners and veterinarians be aware of them so they are quickly recognized. In most cases, much can be done to prevent or correct them.

Increased water consumption and increased urination: are two of the most common side effects of glucocorticoid usage. Although it can be quite disconcerting to the owner of a pet that lives predominately in the home, it is not by itself a serious problem. Glucocorticoids increase the activity of the glomeruli, which are the filtration units of the kidneys. This causes the animal to excrete higher levels of urine. The loss stimulates thirst in an attempt to replace lost fluids. These actions may increase water consumption and urination to the point that the animal can control neither one. Such signs can be observed within hours of initiating steroid therapy if the initial dosages were too high for the individual animal to tolerate. When long-acting injectable forms are used at excessive levels, increased water consumption and urination can continue for several weeks.
Changes in attitude and appetite: Some animals will seem more lethargic or tired while on these medications; others may show increased appetites.

Abortion: If given to an animal during pregnancy, glucocorticoids can cause an abortion. Animals on glucocorticoids may be temporarily infertile until the therapy is discontinued.

Immune suppression: During use, and for a period thereafter, higher doses of glucocorticoids will suppress the immune system to some degree and therefore make the animal more susceptible to viral, bacterial, or fungal diseases. To overcome this problem, antibiotics or other medications are frequently given concurrently with steroid therapy to protect the animal from opportunistic organisms taking advantage of the suppressed immune system.

Changes in protein metabolism: Glucocorticoids will alter the animal’s metabolism of protein and can easily lead to muscular weakness or atrophy. With consistent and long-term use, the signs of this can become quite apparent. The abdominal muscles may weaken, causing the animal to have a sagging or pendulous abdomen. Additional strength can be lost from the legs, causing the animal to have difficulty rising after lying down, climbing steps, or walking long distances.

Pancreatitis: There may be a relationship between the use of glucocorticoids and the development of pancreatitis, however, it has not been proven. Glucocorticoids are not recommended for the treatment of pancreatitis, except if the animal is in shock.

Stomach and intestinal ulcers: Again, there may be a relationship between the use of glucocorticoids, especially dexamethasone, and the development of ulcers in the stomach or intestinal tract. This is especially true if the steroids are given to animals also receiving nonsteroidal anti-inflammatory drugs (NSAIDS) such as carprofen (Rimadyl, Novox), deracoxib (Deramaxx), meloxicam (Metacam), and others.

Changes in liver function: Animals treated with glucocorticoids often have increased liver enzymes. If given excessive glucocorticoids, hepatopathy (a liver disease) may occur.

Cushing’s or Cushing-like disease: Many animals treated with high, continuous levels of glucocorticoids can develop symptoms similar to those in Cushing’s disease: increased thirst and urination, panting, and increased appetite. True Cushing’s disease which is an abnormal response of the adrenal gland to stimulation generally does not occur unless the animal has high and long-term exposure to glucocorticoids.

Diabetes and changes in glucose metabolism: Steroids will also alter glucose metabolism, and their use in a diabetic animal can be disastrous. As excessive glucose is produced, the blood sugar elevates abnormally and the animal’s need for insulin increases dramatically. There appears to be a link between glucocorticoid therapy and the development of diabetes mellitus in dogs.

Changes in calcium utilization: The glucocorticoids also affect calcium utilization in the body. Not only do they cause less calcium to be absorbed through the intestinal wall, but they also cause the kidneys to excrete excessive calcium through the urine. Combined, they cause the body to steal from its own major storage site of calcium, the bones. As it selectively removes calcium from the bones for use in other areas, the bones become weaker and could be more prone to fracture. Although the biochemical pathways in which this can occur are easy to understand, bone problems associated with steroid usage in pets are very, very rare.

Shutdown of the adrenal glands: The most serious and life-threatening side effect of steroid therapy is not always so easy to recognize initially. After use in discontinued, or during prolonged use, steroids can have severe effects on the adrenal glands. The brain and the pituitary gland routinely monitor the levels of the mineralocorticoids and glucocorticoids within the body. When their concentrations are low, they signal the adrenal glands to produce more, or vice versa.

