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# Clinical and epidemiological features and impact of life habits in canine atopic dermatitis in Fortaleza, Brazil<sup>1</sup>

Tiago C. Ferreira<sup>2\*</sup>, Diana Célia S. Nunes-Pinheiro<sup>2</sup> and Marina Gabriela M.C. Mori da Cunha<sup>3</sup>

**ABSTRACT.-** Ferreira T.C., Nunes-Pinheiro D.C.S. & Mori da Cunha M.G.M.C. 2023. **Clinical and epidemiological features and impact of life habits in canine atopic dermatitis in Fortaleza**, **Brazil**. *Pesquisa Veterinária Brasileira 43:e07302, 2023*. Graduate Program in Veterinary Sciences, Faculdade de Veterinária, Universidade Estadual do Ceará, Av. Dr. Silas Munguba 1700, Fortaleza, CE 60714-903, Brazil. E-mail: <u>tiago.cunha@uece.br</u>

Canine atopic dermatitis (cAD) is a worldwide allergic skin disease. The affected dog population can show different clinical patterns according to geographic region, and a lack of studies in Brazil is observed. Therefore, the aim of the present study was to assess the clinical and epidemiological data of cAD in dogs treated in a private clinical practice in Fortaleza, a city located in the Northeast Region of Brazil. cAD was diagnosed in 35% of dogs, being Shih-tzu and Poodle the most affected breeds. Paws and ears were frequently injured sites. Almost 50% of atopic dogs were diagnosed with superficial pyoderma and 36% with cutaneous malasseziosis. Atopic dogs with outdoor habits were less likely to develop cutaneous malassezial infection, and with routine ear, cleaning habits were less likely to develop bacterial otitis externa. In conclusion, canine atopic dermatitis is a prevalent disease in private clinical practice in Fortaleza, and lifestyle habits can be considered a risk factor for cutaneous malasseziosis infection and bacterial otitis externa in atopic dogs.

INDEX TERMS: Canine atopic dermatitis, skin inflammation, epidemiological aspects, clinical aspects, dogs.

**RESUMO.-** [Achados clínicos e epidemiológicos e impacto do estilo de vida na dermatite atópica canina em Fortaleza/ Brasil.] A dermatite atópica canina (DAC) é uma doença alérgica cutânea de ocorrência mundial. A população canina acometida pode apresentar diferentes padrões clínicos de acordo com a região geográfica e observa-se uma carência de estudos no Brasil. Portanto, o objetivo do presente estudo é avaliar os dados clínicos e epidemiológicos da DAC em cães atendidos em uma clínica privada em Fortaleza, cidade localizada na Região Nordeste do Brasil. A DAC foi diagnosticada em 35% dos cães, sendo Shih-tzu e Poodle as raças mais acometidas. As patas e as orelhas foram locais frequentemente afetados. Quase 50% dos cães atópicos foram diagnosticados com piodermite superficial e 36% com malasseziose cutânea. Cães atópicos com hábitos ao ar livre foram menos propensos a desenvolver malasseziose cutânea e com hábitos rotineiros de limpeza auricular foram menos propensos a desenvolver

otite externa bacteriana. Em conclusão, a dermatite atópica canina é uma doença prevalente na prática clínica privada em Fortaleza e os hábitos de vida podem ser considerados como um fator de risco para infecção por malasseziose cutânea e otite externa bacteriana em cães atópicos.

TERMOS DE INDEXAÇÃO: Dermatite atópica canina, inflamação cutânea, aspectos epidemiológicos, aspectos clínicos, caninos.

# **INTRODUCTION**

Canine atopic dermatitis (cAD) is an inflammatory skin syndrome characterized by a hypersensitivity response influenced by a complex interaction between genetic and environmental factors (Nutall et al. 2019, Marsella 2021, Tengvall et al. 2022). This relationship shapes the skin's immune system and barrier function, contributing to epidermal dysfunctions and changes in the cutaneous microbiome, which may perpetuate chronic skin injury (Hoffmann et al. 2014, Nutall et al. 2019, Rostaher et al. 2020).

Environmental exposure can affect the immune system, skin barrier and microbiome (Chatenoud et al. 2020). In humans, factors such as industrialization, air pollution, water hardness and early life exposure to antibiotics have been

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<sup>&</sup>lt;sup>2</sup> Graduate Program in Veterinary Sciences, Faculdade de Veterinária, Universidade Estadual do Ceará (UECE), Av. Prof. Silas Munguba 1700, Fortaleza, CE 60714-903, Brazil. \*Corresponding author: <u>tiago.cunha@uece.br</u> <sup>3</sup> Department of Development and Regeneration, KU Leuven, Leuven, Belgium.

found to contribute to the persistence of atopic dermatitis clinical signs (Harvey et al. 2019). Conversely, ultraviolet ray B (UVB) exposure and helminth infection improve this skin condition (Chatenoud et al. 2020). In the case of atopic dogs, research suggests that *Toxocara canis* infection may reduce pruritus (Fischer et al. 2018), while passive smoking may increase the risk of developing atopic dermatitis (Ka et al. 2014), highlighting the influence of various lifestyle factors on cAD. Therefore, characterizing the dog population affected by cAD is essential to provide epidemiological support for future studies, considering the potential environmental elements that may vary from region to region.

