

BALD ISN'T ALWAYS BEAUTIFUL – THINKING OUTSIDE THE BOX PART TWO – NON-INFLAMMATORY ALOPECIA - WHAT'S NEW

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Canine alopecia is a common presenting complaint in veterinary dermatology. Hair loss can be associated with self-trauma (pruritus due to allergies, ectoparasites, behavioural), inflammation of the hair follicle (folliculitis - Demodex, dermatophyte, bacteria), immune-mediated attack of a follicular component (alopecia areata, pemphigus, other immune-mediated) or clinically non-inflammatory, non-pruritic alopecias of the dog. The latter group can be subdivided into several groups:

- a) **Endocrine alopecias** - hyperadrenocorticism; hypothyroidism; sex hormone imbalances (Sertoli's cell tumor, testicular and ovarian neoplasia, cystic ovaries), and pituitary dwarfism.
- b) **Hair cycle arrest** - Alopecia X, post-clipping alopecia, telogen defluxion, nutritional deficiencies.
- c) **Follicular dysplasia** - cyclical flank alopecia, color dilution alopecia, black hair follicular dysplasia.
- d) **Other** - Pattern baldness; sebaceous adenitis, alopecia areata; congenital alopecia, breed specific alopecias, dermatomyositis

Although all alopecias may look alike, they are not alike in many other ways. Subtle historical and dermatologic findings can help distinguish between the various non-inflammatory alopecias.

Table 1. Alopecias Are Not Alike – some clues that help

Loss of telogenized hairs in frictional areas dorsal muzzle, tail, back	HypoT4, Cushing's, sex hormone, Alopecia X
Telogen phase when hair is shaved Vasoconstriction due to cold temp at shaved area	Post-clipping alopecia
Hair growth at sites of trauma	Alopecia X – due to release of Platelet Derived Growth Factor
Hair loss affecting one colour	Follicular dysplasia – genetic
Hair damage due to abnormal clumping of melanin in hair shafts	Color Dilution Alopecia

Approach to Alopecia in Dogs

Canine Cushing's Syndrome

This condition is a diagnostic dilemma. Classic clinical signs are most helpful and include bilateral symmetric alopecia, recurrent secondary infections, atrophic skin (abdominal blood vessels visible through skin), pot-bellied appearance due to fat redistribution and ventral abdominal muscle atrophy, the Poly Complex (polyuria, polydipsia, polyphagia and polyanting) and calcinosis cutis. Some of the more unusual clinical findings that suggest Cushing's syndrome include loss of muscle mass (temporal muscle loss noted by prominent occipital process), "split ends", coat color change, collagen breakdown (especially noticeable at spay incision), poor healing wounds, anterior cruciate rupture, reproduction failure (FSH – failure to cycle; LH – testicular atrophy) and secondary hypothyroidism (downregulation of TSH receptors – reversible hypothyroidism).

Encompassing clinical signs with a combination of screening and differentiating tests (beyond the scope of this lecture) will help to provide a definitive diagnosis of Cushing's syndrome. When discussing the benefits of treatment with your client, one must also weigh the potential risks/negative effects of treatment including cost of monitoring, relapse of inflammatory conditions such as allergies and arthritis when endogenous steroids are returned to normal levels, Addisonian crisis and potential for adrenal necrosis. Below are key points to consider when selecting a treatment for Cushing's syndrome.

Treatment Options

1. Mitotane (o,p-DDD)

- Adrenolytic agent causing progressive necrosis of the zona fasciculata and reticularis but usually spares the zona glomerulosa.
- Most frequently used in the treatment of dogs with PDH before Trilostane

- Should be dosed between 12.5-25mg/kg/BID given with food for induction, then decreased to 1-3X weekly when appetite and water intake have decreased by 50% or normalized
- Start treatment on Friday as most notable effects seen within 7-10 days of the induction regimen
- Dispense prednisolone (0.5 mg/kg) to mitigate any adverse effects (lethargy, anorexia, V/D)
- Control achieved in well over 80% of cases noted by ACTH stimulation tests that remain within normal pre-stim levels post-ACTH stimulation
- Relapses in 50% of dogs on maintenance therapy during the first year of treatment
- Most common cause for relapse is being too conservative with the initial weekly maintenance dose
- Should try to achieve 50 mg/kg weekly for maintenance
- Addison's disease develops in about 5%; Nelson's syndrome may occur in 10% of patients

