

EUROVET

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1



DEZE KEER:

**A dermatological
perspective on
hormonal disorders**

Hypothyroidism

The primary goal of this article is to discuss skin disorders in a number of hormonal abnormalities with alopecia as special indicator in dogs. Diagnosis and therapy will be described briefly, with no pretence to be complete.

Underproduction by the thyroid gland is the most common hormonal disorder in dogs. The animals are generally older than two years of age, and large breeds such as the Golden Retriever, Giant Schnauzer, Doberman Pinscher and Great Dane make up the most significant group. There is no predisposition related to the sex of the animals.

Primary hypothyroidism can be subdivided into lymphocytic thyroiditis and the much more seldom idiopathic thyroid necrosis with atrophy. It is possible that idiopathic necrosis represents the final phase of lymphocytic thyroiditis. This, however, is irrelevant to the medical signs, the diagnosis and the therapy. Secondary hypothyroidism is a rare disorder resulting from the decreased production of TSH (thyroid-stimulating hormone) in the pituitary gland.

Typical for a dog with hypothyroidism is an excessively low metabolic rate. This affects the entire dog. A classic symptom is the dog with symmetric baldness of the trunk. The dog often is lethargic, overweight and the belly line runs horizontally instead of sloping upwards.

The quality of the fur can vary. The hair is brittle and breaks easily at places where friction occurs such as the elbows, neck, underside of the trunk and tail. The only symptom can be a bald bridge of the nose with hyperpigmentation. If the dog is shaved, the hair no longer grows back, or does so very slowly.

Fur discolouration can occur. The normal moult cycle is disrupted, causing the hair to remain longer. Sunlight causes the fur to turn pale, and brown ends obtain a dark red glow.

Disturbed immunity in the skin makes the dog more sensitive to surface pyoderma. The hair follicles and dermal papillae contain receptors for the thyroid hormone, which is why all animals with an underactive thyroid gland will manifest hair disorders. The symptoms can be subtle, such as a thinner hair diameter, or more telogen hair than is normal in a trichogram.

The fatty acid composition in the skin and blood changes. Seborrhoea in the skin can result, as well as in the external auditory canal. The cerumen changes composition and sticks to the ear canal.



Two dogs with hypothyroidism. The Belgian Shepherd Dog evidences focal alopecia with hyperpigmentation and hair loss on the tail. The Airedale Terrier has very thin fur with hyperpigmentation and a continuous, horizontal belly line

The dry or sometimes also oily seborrhoea on the skin can be focal or generalised. The abnormal fatty acid composition predisposes the dog to bacterial or Malassezia dermatitis. In this, decreased quality of the skin barrier in combination with changed local immunity of the B and T lymphocytes plays a role.

This changed immunity recovers after therapy is begun. The infections can cause pruritus, hence it is possible that a dog with a non-itchy hormonal disorder finally suffers from itching.

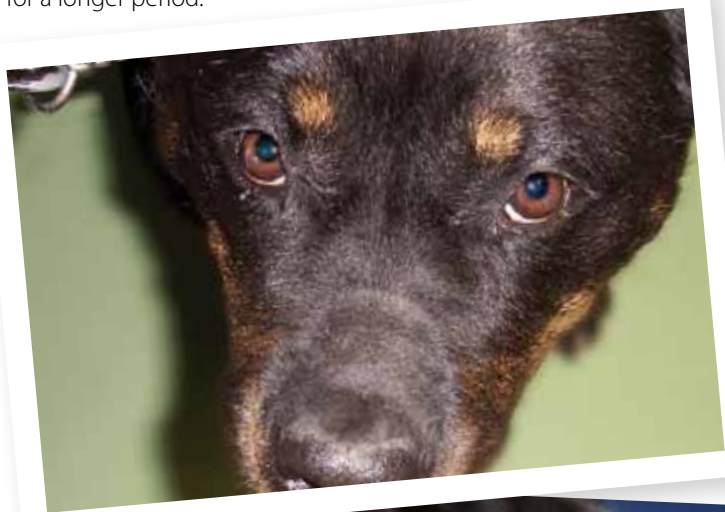
Hyperpigmentation and lichenification of the skin are secondary symptoms that are not specific to this disorder, but rather indicate that the dermatosis has existed for a longer period.

Comedones are a characteristic of seborrhoea and also appear in the case of hyperadrenocorticism and Sertoli cell tumours. The thyroid hormone regulates the production of glycosaminoglycans in the skin.

In the case of an underactive thyroid gland, the hyaluronic acid can build up in the skin, causing myxoedema: the skin thickens and can fall into folds. Heavy eyelids, hanging lips and folds on the forehead cause the familiar sad look.