This system can be fooled by long term administration of glucocorticoids, confusing the synthetic products with those naturally produced by its own adrenal glands. In the presence of higher than normal levels of these compounds, it senses no need for further production and may turn off the adrenal glands completely.

Unfortunately, when the medications are later discontinued, the glands are unable to immediately re-initiate normal levels of production. This leaves the body totally without or with greatly reduced concentrations of its own natural regulating steroids. This condition causes the same symptoms as Addison’s disease, but in almost all cases is reversible with time.

We must stress that by monitoring the dosage and response of the animal, many of these effects of glucocorticoid usage are usually easily prevented and the desired beneficial results obtained. Most of these problems, with the exception of induced abortion, are easy to recognize and quickly reversed when steroid usage is decreased or discontinued.

The above list of potential side effects may frighten the average pet owner. They are, however, the exception. The vast majority of all cases in which steroids are used correctly provide great benefit to the pet without any serious side effects occurring. When serious problems do occur, it is usually in cases in which steroids were administered over very long periods of time or at excessive doses. Large single doses or short-term use at normal levels rarely, if ever, causes a serious problem unless there is some pre-existing condition such as diabetes, pregnancy, or heart disease.

Common Steroids in Medications for Pets

Every veterinary clinic has numerous steroid medications, including injectable solutions, tablets, and topical preparations such as creams, ointment, or skin preparations. They may be single formulas or mixed with other medications. Their most common use is to control or eliminate inflammation. Among other things, they are also used to treat shock and, in the case of autoimmune diseases, they are prescribed to suppress immune systems that are out of control.
Although other compounds could be listed, over 98 percent of all steroids used in pets are either hydrocortisone, prednisone, prednisolone, triamcinolone (Vetalog), methylprednisolone (Depo-Medrol and Medrol), dexamethasone (Azium), or betamethasone (Betasone). We can easily classify the different medications by their strength and time of effectiveness in the body. Many texts use the naturally occurring cortisol as a standard. You can calculate the amount of glucocorticoid activity as being directly proportional to anti-inflammatory effects. That is to say, the higher the glucocorticoid activity, the greater its effect will be on suppressing inflammation and vice versa. Using this method, hydrocortisone has basically the same glucocorticoid or anti-inflammatory strength as the natural cortisol. It is the weakest of the commonly used steroids. Prednisone and prednisolone are both three to four times stronger in their anti-inflammatory effects as cortisol. They have been used for decades and their action is often easier to predict than some of the stronger preparations. Methylprednisolone and triamcinolone are newer synthetics with about five to seven times the strength of cortisol in their glucocorticoid effects. Dexamethasone and betamethasone are the powerhouses of steroids. They are thirty to thirty-five times more powerful than cortisol in their effect on inflammation.

As to the length of activity after a single injection, the relative glucocorticoid strength parallels the duration of action within the body. Cortisol and hydrocortisone only last for twelve hours or less. Oral prednisone, prednisolone, triamcinolone, and methylprednisolone last for twelve to thirty-six hours, while dexamethasone and betamethasone show activity for over forty-eight hours. Injectable forms of the glucocorticoids can vary widely in their duration of action.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Potency</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Hydrocortisone</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Oral Prednisone or prednisolone</td>
<td>4</td>
<td>12-36 hours</td>
</tr>
<tr>
<td>Oral Methylprednisolone</td>
<td>5</td>
<td>12-36 hours</td>
</tr>
<tr>
<td>Oral Triamcinolone</td>
<td>5</td>
<td>12-48 hours</td>
</tr>
<tr>
<td>Oral Dexamethasone</td>
<td>30</td>
<td>&gt; 48 hours</td>
</tr>
<tr>
<td>Oral Betamethasone</td>
<td>35</td>
<td>&gt; 48 hours</td>
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<tr>
<td>Injectable Methylprednisolone</td>
<td>5</td>
<td>3-5 weeks</td>
</tr>
<tr>
<td>Injectable Triamcinolone</td>
<td>5</td>
<td>1-2 weeks</td>
</tr>
<tr>
<td>Injectable Dexamethasone</td>
<td>30</td>
<td>2-4 weeks</td>
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Most veterinarians today prefer not to use the long-acting injectable products like triamcinolone (Vetalog) or the methylprednisolone product Depo-Medrol. They are usually fine for a single injection but their repeated use in the same animal can cause suppression of the hypophysial section of the brain and pituitary gland and other side effects. When long-term therapy is being considered, it is much better and easier to use oral forms like the short-acting prednisone or prednisolone tablets on an every-other-day schedule. With tablets, the dosage can be quickly changed at any time. With long-acting injections, nothing can be done to alter the effect once the product is in the animal’s body.

