# Rapid Fire Allergy/Asthma An attempt to make this hour valuable!

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#### Disclosures

TEACHING
Idaho State University PA Program
ThriveAP

#### **INDUSTRY AFFILIATIONS**

Grifols Pharmaceutical - speaker, consultant
Boehringer Ingelheim Pharmaceuticals – consultant, speaker
Meda Pharmaceuticals – speaker, consultant
Circassia Pharmaceuticals – advisory panel
Genentec Pharmaceuticals - Speaker

#### CLINICAL RESEARCH

2017 – Sub-I, Genetech Zenyatta Severe Asthma Study

2016 – Sub-I, Biota Human Rhinovirus Study

2015 - Sub-I, Sanofi Traverse Severe Asthma Study

2015 - Sub-I, Sanofi Liberty Severe Asthma Study

2013 – Study Coordinator: MediVector Influenza Study

Brian Bizik does not intend to discuss the use of any off-label use/unapproved use of drugs or devices

# The Big Picture

The world of food allergy is changing quickly, seasonal allergy changes have not been as rapid but sometimes tips and tricks can make a big difference!

Start off with amoxicillin allergy and some important info -

This is a thing that essentially does not exist, at least not much . . . and yet it costs the system and our patients dearly

Pharmacist Christopher Bland published in the Open Forum Infectious Diseases journal that 98% of those with a documented PCN or amoxicillin allergy in their chart did not have an PCN allergy when given an allergy test.

In the Journey of Allergy and Clinical Immunology, Labrosse et al. tested 133 children with documented PCN allergy – 3 ended up being positive. Yes, 3.

A summary by the American Academy of Asthma, Allergy and Immunology found that 94% or more of those with a clinically documented amoxicillin allergy can tolerate the medication without a problem

A very nice summary study in the British Medical Journal (Blumental et al. 2018) found that PCN allergy in the chart led to a 69% increase in the risk of getting MRSA and 26% increased risk for C. difficile.

It is important to remember that a true amoxicillin allergy is usually sudden, starting within an hour or so after dosing and presents with hives. Following this phase there are often longer lasting issues like skin blistering or peeling.

Send patients for testing. Multiple studies have show that testing for amoxicillin allergy is inexpensive (around \$300 total in the US) and can save thousands on more expensive (and more broad-spectrum) antibiotics and save on additional treatment for C. diff and MRSA infections.

In JAMA Internal Medicine, 2020;180(5):75-752 Trubiano and his team developed an easy tool to use in your practice called PEN-FAST,

- A. The reaction was five or fewer years ago (2 points)
- B. The patient had angioedema or anaphylaxis with the reaction (2 points)
- C. Severe cutaneous skin reaction (2 points)
- D. Treatment was needed for the reaction itself (1 point) If the patient in question has 3 points or less, the likelihood of having an actual reaction to a prescription you might give was around 3%.

# Meds in Allergy (also in asthma/COPD)

Goal is to help understand how the mechanism of action can treat common allergy symptoms

#### Lets look at SAMAs and LAMAs

#### Ipratropium bromide (SAMA)

- Made from the combination of Isopropyl alcohol and atropine. The name comes from these two words. Isopropyl alcohol and atropine
- 2. By antagonizing the muscarinic receptor they work by INCREASING the degradation of cGMP and by DECREASING Ca2+ in the cells, these all BLOCK contraction. They don't dilate anything really.
- 3. Onset of action . . . 20 minutes or so. Ipratropium half life is 2 hours.
- SAMAs and LABAs also effect one big nerve. . .

#### Lets look at SAMAs and LAMAs

#### Ipratropium bromide

- 1. Vagal tone both LAMAs and SAMAs decrease vagal tone (lungs only). This is why they can be helpful in patients with minimal constriction but have dyspnea.
- 2. So these are very different than SABAs (albuterol) and LABAs, and when combined work very well.
- 3. For patients over the age of 2 years and older nebulized therapy should use both (if they need a SVN, they need both)
- 4. Oh yea, the diffusion of inhaled ipratropium bromide (both nose and lungs) does NOT diffuse into the blood in any significant amount. Yep ©

#### Question:

What do "steroids" really do?

How long does it really take for them to start working?

Hey, wait. . .don't I make my own?

#### **Steroids**

The term "steroid" refers to the structure of the compound, not to the function.

Prednisone -

(1S,2R,10S,11S,14R,15S)-14-hydroxy-14-(2-hydroxyacetyl)-2,15-dimethyltetracyclo[8.7.0.0<sup>2</sup>,<sup>7</sup>.0<sup>11</sup>,<sup>15</sup>]heptadeca-3,6-diene-5,17-dione

Prednisone is metabolized by the liver to prednisolone. A glucocorticoid agonist corticosteroid

One of the first effects is to decreased the leukocyte migration to sites of Inflammation.

