

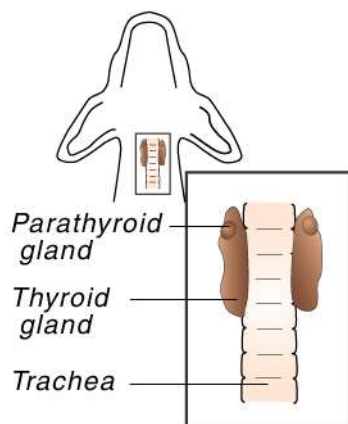
Hypothyroidism in Dogs

Hypothyroidism is the most common hormone imbalance of dogs. It seems like it would be a straight forward problem: the body does not produce enough thyroid hormone, problems result, tests show thyroid hormone levels are low, the hormone replaced given in pill form, problem solved. Unfortunately, it is not always quite so straightforward in real life. This article attempts to review the issues relevant to this condition and the pitfalls that keep it from being a simple problem.



WHAT IS THE THYROID GLAND AND WHAT DOES IT DO?

The thyroid gland is a gland in the throat and upper neck, near the windpipe. It produces two forms of thyroid hormone: T3 is the active form of the hormone, and T4 (also called thyroxine) is the inactive form created to circulate in the bloodstream. When T4 is absorbed from the bloodstream and into tissue cells, it is converted into T3. Most of the circulating T4 is carried by blood proteins and is not available for tissue absorption; the portion that is not carried by proteins (the so-called "free T4") is the portion that is able to enter tissues for activation.



Production of T4 is regulated by the pituitary gland at the base of the brain (this gland is called the "master gland" as it regulates hormone production in the adrenal system, the thyroid system, the reproductive system and more). The pituitary produces a substance called TSH, which stands for thyroid stimulating hormone. When T4 levels are dropping in the normal dog, the pituitary gland produces TSH which in turn stimulates the thyroid gland to make and release more T4, which is converted to T3 when it gets to the tissues.

Active thyroid hormone serves as a sort of a volume dial for metabolism. Since virtually every cell in the body can be affected by reduced levels of thyroid hormone it is not surprising that reduced levels of thyroid hormone lead to symptoms in multiple body systems.

WHAT IS HYPOTHYROIDISM?

If the thyroid is overactive (*hyperthyroidism*), the body's metabolism is elevated. If it is underactive (*hypothyroidism*), the metabolism slows down. In short, hypothyroidism is the deficiency of thyroid hormone. This deficiency is usually produced by destruction of the thyroid gland by the immune system, by natural atrophy of the gland, by dietary iodine deficiency, or as a birth defect. In the dog, the first two causes listed account for almost all cases.

Hypothyroidism generally develops in middle aged or elderly dogs. Breeds with definite predisposition to develop hypothyroidism include: Doberman pinscher, Golden retriever, Irish Setter, Great Dane, Dachshund, Cocker Spaniel, Miniature Schnauzer, Old English Sheepdog, Shetland Sheepdogs (Shelties) and Boxer. Hypothyroidism in cats is extremely rare.

WHAT CAUSES HYPOTHYROIDISM?

Hypothyroidism is usually caused by one of two diseases: *lymphocytic thyroiditis* or *idiopathic thyroid gland atrophy*. The former disease is the most common cause of hypothyroidism and is thought to be an immune-mediated disease. This means that the immune system decides that the thyroid is abnormal or

foreign and attacks it. It is unclear why this occurs. In idiopathic thyroid gland atrophy normal thyroid tissue is replaced by fat tissue. This condition is also poorly understood. In fact "idiopathic" means "of unknown cause." These two causes of hypothyroidism account for more than 95% of the cases in dogs. The other five percent are due to rare diseases, including cancer of the thyroid gland.

MANIFESTATIONS OF HYPOTHYROIDISM

Hypothyroidism has a typical collection of symptoms, which most commonly affects middle aged to older dogs. When the metabolic rate slows down, virtually every organ in the body is affected. The most common problems are those associated with the skin. But there are many other problems that can possibly be caused by low thyroid hormone levels, especially if they are severely low, or if the problem goes untreated for long periods of time. Your hypothyroid pet may have any combination of the problems listed and explained below.