The onset of clinical symptoms in the first years of life can be attributed to genetic and environmental factors (Rostaher et al. 2020), a concept known as the hygiene hypothesis. This theory suggests that early exposure to diverse antigens can shift the immune system towards a non-allergic response, reducing the risk of allergic diseases (Kantor & Silverberg 2017). Evidence from human studies indicates that children with regular exposure to dogs or recurrent infections have a lower risk of developing atopic dermatitis, further supporting the hygiene hypothesis (Chatenoud et al. 2020). In dogs, limited data are available regarding risk and protective factors for cAD, with factors such as flea/tick control, urban living, and overly clean households being identified as risk factors and rural living and contact with other animals being protective (Anturaniemi et al. 2017, Hakanen et al. 2018, Harvey et al. 2019).

Overall atopic dermatitis research in dogs has advanced in the last decades, especially on immunopathogenic, diagnostic and therapeutic aspects (Favrot et al. 2010, Olivry & Banovic 2019, Marsella 2021). On the other hand, worldwide epidemiological data for this disease are scarce (Rostaher et al. 2020). Considering the heterogeneity among the affected individuals (Ferreira et al. 2022) and the possible influence of environment and lifestyle on disease progression (Kantor & Silverberg 2017, Mahdavinia et al. 2021, Suaini et al. 2021), it becomes necessary to combine clinical and epidemiological studies of cAD in different locations around the globe in order to plan a better healthcare strategy.

Brazil has a few epidemiological studies on atopic dermatitis in the canine population (Amarante et al. 2015, Couceiro et al. 2021). However, Brazil has a continental dimension comprising many biological, physical and chemical characteristics. This may provide a data variation on cAD, as it happens in human atopic dermatitis (Suaini et al. 2021).

Therefore, the aim of the present study is to assess the clinical and epidemiological data of cAD in dogs treated in a private clinical practice in Fortaleza, a city located in the Northeast Region of Brazil. Given the potential influence of various dogrelated factors on the development and severity of cAD, this study also aims to investigate the relationship between these characteristics and infection patterns in the disease.

#### MATERIALS AND METHODS

**Animal Ethics.** This study protocol was approved by Ethics Committee in Animal Use of "Universidade Estadual do Ceará" (UECE) under number 9140062/2018.

**Population and clinical data collection.** The study was carried out at a private clinic in Fortaleza, Brazil, in a prospective fashion during 2019 and 2020. Dogs enrolled in this research came from different regions of this city.

All canine patients treated in the given period were submitted to standard clinical procedures, and inclusion criteria were all dogs diagnosed with atopic dermatitis. In the clinical evaluation, the following data were recorded: location of the lesions, bathing, deworming and ear cleaning frequency, and indoor/outdoor habits at the time of diagnosis. The data were expressed descriptively.

**Diagnosis of atopic dermatitis.** The diagnosis of cAD was made through clinical history, signs and exclusion of other pruritic skin diseases (Favrot et al. 2010). In order to rule out other cutaneous pruritic disorders, the dogs were submitted to the elimination diet to assess the diagnosis of food hypersensitivity. They had adequate control of ectoparasites to eliminate allergies to fleas and tick bites. In addition, parasitological and cytological skin tests were carried out to identify mites, cutaneous infection and otitis externa.

**Cytological analysis of skin and ear infections.** Biological samples were collected during dermatological evaluation according to the location and type of injury to characterize the cutaneous and otological infectious processes. Skin samples were collected from epidermal collars, pustules or skin secretions through scarification and imprint, while samples of ear discharges were collected with a swab. The materials were fixed on glass slides, stained with a Diff-Quik kit and evaluated by a dermatologist with optical microscopy to identify microorganisms associated with cAD.

The bacterial types identified by cutaneous and ear cytological examinations were classified as cocci and rods and semi-quantified according to the subjective occupation of the microscope field (1000x amplification). Thus, it was possible to consider subdivisions of bacterial density as mild (with occupation below 30%), moderate (between 30% and 70%) and intense (above 70%). Descriptive data analysis and statistical correlations between infection and lifestyle were applied.

Regarding the fungal evaluation, yeast cells with morphology similar to *Malassezia* spp. were subdivided into groups according to the fungal cell count/field in mild (<20 yeasts/field), moderate (between 20 and 50 yeasts/field) and intense (>50 yeasts/field). Descriptive data analysis and statistical correlations between infection and lifestyle were applied.

**Statistical analysis.** Statistical analysis was performed with Graph Pad<sup>®</sup> software. The correlation between lifestyle data and cutaneous and otological infection was evaluated with Fisher's exact test. Statistical significance was set at P<0.05.