Corticosteroids then bind to the glucocorticoid receptor mediates changes in gene expression that lead to multiple downstream effects over hours to days.

Glucocorticoids inhibit neutrophil apoptosis and demargination; they inhibit phospholipase A2, which decreases the formation of arachidonic acid derivatives; they inhibit NF-Kappa B and other inflammatory transcription factors; they promote anti-inflammatory genes like interleukin.

Lower doses of corticosteroids provide an antiinflammatory effect, while higher doses are immunosuppressive.

Aaaaarrrghhhh! Stop – too many words on one slide!

The point, it shuts down most of the things that drive inflammation.

So EVERY bad part of allergic rhinitis is shut down by steroid nasal sprays. Think of this vs an antihistamine or vs ipratropium

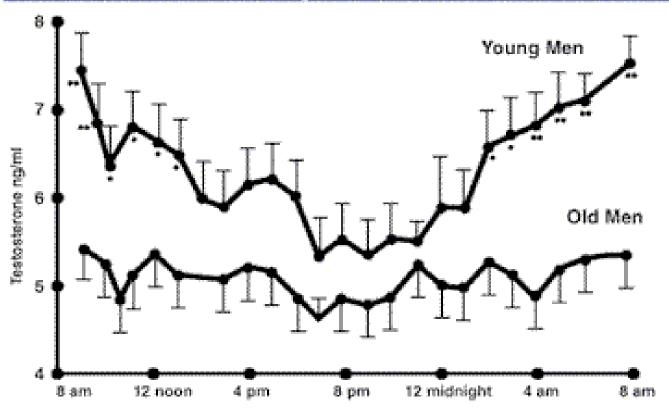
Oral Steroids for ALLERGIES?

Sure, they work great. Lots of questions of course but it can be a wonderful thing

Adults – 2 days of 40 mg works great for most, no need to extend much past this

#### Prednisone – diurnal variation





Diumai rhythm of testosterone in elderly men compared to young men. Note that testosterone levels in young men rise dramatically at night, remain elevated, and drop progressively throughout the day. This diumal rhythm is greatly attenuated in elderly men (Bremer, 1983).

# Nasal Sprays





#### Nasal Sprays

Nasal sprays – Most important thing here is to make sure they are not shooting the spray straight up to the olfactory bulb. Shoot in the left nostril with the right hand – toward the left EAR LOBE. And don't inhale. You don't need to help the mist get back, just let the mist fall, it'll get there I promise.

Any steroid spray works and again at Costco or Amazon a 5-pack of fluticasone is \$30 or so. Very cheap.

## Tips and Tricks:

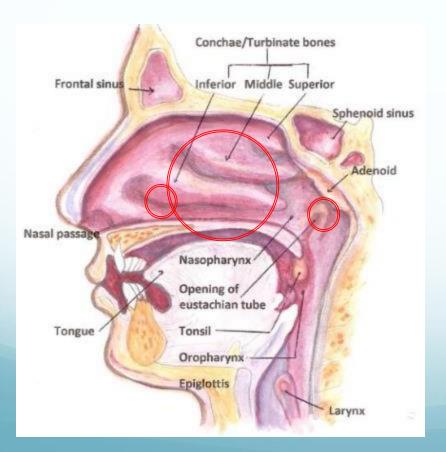
- Nasal Steroids
  - All work great, use daily or BID
  - Make sure to use the opposite hand technique and avoid hitting the septum – where the blood vessels

## Tips and Tricks:



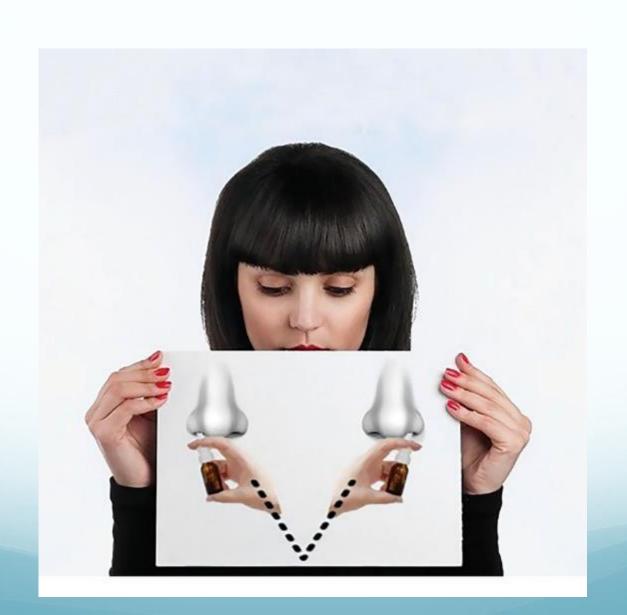
# The Approach:

- Nasal Steroids
  - Any steroid is fine, fluticasone is cheap
  - Use correctly if not can cause epistaxis





### Nasal Sprays



#### Nasal Sprays

Any nasal spray can be used QD or BID. If they have epistaxis from BID use it's because the spray is hitting the septum and they are not aiming for the earlobe with the opposite hand.