2. Trilostane

- Synthetic steroid analogue competitively inhibiting 3β -hydroxysteroid dehydrogenase → reduces synthesis of cortisol and aldosterone; reversible and dose related
- 1 – 2.5 mg/kg q 12h with food
- Improvement of PU/PD/Pphagia within 4 weeks; hair re-growth within 2-3 months
- Monitoring ACTH stim test at 0, and between 4-6 hours post ACTH on day 10, 30, and 90 then every 4 to 6 months thereafter with the goal post-ACTH = 50-150 nmol/L 4-6h post trilostane. If post-ACTH > 250 nmol/L double the dose; if post-ACTH < 20 nmol/L, discontinue trilostane for 2 days, then return to the next lowest pill size.
- Adverse effects: lethargy, decreased appetite, mild electrolyte changes, adrenal cortical necrosis, Addison's disease even after a single dose, Nelson's syndrome
- Consider using prior to adrenalectomy and/or to treat adrenal tumours

3. L-deprenyl/Selegiline HCl (Anipryl)

- An irreversible inhibitor of monoamine oxidase-B of the brain causes decreased ACTH production
- Initially reported to produce partial to complete improvement in signs in 83%
- Others have reported only 20% success rates most likely because this is the incidence of pars intermedia-based Cushing's syndrome.
- May have suppressive effects on the growth of pituitary masses
- Minimal side effects therefore indicated for milder cases of Cushing's syndrome
- Monitoring is solely based on clinical signs

4. Ketoconazole

- Interferes with steroidogenesis by preventing cholesterol side chain cleavage/ 17α -hydroxylase activity.
- Helpful in 50-67% of either PDH or AT
- Side effects are uncommon (anorexia, diarrhea elevated liver enzymes)
- High cost + risk of hepatotoxicity + daily administration

5. Retinoid therapy

- Retinoic acid (isotretinoin) decreases corticotrophin secretion in vitro and in vivo in rodents
- Recently used to treat pituitary dependent Cushing's @ 2 mg/kg q 24h per os
- Clinical signs, plasma ACTH levels, and UCCR improved + size of pituitary adenomas decreased
- No adverse events or signs of hepatotoxicity

6. Gefitinib

- Tyrosine kinase inhibitor targets the Epidermal Growth Factor Receptors (EGFR)
- EGFR is overexpressed by some pituitary adenoma

7. Radiotherapy

- Pituitary macrotumors (> 1 cm in diameter) +/- microtumors
- With or without concurrent neurological
- ACTH production may take many months to decrease

8. Transphenoidal hypophysectomy

- Effective if CT or MRI + an experienced surgeon

- One year survival was 84%; 2 year estimated survival 80%; recurrence rate was 11.6%
- Treat with desmopressin transiently and thyroid hormone indefinitely
- Offers a potential cure for the disease or at least debulk for radiotherapy

9. Bilateral adrenalectomy

- Hi morbidity and mortality
- Currently therapy of choice in cats if minimal response to trilostane

Hypothyroidism

Hypothyroidism has been described as one of the most common endocrinopathies in veterinary medicine. This in part, is most likely due to the over interpretation of baseline thyroxine (T4) concentrations. As well, clinical signs of hypothyroidism may resemble non-thyroidal illnesses (NTI), which in turn may suppress serum thyroxine levels, leading to misdiagnosis of the disease process. The ability of diagnostic thyroid evaluations to differentiate between the hypothyroid and euthyroid-sick individual in veterinary medicine is becoming more refined. One must however always remember to combine results of thyroid tests with clinical impressions to obtain a diagnosis of canine hypothyroidism.

Clinical Signs

The most common reason for presentation is the classic clinical sign of alopecia that tends to be bilaterally symmetric from localized to generalized, predominantly involving the ventrolateral thorax and abdomen, the dorsal muzzle proximal to the planum nasale. Not always present, but when observed a hyperpigmented and alopecic "rat's tail" that is typically noted in the latter stages helps support a diagnosis of hypothyroidism.

