



ADVERSE FOOD REACTIONS: DO THEY EXIST AND HOW DO I DIAGNOSE THEM?

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What is an Adverse Food Reaction?

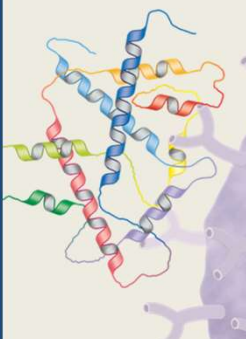
- Many names
 - Food allergy
 - Food intolerance
 - Food hypersensitivity
 - Food induced atopic dermatitis
- Abnormal response related to the ingestion of a food or food additive
 - Intolerance = non-immunologic, physiologic response
 - Allergy = immunologic response to a food antigen



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Cutaneous Adverse Food Reaction

- Food allergy
 - IgE mediated: type I hypersensitivity
 - Non-IgE mediated
 - Type III hypersensitivity (immune complex formation)
 - Type IV hypersensitivity (cell-mediated)
- Reactions occur within hours to days after exposure



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Most common food allergens



- Beef
- Dairy
- Chicken
- Lamb
- Wheat



- Beef
- Fish
- Chicken



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Dog: Common cutaneous signs

- Pruritus
- Recurrent bacterial folliculitis
- Recurrent otitis externa
- Malassezia dermatitis

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Dog: Less common cutaneous signs

- Urticaria
- Perianal fistulae
- SLO
- Acute eosinophilic dermatitis with edema (Well's syndrome)
- Vasculitis
- Erythema multiforme



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Cats: Cutaneous signs

- Pruritus
 - Head and neck pruritus
 - Symmetric self-induced alopecia
- Eosinophilic granuloma complex
- Miliary dermatitis
- Non-pruritic cervical nodules
- Angioedema
- Urticaria

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AFR: Gastrointestinal signs

- Diarrhea
- Vomiting
- Increased frequency of defecation
 - Dog > 3 BM's/day (Stetina et al. Vet Derm 2015)
- Tenesmus
- Salivating
- Flatulence



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AFR: Other non-cutaneous signs

- Dogs
 - Paroxysmal gluten-sensitive dyskinesia of Border terriers
 - Conjunctivitis
 - Asthma
 - Sneezing
 - Anaphylaxis
 - Seizures
- Cats
 - Conjunctivitis
 - Respiratory signs
 - Hyperactive behavior



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CAFR: Do they *actually* exist??

Prevalence in a population	Dogs	Cats
Presenting to a vet	1-2%	<1%
With skin disease	6% (0-24%)	5% (3-6%)
With pruritus	18% (9-40%)	12-21%
Allergic dermatitis	20% (8-62%)	10% (5-13%)
Atopic dermatitis	29% (9-50%)	



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HOW DO WE DIAGNOSE ADVERSE FOOD REACTIONS?

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CAFR diagnosis: diet trial

- Improved pruritus with elimination diet trial
 - Dogs: 80% within 5 weeks, >90% in 8 weeks
 - Cats: 80% within 6 weeks, >90% in 8 weeks
- Worsening on rechallenge
 - Mix 50:50 with previously fed food and treats
 - Dogs: 50% within 5 days, 90% in 14 days
 - Cats: 50% within 4 days, 90% in 7 days
- Symptoms improve again upon restarting elimination diet
- +/- Individual ingredient challenges to find triggers

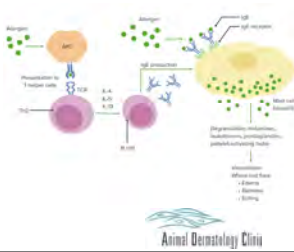


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What about serum testing?

- Low repeatability, highly variable accuracy
 - Negative values *may* help guide choice for diet trial (~80% NPV, Bethlehem et al. *Vet Immunol Immunopathol* 2012)
- Food allergies aren't all Type I hypersensitivities (IgE mediated)
 - We expect IgE mediated disease to flare within hours
 - It can take up to 2 weeks for dogs with food allergies to flare
- Serum testing can't tell us about cell mediated immunity
 - Patch testing measures both Type I and Type IV hypersensitivity



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Hair and saliva testing?

