

# Adrenal steroid hormone concentrations in dogs with hair cycle arrest (Alopecia X) before and during treatment with melatonin and mitotane

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**Abstract** The purpose of the study was to evaluate intermediate adrenal steroid hormones (ISH) in neutered dogs with hair cycle arrest (Alopecia X) during treatment with melatonin, and to see if hair re-growth is associated with sex hormone concentrations within the normal ranges. Twenty-nine neutered, euthyroid, and normocortisolemic dogs were enrolled in the study (23 Pomeranians, three keeshonds, two miniature poodles, and one Siberian husky). Coat assessment and an ACTH stimulation test were performed pre-treatment and approximately every 4 months for a year post treatment. Melatonin was administered initially at 3–6 mg, every 12 h. Based on clinical progression, each dog was continued on the current dose of melatonin, given an increased dose of melatonin or changed to mitotane. Partial to complete hair re-growth occurred in 14/23 Pomeranians, and partial re-growth in 3/3 keeshond and 1/2 poodle dogs. A Siberian husky dog failed to re-grow hair. Fifteen dogs had partial hair re-growth at the first re-evaluation. Melatonin dosage was increased in eight dogs but only one had improved hair re-growth. On mitotane treatment, partial to complete hair re-growth was seen in 4/6 dogs and no re-growth in 2/6 dogs. No significant decrease in sex hormone concentrations were seen during melatonin or mitotane treatment. Concentrations of ISH in dogs with hair re-growth did not differ significantly from pre-treatment values. At the completion of the study, androstenedione, progesterone and 17-hydroxyprogesterone were still above reference ranges in 21, 64 and 36%, respectively, of dogs with partial to complete hair re-growth. In conclusion, 62% of dogs had partial to complete hair re-growth. However, not all dogs with hair re-growth had concentrations of ISH within the normal range.

**Keywords:** adrenal hyperplasia-like syndrome, Alopecia X, dogs, intermediate steroid hormones, melatonin, sex hormones.

## INTRODUCTION

Alopecia X (also known as adrenal hyperplasia-like syndrome, growth hormone-responsive alopecia, biopsy-responsive alopecia, castration-responsive dermatosis, pseudo-Cushing's syndrome, etc.) is a common condition seen in miniature poodles and the Nordic and 'plush-coated' breeds.<sup>1,2</sup> The alopecia occurs in both male and female young adult dogs, regardless of their neuter status. Clinical signs consist of partial to complete alopecia of the neck, tail, caudo-dorsum, perineum, caudal thighs and ultimately trunk, sparing the head and forelimbs. In addition, the skin may become hyperpigmented, primarily in areas of alopecia.

The pathomechanism of this disease is not known. Diagnosis is based on ruling out endocrine diseases such as hypothyroidism and hypercortisolemia (e.g.

Cushing's syndrome). In addition, abnormalities of adrenal steroid intermediates (ISH) and sex hormones may be noted in affected individuals,<sup>3,4</sup> but their significance is still uncertain. Schmeitzel and Lothrop<sup>3</sup> first proposed an adrenal steroid hormone imbalance as the cause of the bilateral alopecia and hyperpigmentation in Pomeranian dogs. The authors theorized that there was a partial deficiency of the 21-hydroxylase enzyme, as described in humans, which could account for the increases in steroid hormone intermediates and the resulting alopecia.

Currently, treatments are varied. Originally, when the condition was thought to be growth hormone related, treatment with growth hormone was recommended, which resulted in hair re-growth in many cases.<sup>5</sup> Unfortunately, growth hormone is difficult to obtain and administration may result in diabetes. More recently mitotane, similar to treatment of hyperadrenocorticism, was used to treat 12 Chow Chow dogs with Alopecia X, resulting in hair re-growth in all 12.<sup>6</sup> This treatment is also not without risk. Most recently there have been anecdotal reports that melatonin administration resulted in hair re-growth in dogs receiving this therapy.<sup>7,8</sup>

