For Vet Professionals only

PET POD

Volume 6
Issue 1
Jan-March
2025

HAPPY NEW YEAR - 2025

Modern Approach to Management of Canine Atopic Dermatitis

Overview

Itchy, scratchy pet is one of the most common reasons owner seeks Veterinary care. Allergic skin diseases can cause not only significant discomfort and distress to individual pet but also cause stress and disruption to pet's family members. Because of the complex nature of allergic skin disease, diagnosis can be time-consuming and may require multiple follow-up visits before a final diagnosis is achieved. Dogs with allergic skin disease often require lifelong management to optimize their quality of life. The challenge is not only to treat the dog successfully, but also to avoid severe flares which requires multifaceted management. Successful remission can only be achieved with a combination of approach in order to control the clinical signs and prevent flares. The following content highlight on management of such multifactorial skin disease which entails a multimodal approach.

Canine atopic dermatitis (CAD) has been the object of investigation for many decades. Discoveries in the clinical, histological, immunological and epidemiological aspects of disease led to the definition of CAD as a genetically predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features associated with immunoglobulin E (IgE) antibodies, most commonly directed against environmental allergens. Despite many years of research, investigations of clinical and histological features of CAD are still of interest to many clinicians and researchers because they allow us not only to diagnose the disease more precisely, but also to obtain an insight into the possible pathomechanism of the condition. Gorman and Halliwell (1989) defined Canine Atopic Dermatitis (referred as atopy) as an inherited predisposition to develop IgE antibodies to environmental allergens resulting in allergic disease. It is frequently encountered in clinical practice, known to negatively impact the quality of life of affected dogs and their owners and oftentimes requires lifelong management.

For Vet Professionals only

PET POD

Dear Vets,

Allergic skin diseases can cause not only significant discomfort and distress to individual pet but also cause stress and disruption to pet's family members. Because of the complex nature of allergic skin disease, diagnosis can be time-consuming and may require multiple follow-up visits before a final diagnosis is achieved. Dogs with Atopic Dermatitis often require lifelong management to optimize their quality of life. The challenge is not only to treat the dog successfully, but also to avoid severe flares which requires multifaceted management. This issue highlights on management of such multifactorial skin disease which entails a multimodal approach.

We welcome Vet practitioner to share their view and experience on management of Atopic Dermatitis. We request you to share your invaluable feedback on this issue of PetPod via e-mail to petpod@intaspharma.com or else by scanning below QR code.

Etiopathogenesis

The cause of CAD is unknown, but a general understanding of the anatomy of skin is vital in understanding what happens to a dog when skin becomes irritated and inflamed as a result of allergens in environment. Some of the predisposing factors may include, direct contact with another animal, object, plant, or irritating chemical substance, excessive rubbing of skin, allergies to food, Yeast or fungi, infection by parasites such as fleas, ticks, mites, lice, worms, skin allergies or hypersensitivity, pyoderma, acne and malnutrition.

The pathogenesis of CAD is incompletely understood, but is believed to involve complex interactions between genetic and environmental factors that lead to epidermal barrier dysfunction, immune dysregulation and dysbiosis of cutaneous microbiome. A significant challenge faced by researchers is determining whether epidermal barrier dysfunction, immune dysregulation and dysbiosis of cutaneous microbiome play critical roles in disease induction or are secondary downstream sequela. Evidence to support a role of genetic and environmental factors, epidermal barrier dysfunction, immune dysregulation and dysbiosis of cutaneous microbiome are discussed herein:

- **Genetic:** Several breeds are well-recognized to be at increased risk for developing CAD. Several lines of evidence have suggested a genetic basis for CAD. First, several pure breeds of dog are well-recognized to be at increased risk for developing CAD, including Golden Retriever, Labrador Retriever, Pit Bull Terrier, German Shepherd, Bulldog, Boxer, Pug, Irish Setter, Dalmatian, Shih Tzu and Miniature Schnauzer. Second, pedigree analyses have demonstrated the heritability of CAD. The studies that have investigated the genetic basis of CAD to date have clearly illustrated that the disease is not a simple dominant or recessive trait. Rather, CAD appears to be a complex, polygenic disorder arising from diverse genetic mutations that vary between breeds and geographic locations.