- Bernstein, et al: Hair and saliva analysis fails to accurately identify atopic dogs or differentiate real and fake samples. *Vet Dermatol.* 2019
- Coyner and Schick: Hair and saliva test fails to identify allergies in dogs. *J Small Anim Pract.* 2019.
- Can not distinguish between allergic dogs, non-allergic dogs and stuffed animals
- No difference in results distribution from those expected by random chance
- Test- retest reliability was poor to slight



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Who *actually* needs a diet trial?

- Non-seasonal pruritus
- Onset of pruritus <1 yr of age
 - 23% of cats, 38% of dogs have symptom onset by 1yr of age
- Geriatric pruritus
- Refractory pruritus
- Constant pruritus in varied geographical locations
- Patients with a history of cutaneous and non-cutaneous signs/ >1 clinical manifestation
 - 20-30% of CAFR have skin + GI symptoms
- Persistent or recurrent urticaria



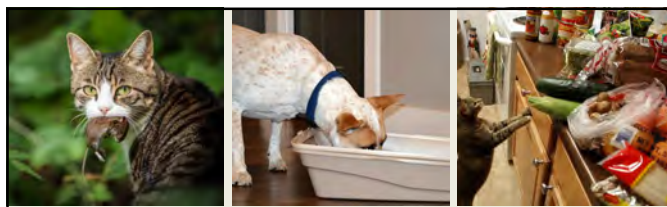
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Variables to consider during a diet trial

- Often require symptom management medications initially
 - Ideally try to withdraw prior to diet rechallenge
- Consider the season in concurrently atopic patients
- Ensure infections are managed
 - Pyoderma, *Malassezia* dermatitis, infectious otitis all cause pruritus
- Ensure adequate flea prevention
 - Consider flavoring in flea/HW preventatives- may cause a flare for the week after administration
 - Consider topicals, Bravecto® at the beginning of a trial



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VARIABLES TO CONSIDER

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Which diet should we choose?

- Dietary history
- Any concurrent disease?
 - Diabetes? Renal disease? Urinary tract disease?
- Is a canned food option needed?
 - Medication administration
 - Cats
- Owner concerns/ preferences

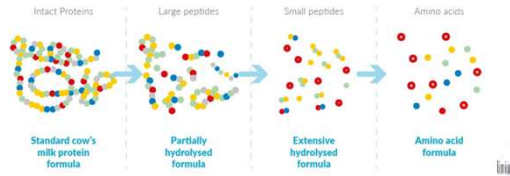
When you were super motivated starting your diet this morning but by the time you get lunch you regret your whole life



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Why choose hydrolyzed?

- No diet history/ rescued pet
- Multiple diets and treats
- Exposure to available novel proteins
- Increased digestibility
- Poor palatability
- Osmotic diarrhea
- Persistent allergenicity



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Hydrolyzed options- Royal Canin

- Ultamino®
 - Poultry feather hydrolysate
- HP® canine
 - Soy hydrolysate
 - Canned version also contains hydrolyzed chicken liver
 - Available for small breeds and moderate calorie
 - Dry approved for use in **growing puppies****
 - Treats
- HP® feline
 - Soy hydrolysate
- HP Multifunction® diets
 - Renal
 - Urinary
 - Satiety



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Hydrolyzed options: Purina

- Purina Elemental***
 - Free amino acids
- HA® vegetarian canine
 - Hydrolyzed soy
 - Gentle snacks® treats
- HA® chicken flavor canine
 - Hydrolyzed soy, hydrolyzed chicken, hydrolyzed chicken liver
 - Canned available
- HA® salmon flavor canine
 - Hydrolyzed soy, hydrolyzed salmon
 - Approved for **growing puppies**
- HA® feline
 - Hydrolyzed soy, hydrolyzed chicken



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Hydrolyzed options: Hill's

- Z/D® canine
 - Hydrolyzed chicken liver
 - Available small bites, canned, treats
- Z/D® feline
 - Hydrolyzed chicken liver
 - Available canned, treats



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Hydrolyzed options: Blue Buffalo

- HF® canine
 - Hydrolyzed salmon, peas and pea protein
 - Available canned
- HF® feline
 - Hydrolyzed salmon, peas and pea protein
 - Available canned



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Hydrolyzed diets are not all equal

- 10 dogs with chicken-induced CAFR
- Diets each fed for 14 days with a 14 day washout between
- Hydrolyzed poultry feather diet (Ultamino®) did not induce pruritus
- Hydrolyzed chicken liver diet (Z/D®) induced a pruritic flare in 40% of dogs
- TAKE HOME MESSAGE:
 - Patients can still react to the hydrolyzed version of their allergen
 - May need more than 1 trial
 - Try to choose smaller Dalton size or novel hydrolyzed



