Treating Unrecognized Cortisol-Based Imbalances Offers Major Healing Benefits for Multiple Disorders

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Summary

During more than three decades of clinical practice involving many thousands of cases, I have repeatedly identified an unrecognized endocrine-immune disturbance as a major trigger of multiple problems in canines and felines, including allergies, viral and other infectious diseases, vaccination failures, inflammatory bowel, autoimmunity, and cancer. In most cases, and for seemingly unrelated conditions, I have restored health by correcting this disturbance with the same hormone replacement program. The basis of the disturbance is genetic or acquired impairment of cortisol. A domino effect ensues, disrupting the hypothalamus-pituitary-adrenal axis. Hormones go awry. Estrogen, from an apparent conversion of adrenal androgens, is overproduced. Thyroid hormones are blocked. Immune function is compromised. I consistently see this scenario in sick patients, including EVERY cancer patient I treat.

The nature of cortisol imbalances

The typical pattern of imbalance involves low/excessively bound/defective cortisol, elevated total estrogen, impaired thyroid function, and low IgA, IgG, and IgM levels.

Cortisol, a steroid hormone, is produced from cholesterol through an enzymatic process in the middle layer of the adrenal cortex, the zona fasciculata. Hormones secreted by the hypothalamus and pituitary in the brain govern this activity.

Cortisol exerts an anti-inflammatory effect, a property that inspired the development of clinically important cortisone (synthetic cortisol) drugs more than fifty years ago. Much has been written about the immunosuppressive properties of elevated cortisol and powerful cortisone drugs, but little attention given to its role as a central regulating agent of the immune system. A normal level of cortisol appears necessary for proper immune and inflammatory responses (see Fig. 1). At a basal, physiologic level this hormone regulates molecular mediators that turn on or turn off activity related to immunity and inflammation (1). A deficiency leads to an unresponsive or destabilized immune system, and increased vulnerability to stresses and infections (2).

From an endocrine standpoint, a lack of active cortisol disturbs the hypothalamus-pituitary-adrenal feedback loop that governs cortisol production. To increase a subnormal cortisol level, the pituitary steps up adrenocorticotropic hormone (ACTH) secretion. This hormone stimulates cortisol release.

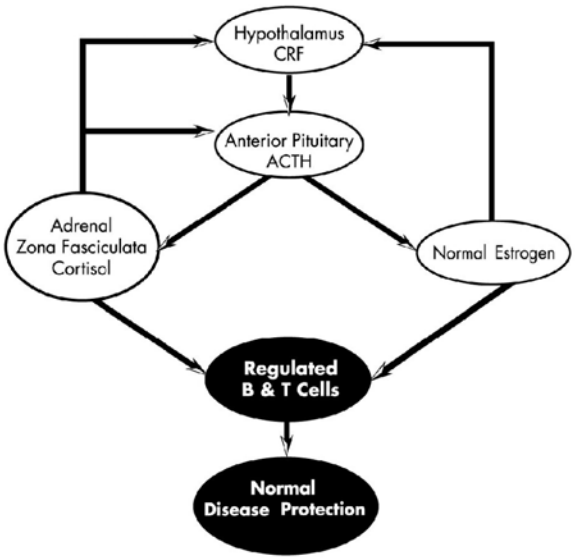

Figure 1. Normal cortisol regulates immune system, promoting disease protection.

However, when the adrenal cortex is unable to produce enough cortisol, or for some reason the cortisol is excessively bound or otherwise inactive, and thus not recognized by the system, the pituitary continues to produce ACTH in order to extract more cortisol.

One consistent consequence of this activity I have observed over the years is a physiologically significant buildup of estrogen compounds that have a further destabilizing effect. I have not seen this phenomenon reported elsewhere. The increased estrogen may come from ACTH-stimulated androgens, produced in the inner layer of the adrenal cortex (zona reticularis), which convert in part to estrogens in peripheral tissue (3) or from "interface" cortical tissue directly secreting estrogen compounds (4, 5). I routinely measure elevated total estrogen in all animals with the endocrine-immune disturbance—male and female, intact or neutered—and thus the excess cannot be attributed to ovarian activity. It is possible, however, that environmental

estrogenic compounds in industrial chemicals and in food (such as soybeans) may contribute to increased estrogen as well.

