

Addressing food allergies can help your atopic patients!

And who doesn't need help with that?!

Alice Jeromin, B.S. Pharmacy, DVM, DACVD

What we'll discuss today:

- **Immunologic aspects** of food allergy-only briefly-I promise!!

Clinical aspects:

1. **Symptoms-cutaneous and noncutaneous**
2. **Diagnostic workup-are serum or skin tests accurate?**
3. **Treatment**
4. How **diet affects atopy** and can help you **better control** atopics

We'll look at a compilation of food allergy studies published by Olivry/Mueller from 1997-2017:

"Critically appraised topics on adverse food reactions"

Adverse Reactions to Food

- Hippocrates—"Let food be your medicine and your medicine be your food"
- Hypersensitivity vs. intolerance—clinically the same, immunologically different.
- Described as early as 1920 in pets.
- Diagnosis-problematic because coexists 20-30% of the time with other allergies.

Wouldn't it be great if we could control chronic skin disease in our patients with diet?!



Wouldn't it be great if we could get owners to perform the diet correctly?!



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Adverse Reactions to Food

- **IgE mediated:**

- Oral allergy syndrome
- Immediate Gi allergy
- Urticaria
- Papular rash/flushing
- Eosinophilic gastroenteritis
- Atopy

- **Non-IgE mediated (cell-mediated)**

- Protein-induced enteropathy

Food affects
you from the
top of your
head to the
tips of your
toes!

- Diet in dogs and cats can play a pivotal role from their head—neurologic diseases/otitis to their feet-- atopy, lupoid onychodystrophy, vasculitis!
- And everywhere in between!



Food can affect your mental state

- Recent report in a woman w/ depression. Her symptoms abated when she avoided certain foods such as casein, gluten, etc.
- When challenged again w/ these ingredients, her depression/anxiety returned.
- You ARE what you eat in more ways than one!

- MPR, Ernst D, Oct. 11, 2019

Incidence of Adverse Food Reactions (AFR) Among Dogs

- 7.6-12% incidence of AFR in dogs.
- Of dogs with adverse food reactions, 9-30.6% have clinical signs compatible with atopy. In humans atopy precedes food allergy-sets up thru eczematous skin.
- GI signs occurred in >20% of dogs and cats with adverse food reactions.
- JAVMA, Sept 1, 2019, Rankovic, A. et al. "Role of carbs in the health of dogs."
- Olivry and Mueller 2017: 1 in 5 cats or dogs with pruritic skin disease---food involved. Incidence is likely underestimated.

Why do some individuals develop allergic reactions to food?

- Largely unknown why some individuals develop allergic reactions to food while the majority do not!

- Interplay between:
 - Genetic factors
 - MICROBIAL COMPOSITION of gut and metabolic activity (dysbiosis)
 - Dietary factors
 - Timing of allergen exposure

Gut Microbiome- Dysbiosis

- Bacterial diversity is essential! The microbiome protects against pathogens, trains/stimulates the immune system, and supplies nutrients-energy, vitamins, SCFA's.
- Dysbiosis-abnormal or unhealthy makeup of the skin or gut microbiome.
- Atopic dermatitis (AD) is associated with dysbiosis of the skin & intestinal microbiome.
- Raw diets-no fermentation in the gut to allow for bacterial diversity.
- Cats-canned food allowed the most bacterial diversity.
- Cave N, Hill's global symposium.com

Microbiome and food allergy

- Relationship between gut bacteria and food allergy.
- Inadequate “good” gut bacteria + inability of the gut to DIGEST foreign food protein-due to large protein size or ALLERGY to a particular protein.
- Inadequate “good” gut bacteria-due to:
 1. antibiotic use
 2. “hygiene hypothesis”
 3. gi parasites
 4. food allergy
 5. poorly digested diet
- ALL OF THE ABOVE CAN SET THE PATIENT UP FOR AN ADVERSE FOOD REACTION (AFR)

Adverse Reactions to Food

- Incidence-10-49% of dogs & cats.
- Cats with IBD-29% found to be food allergic.
- IBD in dogs & cats-histopath results of lymphoplasmacytic +/-eosinophilic gastroenteritis.



Adverse Reactions to Food

- Remember—with gi biopsy results yielding “lymphoplasmacytic enteritis”—the gut is the largest organ populated w/ lymphs/plasma cells. Any gi irritation will result in that reading!