Don't forget that marvelous spray ipratropium bromide. This is just a snot stopper. Use alone or with fluticasone. Use this first for senior patients with chronic or non-allergic rhinitis and they will love you forever.

#### **Antihistamines**

Anithistamines - strongest is Zyrtec, next Claritin then Allegra. All are VERY cheap on Amazon or at Costco (Kirkland Brand), a year supply is about \$15, \$30 for Allegra. Allegra is the least sedating however.

The Antihistamine level needs to match the histamine level. So early in an allergy season one Zyrtec might be enough but mid-season they might need two or even three daily for a short period of time.

My favorite plan is a Zyrtec D 12 hour in the AM and a Zyrtec at night.

PRN -

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Sprays Total



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#### Eye Drops

Eyes – PO antihistamines and nasal sprays do little for eye symptoms. Pataday or any form of the active ingredient olopatadine is great. Pataday just went OTC so is reasonably priced. Keep these drops in the fridge, the cooler drops feel wonderful and the bottle is good for 3 years or so when refrigerated.

#### Eye Drops



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#### Pataday.

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Olopatadine hydrochloride ophthalmic solution 0.2% Antihistamine

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#### Eye Allergy Itch & Redness Relief

#### TWICE

# Food and Pet Allergies – new stuff

First is a bit on component testing, super important to your patients!

# History of Allergy Testing

1872 Blackley<sup>1</sup> performs first skin test with pollen

1920's

Skin prick testing introduced by Lewis and Grant<sup>3</sup> 1974

First RAST test introduced for specific IgE<sup>5</sup>

1972

First total IgE test goes to market<sup>5</sup>

1989

In vitro testing replaces paper disc with solid phase<sup>5</sup>

2005

Component resolved diagnostics

1912 Schloss performs first scratch test

1967

The discovery of IgE<sup>4</sup>

1991

First fully automated in vitro specific IgE testing<sup>5</sup>

1981

Specific IgE testing using enzyme linked assav<sup>5</sup>

for foods<sup>2</sup>

- history http://www.phadia.com/en/About-us/Phadia-History/

# "We got a dog! But don't worry, it's hypoallergenic"

## Pet Allergy

- US has highest percentage of household pets in the world
  - 62% of households
  - Cat owners: 17% are SPT positive
  - Dog owners: 5% are SPT positive
- Incidence of allergy increasing
- Differences in allergens differ between animals but also among breeds

# Pet Allergy

- Major Dog Allergen: Can f 1
- Major Cat Allergen: Fel d 1

- Released from saliva, sebaceous glands, perianal glands
- Allergen harbored in skin particles/flakes, fur

The hair does not cause allergy!

# Cat/Dog Allergens

- Found everywhere, throughout entire home that has a cat/dog
- Found in most public places

- Strict removal of pet(s) from inside home is the ONLY effective method to remove allergen
  - Can take up to 6 months or longer for allergen to be completely eliminated

# Hypoallergenic Pets?

- No such thing!
- Marketing by companies
  - False advertising, non-shedding, short-hair, etc
  - Studies show amount of allergen in the home is the same in shedding vs. nonshedding dogs





# Patient Education & Limiting Exposures

- Remove animal from home or do not get one
- Extensive home cleaning
- Remove carpeting
- Mattress encasing
- Bathing dogs regularly
  - Must be at least 2x per week
  - Rise of allergens back to baseline after 3 days
  - Bathing is more effective at removing allergen than vacuuming of dog hair

# OK, this is cool stuff, hang with me!

Protein Stability Egg & Milk

## Protein Stability - Milk

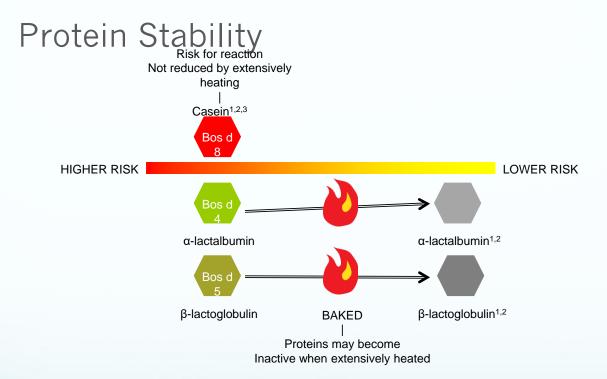


In one study, **75%** of patients sensitized to cow's milk **could** tolerate baked milk<sup>1</sup>

\*Heated to the point of protein denaturation. If a physician determines a patient is a good candidate for an Oral Food Challenge following component testing, that patient should take an Oral Food Challenge with a specialist to determine whether the food in question is safe to consume.