Elevated estrogen disturbs the immune system in a number of ways, including interference with the thymus gland (6), and has been implicated in the initiation of autoimmune disorders (7). Moreover, too much estrogen in the system may impair the synthesis of cortisol (8) as well as bind active cortisol, thus further exacerbating a cortisol abnormality. It is interesting to note that researchers have discovered that phytoestrogens (estrogen compounds) in tofu and soy-based food decrease cortisol production and increase androgens, some of which convert to estrogen and raise the total estrogen level in the body (9).

When considered together, these factors add up to a vicious cycle of cortisol-estrogen interactions.

Medical science regards the hypothalamic-pituitary-adrenal axis, which is part of the neuroendocrine system, as exerting a primary influence on immune function (10). However, researchers are still in the dark about many of the countless details and interactions. My clinical impression over the years has been that cortisol and estrogen have an intimate relationship that affects the homeostasis of the neuroendocrine system. If the relationship becomes disturbed, as it obviously has in so many of the animals I test and treat, the immune system becomes deregulated and disease protection is lost (Fig 2).

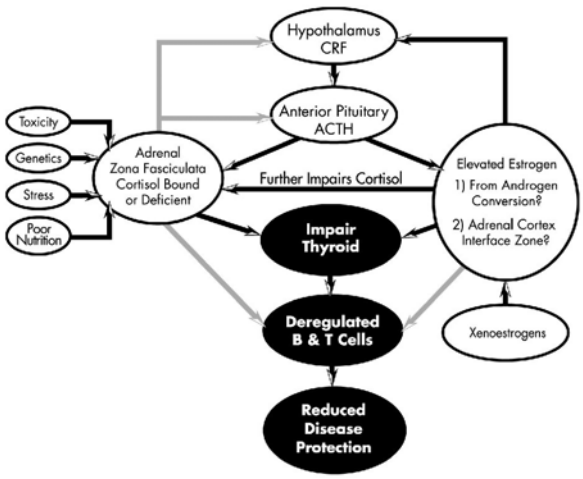

Figure 2. A deficit in active cortisol from a variety of causes stimulates estrogen production, impairs thyroid function, destabilizes the immune system, and undermines disease protection mechanisms.

The combination of deficient cortisol and excess estrogen not only destabilizes the immune system but also has considerable potential to interfere with thyroid function and cause a slowdown of the metabolic rate. Cortisol-estrogen imbalances can impact thyroid function by binding thyroid hormones, decreasing conversion of T4 to T3, and impairing cellular uptake of T3 (11, 12, 13).

In the common endocrine-immune derangement I have identified, there appears to be no discernible involvement of the outer adrenal cortical layer (zona glomerulosa), where aldosterone is manufactured. This hormone helps maintain blood pressure and sodium/water balance in the body.

Causes of cortisol-based imbalances

From my perspective, several primary factors appear to cause the cortisol deficit:

Genetics

For decades, pets have been inbred to attain fashionable structural and cosmetic effects. Many animals, and in particular dogs, are no longer bred for hardiness, function, and work, such as hunting, herding, tracking, and retrieving. This has caused a harmful narrowing of gene pools along with major health problems.

Most popular dog breeds have been bred "almost exclusively to look good," *Time* reported in a 1994 cover article, and this "obsessive focus on show-ring looks is crippling, sometimes fatally, America's purebred dogs" (14). *Time* noted that that there are more than 300 different genetic disorders that may subject animals to enormous pain and suffering. "The astonishing thing," the magazine article reports, "is that despite the scope of these diseases, veterinary researchers know next to nothing about what causes them or how to cure them."

The cortisol-based endocrine-immune mechanism I have identified may be largely the result of such breeding practices. However, this and other genetic problems are not limited to purebreds. Mating between animals of different breeds has thoroughly spread genetic defects throughout the dog and cat world, and today such defects are widely established among all breeds—pure or mixed.