Hyperpigmentation with macular lentigenes involving the trunk, orthokeratotic hyperkeratosis (including the peripinnal margin) resulting in adherent crusts, seborrhea oleosa or seborrhea sicca with lightening of coat color are other cutaneous findings. Often chronic recurrent infections including bacterial pyoderma, ceruminous otitis externa and adult-onset demodicosis can be attributed to hypothyroidism. Myxedema, comprising of increased deposition of dermal mucin, results in a swollen skin appearance, which is typically cool to the touch, and provides the classic "tragic facial expression". Acral lick granuloma are often associated with hypothyroidism as a result of the myxedema causing a "phantom limb" sensation along with a compromised local immune defense system resulting in protracted secondary infections.

Other non-cutaneous clinical signs that suggest hypothyroidism include:

1. GI signs – constipation or diarrhea
2. Cardiovascular signs – bradycardia, decreased blood pressure, decreased contractility, atherosclerosis, cardiomyopathy
3. Reproductive changes - anestrus, irregular cycles, stillborn puppies, azoospermia and decreased libido
4. Neurologic signs – megaesophagus, bilateral laryngeal paralysis (voice changes), muscular atrophy & weakness, polyneuropathy i.e. facial and vestibular nerve involvement as depicted by a droopy eye lid and lip, along with a head tilt, myxedema coma, and hypertrophy of slow twitch/atrophy of fast twitch fibers
5. Ocular - corneal lipid deposits
6. Anterior cruciate ligament ruptures as a result of ligament laxity.

A high index of suspicion for hypothyroidism is based on signalment (middle-aged (6 years); medium to large breed dogs), historical findings including heat seeking, weight gain, lethargy and weakness, consistent dermatologic lesions and physical exam findings of a decreased heart rate and decreased rectal temperature. Unlike Cushing's Syndrome, a definitive diagnosis can be achieved by routine bloodwork. Clinicopathologic changes may include a normocytic/normochromic anemia, elevated cholesterol & triglyceride, elevated creatine phosphokinase, urinalysis with increased WBC due to secondary to a bacterial cystitis and increased activated clotting time and partial thromboplastin time. Thyroid tests of value are the total T4, free T4 and TSH assay as primary diagnostic tools. A low T4, low free T4 and elevated TSH is a classic hypothyroid profile and provides 99.9% certainty. The thyroglobulin autoantibodies may be used as an adjunctive test to help support an early onset hypothyroid condition.

Treatment of concurrent diseases such as bacterial pyodermas, demodicosis, Malassezia dermatitis and seborrhea is advocated as any residual concurrent diseases may alter the response to thyroid supplementation. Thyroid supplementation products on the market can vary in their bioavailability, formulation and consistency. Therefore

use of products with proven pharmacokinetic research is recommended to start with before considering a generic version. The veterinary brand names I tend to rely upon include Leventa® (Merck), Soloxine® (Virbac), and Thyro-Tabs® (Veterinary Healthcare Solutions). Dosing is easily calculated as 0.1 mg per 10 lbs twice daily for pills and once to twice daily for the liquid Leventa®. I typically do not need to exceed 0.8mg BID in a large breed dog, as our dose calculations should ideally be based on body surface area (0.5 mg/M^2). TWICE daily tablet (versus once daily) administration is key to elevating the local immune response, increasing metabolic activity that will help with energy levels (within 7-14 days) hair regrowth/skin integrity (within 4-6 weeks), muscle development and weight loss, and improve ligament strength to minimize anterior cruciate ligament rupture (within 3-6 months). In more mature animals with heart conditions, I will compensate by gradually tapering my dose upwards to avoid cardiac decompensation.