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Hydrolyzed diets- Dalton size

Diet	Dalton size
Purina Elemental	aa's ~110-150
RC Ultamino	95% = <1,000; 5% = <6,000
Blue HF	~2,000
Hill's Z/D	<3,000
RC HP	~10,000
Purina HA	<12,300

Most allergens are 10-70,000 DA



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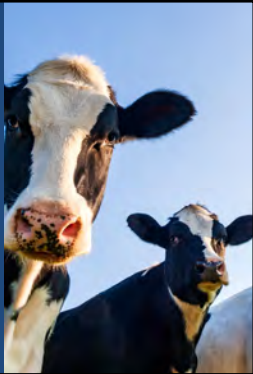
Why choose novel protein?

- Owner preference for whole foods or limited ingredient diets
- Canned option or treats required
- Palatability
- Adverse reactions to hydrolyzed diets
- Ensure no history of prior ingestion
- Multiple OTC novel protein diets may limit options

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Not all novel protein diets are equal

- Undeclared and missing ingredients (Olivry, Mueller, BMC Vet Res, 2018)
 - 33-83% (median, 45%) of novel protein diets have ingredients that are not on the label
 - 0-38% (median 1%) of novel protein diets have missing ingredients based on the label
 - Less likely to have additional/ missing ingredients in hydrolyzed foods
- 9/10 OTC diets contain DNA of animal species other than those listed on the label (Horvath-Ungerboeck: Vet Derm, 2017)
 - Most frequent: beef, pork
 - Tested for: chicken, turkey, beef, mutton, pork



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Consider cross reactive proteins

- Cattle, lamb and venison IgG
- Beef, lamb and dairy
- Duck, chicken and turkey
- Chicken and fish (cod, salmon)
- Chicken and pork
- Chicken, fish and crocodile
- Rice, soy, peanut, corn



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Novel protein diets: Rabbit

- Does your cat hunt rabbits?
- Does your dog eat rabbit poop?
- Rayne Clinical Nutrition® rabbit maintenance and diagnostic diets
 - Canine and feline rabbit maintenance dry diets approved for use in **puppies and kittens**
 - 2 options for carbohydrate source for dogs
 - Available as pate, stew, jerky treats, soft training treats, rabbit meatballs
- Royal Canin PR®
 - Rabbit protein, hydrolyzed soy protein
 - Available as canned and dry for cats and dogs



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Novel protein diets: Alligator

- Blue Buffalo NP®
 - Available as canned and dry for dogs and cats
 - Approved for use in **puppies and kittens**
- Rayne Crocodilla® canine maintenance
 - Alligator protein
 - 2 options for carbohydrate sources
 - Available as jerky treats



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Novel protein diets: Vegetarian

- Rayne Plant-Based® canine
 - Available as stew, gravy topper, compatible treats, sweet potato jerky
- Royal Canin® Vegetarian canine
 - Available as canned



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Novel protein diets: Additional options

- Rayne EcoDerm-BSFL® canine
 - Black soldier fly larva
- Rayne RSS®
 - Pork
 - Struvite and calcium oxalate urolith prevention
 - Available as stew, cans (dog), jerky treats
- Royal Canin® duck, venison, whitefish (canine only)
- Hill's D/D® duck, venison, salmon (canine only)
- Hill's Derm Complete® canine
 - Egg based protein, hydrolyzed chicken flavor
 - **Puppy formula available**
 - Available canned



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Why choose home cooked?

- Often owner driven desire
- Picky eaters
- Still need to ensure novel protein
 - Specialty butcher, avoid ground meats ideally
- Need to ensure nutritionally complete
 - Caution with growing animals and cats
- Recommended to follow the advice of a veterinary nutritionist
 - balance.it
 - www.acvn.org to consult with a nutritionist



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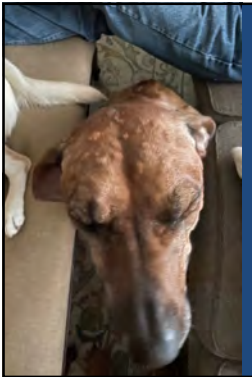
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Case example: Lucy

