

# The evaluation of Canine Atopic Dermatitis Extent and Severity Index (CADESI) test in dogs with Atopic Dermatitis (AD) treated with cyclosporine or prednisone

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## Abstract

The purpose of this study was to assess the clinical state of dogs with atopic dermatitis (AD) by use of CADESI test in own modification during the first visit in the Dermatology Consult Room as well as during the treatment. The study was performed in two groups (I-E and II-C) of 20 dogs in each group. In dogs which were qualified to the I-E group, as antiallergic, anti-inflammatory and antipruritic treatment, prednisone (oral preparation Encorton – Polfa Pabianice) at dose 0.5 mg/kg b.w./day was administered, while in dogs qualified to the II-C group – cyclosporine (oral preparation Sandimmun Neoral – Novartis Pharma) at a dose of 5 mg/kg b.w./day; the treatment was continued for 6 weeks in both groups. During the study, skin lesions were assessed in 15 specified body areas using 4 parameters and 5-point scale. In group I-E and II-C the amount of received points in CADESI test was decreased by 82.26% and by 83% respectively, after the treatment. Statistical analyses of the results obtained revealed no statistically significant ( $P=0.05$ ) differences between means of I-E and II-C groups in consecutive examinations, which indicates comparable clinical efficacy of both drugs. Statistically significant differences ( $P=0.05$ ) of the parameters assessed were found after secondary dermatoses treatment, and after every two weeks of antipruritic and anti-inflammatory treatment.

**Key words:** CADESI, canine atopic dermatitis, AD, prednisone, cyclosporine

## Introduction

Atopic dermatitis in dogs (AD) is erythematous pruritic disease with recurrent, chronic course, characterized by typical morphology and localization of skin lesions. According to published data (Nesbitt 1978, Nesbitt et al. 1984, Scott et al. 2001, Marcella

et al. 2006), 10 to 30% of dogs is affected with the disease, of which in 80%, clinical signs are present throughout the year, therefore patients affected by AD require long-term treatment, mostly lifelong.

According to definition approved by the American College of Veterinary Dermatology (Olivry 2001), atopic dermatitis is “a genetically-predisposed inflam-

matory and pruritic allergic skin disease associated most commonly with IgE antibodies to environmental allergens” such as dust mites, pollens of grass, trees, weeds, fungus, moulds as well as epidermic allergens.

Actual knowledgebase according aetiology, pathogenesis, epidemiology, clinical signs and treatment of the disease is not sufficient, what results in recognizing the disease as incurable. Wide variety of AD clinical signs induced investigators to elaborate the clinical criteria simplifying the diagnostic of disease. They were first published by Willemse (1984, 1986). Features are divided into two groups: major and minor; a dog is diagnosed as afflicted if at least three major and three minor features are found. This criteria have been successively supplemented by other authors. Prelaud et al. (1998) suggested five typical features, characteristically in atopic patient, from which three must be met to set the diagnosis of atopic dermatitis.

Criteria proposed by Willemse (1984, 1986) or Prelaud et al. (1998) are in use nowadays and allow to set the diagnosis of AD in dogs, but they are inadequate to assess patient's clinical signs (DeBoer and Hiller 2001), thereby they are insufficient to objective assessment of therapy.

Therefore, in the nineties of the twentieth century, CADESI test was interposed in veterinary as a objective method of assessment of the severity of disease. It is based on test used in human medicine (Kunz et al. 1997, Gliński et al. 2004) – SCORAD (Severity Scoring of Atopic Dermatitis), in which dermatitis immensity is assessed in scale 0 to 100% in 11 body regions affected by disease. Severity of disease is assessed in scale 0 to 3 and includes six clinical parameters: erythema, erosions, lichenification, papules/oedema, crusts/oozing and skin dryness. Olivry et al. (1997) published the first version of CADESI 01 test for veterinary medicine, which proposed the assessment of skin lesions (erythema, excoriations, lichenification) in 23 body regions. Modification of this test was published by Olivry et al. (2002) as CADESI 02. Currently in veterinary dermatology several versions of CADESI test are used, from which two are the most popular. The test proposed by Germain et al. (2005) is based on the assessment of 3 parameters (erythema, excoriations, lichenification) in 4-points scale from 0 to 3 in 4 body areas (muzzle, feet, axillae and groins). Olivry et al. (2008) suggested to introduce CADESI-03 assessing 4 parameters in a scale from 0 to 5 in 62 body regions. In the own study, the Author used CADESI test in modification worked out in the Sub-department of the Clinical Diagnostics and Veterinary Dermatology, University of Life Sciences in Lublin (Poland), which was applied to clinical assessment of young dogs (1-3 years) affected by atopic dermatitis (AD).

