The Changing Relationship Between the Gastroenterologist and Immunologist in the Treatment of Eosinophilic Esophagitis

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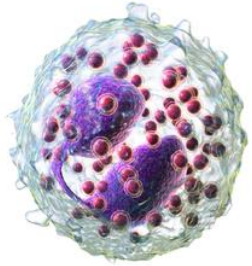
Eosinophilic Esophagitis

EoE represents a chronic, local immune-mediated esophageal disease, characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation.

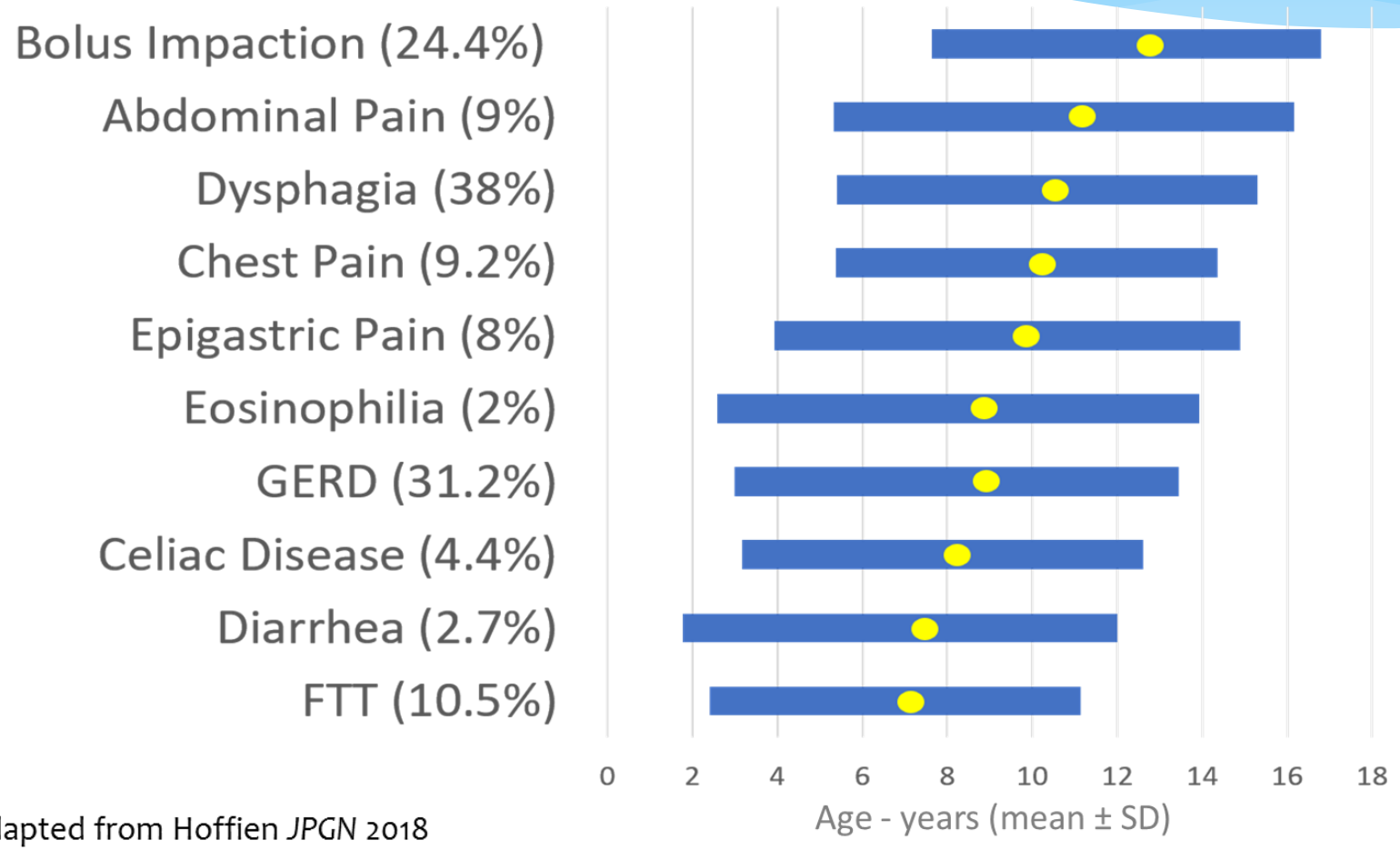
Current prevalence estimates– 1:2000-4000 chidlren and adults