- **Environment:** Studies have been performed to define environmental risk factors associated with CAD. Environmental factors found to be associated with CAD include living in an urban environment or in areas of increasing human density, and living primarily indoors. In fact, the association between an indoor environment and CAD and has led clinical researchers to accept "living in an indoor environment" as one of several diagnostic criteria for the disease. It is well-recognized that clinical signs of CAD fluctuate seasonally in association with changing concentrations of environmental allergens in some dogs. Pets with CAD are known to develop immunoglobulin (Ig)E antibodies against environmental allergens. It is plausible that numerous environmental triggers of CAD exist that have variable effects on disease induction and exacerbation that depend on a dog's individual genetic background, as well as the environments and climates they are exposed to.

- **Epidermal Barrier Dysfunction:** Dysfunction of the epidermal barrier facilitates the percutaneous absorption of chemical irritants, microbes, and environmental allergens that stimulate the local immune system and induce Th2-polarized immune responses. Th2-polarized immune responses are recognized to further impair epidermal barrier integrity and function by downregulating key structural proteins in the skin and by inducing pruritus, scratching, and self-trauma. There is evidence to support the presence of epidermal barrier dysfunction in CAD, it has not been possible to deduce whether epidermal barrier dysfunction in CAD is a primary defect underlying disease induction, or a secondary phenomenon resulting from local skin inflammation and self-trauma. Nonetheless, restoring epidermal barrier function and integrity remains an integral part of the multimodal approach to managing dogs with CAD.

- **Immune Dysregulation:** Inflammation of skin/ Pruritus is a hallmark finding of CAD. Histologically, CAD is characterized by superficial dermal infiltration of T cells, dendritic cells, eosinophils and mast cells. Various studies have demonstrated prominent Th2-polarized immune responses in CAD with variably increased levels of interleukin (IL)-4, IL-5, and IL-13. Th2-polarized immune responses have been proposed to play a critical role in the development and perpetuation of CAD by promoting humoral immunity, including the production of allergen-specific IgE antibodies.

- **Dysbiosis of Cutaneous Microbiome:** Dogs with AD have long been recognized to suffer from recurrent microbial skin infections with S pseudintermedius and M pachydermatis, which are known to exacerbate clinical disease and complicate therapeutic responses. Dogs with CAD complicated by pyoderma, the diversity of bacterial microbiota is found to inversely correlate with clinical disease severity, measures of epidermal barrier function, and relative abundances of *Staphylococcus spp.* Similarly, the fungal microbiota inhabiting the nonlesional skin of dogs with allergic skin disease has also been found to be associated with lipid-dependent yeasts *Malassezia globosa* and *Malassezia restricta* suggested to be driven by the decreased lipid content known to occur in the skin of dogs with CAD. Although dysbiosis of the cutaneous microbiome appears to be a feature of CAD, it remains unknown what specific roles the microbiota play in CAD. Additional research is needed to further define the relationship between the cutaneous microbiome and the induction and exacerbation of CAD.

Clinical Evaluation

CAD commonly present before 3 years of age, may be either perennial or seasonal, and overlap with numerous other pruritic and inflammatory skin diseases. The distribution of skin lesions is known to vary between breeds, but generally involves face, pinnae, ear canals, paws, axillae, ventrum and inguinum (Fig. 1). The most common and clinically significant feature of CAD is moderate to severe pruritus, which is accompanied by erythema, erythematous macular and/or papular eruptions, self-induced alopecia, excoriations, hyperpigmentation, and lichenification (Fig. 2 and 3). Primary lesions are uncommon and consist of erythematous macules, patches and small papules. Common secondary lesions includes; alopecia, erythema, scaling, hemorrhagic crusts and hyperpigmentation (Fig. 4).