The purpose of the present study was the assessment of clinical signs of dogs with AD using CADESI test in the day of the first visit in consulting room and during the treatment.

## Materials and Methods

The study was performed in 2 groups of dogs (20 animals in each group) affected by AD (I-E and II-C) patients of the Dermatology Consult Room of the Veterinary Clinics in the University of Life Sciences in Lublin (Poland).

Group I-E comprised 9 bitches and 11 dogs of various breeds: 5 American Staffordshire Terriers, 3 German Shepherds, 2 crossbreeds, 2 Boxers, 2 West Highland White Terriers and one each of Chow-Chow, Rhodesian Ridgeback, English Bulldog, Beagle, Fox Terrier and Shar-Pei breed.

Group II-C included 7 bitches and 13 dogs of following breeds: 6 American Staffordshire Terriers, 2 mongrels, 2 French Bulldogs, 2 Labradors and one each of German Shepherd, Fox Terrier, Doberman, Central Asian Shepherd, Bernese Mountain Dog, Dalmatian, Cane Corso and Dogo Argentino.

Age of dogs varied between 1.3 and 3.2 years. Average age in the I-E group was 2.4 years, and in II-C group – 2.6 years.

Treatment of secondary dermatoses was performed with the use of antibacterial and antifungal medicines selected individually in relation to the patient's clinical state. The dogs qualified to the I-E group, were administered prednisone (oral preparation Encorton-Polfa Pabianice) at a dose of 0.5 mg/kg b.w./day, and the dogs of the II-C group were treated with cyclosporine (oral preparation Sandimun Neoral -Novartis Pharma) at the dose of 5 mg/kg b.w./day for six weeks in both groups as antiallergic, anti-inflammatory and antipruritic treatment.

During the study, 15 body regions based on Willemse (1984, 1986) and Prelaud et al. (1998) clinical features were clinically inspected: ear auricles, eyes and eyelids, muzzle, chin, interdigital spaces of front and hind feet, axillae, groins and “others” – neck, anus, abdomen and chest. Symmetrically localized body parts were investigated separately i.e. left and right.

4 types of skin lesions: erythema, other primary efflorescences, secondary efflorescences and skin lichenification were assessed in 0-4 scale depending of severity.

Erythema scoring used:

0 – none

1 – erythematous macula without visible oedema

2 – erythema without visible oedema, with elevated temperature towards surrounding tissues

3 – erythema with clearly visible inflammatory oedema

4 – erythema with clearly visible inflammatory oedema, with incidental efflorescences

Primary and secondary efflorescences scoring used:

0 – none

1 – one type of efflorescence except erythema: papules as primary efflorescence or squamas as secondary efflorescence

2 – two types of efflorescences except erythema incidentally present on the skin: papules and pustules as primary efflorescences or squamas and crusts as secondary efflorescences

3 – three types of efflorescences except erythema incidentally present on the skin: papules, pustules and nodules as primary efflorescences or squamas, crusts and erosions as secondary efflorescences

4 – four types of efflorescences except erythema incidentally present on the skin: papules, pustules, nodules and furuncles as primary efflorescences or squamas, crusts, erosions and ulcers as secondary efflorescences

Skin lichenification scoring used:

0 – none

1 – accentuated skin markings

2 – accentuated skin markings and hyperpigmentation

3 – accentuated skin markings, hyperpigmentation and hyperplasia

4 – accentuated skin markings, hyperpigmentation and hyperplasia, with visible loss of skin flexibility, and coexisting ruptures and fissures

CADESI assessment was performed on four occasions:

Examination 0 – the day of first visit in a consulting room.