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The mechanism by which melatonin may result in hair re-growth is not known. Melatonin influences reproductive development and function in a variety of species by altering gonadotropin release and sex hormone concentrations.<sup>9–11</sup> Results of a recent study showed that oral melatonin treatment at 1 mg kg<sup>-1</sup> for 28 days resulted in significant decreases in oestradiol, testosterone and dihydroepiandrosterone sulphate (DHEAS) in intact female beagles and significant decreases in oestradiol and 17-hydroxyprogesterone (17-OHP) in intact male beagles.<sup>12</sup> We theorize that melatonin could result in hair re-growth through normalization of adrenal steroid hormone intermediate and sex hormone concentrations in affected dogs.

The purpose of this study was to evaluate cortisol, sex hormone and ISH concentrations in neutered dogs with Alopecia X before and during treatment with melatonin over a 1-year period, and to see if hair re-growth is associated with concentrations within the normal ranges.

## METHODS AND MATERIALS

### *Dogs*

Twenty-nine neutered dogs (15 males, 14 females) from across the USA were enrolled in the study after physical findings supported a diagnosis of Alopecia X (an endocrine pattern of alopecia), and hypothyroidism and hyperadrenocorticism had been ruled out by the veterinarian. Hypothyroidism was excluded based on normal concentrations of thyroxine (T4) and thyrotropin (TSH) and/or lack of hair re-growth on appropriate supplementation with L-thyroxine. Hyperadrenocorticism was excluded based on lack of other clinico-pathological abnormalities and cortisol concentrations within normal range post-ACTH stimulation, or by suppression of cortisol concentrations at 8 h with the low-dose dexamethasone screening test. While the exact date of neutering was not known in all cases, only one dog was neutered within 6 months of enrollment in the study and all dogs had progression of alopecia in their current neuter status.

### *Samples*

An ACTH stimulation test was performed on all dogs by the veterinarian. Serum was collected before and 1 h after intravenous cosyntropin (Cortrosyn<sup>TM</sup>, Organon, Inc., West Orange, NJ, USA) administration at 5 µg kg<sup>-1</sup>. This dose has been shown to maximally stimulate cortisol production of the adrenal glands.<sup>13</sup> Serum samples were frozen and shipped overnight on ice to the clinical endocrinology laboratory at the University of Tennessee College of Veterinary Medicine. Serum samples were analysed for progesterone (Progesterone [<sup>125</sup>I] radioimmunoassay; Diagnostic Products, Los Angeles, CA, USA), 17-OHP (17-OHP [<sup>125</sup>I] radioimmunoassay; ICN Pharmaceuticals, Costa Mesa, CA, USA), testosterone (Testosterone [<sup>125</sup>I] radioimmunoassay; Diagnostic Products), androstenedione (Androstenedione [<sup>125</sup>I] radioimmunoassay; ICN Pharmaceuticals), oestradiol

(Oestradiol 17-beta [<sup>125</sup>I] radioimmunoassay; ICN Pharmaceuticals) and cortisol (Cortisol [<sup>125</sup>I] radioimmunoassay; Diagnostic Products) concentrations. These tests have been validated in the dog.<sup>14</sup>

After the initial stimulation test, dogs were started on oral melatonin at a dose of 3–6 mg twice daily (≤ 15 kg of body weight, 3 mg twice daily; > 15 kg, 6 mg twice daily).<sup>7</sup> For each dog, an ACTH stimulation test was repeated approximately every 4 months for three additional samplings. The hair coat was assessed by the veterinarian at each visit according to the following two criteria: the percentage of body affected (< 25, 25–50, 50–75, > 75%) and the quality of new hair (1, fine undercoat; 2, moderate undercoat and guard hairs but did not return to normal; 3, total normalization of coat). At each visit a decision was made, based on hair re-growth and the owner's wish, to remain on the current dose of melatonin, increase the dose of melatonin (≤ 15 kg, 4.5 mg twice daily; > 15 kg, 9–12 mg twice daily) or change treatment to mitotane at 25 mg kg<sup>-1</sup>, orally, every 24 h or divided every 12 h for 5–7 days followed by 25 mg kg<sup>-1</sup>, orally, divided twice weekly as maintenance.