Toxicity

Household pets may be intimately exposed to many toxic compounds, including lawn and garden chemicals, rat poison, insect and snake bites, anti-flea chemicals and other pesticides, anesthetic agents, cleaning and disinfecting solutions, building and decorating materials, and a multitude of chemical additives contained in highly processed commercial diets. Sensitive animals may develop a variety of mild to severe symptoms immediately

following exposure, but less appreciated is the potential to damage the adrenal glands, which I have seen occur in many pets.

The adrenals are recognized as the most toxin-vulnerable organ in the endocrine system. The majority of toxic damage has been observed in the cortex, where steroidal hormones, including cortisol, are produced. Indeed, the entire process of adrenal steroidogenesis "poses multiple molecular targets" for disruption (15) and such disturbances can fundamentally affect the whole body physiology and biochemistry (16).

Stress

Mounting evidence in the field of human stress research indicates that hypocortisolism is present in healthy individuals living under chronic stress as well as in patients with stress-related bodily disorders. This new evidence is challenging the widely held belief that stress always results in an increased secretion of cortisol. A persistent lack of cortisol may in fact be a frequent and widespread phenomenon, researchers now say, promoting a greater risk for immune-related disorders and other diseases (17).

Pets are subject to stress just as are humans. I have traced many cases of endocrine-immune imbalances to household upheaval related to divorce, transfer of ownership, constant hassling by children, the addition of a new or incompatible animal in the house, boarding in kennels, and even to excess exercise.

Poor nutrition

A poor quality diet fed over a long period of time contributes to systemic deficits, including lack of proper nutrition to endocrine organs producing hormones. Moreover, the complex nature of processed pet foods may not allow for the adequate absorption of essential nutrients. Digestive enzyme deficiencies are commonplace, particularly in aging animals.

Testing and treatment of imbalances

In the early 1970s I first developed my testing and treatment protocols for cortisol-based imbalances and reported my observations in the veterinary literature (18, 19, 20, 21). A key element in this approach is a blood test that identifies specific imbalances, namely cortisol, total estrogen, T3/T4 levels, and IgA, IgG, and IgM. Table 1 shows the testing values I consider normal.

Originally I also tested for T cell function. Testing showed that T cells, just as B cells and their production of antibodies, were weakened by hormonal imbalances. However, due to the expense of T cell testing to clients, this additional diagnostic procedure was discontinued.

In my analysis of test results, I place no great emphasis on the serum cortisol value by itself because it does not clearly indicate how much of the circulating cortisol is active, bound, or somehow defective, and how much is actually working. I base my therapy decisions on assessing and comparing the other hormonal and antibody measurements in the test. Animals with a cortisol defect typically have elevated estrogen and low antibody levels, even if their cortisol reading is normal.

Standard tests usually measure only one estrogen compound: estradiol. However, I test for total estrogen, which may include endogenous compounds (estradiol, estrone, and estriol) from ovarian and adrenal activity as well as estrogens from environmental and food sources (such as soy). This provides a more accurate measurement for a potential major disrupter of cortisol and thyroid activity. In animals, I have found that even a slight upward variation of total estrogen out of the normal range can be problematic.

The endocrine-immune test is based on a simple blood draw that is spun down in a serum separator tube and refrigerated. It is shipped cold and refrigerated at the lab until testing. If blood is not kept cold, hormone and antibody results tend to be excessively and erroneously high. Correct handling of the blood sample is critical.

