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Atopic Dermatitis

- Allergens
  - Pollens (trees, grasses,weeds)
  - Dust
  - Storage mites
  - Mold spores
  - Epidermal antigens
  - Insect antigens (dust mites, cockroach, moth, others)
  - Misc. allergens
- History
- Clinical signs
  - Pruritus
  - Feet, ventrum, ears, face, extremities
  - Generalized
  - Erythema
  - Otitis – can be only clinical sign
  - Secondary infections w/or w/o pruritus
  - Acute moist dermatitis
  - Acral lick dermatitis
  - Seborrhea – not a common primary diagnosis (there is almost always an underlying cause)
  - Anal gland disease
  - Conjunctivitis, qualitative tear film deficiency-leads to corneal ulcers

- Rhinitis, asthma
- Salivary staining, hyperpigmentation, licenification, scaling, crusting

- Diagnosis of exclusion
  - Rule out
    - ectoparasites (fleas, scabies, demodex, etc.)
    - food allergy
- Do NOT perform blood allergy test; must do food trial
    - bacterial and/or yeast infections
    - dermatophytes
    - cornification disorders
    - contact dermatitis
- Treatment
  - **Definitive Treatment**
    - Allergen specific Immunotherapy
      - Alter disease state
      - Chance for cure
  - **Symptom only treatments**
    - Apoquel
    - Steroids
    - Atopica
    - Cytopoint/CADI
    - Antibiotics
    - Antifungals
    - Antihistamines
    - Fatty Acids

- Topical therapies
- Diets

- Allergen Specific Immunotherapy
  - Treatment of Choice!
  - Only proven therapy for atopic dermatitis that actually works by reversing the underlying immunopathogenesis of the disease
  - Actually corrects elevated pro-inflammatory cell numbers and their associated cytokines does not suppress them
  - Decreases development of new allergies due to the more appropriate interaction of the immune system
  - Can = CURE
  - Best chance to avoid long term drug therapy
  - No long term side effects
  - Low risk short term side effects
  - Natural desensitization
  - Usually lifelong therapy
  - In humans it is recommended to start as early as possible because it may prevent development of additional sensitivities and prevent progression of disease severity
    - I recommend this for veterinary patients as well
  - Do not stop it even if appears to have cured a patient
  - Inhibits immediate-phase responses after allergen challenge
  - Success rates in clinical practice 60-90%
    - Breed variations
- Allergy testing
  - After clinical diagnosis has been made
  - To implement allergy specific immunotherapy

- Intradermal allergy test performed by experienced clinician is the gold standard and most reliable
- Blood allergy testing for environmental allergens is not as reliable in author's opinion
    - Blood allergy testing should NEVER be used for food allergy testing

- Allergen Specific Immunotherapy
    - SCIT
        - Subcutaneous injection every 7-30 days long term
        - Needles
        - Patient cooperation & owner compliance
        - Molds separate??
        - 3-12 months for full efficacy
        - Initial efficacy similar
        - May be efficacious for patients that fail SLIT
        - can be adjusted at any time to fit the patient
        - Possible reactions: Increased pruritus, facial swelling, erythema/hives, vomiting/diarrhea, lethargy, and very rare anaphylaxis
    - SLIT
        - Sublingual (oral) application usually once to twice daily long term
        - No needles
        - Patient cooperation & owner compliance
        - Molds mixed
        - 3-6 months for full efficacy
        - Initial efficacy similar
        - Safer for pets that have had reactions to SCIT
        - May be efficacious for patients that fail SCIT can be adjusted at any time to fit the patient

- May be more efficacious for patients with allergic airway disease (author hypothesis)
- May be more efficacious for patients with recurrent corneal ulcers (author hypothesis)
- Possible reactions (in author's experience very rare): Increased pruritus (esp. face and mouth), facial swelling, vomiting/diarrhea, erythema/hives, lethargy, coughing/reverse sneezing, bad breath, flatulence, and extremely rare anaphylaxis

- Intra-lymphatic immunotherapy – still experimental

- Symptom treatments
- Apoquel® (oclacitinib)
  - Janus kinase inhibitor
  - Janus kinases are a family of intracellular tyrosine kinases that transduce cytokinemediated signals via the JAK-STAT pathway
  - They are cytosolic tyrosine kinases that are specifically associated with cytokine receptors
  - What are we suppressing?
  - JAKS are important for…
    - normal growth and development
    - normal apoptosis (cell death)
    - policing the body against tumor formation
    - function in formation of RBCs and WBCs
    - appropriately functioning T cells and B cells
    - regulating normal inflammatory response against parasites, bacteria, fungi, and viruses
  - Cross talk
    - JAKs communicate with each other and influence actions of others

- So what happens when one is not working/is being suppressed?—It will affect the others

