Managing Pruritus in Dogs – Parts 1, 2, 3

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Pruritus is the most common symptom of skin disease and knowing how to approach this symptom is critical to successful management of skin disease in practice. Your approach to this clinical symptom should follow a stepwise process. First and foremost is taking a complete history. Next define key features on physical examination, including primary and secondary lesions that fit differential diagnoses. Follow with the essential diagnostic tests. Based on your history, physical findings and diagnostics initiate appropriate therapeutic approaches. All of this depends upon client compliance, which can sometimes be challenging.

Causes of pruritus

Pruritus can be associated with a variety of different diseases. Some cases can develop pruritus as a result of a typically non-pruritic disease and other animals with classic pruritic diseases may not manifest pruritus. It is important to realize that even though a wide manifestation of diseases may be involved there are really only a few common consistent causes. A good practitioner will learn to rapidly identify and deal with the common causes. For those cases not determined to have the typical causes of pruritus or that do not respond to the therapies that should normally be effective further diagnostics or referral to a specialist should be consider.

The most common causes of pruritus in clinical practice include allergic skin diseases (atopic dermatitis, flea allergy, adverse food reactions) and parasitic infections (scabies, cheyletiella, demodex, fleas). All of these are also complicated by secondary infections (bacteria and yeast infections). Less common causes of pruritus include keratinization defects, dermatophyte infections, autoimmune skin disease, neoplasia and psychogenic causes. These less common causes can also be complicated by secondary infection, intensifying the level of pruritus.

History

Accurate history is absolutely critical. Specifically for dermatology cases you should create a dermatology history questionnaire. For example consider the following questions: Where is the pruritus? Is the pruritus seasonal or year round? Seasonal symptoms usually indicate atopy, fleas or other insect hypersensitivity. Some symptoms may be seasonal while others are not. What is the age of onset? Young age of onset, less than 6 months of age would rate adverse food reaction or parasitic. Older onset, greater than 10 years, suggests parasites, infections or neoplasia. Where was the initial body location? Most pruritic diseases have a typical pattern. For example for atopic dermatitis aural, paw, axilla and flexor areas of the extremities are most commonly involved. Food allergy can mimic this distribution but may target the perineal or lumbosacral area in the canine. How effective were prior treatments? Failure to continue to respond to glucocorticoids suggests secondary pyoderma, bacterial overgrowth or Malassezia dermatitis. The development of odors may indicate secondary infections. Are other pets/humans affected? Identifying if other pets or in contact humans would increase concerns for zoonotic diseases such as parasites or dermatophytes. Is the condition worse indoors/outdoors? Symptoms worsening when indoors would suggest indoor allergens like house dust mites. Is there a familial history? Atopic dermatitis tends to run in some breeds and specific lines. Are there other abnormalities noted from the history related to bowel habits, general health, activity, eating, drinking and urinating. Some adverse food reactions can have histories of gastrointestinal disease with more frequent bowel movements or history of inflammatory bowel disease. Often you need to question the owner for all of the various synonyms for pruritus, i.e. scratching, biting, chewing licking, gnawing, rubbing, rolling, shaking, as many owners do not equate all of these descriptions as pruritic symptoms. Lastly attempt to get a grade of the pruritus on a scale from 1 – 10. Many dermatologists are using pruritus scoring index systems so that the cases can be assessed by the owner and the practitioner at initially and recheck visits. This aids in the assessment of cases before and during therapy.

Physical exam

When performing your exam your lesions are often secondary and most consistent with self-trauma, in the form of excoriations, erosions, ulcers, scaling, crusting, alopecia, lichenification and hyperpigmentation. Primary lesions such as papules, macules, pustules may also be present depending upon the underlying etiology. Papules are a very common lesion in canine pruritic skin diseases and can be seen in an unlimited number of disorders. Pustules are more common in the canine. When present in the canine consider primary infectious conditions and other sterile pustular diseases (ie pemphigus foliaceus) as top differentials. Secondary lesions such as erosions and ulcers are often due to self-trauma and excoriations. If the erosions and ulcers are due to scratching there should be linearity. When erosions are induced from licking the lesions tend to be more oval or circular and may appear more in groups.

The location or distribution of the lesions should correlate with sites of pruritus and your major differential diagnoses. For example, when dealing with atopic dermatitis there is often secondary lesions of self-trauma over the face, muzzle, periocular, pinnae, antebrachial, pedal, axilla, groin and perineal regions. Canine scabies cases often have pinnae, elbow and ventral truncal lesions. Many canine scabies cases will have a positive femoral pinnal reflex when the edge of the pinnae are rubbed vigorously created the same unilateral pruritic reflex from the rear leg. Dogs with flea allergy and occasionally adverse food reactions will have dorsal lumbosacral

involvement. Ventral lesion distribution is more common in atopic dermatitis, scabies and contact allergies. After performing your exam you may also notice other areas on the body that have skin lesions that the owner did not report in the initial history, warranting further questioning regarding pruritic sites or habits. All of this information aids in the formation of your differential diagnosis and which testing would be indicated to narrow your differential or identify your secondary infections.

Initial diagnostic testing

Which diagnostic tests should be performed on an initial or follow up exam in a pruritic dog depends on many factors. Of course performing tests that are cost effective and those that are going to give you the answer to support or rule out your differentials are most appropriate. Many times we are restricted by finances of what we can do and prioritizing your testing procedures is very important.