### *Data analysis*

Dogs were classified into one of three groups based on hair re-growth and quality of new hair: no hair re-growth (percentage of body area affected was unchanged and either no hair re-growth or quality of hair re-growth was scored as a 1); partial hair re-growth (percentage of body area affected decreased and quality of hair re-growth scored as a 2 or 3); or complete hair re-growth (< 25% of the body area remained affected and quality of hair re-growth scored as a 2 or 3).

For individual dogs, it was determined whether each hormone concentration was greater than the normal hormone ranges recently established.<sup>14</sup> These numbers were then tabulated as to percentage of dogs with abnormalities for a given hormone. Descriptive comparisons were made among the three groups (no hair re-growth, partial hair re-growth, complete hair re-growth).

To evaluate whether melatonin altered steroid hormone intermediate and sex hormone concentrations, paired *t*-tests were used to compare baseline and post-ACTH stimulation steroid hormone intermediates between pre-treatment and first re-evaluation, when all dogs were on melatonin (Sigmastat® 2.0 for Windows, SPSS Inc., Chicago, IL, USA). To determine whether hair re-growth was associated with a change in hormone concentrations, cortisol, steroid hormone intermediate and sex hormone concentrations for Pomeranian dogs in each category (no hair re-growth, partial hair re-growth, complete hair re-growth) were compared to their pre-treatment concentrations using paired *t*-tests. This allowed each dog to serve as its own control. To evaluate whether there was a difference in hormone concentrations before or after treatment among dogs with no, partial, or complete hair re-growth, ANOVA was run on all hormone concentration data from the initial to final evaluations. Because of apparent differences

in steroid hormone intermediate and sex hormone concentrations among breeds,<sup>4</sup> Pomeranian dogs were the only breed included in all analyses.

## RESULTS

Twenty-three Pomeranian dogs (9 female, 14 male), three female keeshond dogs, two miniature poodle dogs (one female, one male) and one female Siberian husky dog were enrolled in the study. A total of 25 dogs (20 Pomeranians, three keeshonds, one miniature poodle and one Siberian husky) had at least two re-evaluations, and 23 dogs completed the 1-year study. The median age of dogs upon entering the study was 4 years, with a range of 1.5–11 years. The median age at which clinical signs began was also 4 years (range 10 months to 10 years) and the median duration of clinical signs was 5.5 months (range 2 weeks to 3 years). The mean initial melatonin dosage for Pomeranians and poodles was 1.4 mg kg<sup>-1</sup>, every 12 h (range 0.5–4.4 mg kg<sup>-1</sup>, every 12 h) and for keeshonds and the Siberian husky was 0.3 mg kg<sup>-1</sup>, every 12 h (range 0.2–0.4 mg kg<sup>-1</sup>, every 12 h).

Complete hair re-growth (defined as < 25% of the body affected and moderate undercoat with partial to complete guard hair re-growth) was seen in 4/23 Pomeranian dogs and partial hair re-growth in 10/23, 3/3 keeshonds, and 1/2 miniature poodles during the study. Therefore, a total of 18/29 (62%) had partial to complete hair re-growth during the initial melatonin treatment. Of these 18 dogs, 15 (11 Pomeranians, three keeshonds, and one miniature poodle) showed only partial hair re-growth (none had complete hair re-growth) at the first re-evaluation after approximately 4 months of therapy. Three Pomeranian dogs with no hair re-growth at the first re-evaluation had partial to complete hair re-growth on continued melatonin treatment (one had partial re-growth of hair and one had complete re-growth of hair by the 8-month re-evaluation, and one had partial re-growth of hair by the 12-month re-evaluation). Two Pomeranian dogs