Monitoring is achieved by serologic evaluation of a 6-hour post-pill T4 at 4-6 weeks after the initiation of therapy. Ideal peak supplementation levels should fall within 10% of the upper normal reference range. Once ideal post-pill supplementation levels have been achieved, I recommend rechecking 6-hour post-pill T4 levels every 6 to 12 months throughout the patient's life. If suboptimal thyroid supplementation is noted on appropriate doses, consider one or more of the following: improper administration, incorrect dosage, poor bioavailability of the brand of synthetic thyroxine (switch to Leventa® - 200% increased bioavailability), improper diagnosis or concurrent condition exists (Euthyroid Sick Syndrome; ESS). ESS is a condition whereby the thyroid is still functional but its activity is decreased due to non-thyroidal illnesses such as chronic renal failure, Cushing's, Addison's, diabetes, hepatopathies and chronic skin disease. The severity of the illness is directly correlated to severity of serum T4 suppression. Medications may also cause falsely lowered thyroid values and result in misinterpretation of the results. Drugs such as glucocorticoids, phenylbutazone, anticonvulsants, anesthetics, long-term sulfonamides, and radiocontrast dyes all may either inhibit TSH secretion or serum thyroid hormone synthesis, release, binding or conversion, or they may impair thyroglobulin iodination and coupling of tyrosinases. Therefore ESS must always be taken into consideration when a complete response to thyroid supplementation has not been achieved within 3 months.

Alopecia-X of the Nordic breeds

Also known as pseudo-Cushing's, adrenal sex hormone imbalance, congenital adrenal hyperplasia-like syndrome, Lysodren responsive dermatosis, follicular dysplasia of Nordic breeds, growth hormone deficiency, hyposomatotropism, growth hormone-responsive alopecia, biopsy responsive alopecia, post-clipping alopecia, castration-responsive dermatosis, gonadal sex hormone alopecia, sex hormone/growth hormone dermatoses, Siberian husky follicular dysplasia, and follicular growth dysfunction of the plush-coated breeds, the term Alopecia X encompasses multiple dysplastic follicular conditions that potentially have many underlying pathogenic mechanisms that are not completely understood with an end-result of hair cycle arrest.

In general, there does appear to be a genetic predisposition to a hormonal/growth factor imbalance systemically or perhaps more likely at the level of the hair follicle receptors. Similar to congenital adrenal hyperplasia-like syndrome in humans, Lothrop et al (1990) proposed that a partial 21-hydroxylase adrenal enzyme deficiency resulting in overproduction of progesterone, 17-OH progesterone, androstenedione, estradiol and other sex hormones was responsible for the changes seen especially in Nordic breed dogs. Unfortunately, both affected and unaffected individuals may have similar changes in circulating levels pre- and post-ACTH stimulation. These post-ACTH findings are not unlike Atypical Cushing's Syndrome noted in some dogs with normal cortisol results on screening tests for hyperadrenocorticism. Although polyuria and polydipsia are not typically noted in Alopecia X patients, it has been proposed that the bilateral symmetric alopecia may categorize these patients as Atypical Cushing's Syndrome; after all, they do respond favourably to medications used to treat Cushing's syndrome (Trilostane, Mitotane). Interestingly, treatment does not appear to alter the sex hormone profiles and in some patients, discontinuation of therapy without a relapse of clinical signs is possible. Lastly, several Alopecia X patients will respond to neutering, while others may resolve spontaneously casting doubt as to whether this condition is mediated strictly by a circulating hormone imbalance and rather emphasizing the need for more focus on the effects of local hormones and growth factor levels on hair follicular arrest.

Clinical Signs

Typically, a non-pruritic bilaterally symmetric alopecia with marked hyperpigmentation in later stages, Alopecia X involves the neck, trunk, and tail, while sparing the head and distal limbs. Hair regrowth at areas of trauma is common. The mean age of onset is 2 years (9 months to 11 years) and is more frequently seen in intact or neutered

male dogs. Miniature poodles and Nordic breeds with a plush coat are predisposed, in particular Pomeranians, Chow Chows, Keeshondens, Samoyeds, Malamutes, and Huskies. Diagnosis is made by ruling out other endocrinopathies and histopathologic findings consistent with catagen arrest/flame follicles. Evaluation of gonadal and adrenal sex hormones pre- and post-ACTH stimulation has questionable value but is typically recommended if Lysodren or Trilostane are being considered for treatment.