Lucendo et al UEG j 2017

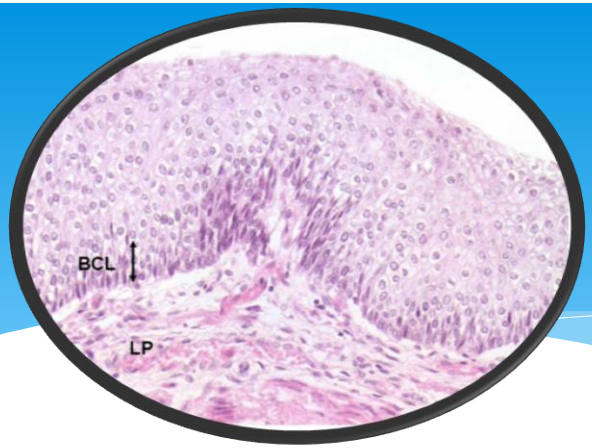
Symptoms

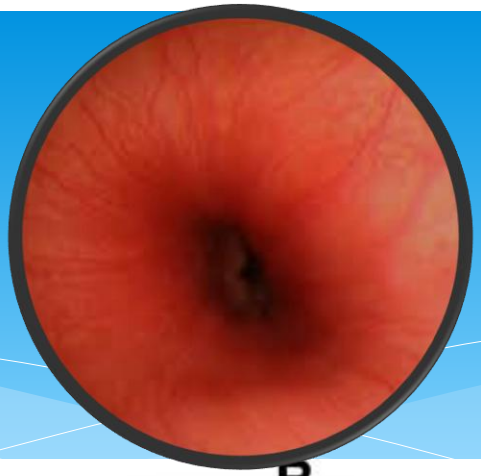
Symptom	Infants/young children	Teenagers/adults
Vomiting	++++	++
GE-Reflux	++++	++
Poor Weight Gain	++++	+
Epigastric Pain	++	+++
Dysphagia	++	++++
Food Bolus Impaction	+	++++