1. Nowak-Wegrzyn A, Bloom KA, Sicherer SH, et al. Tolerance to extensively heated milk in children with cow's milk allergy. J Allergy Clin Immunol. 2008;122(2):342-347.

# Likelihood of Causing a Reaction When Sensitized



<sup>1.</sup> Shek LP, Bardina L, Castro R, Sampson HA, Beyer K. Humoral and cellular responses to cow milk proteins in patients with milk-induced IgE-mediated and non-IgE mediated disorders. Allerav. 2005;60(7):912-919.

<sup>2.</sup> Nowak-Wegrzyn A, Bloom KA, Sicherer SH, et al. Tolerance to extensively heated milk in children with cow's milk allergy. J Allergy Clin Immunol. 2008; 122 (2):342-347.

<sup>3.</sup> Boyano-Martínez T, García-Ara C, Pedrosa M, Díaz-Pena JM, Quirce S. Accidental allergic reactions in children allergic to cow's milk proteins. *J Allergy Clin Immunol.* 2009;123(4):883-888.

# Protein Stability - Egg



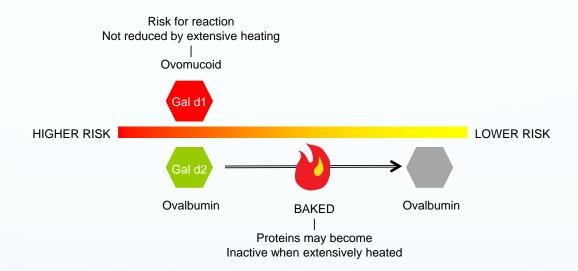
In one study, **70%** of patients sensitized to egg **could tolerate baked\* egg**<sup>1</sup>

<sup>\*</sup>Heated to the point of protein denaturation. If a physician determines a patient is a good candidate for an Oral Food Challenge following component testing, that patient should take an Oral Food Challenge with a specialist to determine whether the food in question is safe to consume.

<sup>1.</sup> Lemon-Mule et al. Immunologic changes in children with egg allergy ingesting extensively heated egg. J Allergy Clin Immunol. 2008;122(5):997-983.

### Basics of Allergen Components

#### **Protein Stability**



Benhamou AH, et al. State of the art and new horizons in the diagnosis and management of egg allergy. Allergy. 2010;65(3):283-289.

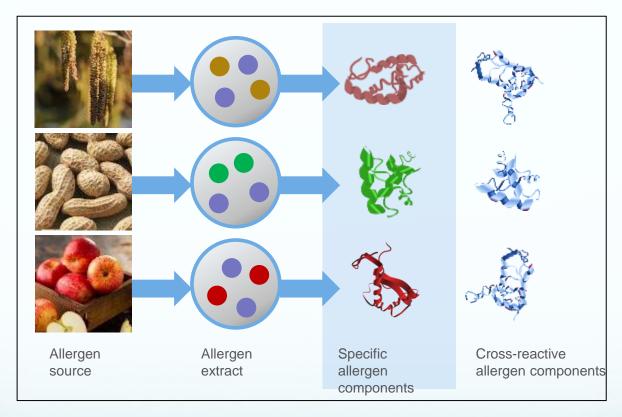
# Cross-Reactivity- Peanut

# Important Allergen Component Families

- The same protein families are present in different species
- Specific IgE antibodies often cross react to proteins in the same protein family



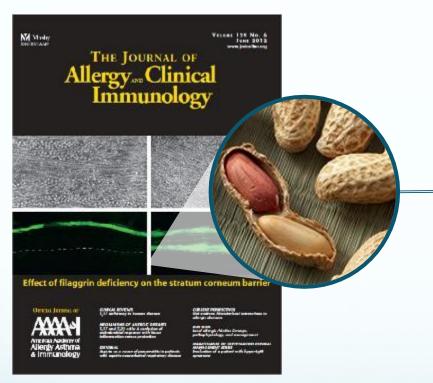
## Cross-Reactivity



Traditional diagnostics

Allergen component slgE testing can help distinguish genuine sensitization from cross-reactivity