Treatment Options:

1. Neuter and assess response within 3-6 months.
 - Regrowth in up to 50 to 75% of cases
 - Expected resolution for months to years post-neutering.
2. Trial melatonin therapy
 - Oral melatonin - 1 mg/kg divided TID
 - Injectable melatonin – 20mg SQ q 2weeks for 3 treatments then as needed
 - Implantable melatonin – 3 constant-release implants of 12mg each at one time
 - A product of the multistep conversion of L-tryptophan → serotonin → melatonin
 - Production is directly proportional to the length of the dark period
 - Centrally stimulates the pulsatile LHRH activity from the hypothalamus
 - Controls photoperiod-dependent molting and/or coat color via direct effects on hair follicles or within the pars tuberalis to alter secretion of melanocyte-stimulating hormone and/or prolactin
 - 50-60% response rates are noted within 3-6 months.
 - Discontinue once hair regrowth is noted so that the treatment can be used again in the future if needed
3. Trilostane
 - Inhibitor of 3-beta hydroxysteroid dehydrogenase
 - Complete hair regrowth within 6 months
 - Study: 14/16 Pomeranians and 8/8 miniatures poodles (@ 11 mg/kg)
 - 3/3 Malamutes (@ 3.0-3.6 mg/kg)
 - Hypoadrenocorticism, expense, death due to adrenal necrosis reported
4. Low dose Lysodren therapy
 - Necrosis of zona reticularis & fasciculata of adrenal gland and usually spares zona glomerulosa
 - 15 - 25 mg/kg PO daily for 5-7 days induction
 - Maintain between normal resting cortisol levels both pre- & post-ACTH stimulation
 - May require 1 to 5 times per week dosing
 - Gradually lower the dosage once a full coat has returned
 - 50-100% response rates reported; good response documented in chow-chows
5. Others
 - Leuprolide acetate – expensive anti-gonadotropic drug used if elevated estradiols
 - Deslorelin implant (Suprelorin®; GnRH-agonist)- with two 4.7 mg/dog 6 months apart (and 1 year follow up) hair regrowth is visible within 3 months in 12 of 16 intact male dogs (75%); no hair regrowth was noted in any neutered female dogs. Adverse effects were not noted, other than a decreased testicular size in intact males (Cerundulo 2013 ESVD/ECVD).
 - Dutasteride, osaterone – anti-androgenic that decreases estradiol and progesterone
 - Cyclosporine prolongs the anagen phase of the hair cycle by inhibiting expression of Protein kinase C thus stimulating hair follicle growth and hair fiber production
 - Medroxyprogesterone acetate injections (5mg/kg every 4 weeks for 4 times) has been described in Pomeranians with partial results and new loss one year after withdrawal of the therapy (Frank et al 2013)
 - Low-Level Laser Therapy - 5 min/administration twice weekly for a maximum of 2 months with a therapeutic laser with a cluster probe (470nm/685 nm/830 nm). 4/7 received 16 laser treatments and 3/7 only 10. Complete hair regrowth in 5/7 animals; 2/7 an improvement in hair density/length. Biopsies revealed an increase in anagen hairs at treated sites. (Olivieri 2013 ESVD/ECVD)
 - Micro-needling - successful in 2 FS 4yr Pomeranian siblings with clinical and histologic changes compatible

with alopecia X no response to melatonin, deslorelin or topical minoxidil helped. The procedure is done under general anesthesia where the sterile microneedling device (Dermaroller MC925) was rolled with moderate pressure vertically, horizontally and diagonally until microbleeding noted. Five weeks post-micro-needling hair re-growth + reduction of hyperpigmentation; 12 weeks 90% of the coat had regrown + skin hyperpigmentation started to subside. No adverse effects were observed. Coat quality had not deteriorated at 12 months follow-up. (Stoll 2015 ECVD/ESVD)

Canine Recurrent Flank Alopecia (CRFA)

Based on the breed predispositions (Airedale, Boxer and Bulldog), CRFA is considered to be a genetically influenced photoperiod-related melatonin deficiency resulting in the recurrent alopecia directly or indirectly by its effects on prolactin, androgens, estrogens and/or growth hormone.