#### RESULTS

#### Epidemiological data and lifestyle

The total studied population consisted of 953 dogs from January 2019 to December 2020. Five hundred eighty-two animals (582, 61%) went to the general clinical practice, and 371 (39%) went to the dermatological service. Among the dogs with skin disease, cAD was diagnosed in 130 (35%). Epidemiological data and lifestyle of the animals are shown in Figure 1 and Table 1. It should be noted that cAD was more prevalent in Shih-Tzu (22.3%), Poodle (16.9%) and mixed-breed dogs (14.6%). Regarding the age of the patients, the disease was most frequently diagnosed in animals between one and three years old (36.9%). However, dogs younger than 1-year-old (10%), between three and five years old (24.6%), between five and eight years old (12.5%) and above eight years old (10%) were also diagnosed with cAD.

## **Injury location**

The lesion distribution data are described in Figure 2. In atopic animals, inflammatory and/or infectious signs were observed in the ears (70.7%), paws (60.3%), axillae/thorax (50%), groin/abdomen (46.9%), chin/neck (43.8%), back (26.9%), periocular (15.3%) and flank (10%). Some animals showed multiple lesions in different regions. Clinical lesions associated with cAD are shown in Figure 3-5.

## **Cutaneous infections**

Almost 50% (64/130) of the dogs were diagnosed with superficial pyoderma, while 36.1% (47/130) were diagnosed with cutaneous malasseziosis. Within such groups, infections with a moderate number of cocci (75%) and a discrete amount of yeasts (78.7%) predominated. The data are described in Table 2. Regarding correlations between cutaneous infections and lifestyle, it was observed that atopic dogs with outdoor habits were less likely to develop cutaneous malasseziosis (P<0.05). Correlation data are shown in Table 3 and 4.

#### Ear infections

Regarding otitis externa, this disease was diagnosed in 70.7% of dogs with cAD. Yeasts were the microorganisms most frequently identified by cytological examination (85.8% of cases of otitis), followed by cocci (51%) and rods (19.5%). The division according to the density of microorganisms is described in Table 2. Regarding correlations between otological infections and lifestyle, it was observed that atopic dogs with ear hygiene habits were less likely to develop bacterial otitis externa (P<0.05). Correlation data are shown in Table 3 and 4.

#### DISCUSSION

This study provides insights into the epidemiological patterns and lifestyle of dogs affected by cAD in Fortaleza, a city located in a tropical region with coast environmental characteristics such as solar incidence (12-hour average) and air humidity (>70% average), according to "Fundação Cearense de Meteorologia e Recursos Hídricos" (FUNCEME). This study is the first of its kind in this city, exploring the prevalence of cAD







Fig.2. Lesion distribution in dogs with canine atopic dermatitis from private clinical practice in Fortaleza, Brazil.

Lifestyle	variables	Absolute value	Relative value (%)
Recurrent skin disease	Yes	111	85.4%
	No	19	14.6%
Bathing frequency	2x/week	14	10.8%
	1x/week	81	62.3%
	1x/15 days	12	9.2%
	1x/month	23	17.7%
Ear hygiene	Yes	50	38.5%
	No	80	61.5%
Outdoor habits*	No	64	49.3%
	Up to 3x/week	50	38.4%
	Above 3x/week	16	12.3%
Deworming frequency	1x/year	12	9.2%
	2x/year	58	44.6%
	3x/year	32	24.7%
	4x/vear	28	21.5%

#### Table 1. Clinical dermatological history and lifestyle of dogs with canine atopic dermatitis at the time of diagnosis

\*Street access, dog meetings, environmental exposure.

and its infectious patterns/associations. The most important observations are: 1) atopic dogs with outdoor habits were less likely to develop yeast infections; 2) cleaning ear habits affect bacterial otitis externa development in atopic dogs.

Human studies indicate that children with frequent contact with dogs or who had sequential infections had a reduced risk of developing atopic dermatitis, supporting the hypothesis that early exposure to environmental factors may promote an adequate balance of the immune response (Chatenoud et al. 2020). In dogs, the data are scarce and involve flea/tick control, castration (Harvey et al. 2019), urban living (Hakanen et al. 2018) and extremely clean household (Anturaniemi



Fig.3-5. Clinical lesions in canine atopic dermatitis. (3) Otitis externa with hyperpigmented and lichenified ear skin. (4 and 5) Alopecic, hyperpigmented and erythema in groin/abdomen.

#### Table 2. Cutaneous and otological infections assessment in canine atopic dermatitis

Atopic dogs (N=130)	c dogs Otitis 130) (N=92, 70.7%)		Cutaneous malasseziosis (N=47, 36.1%)		
Yeasts (<20/field)	37 (40.2%)	-	37 (78.7%)		
Yeasts (20-50/field)	30 (32.6%)	-	7 (14.8%)		
Yeasts (>50/field)	12 (13%)	-	3 (6.3%)		
Cocci – Mild <sup>a</sup>	22 (23.9%)	10 (15.6%)	-		
Cocci – Moderate <sup>b</sup>	21 (22.8%)	48 (75%)	-		
Cocci – Intense <sup>c</sup>	4 (4.3%)	6 (9.4%)	-		
Rods – Mild <sup>a</sup>	4 (4.3%)	-	-		
Rods – Moderate <sup>b</sup>	9 (9.7%)	-	-		
Rods – Intense <sup>c</sup>	5 (5.4%)	-	-		

<sup>a</sup> Microscope field occupancy up to 30%, <sup>b</sup> microscope field occupancy between 30% and 70%, <sup>c</sup> microscope field occupancy above 70%.