The imbalances and their associated medical effects are typically corrected with the long-term use of very low-dosage cortisone preparations that serve as a cortisol replacement (Fig. 3). I use only enough

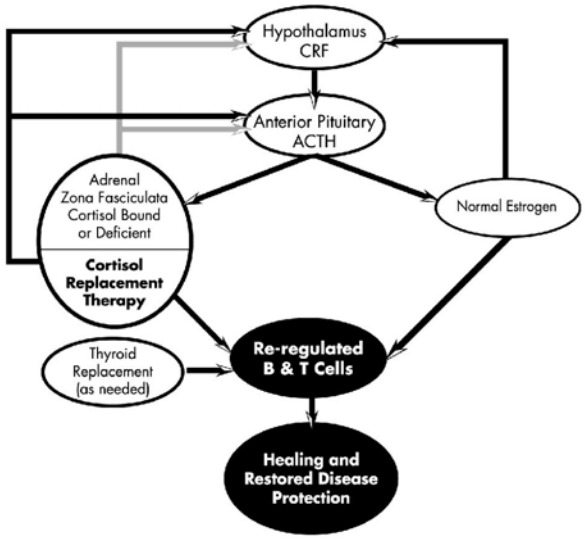

Figure 3. Cortisol replacement therapy (along with T4 medication in dogs) promotes healing and restores disturbed immune function.

steroid replacement to eliminate the imbalances, and this in turn usually resolves the medical effects. Depending on the individual case, I use either pharmaceutical cortisone medications or a bio-identical "natural" plant-based hydrocortisone obtained from a compounding pharmacy. Starting daily oral dosages are as follows: Medrol (methylprednisolone) or Prednisolone, 1 mg per 10 pounds of body weight, or Vetalog (triamcinolone acetonide), 125 mg per 10 pounds; hydrocortisone, available through compounding pharmacies, 1/2-mg per 1 pound of body weight.

Most dogs, but very few cats, also require a T4 thyroid prescription, such as Soloxine (levothyroxine sodium) at .10 mg per 10 pounds of body weight twice daily. Thyroid supplementation serves a dual purpose: to overcome any resistant thyroid impairment or binding effect due to endogenous cortisol-estrogen imbalances, and to guarantee proper metabolizing/breakdown of the cortisol replacement medication within twenty-four hours. I have found that with dogs, but not with cats, even very low physiological dosages of steroid replacement have the potential in some cases to build up in the body and cause side effects unless T4 is taken as a daily accompaniment. Most cats do not require the extra thyroid. The exceptions are cases involving FIP or frank hypothyroidism.

Special attention must be given to the IgA level. IgA is the most abundant antibody and is especially important in mucosal immunity. It is an essential protective factor against infectious agents, allergens and foreign proteins that enter the body via the mouth, nose and upper respiratory tracts, the intestines, and reproductive tract (22). In humans, IgA deficiency is recognized as the most frequent immunodeficiency (23).

Clinical experience has taught me that IgA levels well below 60 mg/dl reflect dysfunction in the intestinal mucosa. By this I mean probable inflammation and malabsorption, including an inability to absorb medication. Low IgA is often the overlooked basis for inflammatory bowel disease. Animals with chronic bowel disorders (including food allergies), respiratory and urinary tract disorders, and anaphylactic and vaccine reactions invariably have abnormal IgA levels.

When IgA is moderately or substantially low I do not take a chance with oral medication, and certainly not for critical patients with an advanced, life-threatening disease. To ensure proper delivery of medication, I use intravenous drips or an intramuscular injection. My formula for IM injections is Vetalog (1 mg per 10 pounds of body weight) in combination with Depomedrol (methylprednisolone acetate, 1 mg per 1 pound of body weight). In very critical cases I often double the quantity of both compounds. The former medication is an immediate-acting steroid, the latter a long-acting steroid that becomes active after five to seven days. Once the IgA level returns to near normal or normal, I switch patients to an oral steroid. However, some patients who have had prolonged intestinal dysfunction because of low IgA may require monthly IM injections on a long-term basis.

Two weeks after therapy begins (or three weeks, if using IM initially) I retest to see how values have shifted. I adjust the program accordingly. Once values normalize and clinical signs abate, I retest on a six-month or annual basis.

Table 1: Normal endocrine-immune serum values for dogs and cats

Cortisol	Total Estrogen	T3	T4	IgA	IgG	IgM
mcg/dl	pg/ml	ng/dl	mcg/dl	mg/dl	mg/dl	mg/dl
1.0-2.5	30-35 female* 20-25 male	100-200	2.0-4.5	70-170	1000-2000	100-200

*Spayed and out-of-estrus females.