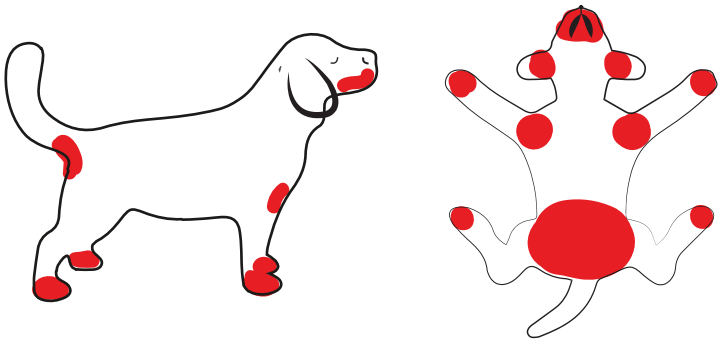


Fig. 1: Typical distribution pattern of skin lesions

Fig. 2: Erythema and alopecia of face

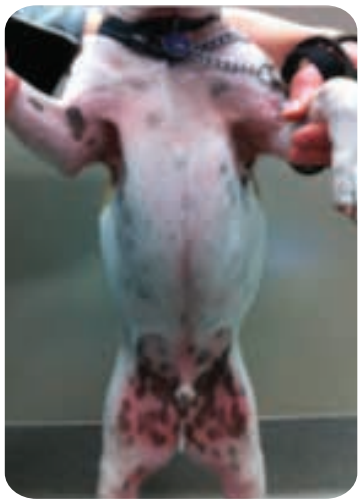


Fig. 3: Erythema of ventral abdomen and axillae

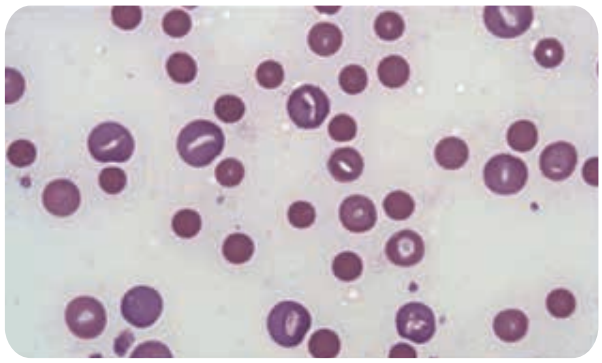
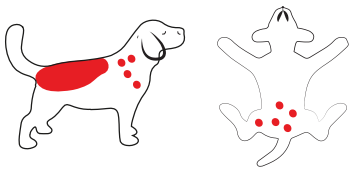
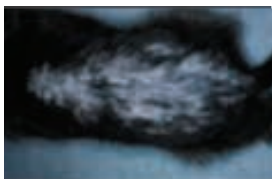
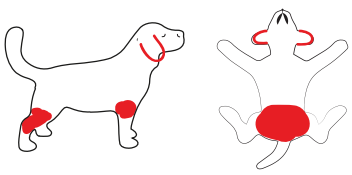
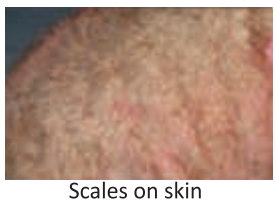
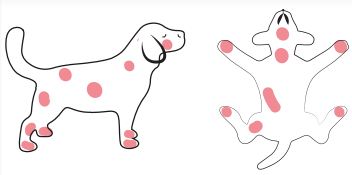
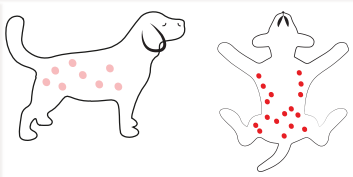
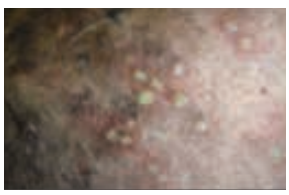
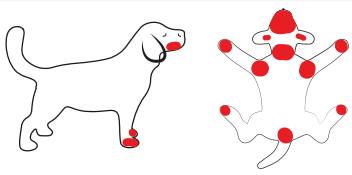
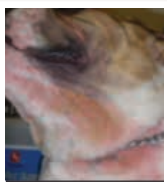
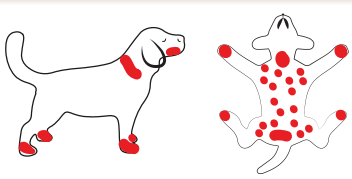
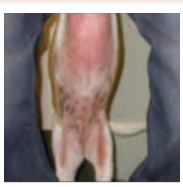