Other non-dermatological symptoms can include:

lameness, bradycardia and/or heart rhythm disorders, corneal dystrophy, anaemia, decreased fertility and megaesophagus.



A Rottweiler with alopecia of the bridge of the nose.

The dog also suffers from seborrhoea of the ear edges.



Diagnosis

A lowered T4 (here total T4 is intended) together with elevated TSH (thyroid stimulating hormone) levels confirm primary hypothyroidism. TSH is not increased in all cases, in which case one speaks of a 'sick thyroid'. Only the T4 is reduced. Further blood tests are required. Medication such as corticosteroids, phenobarbital and trimethoprim-sulfa can also influence the T4 and/or TSH values. It is then necessary to repeat the T4 test after the dog has taken no medication for a few weeks. The following abnormalities can also be present in the animal's blood: normocytic normochromic non-regenerative anaemia, raised cholesterol and triglyceride levels, increased creatinine, increased CPK (creatinine phosphokinase).

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Therapy

A supplement with a levothyroxine preparation (Forthyron®) according to the indicated dosage almost always yields a good result. It can happen that the animals first lose more hair and even begin to itch just after the therapy is started. Once the thyroid hormone has been replenished, normal metabolism resumes. The hair follicle becomes active and the keratinisation recovers. The keratin plugs loosen. The abnormal epidermis returns to its normal, supple state. The old hair falls out before the new hair appears. It is advisable to inform the owner of this beforehand. The secondary bacterial and Malassezia infections, as well as possible otitis externa, must be treated separately.

The use of an anti-seborrhoea shampoo is advised.

The abnormal behaviour often disappears within 2 to 4 weeks, while the skin takes much longer to return to normal.

If the dog does not respond, a different hormonal disorder might be present, such as hyperadrenocorticism or an oestrogen-producing tumour in the testicle.

Prognosis

The prognosis is good.

Hyperadrenocorticism (Cushing's syndrome)

Raised concentrations of glucocorticosteroids in the body are responsible for the symptoms of this disease. A tumour in the adrenal cortex or continuous stimulation of the adrenal cortex can result in the production of abnormal amounts of this hormone in dogs. Corticosteroids can also be administered as medication. If disorders arise due to this treatment, we speak of iatrogenic Cushing's syndrome, a frequent disorder in older dogs.



Left: Yorkshire Terrier with alopecia, macula and muscle atrophy.

Right: Maltese male. Extensive comedo formation on preputium. Calcosinosis cutis to the left and right of the preputium. The blood vessels are visible due to the thin skin.

The traditional symptoms are symmetric baldness, high levels of drinking and urination, and muscle weakness. Patients exhibit multiple symptoms, internally as well as dermatologically. The disorder can appear more frequently in female than in male animals. Breeds for which spontaneous Cushing's syndrome is frequently observed are the Poodle, Dandie Dinmont Terrier, Boston Terrier, Dachshund and Yorkshire Terrier. In contrast to breeds typically affected by hypothyroidism, these are smaller breeds. It is clear, however, that iatrogenic Cushing's syndrome can occur in all breeds and at all ages. These often are animals with allergic symptoms that have been subjected to long-term treatment with (too high dosages of) corticosteroids.

Dermatological symptoms

The typical dog with cushingoid habitus has bald flanks, little muscle in the head musculature, drooping preputium, with a thick, round belly. In these patients, the skin and adnexa are inactive and atrophic, in contrast to hypothyroidism, where the skin thickens.

In the case of Cushing's syndrome, hair also does not grow, but hyperpigmentation is often lacking. The skin is very thin, and the underlying blood vessels can clearly be seen on the belly.

Conspicuous comedones can be present on the belly and also, for example, in a pinna. The moult is disrupted and hair remains longer, resulting in coloured ends. New hair does not form, finally resulting in baldness. The hair loss is usually symmetric on the trunk, while the hair on the head and extremities is normal. Studies have revealed a regional difference in the hormonal sensitivity of the hormone receptors in hair follicles. They are more sensitive and greater in number at the flanks. This might explain the baldness at the flanks in the case of hormonally induced alopecia. The skin immunity of these patients is disrupted, resulting in possible secondary bacterial infections. The reduced immunity is the reason that pustules become larger than normal. The erythema frequently present around a pustule is often absent in dogs with Cushing's syndrome.

Calcinosis cutis can remain confined to a small patch, but if the condition persists for a longer period, it can expand enormously. For differential diagnosis, consideration must be given to neoplasia, deep pyoderma and a deep fungal infection. A skin biopsy is indicated.