Food Allergy-- Dogs

- **Age of onset:** 4 mos-14 years-
extremely variable!
- **Incidence:**
 1. in 1/3rd of dogs < 1 year of
age
 2. other reports- 48% in < 1
year of age
 3. 83% incidence in < 3 years
of age
- **Nonseasonal**-variable
response to steroids and/or
Apoquel.



Food Allergy-- Dogs

- Areas affected: face, feet, axillae, perineum, inguinum, ears.
- 1 study-25% ears only affected-MAY BE UNILATERAL
- Papules, erythema, excoriations, hyperpigmentation, seborrhea, recurrent bacterial/fungal infections.
- **Unusual manifestations:** erythema multiforme, seizures (10%), lupoid onychodystrophy, vasculitis, pemphigus.
- **Severe:** angioedema (pollen-food syndrome) where pollens cross react with food allergens i.e.. Cedar/tomato, ragweed/strawberries.

Food Allergy-- Dogs

- Gastrointestinal areas affected: stomach, small bowel, colon
- Vomiting, diarrhea, weight loss, flatulence, soft feces, increased frequency of feces (up to 3x/day), abdominal pain
- Gi problems occur in up to 50% of food allergic dogs and cats. Ask the owner!

Food Allergy- Dogs

- Why do owners feel occasional or frequent diarrhea, vomiting, belching, or flatulence are normal??!!

Food Allergy— Dogs-breeds and cutaneous signs

- Breeds: Shar pei, German Shepherd, Boxer, Pug, Westie, Rhodesian Ridgeback, Labrador Retriever, Golden Retriever
- Atopy—37%,
- Otitis externa 40%
- Pyoderma 37%
- Pyotraumatic dermatitis 6%



Food Allergy -- Cats

- Age of onset 6 mos-12 years.
Incidence in one study-6%
- 1/3rd Siamese or Siamese crosses
- Nonseasonal-variable response to steroids



Food Allergy-- Cats

- Pruritus without lesions, miliary dermatitis, head/neck/ear pruritus, scaling, EGC, self-induced alopecia
- 30%-lymphadenopathy
- 30%-FAD or atopy
- Onset of clinical signs may be later in cats than in dogs.



Food Allergy- Cats Noncutaneous signs

- Anaphylaxis (Rostaher 2017)
- Asthma (Watson 1967)
- Conjunctivitis (Hagen-Plantinga 2017)
- Sneezing (Leistra 2001)
- Diarrhea, vomiting, flatulence, increased defecation



Food Allergy- Mechanism of Action

- Enhanced gi permeability due to dysbiosis, parasites, antibiotics, etc.-food allergy perpetuates IBD--may not be primary cause of IBD.
- Need a normal mucosal barrier and IgA level-1st step in body's recognition & elimination of foreign antigens.
- An absent INTACT SKIN BARRIER may enhance development of food allergy-relationship between skin and the gut!

Food Allergy- Mechanism of Action- digestibility important

- “Good” Digestion-results in free amino acids & SMALL PEPTIDES=POOR ANTIGENS (**we like those SMALL peptides!**)
- Poor digestion-LARGE POLYPEPTIDES & residual antigenic proteins—HIGHLY REACTIVE in the gut and activate the immune system.
- Type I,II, III, IV, V reactions involved-why serum testing for food is not valid-appears that a lymphocyte component exists.

How does sensitization occur?

- Induced via different routes:
 - Oral
 - Intranasal
 - Sublingual
 - Cutaneous
- In cutaneous exposure-the impairment of the skin barrier plays a role.
- Impairment of gastric digestion is crucial for food allergy to “set up”.

Food Allergy- Most Common Allergens

- Dog-most studies show beef, dairy, wheat, & chicken are the most common allergens but corn, wheat, egg, beef, chicken, soy, dairy, +/-lamb should be avoided.
- Mueller/Olivry 2016.



Food Allergy- Most Common Allergens

- Cat—beef, fish, and chicken but corn, wheat, egg, beef, soy, dairy, +/-lamb should be avoided.
- Mueller/Olivry 2016



Food Allergy-- Additives

- What about food additives?
- Often blamed but few data support their being a cause of allergies.



Testing for food allergy- elimination diet still the best!

- Gold standard for testing--**elimination diet** with subsequent provocation trials.
- Serum IgE/IgG/IgA testing considered unsuitable after poor reproducibility of test results. Food allergy may be more lymphocyte driven than an antibody response (IgE/IgG).
- **Lymphocyte proliferation** testing-higher accuracy but technically difficult to do-not available via commercial labs.
- Intradermal testing for foods-atopics tested positive. Positives may reflect dietary exposure or cross reactivity with environmental allergens.
-
- **Patch testing** with food allergens has high negative predictability...but difficult to do!!
- Mueller/Olivry 2017.