Fig. 4: Chronic dermatitis, lichenification and hyperpigmentation of ventrum

Diagnosis

Diagnosis of CAD is challenging and is based on signalment, clinical signs, history, physical examination, and the exclusion of other pruritic skin diseases, *viz.* ectoparasites (scabies, demodecosis, pediculosis, otocariosis), microbial infections (Staphalococcal pyoderma, Malassezia dermatitis etc), food allergy, contact dermatitis, flea allergy dermatitis, food allergy, insect bite hypersensitivity and neoplasia. Distribution of skin lesions is one of the most important clinical features used to prioritise the differential diagnosis list, which are summarized below;

Table 1: Typical distribution pattern of skin lesions

Sr. No	Disease	Predominant lesions	Typical Distribution Pattern	Clinical Presentation
	PARASITIC SKIN DISEASES			
1	Flea Allergy Dermatitis	Acute: erythematous macules, papules, crusted papules, acute moist dermatitis (hot spots). Chronic: self-induced alopecia, lichenification, hyperpigmentation		 Flea bite hypersensitivity
2	Sarcoptic mange	Papular eruption, erythema, scaling, excoriations. In severe cases the lesions may extend over the entire body.		 Scales on skin
3	Demodicosis	Patches of focal, multifocal or diffuse alopecia; erythema in pink-skinned dogs; comedones, follicular casts, scale and lichenification		 Lichenification on head
	INFECTIOUS SKIN DISEASES			
4	Staphylococcal pyoderma	Acute: papules, pustules, epidermal collarettes, Staphylococcal rings and circular patches of alopecia. Chronic: lichenification, hyperpigmentation, greasiness and scaling.		 Pustules on skin
5	Malassezia Dermatitis	Erythema, yellowish or brownish greasy scale, hyperpigmentation with chronicity.		 Seborrhoea with Malassezia Infection
	ALLERGIC SKIN DISEASE			
6.	Contact Dermatitis	Erythematous macules, papules, lichenification, hyperpigmentation, erosions.		 Lesions on ventral chest

Comprehensive Therapeutic Approach

Pruritus is a hallmark clinical sign of CAD and is often the main presenting complaint when owners of dogs with CAD seek veterinary care. As such, providing immediate and sustained anti-itch relief is a primary therapeutic goal in managing CAD. It is important to recognize that the pruritus experienced by each individual dog with CAD may be complicated by various flare factors, including exposure to environmental allergens (e.g., pollens, molds and house dust mites), dietary components, concurrent uncontrolled flea allergy dermatitis, and the development of microbial skin infections. For these reasons, a multimodal approach is typically required when managing CAD to ensure all contributing flare factors of disease are identified and addressed.

- **Avoidance of Allergens:** The most common causal allergens are house dust mite glycoproteins and aeroallergens *viz.* pollens, prevention of allergen contact is difficult or impossible to achieve. The exposure can be limited using, environmental benzyl benzoate acaricide spray, dust mite-free mattresses, regular vacuuming, and washing blankets regularly.
- **Repairing Skin Barrier:** It is well known that atopic dogs suffer from an impaired epidermal barrier, which results in an increased transepidermal water loss (TEWL). Dry and scaly skin may be seen in some breeds. Supporting the epidermal barrier with topical products *viz.* glycerol, glycerin, propylene glycol, panthenol and urea will increase the water-binding capacity of epidermis, especially when used after bathing. Atopic dogs also have disrupted intercellular lipid lamellae of their stratum corneum. To restore this, oral essential fatty acids (EFAs), either as supplements or incorporated in diet, have been deployed with varying results. Topical formulations including shampoo, sprays and lotions containing fatty acids and ceramides can be used to manage CAD (**Conaseb shampoo**).
- **Controlling Secondary Skin Infections:** Most atopic dogs are prone to recurrent superficial pyoderma, and papules, pustules, collarettes, squames and seborrhea are commonly seen. Colonization of the atopic skin by pathogenic *Staphylococcus* spp. (usually *S. pseudintermedius*) is increased compared to healthy skin, which may be partly explained by lower antimicrobial activity of the cutaneous antimicrobial peptides of the innate immune system. During flares, dysbiosis of atopic skin microbiota develops, with a relative increase in *Staphylococcus* spp. About 40% of atopic dogs have recurrent skin infections with the yeast *Malassezia pachydermatis*, with a strong odor, greasiness, honeycomb crusts, squames and paronychia. A type I hypersensitivity reaction to Malassezia can also occur, leading to severe pruritus. Secondary skin infections by bacteria and yeasts must therefore always be controlled, and is achieved by regular use of topical antimicrobial therapy (shampoos, mousses, sprays, wipes and gels). Shampoo containing Chlorhexidine, Miconazole/Ketoconazole has shown to be clinically effective against bacteria and yeasts (**Conaseb and Micodin shampoo**). Oral Itraconazole can be effectively used (**Izopet suspension**) to manage secondary yeast infections.
- **Controlling Skin Inflammation and Pruritus:** Symptomatic therapy that has shown good evidence for reducing pruritus and dermatitis in CAD includes; Glucocorticosteroids, Cyclosporine, Tacrolimus, Oclacitinib and Lokivetmab. Topical antimicrobial therapy is recommended for the long-term maintenance of CAD to decrease surface colonization of pathogenic microbes in attempts to prevent, or at least decrease the frequency of recurrent skin infections. As with antimicrobial topical therapy, use of lipid-containing topical therapies are recommended for the long-term maintenance of dogs with CAD. To that goal, various antimicrobial topical therapies are now formulated with lipid complexes, thereby allowing managing clinicians and owners to treat and prevent microbial skin infections, as well as