Skin scrape

Skin scraping is one of the most frequently used tests in veterinary dermatology and is recommended anytime the differential diagnosis includes microscopic ectoparasitic diseases. Skin scraping is most commonly used to verify or rule out the diagnosis of demodectic mange. It is also commonly used to try to establish the diagnosis of sarcoptes, cheyletiella infestations and other ectoparasitic diseases, although it does not effectively rule out sarcoptic mange. Not all skin scrapings are performed in the same way. The method of scraping for demodectic mites is different from that of scraping for sarcoptic mites. Demodectic Mites: Generally multiple scrapings from new lesions should be obtained until capillary bleeding is produced. An alternative technique that can be used in areas where skin scrapings may be more difficult, ie periocular or interdigital, is the hair plucking technique. In this technique hairs are gently plucked and the hairs are examined in mineral oil on a glass slide as you would with a skin scraping. Many times mites can be identified at the level of the hair bulb. Canine sarcoptic mites reside within the superficial epidermis however, because small numbers of mites are usually present in canine scabies they are difficult to find. Multiple superficial scrapings are indicated with emphasis on the pinnal margins and elbow. The more scrapings performed, the more likely a diagnosis, however even with numerous scrapings, scabies cannot be ruled out because of negative results. Many cases of sarcoptic mange are ultimately diagnosed by response to therapy. Despite this, skin scrapings should be performed in any chronically, poorly responsive pruritic dog.

Scotch tape preps

Clear scotch tape preps can be helpful in picking up ectoparasites. In particular this method is one of the preferred techniques used to identify cheyletiellosis. The tape is impressed onto the surface of the hair and skin and then placed on a glass slide and scanned for parasites.

Hair coat collections

Combing the coat and collecting dander scale and hair with a flea comb and examining on a glass slide with some mineral oil is an excellent technique to identify many parasites. It has been shown to be the most successful technique of cheyletiellosis identification and can be helpful in flea and flea feces detection.

Trichogram and direct hair exams

Plucking hairs from affected areas of partial alopecia can be very helpful to determine if the hairs are being removed by self-trauma by looking at the normal tapered tip of the hair. Identification of primary hair disorders (ie, follicular dystrophies, color dilution alopecia) can also be made by examining hairs for abnormal melanin clumping or breaks in the cuticle of the hair shaft. In cases where self-trauma is causing the alopecia the tip of the hair will appear fractured and jagged. The stage of the hair growth cycle can also be identified by the appearance of the follicular bulb area. Actively growing hairs have a larger anagen bulb region compared to resting (catagen) or non-growing (telogen) phases. Direct hair exams can also be a method of identifying dermatophytosis. By turning the condenser down you can visualize fungal hyphae and spores in many cases of dermatophytosis.

Cytology

Cutaneous cytology is one of the most valuable tools in the practice of veterinary dermatology. It gives immediate information regarding presence of infectious organisms, inflammatory cells and neoplastic conditions in the skin. It is inexpensive to do and will often allows for immediate decisions on the direction of further diagnostics. The basic equipment required includes: Microscope, cytologic stain, microscope slides and transparent acetate tape, syringes and needles, cotton-tipped applicators and a heat source. The easiest stain to use is a commercial modified Wright's stain like Diff Quik®. This is a Romanovsky-type stain that gives less nuclear detail than a vital stain such as New Methylene blue (NMB). Heat fixing the slides prior to staining can be beneficial, as this prevents sample loss during the staining process. It is particularly important for samples that are waxy, greasy or exudative. The easiest and often the most effective way to obtain a sample for skin cytology is doing a direct impression with a glass slide. The glass slide can be pressed against the site you want to sample or you can place the slide at a slight angel to the skin surface and then scrape the surface of the skin while dragging the slide onto the abraded surface that you have created. Another sampling technique that can be utilized is the transparent acetate tape prep. This can be used to pick up epidermal debris, obtain samples from dry lesions that will not stick to a glass slide easily or to obtain samples from areas that are difficult to get to with a glass slide. When this technique is used you will not do heat fixation and will also skip the fixation (clear) solution as this will prevent the tape from laying flat on the glass slide. Cotton-tipped applicators are used to obtain samples from exudative or purulent areas such as ears, skin folds and interdigital spaces, where it

is difficult to lay a microscopy slide flat. When examining a sample, it is best to scan slides under low power initially to identify location and types of cells before choosing an area to examine under oil immersion. It is best to look more closely at sites where inflammatory or neoplastic cells are seen under low power. Examining under higher magnification (oil immersion) can aid in identifying more detailed cellular morphology, the presence of microbes or cellular atypica. The presence of intracellular organisms indicates that the microbes are pathogens and associated with a true infection. Details on the technique, common organisms, inflammatory cells and artifacts that can be identified from skin cytology can be found in more comprehensive references.

DTM

Dermatophyte test media (DTM) is a convenient fungal culture media commonly used by practitioners. Dermatophytes utilize protein and produce an alkaline by product that produces a red color change. However, after all the carbohydrates are utilized, the saprophytes can utilize the protein and turn the media red. The DTM cultures should be inspected daily. Suspected fungal growth can be lifted with clear plastic tape and stained with lactophenol cotton blue for characteristic macroconidia and fungal identification. The author prefers either Vet Lab or Hardy Diagnostics for optimal sample handling and fungal growth and macroconidia identification.

