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DRUGS FOR ITCHY ANIMALS
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Introduction

A. Pruritic skin diseases often can mimic each other. Atopic dermatitis, flea allergy dermatitis, food allergy, scabies, and pyoderma or Malassezia dermatitis without underlying allergic skin disease all can be differential diagnoses for each other!

B. The presence of one allergic skin disease seems to predispose to the development of other allergic skin diseases. Therefore, remembering the concepts of the ‘Threshold Phenomenon’ and ‘Summation of Effect’ discussed earlier, it always is important not to consider ones diagnostic work finished when one allergic or pruritic skin disease is diagnosed.

C. The concept of triggering flare factors is crucial to the successful management of allergic skin diseases. The signs and severity of allergy will vary with antigen exposure, changes in environment, and may vary with seasonality. Coexistent flea allergy dermatitis and/or food allergy will dramatically impact the severity of pruritus seen in dogs with atopic dermatitis. Pyoderma and Malassezia dermatitis can markedly increase pruritus seen with any allergic skin disease.

D. Systemic and topical antipruritic medications are much less likely to be successful if total case management is not practiced.

General Principals in the Total Case Management of Pruritic Animals

A. Veterinary and owner commitment and vigilance
B. Allergen avoidance and the prevention of allergen contact
C. Stringent long-term flea control
D. Control coexistent allergic skin disease(s)
E. Control secondary bacterial overgrowth, pyoderma, or yeast infection
F. Anti-inflammatory systemic medical management
G. Topical therapy
H. Allergen-specific immunotherapy

Veterinary and Owner Commitment and Vigilance

A. Successful long-term management requires substantial and ongoing owner commitment. Owner and veterinarian must develop a rapport resulting in frequent appointments and conscientious ongoing reevaluations and surveillance. The owner may be visiting their veterinarian regularly for the rest of the dog’s life.

B. Owner must buy into the concepts of ‘threshold phenomenon’ and ‘summation of effect’ so they can determine triggering flare factors.

C. Dogs with atopic dermatitis that respond well to allergen-specific immunotherapy will require considerably less ongoing care.

Allergen Avoidance and the Prevention of Allergen Contact
A. Triggering flare factors for allergic skin disease include aeroallergens (pollens, mold spores) in atopic dermatitis, plus food (food allergy, atopic dermatitis), and arthropod antigens for flea allergy dermatitis and atopic dermatitis (house dust mite, cockroach antigen, etc.)

B. Reduction of outdoor exposure when pollens and molds are present in highest concentration. Wind increases antigen exposure.

C. If allergy to *Dermatophagoides* house dust mite allergens is confirmed, owners can utilize pillow and mattress covers made of low-diameter pore fabrics impenetrable to house dust mite allergens.

D. Purchase washable animal beds (filled with polystyrene beads), wash the bedding every 2 weeks, replace beds every 2 years.

E. Avoidance of direct allergen contact – For example, limit exposure to grass (especially when grass or dog is wet) if allergy to grasses.

F. Bathing - Frequent bathing physically remove allergens.

G. House dust mite control with topical acaricides, arthropod growth regulators, and desiccants is a potentially important future possibility.

H. Atopic animals may have defective epidermal lipid barriers. Attempt to restore epidermal ceramides by a diet rich in linoleic acid? Topical products that restore this barrier may be possible in the future.

**Stringent Long-Term Flea Control**

A. New, less toxic prescription products that are much easier to use kill adult fleas and disrupt the flea life-cycle. Preventing reinestation via insuring long-term pet owner compliance is the key to success.

B. The goals of flea control should be (1) elimination of existing fleas on affected animals, (2) continued elimination of fleas acquired from infested premises, and (3) the prevention of reinestation. To accomplish these 3 goals, an integrated flea control plan must be instituted.

C. Agents that have revolutionized flea control include lufenuron, imidacloprid, fipronil, selamectin, nitenpyram, IGRs, and permethrin.

**Control Coexistent Allergic Skin Diseases**

A. Diagnose and manage all allergic skin diseases present.

B. Long-term surveillance for newly emerging allergies

C. Controversial – Use of limited antigen or hydrolyzed diets?

**Control Secondary Bacterial Overgrowth, Pyoderma, or Yeast Infection**

A. Skin pathogens such as *Staphylococcus intermedius* and *Malassezia pachydermatis* may act as important flare factors.

B. Long-term surveillance using cytology is essential.

**Anti-Inflammatory Systemic Medical Management**
A. The goal of anti-inflammatory therapy is to find the product or combination of products that offer maximum efficacy with minimal cost and side effects.

B. Drugs that inhibit the allergic immediate phase reaction
   1. Cyclosporin A, cromoglycate – Prevent mast cell degranulation and the release of preformed mediators
   2. Antihistamines (anti-H₁ type) - Prevent vasoactive and pruritogenic effects of histamine

C. Drugs that inhibit the allergic late phase reaction
   1. Corticosteroids, cyclosporin A, tacrolimus, pentoxifylline, misoprostol, zileuton - Prevent the activation and release of mediators with chemoattractant effects.

D. Corticosteroids and cyclosporin A - Drugs with the best clinical efficacy, inhibit both immediate and late phase reactions.