with partial hair re-growth at the 4-month re-evaluation had complete hair re-growth on continued melatonin treatment (one by the 8-month re-evaluation and one by the 12-month re-evaluation). The mean initial melatonin dosage received by Pomeranian dogs with partial to complete hair re-growth was 0.7 mg kg<sup>-1</sup>, every 12 h whereas the mean initial melatonin dosage received by Pomeranian dogs that failed to re-grow hair was 1.2 mg kg<sup>-1</sup>, every 12 h. Melatonin dosage was increased in eight dogs with no or partial hair re-growth (five Pomeranian dogs, mean dosage 1.6 mg kg<sup>-1</sup>, every 12 h, and all three keeshonds, mean dosage 0.5 mg kg<sup>-1</sup>, every 12 h). One Pomeranian with partial hair re-growth had complete re-growth of hair following increased dosage of melatonin (from 0.73 to 1.1 mg kg<sup>-1</sup>, every 12 h).

Adverse events reported while the dogs were receiving melatonin were all in keeshond dogs. Two dogs had occasional lethargy; one had increased flatulence.

Baseline ISH and sex hormone concentrations after 4 months of melatonin treatment were not significantly decreased in relation to pre-treatment values (Table 1). Post-stimulation 17-OHP was significantly increased after 4 months of melatonin treatment compared with the pre-treatment concentrations. This hormone was higher than reference ranges in the baseline samples, although this was not statistically significant.

Mitotane was used to treat six Pomeranian dogs whose hair either failed to re-grow (five dogs) or exhibited partial hair re-growth (one dog) while receiving melatonin. Of the five dogs whose hair failed to re-grow while receiving melatonin, two exhibited complete hair re-growth, one partial hair re-growth and two failed to re-grow hair while receiving mitotane. The dog that exhibited partial hair re-growth while receiving melatonin had complete hair re-growth while receiving mitotane.

Mitotane did not always result in suppression of cortisol, ISH or sex hormone concentrations. The two dogs that failed to re-grow hair while receiving mitotane and two of the three dogs with complete hair re-growth while receiving mitotane had cortisol concentrations post-ACTH stimulation greater than

**Table 1.** Mean (SD) cortisol (ng mL<sup>-1</sup>) and adrenal steroid hormone concentrations (ng mL<sup>-1</sup>) (baseline and post-ACTH stimulation) pre-treatment and after 4 months of melatonin

Hormone	Pre-treatment		On melatonin		Normal range	
	Base	Post	Base	Post	Base	Post
Cortisol	49.9 (27.9)	151.9 (38.0)	56.6 (33.1)	149.5 (28.7)	2.2–58.8	70.6–167.5
Androstenedione	12.4 (12.4)	34.6 (32.3)	11.2 (12.8)	29.5 (20.6)	0.7–5.85	5.9–47.6
Oestradiol (pg mL <sup>-1</sup> )	47.5 (19.8)	46.0 (16.9)	47.5 (15.4)	45.4 (13.3)	29.0–69.6	25.7–69.2
Progesterone	0.46 (0.36)	2.27 (0.80)	0.61 (0.49)	2.26 (0.71)	0.01–0.17	0.31–1.48
Testosterone	0.04 (0.06)	0.04 (0.05)	0.03 (0.01)	0.03 (0.02)	0.01–0.12	0.02–0.10
17-OH Progesterone	0.30 (0.24)	2.03* (1.06)	0.50 (0.54)	2.74* (1.92)	0.03–0.37	0.32–2.76

\*Statistical significance:  $P < 0.05$ .

**Table 2.** Mean (SD) cortisol (ng mL<sup>-1</sup>) and adrenal steroid hormone concentrations (ng mL<sup>-1</sup>) before and post-ACTH stimulation of Pomeranian dogs with complete hair re-growth, partial hair re-growth or no hair re-growth as compared to their pre-treatment values