# Table 3. Correlation between lifestyle habits and cutaneous and otological yeast infections in dogs with canine atopic dermatitis in Fortaleza, Brazil

Lifestyle variał	oles	Cutaneous m	alasseziosis	Otological m	alasseziosis	Р	Odds ratio	Relative risk
		Yes	No	Yes	No			
Bathing frequency	Frequent <sup>a</sup>	38	57			0.15	1.92	1.17
	Infrequent <sup>b</sup>	9	26					
Ear hygiene	Frequent <sup>a</sup>			25	25	0.06	0.48	0.64
	Infrequent <sup>b</sup>			54	26			
Outdoor habits	Present <sup>c</sup>	16	50			0.006*	2.93	1.65
	Absent	31	33					
Deworming frequency	Frequent <sup>d</sup>	19	41			0.46	0.74	0.85
	Infrequent <sup>e</sup>	27	43					

<sup>a</sup> Up to three times per week, <sup>b</sup> less than once per week, <sup>c</sup> up to seven times per week, <sup>d</sup> between three to four times per year, <sup>e</sup> between once or twice per year.

et al. 2017) as risk factors and rural living and contact with other animals (Hakanen et al. 2018) as protective factors. Since other dog habits may potentially influence the cAD development and severity, we investigated the relation between these characteristics and infection patterns in this disease.

Among the dermatological conditions, cAD had a general prevalence of 35% in the studied population. This prevalence is considered high, given the variety of existing cutaneous diseases. However, this value may be underestimated due to some dogs not meeting the (strict) diagnostic inclusion criteria. Previous studies have reported similar results, with cAD being diagnosed in 52% (Favrot et al. 2020) and 36% (Amarante et al. 2015) of dogs. The latter study, a retrospective research conducted in Brazil, is likely to represent the situation of dogs in the present study more accurately.

It is believed that the high prevalence of cAD in Shih-Tzu and Poodle may be related to the popularity of these breeds in the study location, as the results differ from previous literature (Tarpataki et al. 2006). Nonetheless, there is an agreement when evaluating the general scenario of pure-breed or mixed-breed dogs, as atopic dermatitis was also found to be more prevalent in the former group (Amarante et al. 2015), suggesting a genetic contribution to the development and progression of cAD. Canine atopy was also more frequently diagnosed in adult animals, the common age of disease onset (Favrot et al. 2010). However, it is important to highlight that young animals may also present cAD, requiring a correct diagnosis and therapeutic approaches when consistent signs of cAD are observed (Favrot et al. 2020).

In this study, most atopic dogs were found to be indoor pets (49.3%), given weekly baths (62.3%), and dewormed more than once a year (90.8%). Although no risk factor was identified for the characteristics above in developing cAD signs, atopic dogs with outdoor habits were less prone to developing yeast infections. The reduced exposure to environmental antigens in indoor animals could explain this observation, leading to an inadequate polarization of the immune system and favoring a pro-inflammation disrupts the skin (Chatenoud et al. 2020). This inflammation disrupts the skin barrier, facilitating dysbiosis (Geoghegan et al. 2018). The high air humidity in Fortaleza may also contribute to the development of cutaneous yeast since, in other global regions, malassezial dermatitis was uncommon in atopic dogs (Saridomichelakis et al. 1999).

On the other hand, outdoor habits did not significantly impact bacterial skin infections. Given the potential role of environmental factors in exacerbating human atopic dermatitis (Suaini et al. 2021), further studies are encouraged in this region to understand better the complex relationship among environmental exposure, skin inflammation and development of bacterial infections in cAD.

The current investigation revealed that 49.2% of atopic animals were affected by bacterial skin infections, while fungal infections were observed in 36.1% of the cases. These findings highlight the high incidence of infections in cAD and emphasize the importance of accurate clinical recognition for improving the diagnosis and treatment of this condition. Interestingly, 85.4% of the dogs experienced relapses of skin disease, which could be attributed to the persistence of antigenic stimuli, inadequate drug control or lack of definitive diagnosis. Moreover, the owners of atopic dogs reported difficulties in maintaining the regular use of skin care products (Spitznagel et al. 2021), which may be the reason for relapse.

It is widely acknowledged that atopic skin lesions can exhibit disordered growth of microorganisms due to the altered cutaneous microbiota of affected animals (Hoffmann et al. 2014, Santoro et al., 2015, Brunner et al., 2018). This dysbiosis predisposes to cutaneous infections, particularly those caused by *Staphylococcus pseudintermedius* and *Malassezia* spp., which triggers abnormal inflammatory responses associated with the pathogenesis of atopic dermatitis (Gallo & Nakatsuji 2011). Such infections can affect both the skin and the ears, hindering the resolution of cutaneous inflammation related to cAD by promoting immune polarization towards the Th2 pathway and consequent production of pro-inflammatory cytokines (Williams & Gallo 2015, Sakamoto et al. 2016, Ruchti & Leibundgut-Landmann 2023).