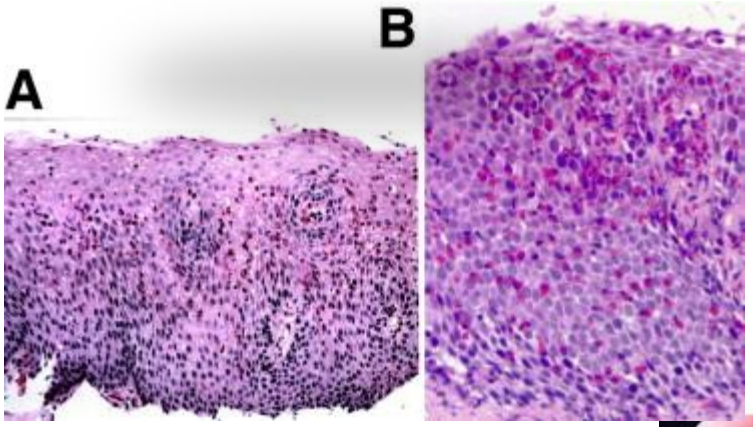
Adapted from Hoffien *JPGN* 2018

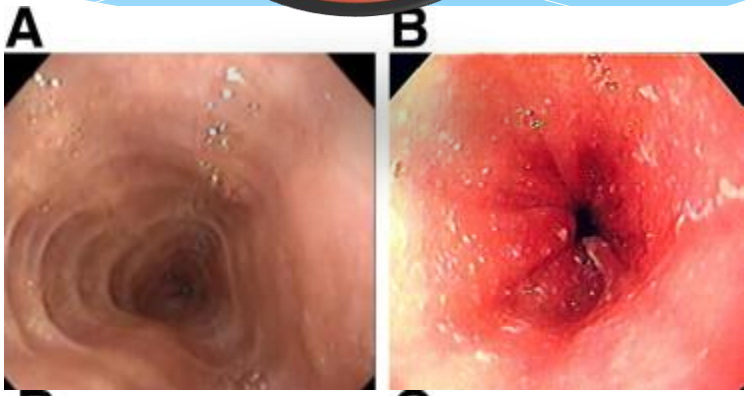
Normal

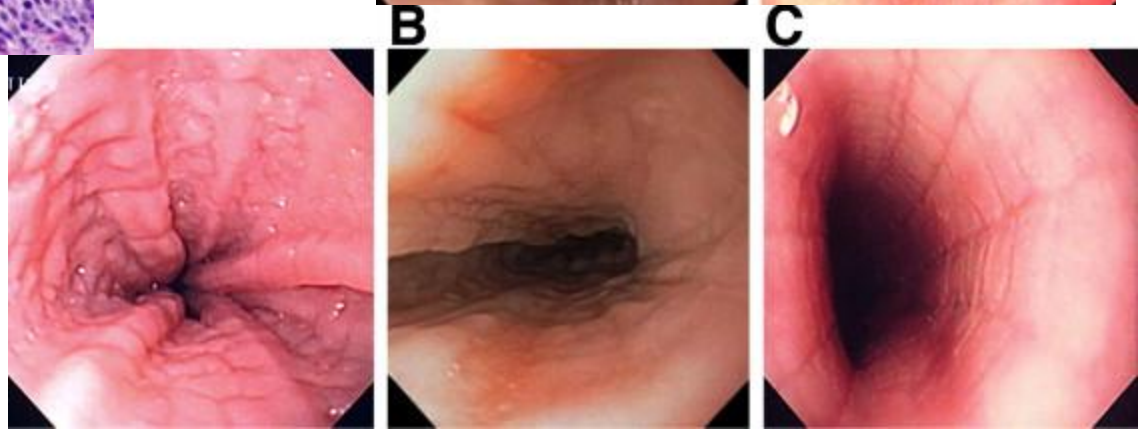




EoE







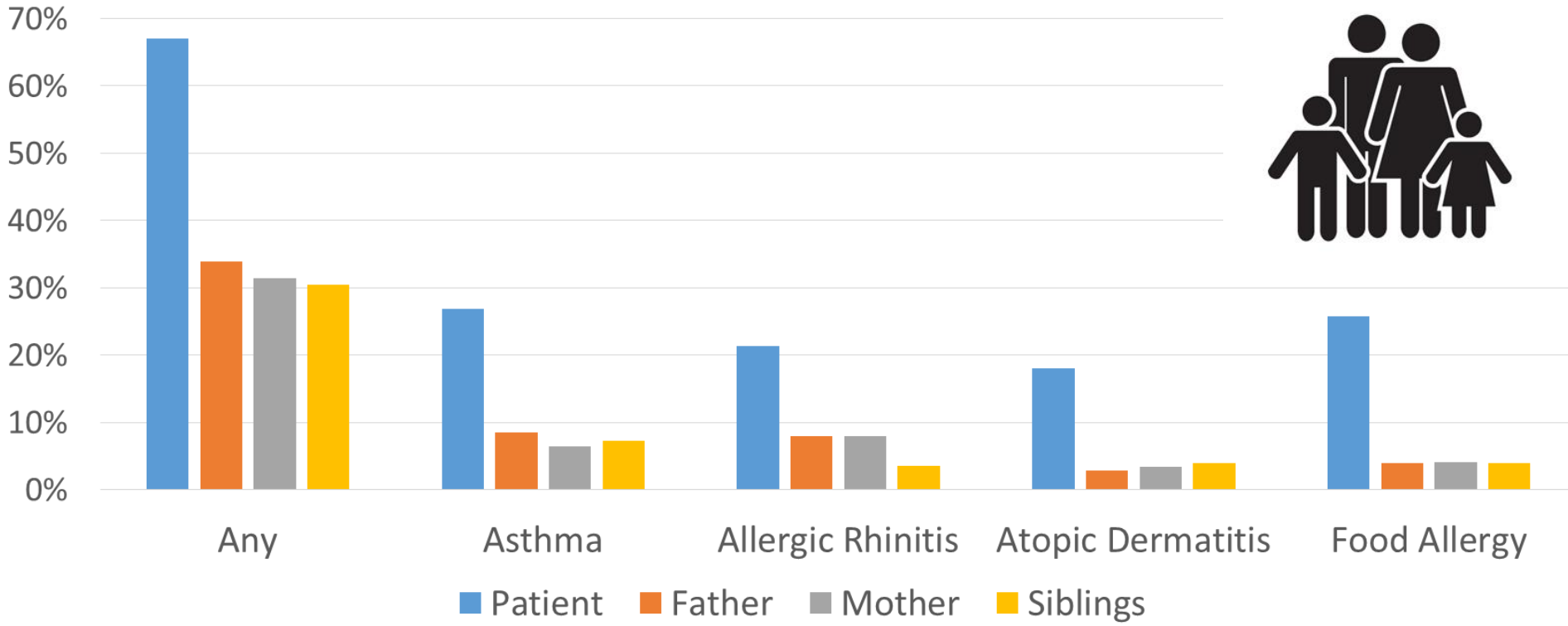
Furuta *Gastroenterol 2007*

* 1977-1995 sporadic reports of eosinophilic infiltrates resistant to GERD treatment.
* 1995 Kelly et al 10 patients resistant to GERD treatment (2 fundo's) all responded to amino acid formula.