Practical tips for taking a skin biopsy:

The medical history is also very important for the pathologist. A description of the clinical symptoms, a differential diagnosis, the possible treatments begun and a detailed description of the biopsied lesions increase the quality of the pathologist's diagnosis. The inclusion of a photo can be extremely valuable. The skin should not be disinfected prior to the biopsy: mechanical cleaning can remove important information. If multiple lesions are present, a biopsy should be taken of all the different lesions. If an intact pustule is present, a biopsy should be taken of the entire intact pustule. If alopecia is present, a biopsy should be taken not only of the alopecia but also of the transitions to normal skin and a normal piece of skin with hair.

An alternative is the taking of a large, oval-shaped biopsy. The longitudinal direction of the biopsy should run diagonally to the transition from skin with hair to bald skin. A marker pen can be used to indicate the direction of hair growth. Once the locations of the biopsied material have been determined and indicated with a marker pen, the skin is locally anaesthetised with lidocaine with adrenaline. Noses, soles and other locations that do not easily lend themselves to a biopsy, require sedation. After a few minutes, a 4, 6 or 8 mm biopsy tool can be used to take the biopsy by rotating the tool in a single direction.

When the biopsy material comes loose, and the biopsy tool has reached the subcutaneous layer of fat, a small tweezers can be used to grasp the biopsy on the underside at the subcutaneous fat.

Avoid squeezing the biopsy material. Squeeze artefacts can easily occur, and the biopsy material is then unsuitable for a proper evaluation. Use a small scissors to cut away the biopsy material and immediately place it in the pot filled with formalin. If there is blood on the biopsy material, first carefully dab the biopsy material clean on a tampon before placing it in the formalin.

Most laboratories provide the bottles, already filled with formalin, in various sizes. If biopsies are taken of several lesions, consider placing the different biopsy material in separate bottles, so that the pathologist knows which biopsy material comes from which lesion. Then the skin can be closed with a few sutures.



Boston Terrier with extensive calcinosis cutis plaque. The muscle atrophy of the extremities is striking.

Diagnosis

In addition to the typical medical signs of a dog with poor quality fur extending to baldness, hanging belly/preputium and muscle atrophy, the dog will drink and urinate excessively. Overeating is frequently noted. Blood tests will reveal the following abnormalities: slightly elevated liver enzymes and glucose, lymphocytopenia and eosinopenia. In the Netherlands, an abnormal cortisol/creatinine ratio is often used as a first test. This article will not go further into the examination and diagnosis necessary for correct treatment. Calcinosis cutis can be diagnosed using a skin biopsy.

Prognosis

The prognosis is reserved.

Diagnosis

The medical signs are convincing in many cases. An older male with asymmetric testicles, or a swelling palpable in a testicle, or cryptorchidism in combination with the dermatological abnormalities is very suggestive. It becomes more difficult when no abnormalities are palpable. Regarding differential diagnosis, hypothyroidism, hyperadrenocorticism and the much rarer hypogonadism and sex hormone imbalance should be considered. The usual ambiguity exists concerning the latter two disorders. A skin biopsy provides no diagnostic information except that the alopecia has a hormonal cause. Elevated oestrogen levels are by no means always present. An echographic examination of the testicle can make a non-palpable neoplasia visible. A histopathological examination of the neoplastic testicle finally yields the definitive diagnosis.

Therapy

Castration is the only correct therapy. Metastasis is theoretically possible, especially if an enlarged excretory duct of seminal gland or enlarged regional lymph nodes are detected during castration. Clinical restoration of the skin and fur takes three months on average. Aplastic anaemia and thrombocytopenia can be life threatening. It is advisable to examine bone marrow functioning before a surgical intervention.

Seminomas occur frequently in cryptorchid testicles. They seldom produce hormones and in most cases also cause no skin and fur problems. Many testicle tumours consist not of one tumour but of multiple tumours of differing cell types.

Interstitial tumours occur most often in the Boxer. They seldom metastasise, but the Cornell study found indications of malignancy in 12.9% of the cases. If this tumour produces hormones, the clinical symptoms are circumanal gland hyperplasia, tail gland hyperplasia and maculae.

Prognosis

The prognosis is good.

Testicular tumour

Neoplasia in the testicle occurs regularly in older males. Cornell University's College of Veterinary Medicine, USA, studied 1971 testicular tumours: 750 tumours were found to have an interstitial origin, 690 were a seminoma, and 531 a Sertoli cell tumour. Cryptorchid testicles have a ten times greater likelihood of degenerating into a tumour. The Sertoli cell is the tumour that most frequently produces oestrogens, hence symmetric alopecia occurs most frequently with this tumour. In addition to decreased fertility, an elevated oestrogen level can also cause a bone marrow depression.