Hormone	Complete hair re-growth†				Partial hair re-growth‡				No hair re-growth§			
	Pre-treatment		Final sample		Pre-treatment		Final sample		Pre-treatment		Final sample	
	Base	Post	Base	Post	Base	Post	Base	Post	Base	Post	Base	Post
Cortisol	40.3 (4.6)	149.7 (33.4)	38.6 (19.9)	123.9 (40.2)	58.5 (35.0)	166 (47.7)	51.7 (40.5)	132 (53.3)	53 (32.1)	140 (24.3)	71.5 (50.6)	143.3 (23.9)
Androstenedione	9.2 (6.8)	38.4 (21.4)	8.4 (9.7)	31.3 (24.1)	13 (12.7)	46.6 (45.8)	15.5 (14.7)	27.5 (21.2)	10.5 (6.5)	21.5 (10.6)	14.7 (10.6)	45.5 (39.7)
Oestradiol (pg mL <sup>-1</sup> )	32.7* (12.2)	35.5* (8.8)	46.4 (17.2)	40.2 (17.1)	52.5* (13.6)	49.8* (12.4)	58.9 (11.6)	55.6 (10.2)	39.6 (10.1)	36.7 (8.3)	44.7 (11.4)	37.4 (10.3)
Progesterone	0.25 (0.12)	2.12 (1.23)	0.47 (0.54)	1.97 (0.82)	0.57 (0.40)	2.61 (0.62)	0.60 (0.33)	1.93 (0.83)	0.56 (0.40)	2.25 (0.74)	0.82 (0.70)	1.98 (0.59)
Testosterone	0.07 (0.13)	0.07 (0.11)	0.04 (0.02)	0.05 (0.02)	0.03 (0.01)	0.03 (0.02)	0.04 (0.02)	0.04 (0.02)	0.03 (0.01)	0.03 (0.01)	0.02 (0.01)	0.03 (0.01)
17-OH Progesterone	0.29 (0.23)	2.58 (1.51)	0.75 (0.94)	4.22 (3.69)	0.30 (0.24)	2.10 (1.03)	0.39 (0.29)	2.65 (2.37)	0.37 (0.27)	1.78* (0.80)	0.68 (0.52)	3.01* (0.94)

\*Statistical difference:  $P < 0.05$ .

† $< 25\%$  of the body area remained affected with moderate undercoat and partial to complete guard hair re-growth.

‡Percentage of body area affected decreased with moderate undercoat and partial to complete guard hair re-growth in haired areas.

§Percentage of body area affected was unchanged and either no hair or only fine undercoat re-growth.

100 ng mL<sup>-1</sup>. Both dogs whose cortisol suppressed on mitotane to  $< 30$  ng mL<sup>-1</sup> post-ACTH stimulation (one with partial hair re-growth and one with complete hair re-growth) had baseline concentrations of androstenedione, progesterone and 17-OHP greater than the normal range at all sampling times.

Pre-treatment baseline concentrations of androstenedione were above reference range in 65.2%, progesterone in 68.2% and 17-OHP in 34.8% of Pomeranian dogs. Only one Pomeranian dog each had above reference range concentrations of oestradiol and testosterone. Post-ACTH stimulation concentrations of androstenedione and 17-OHP were above reference range in 26.1% and progesterone was above reference range in 86.4% of Pomeranian dogs. At the completion of the study 9/14 (64%) of Pomeranian dogs with partial to complete hair re-growth had post-stimulation progesterone concentrations, 5/14 (35.7%) had post-stimulation 17-OHP concentrations and 3/14 (21.4%) had post-stimulation androstenedione concentrations above the reference range.

Cortisol, ISH and sex hormone concentrations in Pomeranian dogs with partial or complete hair re-growth were not significantly different from pre-treatment concentrations (Table 2). Post-stimulation 17-OHP was significantly increased ( $P < 0.05$ ) in dogs that failed to re-grow hair on treatment as compared to pre-treatment concentrations. Pre-treatment oestradiol concentrations were significantly different between groups at the start of the study so no conclusions can be drawn about changes during the study. No other differences among the groups were detected.