Examination 1 – after completion of secondary dermatoses treatment with use of oral antibiotics, shampoos, creams, lotions containing no glucocorticosteroids or immunomodulating and antihistaminic compounds.

Examination 2 – after two weeks of treatment with the use of prednisone (I-E group) or cyclosporine (II-C group).

Examination 3 – after six weeks of treatment anti-inflammatory and antipruritic treatment with the use of prednisone (I-E group) or cyclosporine (II-C group).

### Statistical analysis

The results were analyzed statistically using Excel 2007 and STATISTICA9 PL software. The data investigated were typically distributed. Arithmetical means

( $\bar{x}$ ) and standard deviations ( $\pm$  SD) were determined in investigated groups and in subsequent measurements. Test t-Student was used to assess the difference between means in investigated groups and in subsequent measurements. T Critical Value and F variance value were investigated. The significance level was set at  $P \leq 0.05$ .

### Results

In the examination 0, the dogs qualified to the I-E group obtained total 1285 points, while to the II-C group – 1423. These results are presented in Table 1. In both I-E and II-C groups the dogs obtained most of points from the assessment of erythema – 529 points (41.17% of total points received by group) and 518 points (36.4%), respectively.

After the treatment, in I-E group the total sum of points obtained from CADESI test decreased from 1285 to 228 i.e. by 82.26%. In II-C group the results were similar – the total sum of points decreased from 1423 to 242 i.e. by 83%.

During examination 1, the significant reduction of primary efflorescences and skin erythema were ascertained. In I-E group, points obtained from assessing primary efflorescences was reduced from 268 to 19 i.e. by 93%, and in II-C group was reduced from 249 to 16 i.e. by 93.6%; whereas erythema was reduced by 30% and 24%, respectively.

At the same time, in both investigated groups, points assessing secondary efflorescences and clinical signs of lichenification were increased.

CADESI assessment in examination 2, i.e. two weeks after anti-inflammatory and antipruritic treatment, revealed the elimination of primary efflorescences and reduction of erythema, secondary efflorescences and lichenification both in group I-E and II-C. Overall, observed points reduction in I-E group was by 64.5% with reference to examination 1, and in II-C group by 71.5%.

No primary efflorescences were found in dogs of I-E group in examination 2, and erythema reduction was by 59.5%, secondary efflorescences by 55.1% and signs of skin lichenification by 44.6% in comparison with those observed in examination 1. However, in II-C group the reduction of erythema was by 75% against examination 1, secondary efflorescences by 56.2% and lichenification signs by 47.6%. One primary efflorescence was also found.

In dogs qualified to I-E group in examination 3, the clinical state was assessed with the use of CADESI test to 228 points, and in II-C group to 242 points. In both groups, most points were gained during the assessment of lichenification – in I-E group it was 47.81% of total points of examination 3, and in

Table 1. Results of CADESI test in dogs with atopic dermatitis qualified to groups I-E and II-C during the study.

Examination	Group	Erythema sum of points, (% total points)	Primary efflorescences sum of points, (% total points)	Secondary efflorescences sum of points, (% total points)	Lichenification sum of points, (% total points)	Total (max=4800)
0	I-E	529 (41.17%)	268 (20.86%)	270 (21.01%)	218 (16.96%)	1285
	II-C	518 (36.4%)	249 (17.5%)	323 (22.7%)	333 (23.4%)	1423
1	I-E	375 (37.42%)	19 (1.9%)	314 (31.34%)	294 (29.34%)	1002
	II-C	395 (37.84%)	16 (1.53%)	299 (28.64%)	334 (31.99%)	1044
2	I-E	152 (33.33%)	0 (0%)	141 (30.92%)	163 (35.75%)	456
	II-C	99 (24.38%)	1 (0.25%)	131 (32.27%)	175 (43.1%)	406
3	I-E	68 (29.82%)	0 (0%)	51 (22.37%)	109 (47.81%)	228
	II-C	61 (25.21%)	0 (0%)	57 (23.55%)	124 (51.24%)	242