Testing for food allergies-continued

- JAVMA 10/19, Andrea et.al. "Assessment of the clinical accuracy of serum and saliva assays for identification of AFR in dogs WITHOUT clinical signs of disease". (aka not FOOD ALLERGIC)
- 30 dogs
- Tests: Food-specific IgA, IgG-saliva, IgE-serum testing.
- All dogs, despite not being food allergic, showed positive results for food allergies in these tests.
- Elimination diets **STILL** the best test!

Diagnosis & Management: Selecting a Diet

- A thorough dietary history is essential! What has the pet previously eaten including foods and treats? Do owners even know?
- Protein exposure: study by Raditic et al—3 out of 4 “limited ingredient” venison diets contained soy, poultry, and beef—all not listed on the label.
- Follow-up study evaluated OTC “no soy” diets—3 out of 4 were positive for soy antigen.
- Up to 50% of prescription protein hydrolysate diets—soy or chicken based, may cause reactions in dogs allergic to chicken or soy proteins. (Olivry 2017)

Another study shows why OTC “limited ingredient diets” are not!!

- Fossati L, et al- “Determination of Mammalian DNA in Commercial Canine Diets with Uncommon and Limited Ingredients”, AAVN meeting 2018
- DNA testing of 21 OTC “limited ingredient” diets found in all 21 diets DNA consistent with species not declared on the label-bovine, porcine, caprine, bison, ovine--ALL PRESENT.

Selecting a Diet

- We must use a PRESCRIPTION novel protein or protein hydrolysate diet or home-cooked diet as our test for food allergy! WHY??
- Ex. Blue Buffalo prescription diets are tested for contaminant proteins! OTC diets are not!
- Royal Canin and Rayne also tests.



ELISA/PCR testing for contaminant proteins

- Samples of Blue Buffalo HF and NP finished product from EVERY production line subjected to protein contamination testing via ELISA-TEK.
- Highly sensitive testing.
- ELISA-TEK tests for beef, poultry, egg, soy and common food protein sources.
- Testing is done on the product AND during the manufacturing process i.e. cleanout and burnout before each run.

Adverse Reactions to Food- importance of novel proteins

- For food allergic pets-ingredient EXCLUSIONS are just as important as INCLUSIONS!
- Novel proteins are now hard to come by with the advent of OTC “limited ingredient diets”--these are not suitable for use in testing for food allergies in pets.
- A thorough dietary history is essential!-- What has the pet eaten in the past?

Adverse Reactions to Food-OTC “limited ingredient” diets

- Of 210 pet foods tested including over the counter (OTC) “limited ingredient diets”, 83% detected ingredients in the food that were not on the label!
- Up to 38% of foods had missing ingredients.
- Pork was the most common “undeclared” protein.
- Another study of 21 over-the-counter “limited ingredient” diets found all contained EVERY protein except dog, cat, and horse!
- Olivry T, et.al BMC Veterinary Research, 2017.

OTC “limited ingredient” diets- continued

- So it’s not enough to say “avoid chicken” or whatever protein you’re suggesting as you can’t trust ingredient labels for OTC diets!
- Digestibility of diet is also important and AAFCO doesn’t require food manufacturers to provide digestibility information on their products.

Selecting a Diet-Many prescription diets available, thankfully!



Selecting a Diet



Selecting a Diet



Selecting a diet-length of testing period

- How long to feed the restrictive diet to make the diagnosis of food allergy?
- By 5 weeks in dogs and 6 weeks in cats >80% of patients had achieved remission of their clinical food allergy signs. Increasing the diet trial to **8 weeks** led to complete remission in **>90%** of dogs/cats.
- Mueller/Olivry 2015.

Food Allergy- Cats

- LET'S FACE IT--THE MAIN PROBLEM IN CATS IS GETTING THEM TO EAT A NEW FOOD!



What about homemade diets?

- Homemade diets-sometimes more successful-- BUT may be calcium, omega-3, micronutrient deficient, too high in protein, and incorrect Ca:Po₄ ratio. Recent study showed homemade diets devised by the owner were nutrient deficient in at least 3 nutrients, if not more!
- If homemade diets are attempted-- need to be done under veterinary supervision or www.balanceit.com

How long does it take to flare when rechallenged?

- Cats: >90% flare by day 7 when rechallenged with former diet.
- Dogs: >90% flare by day 14 after food challenge.
- Some cats and dogs will flare immediately!
- Olivry/Mueller 2017.