Allergy ???

Kelly Gastroenterol 1995

Patient and family atopic background

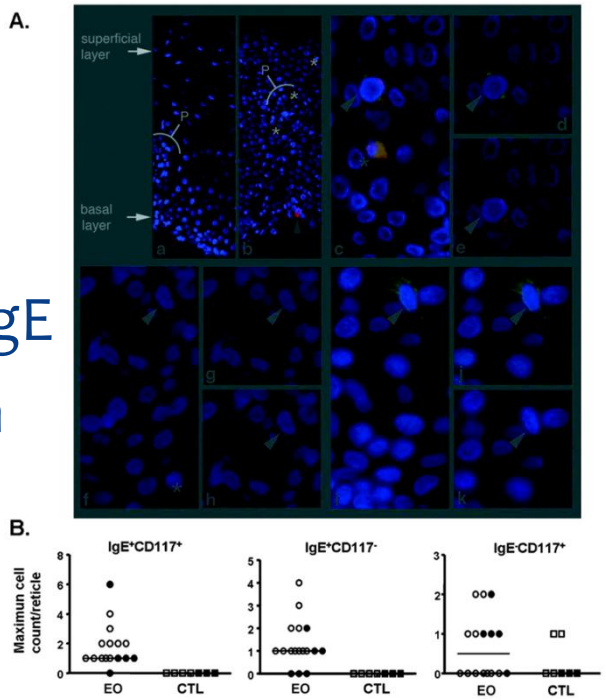


n= 410 European children (RetroPEER)

Hoffien et al *JPGN* 2018

Is EoE IgE mediated?

* The majority of EoE patients have concomitant allergic diseases
* ~70% have elevated IgE
* ~75% have sensitization to food or aeroallergens
* Evidence of localized class switch to IgE
* High responses to antigen elimination