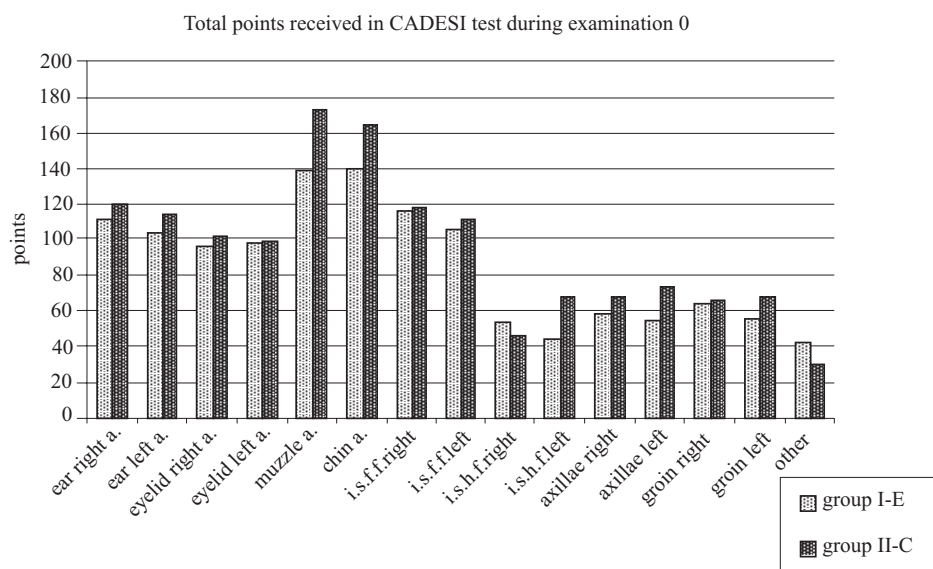


Fig. 1. Results of CADESI test in fixed localisation of skin lesions during examination 0 obtained from dogs qualified to I-E and II-C groups.

Explanation:

ear right/left a. – ear auricles right/left area

eyelids right/left a. – eyes and eyelids right/left area

muzzle/chin a. – muzzle/chin area

i. s. f. f. right/left – interdigital spaces of front feet right/left

i. s. h. f. right/left – interdigital spaces of hind feet right/left

other – neck, anus, abdomen, chest area

II-C group- 51.24%. In I-E group the reduction of erythema was by 81.9% with reference to examination 1, secondary efflorescences by 83.8% and skin lichenification by 62.9%. Instead, the results obtained in II-C group revealed erythema reduction by 84.6%, secondary efflorescences by 81.9% and skin lichenification by 62.9%, in comparison with that found in the examination 1.

In assessment of localization of skin lesions in examination 0, in dogs qualified to both group I-E and IIC, skin lesions was observed mostly on the muzzle,

on the chin, on the ear auricles, around eyes and in interdigital spaces of front feet (Fig. 1).

Examination 3 conducted after 6 weeks of treatment with the use of prednisone (I-E group) or cyclosporine (II-C group) showed, that total remission of skin lesions was not achieved (Fig. 2), and observed skin lesions were localised steadily in body regions investigated.

In examination 3, dogs qualified to I-E group revealed skin lesions which were mostly localized on internal side of ear auricles and in interdigital spaces of

