Reference Point

Growth hormone-responsive alopecia in dogs

Linda A. Frank, MS, DVM

For years, breeders of dogs that are double coated and have a dense undercoat, such as Pomeranians, Alaskan Malamutes, Chow Chows, and Keeshonds, have been aware that their dogs might develop bilaterally symmetrical alopecia with hyperpigmentation of the skin that is not caused by hypothyroidism or hypercortisolemia. This problem has also been described in Miniature and Toy Poodles. The breeders refer to this condition as "black skin disease" or "coat funk," depending on the breed affected; in the veterinary literature, it has been known by many names including adult-onset growth hormone deficiency (hyposomatotropism), growth hormone-responsive alopecia, castration-responsive alopecia, biopsy-responsive alopecia, congenital adrenal hyperplasia-like syndrome, and, most recently, alopecia X. The intent of this article is to provide a review of the investigations into the pathologic mechanisms associated with the alopecia and an overview of the current perspectives regarding this disease. For clarity, the term hair cycle arrest will be used when referring to the syndrome.

Hair cycle arrest was first described in dogs by Siegel[1] in 1977. He termed the condition pseudo-Cushing syndrome because the clinical signs resembled those of hyperadrenocorticism; however, in affected dogs, results of serum biochemical analyses, urinalysis, and adrenal gland and thyroid gland function tests were within reference limits. These dogs regrew hair when treated with bovine growth hormone. In light of this, the name growth hormone-responsive dermatosis was coined and attempts to determine the association of growth hormone with the hair cycle arrest were undertaken. In an initial study[2] of dogs with alopecia and hyperpigmentation of the skin that had no abnormalities detected via thyroid gland hormone and ACTH response assessments, basal plasma growth hormone concentrations were low in 2 dogs; however, the validity of those basal concentrations was questioned.[3]

Dynamic function testing of plasma growth hormone concentrations involving the use of clonidine or xylazine has provided a better assessment of growth hormone deficiencies in dogs.[3] Clonidine and xylazine are α_2-adrenoceptor agonists that stimulate growth hormone secretion at the hypothalamus, probably via release of **growth hormone-releasing hormone (GHRH)**.[3] Adult-onset hyposomatotropism was suggested as the pathologic mechanism of the hair cycle arrest when researchers detected growth hormone deficiency via clonidine stimulation in 9 dogs (4 Miniature Poodles, 4 Pomeranians, and 1 Lhasa Apso) with clinical signs associated with hair cycle arrest.[4] Hyposomatotropism was further supported by findings of a case study conducted by Scott and Walton,[5] in which plasma growth hormone concentrations of 22 affected dogs failed to increase in response to xylazine stimulation. In addition to Pomeranians and Poodles, the breeds of dog in that case study included Airedale, Chow Chow, Keeshond, Portuguese Water Dog, Dachshund, and German Wirehaired Pointer. Both neutered and sexually intact dogs were represented. In that study,[5] the Dachshund and German Wirehaired Pointer did not have hyperpigmented skin, and alopecia was limited to the flanks in the Airedale and Portuguese Water Dog. Histologically, 6 of 15 of the dogs from which skin biopsy specimens were obtained had decreased dermal elastin, although no comparison to clinically normal dogs was made; this is similar to a finding reported in dogs with hyposomatotropism. However, conclusions from the finding of Scott and Walton[5] are difficult to draw because clinically normal dogs do not have abundant elastic fibers in the dermis.[6] Of 6 dogs treated with bovine growth hormone, 5 had complete regrowth of hair; however, clinical signs returned 7 months later in 2 of those dogs.[5] Seven dogs treated with ovine growth hormone failed to respond.[5] This discrepancy was attributed to differences in structure or possibly function of ovine growth hormone, compared with bovine or canine growth hormone. Ten dogs in the case study[5] were not treated. Of these, 1 dog (a Pomeranian) spontaneously regrew hair 4 months after initial evaluation. Adult-onset growth hormone deficiency has also been reported in 2 sibling Airedale Terriers,[7] 2 Chow Chows,[8] and a Toy Poodle.[8] Interestingly, Airedales are no longer typically listed as a breed predisposed to hair cycle arrest.[9] Most likely, these affected dogs had cyclic flank alopecia, a condition known to affect Airedales, Boxers, and English Bulldogs.[10]