- Apoquel could seriously undermine a dog's immune system
- Apoquel
  - Control of pruritus associated with allergic dermatitis
  - NOT all pruritus regardless of cause
  - **NOT a replacement for appropriate diagnostic work-up**
  - Worse case of Scabies I have ever seen, no skin scrapings, placed on Apoquel forever!
  - No major concerns with short term or acute use
  - Purpose is to give the clinician time to correctly diagnosis and treat the underlying cause
  - Rapid onset
  - Goal is NOT long term use
  - Appropriate diagnostics to rule out mites and other infectious causes of pruritus
  - Appropriate food trial to rule out food allergy
  - Diagnosed definitively with atopic dermatitis
  - Owners offered allergy testing and immunotherapy first (document)
  - Discuss all main allergy medications: steroids, Atopica, Apoquel, Cytopoint… and their associated side effects in detail with the owner and each drugs unique pros/cons (document)
- Apoquel side effects
  - Gastrointestinal
  - Diarrhea
  - Vomiting
  - Anorexia
  - Nausea
  - Weight loss

- Increased appetite
- Aggression
- Lethargy
- Polydipsia
- Lymphadenopathy
- Neoplasia
    - New dermal/cutaneous or subcutaneous lump
    - Mast cell tumor, malignant melanoma
    - histiocytoma *see new abstract that I included at the end of notes*
    - lipoma
    - malignant neoplasms: thoracic metastatic, abdominal metastatic, heart base, splenic, frontal sinus, intracranial, and transitional cell carcinoma
    - low grade B-cell lymphoma
    - low grade oral spindle cell sarcoma
    - apocrine gland adenocarcinomas
- Lab work
    - reticulocytosis, mild decrease in RBC (subclinical bleeding)
    - decreased WBC
    - increased cholesterol
    - elevated liver values
    - decreased serum globulin
    - increased lipase
- Bleeding
- Pododermatitis
- Fever

- Infections
    - pyoderma
    - *Malassezia* dermatitis or other yeast infections
    - otitis
    - cystitis
    - demodicosis
    - pneumonia
    - dermal pigmented viral plaques
    - papillomas
- Abdominal ascites and pleural effusion
- Darkening areas of skin and fur
- Worsening of dermatitisand pruritus
- Cutaneous drug reaction

- Apoquel warnings
    - Should not be used with other systemic immunosuppressive medications
        - Safety has not been evaluated
        - Wash out period w/ steroids or Atopica?
    - Do not use in breeding, pregnant, lactating animals
    - Do not use in dogs under 1 year of age
    - May increase susceptibility of infections
    - Do not use in dogs with serious infections
    - Exacerbation of neoplastic conditions
- Always dose at SID (author's opinion)
    - Some experience unsuccessful tapering from BID to SID
    - 30 to 50% of cases

- Some reports of more severe pruritus than pre-Apoquel
- Major safety concerns with long term BID dosing

- Apoquel long term?
  - "I am concerned that we do not have long term safety studies on large numbers of dogs on this drug. Until we do, I have a difficult time recommending it unless all other options have been tried" (quote I agree with)

- Apoquel monitoring
  - PE
  - CBC, Chemistry Profile
  - Urinalysis?
  - For development of infections, demodex, and neoplasia
  - Skin scrapings, fungal cultures, cytologies
  - Frequency depends on frequency of use, dose, etc.

- Apoquel - Cats?
  - My personal experience – not very effective
  - Have owners sign statement about off label use and unknown side effects

- mAb therapy
  - Cytopoint/CADI (Zoetis)
  - Remember= only a SYMPTOM treatment
  - Subcutaneous injection given in hospital
  - Anti-itch for about 3-4 weeks
  - 80% effective
  - Loss of efficacy over time
  - Side Effects: gastrointestinal, facial angioedema
  - What will happen over time suppressing a normal part of the immune system
  - In human medicine these are used for much more serious diseases

- In human medicine, now mAbs have been used for a longer period of time they are starting to appreciate there are side effects

- Secondary infections with allergies
- *Staphylococcus*
  - Gram +
  - Facultative anaerobic cocci
  - Normal cutaneous and mucosal microflora
  - Coagulase positive
    - *S. pseudintermedius*
    - *S. aureus*
    - *S. schleiferi ssp. coagulans*
  - Coagulase negative
    - *S. schleiferi ssp. schleiferi*
  - Beware,methicillin resistant *Staphylococci* infections = MRS (MRSA/MRSP/MRSS) are on the rise
- Methicillin resistance
  - Use of fluoroquinolone antibiotics select for super resistant MRS
  - Never use ciprofloxacin to treat *Staphylococcus*
    - Limited bioavailability
    - author's opinion that we should not use it at all in veterinary medicine
  - Antibiotic use inpatients with MR may be a risk factor for development of resistance to other categories of antimicrobials
    - Provocation of heterogeneous resistance in MR strains has been documented
  - Zoonosis
  - Diagnosis

- Swab for superficial infections (should rupture an intact pustule)
- Deep tissue punch for deep infections
- laboratory must be successful at phenotypic differentiation of *Staphylococcal* species. Ie. Is your lab telling you if a strain of *S. schleiferi* is coagulase positive or negative? Are they able to speciate out all *Staphylococcal* species?