- Syr old, f/s Rhodesian ridgeback
- History of recurring hives since 6wks of age
 - Initially intermittent and few
 - Past 3 years persistent with waxing and waning severity
- Hives respond well to Benadryl®, no improvement with Apoquel®
- When more severely affected Lucy feels systemically unwell
 - Vomiting, gagging, lethargic
 - 2 ER visits in the months leading up to exam
- History of head shaking and otic pruritus as well as waxing and waning generalized pruritus



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Lucy: Current medications

- Diphenhydramine 3x25mg (1.7mg/kg) q4-6hrs
- Apoquel® 16mg (0.38mg/kg) SID
- Motizol® AU prn (~3d's/mo)
- Proin® 75mg (1.8mg/kg) in the am and pm with ½ dose at noon
- Heartgard® and Nexgard® monthly
- Coconut oil on ear tips SID
- VetraSeb CeraDerm® shampoo monthly prn

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URTICARIA TOP DIFFERENTIALS

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Lucy: Diet history

- Hives worsen immediately after eating shellfish and within 24 hours of eating chicken
- Symptoms seem improved on current diet of Kirkland® lamb and rice
- Peanut butter treats
- Eats rabbit poop on acreage
- 2 other dogs and a cat at home who are unaffected
- Lucy is a “vacuum cleaner” and likes to clean up after the other dogs



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Lucy: Diagnostic plan

- Elimination diet trial with Royal Canin Ultamino®
 - Small DA size, history of known food triggers so attempt to avoid whole proteins due to possible cross-reactivity
 - Instructed owner how to “pill” Lucy to avoid peanut butter for medications
 - Basket muzzle for outside if needed
 - Feed the other dogs in a separate room, owner to p/u dishes after use and sweep the floor after they eat
- Discontinue: Apoquel®, Heartgard® (beef flavor), Nexgard® (soy based beef flavor), Proin® (liver flavor)
- Advantage Multi® monthly
- Compounded PPA capsules
- Benadryl® increase to 100mg (2.3mg/kg) BID & up to 150mg (3.5mg/kg) q6hrs prn
- Rescue doses of prednisone



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Lucy: Bump in the road

- 1mo into the diet trial and changing from Proin® to compounded PPA Lucy's incontinence has been dramatically worse
 - Historically no response to Incurin
 - Using reliable compounding pharmacy
- Advised exam with pDVM and urinalysis to r/o UTI
 - NSF on exam, lab work, u/a
- Possible poor response to compounded PPA??
 - Increased dose to 75mg TID (was previously getting ½ dose at noon)



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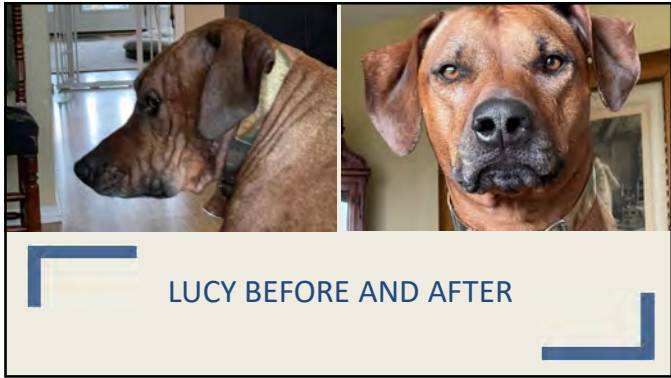


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Lucy: Follow up

- Diet changed from Ultamino® to Purina HA® vegetarian
 - Within 24hrs pu/pd, incontinence resolved
 - Worsening hives 3d's into the diet change (had been on Ultamino® for 1mo prior to this): improved with increased dose of Benadryl®
 - Elected to give it some more time but advise if continued
- 2mo after starting diet trial, 1mo after change to Purina HA® Vegetarian
 - Medications: Advantage Multi®, compounded PPA, Benadryl® 100mg BID
 - Significant improvement with 4 small hives on top of head and one on RH leg
- Plan: Continue HA® vegetarian for another 4 weeks, attempt to withdraw Benadryl® at that time if no residual hives, then consider individual ingredient challenge

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Recommended Reading

- <https://www.biomedcentral.com/collections/catsfoodreactions>
 - Multiple review articles related to food allergies in dogs and cats
 - Quick and easy reading
 - Great overview of the topic

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