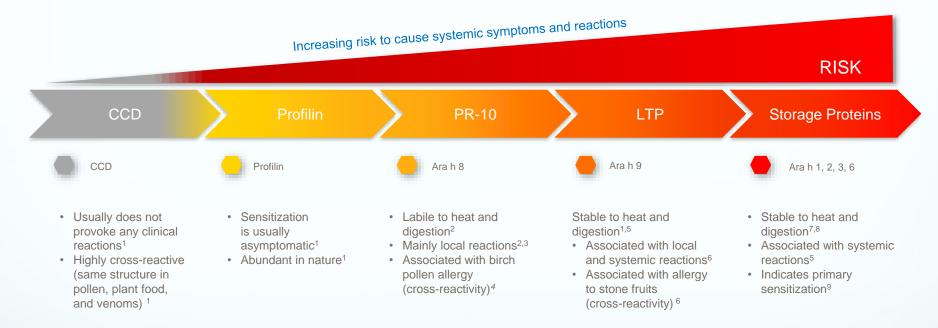
## Protein Stability – Peanut



In one study, 77% of patients sensitized to peanut are not at risk of a severe reaction<sup>1</sup>

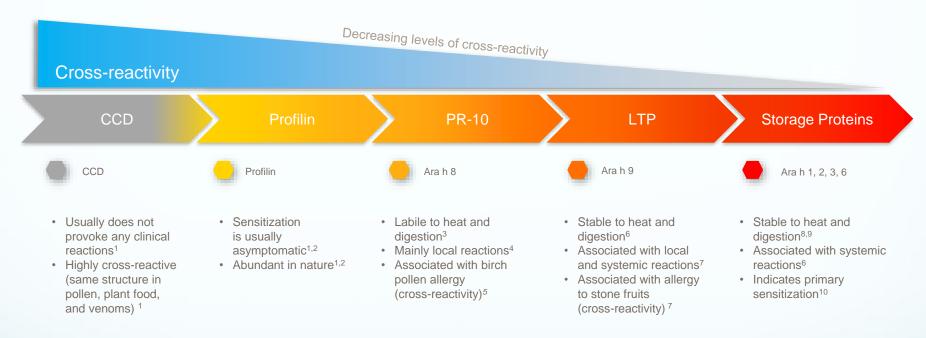
<sup>1.</sup> Nicolaou, N. et al. Allergy or tolerance in children sensitized to peanut: prevalence and differentiation using component-resolved diagnostics. J Allergy Clin Immunol. 2010;125(1):191-197

# Characteristics of Protein Families



- 1. Bradshaw N, A Clinical Reference Guide to Molecular Allergy. Go Molecular! Molecular Allergy The Basics, 2014.
- 2. Canonica et al. World Allergy Organization Journal 2013, 6:17
- 3. Nucera E, et al. Hypersensitivity to major panallergens in a population of 120 patients. Postepy Dermatol Alergol. 2015 Aug; 32(4): 255–261
- 4. Mittag D. Akkedaas J, Ballmer-Weber BK, et al. Ara h 8, a bet v 1-homologous allergen from peanut, is a major allergen in patients with combined birch pollen and peanut allergy. J Allergy Clin Immunol. 2004;114(6):1410-1417.
- 5. Sastre J: Molecular diagnosis in allergy. Clin Exp Allergy 2010, 40:1442-1460.
- 6. Lauer I, Dueringer N, Pokoj S, et al. The non-specfic lipid transfer protein, Ara h 9, is an important allergen in peanut. Clin Exp. Allergy. 2009;39(9):1427-1437.
- 7. Peeters KA, Koppelman SJ, van Hoffen E, et al. Does skin prick test reactivity to purified allergens correlate with clinical severity of peanut allergy? Clin Exp Allergy. 2007; 37(1): 108-115.
- 8. Asarnoj A, Moverare R, Östblom E, et al. IgE to peanut allergen components: relation to peanut symptoms and pollen sensitization in 8-year-olds. Allery. 2010; 65(9): 1189-1195.
- 9. Asarnoj A, Nilsson C, Lidholm J, et al. Peanut component Ara h 8 sensitization and tolerance to peanut. J Allergy Clin Immunol. 2012;130(2):468-472.

# Characteristics of Protein Families



- 1. Bradshaw N, A Clinical Reference Guide to Molecular Allergy. Go Molecular! Molecular Allergy The Basics, 2014.
- 2. Katelaris CH: Food allergy and oral allergy or pollen-food syndrome. Curr Opin Allergy Clin Immunol 2010, 10:246–251.20.
- 3. Canonica et al. World Allergy Organization Journal 2013, 6:17
- 4. Nucera E, et al. Hypersensitivity to major panallergens in a population of 120 patients. Postepy Dermatol Alergol. 2015 Aug; 32(4): 255-261
- 5. Mittag D. Akkedaas J, Ballmer-Weber BK, et al. Ara h 8, a bet v 1-homologous allergen from peanut, is a major allergen in patients with combined birch pollen and peanut allergy. J Allergy Clin Immunol. 2004;114(6):1410-1417.
- 6. Sastre J: Molecular diagnosis in allergy. Clin Exp Allergy 2010, 40:1442-1460.
- 7. Lauer I, Dueringer N, Pokoj S, et al. The non-specfic lipid transfer protein, Ara h 9, is an important allergen in peanut. Clin Exp. Allergy. 2009;39(9):1427-1437.
- 8. Peeters KA, Koppelman SJ, van Hoffen E, et al. Does skin prick test reactivity to purified allergens correlate with clinical severity of peanut allergy? Clin Exp Allergy. 2007; 37(1): 108-115.
- 9. Asarnoj A, Movérare R, Östblom E, et al. IgE to peanut allergen components: relation to peanut symptoms and pollen sensitization in 8-year-olds. Allery. 2010; 65(9): 1189-1195.
- 10.Asarnoj A, Nilsson C, Lidholm J, et al. Peanut component Ara h 8 sensitization and tolerance to peanut. J Allergy Clin Immunol. 2012;130(2):468-472.