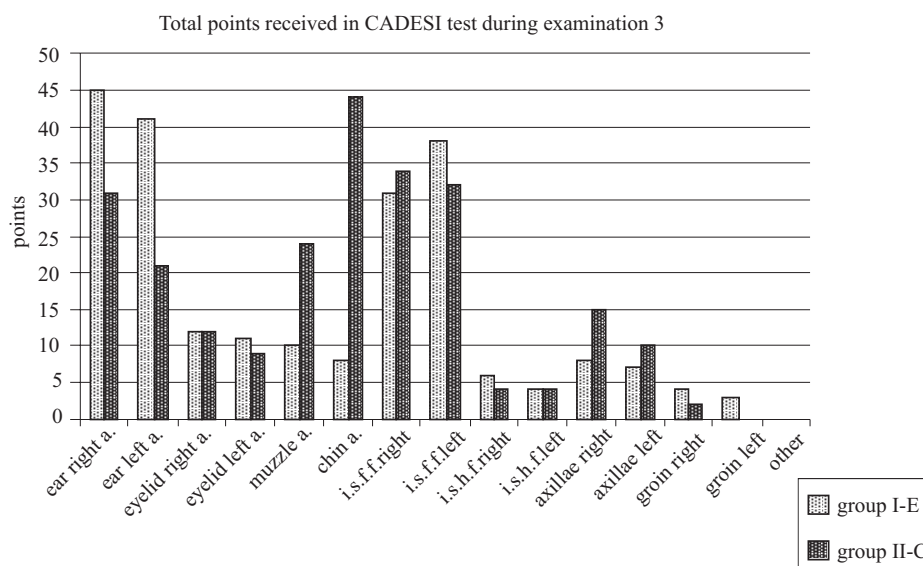


Fig. 2. Results of CADESI test in fixed localisation of skin lesions during examination 3 from dogs qualified to I-E and II-C groups.

Explanation:

ear right/left a. – ear auricles right/left area

eyelids right/left a. – eyes and eyelids right/left area

muzzle/chin a. – muzzle/chin area

i. s. f. f. right/left – interdigital spaces of front feet right/left

i. s. h. f. right/left – interdigital spaces of hind feet right/left

other – neck, anus, abdomen, chest area

Table 2. Statistical analysis (Student's *t*-test) of differences between groups I-E and II-C dogs from CADESI test. Arithmetical mean value ( $\bar{x}$ ), standard deviation ( $\pm$  SD), significance level (P) and quotient of variation (F) obtained from subsequent measurements in groups I-E and II-C (n=80). Significance level was set at  $P \leq 0.05$ .

	Group I-E n=80	Group II-C n=80	Values from Students T-test	
	$\bar{x} \pm$ SD	$\bar{x} \pm$ SD	Significance level (P)	Quotient of variation (F)
Examination 0	16.063 $\pm$ 8.265	17.787 $\pm$ 7.281	0.163 (No)	1.288
Examination 1	12.525 $\pm$ 7.821	13.05 $\pm$ 8.38	0.683 (No)	1.148
Examination 2	5.7 $\pm$ 4.465	5.075 $\pm$ 4.194	0.363 (No)	1.133
Examination 3	2.85 $\pm$ 2.938	3.025 $\pm$ 3.166	0.397 (No)	1.161

front feet, whereas in II-C group skin lesions were mostly observed on chin, in interdigital spaces of front feet, on muzzle and on internal side of ear auricles.

Statistical analyses of the results obtained revealed no statistically significant differences between the means in I-E group and II-C group at  $P=0.05$  in sequent examinations, present comparable level of clinical efficacy of both drugs. Statistical analysis of differences between both groups were shown in Table 2.

However, in both investigated groups, statistically significant differences ( $P \leq 0.05$ ) between results from CADESI test were observed, what proves the efficacy of the treatment of both secondary dermatoses and pruritic lesions to eliminate clinical signs of AD (Table 3). Statistically significant differences between measurements 0 and 1, 0 and 2 as well as 1 and 2, 1 and 3 also 2 and 3 were observed in both groups.

## Discussion

Statistical analysis of the literature performed by Favrot et al. (2010), basing on the results of the studies performed by 34 dermatologists in 15 countries including 1542 dogs, from which 843 had confirmed diagnosis of AD, allowed to ascertain diagnostic criteria of the disease. The analyze proceedings are that gender of dogs is not statistically relevant in disease development, the average age of dogs affected by AD is 2.2 years and 68% of the investigated animals show clinical signs before the third year of life. In the study performed by the Author, the average age of qualified dogs was 2.4 years (I-E group) and 2.6 years (II-C group). Dogs breeds with more frequent occurrence of disease (Favrot et al. 2010) are West Highland

Table 3. Statistical analysis (Student's *t*-test) of results obtained from particular examinations in fixed localisations (n=15) with reference to measurement 0. Presented data concerns arithmetical mean ( $\bar{x}$ ), standard deviation ( $\pm$  SD), significance level (P) and quotient of variation (F) with reference to measurement 0 in groups I-E ( $\bar{x} \pm$  SD= 85.667  $\pm$  34.868) and II-C ( $\bar{x} \pm$  SD = 94.867  $\pm$  38.258).