One particularly well published survey of 162 confirmed hypothyroid dogs showed the following common findings:

- 88% had some kind of skin abnormality
- 40% had hair loss and sometimes darkened skin (often this starts on the tail leading to a "rat tail" appearance, or a bald area around the collar is created)
- 22% had skin infection (often dogs are scaly and smelly due to an excessively oily coat)
- 14% had brittle or dry flaky coats (often the outer hairs break off, leaving a short, softer under coat, classically described as a "puppy-like coat")
- 49% were overweight, and had weight gain without increased appetite
- 48% were described as lethargic or listless at home
- 36% were mildly anemic (had a reduced number of red blood cells due to slowed red blood cell production in the bone marrow)

Hypothyroid dogs also get cold easily, seek out warm places to rest, have flaky skin, are susceptible to ear infections, have high cholesterol and fail to grow hair back normally after clipping.



Skin Problems – Skin problems caused by low thyroid hormone levels are listed above. Fortunately, they usually resolve within weeks to months of starting thyroid hormone replacement treatment. One classical finding in hypothyroid dogs is a thickening of some skin tissues, especially of the face and head. The skin in particular thickens leading to more skin folds and what is classically referred to as a "tragic face" (see photo to the left). This skin thickening is called "myxedema" and can occur in some other tissues as well (such as nerves of the face- see later).

Hormonal Problems – Low thyroid function can make it so that insulin doesn't work properly in dogs that are also diabetic. When a dog has more than one hormonal abnormality (including low thyroid function, diabetes, and low adrenal gland function), the medical term for the syndrome is "polyendocrine syndrome." "Poly" means many, and "endocrine" means hormonal systems, so the term means Disease of many hormone systems. When a diabetic dog is started on thyroid replacement, be sure to watch carefully for signs of low blood sugar, because sometimes insulin requirements will decrease (maybe drastically) once thyroid hormone levels are brought back to normal. If your dog has two of the three problems listed in the polyendocrine syndrome, keep an eye out for the other one. Here are some things to look for:

- Diabetes – increased water drinking, increase urination, weight loss, cataracts, low energy, etc.
- Low adrenal gland activity (hypoadrenocorticism or Addison's Disease) – vomiting, diarrhea (especially with blood), weakness, poor appetite, collapse, etc.
- Fertility problems – lack of heat cycles, infertility and abortion in females. Reluctance to breed and failure to breed successfully in males.

Heart Problems - Hypothyroidism can interfere with the electrical fibers that more or less provide the wiring for the heart, as the rhythmic contractions of heart muscle are normally stimulated by these electrochemical fibers. Abnormal rhythms or slow heart rate occur in as many as 26% of hypothyroid dogs; still, the significance of this in terms of overall lifestyle is not clear. Many specialists feel thyroid supplementation should be started at a lower dose for many patients with obvious heart disease, and then increased gradually, to avoid overtaxing the weak heart. Hypothyroidism has been identified as a cause of a heart disease called Dilated Cardiomyopathy, where the heart becomes enlarged and beats very weakly. Hypothyroidism can also cause a low resting heart rate.

Neurologic Problems - According to surveys of confirmed hypothyroid dogs, only about 2% to 4% have nerve problems. There are several syndromes reported.

- **Polyneuropathy** – “Poly” means many, “neuro” means nerve, and “opathy” means disease, so in medical terms, polyneuropathy means disease of many nerves. In advanced hypothyroidism, nerves may not conduct electrical impulses normally. This may account for some of the general weakness and listlessness seen in hypothyroidism, dragging the toes while walking, or poor coordination. Response to thyroid hormone therapy for this problem is rapid (improvement within the first week of treatment).
- **Focal Neuropathy** – “Focal” means one place, so focal neuropathy means nerve disease in one place. Single nerves can get entrapped as they exit the skull or spinal cord as they (like other tissues) swell with myxedema. Pressure on these nerves can lead to paralysis of the facial muscles and/or head tilt, bizarre eye motions and balance disruption (vestibular disease). When there is facial nerve paralysis, the face will be asymmetrical and droopy on one side, as in the photo to the right. This dog's face droops on the right side (left side of the photo).
- **Brain and Spinal Cord Problems (Central Nervous System)** – hypothyroidism may cause abnormal electrical conduction within nerves in the brain and spinal cord; however, disease of the blood vessels has been found in hypothyroid dogs with central nervous system signs. Clinical signs have involved drunken gait (ataxia), weakness in front and back legs on the same side of the body (hemiparesis), exaggerated steps (hypermetria), head tilt, circling and abnormalities in the nerves of the head. It may take several months of therapy to see a response when these problems exist. Changes in behavior, aggression and even seizures can occasionally result in severely affected dogs. Coma from myxedema in the brain's tissues is a rare possibility but has been known to occur in very severe cases.