At first, adult-onset growth hormone deficiency seemed like a plausible explanation for the hair cycle arrest in these dogs. Growth hormone may have a direct action or an indirect action via **insulin-like growth factor 1 (IGF-1)** on the skin and appendages. In dogs with congenital hyposomatotropism (pituitary dwarfism), alopecia and hyperpigmentation of the skin are common clinical findings.[11,12] In addition, trans-

From the Department of Small Animal Clinical Sciences, Veterinary Teaching Hospital, College of Veterinary Medicine, University of Tennessee, Knoxville, TN 37996-4544.

genic rats in which growth hormone expression was suppressed completed 2 normal hair cycles shortly after birth and then entered a long telogen phase.[13]

Doubt as to whether growth hormone deficiency was truly the pathologic mechanism of the hair cycle arrest first emerged in 1988. In 95 dogs with clinical signs suggestive of this syndrome, 32 (34%) had serum or plasma growth hormone concentrations that were within reference limits in response to administration of xylazine or GHRH.[14] Most of the Chow Chows (14/19) and Keeshonds (3/4) in that study had normal growth hormone responses, and serum or plasma IGF-1 concentration was within reference limits in all 16 dogs tested. Pomeranians and Poodles had lower serum or plasma concentrations of IGF-1, compared with 8 clinically normal dogs, which was attributed to their smaller body size.[14,15] Dogs with congenital hyposomatotropism have substantially decreased plasma concentrations of IGF-1 and growth hormone.[11] In another study,[16] serum growth hormone concentrations were evaluated in 5 of 6 sexually intact male dogs with hair cycle arrest that subsequently underwent castration. In 4 of 5 of these dogs, serum growth hormone concentrations before and after stimulation with xylazine were less than the lower limit of the reference range. After surgery, hair regrew in all dogs (thus, the term castration-responsive dermatosis was proposed); however, serum growth hormone concentrations remained low in the 4 dogs evaluated.

In adult dogs, there have to be disturbances in growth hormone secretion either at the pituitary gland or hypothalamus for development of growth hormone deficiency.[17] Isolated pituitary gland deficiencies are rare and have been attributed to an autoimmune disorder in humans.[18] Because the dogs with hair cycle arrest (for which serum or plasma growth hormone concentrations have been reported) have low but detectable amounts of growth hormone, a pituitary gland deficiency of growth hormone is an unlikely cause of the syndrome. Growth hormone secretion is regulated by GHRH and somatostatin, both of which are produced by the hypothalamus.[19] There could be a selective decrease in the number of cells that produce and secrete GHRH; however, this is unlikely because repeated administration of GHRH did not result in normal growth hormone secretion in 2 Miniature Poodles with alopecia.[17] A more likely explanation is an increase in the inhibitory control of growth hormone secretion by somatostatin.[17]

Glucocorticoids interfere with growth hormone release, presumably via increased somatostatin release.[20-22] Dogs with hyperadrenocorticism have decreased responses to stimulation with xylazine[23] or GHRH and clonidine,[24] compared with responses of clinically normal control dogs. In 1 study,[23] 3 dogs with hyperadrenocorticism and decreased plasma growth hormone concentrations after xylazine stimulation (compared with baseline values) were treated with mitotane, after which 2 of the dogs had a significant increase in plasma growth hormone concentration after xylazine stimulation; however, 1 dog still had plasma growth hormone concentrations less than the lower limit of the established reference range. This latter finding may be attributed to a residual corticosteroid influence. In humans, 1 dose of cortisone administered orally 60 minutes prior to a growth hormone stimulation test involving GHRH significantly decreased growth hormone responsiveness.[25] In many studies[4,5,7,14] of growth hormone hyporesponsiveness in dogs, multiple endocrine function tests were performed, including ACTH stimulation and low-dose dexamethasone suppression tests; the order in which these tests were performed in relation to growth-hormone response testing was not provided in those reports. But because hypothyroidism and hyperadrenocorticism are usually ruled out prior to growth hormone response testing, it can be assumed that adrenal gland function assessments were performed first. In humans, plasma growth hormone concentrations and responses to external stimulation may take 6 to 12 months to normalize once hyperadrenocorticism has been corrected.[26] It is not known what withdrawal period is required after short-term corticosteroid treatment before systemic effects of treatment are eliminated or what influence endogenous corticosteroid release associated with stress may have on the results of plasma or serum growth hormone concentrations. Therefore, if the adrenal gland function tests were performed in close temporal association with the growth hormone stimulation test involving any of the known secretagogs, the results of the latter could be affected by the iatrogenic increase in circulating cortisol concentration. In light of these observations, the possibility of adult-onset growth hormone deficiency as a cause of hair cycle arrest is highly unlikely.