# Food Allergy - Summary

- Prevalence of Food Allergy continues to increase
- Impact can be both physical and psychological
- Diagnosis Challenging
  - Adverse Reactions -vs- IgE Mediated Allergy
  - Over-reporting is common
  - Accepted whole allergen extract testing cut off values -Insufficient
- Component Resolved Diagnosis
  - Adds to available information
  - Assists clinicians in management decisions
  - Evolving to include additional allergen groups

## Pet Allergy

Allergies to dogs and cats affect **10%–20%** of the population worldwide<sup>1</sup>

Approximately **48 Million Americans** are sensitized to dog and/or cat allergens<sup>2</sup>

**50% of people** with exposure to horse barns report respiratory symptoms such as wheezing, coughing and shortness of breath<sup>3</sup>





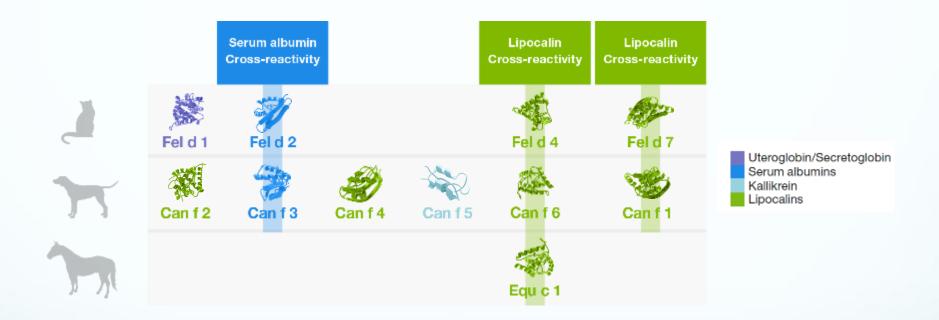


<sup>1.</sup> Chan SK, Leung DYM, Dog and Cat Allergies: Current State of Diagnostic Approaches and Challenges, Allergy Asthma Immunol Res. 2018;10(2):97-10.

<sup>2.</sup> Konradsen W, et al. J Allergy Clin Immunol. 2015;135:616-2

<sup>3.</sup> Mazan MR, Svatek J, Maranda L, et al. Questionnaire Assessment of Airway Symptoms in Equine Barn Personnel. Occup Med. 2009;59:220-

#### Provide a More Precise Diagnosis<sup>1</sup>



Species-specific or cross-reactive sensitization?

ImmunoCAP Pet Allergen Components can help you decide

# Pet Selection And Human Semen Allergy Relationship

Up to 30% of dog-allergic patients are monosensitized to Can f 51\*

Patients who are monosensitized may tolerate female dogs or castrated males dogs.<sup>2,3</sup>

In women allergic to dog that refer to reactions following contact with human seminal fluid, it would be advisable to determine IgE against Can f 5.3

A comprehensive allergen component profile may help healthcare providers determine if monosensitization to Can f 5 is causing symptoms<sup>1-3</sup>



\*Can f 5 is a androgen-regulated protein expressed in the prostate, hence present only in male dogs

<sup>1.</sup> Konradsen W, et al. J Allergy Clin Immunol. 2015;135:616-25.

<sup>2.</sup> Matricardi P. M. et al. *EAACI Molecular Allergology User's Guide*. PAI 2016: 27: (suppl23): 1–250 (165-170).

<sup>3.</sup> Davila I. et al. Allergy. 2018 Jun;73(6):1206-1222.