What's involved with protein hydrolysate diets?

- Formed by enzymatic hydrolysis of native proteins from chicken liver (Z/D), poultry feathers (Ultamino), soybeans (HA, HP) or salmon (HF, HA).
- Reduction of antigenicity following cleavage of protein bonds.
- Most common reason for allergic reaction to these diets is presence of large incompletely hydrolyzed peptides.

Food Allergy- Protein Size

- Protein hydrolysates of <10,000 Daltons (10 kDa)-less likely to elicit an allergic response.
- Studies show protein hydrolysate diets have similar efficacy as novel protein diets when used in food allergies.
- Estimated 10% diarrhea occurrence.
- PH results in bitter taste-palatability issues but clinically doesn't seem to be a problem.
- Bizkova/Olivry Vet Derm 2016;27:289e70.

Protein hydrolysate diets

- Royal Canin Ultamino-99% of peptides in final product are <6 kDa with larger peptides originating from chicory root fiber.
- Hill's Z/D-avg size of animal derived peptides <1 kDa with 7%>5 k Da.
- Blue Buffalo HF-97.3% of peptides of salmon hydrolysate have a mean molecular weight of 2 kDa or less.

Hydrolyzed diets may stimulate food-reactive lymphocytes

- Evaluated Z/D and Amino-peptide Formula-Royal Canin (Japan)-Ultamino-both contained peptides large enough to activate lymphocytes when studied in dogs.
- Their conclusion: the 2 diets may contain proteins that stimulate T-Helper lymphocytes to activate food allergies.
- Masuda K, et al. JVetMedSci Feb 2020 82(2)177-183

Blue Buffalo HF vs. Royal Canin Ultamino

- Lewis T, et. al presentation at ACVD, April 2019, comparing HF and Ultamino.
- Both were equally effective for managing food allergy after feeding for 8 weeks.
- 16 of the Ultamino fed dogs experienced “adverse effects” compared to 7 of the dogs fed HF.

What about using raw diets for food allergy trials?

- Cox A, et al "Detection of DNA for undeclared animal species in commercial canine & feline raw meat diets using qPCR" April, 2019 ACVD meeting.
- 78% of canine raw diets/56% of feline diets contained other meat species. (lamb most common contaminant in dog diets, turkey in cat diets).

What about using prescription vegetarian diets for food trials?

- PCR analysis of Royal Canin Vegetarian diet (RCV) for 11 species of mammals and poultry-negative for animal and avian proteins.
- 3 dogs with AFR on RCV diet successfully used for testing and maintenance.
- RCV-oat groats, brewer's rice, potato protein
- Aufox E, et. al, Vet. Dermatology 2018;29:345-e122.

Insect-based protein diets

- Mealworm-based diet in France fed to atotics for 2 months.
- Approximately 50% improved w/ less itching. Coat/skin quality improved for 63%.
- No cross reactivity with fleas.
- Chala V., Virbac, France, 2018.

Initial 2 week steroid Rx when starting food trial

- 53 dogs with nonseasonal dermatitis-Rx anti-inflammatory prednisolone dose x 2 wks when starting hydrolyzed diet trial.
- 2 wks after off pred when rechallenged w/ original diet-10 dogs flared—"food-induced atopic dermatitis"
- Diesel A, Vet Derm 2019;30(6)

Why use a prescription hypoallergenic diet in atopics?



Food cross reacts with inhalants- interaction between atopy and food allergens.

- Shellfish/dust mites/glucosamine & chondroitin
- Cereals/grasses
- Birch/stone fruits, celery, nuts, soy, carrots
- Duck/avian meats
- Ragweed/melon
- Mugwort/celery



Food and pollens---food- induced atopic dermatitis

- Pollen-Food Syndrome in humans—during a pollen season if person eats food that cross reacts with pollen—allergy flares.
- Found to occur in dogs-cedar/tomatoes.
- Ragweed/strawberries, melon, zucchini, cucumbers
- Walnut/mango
- A new area to investigate in our atopic patients!

Atopic dermatitis (AD) and Food- their connection

- “AD” has always been used in relation to environmental allergens.
- Food-driven skin disease may look indistinguishable from pollen driven allergy.
- AD and food allergy no longer separate!
- A patient’s microbiome (combination of microorganisms and their genetic material) involves SKIN AND MUCOSAL BARRIER--Any alteration of that can result in clinical disease.

AD and food allergy-the combo!