Bacterial C/S

Culture and sensitivity testing is indicated in cases that have not responded to appropriate empirical therapy based on cytology, in cases of suspected MRS infections, in cases of severe immune suppression, and when there is a differential that includes a sterile inflammatory disease. Depending on the type of lesion and the differential you are concerned with, the culture may be obtained by using a sterile swab or preferably by using a sterile biopsy punch technique. The sample is then sent to the lab; the tissue is emulsified and then cultured. Lesions that are not already open to the surface are the best samples to obtain. Deeper, and in particular more nodular or granulomatous lesions, may require additional culture techniques in the laboratory. This is particularly true when anaerobic or mycobacterium infections are suspected. Laboratories that offer minimum inhibitory concentrations (MICs) are preferable to enable selection of not only a sensitive antibiotic but also one that may be effective even at lower serum concentrations. Even though most MICs reflect serum levels, the information can still be valuable because of the likelihood that it will also reflect better tissue levels of that particular antibiotic. Culture and sensitivity testing has been particularly valuable in identifying the increasing frequency of MRS infections. Since methicillin is no longer commercially available, it does not appear on antibiotic susceptibility panels. Oxacillin is the stand-in for methicillin, and assume methicillin resistance if an organism is reported as being oxacillin-resistant. If oxacillin is resistant, the lab should automatically report all beta-lactam agents as resistant even if in vitro testing shows susceptibility. This means an “R” is populated next to all penicillins, synthetic penicillins, clavulanic acid-augmented penicillins, cephalosporins, carbapenems, and cephems.

Work in human and now veterinary medicine has looked at resistance prevention by using a newer concept called “the mutant prevention concentration” (MPC). MPC can help evaluate an antibiotic’s ability to minimize or limit development of resistant organisms. The MPC defines the antimicrobial drug concentration threshold that obtains inhibition of fully susceptible, as well as resistant, strains of bacteria. Another definition is the drug concentration that prevents growth of first-step resistant mutants or the MIC of the most resistant organism present in the heterogeneous bacterial population when tested against ≥ 109 organisms. A mutant section window (MSW) describes a danger zone in the dosing of antibiotics at which drug concentrations in serum or other body fluids is considered too low and resistance is likely to occur. Ideally antibiotics should exceed the MPC and be in the upper end of the mutant section window. MPC testing has been established for many fluoroquinolones but is now available for many other antibiotics. Much of the data show the importance of using antibiotics at or above their recommended dosing during the early stages of therapy, during treatment of the infection, and beyond clinical resolution.

Elimination diet trials

Vegetable based home cooked diets (pinto or kidney beans, tofu mixed with pumpkin or yams) are considered the most optimal for canine cases but not all pets will eat or tolerate such diets and these are nutritionally deficient for long term use in most dogs especially in young actively growing dogs. In the feline limited meat protein diets without carbohydrates are optimal. Often other novel protein sources need to be considered. Options for protein sources include; lamb, duck, turkey and wild game including venison, rabbit, alligator, kangaroo, and ostrich, assuming these have not been previously fed in a home cooked or commercial diet. Carbohydrates should also be novel as many also contain some amounts of protein. Some examples include potatoes, sweet potatoes, yams, rice, green pea, oatmeal, quinoa or turnip. It is also necessary to eliminate all other sources of potential antigens including treats, rawhide, chew toys, chewable heartworm preventatives and additive-containing vitamin and mineral supplements and flavored medications and toothpaste. The duration of the elimination diet again depends on the pet. Most specialists utilize an 8 - 12 week elimination trial to make a diagnosis of food allergy. If a pet is showing no or limited improvement at 6 weeks but if food allergy is highly suspected then the trial should be extended for an additional 2-6 weeks. Although home cooked diets are optimal they can be impractical and difficult to feed for both the owner and pet. In this situation there are many novel and hydrolyzed commercial protein diets available on the market. The author has had success with the limited commercial canine protein diets made from the Iams

Company (KO), Royal Canin, Hills and Waltham (Duck and Rabbit). Canine hydrolyzed diets can also be of value and include Purina CNM-HA (cornstarch and hydrolyzed soy) and Hills ZD (hydrolyzed chicken) and Royal Canin HP.

Skin biopsies

Biopsies and histopathologic interpretations can often be an invaluable tool in helping to establish definitive diagnoses or disease categories. Some of the ways in which histopathology can be helpful include giving specific diagnoses or at least limiting your differential diagnosis, showing evidence of multiple diseases or secondary disease factors, helping to establish treatment protocols and helping to gave a prognosis especially when more serious life threatening diseases are a concern. In addition, there are some diseases that require histopathology for diagnosis, such as the autoimmune or neoplastic diseases. Cell types and patterns of inflammation can also be very helpful in formulating differential diagnoses. Biopsies are also indicated when there is a lack of response to what is perceived to be appropriate therapy. Site selection to determine which areas to biopsy is an art, but there are multiple guidelines to follow which can be helpful in assuring that biopsied areas are more likely to be representative for specific diseases. Sampling multiple sites or a continuum of the disease can be extremely helpful in establishing how a disease is progressing. It is also important to biopsy lesions early in the course of the disease. You are much more likely to find diagnostic changes in an early lesion than one that is older, scarred, ulcerated or crusted. The clinician should also pick lesions that are needed for the diagnosis of the suspected disease. Samples should be sent to a pathologist who has expertise and interest in dermatopathology.

Allergy testing

Allergy testing is indicated when a clinical diagnosis of atopic dermatitis has been made and allergen specific immunotherapy (ASIT) is being considered as the therapy of choice. Allergy testing may be done by intradermal testing (IDT) or serum in vitro testing (SIVT). In general IDT is considered preferable by most veterinary dermatologists but neither test is perfect. SIVT is not performed to diagnose AD and can have many positives in normal dogs and dogs with other skin diseases. IDT has much fewer irrelevant positives and to some degree may be an aid to diagnosis of AD, but less so when reactions are weaker. When to perform allergy testing is determined by the probability that atopic dermatitis is present and how likely other concurrent diseases may be present. It may also reflect how quickly an owner wants results, their willingness to complete an elimination diet trial and how interested they are in ASIT vs other therapeutic options for AD. In the feline the author typically utilizes SIVT for pollens. (Details on allergy testing will be presented in another section).