E. Evidence-based medicine has fostered new ‘quality of evidence’ and ‘strength of recommendation’ grading schemes allowing standardized evaluation of published clinical trials.

F. ‘Good evidence’ - oral prednisolone/prednisone and cyclosporine. Studies show that prednisolone is more predictably absorbed than prednisone in the cat and horse. Studies in the dog have not been done.

G. ‘Fair evidence’ - misoprostol and pentoxifylline

H. ‘Insufficient evidence’ is available to recommend for or against antihistamines, essential fatty acids, tacrolimus, leukotriene inhibitors, serotonin-reuptake antagonists, and capsaicin

I. Corticosteroids - Very effective, however, frequent serious side effects if improperly used - If corticosteroids are used long-term, short acting (prednisolone, prednisone, methylprednisolone) corticosteroids should be used on an alternate day basis only. Oral corticosteroids may be the treatment of choice, if only short-term seasonal pruritus. Diminishing corticosteroid dosage down to every other day is most beneficial as the adrenal-pituitary axis is substantially less suppressed. Prednisolone: 0.50 mg/kg BID for 7 days, 0.50 mg/kg SID for 7 days. 0.50 mg/kg q 48h for 7 days, then decrease the dosage every other day until the lowest dose that will control the pruritus is established
   Temaril-P[^R] (Pfizer) – A combination product containing 2 mg of prednisolone and trimeprazine tartrate (an antihistamine) equivalent to 5mg. of trimeprazine. The use of this combination product frequently decreases the total dosage of prednisolone required to manage pruritus! It is not unusual for this product to allow using half the dosage of prednisolone to manage pruritus.

J. Cyclosporine A (CsA) - Atopica® (Novartis) is a micro emulsion formulation that improves absorption of the drug. The standard dosage for atopic dermatitis is 5mg/kg per day. It is available in capsules of 10mg, 25mg, 50 mg and 100mg. Cyclosporine therapy may be more practical in small dogs and cats due to expense. Atopica ® is most consistently absorbed when given without food. However, giving with food may decrease the likelihood of vomiting and other gastrointestinal
side effects. A recent study suggests that the administration of CsA with food does not influence the clinical response or the frequency of adverse events. CsA is metabolized by cytochrome P-450 enzymes. Drugs that induce Cytochrome P-450 enzymes (phenobarbital and rifampin) may decrease serum CsA levels. Likewise, drugs that inhibit P-450 enzymes may increase CsA levels. Commonly used drugs that inhibit P-450 enzyme systems include antifungals (ketoconazole, itraconazole, fluconazole), furosemide, calcium channel blockers, metaclopramide, methylprednisolone and doxycycline. Ketoconazole specifically inhibits hepatic microsomal cytochrome P-450(CYP) 3A12 enzyme, the CYP that metabolizes cyclosporine and dexamethasone. Consequently, ketoconazole may be given with cyclosporine to decrease the amount of cyclosporine needed and decrease the cost of therapy. This is especially important when considering cyclosporine therapy in large dogs. Dosages of Atopica® of 2.5 -3 mg/kg per day may be as effective as 5 mg/kg per day when given with generic ketoconazole at 5 mg/kg per day. We recommend dosage of CsA alone initially and establishing efficacy, before administration with ketoconazole. After control of pruritus is achieved, the clinician may be able to reduce the daily dosage or switch to every second or third day therapy.

Herbal therapy

Herbal therapy using medicinal herbs currently is being explored in veterinary medicine. Several studies indicate benefit from an extract made from a mixture of Rehmannia glutinosa, Paeonia lactiflora, and Glycyrrhiza uralensis (Phytopharm).

Topical Therapy

A. Shampoos can remove allergens before allergy can be initiated. Shampoo therapy must be gentle in order to remove surface allergens, bacteria, and yeast with minimal disruption to the epidermal lipid barrier. The ideal shampoo for the management of an allergic animal should be gentle, lipid barrier sparing, and prevent surface bacterial and yeast overgrowth.

B. Antimicrobial shampoos are beneficial for animals with recurrent surface bacterial overgrowth or bacterial and/or Malassezia infection.

C. Glycotechnology, the use of sugars in topical products, is encouraging because of the potential benefits of preventing microbial adherence and by reducing the inflammatory response to allergy challenge. Microbial carbohydrate receptors (lectins) recognize specific sugars on host cell membranes thus preventing adherence. Sugars also can down regulate inflammation by inhibiting the secretion of pro-inflammatory cytokines. AllermylR shampoo (Virbac) offers this new technology.

D. Shampoos, rinses or sprays containing oatmeal can offer soothing, antipruritic benefit. ReliefR (DVM/IVX), Epi-SootheR (Virbac)
E. Longevity of residual topical products after shampooing, has been disappointing. Available products contain oatmeal, corticosteroids (hydrocortisone), and antihistamines.

F. Topical low-dose (.015%) triamcinolone (Genesis™ Spray [Virbac]) sprays can be beneficial, but care must be taken not to induce topical application iatrogenic hyperglucocorticoidism.

G. Tacrolimus (Protopic® [Astellas Pharma] and topical pimecrolimus (Elidel® [Novartis]) are topical macrolide immunomodulatory agents related to Cyclosporine A. Tacrolimus shows promise in the management of dogs with atopic dermatitis, especially if affected body area is small.

Recommended Reading