#### Food Allergies - What is New!

Think about two groups –

Infants born with a high likelihood of having a peanut allergy

Children through adults who already have had an anaphylactic reaction to a food (especially nuts)



#### **PEANUT SNIFFING DOG**

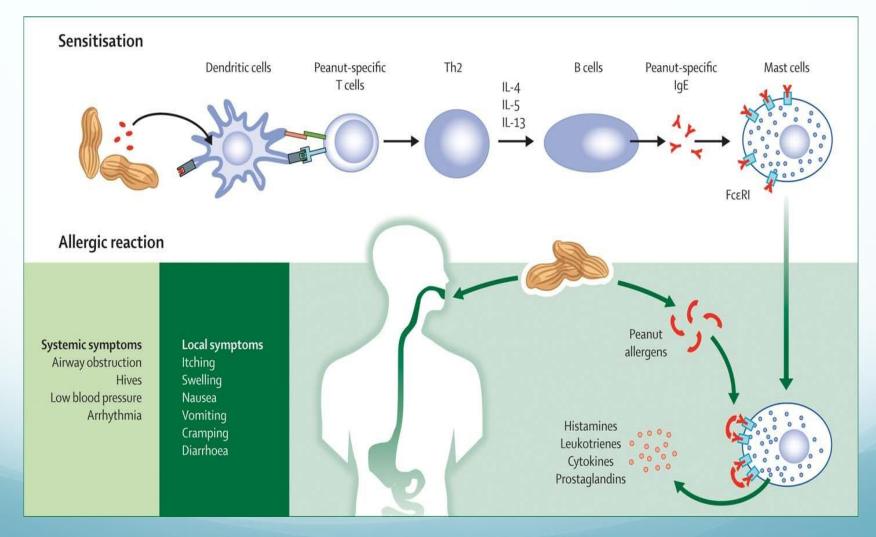


# First Group – infants with a high likelihood of having a peanut allergy

Is there a way to reduce this risk SIGNIFICANTLY?

• What do we know from dogs for example?

#### **Peanut Sensitization**



#### **INCIDENCE OF PEANUT ALLERGY**

- 1-3 % of all children in the U.S. have a peanut allergy
- Doubled in the past 10 years in Western countries
- Peak incidence is by one year of age
- Only 20% of children outgrow a peanut allergy
- Question what percent of children outgrow milk allergy?

Osborne NJ, Koplin JJ, et. al., Prevalence of challenge – proven IgE – mediated food allergy using population based sampling and predetermined challenge criteria in infants. J. Allergy Clin Immunol. 2011;127(3):668.

#### WHO IS AT HIGHEST RISK?

- Family history of food allergy
- Moderate severe atopic dermatitis
- Egg allergic
- History of other allergic diseases, for example, children with allergic asthma

# Randomized trial of peanut consumption in infants at risk for peanut allergy

DuTort G., Roberts, G., etal. Randomized trial of peanut comsumption in infants at risk for peanut allergy. N Engl J Med. 2015;372(9):803

#### STUDY RESULTS

530 Infants in the intention to treat

- At 60 months
  - >13.7% in the avoidance were peanut allergic
  - >1.9% in the consumption group (P<0.001)

DuTort G, Roberts G., et al., Randomized trial of peanut consumption in infants at risk for peanut allergy. N.Engl J Med. 2015; 372(9):803

#### CONCLUSION

"THE EARLY INTRODUCTION OF PEANUTS
 SIGNIFICANTLY DECREASED THE FREQUENCY OF THE
 DEVELOPMENT OF PEANUT ALLERGY AMOUNG
 CHILDREN AT HIGH RISK FOR THIS ALLERGY AND
 MODULATED IMMUNE RESPONSE TO PEANUT"

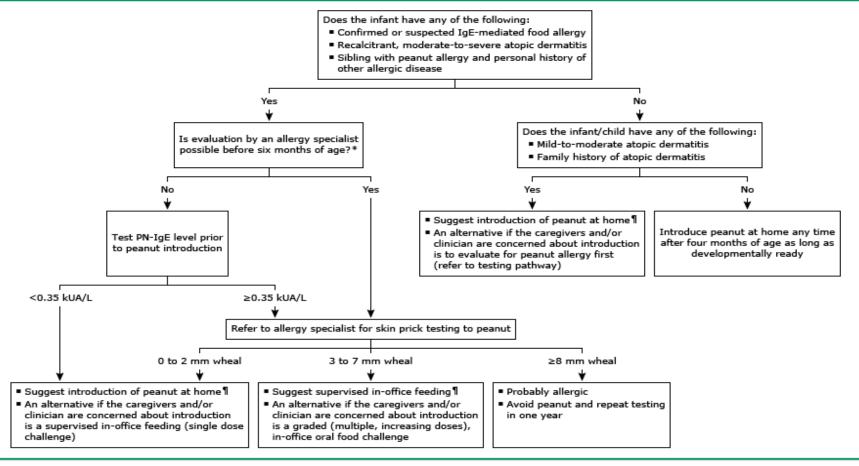
DuTort G, Roberts G., et al., Randomized trial of peanut consumption in infants at risk for peanut allergy. N.Engl J Med. 2015; 372(9):803

# Learning Early About Peanut Allergy (LEAP)

#### **NEW PEANUT INTRODUCTION**

- LEAP (Learning Early About Peanut Allergy) trial
- Introduction at 4-6 months of age but not the first food introduced
- Most common food allergies: Cow's milk, hens egg, peanut, tree nuts, fish and shellfish
- Formal guidelines have been revised in 2017 by the National Institute of Allergy and Infectious Disease

#### Introduction of peanut into the diet during infancy/early childhood



IgE: immunoglobulin E; PN-IgE: peanut-specific immunoglobulin E.