Initial therapeutic trials

Treat secondary infections

Appropriate treatment for secondary bacterial and yeast infections is critical in all pruritic cases. By eliminating the infection there can be huge improvements in the level of the pruritus. Antibiotics can be chosen empirically from cytology or based on culture results. Appropriate duration and dosing is critical for skin infections and if both yeast and bacterial infections are identified both must be addressed.

Bacterial infection - Topical therapy

Shampoo therapy is the author's favorite topical antimicrobial therapy. The most common antibacterial agents found in shampoos include benzoyl peroxide with or without sulfur, chlorhexidine with and without phytosphingosine, ethyl lactate and triclosan. Benzoyl peroxide is very effective for S. intermedius and it is also an excellent follicular flushing agent, which promotes removal of inspissated debris and is comedolytic. It also has excellent keratolytic and degreasing effects. It is available in several different products. (OxyDex® and Sulf/OxyDex®, Teva Animal Health, Pyoben®, Virbac, Micro Pearls Benzoyl Peroxide®, Vetoquinol, Benzoyl Peroxide Plus® -Dechra). Another favorite antibacterial agent is chlorhexidine. It is less drying and irritating than benzoyl peroxide, but at the 2% concentration is not as effective as higher 3 -4% concentrations. Newer formulations have been impressive in clinical cases (Douxo Chlorhexidine PS, Sogeval, ChlorhexiDerm®, Teva Animal Health, Hexedene® and Ketochlor®, Virbac,). The Douxo chlorhexidine PS, Sogeval product also combines phytosphingosine with the chlorhexidine giving added antimicrobial efficacy. Cases that are complicated by concurrent Malassezia are best treated with a combination shampoo products that contain and antibacterial and antiyeast agent such as chlorhexidine with phytosphingosine (Douxo Chlorhexidine PS®, Sogeval), chlorhexidine and miconazole (Malaseb®, Teva Animal Health) chlorhexidine and ketoconazole (Ketochlor®, Virbac) or chlorhexidine and TRIZ edta (Triz CHLOR, Dechra).

Localized topical therapy has value in some pyoderma cases. A number of companies that make chlorhexidine-based shampoos also make topical sprays, wipes and towelettes that can be used in between or as an option for bathing. Mupirocin, an antibiotic developed from the fermentation of Pseudomonas fluorescens works very well for localized deep folliculitis and furunculosis cases. Mupirocin is available in a polyethylene glycol ointment (Dechra).

Bacterial infection - Systemic therapy

The author's personal favorite antibiotics in clinical dermatology practice are based on many variables. Selection factors include appropriate sensitivity, chronicity, degree of scarring, depth of infection, immune suppression, and client concerns, (cost, frequency of administration, and incidence of side effects). The most commonly used antibiotics at the author's practice include cephalosporins, amoxicillin- clavulanate, clindamycin, ormetoprim-potentiated sulfonamides, fluoroquinolones and chloramphenicol.

Cephalosporins

Cephalexin is the work horse antibiotic used in our clinical practices. It is a broad-spectrum, first generation bactericidal cephalosporin. It is a twice a day antibiotic, with excellent tissue penetration, rarely creates resistance and the generics are inexpensive. It is commonly dosed at 20 -30mg/kg q 12h. The classification of cephalosporins into first, second and third generations is based upon their increasing activity against beta-lactamase producing gram-negative bacteria. Cefpodoxime proxetil (Simpicef, Pfizer) an orally administered extended spectrum, semi synthetic cephalosporins and is classified as a third generation cephalosporins with increased gram-negative activity with still having good gram positive activity with limited anaerobic spectrum. Tablets are available in 100 and 200mg and dosed at 5 – 10mg/kg q 24h. Cefovecin (Convenia®, Pfizer) is a new third generation cephalosporin developed for the treatment of aerobic and anaerobic gram negative and gram positive. Cefovecin is a bactericidal against Staphylococcus and Streptococcus spp, Escherichia coli, Pasteurella multocida, Klebsciella and Proteus spp, but is not active against Pseudomonas or Enterococcus spp. Cefovecin has a long half-life of 6.9 days in cats and 5.4 days in dogs and demonstrates prolonged concentrations in extracellular fluid allowing for dosing every 14 days. If required, the dose of 8 mg/kg subcutaneously can be repeated every 14 days for a total of three doses.

Amoxicillin-clavalanate

Clavamox®, Pfizer (amoxicillin trihydrate/clavulanate potassium) is an orally administered formulation comprised of the broad-spectrum antibiotic Amoxi® (amoxicillin trihydrate) and the β-lactamase inhibitor, clavulanate potassium (the potassium salt of clavulanic acid). Amoxicillin trihydrate is a semi-synthetic antibiotic with a broad spectrum of bactericidal activity against many gram-positive and gram-negative, aerobic and anaerobic microorganisms. It does not resist destruction by β-lactamases; therefore, it is not effective against β-lactamase producing bacteria. It is dosed at 12.5-22 mg/kg q12h. It has been a very good choice for many canine Staphylococcal pyoderma cases at the author's practice and is one of most commonly used antibiotics for cats in our practices.

