REACTION BY CONSUMERS
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OVERVIEW
An adverse reaction to food (AFR) is defined as a clinically abnormal response attributed to an ingested food substance, and may be further categorized as immunologic or non-immunologic in nature. Food allergy is an immunologically mediated, reaction to ingested food. This is different than food intolerance, which is a non-immunologically mediated adverse reaction including toxic reactions, pharmacological reactions, metabolic reactions, and idiosyncratic reactions.

Immunologic adverse food reactions can result in dermatological diseases, and/or gastrointestinal diseases as well as potentially other disorders. Patients with immunological adverse food reactions may be more common and a patient with repeated gastrointestinal and/or dermatological signs should be suspect. Immunological AFR can be an underlying cause for food allergies, chronic enteropathies, inflammatory bowel disease, perianal fistulas, idiopathic seizures, behavioral disorders and asthma.

We believe the general practitioner is seeing potential cases of immunological adverse food reactions in patients with skin (itching, licking, chewing, otitis, head shaking, anal glands) and GI signs (vomiting and/or diarrhea, flatulence, perianal fistulae, anal gland disease, poor appetite/ anorexic patients) on a daily basis. It is important for the practitioner to identify patients with immunological AFR as they can often be treated with diets and supplements successfully.

FOOD INTOLERANCE
• A non-immunological abnormal physiological response to a food item
• Recognizing food-associated illness can be difficult as often cases present sporadically with no apparent connection
• May involve, toxic, pharmacological, or metabolic reactions or dietary idiosyncrasies
• Examples of food intolerance include lactose intolerance, gluten intolerance, reaction to vasoactive amines in diet
• Reactions to food additives
• Reporting potential adverse reactions:
  o Contact the manufacturer – they should be willing to listen and take information as well as answer questions as to whether other complaints have occurred
  o FDA: http://www.fda.gov
  o AVMA: http://www.avma.org – specifically, this link for reporting adverse events with drugs, vaccines, and pet food:
    http://www.avma.org/animal_health/reporting_adverse_events.asp
  o Example Jerky treats
  o Recent example of recalls for pentobarbital, hyperthyroidism in dogs
THE ETIOLOGY OF IMMUNOLOGICAL ADVERSE FOOD REACTIONS

- Antigens are heat- and acid-stable glycoproteins (carbohydrate and protein) with molecular weights of 18,000-30,000 Daltons
  - Processing of proteins w/ CHO, fats, create glycoproteins, lipoproteins which may be antigenic
  - Hypersensitivity reactions involved in food allergies have been shown to involve types I, III, and IV reactions
  - Some studies indicate that IgE is implicated in some instances and the reactions involved include both the classic, immediate Type I reaction and the late-phase IgE-mediated reactions
- Factors that determine the extent of absorption of allergens by the intestine are not fully understood, although local vasodilation is clearly facilitatory
  - Once local vasodilation is stimulated by local reactions, the cycle feeds on itself
  - What initiates the original immunologic reaction is not clear
- Immune tolerance does not develop appropriately
- If clinical or subclinical GI disease occurs which alters mucosal integrity, absorption of antigenic proteins may occur which may initiate/continue the processes
- Most basic food ingredients have potential to induce an allergic response, although proteins cause the majority of reactions
- Dietary components reported to cause food sensitivity in dogs and cats include: cow’s milk, beef, mutton, pork, chicken, rabbit, horse meat, fish, eggs, oatmeal, wheat, corn, soy, rice flour, potatoes, kidney beans, canned foods, cod liver oil, dry food, pet treats, and food additives.
- Clinical signs of food allergy relate primarily to dermatologic and gastrointestinal
  - Dermatologic signs often include pruritis, erythema, and secondary pyoderma
  - Gastrointestinal signs may include vomiting and/or diarrhea, flatulence, perianal fistulae, and anorexia.
  - Other potentially associated disorders include cholangiohepatitis/cholangitis, feline asthma, idiopathic epilepsy, and feline urinary tract disease

PERSPECTIVES ON IMMUNOLOGICAL ADVERSE FOOD REACTION, FOOD ALLERGY, CANINE ATOPIC DISEASE, CHRONIC ENTEROPATHY AND INFLAMMATORY BOWEL DISEASE:
We would suggest that immunological adverse food reactions may play a significant role in food allergy, canine atopic dermatitis, chronic enteropathies and IBD. And it has been reported that food allergy and canine atopic disease can be clinically indistinguishable. This would suggest that the astute practitioner would benefit from considering the canine with recurrent dermatological and/or gastrointestinal disease as having some underlying immunological adverse food reaction(s) and diet should be part of the treatment plan.