Clinical Signs

CRFA is a non-scarring, initially cyclical alopecia of the thoracolumbar region that is usually bilaterally symmetric but can favour or affect one side only. Lesions are well demarcated often with marked hyperpigmentation and most commonly seen in Boxers, Airedales, English bulldogs and Schnauzers of either sex. Although it can affect any breed, CRFA seems rare in plush-coated Nordic breeds, German Shepherds and Cocker. As the condition may also involve the dorsum of the nose, base of the ears, base of tail and perineum in Airedales, Golden Retrievers, Doberman and Giant Schnauzer, hypothyroidism and Cushing's syndrome must be considered strong differentials, especially on non-seasonal patients. Most often however, both the early mean age onset of 4 years (8 months to 11 years) and the seasonality of the hairloss (November or March north of the 45th parallel) with spontaneous complete regrowth, move the progressive endocrinopathies lower on the rule-out list. As well, 20% of cases may have only one isolated episode, and some may skip a year. The alopecia may worsen from year to year, eventually becoming permanent. When regrowth is noted, it may vary from a normal return of hair to coat color changes (darker to aurotrichia). A classic history of recurrent hairloss is typically sufficient to diagnose this condition. Histopathologic findings of a follicular dystrophy ("witch's feet") will help support the diagnosis.

Treatment Options.

1. Benign neglect
2. Trial melatonin therapy
 - Oral melatonin - 1 mg/kg divided TID
 - Injectable melatonin – 20mg SQ q 2weeks for 3 treatments then as needed
 - Implantable melatonin – 3 constant-release implants of 12mg each at one time
 - On subsequent years, treatment should be initiated one to two months before expected onset of alopecia
 - Apparent success rate ~ 50-75%

Canine Pattern Alopecia (CPA)

CPA is a relatively common disorder resulting in alopecia of the post-auricular regions, ventral neck, thorax, abdomen and caudomedial thighs. The age of onset is typically at 6 months with gradual progression over months to years. Although primarily a condition of the Dachshund, CPA may also be seen in Chihuahuas, Miniature Pinschers, Whippets, Greyhounds, Boston terriers and Boxers. Diagnosis is based on history, dermatologic findings, ruling-out other endocrinopathies (HAC, estrogen-responsive dermatosis, congenital hypothyroidism) and dermatohistopathologic evidence of miniaturized hair follicles.

Treatment

1. Trial melatonin therapy
 - Oral melatonin - 1 mg/kg divided TID
 - Injectable melatonin – 20mg SQ q 2weeks for 3 treatments then as needed
 - Implantable melatonin – 3 constant-release implants of 12mg each at one time
 - Hair growth noted within 6 weeks; maximum growth in 3 to 4 months
 - 60-70% response rate

Post-clipping Alopecia

Protracted alopecia is sometimes noted after preparation for a surgical or epidural procedure. The lower back and dorsal pelvic region tend to be predisposed and often present with hyperpigmentation pending the duration. This syndrome is seen most commonly in long-coated breeds (e.g. "plush-coated" breeds, such as Samoyed and Chow

Chows, German Shepherds). Similar to Alopecia X patients, tufts of hair may be seen to regrow at sites of trauma. It is thought that the alopecia results from decreased vascular perfusion/vasoconstriction in response to decreased skin temperatures at the sites of hair clipping. Another theory is that the hair that was clipped happened during a normal catagen stage of hair growth, and that the time to regrow hair is dependent on the proximity of the anagen phase of the hair cycle. Therefore, with benign neglect, it may take 6 to 24 months for hair to regrow.

Treatment options:

1. Pentoxifylline

- Phosphodiesterase inhibitor that promotes increased rheologic activity, hence increased blood flow and nourishment of hair follicles
- 10-30mg/kg TID for a minimum of 3 months
- Caution with natural or chemically induced blood dyscrasias

2. Cyclosporine

- Prolongs the anagen phase of the hair cycle by inhibiting expression of Protein kinase C thus stimulating hair follicle growth and hair fiber production
- 5mg/kg daily until hair regrowth, then discontinue

3. Thyroxine supplementation

- Stimulate hairs to non-specifically move into the anagen (growth) phase of the hair cycle
- Acquire baseline thyroid values, then administer 0.05 to 0.1 mg/10lbs once to twice daily to stimulate anagen growth
- Supplementation for 3 months will not result in permanent thyroid shut down.