Clindamycin

Clindamycin is a lincosaminide antimicrobial agent with activity against a wide variety of aerobic and anaerobic bacterial pathogens. Unlike penicillin and cephalosporin, it does not have a beta-lactamase enzyme. Therefore bacteria that produce beta-lactamase enzymes are often susceptible to clindamycin, making it a good choice for many methicillin resistant Staphylococcal pyodermas. It has a high oral bioavailability and large volume of distribution and therefore penetrates tissues well. The author likes this antibiotic for deep scarring pyodermas but uses it at a higher dose at 15-20mg/kg q 24h, making it more client user friendly. Side effects are minimal but can include gastrointestinal upsets.

Ormetoprim-potentiated sulfonamides

Two different antibiotics, sulfadimethoxine and ormetoprim, are compounded into one drug (Primor®, Pfizer). Sulfadimethoxine is a long-acting sulphonamide and ormetoprim is a diaminopyrimidine structurally related to trimethoprim. These antibiotics potentiate each other as they block two sequential steps in bacterial folic acid synthesis, thus inhibiting bacterial thymidine synthesis. Potentiated sulfas have a broad spectrum of antimicrobial activity. Susceptible Gram-positive bacteria include: most Streptococci, most Staphylococci and Nocardia. In dogs, the usual dose is 55 mg/kg q 24h orally for the first day and then 27.5 mg/kg q 24h until the end of the course of treatment. Although the incidence of sulfa reactions is lower with ormetoprim-potentiated sulfonamides, it should be avoided in animals with known hypersensitivity to either drug or other sulfonamides. In particular it should be avoided in liver problems, thyroid disease, or blood dyscrasias. Keratoconjunctivitis is a possible sequel to the use of this combination. In addition, toxic hepatopathy, seizures, vomiting, diarrhea, fever, hemolytic anemia, hematuria, polydipsia/polyuria, urticaria, and polyarthritis are all possible side effects. The Doberman breed may be particularly predisposed to sulfa reactions.

Fluoroquinolones

Enrofloxacin, ciprofloxacin, orbifloxacin, difloxacin (5-10mg/kg q24h) and marbofloxacin (2-5mg/kg q24h) and other fluoroquinolones are broad-spectrum bactericidal antibiotics that have excellent activity against multiresistant organisms with very rapid killing activity. Their high lipophilicity allows penetration into gram-positive and gram-negative bacteria. . Their mode of action is by inhibition of an enzyme called DNA gyrase. Once a day dosing with most fluoroquinolones is preferred due to higher sustained concentrations. As mentioned potent tissue penetration is partially related to uptake into macrophages in chronic inflammatory tissue. Its major disadvantages are cost and it is not recommended to be used in growing dogs because of possible particular cartilage. The

author also has had success in treating feline pyoderma with fluoroquinolones. It is recommended when using enrofloxacin to not exceed 5mg/kg in the feline to avoid an idiosyncratic retinal reaction, which can lead to blindness.

Chloramphenicol

Chloramphenicol has an especially broad spectrum of activity against numerous aerobic bacteria, mycoplasma, chlamydial organisms, and anaerobic bacteria. It has the ability to kill some of these infectious organisms intracellularly. The recommended dosing is 50mg/kg q8h. This schedule is relatively inconvenient for most pet owners. Cats have increased sensitivity to blood dyscrasias and for this reason it has never been a common feline treatment. This antibiotic is an especially good choice for skin infections where there is a necrotic or walled off area or in many of the recently isolated methicillin resistant Staphylococcal infections. In some dogs, chloramphenicol use may also induce blood dyscrasias. Chloramphenicol should not be used in patients with abnormal bone marrow, non-regenerative anemia, or circulating abnormal blood cells. Chloramphenicol is removed from the body via the liver's detoxification mechanisms. If a patient is in liver or kidney failure, another antibiotic is probably a better choice. Humans may develop fatal aplastic anemia if exposed orally to chloramphenicol (risk is approximately one person in 25,000). This condition is irreversible and is not dependent upon dosages. For this reason, chloramphenicol has been banned from food animal use in the United States as well as from human use. Washing hands after handling this medication or preferable wearing gloves is recommended. Lastly the author and others have recognized what appears to be a rare peripheral neuropathy which presents as urinary incontinence and hind leg paresis that responds to dosage reduction or discontinuation of the drug.

Malassezia topical therapy

Topical therapy includes a variety of products, most contain one or a combination of the following ingredients: miconazole ≥1%, clotrimazole ≥1%; chlorhexidine ≥ 2%, phytosphingosine, ketoconazole >1%, acetic acid/boric acid, benzoyl peroxide ≥ 2%, and selenium sulfide. Lotions, sprays and wipe on products may be used for localized areas and shampoo for diffuse or large areas. The author’s favorite topical products for Malassezia dermatitis are 3% chlorhexidine and phytosphingosine (Douxo Chlorhexidine PS, Sogeval) and 2% miconazole and 2% chlorhexidine (Malaseb®, Teva Animal Health), both also have topical leave on sprays and/or wipe on products for more difficult localized areas of treatment.