Discussion

About two years ago I learned about the work of William Jefferies, M.D., professor emeritus of internal medicine at the University of Virginia. For decades, Jefferies has championed the use of long-term physiologic dosages of cortisone in human patients with "adrenocortical deficiency," that is, a mild deficiency of cortisol. Among other conditions, he has reported significant improvement of allergies, autoimmune disorders, and chronic fatigue, and he also suggests potential benefits of this approach as part of a comprehensive cancer treatment program. In his book, *Safe Uses of Cortisol*, he notes that the persistent application of physiologic dosages of appropriate steroids "might help patients with any type of malignancy by improving their resistance to cancer" (24). In my experience, Jefferies' suggestion is understated. In animals, I have found that cortisol replacement therapy actually represents a primary healing modality, even in advanced cancer cases. (25).

Defective/bound/deficient cortisol is grossly underdiagnosed in veterinary medicine and appears to be so as well in human medicine (26). Moreover, many doctors fear long-term cortisone usage at any dosage because of the drug's well-known side effects and its immunosuppressant properties. This stigma has created a "unique situation in which a normal hormone, one that is essential for life, has developed such a bad reputation that many physicians and

patients are afraid to use it under any circumstances," says Jefferies (27).

As Jefferies points out, it is not generally recognized that the dangerous side effects of steroid therapy "occur only with certain dosages and not with others. That there is a tremendous difference between the effects of small 'physiologic' dosages and those of larger 'pharmacologic' dosages has not been emphasized" (28).

In recent years, a variety of successful applications of low-dosage cortisone has been reported in the medical literature. They include rheumatoid arthritis (29), polymyalgia rheumatica, a systematic inflammatory disorder of the aged (30), and sepsis (31). Recognition of the safety and benefits of long-term, low-dosage cortisone therapy thus appears on the increase. Hopefully, in the process it will bring attention to the centrality of cortisol's immune regulating role.

Both Jefferies, in humans, and I, in animals, have found that replacement with physiologic dosages of cortisone should not be stopped upon initial remission of symptoms and signs. When medication is stopped, the medical effects return. This is long-term therapy, usually for a lifetime.

The method I have briefly described in this paper introduces a potentially major healing tool for many of the most challenging conditions confronted by veterinarians. The treatment funds a deficit, realigns a hormonal derangement, resets the metabolism, and restores coherence to an incoherent immune system. It controls disease and supports the health of patients for as long as the program is maintained. It can often save animals who might otherwise be destined for euthanasia. Among other conditions, I have found this approach effective for the following: chronic allergies; malabsorption and digestive tract disorders; respiratory and urinary tract disorders, including FLUTD; bacterial, fungal and viral infections, including parvo, FeLV, FIP, and FIV; vaccination failures and complications; autoimmunity; obesity; chronic kidney and liver diseases; Von Willebrand's Disease; epilepsy; aggression and other behavioral problems; and cancer.

This approach can also be applied preventively to determine the presence of imbalances in outwardly healthy animals. Used thusly it can help avoid future suffering and premature death brought about by an unsuspected adrenal defect with systemic repercussions.

Based on my experience with animals, and other veterinarians who use it in their clinics, and the work of Jefferies and other researchers in human medicine, I strongly believe that addressing cortisol-based endocrine-immune imbalances offers significantly promising solutions for disease prevention and control—for both people and pets.

Dr. Plechner welcomes inquiries about his method from interested veterinarians. He can be contacted at the California Animal Hospital, 1736 S. Sepulveda Blvd., Los Angeles CA 90025. Phone: 310-473-0969. E-mail: drplechner@hotmail.com. Web site: www.drplechner.com. His newest book, **Pets at Risk: From Allergies to Cancer, Remedies for an Unsuspected Epidemic,** *was published in 2003 by NewSage Press (**www.newsagepress.com**).*

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