4. Low Level LASER Therapy – see under Alopecia X above (Olivieri 2013)

Bald Belly Bald Thigh Syndrome (BBBTS)

BBBTS is a non-pruritic, non-inflammatory alopecia that affects the caudal aspect of the pelvic limbs and can progress to involve the abdomen, often noted in breeds with very little subcutaneous fat such as greyhounds and whippets. The hairloss may be caused by decreased oxygen tension at the skin as a result of muscle to skin compression of superficial blood vessels with very little subcutaneous fat to act as padding, in essence and ischemic folliculopathy. Ruling-out other endocrinopathies, in particular hypothyroidism, is important in these patients to help confirm a diagnosis.

Treatment options:

1. Pentoxifylline

- 10-30mg/kg TID for a minimum of 3 months before tapering the dose
- Other ischemic folliculopathies that might be considered pentoxifylline candidates include: traction alopecia, elbow/hock calluses and deep scarring pyoderma/pododermatitis

2. Melatonin

- 1mg/kg divided TID for a minimum of 3 months before adjusting the dose

3. Thyroxine

- 0.05 to 0.1mg/10lbs BID as a non-specific anagen hair growth stimulator
- Discontinue at 3 months regardless of whether or not hair growth is noted

4. Cyclosporine

- Prolongs the anagen phase of the hair cycle by inhibiting expression of Protein kinase C thus stimulating hair follicle growth and hair fiber production
- 5mg/kg daily until hair regrowth, then discontinue

5. Soft, warm bedding and LLLT

- To minimize compression of the superficial blood vessels and promote increased circulation

Color dilution alopecia (CDA)

CDA is the result of the dilute mutation causing abnormal clumping of melanin within the hair shaft with subsequent fracturing and alopecia. Age of onset is typically between 3 months to 3 years. Predisposed breeds include blue/fawn/red-coated Doberman Pinschers, Great Danes, Whippets, Dachshunds, Standard Poodles, Chow Chows and fawn Irish Setters. The patients are normal at birth and then progress gradually to develop a dry and dull coat with partial to complete alopecia on the dorsum of the trunk. Seborrhea, comedones and secondary bacterial folliculitis often present in affected areas. Aggressive bathing may hasten the presentation of affected individuals. Diagnosis is based on signalment, trichoscopy and dermatohistopathologic findings of melanin clumping within the epidermis of the hair follicle, increased melanophagic activity, and varying degrees of follicular dysplasia.

Treatment options

1. To help minimize scale and seborrhea - Oral retinoids (vit A, isotretinoin, acitretin), Omega 3 AND 6 fatty acids, epidermal barrier repair products (Allerderm Spot-On, Douxo Antiseborrheic pipettes)
2. To help address secondary infections - Topical and/or oral antibiotics
3. To help improve hair regrowth - Melatonin

Suggested Reading:

General Hair Loss

Gross TL, Ihrke PJ, Walder EJ, Affolter VK. *Skin Diseases of the Dog and Cat. Clinical and Histopathologic Diagnosis*, 2nd edition. Oxford, Blackwell Science, 2005.

Mecklenburg L, Linek M, Tobin DJ. *Hair Loss Disorders in Domestic Animals*. Ames: Wiley-Blackwell, 2009

Cushing's Syndrome

Barker EN, Campbell S, Tebb AJ, *et al*. A comparison of the survival times of dogs treated with mitotane or trilostane for pituitary-dependent hyperadrenocorticism. *Journal of Veterinary Internal Medicine* 2005;**19**(6): 810-5.

Castillo VA, Giacomini D, Páez-Pereda M, *et al*. Retinoic acid as a novel medical therapy for Cushing's disease in dogs. *Endocrinology*. 2006;**147**(9): 4438-44.

Castillo VA, Cabrera Blatter MF, Gómez NV, *et al*. Diurnal ACTH and plasma cortisol variations in healthy dogs and in those with pituitary-dependent Cushing's syndrome before and after treatment with retinoic acid. *Research in Veterinary Science*. 2009;**86**:223-9.