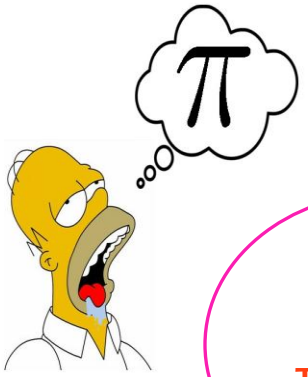


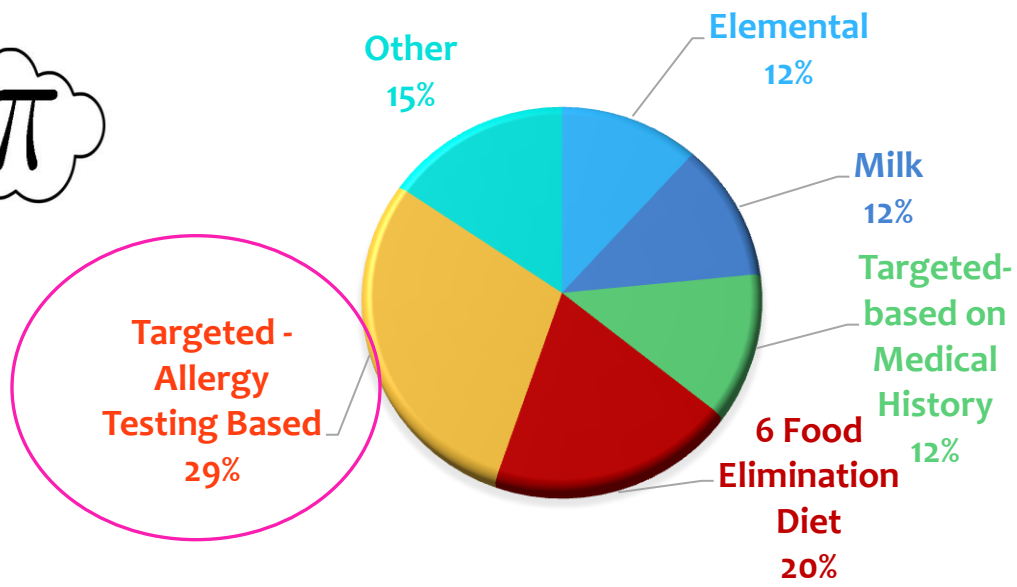
Simon D et al Allergy 2016

M Vicario et al. Gut 2010;59:12-20

Elimination diets – Patients treated only with diet (n=154) RetroPEER

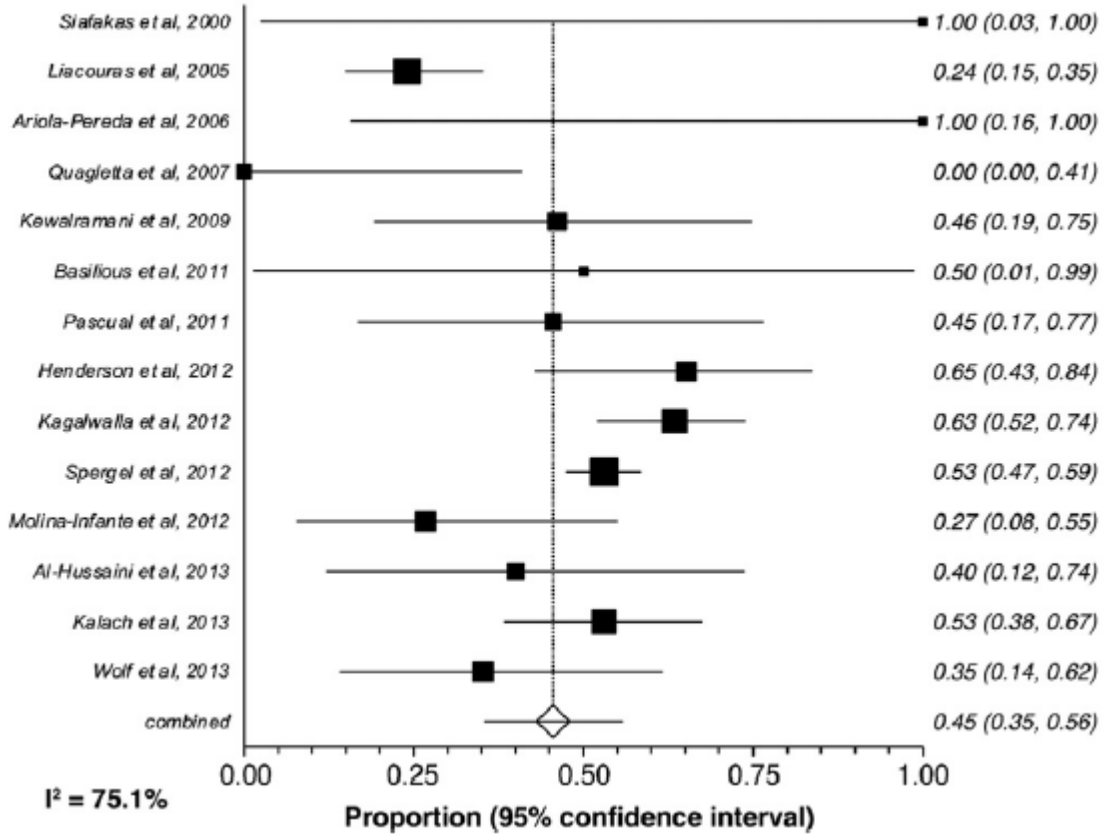
- Most patients were referred to allergists for allergy testing – prick/RAST to assess for list of causative antigens.
- Targeted elimination diets were formulated.