Interestingly, some adult dogs with alopecia and serum or plasma growth hormone concentrations that were within reference range regrew hair in response to growth hormone injections; thus, the term growth hormone-responsive alopecia was adopted.[14] It has been proposed that growth hormone simply induces resting hair follicles to begin an anagen cycle; however, the exact mechanism by which this hormone works is not known.

Because of the questionable association of alopecia and growth hormone deficiency in dogs with hair cycle arrest, other hormonal abnormalities were investigated. In 1990, Schmeitzel and Lothrop[27] suggested that the alopecia and hyperpigmentation associated with this condition may be attributed to an imbalance of adrenal gland steroid hormone intermediates. In their study,[27] 7 Pomeranians (6 of which were sexually intact) with bilateral alopecia and hyperpigmentation of the trunk, caudal portion of the thighs, and ventral neck region and 12 normal-coated sexually intact Pomeranians were evaluated. Both abnormal- and normal-coated dogs had abnormal serum concentrations of adrenal gland steroid intermediates and sex hormones, compared with values in 19 mixed-breed control dogs[27]; most notable was the high serum **17-hydroxyprogesterone (17-OHP)** concentration in the affected and unaffected Pomeranians. The authors theorized that there may be a partial deficiency of the 21-hydroxylase enzyme (as described in humans with congenital adrenal gland hyperplasia) that may account for the laboratory and clinical findings in these dogs. This enzyme deficiency results in an increase in serum 17-OHP concentration, which provides more substrate for the formation of androstenedione and, subsequently, estradiol. In humans with late-onset congenital adrenal gland hyperplasia, clinical signs are associated with

hyperandrogenism and may include premature development of pubic hair in children, hirsutism in women, early fusion of epiphyseal growth plates, and severe cystic acne[28]; in addition, male pattern baldness may be the sole clinical sign in young women.[28] Diagnosis in humans is made on the basis of detection of substantial increases in serum 17-OHP concentrations following ACTH stimulation; treatment involves administration of low doses of corticosteroids to decrease ACTH secretion from the pituitary gland via negative feedback, thus decreasing serum 17-OHP concentration.[29]

Although an imbalance in adrenal gland hormones resulting in hyperandrogenism is a very appealing explanation of hair cycle arrest, dogs do not have androgen-dependent hair follicles and administration of methyltestosterone has resulted in hair regrowth in some dogs with this condition.[14,16] Furthermore, in humans with late-onset congenital adrenal gland hyperplasia, there may be systemic clinical signs in addition to pattern baldness.[28] Yet, the hallmark of hair cycle arrest in dogs is that they have no systemic clinical signs associated with the coat abnormality. In addition, there are no reports of hair regrowth in dogs with hair cycle arrest as a result of treatment with corticosteroids.

Since the study by Schmeitzel and Lothrop[27] was undertaken, findings of further research did not support adrenal hyperplasia as the pathologic mechanism for hair cycle arrest. In a retrospective evaluation[30] of dogs with alopecia in which hypothyroidism and hypercortisolemia had been excluded as a possible cause, not all dogs had detectable abnormalities in serum concentrations of sex hormones and steroid hormone intermediates and seldom were the values substantially greater than the upper limits of the reference ranges. Breed differences were also evident in that study[30]; among the different breeds of dogs evaluated, greater proportions of Chow Chows, Samoyeds, and Alaskan Malamutes had serum concentrations of steroid hormone intermediates that were within reference limits. Serum 17-OHP concentrations before and after ACTH stimulation were high in only 17.8% and 6.9% of the samples analyzed in that study, respectively. In a prospective study[31] to evaluate serum concentrations of adrenal gland steroid hormones in dogs with hair cycle arrest during treatment with melatonin or mitotane, partial to complete hair regrowth occurred in 18 of 29 dogs receiving melatonin and 4 of 6 dogs receiving mitotane; however, hair regrowth was not associated with decreases of serum concentrations of adrenal gland steroid hormones to within reference ranges. After treatment with melatonin or mitotane, hormonal imbalances associated with androstenedione, progesterone, and 17-OHP were still detected in 21%, 64%, and 36% of dogs with partial to complete hair regrowth, respectively. Finally, cloning and sequencing of the canine 21-hydroxylase gene in Pomeranians with alopecia did not reveal any mutations in the gene, compared with that of control dogs without alopecia.[32]