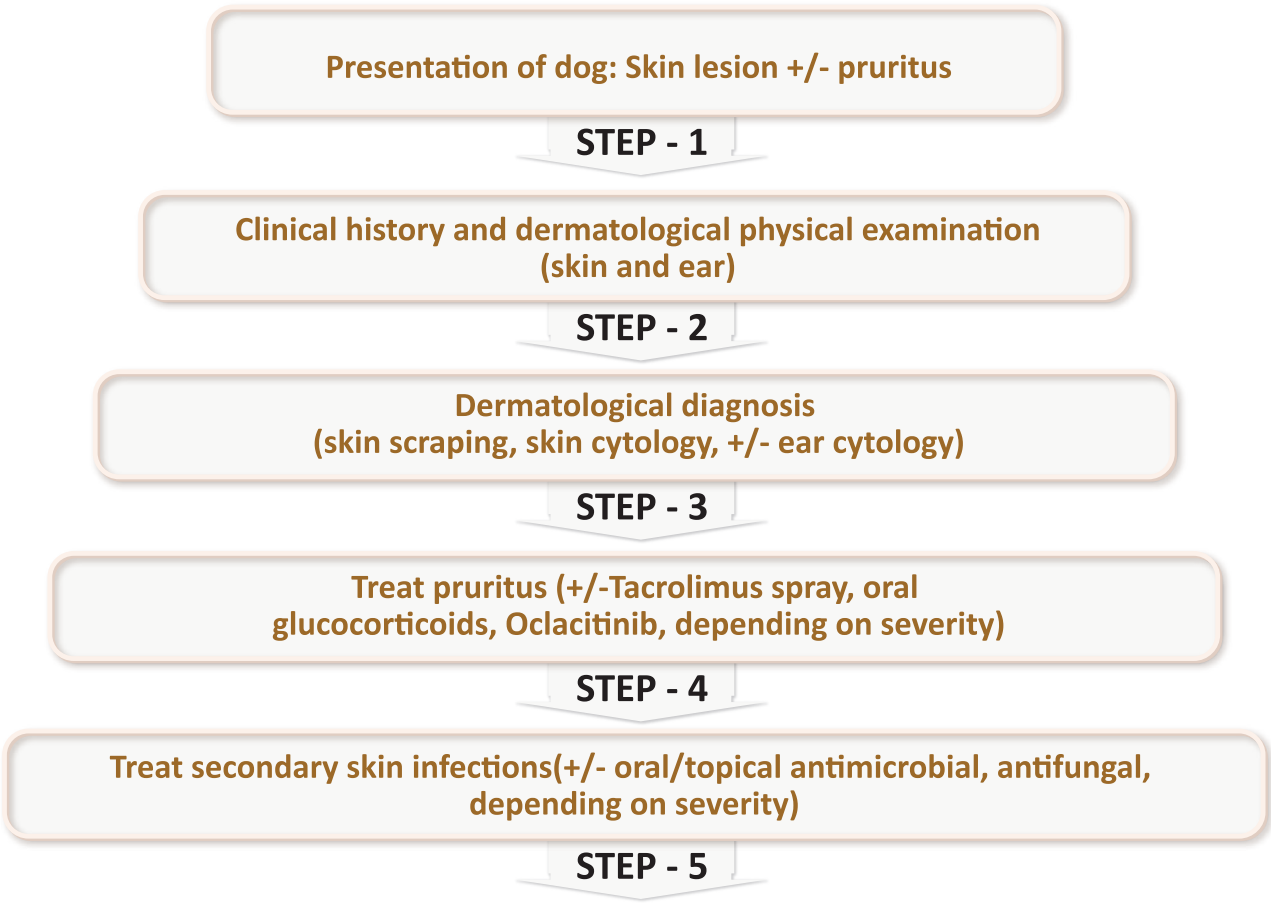
restore epidermal barrier integrity function with only one product. Tacrolimus is one such macrolide antibiotic that is widely used to treat CAD in dogs. It is basically calcineurin inhibitor which has both anti-inflammatory and immune-modulator property. Therefore it is a powerful topical immunomodulator that can effectively decrease inflammation and allergic reactions. It has been reported that, Tacrolimus significantly decreases pruritus and erythema, when used in a compounded lotion formulation for four weeks and also reported that it has better absorption by easily penetrating through skin and has rapid onset of action and exerts sustaining therapeutic effects, with an efficacy similar to that of moderate to potent topical corticosteroid but without causing skin atrophy (**TakfaPet spray**).