Adapted from Hoffien *JPGN* 2018

Allergy test based elimination diets fail to induce remission in majority



Most common triggering allergens identified:





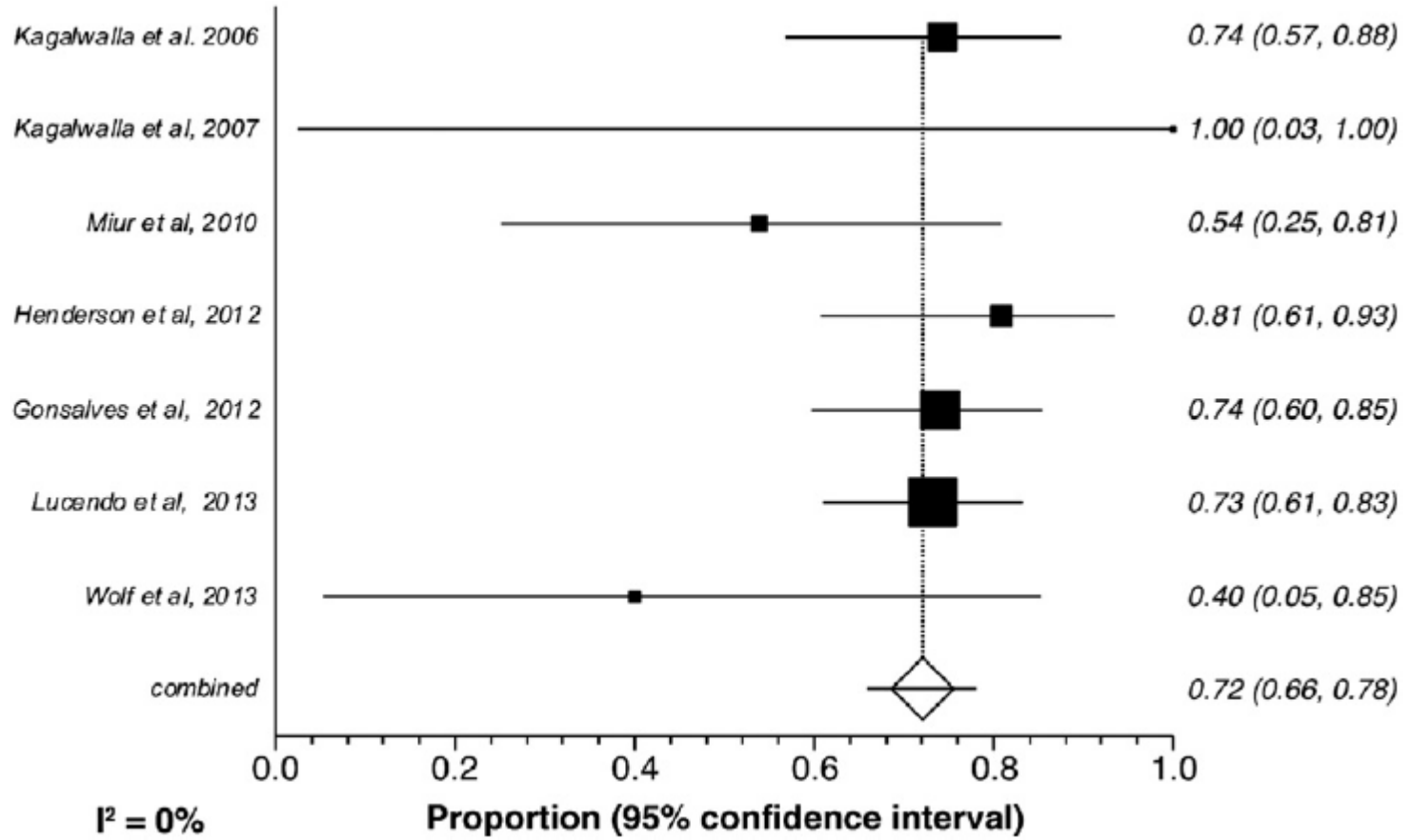


	ESPGHAN RetroPEER (current study)	Spergel *et al.* 2012 (Children's Hospital of Philadelphia)
Milk	40.3%	24%
Egg	17.4%	13%
Wheat/Gluten	10.3%	9%
Peanut	9.5%	7%
Tree nuts	8.3%	
Soy	8%	9%
Fish & Seafood	6.5%	
Sesame	3.4%	
Potato	1.2%	4%
Tomato	1%	
Beef	1%	6%
Corn	0.7%	6%
Chicken	0.7%	5%






Empiric Six Food Elimination Diet



Anti-IgE Treatment (Omalizumab)

* Induced remission in only 33% of EoE patients in an open label study despite decreasing tissue IgE levels. n=15
* Failed to induce remission or reduce symptoms compared to placebo in a DBPC trial (n=30). Most patients had granular IgG4 deposits.
* Omalimumab failed to improve tissue histology and Eos counts in 2 children
* Sporadic Successful treatments reported.