Eye Problems (Ocular Problems)- Ocular changes are not common in hypothyroidism but the high levels of blood cholesterol and circulating fat can sometimes lead to eye changes. When these changes are seen, often thyroid testing is recommended. Corneal dystrophy, an abnormal change in the clear covering of the eye, is such an eye sign. This finding is usually represented as a small white spot (sometimes a white circle) on the eye surface (see photo on the left). At this degree it is only a cosmetic problem and does not interfere with vision. In more severe

forms, painful bubbles can erupt on the corneal surface leading to ulceration. Obviously, this more severe form would require treatment.

Hypothyroidism can also cause dryness in the eyes called “keratoconjunctivitis sicca” (KCS), that may need to be treated even after the thyroid hormone levels are returned to normal. Dry eyes will appear dull, may collect more matter than usual, and are often red and irritated. If left untreated, dry eyes can become blackened causing blindness, and are susceptible to ulcers which fail to heal well. In the most severe cases, long term ulcers left untreated can result in rupture of the eye and blindness. The photo at the right shows an eye severely affected by KCS. Dry eye is diagnosed by doing a Schirmer Tear Test.



Other Conditions suspected or proven to be associated with hypothyroidism:

- Enlarged esophagus (megaesophagus) – causes regurgitation of food and fluid, and can result in severe pneumonia.
- Paralysis of the muscles in the voice box (laryngeal paralysis) – causes loud noises when breathing (often referred to as “roaring”), or difficulty breathing. Can also result in pneumonia eventually.

VON WILLEBRAND'S DISEASE

For a long time, von Willebrand's disease, a hereditary blood clotting disease, was felt to have an association with hypothyroidism (when a dog borderline for von Willebrand's factor levels became hypothyroid later in life, the abnormal clotting ability would become evident). This theory has largely been abandoned but there does seem to be a positive effect when a von Willebrand's dog is treated with thyroid hormone.

TESTING FOR HYPOTHYROIDISM

Measurement of Total T4: The T4 level (also called the total T4 level) is measured commonly and is included in some routine blood panels. It would seem that a low T4 would indicate hypothyroidism and a normal T4 would indicate normal thyroid function. Unfortunately, it isn't that simple. Dogs on certain drugs (most notably phenobarbital, prednisone or other corticosteroids, or trimethoprim sulfa) or with illnesses other than thyroid disease often have depressed T4 secretion. These dogs will have temporarily low T4's but are not hypothyroid. This means a normal T4 indicates normal thyroid function but a low T4 may or may not indicate hypothyroidism. As well, there are cases where dogs are truly hypothyroid, but have normal T4 levels. One example is when a dog's immune system is destroying the thyroid gland, and there are antibodies to thyroid hormones in the blood stream. The usual test for total T4 (uses the RIA or “radioimmunoassay” method) counts both T4 and antibody for T4, and adds them together. So a dog with T4 antibodies in its bloodstream may have a total T4 result that looks higher than it really is. To rule out this problem, a special test called “free T4 by equilibrium dialysis” is requested.

Free T4 - T4 exists in two forms: the form which is carried around bonded to a blood protein (this is called bound T4) and T4 floating around loose in the bloodstream (called free T4). Only free T4 can enter cells and be converted to T3 and the concentration of free T4 corresponds to thyroid hormone activity where it counts (i.e., at the tissue level). Free T4 levels are less subject to fluctuate into a falsely low range in response to non-thyroidal diseases or drugs than is a total T4 level. Because free T4 levels are typically 1000 times smaller than total T4 levels and tests for free T4 have to work in such a way so as not to convert bound T4 into free T4 and thus interfere with results. At some labs, free T4 by equilibrium dialysis is considerably more expensive than the regular T4 tests.