\* Alternatively, the allergy specialist may chose to perform PN-IgE testing, or both skin prick and PN-IgE testing, for the initial evaluation.

¶ Prior to introduction of highly allergenic foods, the infant/child should:

- Be at least four months of age.
- · Show developmental readiness to consume complementary foods.
- Have tolerated a few of the more typical, initial complementary foods (eg, cereals, fruits, vegetables).

## 2016 NIAID FOOD GUIDELINES UPDATE

#### **Summary of Addendum Guidelines**

Addendum Guideline	Infant Criteria	Recommendations	Earliest Age of Peanut Introduction
1	Severe eczema, egg allergy, or both	Strongly consider evaluation with peanut- specific IgE and/or skin prick test and, if necessary, an oral food challenge. Based on test results, introduce peanut- containing foods.	4 to 6 months
2	Mild to moderate eczema	Introduce peanut-containing foods.	Around 6 months
3	No eczema or any food allergy	Introduce peanut-containing foods.	Age-appropriate and in accordance with family preferences and cultural practices

#### PEANUT containing products for infants





#### **SUMMARY**

- The incidence of peanut allergy is on the rise
- New studies, in particular, the LEAP study have proven that is essential to start peanut early in an infants life
- Remember who is at risk: children with eczema, egg allergy or other food allergies, family history of food allergies, and other allergic diseases such as asthma
- In primary care, utilize specific IgE testing to peanut and refer appropriately
- The new guidelines should decrease peanut allergy in the U.S.

# Second Group – Any person with a known anaphylactic food reaction

Can we treat this like a pollen or pet allergy?

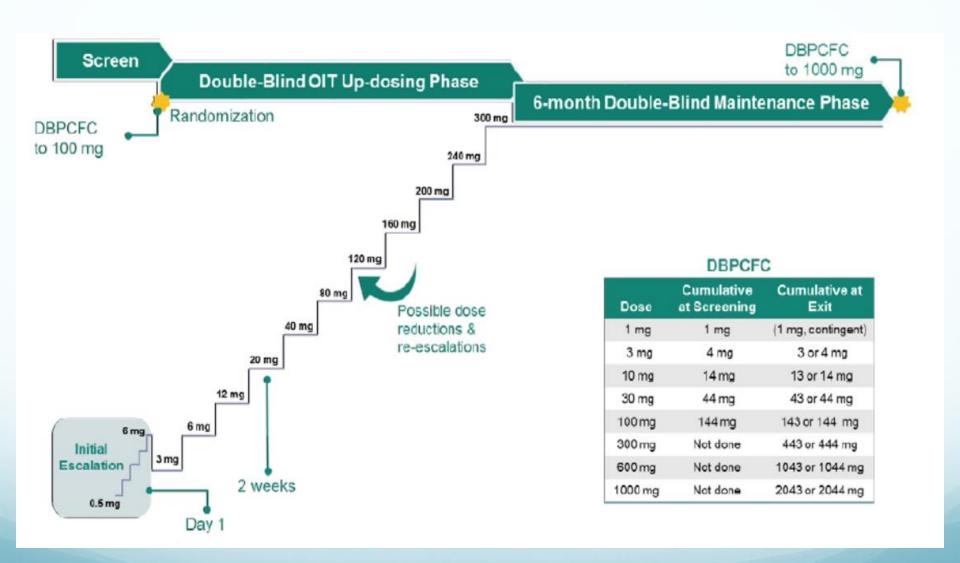
Can we take away the very real fear?

# Second Group – Any person with a known anaphylactic food reaction

 The goal is to desensitize the patient to achieve tolerance

 The goal is not to eat anything but to allow for accidental exposure to foods

#### **Peanut Trials**

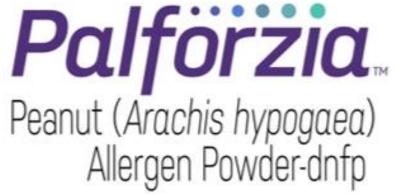


# Second Group – Any person with a known anaphylactic food reaction

 By slowly increasing the amount ingested tolerance is achieved

 90% of all accidental peanut exposures are less than 600 mg

# Second Group – Any person with a known anaphylactic food reaction





#### **Take Home**

- High risk infants need to have peanut introduced early – 80% percent reduced risk of a life threatening peanut allergy
- If anyone over the age of 3 has a serious food allergy, refer if desensitization is desired.

# Rapid Fire is over ©

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