Malassezia systemic therapy

The most common drug used is ketoconazole. Ketoconazole works by interfering with the synthesis of ergosterol in the fungal cell membrane. It is lipophilic and is actively secreted by the sebaceous glands. Possible adverse effects seen include gastroenteritis (vomiting, diarrhea, anorexia), and malaise. Administering the medication with food is helpful in preventing gastrointestinal upset and improving drug absorption. Absorption is enhanced in an acid environment; thus it should not be administered concurrently with antacids or H2 blockers. Other reported side effects include elevated serum liver enzymes, icterus, and anecdotal transient lightening of the coat. Monitoring blood work with long-term use is recommended. Pre-treatment blood work is not usually performed unless warranted by the dog's age or physical condition. Other systemic antifungals include itraconazole, fluconazole and terbinafine. Itraconazole and terbinafine are more expensive than ketoconazole however fluconazole has come down in price with the availability of generic formulations. Itraconazole and fluconazole are first choice systemic drugs in cats as ketoconazole is often associated with more hepatic side effects in felines. All of the azoles are dosed similarly at 2.5 - 10mg/kg q24. Although most specialists like daily therapy for 2-4 weeks, I have seen responses when the drug is used daily for 7- 14 days, and once a response is seen then q 48-hour therapy is continued until complete remission, which usually is 14-21 days. An option to the azoles includes using terbinafine (Lamisil® 250 mg, Novartis), an allylamine antifungal that blocks ergosterol biosynthesis by inhibiting squalene eposidase. It is well distributed in the skin, which has been shown at 30mg/kg q 24h to be as effective as ketoconazole.

Ectoparasites

Ruling out ectoparasites and fleas is critical in any pruritic dog. Trial therapy with selamectin (Revolution®, Pfizer) or imidacloprid-moxidectin (Advantage Multi®, Advocate®, Bayer) every two weeks for at least three treatments is the preferred way to rule out scabies, otodectes or cheyletiella. All in contact dogs should be treated if scabies is to be ruled out. Dogs, cats and rabbits must also be treated if cheyletiella is to be ruled out. Scabies and cheyletiella should be ruled out anytime that it appears contagious pruritus may be present. Also when in contact humans develop a papular pruritic rash, there is a positive pinnal femoral reflex, and perennial pruritus with a papular rash is present and little to no infection is present. Always keep in mind that asymptomatic carriers can be present with many of these ectoparasites and these pets still need to be treated.

Flea allergy

When flea allergy is suspected trial therapy is now available that is fairly reliable in ruling out fleas. This should be done in the canine when dorsal lumbar pruritus is present or is some cases when there is a primary papular rash. There are many excellent products on the market and I like to divide these into traditional and new flea control options.

Traditional flea products

Insect growth regulators (IGR's) and insect development inhibitors (IDI's)

These products are very safe and highly effective for both environmental flea control and for on animal use. Methoprene and pyriproxifen are the two currently marketed IGR's in the US and Europe. The current IDI is lufenuron (Program® and Sentinel®, Novartis). These agents are administered orally, by injection (lufenuron) or topically (pyriproxifen, methoprene), and provide long-term (usually 30 days or longer) ovicidal and larvicidal effects. Methoprene is quickly inactivated by ultraviolet light, which is not the case with the other two. All IGR's are analogues of the insect juvenile hormone. Juvenile hormone regulates larval DNA transcription, maintaining larval information. Other hormones then trigger the fall in the level of juvenile hormone, which allows DNA that codes for adult characteristics. Thus, when the apparent level of juvenile hormone does not fall, pupation cannot occur. This leads to very large larvae, which generally die, or to abnormal pupae, which cannot hatch. They are also ovicidal. Lufenuron is a benzoyl urea that inhibits chitin development if present in blood ingested by the flea. It interrupts embryogenesis, hatching and molting. The fleas are unable to exit from the egg. Pyriproxifen Nylar® has the longest action, and is the most stable remains 100% effective for 150 days after a single spray application. It is an excellent option in cases when Program® may be too expensive because of a multiple pet household or in situations where Program® is ineffective. It is presently available as a spray on and as a topical spot on in combination with permethrin for dogs and a spray with pyrethrins for cats and is included in the new product line, Vectra®. Environmental foggers and sprays are also being marketed and many professionals use this chemical for home treatments.

- Fipronil based products
- Frontline® Spray, Frontline Plus® and Frontline Top Spot®– Merial
- ParastarTM/EasySpotTM Novartis
- PetArmorTM Fidopharm
- CERTIFECT™ (amitraz-methoprene) Merial

Fipronil is a phenylpyrazole, which blocks the action of GABA – an essential neurotransmitter. The Frontline plus contains the insect growth regulator S-methoprene. These products are available as either a spray (Frontline spray®, 0.29% w/w alcohol) or a more convenient spot-formulation (Frontline® and Frontline plus®)(9.7%), ParastarTM and EasySpotTM Novartis, PetArmorTM Fidopharm and CERTIFECT™ (also contains amitraz-methoprene) Merial. One major problem with the spray formulation is the high volume of alcohol-based product that must be applied when the spray product is used. Many cats will show minor adverse reactions with this application technique and many owners will apply insufficient amounts of the product. It has around a month's activity with 95% or greater removal of fleas. Immersion in water has little effect, as it is lipid soluble. However, the author does recommend that dogs should not be bathed 2 days prior or 2 days after applications. It is also effective against ticks, although it kills much more slowly than does amitraz. It also seems to be effective against sarcoptes and cheyletiella, although it has a somewhat slow action. It is very safe with less than one adverse reaction in 200,000. The author routinely uses these products on dogs and cats and may use them at 2-3 week intervals for more complete control in flea allergic animals. The newest fipronil based product CERTIFECT also contains methoprene but also contains amitraz and if more of a tick control based product and cannot be used in cats due to the amitraz.