Parameter	Group	Examination 1	Examination 2	Examination 3
$\bar{x} \pm$ SD	I-E (n =15)	66.8 $\pm$ 23.752	30.4 $\pm$ 13.824	15.2 $\pm$ 8.143
	II-C (n =15)	69.6 $\pm$ 22.658	27.067 $\pm$ 13.982	16.133 $\pm$ 8.601
Significance level P	I-E (n =15)	0.0094*	0.000004*	0.000001*
	II-C (n =15)	0.0361*	0.000001*	0.000000*
Quotient of variation (F)	I-E (n =15)	2.155	6.362	18.334
	II-C (n =15)	2.851	7.487	19.785

\* – P $\leq$ 0.05

White Terrier, Labrador Retriever, German Shepherd, Golden Retriever, Boxer, Bulldog, but the area of study range did not enabled to determine genetic predisposition to disease development. Dogs qualified to the Author's study belonged mostly to the breeds mentioned above. Favrot et al. (2010) also revealed, that statistically relevant ( $p < 0.0001$ ) for diagnosis of AD, except patient's age ( $< 3$  years), were: indoor pet residence by most of time, pruritus as first clinical sign, pruritus receptivity for glucocorticosteroids treatment and typical location of skin lesions. Other statistically significant signs were chronic/recurrent pyoderms receptive for antibiotic treatment, inflammation of the external ear canal – otitis externa, conjunctivitis occurring in spring/summer and hyperhidrosis. However, skin dryness and adipose seborrhoea were statistically less significant. Localization of skin lesions was assessed in 30 body regions and statistically significant ( $p < 0.0001$ ) differences were: the presence of otitis externa as first clinical sign of disease and the localization of skin lesions in interdigital spaces of front and hind feet, abdomen/groins, elbows, ear auricles, flews, eyelids.

No relevance were ascertained when lesions were localized on elbows, on edges of ear auricles and in lumbosacral area. Statistically significant were also positive results of intradermal skin test and/or serological test and fulfilment of three primary major Willemse's features. Dogs qualified to the present study met all the criteria mentioned above, including localizations of skin lesions.

In CADESI 03 test (Olivry et al. 2008), patients can be assessed with maximum of 1240 points, and results showed, that dogs affected by AD obtained no more than 400 points i.e. 32.2%. In the present study the total sum of points obtained by all dogs in measurement 0 were 28.21%. Four clinical parameters were assessed: in addition to erythema and lichenification also primary efflorescences – being the

evidence of pyoderms, and secondary efflorescences – descended from primary efflorescences or caused by scratching, e.g. abrasions.

In the treatment of AD in dogs, orally administered cyclosporine at a dose of 5 mg/kg b.w./day and prednisone/prednisolone at dose of 0.5-1 mg/kg b.w./day are recommended (Reedy et al. 1997, Scott et al. 2001, Steffan et al. 2003, Olivry et al. 2010). In the present study, cyclosporine was administered at a dose of 5 mg/kg b.w./day and prednisone at a dose of 0.5 mg/kg b.w./day.

The present study revealed, that used dosage of prednisone or cyclosporine in young dogs with AD reduced skin lesions by 83% and no statistically significant differences were observed. Other publications reports the similar efficacy of both drugs, although there are differences between authors. Olivry et al. (2002) and Steffan et al. (2003) were unanimous, that clinical efficacy of both glucocorticosteroids and cyclosporine administered orally at dosage mentioned earlier were comparable.