TSH (Thyroid Stimulating Hormone) - The idea is that if a patient is hypothyroid, the pituitary gland should be secreting high levels of TSH in a futile attempt to stimulate a diseased thyroid gland. Measurement of TSH level is apparently a very important means of diagnosing hypothyroidism in humans and a canine version of the test was long sought. Unfortunately, when it finally became available, it was found that many dogs with true hypothyroidism did not have elevated TSH levels as one would expect; still, this test is often helpful in making the diagnosis of hypothyroidism, when the TSH level happens to be high.

Testing with a Trial of Medication - Sometimes the only way to test for hypothyroidism is to simply administer the medication for several months and see if the problems suspected to be caused by hypothyroidism go away. Often an improvement in attitude and energy level is seen within the first week if the dog was truly hypothyroid. Hair re-growth takes substantially longer (typically 4 months minimum) as the follicles must "reawaken" and then grow a hair long enough to create a visible coat change.

TREATMENT OF HYPOTHYROIDISM

At least treatment of hypothyroidism is relatively straight-forward. Hypothyroidism is treated with oral administration of thyroid hormone (T4). Most hypothyroid dogs are perfectly capable of converting T4 to T3. Pills are given usually twice daily to start but may be dropped to once a day after good thyroid control has been achieved. There are many brands of thyroid supplementation available and prices are somewhat variable depending on the manufacturer. Treatment of hypothyroidism is for life.

Occasionally we are asked if it is reasonable to use dried or powdered thyroid glands of hogs or cattle as a more natural form of treatment. While some people prefer natural therapies, we have to keep in mind that because they are natural, these products are not as consistent in the amount of thyroid hormone they contain. Each brand, lot or even dose may be completely different when using natural products. When using natural products, it is important to buy from a reliable manufacturer, and stick with it. It might take much longer to determine the proper dose, and dosage changes may be needed from time to time. Therapy with prescription thyroid hormone produces much more consistent results.

Re-testing later on. Whenever an animal goes on a medication long term, periodic blood testing is a good idea. In the case of hypothyroidism treatment, it is important to know if the medication dose is too low or too high. Thyroxine (T4) is a very safe medication but if it is not given in adequate doses, obviously the patient will not be adequately treated. If the dose is too high and given for too long a time, excessive water consumption, weight loss, and restlessness can result. T4 is first checked 1-2 months after beginning thyroid supplementation, and then checked once to twice a year thereafter. Ideally, T4 should be checked 4-6 hours after giving the pill.

Monitoring with TSH level. The canine thyroid stimulating hormone level (abbreviated cTSH) does not seem to require any particular timing issues and can be run on a blood sample taken any time of the day. The cTSH level will not indicate whether or not the thyroid dose is too high but is quite accurate at determining if the level is too low (inadequate treatment is associated with high TSH levels indicating that the pituitary gland is vainly trying to stimulate the thyroid gland with high levels of stimulating hormone). This test may be run instead of or in addition to a T4 level when it comes time to monitor thyroid hormone treatment.

IS THE DIAGNOSIS CORRECT?

Because of difficulties in diagnostic testing methods (especially before 1995), many dogs have been erroneously diagnosed with hypothyroidism and have been on medication for years. If there is any question about a patient and one wishes to re-test now that newer testing methodologies are available, thyroid hormone supplementation must be discontinued at least 2 months for blood testing to be valid. If possible, medications known to interfere with testing should be discontinued for testing (though this is obviously not always possible, depending on the medication and the reason for giving it).

WHAT IS THE PROGNOSIS?

Hypothyroidism is easily treatable but not curable. It is treated with oral administration of thyroid replacement hormone. This drug must be given for the rest of the dog's life. Fortunately, it is an inexpensive prescription drug, and it is well tolerated. Ninety-five percent of the time, the prognosis for hypothyroidism is excellent, despite how long it has been going on and how severely affected the dog is. This type of low thyroid function is called *primary hypothyroidism*.

Five percent of the time, the low thyroid function is caused by a dysfunction of the master gland (pituitary) which sends the signal to the thyroid gland to get to work, rather than a failure of the thyroid gland. This kind of hypothyroidism is rare, but can be much more difficult to treat successfully, as other organs are affected by the master gland. In order to diagnose this rare condition, an expensive test called the TSH stimulation test must be performed. This type of low thyroid function is called *secondary hypothyroidism*.

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