Most recently, hypercortisolemia as the cause of the alopecia in dogs has been hypothesized.[33] Miniature Poodles and Pomeranians with hair cycle arrest were found to have increased urinary cortisol-to-creatinine ratios; however, serum cortisol concentrations after ACTH stimulation were within reference limits. Although this theory remains to be further evaluated, a question of interest is why these dogs do not show other clinical signs associated with increased serum cortisol concentrations such as dilute urine, polyuria, polydipsia, urinary tract infections, or polyphagia. One of the unique occurrences associated with hair cycle arrest in dogs is that hair will regrow at a site of trauma such as a biopsy or surgical site (thus, the term biopsy-responsive alopecia has been proposed). Trauma-induced anagen is a known phenomenon of the hair follicle.[34] Hormones such as corticosteroids have an inhibitory effect on anagen that overrides the local stimulation from trauma.[35] Therefore, if glucocorticoid suppression of anagen was the pathologic mechanism of hair cycle arrest, then hair should not grow following trauma at a biopsy or surgical site. The fact that hair regrows at a site of trauma in dogs with hair cycle arrest implies a local inhibition of anagen at the level of the follicle rather than a systemic hormonal inhibition.

Many treatments of dogs with hair cycle arrest (eg, castration[16] or administration of growth hormone,[1,2,5,7,14,16] methyltestosterone,[14,16] mitotane,[31,a] and melatonin[31,33]) have been associated with hair regrowth; however, the various treatments are not always effective. In addition, as reported[5] and in the author's experience, the new hair is rarely permanent and will often fall out in months to years. This suggests a failure of the hair follicle to cycle properly and that the treatments merely serve as an anagen jump start. Hormones are known to have stimulatory and inhibitory effects on the hair follicle cycle.[35,36] Castration or administration of methyltestosterone or mitotane may result in hair regrowth by merely manipulating serum hormone concentrations. Melatonin may influence hair growth via alterations in serum sex hormone concentrations in sexually intact dogs.[37] However, in neutered dogs, this mechanism is unlikely.[31] Melatonin may indirectly influence hair growth via increases of serum growth hormone or IGF-1 concentrations.[38,39] In addition, melatonin has been shown to block estrogen receptors in human breast cancer cells.[40,41] Estrogen receptors are present in telogen follicles and appear to have a regulatory role in the hair cycle.[42-44]

New theories regarding the pathologic mechanism of hair cycle arrest in dogs are focusing on genetics and hair follicle receptors. Both extrinsic (hormones) and intrinsic factors (cytokines, growth factors, and receptors) influence the hair follicle cycle.[35,44] Current research into the normal canine hair follicle cycle may help shed some light on the pathogenesis of this disease. Recent investigations have revealed that breeds such as the Nordic breeds have hairs in a prolonged telogen phase, which may last for years.[45,46] This is in contrast to Poodles in which the hair cycle has a prolonged anagen phase, similar to that found in humans.[45,46] Interestingly, both of these breed types develop hair cycle arrest.

Proposed pathologic mechanisms, from hyposomatotropism to adrenal androgen imbalance, have been investigated as causes of hair cycle arrest. This has resulted in many different names being assigned to the alopecic condition, with the most recent being alopecia X. Although the latter term does reflect the mystery behind the cause of the alopecia, it fails to reflect what we do know about the condition. Therefore, until more

is known about the pathologic mechanism of this syndrome, the author recommends that the alopecic condition in dogs be referred to as hair cycle arrest (of breeds that are double coated and have a dense undercoat).

a. Rosenkrantz WS, Griffin C. Lysodren therapy in suspect adrenal sex hormone dermatosis (abstr), in *Proceedings*. 2nd World Cong Vet Dermatol 1992;121.