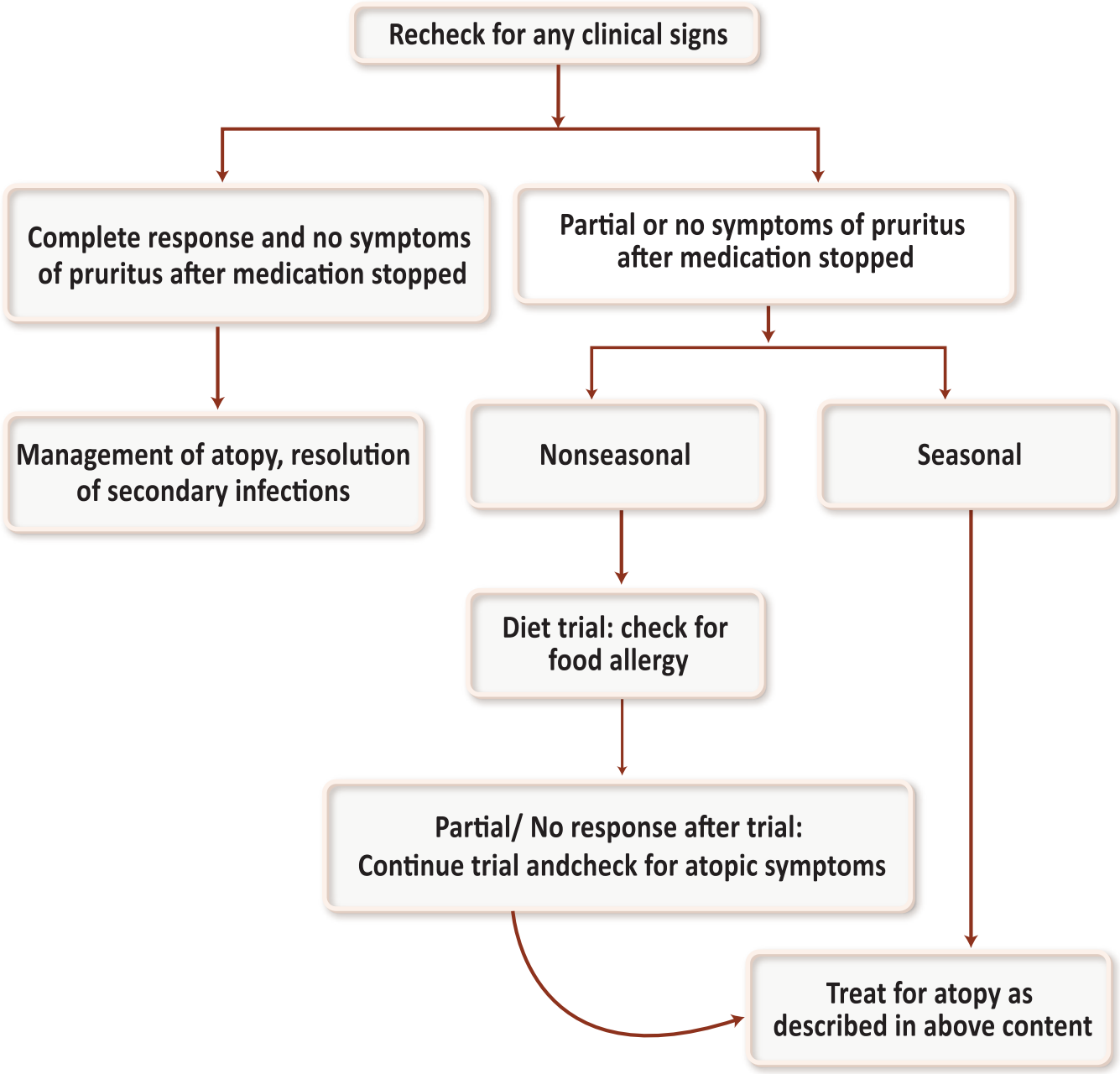
- **Allergen-Specific Immunotherapy:** Altering the immune response by allergen-specific immunotherapy (ASIT), also known as desensitization or hyposensitization, is the only disease-modifying therapy that neutralizes a hyper-responsive immune system to environmental allergens by inducing tolerance. Subcutaneous immunotherapy (SCIT) has been the mainstay of ASIT since the early 1980s. Two formulations are available for dogs, namely aqueous and alum-based solutions, and if the correct protocols are followed systemic side-effects are rarely seen.