Statistical analysis of literature data published in years 2001-2005, concerning the efficacy of cyclosporine in treatment of AD, conducted by Steffan et al. (2006) has revealed, that after four weeks of application of cyclosporine, the reduction of lesions was usually by 30-52%, however in some dogs even after 2 weeks of treatment the reduction of lesions by 60% was observed. Average efficacy of cyclosporine in reduction of clinical lesions is assessed as for 44%, and glucocorticosteroids for 53%. After 4 weeks of treatment with the use of cyclosporine, the reduction of skin lesions is assessed as for 30-51%, and after 8 weeks – for 53-69%, whereas the reduction of skin lesions by more than 50% is observed in 66-75% of patients. Longer application of cyclosporine (12-16 weeks) did not reduced the skin lesions and pruritus; on the contrary, it went up after the development of secondary dermatoses.

According to Burton et al. (2004), statistically significant differences are observed after 27-42 days of the treatment with the use of cyclosporine at a dose of 0.5 mg/kg b.w./day administered orally.

A review of pharmacotherapy in AD published by Olivry et al. (2003), concerning the data published in years 1980-2002, revealed that orally administered glucocorticosteroids (prednisone, prednisolone, methylprednisolone) reduces the skin lesions by 45-83%, and by more than 50% in 58-86% of treated dogs. Similar data were obtained after assessment of clinical efficacy of cyclosporine, which administered orally reduces skin lesions by 52-67%, and by more than 50% in 40-86 of treated dogs.

Assessment of clinical efficacy of medicines used to reduce erythematous pruritic lesions in dogs with AD in age of 1.2-11 years old, presented by Olivry et al. (2010), indicates, that cyclosporine administered orally (5 mg/kg/day) for 4-6 weeks reduces skin pruritus and clinical signs of disease by over 50% in a half of cases described, and by 90% in 13-27% described cases of AD. However, glucocorticosteroids (prednisone, prednisolone or methylprednisolone), administered orally (0.5-1 mg/kg/day) reduce skin pruritus and clinical signs by 50% in 69% of examined dogs already in one week.

CADESI test is a useful tool for veterinary dermatology study scientists and for veterinary practitioners to objective assessment of skin lesions in dogs with AD and efficacy of treatment. Presently, however, due to the lack of validation methods, providing results reliability, and due to the lack of measurement uncertainty estimation, several test modifications are available (Olivry et al. 1997, 2002, 2008, Steffan et al. 2003, 2004, Germain et al. 2005, Hill et al. 2007, Rybnicek et al. 2008). The common use of uniform CADESI test would standardise study results, and allow objective assessment of the clinical efficacy of the therapy.

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### References

Burton G, Burrows A, Walker R, Robson D, Bassett R, Bryden S, Hill S (2004) Efficacy of cyclosporin in the treatment of atopic dermatitis in dogs – combined results