Dermatological symptoms

The fur can become stiff and brittle, and easily break off. This is also called puppy fur. The hair breaks off as a result of trauma (the area under the dog collar, and the elbows and thighs). Alopecia develops on the flanks due to decreased hair growth rather than due to trauma. This has to do with the above-mentioned changed sensitivity of the sex hormone receptors in the primary hair follicle. The secondary follicles remain, and as a result, puppy-like fur develops.



Shetland Sheepdog with Sertoli cell tumour. The underfur has disappeared. The hair is brittle and has broken off, resulting in alopecia and hyperpigmentation.

The fur changes colour, possibly because the normal hair follicle cycle is disrupted, but also due to the effect of the oestrogens on pigment production and the melanocyte transfer to the hair.

A stripe of pigment can develop at the preputium that extends to the testicle. The cause for the pigment stripe remains unclear, but it is related to an elevated oestrogen level. Maculae can also develop on the belly, anus, perineum and scrotum. Multiple comedones form, which are clearly visible on the thin-haired belly.



Preputium with pigment stripe.

Specific to the Sertoli cell tumour is the feminisation syndrome in addition to the symmetric alopecia. All dogs do not necessarily correspond to this ideal picture, but one third of the animals with a Sertoli cell tumour exhibit both medical signs.

The feminisation syndrome is characterised by (possibly symmetric) alopecia, enlarged nipples, drooping preputium and being attractive to other male dogs.



Labrador with pigment stripe and enlarged nipples.

Alopecia X

The name of the above-mentioned disorder provides a good summary of all the ambiguity concerning the pathogenesis. This condition has also been described in the past as congenital adrenal gland hyperplasia, pseudo-Cushing's syndrome, castration responsive dermatosis, and growth hormone responsive dermatosis. These designations are often based on the clinical symptoms or on the response to a given treatment.

Various parts of the world think differently about the pathogenesis of this disorder. In "Small Animal Dermatology", the author suspects it is related to the growth hormone. Pseudo-Cushing's syndrome and growth hormone responsive dermatosis are mentioned in one sentence. He refers to Rijnberk et al. who in 1993 described in the Veterinary Record the abnormal response of a growth hormone stimulation test. In 1999, Schmeitzel et al. spoke of alopecia X at the AAVD/ACVD congress. She cites the effect of castration and the use of melatonin. Here again the term "lysodren responsive dermatosis" is used. Both male and female dogs can suffer from this condition.

Breeds in which this disorder has been identified include Malamute, Chow Chow, Keeshond, Pomeranian, Samoyed and the Miniature Poodle.

Dermatological symptoms

The classic symptoms consist of symmetric baldness of the trunk without itching. The animals exhibit no other symptoms than the baldness with secondary hyperpigmentation. The baldness usually develops in the neck or on the flanks, and can lead to baldness of the trunk. Secondary infections are seldom seen.



Pomeranian with alopecia X.

Diagnosis

The medical signs with the associated breed are very suggestive for this condition. To exclude the possibility of other hormonal abnormalities, the functioning of the thyroid gland and adrenal gland needs to be examined. Careful testicle palpation can make testicle neoplasia less probable, but never exclude it completely.

The general blood and/or urine test is normal. A skin biopsy exhibits the signs of endocrine alopecia. The so-called "flame follicle" in the skin biopsy is frequently seen by the pathologist in cases of alopecia X.

This is not specific to this disorder, but more specific to the breeds that exhibit alopecia X. Striking is the focal hair growth at the location where the biopsy was taken.

Therapy

As has become clear from the many descriptions of this disorder, in the past there were multiple treatments proposed with a varying results: castration, thyroid gland hormone supplement, melatonin, treatment with trilostane or lysodren and growth hormone.

Cerundulo treated 16 Pomeranians and 8 Poodles with Vetoryl® (trilostane). The underlying idea was that the increased concentrations of 17-hydroxyprogesterone in the blood were a result of abnormal activity of the enzyme 21-hydroxylase. This study also demonstrates that the animals have slightly elevated cortisol production. A mild, breed-related variation of pituitary-dependent Cushing's syndrome is likely. A restoration of hair growth can be expected by decreasing steroid production in the adrenal gland. Hair growth returned in 85% of Pomeranians and in all Poodles. Two Pomeranians died in the follow-up period. It could not be established whether this resulted from the therapy. The question remains why hair growth did not return in all dogs.

Prognosis

The prognosis varies.

Colofon

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