It has been established in dogs that nematode infections can alleviate signs associated with cAD (Fischer et al. 2018). Therefore, it was hypothesized that atopic dogs subjected to frequent deworming cycles might exhibit more signs of cAD. However, the present study failed to establish a correlation between deworming frequency and cutaneous infections in cAD. Since this was beyond the aim of this research, further studies with atopic dogs, local nematode infections and more in-depth analyses still need to be carried out to investigate this fact.

Concerning the locations of the injuries, they are consistent with the disease pattern identified by Favrot et al. (2020), wherein the feet and ears are the most frequently affected sites. In the current investigation, these regions were observed to be sporadically affected, indicating a mild form

 Table 4. Correlation between lifestyle habits and cutaneous and otological bacterial infections in dogs with canine atopic dermatitis in Fortaleza, Brazil

Lifestyle variables		Superficial pyoderma		Bacterial otitis externa		Р	Odds ratio	Relative risk
		Yes	No	Yes	No			
Bathing frequency	Frequent <sup>a</sup> Infrequent <sup>b</sup>	44 20	51 15			0.32	0.65	0.89
Ear hygiene	Frequent <sup>a</sup> Infrequent <sup>b</sup>			14 41	36 39	0.01*	0.37	0.53
Outdoor habits	Present <sup>c</sup> Absent	37 27	29 37			0.12	0.57	0.75
Deworming frequency	Frequent <sup>d</sup> Infrequent <sup>e</sup>	31 33	29 37			0.72	1.19	1.10

<sup>a</sup> Up to three times per week, <sup>b</sup> less than once per week, <sup>c</sup> up to seven times per week, <sup>d</sup> between three to four times per year, <sup>e</sup> between once or twice per year.

of cAD that can be managed locally. Furthermore, given the common involvement of the paws in this disease, a thorough examination is recommended for patients who habitually lick the extremities of their limbs. Concerning the distribution of lesions, it was noted that affected areas varied according to breed, likely due to racial phenotype (Wilhem et al. 2010).

Otitis was present in 70.7% of the studied population. Interestingly, atopic dogs with frequent ear hygiene had a lower risk of otologic bacterial infection, possibly due to the mechanical removal of bacterial cells during cleaning. It is also important to consider the possibility of a direct effect of the product on bacterial growth since acid products can inhibit bacterial growth (Swinney et al. 2008). However, the cleaner type was not accessed in this research, and thus, this hypothesis could not be confirmed.

Since cAD is a chronic immune-inflammatory disease, it is expected the presence of flares triggered by exposure to allergens and the effectiveness of the therapy used (Olivry et al. 2010). In the present study, it was observed that the clinical reappearance manifested itself in different ways in each animal. While some dogs had otitis repeatedly, others had skin abrasions due to the intense itching. The different clinical manifestation of flares highlights the need for personalized therapy, in which the therapeutic approach is tailored according to the problem/signs of each patient. This identification will therefore allow the adoption of proactive measures to delay or prevent the recurrence of the clinical disease and provide adequate comfort to the animal (Olivry & Banovic 2019). Furthermore, new studies should be conducted in this global region to establish possible local allergens and seasonal variations contributing to the periodicity of crises in atopic dogs.

#### CONCLUSION

Canine atopic dermatitis is a prevalent disease in private clinical practice in Fortaleza, and lifestyle habits may be considered a risk factor for cutaneous malasseziosis infection and bacterial otitis externa in atopic dogs. Further investigations are required to determine the true impact of these habits on injury intensity and cutaneous microbiome in Brazilian atopic dogs. Considering that cutaneous and ear infections were regularly identified in atopic dogs, it is recommended that cAD be considered as an important underlying disease associated with them.

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**Conflict of interest statement.**- The authors declare that there are no conflicts of interest.

#### REFERENCES

- Amarante C.F., Ramadinha R.R. & Pereira M.J.S. 2015. Atopic dermatitis: a retrospective study of associated factors in a dermopathic canine population. Revta. Bras. Med. Vet. 37(Supl.1):13-17.
- Anturaniemi J., Uusitalo L. & Hielm-Bjorkman A.H. 2017. Environmental and phenotype-related risk factors for owner reported allergic/atopic skin symptoms and for canine atopic dermatitis verified by veterinarian in a Finnish dog population. PLoS One 12(6):e0178771. <a href="https://dx.doi.org/10.1371/journal.pone.0178771">https://dx.doi. org/10.1371/journal.pone.0178771</a> <a href="https://dx.doi">PMId:28570617</a>