Topical treatments are also very common in veterinary medicine. Many of the topical preparations contain steroids for two purposes. Not only do they help reduce the inflammation present but they also quickly eliminate pain and itching. If we can get the animal to leave the affected tissue alone, it will usually heal much quicker. In many cases, the self-inflicted damage done by the pet is greater than that done by the inflammation. Most medications for ear infections or skin sores utilize steroids for these reasons. Many will contain hydrocortisone, which is rarely used except in topical preparations. Many are produced in combination with antibacterial or antifungal medications. Examples of these would be Panolog, Tresaderm, and Otomax. Topical glucocorticoids are absorbed through the skin and cause the same side effects as steroids given orally or by injection.
Dosage

From the veterinarian's point of view, an additional problem with steroid therapy is that none of the products or the disease syndromes treated have exact dosages. It varies with each condition and each animal. As with an anesthetic agent, the goal is to use only the minimum amount necessary to produce the desired effect. Two animals weighing exactly the same and having the same disorder may require very different dosages of steroids to control the condition and/or prevent side effects. Veterinarians are constantly doing a balancing act between these two extremes of steroid usage. When an animal is sent home under the observation of the owner, frequent communication with the veterinarian is necessary to describe how the disease is responding and how the animal is dealing with the medication. One of the first problems that owners will see at home will be excessive water consumption and urination. If side effects occur, then the dosage needs to be lowered, a different medication used, or possibly all steroids usage discontinued.

Additionally, the dosage for steroids usually changes with each animal over time. The animal is usually started at a high or 'loading' dose for a few days, and is then dropped to a long term maintenance level. Finally, a reduced dosage is utilized that slowly weans the animal's body off the medication. During the maintenance stage, it is preferred to use oral medications and give them only every other day in the morning. This also reduces the chance of suppressing the hypophyseal/pituitary gland feedback system on the adrenal glands.

By gradually decreasing the level of steroids at the end of the treatment, veterinarians greatly reduce or eliminate potential problems with the adrenal glands being unable to function normally as described above.

Summary

The glucocorticoids can be a veterinarian's and pet's best friend when the latter suffers from some form of inflammation or autoimmune disease, or is in shock or diagnosed with certain types of cancer. They can also be an enemy if abused. Glucocorticoids can be abused just like any other medication with doses that are too high, last for too long, or are used in situations where they will do more harm than good. They are sometimes used without a diagnosis, hoping that their euphoric effects will make the animal feel better for a few days. By then, whatever was bothering the animal will have passed and the case will be classified as a successful cure. With rare exceptions, steroids should only be used when the diagnosis is known and their effects on the case understood.

In most instances, the beneficial actions of glucocorticoids only suppress the harmful effects of the disorders (e.g., allergies) while they are being used. As soon as these medications are withdrawn, the problem may reappear. They can, in some cases, suppress the body’s actions long enough for tissues to heal correctly on their own, but the steroids play no part in the actual repair, and in some cases can actually delay healing.