- from two veterinary dermatology referral centres. *Aust Vet J*, 82: 681-685
- Carlotti D, Madiot G, Ducret J, Jasmin P, Gardey L (2004) Use of recombinant omega interferon therapy in canine atopic dermatitis: a pilot study. *Vet Dermatol* 15: 32-28
- DeBoer DJ, Hiller A (2001) The ACVD task force on canine atopic dermatitis (XV): Fundamental concepts in clinical diagnosis. *Vet Immunol Immunopathol* 81: 271-276
- Favrot C, Linek M, Mueller R, Zini E, International Task Force on Canine Atopic Dermatitis (2010) Development of a questionnaire to assess the impact of atopic dermatitis on health-related quality of life of affected dogs and their owners. *Vet Dermatol* 21: 63-69
- Favrot C, Steffan J, Seewald W, Picco F (2010) A prospective study on the clinical features of chronic canine atopic dermatitis and its diagnosis. *Vet Dermatol* 21: 23-31
- Germain PA, Prelaud P, Bensignor E (2005) CADESI (Canine Atopic Dermatitis Extent and Severity Index) reproducibility. *Rev Med Vet-Toulouse* 156: 382-385
- Gliński W, Kruszewski J, Silny W, Kurzawa R, Czarnecka-Operacz M, Baran E, Szepietowski J (2004) Diagnostic prophylactic and therapeutic guidelines in patients with atopic dermatitis. Position paper by the task force on the national specialists on dermatology and venereology and allergology. *Postep Derm Alergol* 21: 265-277
- Kunz B, Oranje AP, Labréze L., Stalder JF, Ring J, Taieb A (1997) Clinical validation and guidelines for the SCORAD index: consensus report of the European Task Force on Atopic Dermatitis. *Dermatology* 195: 10-19
- Marsella R, Olivry T, Nicklin C, Lopez J (2006) Pilot investigation of a model for canine atopic dermatitis: environmental house dust mite challenge of high-IgE-producing beagles, mite hypersensitive dogs with atopic dermatitis and normal dogs. *Vet Dermatol* 17: 24-35
- Nesbitt GH (1978) Canine allergic inhalant dermatitis: a review of 230 cases. *J Am Vet Med Assoc* 172: 55-60
- Nesbitt GH, Kedan GS, Cacciolo P (1984) Canine atopy.1. Etiology and diagnosis. *Compendium on Continuing Education of Practicing Veterinarian* 6: 73-84
- Olivry T, Guaguère E, Heripret D (1997) Treatment of canine atopic dermatitis with misoprostol, a prostaglandin E1 analogue: an open study. *J Dermatol Treat* 8: 243-247
- Olivry T (2001) The American Collage of Veterinary Dermatology Task Force on Canine Atopic Dermatitis. Special Issue. Elsevier Science BV
- Olivry T, Rivierre C, Jackson HA, Murphy MK, Davidson G, Sousa CA (2002) Cyclosporine decreases skin lesions and pruritus in dogs with atopic dermatitis: a blinded randomized prednisolone-controlled trial. *Vet Dermatol* 13: 77-87
- Olivry T, Mueller RS, International Task Force on Canine Atopic Dermatitis (2003) Evidence-based veterinary dermatology : a systematic review of pharmacotherapy of canine atopic dermatitis. *Vet Dermatol* 14: 121-146
- Olivry T, Marsella R, Iwasaki T, Mueller RS, International Task Force on Canine Atopic Dermatitis (2007) Validation of CADESI-03, a severity scale for clinical trials enrolling dogs with atopic dermatitis. *Vet Dermatol* 18: 78-86
- Olivry T, Mueller R, Nuttall T, Favrot C, Prelaud P, International Task Force on Canine Atopic Dermatitis (2008) Determination of CADESI-03 thresholds for increasing severity levels of canine atopic dermatitis. *Vet Dermatol* 19: 115-119

- Prelaud P, Guaguère E, Alhaidari Z, Faivre N, Heripret D (1998) Reevaluation of diagnostic criteria of canine atopic dermatitis. *Rev Med Vet-Toulouse* 149: 1057-64
- Reedy L M., Miller WH., Willemse JRT (1997) Allergic skin diseases of dogs and cats. 2nd ed, WB Saunders Comp. Ltd, Philadelphia
- Scott D, Miller W, Griffin C (2001) Muller and Kirk's Small Animal Dermatology, 6th ed, WB Saunders Comp., Philadelphia
- Steffan J, Alexander D, Brovedani F, Fisch RD (2003) Comparison of cyclosporine A with methylprednisolone for treatment of canine atopic dermatitis: a parallel blinded, randomized controlled trial. *Vet Dermatol* 14: 11-22
- Steffan J, Horn J, Gruet P, Strehlau G, Fondati A, Ferrer L, Noli C (2004) Remission of the clinical signs of atopic dermatitis in dogs after cessation of treatment with cyclosporin A or methylprednisolone. *Vet Rec* 154: 681-684
- Willemse A (1984) Investigation of symptomatology and the significance of immediate skin test reactivity in canine atopic dermatitis. *Res Vet Sci* 34: 261-266
- Willemse A (1986) Atopic skin disease: a review and a re-consideration of diagnostic criteria. *J Small Anim Pract* 27: 771-778