- Prevention
  - Avoid use of fluoroquinolones unless necessary
  - Don't treat skin infections with 3rd generation cephalosporins unless they stop responding to 1st generation cephalosporins
  - Do more cultures
  - Don't change or switch around antibiotics
  - Topical therapy for superficial infections instead of systemic therapy
    - Shampoos, rinses, sprays, wipes
  - Do not use pulse therapy antibiotics
  - In hospital
    - Guidelines
    - Active surveillance
    - ***Hand hygiene***
    - Barrier precautions
    - Fomites
    - Antibiotic stewardship
    - Prevention of patient to patient AND person to patient spread
    - Cover cuts/wounds
  - For owners
    - Use of systemic antibiotics for colonized pets should be discouraged in favor of barrier precautions

- Do not share personal items
- Towels
- Clippers
- Utensils
- NO kissing/licking of face/open sores
- Wash hands after petting or playing with pet
- Avoid contact with nose, mouth or rectum
- Pick-up feces and discard
- Wash toys bedding frequently and dry on high heat
- Keep off peoples beds and pillows
- Decrease exposure to other animals to prevent spread

This is one of the abstracts from the recent yearly derm meeting...which confirms my concern about neoplasia and Apoquel.

A retrospective study comparing the incidence of cutaneous histiocytoma development in atopic dogs treated with oclacitinib and ciclosporin.

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Abstract:

Oclacitinib (Apoquel, Zoetis, Inc, Florham Park, NJ, USA) is a Janus kinase inhibitor licensed for the treatment of allergic dermatitis in dogs. Clinical trials have demonstrated a high margin of safety with few adverse reactions. One of these reactions reported is development of benign skin tumors, especially cutaneous histiocytomas, although a causal relationship has not been established. The objective of this retrospective study was to report and compare the incidence of cutaneous histiocytoma development in confirmed atopic dogs treated with oclacitinib versus ciclosporin (Atopica, Elanco USA Inc., Greenfield,IN, USA).

A review of Tufts University's medical records between 2013 and 2016 identified dogs with a diagnosis of atopic dermatitis treated with oclacitinib (n=533) or ciclosporin (n=654). The signalment, diagnosis, treatment, dose, duration of therapy, location of lesion, and remission information were recorded.

There were 14/533 and 4/654 patients who developed histiocytomas while on oclacitinib and ciclosporin, respectively. There was a significantly higher percentage of dogs with histiocytomas on oclacitinib (2.6%) versus ciclosporin (0.6%) (P=0.0041). The mean age of dogs with histiocytomas on oclacitinib (mean=7.0 years) was significantly higher than the dogs on ciclosporin (mean=1.5 years) (P=0.0002). Also, there was a significant difference in duration of treatment between dogs with histiocytomas on oclacitinib (mean=14.8 weeks) versus on ciclosporin (mean=4.8 weeks) (P=0.018). The results of this study demonstrate that histiocytoma development may be higher in patients treated with oclacitinib compared to those treated with ciclosporin. Additional research is needed to determine a causal relationship and pathomechanisms between oclacitinib and cutaneous histiocytomas.

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Allergies in Feline Patients

Feline common clinical signs

- Eosinophilic granuloma complex
  - 1. Indolent ulcer (aka rodent ulcer)
    - Unilateralor bilateral well circumscribed ulcer w/ raised border
    - Regional lymphadenopathy may be present
    - Peripheral eosinophilia rare
    - Rarely undergo malignant transformationin to SCC
    - Can be from all allergies but flea allergy most common underlying cause
  - 2. Linear or collagenolytic granuloma
    - Yellow to pink, raised, well-circumscribed lesions w/ linear, papular, or nodular appearance
    - Common on caudal thighs
    - Swollen chin or lips, intra-oral, on footpads
    - Asymptomatic or very pruritic
    - Peripheral eosinophilia variable
  - 3. Eosinophilic plaques
    - Common reaction pattern, Siamese may be over represented

- Single or multiple well-circumscribed, raised, round, erythematous, moist, eroded and pruritic lesions
- Most common on ventral abdomen, in inguinal area, and medial thighs
- Regional lymphadenopathy may be present
- Tissue as well as blood eosinophilia usually present

- Miliary dermatitis
  - Small, multifocal, crusted papules
  - Head and trunk
  - Variable pruritus
  - Represent primary hypersensitivity reaction
  - All allergies but fleas most common cause, other ectoparasites, dermatophytes
- Self-induced alopecia (feline symmetrical alopecia)
  - Over-grooming behavior
  - Often symmetrical and non-inflammatory, rare secondary lesions, ventrum most commonly affected
  - Perform in secret
  - Very RARELY endocrine or behavioral (psychogenic)
  - May be most common sign in cats with atopic dermatitis
  - Also consider ectoparasites (demodex), anal sac disease
- Cervicofacial pruritus—intense pruritus
  - Severe erosions and ulcers from self trauma
  - May be more common with food allergy