- Brunner P.M., Leung D.Y.M. & Guttman-Yasky E. 2018. Immunologic, microbial, and epithelial interactions in atopic dermatitis. Ann. Allergy Asthma Immunol. 120(1):34-41. <a href="https://dx.doi.org/10.1016/j.anai.2017.09.055">https://dx.doi.org/10.1016/j.anai.2017.09.055</a>
- Chatenoud L., Bertuccio P., Turati F., Galeone C., Naldi L., Chatenoud L., Vecchia C.L. & Bach J.-F. 2020. Markers of microbial exposure lower the incidence of atopic dermatitis. Allergy. 75(1):104-115. <a href="https://dx.doi.org/10.1111/all.13990">https://dx.doi.org/10.1111/all.13990</a> <a href="https://dx.doi.org/10.1111/all.13990">></a> </a> <a href="https://dx.doi.org/10.1111/all.1390">></a> <a href="https://dx.doi.org/10.1111/all.1390">></a> <a href="https://dx.doi.org/10.1111/all.1390">></a> </a>
- Couceiro G.A., Ribeiro S.M.M., Monteiro M.M., Meneses A.M.C., Sousa S.K.S.A. & Coutinho L.N. 2021. Prevalence of canine atopic dermatitis at the Veterinary Hospital of the Universidade Federal Rural da Amazônia in Belém/Pará, Brazil. Pesq. Vet. Bras. 41:e06778. <a href="https://dx.doi.org/10.1590/1678-5150-PVB-6778">https://dx.doi.org/10.1590/1678-5150-PVB-6778</a>
- Favrot C., Fischer N., Olivry T., Zwickl L., Audergon S. & Rostaher A. 2020. Atopic dermatitis in West Highland white terriers – part I: natural history of atopic dermatitis in the first three years of life. Vet. Dermatol. 31(2):106-e16. <https://dx.doi.org/10.1111/vde.12801> <PMid:31646697>
- 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(1):23-31. <a href="https://dx.doi.org/10.1111/j.1365-3164.2009.00758.x>">https://dx.doi.org/10.1111/j.1365-3164.2009.00758.x</a>
- Ferreira T.C., Carvalho V.M., Cunha M.G.M.C.M. & Pinheiro D.C.S.N. 2022. Canine atopic dermatitis: report of 10 cases. Res. Soc. Develop. 11(4):e12411427258. <https://dx.doi.org/10.33448/rsd-v11i4.27258>
- Fischer N., Rostaher A., Zwickl L., Deplazes P., Olivry T. & Favrot C. 2018. A Toxocara canis infection influences the immune response to house dust mite allergens in dogs. Vet. Immunol. Immunopathol. 202:11-17. <a href="https://dx.doi.org/10.1016/j.vetimm.2018.06.009">https://dx.doi.org/10.1016/j.vetimm.2018.06.009</a> <a href="https://dx.doi.org/10.1016/j.vetimm.2018.06.009">PMid:30078584</a>
- Gallo R.L. & Nakatsuji T. 2011. Microbial symbiosis with the innate immune defense system of the skin. J. Invest. Dermatol. 131(10):1974-1980. <a href="https://dx.doi.org/10.1038/jid.2011.182">https://dx.doi.org/10.1038/jid.2011.182</a> <a href="https://dx.doi.org/10.1038/jid.2011.182">https://dx.doi.001</a> <a href="https://dx.doi.org/10.1038/jid.2011.182">https://dx.doi.001</a> <a href="https://dx.doi.org/10.182">https://dx.doi.001</a> <a href="https://dx.doi.org/10.182">https://dx.doi.001</a> <a href="https://dx.doi.org/10.182">https://dx.doi.001</a> <a href="https://dx.doi.001">https://dx.doi.001</a> <a href="https://dx.doi.001">https://dx.doi.001</a> <a href="https://dx.doi.001">https://dx.doi.001</a> <a href="https://dx.doi.001">https://dx.doi.001</a> <a href="https://dx.doi.001">https://dx.doi.001</a> <a href="https://dx.doi.001">https://dx.doi.001</a> <a href="https://dx.doi.001">https://dx.doi.00
- Geoghegan J.A., Irvine A.D. & Foster T.J. 2018. *Staphylococcus aureus* and atopic dermatitis: a complex and evolving relationship. Trends Microbiol. 26(6):484-497. <a href="https://dx.doi.org/10.1016/j.tim.2017.11.008">https://dx.doi.org/10.1016/j.tim.2017.11.008</a> <a href="https://dx.doi.org/10.1016/j.tim.2017.11.008">https://dx.doi.org/10.1016/j.tim.2018</a> <a href="https://dx.doi.org/10.1016/j.tim.2017.11.008">https://dx.doi.0018</a> <a href="https://dx.doi.org/10.1016/j.tim.2017.11.008">https://dx.doi.0018</a> <a href="https://dx.doi.org/10.1016/j.tim.2017.11.008">https://dx.doi.org/10.1016/j.tim.2017.11.008</a> <a href="https://dx.doi.org/10.1016/j.tim.2017.11.008">https://dx.doi.org/10.1016/j.tim.2018</a> <a href="https://dx.doi.org/10.1016/j.tim.2017.11.008">https://dx.doi.org/10.1016/j.tim.2018</a> <a href="https://dx.doi.org/10.1016/j.tim.2017.11.0116/j.tim.2017.11.0116/j.tim.
- Hakanen E., Lehtimaki J., Salmela E., Tiira K., Anturaniemi J., Hielm-Bjorkman A., Ruokolainen L. & Lohi H. 2018. Urban environment pre-disposes dogs and their owners to allergic symptoms. Sci. Rep. 8:1585. <a href="https://dx.doi.org/10.1038/s41598-018-19953-3">https://dx.doi.org/10.1038/s41598-018-19953-3</a> <a href="https://dx.doi"></a> org/10.1038/s41598-018-19953-3</a> <a href="https://dx.doi"></a> org/10.1038/s41598-018-19953-3</a> <a href="https://dx.doi"></a> org/10.1038/s41598-018-19953-3</a> <a href="https://dx.doi">></a> org/10.1038/s41598-018-19953-3</a> </a>
- Harvey N.D., Shaw S.C., Craigon P.J., Blott S.C. & England G.C.W. 2019. Environmental risk factors for canine atopic dermatitis: a retrospective largescale study in labrador and golden retrievers. Vet. Dermatol. 30(5):396-e119. <https://dx.doi.org/10.1111/vde.12782> <PMid:31407839>
- Hoffmann A.R., Patterson A.P., Diesel A., Lawhon S.D., Ly H.J., Stephenson C.E., Mansell J., Steiner J.M., Dowd S.E., Olivry T. & Suchodolski J.S. 2014. The skin microbiome in healthy and allergic dogs. Plos One 9(1):e83197. <a href="https://dx.doi.org/10.1371/journal.pone.0083197">https://dx.doi.org/10.1371/journal.pone.0083197</a> <a href="https://dx.doi.org/10.1371/journal.pone.0083197">Https://dx.doi.org/10.1371/journal.pone.0083197</a> <a href="https://dx.doi.org/10.1371/journal.pone.0083197">https://dx.doi.org/10.1371/journal.pone.0083197</a> </a>
- Ka D., Marignac G., Desquilbet L., Freyburger L., Hubert B., Garelik D. & Perrot S. 2014. Association between passive smoking and atopic dermatitis in dogs. Food Chem. Toxicol. 66:329-333. <a href="https://dx.doi.org/10.1016/j.fct.2014.01.015">https://dx.doi.org/10.1016/j. fct.2014.01.015</a> <a href="https://dx.doi.org/10.1016/j">PMId:24491262</a>>
- Kantor R. & Silverberg J.I. 2017. Environmental risk factors and their role in the management of atopic dermatitis. Expert Rev. Clin. Immunol. 13(1):15-26. <a href="https://dx.doi.org/10.1080/1744666X.2016.1212660">https://dx.doi.org/10.1080/1744666X.2016.1212660</a> PMid:27417220>
- Mahdavinia M., Greenfield L.R., Moore D., Botha M., Engen P., Gray C., Lunjani N., Hlela C., Basera W., Hobane L., Watkins A., Mankahla A., Gaunt B., Facey-Thomas H., Landay A., Keshavarzian A. & Levin M.E. 2021. House dust microbiota and atopic dermatitis: effect of urbanization. Pediatr. Allergy Immunol. 32(5):1006-1012. <a href="https://dx.doi.org/10.1111/pai.13471">https://dx.doi.org/10.1111/pai.13471</a> <a href="https://dx.doi.org/10.1111/pai.13471">></a> <a href="https://dx.doi.org/10.11111/pai