References

1. Siegel ET. Hypofunction of the anterior pituitary gland. In: *Endocrine diseases of the dog*. Philadelphia: Lea & Febiger, 1977;23–32.
2. Parker WM, Scott DW. Growth hormone responsive alopecia in the mature dog: a discussion of 13 cases. *J Am Anim Hosp Assoc* 1980;16:824–828.
3. Hampshire J, Altszuler N. Clonidine or xylazine as provocative tests for growth hormone secretion in the dog. *Am J Vet Res* 1981; 42:1073–1076.
4. Eigenmann JE, Patterson DF. Growth hormone deficiency in the mature dog. *J Am Anim Hosp Assoc* 1984;20:741–746.
5. Scott DW, Walton DK. Hyposomatotropism in the mature dog: a discussion of 22 cases. *J Am Anim Hosp Assoc* 1986;22: 467–473.
6. Frank LA, Calderwood-Mays MB, Kunkle GA. Distribution and appearance of elastic fibers in the dermis of clinically normal dogs and dogs with solar dermatitis and other dermatoses. *Am J Vet Res* 1996;57:178–181.
7. Shanley KJ, Miller WH. Adult-onset growth hormone deficiency in sibling Airedale terriers. *Comp Small Anim Pract* 1987;9: 1076–1982.
8. Bell AG, Jones BR, Scott MF. Growth hormone responsive dermatosis in three dogs. *N Z Vet J* 1993;41:195–199.
9. Scott DW, Miller WH, Griffin CE. Endocrine and metabolic diseases. In: *Muller and Kirk's small animal dermatology*. 6th ed. Philadelphia: WB Saunders Co, 2001;780–886.
10. Miller MA, Dunstan RW. Seasonal flank alopecia in Boxers and Airedale terriers: 24 cases (1985–1992). *J Am Vet Med Assoc* 1993;203:1567–1572.
11. Campbell KL. Growth hormone-related disorders in dogs. *Comp Small Anim Pract* 1988;10:477–481.
12. Schmeitzel LP. Sex hormone-related and growth hormone related alopecias. *Vet Clin North Am Small Anim Pract* 1990;20:1579–1601.
13. Ikawa A, Ishil Y, Suzuki K, et al. Age-related changes in the dorsal skin histology in Mini and Wistar rats. *Histol Histopathol* 2002;17:419–426.
14. Lothrop CD. Pathophysiology of canine growth hormone-responsive alopecia. *Comp Small Anim Pract* 1988;10:1346–1349.
15. Eigenmann JE, Patterson DR, Froesch ER. Body size parallels insulin-like growth factor I levels but not growth hormone secretory capacity. *Acta Endocrinol* 1984;106:448–453.
16. Rosser EJ. Castration responsive dermatosis in the dog. In: von Tscharner C, Halliwell REW, eds. *Advances in veterinary dermatology*. Vol 1. Philadelphia: Baillière Tindall, 1990;34–42.
17. Rijnberk A, van Herpen H, Mol JA, et al. Disturbed release of growth hormone in mature dogs: a comparison with congenital growth hormone deficiency. *Vet Rec* 1993;133:542–545.
18. Kikuchi T, Yabe S, Kanda T, et al. Antipituitary antibodies as pathogenetic factors in patients with pituitary disorders. *Endocrinol J* 2000;47:407–416.
19. Feldman EC, Nelson RW. Disorders of growth hormone. In: *Canine and feline endocrinology and reproduction*. 3rd ed. St Louis: Saunders 2004;45–83.
20. Wehrenberg WB, Janowski BA, Piering AW, et al. Glucocorticoids: potent inhibitors and stimulators of growth hormone secretion. *Endocrinology* 1990;126:3200–3203.
21. Takahashi H, Brando H, Zhang C, et al. Mechanism of impaired growth hormone secretion in patients with Cushing's disease. *Acta Endocrinol (Copenh)* 1992;127:13–17.
22. Lee WM, Meij BP, Bhatti SFM, et al. Pulsatile secretion pattern of growth hormone in dogs with pituitary-dependent hyperadrenocorticism. *Domest Anim Endocrinol* 2003;24:59–68.
23. Peterson ME, Altszuler N. Suppression of growth hormone secretion in spontaneous canine hyperadrenocorticism and its reversal after treatment. *Am J Vet Res* 1981;42:1881–1883.
24. Regnier A, Garnier F. Growth hormone responses to growth hormone-releasing hormone and clonidine in dogs with Cushing's syndrome. *Res Vet Sci* 1995;58:169–173.