When managing CAD, it is important to determine the right combination of therapies for each individual dog that will provide a safe, effective, and affordable management strategy that the respective pet owner can reliably and willingly execute. A common pitfall in the management of CAD is a failure to identify and address all disease flare factors. Therapeutic recommendations for CAD need to be tailored to each individual dog, including their stage and severity of disease, using a combination of topical and systemic therapies.

Clinical Assesment of Dog with Pruritus

In an attempt to provide Veterinarians with sound guidance, dog presented with pruritus to follow below mentioned steps for assessing proper treatment;





Summary

- Atopic Dermatitis is a common, chronic disease which affects the quality of life for many dogs and their owners.
- The various factors that influence the pruritus threshold should be addressed simultaneously in order to achieve successful treatment, especially when flares are present.
- Exacerbations of pruritus and dermatitis by secondary skin infections should be controlled with topical treatment, taking into account the repair of the epidermal barrier.
- Management of CAD should be individualized and adjusted for flares, seasonality and the general health of the pets.
- Atopic dog needs long-term multimodal treatment management to secure a good quality of life, and there is a need for education, clear explanation, and coaching of owners to achieve the best treatment outcome.

References

Annette van der Lee (**2021**). Treating Canine Atopic Dermatitis. *Vet. Focus.* p. 08-13.

Bizikova, P., Santoro, D., Marsella, R., Nuttall, T., Eisenschenk, M.N.C. and Pucheu-Haston, C.M. (**2015**). Review: Clinical and histological manifestations of canine atopic dermatitis. *Vet. Dermatol.* 1-6.

https://www2.zoetis.com.au/content/_assets/docs/Resource-center/AVDAP-Guidelines.pdf.

Miller, J., Simpson, A., Bloom, P., Diesel, A., Friedeck, A., Peterson, T., Wisecup, M. and Chih-Ming, Yu. **(2023)**. AAHA Management of Allergic Skin Diseases in Dogs and Cats Guidelines. *J. Am. Anim. Hosp. Assoc.* **59:** 1-30.

Outerbridge, C.A. and Jordan, T.J.M. (**2021**). Current Knowledge on Canine Atopic Dermatitis: Pathogenesis and Treatment. *Adv. Small Anim. Care* **2:** 101-115.

For suggestions and comments, please write to us

INTAS ANIMAL HEALTH

TECHNICAL CELL

INTAS ANIMAL HEALTH

INTAS PHARMACEUTICALS LIMITED,

Corporate House, Near Sola Bridge, Sarkhej-Gandhinagar Highway, Thaltej, Ahmedabad - 380054. Gujarat. INDIA

E-mail: Petpod@intaspharma.com | Telephone: +91 (79) 61577000, 61577843

Website: www.intasanimalhealth.com | Corporate website: www.Intaspharma.com

2212439