- Marsella R. 2021. Advances in our understanding of canine atopic dermatitis. Vet. Dermatol. 32(6):547-e151. <a href="https://dx.doi.org/10.1111/vde.12965">https://dx.doi.org/10.1111/vde.12965</a> <a href="https://dx.doi.org/10.1111/vde.12965">></a> <a href="https://dx.doi.org/10.1111/vde.1296">><
- Nutall T.J., Marsella R., Rosenbaum M.R., Gonzales A.J. & Fadok V.A. 2019. Update on pathogenesis, diagnosis, and treatment of atopic dermatitis in dogs. J. Am. Vet. Med. Assoc. 254(11):1291-1300. <a href="https://dx.doi.org/10.2460/javma.254.11.1291">https://dx.doi.org/10.2460/javma.254.11.1291</a> <a href="https://dx.doi"></a> <a href="https://dx.doi">NIGON Contemport</a>
- Olivry T. & Banovic F. 2019. Treatment of canine atopic dermatitis: time to revise our strategy? Vet. Dermatol. 30(2):87-90. <a href="https://dx.doi.org/10.1111/vde.12740">https://dx.doi.org/10.1111/vde.12740</a> <a href="https://dx.doi"></a> </a> </a>
- Olivry T., DeBoer D.J., Favrot C., Jackson H.A., Mueller R.S., Nuttall T. & Prélaud P. 2010. Treatment of canine atopic dermatitis: 2010 clinical practice guidelines from the international task force on canine atopic dermatitis. Vet. Dermatol. 21(3):233-248. <a href="https://dx.doi.org/10.1111/j.1365-3164.2010.00889.x">https://dx.doi.org/10.1111/j.1365-3164.2010.00889.x</a> PMid:20456716>
- Rostaher A., Dolf G., Fischer N.M., Silaghi C., Akdis C., Zwickl L., Audergon S. & Favrot C. 2020. Atopic dermatitis in a cohort of West Highland white terriers in Switzerland. Part II: estimates of early factors and heritability. Vet. Dermatol. 31(4):276-e66. <a href="https://dx.doi.org/10.1111/vde.12843">https://dx.doi.org/10.1111/vde.12843</a> <PMid:32077169>
- Ruchti F. & Leibundgut-Landmann S. 2023. New insights into immunity to skin fungi shape our understanding of health and disease. Parasite Immunol. 45(2):e12948. <https://dx.doi.org/10.1111/pim.12948> <PMid:36047038>
- Sakamoto M., Asahina R., Kamishina H. & Maeda S. 2016. Transcription of thymic stromal lymphopoietin via Toll-like receptor 2 in canine keratinocytes: a possible association of Staphylococcus spp. in the deterioration of allergic inflammation in canine atopic dermatitis. Vet. Dermatol. 27(3):184-e46. <https://dx.doi.org/10.1111/vde.12301> <PMid:27018172>
- Santoro D., Marsella R., Pucheu-Haston C.M., Eisenschenk M.N.C., Nutall T. & Bizikova P. 2015. Review: pathogenesis of canine atopic dermatitis: skin barrier and host microorganism interaction. Vet. Dermatol. 26(2):84-e25. <https://dx.doi.org/10.1111/vde.12197> <PMid:25683702>