## DISCUSSION

Alopecia X is so named because the syndrome is associated with truncal hair loss but the pathogenesis of the

alopecia is unknown. The literature describes the condition as occurring in young adults between 1 and 3 years of age. In our study, the median age of onset of clinical signs was 4 years with a range of 10 months to 10 years, which is older than previous reports.<sup>1,2</sup>

A number of hormone abnormalities were present in dogs with Alopecia X enrolled in the study, with the most frequent being increased concentrations of progesterone, androstenedione and 17-OHP, similar to previous findings.<sup>3,4</sup> In agreement with our previous study,<sup>4</sup> not all dogs with Alopecia X exhibited adrenal steroid hormone concentrations above the reference range. The role that increases in steroid hormone intermediates and sex hormones play with regard to the pathogenesis of this syndrome is unknown.

Melatonin is a neurohormone produced in all vertebrate species by the pineal gland in response to darkness and decreasing day length.<sup>15-17</sup> Melatonin therefore controls the circadian and seasonal reproductive and hair growth cycles. In a previous study, melatonin treatment for 28 days resulted in decreases in oestradiol, testosterone and DHEAS in intact female dogs, and decreases in oestradiol and 17-OHP in intact male dogs.<sup>12</sup> We hypothesized that it is through the alterations in sex hormones that melatonin may influence hair growth in dogs. In this study there were no significant decreases in hormone concentrations after 4 months of melatonin treatment at the prescribed dosage and regimen. This difference between the two studies may be related to the fact that our study utilized only neutered dogs, and melatonin's primary influence on sex hormones is via gonadotropin secretion and their effect on gonadal production of sex hormones. It is also possible that we failed to detect biologically relevant differences as significant because of insufficient power.

Melatonin may also inhibit ACTH-stimulated cortisol production by the adrenal glands; however, this is

controversial. While melatonin receptors have recently been identified in primate adrenal cortices,<sup>18</sup> studies in rats, horses and humans in which melatonin and cortisol were compared under various natural and experimental conditions failed to show an association between the two hormones.<sup>19–21</sup> In our study, cortisol concentrations in dogs after 4 months of melatonin were similar to their pre-treatment values.

During the treatment regimen with melatonin there was partial to complete hair re-growth in 62% of dogs with Alopecia X; however, hair re-growth in individual dogs was not associated with changes in cortisol or steroid hormone intermediate concentrations. Only 17-OHP was significantly increased in dogs that failed to re-grow hair compared with pre-treatment concentrations. However, even this was not significantly different from dogs with partial or complete hair re-growth. The hormone concentration of 17-OHP was not within the normal range in dogs with hair re-growth indicating that the concentration of this ISH is not associated with either hair re-growth or melatonin treatment.

Not all dogs with Alopecia X re-grew hair while on melatonin. Possible explanations include incorrect dosage and poor absorption of the drug. Because melatonin is classified as a nutraceutical, there is a lack of standardization of the product, which may result in variable drug content in the preparation, as well as variable absorption and bioavailability. There was no attempt to standardize the product used in our study, and serum melatonin concentrations were not measured. The third, and probably most important factor, involves the timing of melatonin administration. In studies with humans, ponies and sheep in which melatonin was administered orally, melatonin was given in the evening preceding nightfall or after 8 h of daylight to mimic a shortened daylength.<sup>20–22</sup> In our study, although medications were given twice daily, no specific recommendations were given as to the timing of the evening dose. The seasonal timing of treatment also appears to be important in other species such as Cashmere goats<sup>23,24</sup> and horses.<sup>25</sup> In our study, dogs were entered into the study throughout the year, were from many different parts of the United States, and had different environmental influences depending on whether they resided primarily indoors or outdoors. If a seasonal effect existed, it would not have been possible to detect because of the number of variables present.