25. Giustina A, Doga M, Bodini C, et al. Acute effects of cortisone acetate on growth hormone response to growth hormone-releasing hormone in normal adult subjects. *Acta Endocrinol (Copenh)* 1990;122:206–210.
26. Suda T, Demura H, Demura R, et al. Anterior pituitary hormones in plasma and pituitaries from patients with Cushing's disease. *J Clin Endocrinol Metab* 1980;51:1048–1053.
27. Schmeitzel LP, Lothrop CD. Hormonal abnormalities in Pomeranians with normal coat and in Pomeranians with growth hormone-responsive dermatosis. *J Am Vet Med Assoc* 1990;197:1333–1341.
28. Speiser PW, White PC, New MI. Congenital adrenal hyperplasia. In: James VHT, ed. *The adrenal gland*. 2nd ed. New York: Raven Press, 1992;327–371.
29. Vermeulen A, Rubens R. Adrenal virilism. In: James VHT, ed. *The adrenal gland*. 2nd ed. New York: Raven Press, 1992;413–440.
30. Frank LA, Hnilica KA, Rohrbach BW, et al. Retrospective evaluation of sex hormones and steroid hormone intermediates in dogs with alopecia. *Vet Dermatol* 2003;14:91–97.
31. 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. *Vet Dermatol* 2004;15:278–284.
32. Takada K, Kitamura H, Takiguchi M, et al. Cloning of canine 21-hydroxylase gene and its polymorphic analysis as a candidate gene for congenital adrenal hyperplasia-like syndrome in Pomeranians. *Res Vet Sci* 2002;73:159–163.
33. Paradis M. Alopecia-X. *Am Acad Vet Dermatol Newslett* 2002;summer:12–14.
34. Argyris TS. Hair growth induced by damage. *Adv Biol Skin* 1967;9:339–356.
35. Stenn KS, Paus R. Controls of hair follicle cycling. *Physiol Rev* 2001;81:449–494.
36. Ebling FJG. The hormonal control of hair growth. In: Organos CE, Happle R, eds. *Hair and hair diseases*. New York: Springer-Verlag Inc, 1990;267–299.
37. Ashley PF, Frank LA, Schmeitzel LP, et al. Effect of oral melatonin administration on sex hormone, prolactin, and thyroid hormone concentrations in adult dogs. *J Am Vet Med Assoc* 1999;215:1111–1115.
38. Ostrowska Z, Kos-Kudla B, Swietochowska E, et al. Influence of pinealectomy and long term melatonin on GH-ICF-1 axis function in male rats. *Neuroendocrinol Lett* 2001;22:255–262.
39. Pawlikowski M, Kolomecka M, Wojtczak A, et al. Effects of six months melatonin treatment on sleep quality and serum concentrations of estradiol, cortisol, dehydroepiandrosterone sulfate, and somatomedin C in elderly women. *Neuroendocrinol Lett* 2002;23(suppl 1):17–19.
40. Avelina GR, Pedrero JG, Martinez AM, et al. Melatonin blocks the activation of estrogen receptor for DNA binding. *FASEB J* 1999;13:857–868.
41. Kiefer T, Ram RT, Yuan L, et al. Melatonin inhibits estrogen receptor transactivation and cAMP levels in breast cancer cells. *Breast Cancer Res Treat* 2002;71:37–45.
42. Oh HS, Smart RC. An estrogen receptor pathway regulates the telogen-anagen hair follicle transition and influences epidermal cell proliferation. *Proc Natl Acad Sci U S A* 1996;93:12525–12530.
43. Smart RC, Oh HS, Chanda S, et al. Effects of 17-β-estradiol and ICI 182 780 on hair growth in various strains of mice. *J Invest Dermatol Symp Proc* 1999;4:285–289.
44. Botchkarev VA, Kishimoto J. Molecular control of epithelial-mesenchymal interactions during hair follicle cycling. *J Invest Dermatol Symp Proc* 2003;8:46–55.
45. Credille KM, Lupton CJ, Kennis RA, et al. The role of nutrition on the canine hair follicles: a preliminary report. In: Reinhart GA, Carey DP, eds. *Recent advances in canine and feline nutrition*. Vol III. Wilmington, Del: Orange Frazer Press, 2000;37–53.
46. Dunstan RW, Credille KM, Mansell J, et al. A common sense approach to the morphology of alopecia: addressing 10 points of follicular confusion, in *Proceedings*. 16th Annu Am Acad Vet Dermatol Am Coll Vet Dermatol Meet 2001;43–47.