- Saridomichelakis M.N., Koutinas A.F., Gioulekas D. & Leontidis L. 1999. Canine atopic dermatitis in Greece: clinical observations and the prevalence of positive intradermal test reactions in 91 spontaneous cases. Vet. Immunol. Immunopathol. 69(1):61-73. <a href="https://dx.doi.org/10.1016/S0165-2427">https://dx.doi.org/10.1016/S0165-2427</a>
- Spitznagel M.B., Hillier A., Gober M. & Carlson M.D. 2021. Treatment complexity and caregiver burden are linked in owners of dogs with allergic/atopic dermatitis. Vet. Dermatol. 32(2):192-e50. <a href="https://dx.doi.org/10.1111/vde.12938">https://dx.doi.org/10.1111/vde.12938</a> PMid:33554382>
- Suaini N.H.A., Tan C.P.T., Loo E.X.L. & Tham E.H. 2021. Global differences in atopic dermatitis. Pediatr. Allergy Immunol. 32(1):23-33. <a href="https://dx.doi.org/10.1111/pai.13335">https://dx.doi.org/10.1111/pai.13335</a> <a href="https://dx.doi">PMId:32841425</a></a>
- Tarpataki N., Pápa K., Reiczigel J., Vajdovich P. & Vörösi K. 2006. Prevalence and features of canine atopic dermatitis in Hungary. Acta Vet. Hung. 54(3):353-366. <a href="https://dx.doi.org/10.1556/avet.54.2006.3.6">https://dx.doi.org/10.1556/avet.54.2006.3.6</a> <a href="https://dx.doi.org/10.1556/avet.54.2006.3.6">https://dx.doi.org/10.1556/avet.54.2006.3.6</a> <a href="https://dx.doi.org/10.1556/avet.54.2006.3.6">https://dx.doi.org/10.1556/avet.54.2006.3.6</a> <a href="https://dx.doi.org/10.1556/avet.54.2006.3.6">https://dx.doi.org/10.1556/avet.54.2006.3.6</a> </a> </a>
- Tengvall K., Sundstrom E., Wang C., Bergvall K., Wallerman O., Pederson E., Karlsson A., Harvey N.D., Blott S.C., Olby N., Olivry T., Brander G., Meadows J.R.S., Roosje P., Leeb T., Hedhammar A., Andersson G. & Lindblad-Toh K. 2022. Bayesian model and selection signature analyses reveal risk factors for canine atopic dermatitis. Commun. Biol. 5:1348. <https://dx.doi. org/10.1038/s42003-022-04279-8> <PMid:36482174>
- Wilhem S., Kovalik M. & Favrot C. 2010. Breed-associated phenotypes in canine atopic dermatitis. Vet. Dermatol. 22(2):143-149. <a href="https://dx.doi.org/10.1111/j.1365-3164.2010.00925.x">https://dx.doi.org/10.1111/j.1365-3164.2010.00925.x</a> <a href="https://dx.doi">< https://dx.doi</a>.
- Williams M.R. & Gallo R.L. 2015. The role of the skin microbiome in atopic dermatitis. Curr. Allergy Asthma Rep. 15(11):65. <a href="https://dx.doi.org/10.1007/s11882-015-0567-4">https://dx.doi.org/10.1007/s11882-015-0567-4</a>