Mitotane was used to treat six dogs in which hair re-growth did not occur while receiving melatonin. Partial to complete hair re-growth was noted in 4/6 dogs. Mitotane has a direct toxic effect on the adrenal cortex, resulting in destruction of the zonae fasciculata and reticularis.<sup>26,27</sup> In addition to the cytotoxic effect, mitotane also interferes with steroid biosynthesis by inhibiting the 11 $\beta$ -hydroxylase enzyme.<sup>26,27</sup> The net result is decreased cortisol secretion. The cytotoxic mechanism should result in decreased secretion of all precursors of cortisol. However, the 11 $\beta$ -hydroxylase enzyme just precedes cortisol production. Therefore, its inhibition alone should not result in decreased concentrations of

ISH. It has been observed by one of the authors (JWO) through experience running these assays that androstenedione, progesterone and 17-OHP are routinely suppressed similar to cortisol by mitotane, whereas oestradiol may be resistant to the drug's effect (unpublished observation). In our study, neither cortisol nor ISH were suppressed in all dogs, whether or not there was hair re-growth. It is possible that the hormone which influences hair re-growth was not measured, or that there was a substantial decrease in the total daily production of cortisol or one of its precursors not reflected in a one-time measurement. It is also possible that, despite the known action of mitotane on the adrenal, effects on hair growth are not hormone dependent.

Most of the studies that discussed hair growth in experimental animals used exogenous hormones or surgical ablation to manipulate a *normal* cycling follicle.<sup>20,23,24,28–34</sup> Hair follicles from dogs with Alopecia X do not appear to be cycling normally. Results of the present study suggest that hair re-growth in dogs with Alopecia X is not mediated through alterations in adrenal steroid hormone concentrations.

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**Résumé** Le but de cette étude était d'évaluer les taux d'hormones stéroïdes d'origine adrénaliennne chez des chiens castrés, présentant un arrêt du cycle folliculaire (alopécie X) pendant un traitement avec la mélatonine, et de corrélér la repousse pilaire avec les modifications des taux d'hormones sexuelles. Vingt-neuf chiens stérilisés, euthyroïdes et normo-cortisolémiques ont été étudiés (23 Pomeranians, 3 keeshonds, 2 Caniche, et un Siberian husky). Une évaluation du pelage et un test de stimulation à l'ACTH ont été réalisés avant traitement et environ tous les 4 mois pendant un an. La mélatonine a été administrée initialement à la dose de at 3–6 mg, deux fois par jour. En fonction du résultat clinique, la posologie a été maintenue, augmentée, ou le traitement a été changé pour le mitotane. Le traitement avec la mélatonine a permis une repousse partielle ou complète des poils chez 14/23 Poméranians, et une repousse partielle chez 3/3 keeshond et 1 Caniche sur deux. Un Siberian husky n'a

pas présenté de repousse pilaire. Quinze chiens avaient une repousse partielle à la première ré-évaluation. La dose de mélatonine a été augmentée chez 8 chiens, avec un résultat médiocre (amélioration de la repousse pilaire chez 1 Poméranien). Le mitotane a permis une repousse partielle ou complète chez 4/6 chiens et n'a pas été efficace dans 2 cas sur 6. La mélatonine, à la dose utilisée, n'a pas diminué significativement les taux d'hormones sexuelles. Les concentrations hormonales chez les chiens dont le poil a repoussé n'étaient pas significativement différentes de celles avant traitement. A la fin de l'étude, l'androstenedione, la progestérone, et la 17-hydroxyprogestérone étaient augmentées chez 21%, 64%, et 36%, respectivement, des chiens avec une repousse pilaire partielle ou complète. En conclusion, 62% des chiens ont présenté une repousse pilaire partielle ou totale avec la mélatonine; cependant la repousse pilaire n'était pas liée à des modifications des concentrations en hormones sexuelles.