- In some dogs with atopy, food allergens trigger their disease.
- Termed “food-induced” AD.
- Predisposed breeds to food-induced AD: Westies, Boxers, Ridgebacks, Pugs, GSD’s
- Clinical signs usually start <12 mos of age in 60% of dogs. GI issues seen in 31%, Malassezia seen in 43%.
- Young age of onset in dogs very much like in humans.
- Pucheu-Haston, et al Vet Derm 2015.

Atopy-food induced

- Study by Fiora, P (France) showed that in dust mite allergic (nonseasonal) atopics (36/123) fed a prescription hydrolyzed protein diet (Z/D) strictly remained in remission for 1 yr (free of their atopy symptoms).
- 50/123 underwent food challenges when fed OTC diets that triggered their atopy symptoms.

What we know about the relationship between food & AD

- Atopy (AD) may be a manifestation of food allergy—food allergens may trigger flares of AD in some dogs.
- AD and food allergy are almost impossible to distinguish clinically and both may be present in the same dog.
- “Cross over” syndromes may be present-Oral Allergy Syndrome, worsening of AD by ingesting inhalants such as storage mites or pollens.

Food and Inhalants

- Based on these studies changing the diet of atopic dogs to a prescription novel protein diet or hydrolyzed protein diet may be a useful adjunctive measure in the treatment of atopy!
- Probiotics-
- If used in puppies <4 mos old, may impede the development of atopy as the dog ages (improves gi immunity?)
- Probiotics, prebiotics, and fiber may also play a role in food allergy.
- Use an unflavored probiotic such as Provable.

So...what can
WE do?



How we can help!

- Get a thorough diet history-what protein source has been fed previously?
- **Select a PRESCRIPTION hypoallergenic diet.** No treats-make this clear!!
- Remember that some soy or chicken-based hydrolysate diets may trigger allergic symptoms in soy/chicken allergic pets. Blue Buffalo HF is great alternative.
- Single protein PRESCRIPTION diets-duck, venison, rabbit, fish, kangaroo, alligator.

How we can help, continued

- Choose a diet with high digestibility. Be sure the diet is approved for long term use if keeping the pet on it permanently.
- Wean onto the new diet slowly over 7 days, do not abruptly stop current diet and start the new one!
- Consider a non-flavored probiotic to maintain/correct dysbiosis.

Elimination diets approved for growth

- **Dogs:**

- Royal Canin HP dry, duck/potato dry
- Rayne rabbit maintenance
- Blue Buffalo NP

- **Cats:**

- Royal Canin PR dry, PD dry, PV dry
- Rayne rabbit maintenance
- Blue Buffalo NP

Finally-a few take home points!

- OTC “limited ingredient diets” cannot be trusted!! Not suitable as an elimination diet to test for food allergy!
- Inhalants/pollens cross react with fruits, vegetables, nuts.
- Atopics should be on a novel protein or protein hydrolysate prescription hypoallergenic diet--Results show that it results in less allergy flareups.
- Consider probiotics such as Proviabio (no protein flavoring).

Protein hydrolysate diet for food allergic/atopic patients



- Since up to 50% of chicken or soy-based hydrolysate diets can cause reactions in chicken or soy allergic patients, HF is a good option- provides fatty acids, small protein size, and hypoallergenic.

So when should I use a prescription hypoallergenic diet?

- If **food allergy** is suspected.
- If **atopy** is suspected.
- **Lupoid onychodystrophy**
- **Immune mediated disease**
- If patient has **seizures** (10% of dogs with seizures may be due to food allergy)-Rosser, JAVMA 1993
- Veterinary therapeutic diets in general are held to a higher standard-more research goes into them, quality control, and if for food allergy-diets are DNA tested for extraneous proteins.

Veterinary Therapeutic Diets (VTD)

- Digestibility of VTD's reportedly higher than OTC diets.
- ELISA tested for protein contaminants.
- Better quality control.
- Fatty acid balance based on studies.
- When costs of both VTD and OTC diets on a per 100 kcal basis of comparison-VTD's are competitively priced.
- Hydrolyzed .21 VTD
- .08 Grocery store
- .31 Pet store

And finally...

- There is a confusing array of diets available to pet owners-they need guidance in wading through terms such as “premium” which has no legal definition but suggests superior quality.
- We now know that labels ARE NOT accurate in revealing what is in OTC pet foods as far as protein content.
- OWNERS NEED OUR HELP AND GUIDANCE!

Thanks to
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THANKS FOR
ALL YOU DO!!

ajeromin@perfectpet.com



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