Imidacloprid based products

Advantage® K9 Advantix® (permethrin), Advantage Multi® and Advocate® (moxidectin)- Bayer

These products are available as topical spot on treatments for either dogs or cats. Imidacloprid is the common ingredient in all of these products and is a chloronicotyl nitroguanidine that acts by binding to the nicotinergic receptors in the postsynaptic nerve region, thus preventing binding of acetylcholine. It acts for approximately the same length of time as Fipronil, but is water soluble and more readily removed by water. It has no effect against ticks and no apparent flea repellent effects unless the combined product (imidacloprid and Permethrin - Advantix®) is used. Advantage Multi® is a prescription drug that also is a heartworm preventive (moxidectin) and also has efficacy for other ectoparasites including scabies and cheyletiella. Imidacloprid when applied at its target dosage of 10mg/kg achieved an 86.6% flea control within 6 hours and up to 97.6% within 12 hours. Efficacies are maintained at between 97.8% and 100% for dogs and between 90% and 96% for cats through day 28. The product appears to be affected by water and shampooing and should be reapplied every 2 weeks if frequent bathing is performed. The author has had excellent results and no adverse reactions at this frequency in both dogs and cats and it are the first choice product for flea control in the feline.

- Selamectin based products
- Revolution® - Pfizer

Selamectin is a semi-synthetic avermectin, derived from doramecin. It is available as a isopropanol/diproylene glycol mono-methyl ether-based topical liquid (6% or 12 % w/v active) for spot on application in both dogs and cats. It is also effective against ticks, sarcoptes, cheyletiella, heartworm prevention, otodectes and some internal parasites. Its efficacy against fleas in both dogs and cats was greater than 90% after the first month of administration and exceeded 99% on day 90 following three consecutive monthly applications. It appears that selamectin is fairly water-resistant as long as it is delayed for at least 2 hours after application. The author has also safely used this product on an every 2-week basis without adverse reactions. Selamectin has been shown to be as effective as fipronil and imidacloprid in reducing C. felis infestation in dogs housed for 3 months in a flea-infested environment. The safety of

selamectin is well established and additional studies have been performed in ivermectin – sensitive collies establishing its safety in this breed. The author tends to use this product more in situations where flea control and additional parasite management are indicated. And also finds it very effective and well tolerated in cats.

Nitenpyram based products

Capstar® - Novartis

Nitenpyram is at neonicotinoid flea adulticide. It is chemically similar to imidacloprid, but differs as it is orally administered at a minimum target dose of 1mg/kg. It is rapid in onset, but short acting. It removes over 95% of adult fleas from dogs and cats within 4 – 6 hours of oral administration and has residual activity for 48 -72 hours. It is incredibly safe to use in both dogs and cats. The author will use this product in conjunction with lufenuron as an alternative to topical control in situations where the pets are bathed very frequently or in situations where topical control is not effective or feasible for the client. When used 2 -3 times a week with monthly lufenuron, excellent control flea control has been accomplished. Nitenpyram can also be used for situations of high-risk flea exposure as a one or two time treatment, ie kenneling, dog or cat shows, trips to the veterinarian or groomers, dog parks, etc.

The newer flea control products include the following

- Spinosad and Spinetoram based products
- Spinosad - Comfortis ®for Dogs and Trifexis (with milbemycin) for Dogs - Elanco

Spinetoram - Assurity® for Cats – Elanco

This is the newest most impressive group of flea products that have been released. The spinosad-based products are only approved for use in the canine and have a novel mode of action at nicotinic acetylcholine D alpha receptors with some effects on GABA resulting in nerve excitation paralysis and death of the flea. Spinosad is felt to be safe in conjunction with all other flea control products and heartworm preventives. There is one interaction that has recently come to note: spinosad can increase the risk of ivermectin side effects when ivermectin is used at the super high doses required to treat skin parasites such as demodicosis. Low doses of ivermectin as used in heartworm prevention are not problematic for this interaction. It does not kill other internal or external parasites. It is for dogs 14 weeks of age an older. Comfortis® tablets are beef flavored but contain pork protein and hydrolyzed soy. That should not be a problem for dogs with beef allergy but could be a problem for a dog with a pork allergy or possibly soy, rare as that might be. It is highly effective and starts working within 30 minutes and has 100% kill rate by 4 hr and lasting 30 days or longer. It is best given with food for the highest C max and longest duration of effectiveness. Because it kills fleas so rapidly, egg formation does not occur. Clinical trials in dogs have shown excellent results for not only flea control but in flea allergic dogs with reduced clinical symptoms. It is not approved in cats but toxicity work has been done in cats to show that vomiting may occur when ingested at very high dosages. At this point in time no feline product is planned. Trifexis has the added benefit of milbemycin giving additional prevention of heartworm disease (Dirofilaria immitis) and treatment and control of adult hookworm (Ancylostoma caninum), adult roundworm (Toxocara canis and Toxascaris leonina) and adult whipworm (Trichuris vulpis) infections. Spinetoram, Assurity® like spinosad is a spinosyn based insecticide derived from the actinomycete bacterium Saccharopolyspora spinosa, and is a macrocyclic lactone insecticide. It acts by causing persistent activation of insect nicotinic acetylcholine receptors. It is available as a spot on low dose volume product for cats. It kills 98-100% of fleas in 12 hours and also kills fleas before they lay eggs. It has good residual activity lasting >99% at 12 hours on Day 35 and has 100% efficacy from 24 hours through Day 37 in manufacture drug trials. To date the author has had limited direct experience with the product but will be available shortly in California.