Chapman PS, Kelly DF, Archer J, *et al*. Adrenal necrosis in a dog receiving trilostane for the treatment of hyperadrenocorticism. *Journal of Small Animal Practice* 2004;**45**:307-10.

Feldman EC. Evaluation of twice-daily lower-dose trilostane treatment administered orally in dogs with naturally occurring hyperadrenocorticism. *Journal of American Veterinary Medical Association* 2011;**238**:1441-51.

Kintzer PP, Peterson ME. Mitotane (o,p'-DDD) treatment of 200 dogs with pituitary-dependent hyperadrenocorticism. *Journal of Veterinary Internal Medicine*. 1991;**5**:182-190.

Lien YH, Huang HP. Use of ketoconazole to treat dogs with pituitary-dependent hyperadrenocorticism: 48 cases (1994-2007). *Journal of American Veterinary Medical Association* 2008;**233**:1896-901

Neiger R, Ramsey I, O'Connor J, *et al*. Trilostane treatment of 78 dogs with pituitary dependent hyperadrenocorticism. *The Veterinary Record* 2002;**150**:799-804.

Reine NJ. Medical management of pituitary-dependent hyperadrenocorticism: mitotane versus trilostane. *Clinical Technique in Small Animal Practice* 2007;**22**(1):18-25.

Vaughan MA, Feldman EC, Hoar BR, *et al*. Evaluation of twice daily, low-dose trilostane treatment administered orally in dogs with naturally occurring hyperadrenocorticism. *Journal of American Veterinary Medical Association* 2008;**232**:1321-8.

Alopecia X

Cerundolo R, Warren S. The use of deslorelin to promote hair regrowth in dogs with Alopecia X. *ESVD/ECVD Annual Conference Proceedings*. 2013: p 185.

Cerundolo R, Lloyd DH, Persechino A, *et al*: Treatment of canine alopecia X with trilostane. *Veterinary Dermatology* 2004;**15**:285-293.

Frank LA, Watson JB. Treatment of alopecia X with medroxyprogesterone acetate. *Veterinary Dermatology* 2013; **24**:624-7.

Frank LA. Alopecia X. In: *Hair loss disorders in domestic animals*. Mecklenburg L, Linek M, and Tobin DJ ed. Wiley-Blackwell. 2009, pp. 148-155.

Frank LA, Hnilica KA, Oliver, JW. Adrenal steroid hormone concentrations in dogs with hair cycle arrest (Alopecia X) before and during treatment with melatonin and mitotane. *Veterinary Dermatology* 2004;**15**:278-284.

Olivieri L, Cavina D, Radicchi G, Miragliotta V, Abramo F. Efficacy of the low-level laser therapy on hair regrowth: a preliminary study on 8 cases of noninflammatory alopecia in dog. *ESVD/ECVD Annual Veterinary Dermatology Conference*

Proceedings. 2013:p 206

Paradis M. Alopecia X. Clinical Veterinary Advisor Dogs and Cats. Second edition. E. Coté ed. Mosby Elsevier. 2011, pp. 58-59.

Paradis M. Melatonin therapy in canine alopecia. Current Veterinary Therapy XIII. Kirk ed. WB Saunders Co. Philadelphia, 2000, pp. 546-549.

Stoll S, Dietlin C, Nett-Mettler CS. Microneedling as a successful treatment of alopecia X in two Pomeranians. ESVD/ECVD Annual Conference Proceedings. 2015: p 130.

Canine Recurrent Flank Alopecia

Paradis M. Canine recurrent flank alopecia in: Hair loss disorders in domestic animals. L. Mecklenburg, M.Linek, D.J. Tobin ed. Willey-Blackwell. 2009, pp. 155-161.

Canine Pattern Alopecia

Paradis M. Canine pattern alopecia. Hair loss disorders in domestic animals. L. Mecklenburg, M.Linek, D.J. Tobin ed. Willey-Blackwell. 2009, pp. 164-169.

Paradis M. Melatonin in the treatment of canine pattern baldness. Proceedings of the Third World Congress in Veterinary Dermatology. Edinburg, Scotland, 1996, p. 53.