AFR AND DERMATOLOGICAL CANINE PATIENTS

- Index of suspicion of immunological cutaneous adverse food reactions and genetics
  - Top breeds Soft Coat Wheaton, Dalmatian, West Highland White, Bichon, Cairn terrier, Irish/English Setter, Golden retriever, G. Shepherd, Vizla
- Think breed and age as risk factors
  - Age typically < 1 year with 33-52% 2 month- 16 yr
• Think immunological AFR with onset pruritus or other dermatological signs prior to age 6 months and after 6 years of age!
• Pruritic dermatopathies include atopy, flea allergy, food allergy, Malassezia dermatitis, and superficial staphylococcus pyoderma occur together/simultaneously/overlap and immunological adverse food reaction may play role
  o Skin signs pruritus, erythema, epidermal hyperplasia, papular eruption, secondary scales and crusts and more chronic seborrhea w/recurrent bacterial or Malassezia infection
• GI signs present in 32% - we suspect this is much higher
• Use dermatological patterns especially “Ears and Rears”
  o Ear region (otitis, inflamed pinna, pruritic ears) was most consistently involved (80%), Feet (61%), Inguinal/perineal region (53%)
  o Axillary, anterior foreleg and periorbital regions (31–37%)
  o Similar pattern to flea allergy dermatitis affecting the lower back, tail head region and caudolateral thighs
  o Dorsal lesions extend beyond the thoracolumbar junction over the chest area think AFR
Specific dermatological diseases that suggest AFR
• Cocker Spaniels idiopathic seborrhea,
• Seborrhea +/- recurrent secondary bacterial or Malassezia dermatitis
• Symmetric lupoid onchodystrophy, sterile interdigital cysts
• Secondary recurrent pyoderma
• Malassezia pachydermatis infection (may be the only sign)
• Acral lick dermatoses
• Perianal pruritus is almost exclusively due AFR NOT anal gland infection, full anals, etc.
AFR and Canine Atopic Disease
• Prospective studies have documented that CAD and CAFR are often clinically indistinguishable
• Contrary to popular opinion, dogs with CAFR can be steroid responsive.
• Food allergens are often the first to which children with atopic dermatitis become hypersensitive
  o Study, 48% of dogs w/ CAFR had clinical signs develop at less than 1 year of age compared to only 16% of dogs w/ CAD
  o As with children, a higher percentage of dogs with cutaneous adverse food reactions (CAFR) develop clinical signs earlier than dogs with CAD
Dietary treatment and the dermatologic canine patient
• Veterinary therapeutic diets (VTD) antigen restricted/novel protein
• Veterinary therapeutic diets protein hydrolyzed
• Homemade and raw diets
• Treats

AFR AND GASTROINTESTINAL CANINE PATIENTS
• Index of suspicion of AFR and Genetics
  o Boxer and ulcerative colitis
  o Soft Wheaton, G Shepherd and PLE
  o G. Shepherd and Shar Pei and IBD
  o Irish setter and gluten enteropathy,
• Small terrier breeds and intestinal lymphangiectasia
• GDV presents in dogs that are a large or giant breed
• Chronic pancreatitis such as spaniels (Cockers and Cavaliers),
• IBD definition a collective term for a group of chronic enteropathies characterized by persistent or recurrent GI signs, inflammatory infiltrate, and response to treatment (diet, antibiotics and/or immunosuppressive drugs) whereby the basis for different response or lack of response is not known.
• Diagnosis of IBD involves a systematic integration of signalment, medical and dietary history, physical findings, clinic-pathologic testing, diagnostic imaging, and intestinal histopathology
• Canine inflammatory bowel disease activity index (CIBDAI) – a scoring system has been suggested to stage the degree of clinical signs and to better quantify response to therapy
• IBD may be defined by genetic criteria in several animal species
  • Crohn's disease and ulcerative colitis are more common in certain human genotypes
  • A mutation in the NOD2 gene (nucleotide-binding oligomerization domain2) found in a sub-group of patients with Crohn's disease
  • Genetic influences not yet been identified in canine IBD, but certain breeds (e.g., German shepherds, Boxers) appear to be at increased risk for the disease
    • Unknown in any given patient is whether any abnormal immune response to the diet is the cause or result of a mucosal infiltrate
    • If the cause, it is expected that removal of the inciting antigen would lead to improvement
    • If the effect, it still may be that removing the largest single source of antigen during an elimination-diet trial is sufficient to reduce the inflammatory stimulus
    • Because of the consistent partial or complete response, restriction or manipulation of individual dietary components is perhaps the single most important factor in the treatment of IBD, and may be sufficient in mild cases

**MANAGEMENT OF CHRONIC ENTEROPATHIES AND IBD**
• Considering the dietary studies as a whole, a positive response to diet is reported in approximately 50% of dogs with chronic GI signs and IBD
• The descriptive terms 'food responsive' or 'dietary intolerant' have been suggested
• Focuses of dietary therapies are antigenic modification (antigen-restricted/novel protein source or protein hydrolysate) or optimized assimilation (highly digestible, fat restricted and/or restricted fiber)

**Diet Selection**
• VTD novel protein therapeutic single protein source diets available include duck, venison, lamb, fish, rabbit, kangaroo, and alligator
• VTD protein hydrolysate
• VTD GI Hill’s, Purina, Royal canin, Blue Buffalo, Rayne
  • Large bowel signs primarily – fiber diets such as Purina OM, Hill’s w/d, RC GI Fiber Response
  • Small bowel signs – highly digestible Purina EN, Hill’s i/d, RC Mod Calorie
• Low moderate fat in upper GI, motility (GERD) Hill’s i/d low fat, RC Low Fat, Purina OM
• Homemade or raw diets see ACVN (http://www.acvn.org)

Other Therapies
• Vitamin B12 (cobalamin): patients with small intestinal disease even if not SIBO may have systemic B12 deficiency
  o With GI disease, oral replacement may not effective?
  o Parenteral B12 therapy is required. Treatment includes: 1000 mcg SQ q 2-3 weeks, dogs/cats; Cats and dogs <5kg 250 mcg SQ q 7 days for 6 weeks, then q 2 weeks for 6 weeks, then q 4 weeks; Dogs 5-15 kg, 500 mcg/injection; Dogs > 15 kg, 1000mcg/injection
• Probiotics, prebiotics, symbiotics
• Omega-3 fatty acids
• Pancreatic enzymes
• Parental Corticosteroids, Iron, Vitamin A & D, B complex

References by request