Metaflumizone based products

- ProMeris Duo for Dogs® (metaflumizone/amitraz) - Pfizer
- ProMeris for Cats® (metaflumizone) - Pfizer

Metaflumizone is a novel insecticide that blocks the influx of sodium required to propagate a nerve impulse along the axon and dendrite of the neuron. This results in reduced feeding, loss of coordination, paralysis and death of the flea. Studies have shown excellent flea and flea egg reduction up to 7 weeks with a high margin of safety. The canine product also contains amitraz and should not be used in cats. The addition of amitraz gives protection against ticks when used in dogs and there are reports of it also working for demodecosis in dogs. The author has evaluated this product in cases of demodicosis and has been impressed with responses seen with every two-week application. The product remains effective if the animal becomes wet. However, prolonged, intense exposure to water should be avoided. This product prevents flea infestation for up to 6 weeks and tick infestation for 4 weeks. Do not use on puppies under 8 weeks of age. Do not administer to cats, sick or debilitated dogs or animals suffering from heat stress. Do not administer to pregnant and lactating animals. This product does have a strong odor that some clients do find unpleasant. There has been a low incidence of pemphigus foliaceus like drug eruptions associated with its use and this may have led to the product being discontinued. The feline product is also a spot-on application of metaflumizone that does not contain amitraz. It binds to the hair and skin surface, and stands up to some shampooing. It can be administered at 4 to 6 week intervals. Do not use on kittens under 8 weeks of age. Do not allow animals to groom each other following application. It may produce a local, temporary, oily appearance, and clumping of the hair at the application site and the volume of application is rather large. Rare topical reactions have been seen, but no pemphigus like reactions as seen in the canine product.

Dinotefuran based products

Vectra 3-D for Dogs® (dinotefuran, permethrin, pyriproxifen) - Summit Vet Pharm/Ceva

This product is a monthly spot-on application for flea, tick and mosquito control with an insect growth regulator. It contains 4.95% dinotefuran (flea adulticide), 0.44% Pyriproxyfen (IGR) and 36% permethrin (tick, mosquito & flea parasiticide/repellent). The advantages of this product include three ingredients and is labeled for fleas, ticks and mosquitoes. Also, it has a quick kill (96% of fleas within 6 hours). Like all topical products, efficacy decreases when animal is bathed. Water and shampooing can lower efficacy after 14 days. It does contain a large dosing volume (large dog--8mL) and needs to be applied in multiple sites or spread along the entire dorsal surface of the body. Care needs to be taken to avoid inadvertent application of the canine product on cats, as permethrin is toxic to cats and extra care should be used when prescribed in households where cats are present. Dinotefuran is a novel 3rd generation neonicotinoid, it is a flea adulticide: it binds permanently to insect nAchR gated Na+ channels leading to tremors, uncoordinated movement and death. It kills by contact--ingestion is not necessary thus this is very beneficial for flea allergic animals. A recent study performed by Blagburn showed that Vectra 3D® successfully inhibited flea feeding immediately after flea infestation, with overall reduction in feeding of 79% within the first hr after application compare to non treated placebo controls. Results of this flea feeding inhibition were seen as quickly as 5 minutes after fleas were placed on the treated dogs. The author has been using this product as an option for Frontline and Advantix and in particularly when there is concern and sensitivity to other biting insects for its repellent effects due to the high permethrin concentration.

Vectra for Dogs and Puppies® (dinotefuran and pyriproxifen) - Summit Vet Pharm/Ceva

This product does not contain permethrin but has a higher concentration of dinotefuran (22%) and pyriproxifen (3%) designed for pure flea control. It has a rapid onset of activity with good residual activity. In particular it would be indicated in cases of FAD where rapid kill is critical for the control of pruritus in the hypersensitive patient. Studies performed by Dryden showed that both of the above mentioned dinotefuran topical formulations were highly effective against flea infested dogs throughout a study period of 28 days post treatment.

Vectra for Cats® (dinotefuran, pyriproxifen) - Summit Vet Pharm/Ceva

This product is a monthly spot-on application for flea, tick and mosquito control with an insect growth regulator. It provides long-lasting repellent, and is a fast acting adult flea killer that also provides control for the egg stage of the flea for at least 30 days. Permethrin is added to provide tick control and as an insect repellant. Pyriproxifen (Nylar) is added for flea egg control. Water and shampooing can lower efficacy after 14 days. Do not use on cats (because of the high concentration of permethrin). This product is fast acting and should be very useful for households with flea allergy patients. The author will also use this product in dogs when there is concern and sensitivity to other biting insects for its repellent effects due to the high permethrin concentration. This product is similar to the canine product but does not contain permethrin due to toxicity concerns.

Adverse food reactions

Dietary trials are also considered trial therapies as well as diagnostic tests and should be performed as listed above. It is critical that diet trials be performed strictly and for adequate time periods. In some cases only partial responses may be seen as the majority of adverse food reactions are seen in dogs with atopic dermatitis. Unfortunately in some cases a therapy for either individual disease may be ineffective unless both diseases are treated concurrently. This may mean in some cases the only time a diet trial will be effective is when AD is being managed by avoidance of the allergen or ASIT.

Topical therapeutic trials

There is a variety of excellent topical shampoos and rinses that can be used to minimize and in some situations control pruritus. The author prefers shampoos and rinses that contain specific antipruritic agents (Colloidal oatmeal, pramoxine, hydrocortisone and phytosphingosine). There are many excellent veterinary dermatologic therapeutic companies that make specific products with different vehicle and delivery systems.

Antihistamines and fatty acid trials

In the author's experience these therapies have limited success and can be utilized as adjunctive therapies in moderate to severe pruritic cases. They may be more effective trial treatments in mild cases of AD. These treatments will only have a chance of being effective if ectoparasites and skin infections are controlled.

Cyclosporine and glucocorticoids

In many cases of AD alterative treatments with other immunosuppressives need to be utilized. The author prefers Cyclosporine to glucocorticoids for long-term use, as it has less outward complications and less long-term side effects. The details of use of these drugs will be covered in another lecture.

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