**Resumen** El propósito de este estudio fue evaluar las hormonas esteroideas adrenales intermediarias en perros castrados con parada de ciclo celular (Alopecia X) durante el tratamiento con melatonina, y correlacionar el recrecimiento del pelo con cambios en las concentraciones de hormonas sexuales. El estudio incluía veintinueve perros castrados, eutiroides y normo-cortisolémicos (23 Pomeranios, 3 keeshonds, 2 caniches miniatura, y un husky Siberiano). Se llevó a cabo una revisión del estado del pelo y un test de estimulación de ACTH aproximadamente cada 4 meses durante un año. Se administró melatonina inicialmente a 3–6 mg, q 12 hr. Basándonos en la evolución clínica, se continuó con igual dosis de melatonina, una dosis aumentada, o se cambió a mitotane. El tratamiento con melatonina se asoció a un recrecimiento del pelo parcial a completo en 14/23 Pomeranios, un recrecimiento parcial en 3/3 keeshonds y 1/2 caniches. A un husky siberiano no le volvió a crecer el pelo. Quince perros mostraron un recrecimiento parcial después de la primera reevaluación. Se incrementó la dosis de melatonina en 8 perros con efectos mínimos (mejora en el recrecimiento del pelo en 1 Pomeranio). El mitotane produjo un recrecimiento parcial a completo en 4/6 perros y no produjo recrecimiento en 2/6 perros. La melatonina, a las dosis empleadas, no redujo significativamente las concentraciones de hormonas sexuales. Las concentraciones en hormonas esteroideas intermediarias en perros con recrecimiento de pelo no fueron significativamente diferentes de los valores anteriores al tratamiento. Al final del estudio la androstenediona, progesterona, y la 17-hidroxiprogesteron de los perros con recrecimiento parcial a completo de pelo, se encontraban incrementadas un 21%, 64%, y 36%, respectivamente. En conclusión, el 62% de los perros mostraron recrecimiento de pelo parcial a completo mientras fueron tratados con melatonina; sin embargo, el recrecimiento no se encontraba correlacionada con alteraciones en las concentraciones de hormonas esteroideas intermedias.

**Zusammenfassung** Ziel der Studie war, bei kastrierten Hunden mit Haarzyklusarrest (Alopecia X) während der Therapie mit Melatonin adrenele Steroidhormonzwischenprodukte auszuwerten und erneutes Haarwachstum mit Veränderungen von Geschlechtshormonkonzentrationen in Beziehung zu setzen. Neunundzwanzig kastrierte, euthyreote und normocortisolämische Hunde wurden in die Studie aufgenommen (23 Pomeranians, 3 Keeshonds, 2 Zwergpudel und ein Sibirischer Husky). Beurteilung des Haarkleides und ACTH-Stimulationstest wurden vor der Behandlung und ca. alle 4 Monate für ein Jahr durchgeführt. Zu Beginn wurde Melatonin in einer Dosis von 3-6mg alle 12 Stunden gegeben. Je nach klinischer Verbesserung wurde die gleiche Dosis fortgesetzt, erhöht oder zu Mitotane gewechselt. Melatoninbehandlung war bei 14/23 Pomeranians mit vollständigem Wiederwachsen der Haare, bei 3/3 Keeshonds und 1/2 Pudeln mit partiellen Wiederwachsen der Haare verbunden. Bei einem Sibirischen Husky wuchsen die Haare nicht mehr nach. 15 Hunde zeigten bei der ersten Kontrolle erneutes Haarwachstum. Bei 8 Hunden wurde die Melatoninindosierung mit minimalem Effekt erhöht (verbessertes Haarwachstum bei einem Pomeranian). Mitotane führte bei 4/6 Hunden zu partiellem bis komplettem Neuwachstum der Haare und keinem erneutem Haarwachstum bei 2/6 Hunden. Mit den verwandten Melatoninindosierungen konnte keine signifikante Verminderung der Geschlechtshormone erzielt werden. Konzentrationen von Steroidhormonzwischenprodukten bei Hunden, die erneutes Haarwachstum zeigten unterschieden sich von Werten vor der Behandlung nicht signifikant. Bei Beendigung der Studie waren Androstendion, Progesteron und 17-hydroxy-Progesteron bei 21%, 64% bzw. 36% der Hunde mit partiellen Neuwachstum der Haare erhöht. Als Schlußfolgerung läßt sich sagen, daß 62% der Hunde während der Behandlung mit Melatonin partielles bis komplettes Neuwachstum an Haaren zeigte; jedoch war das Nachwachsen der Haare nicht mit Veränderungen der Konzentrationen an Steroidhormonzwischenprodukten korreliert.