Louizou PLoS One 2015 ; Rocha Eur J Ped 2011; Clayton Gastroenterology 2014

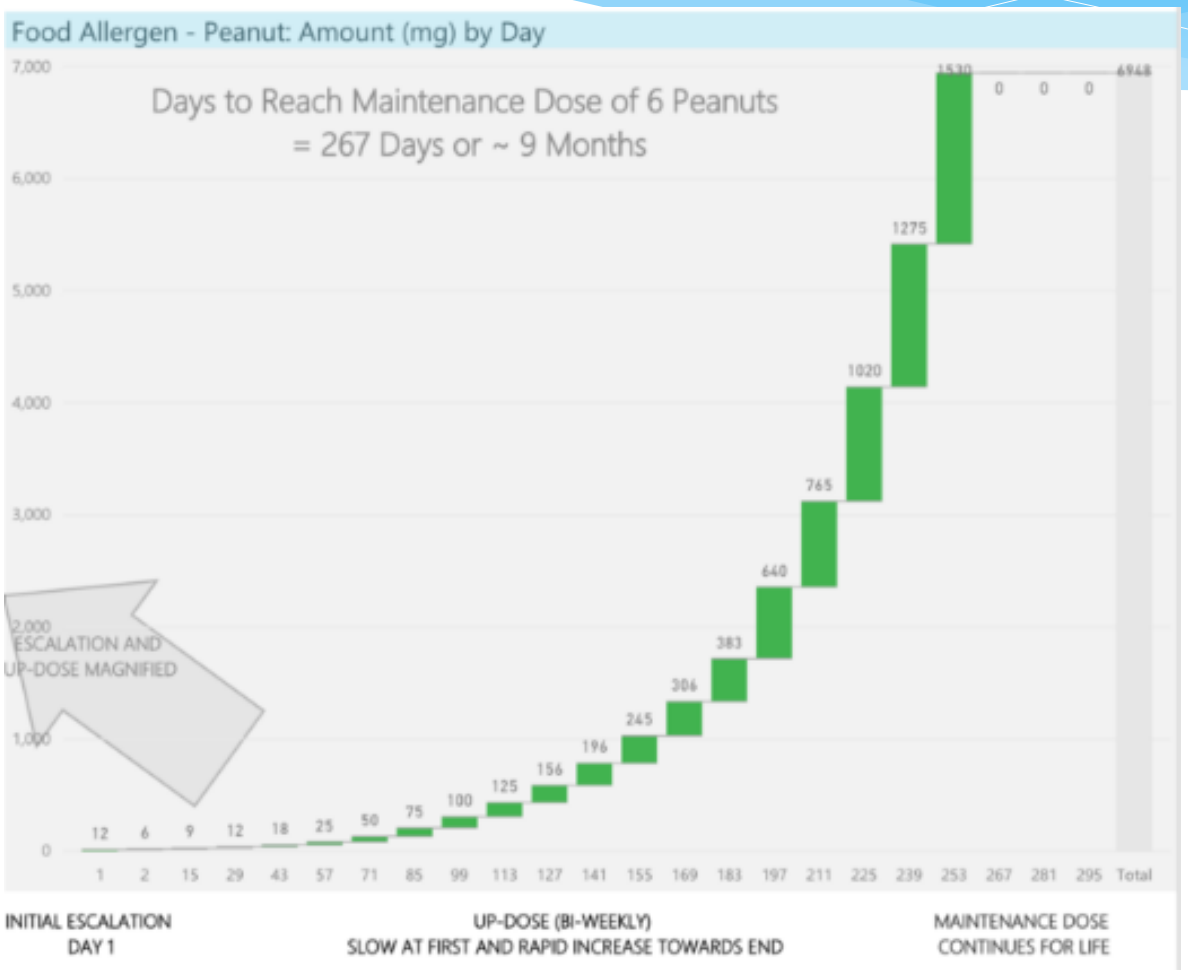
Some children who outgrow their IgE mediated allergies may develop EoE to the same allergen.

Maggadottir JACI 2014

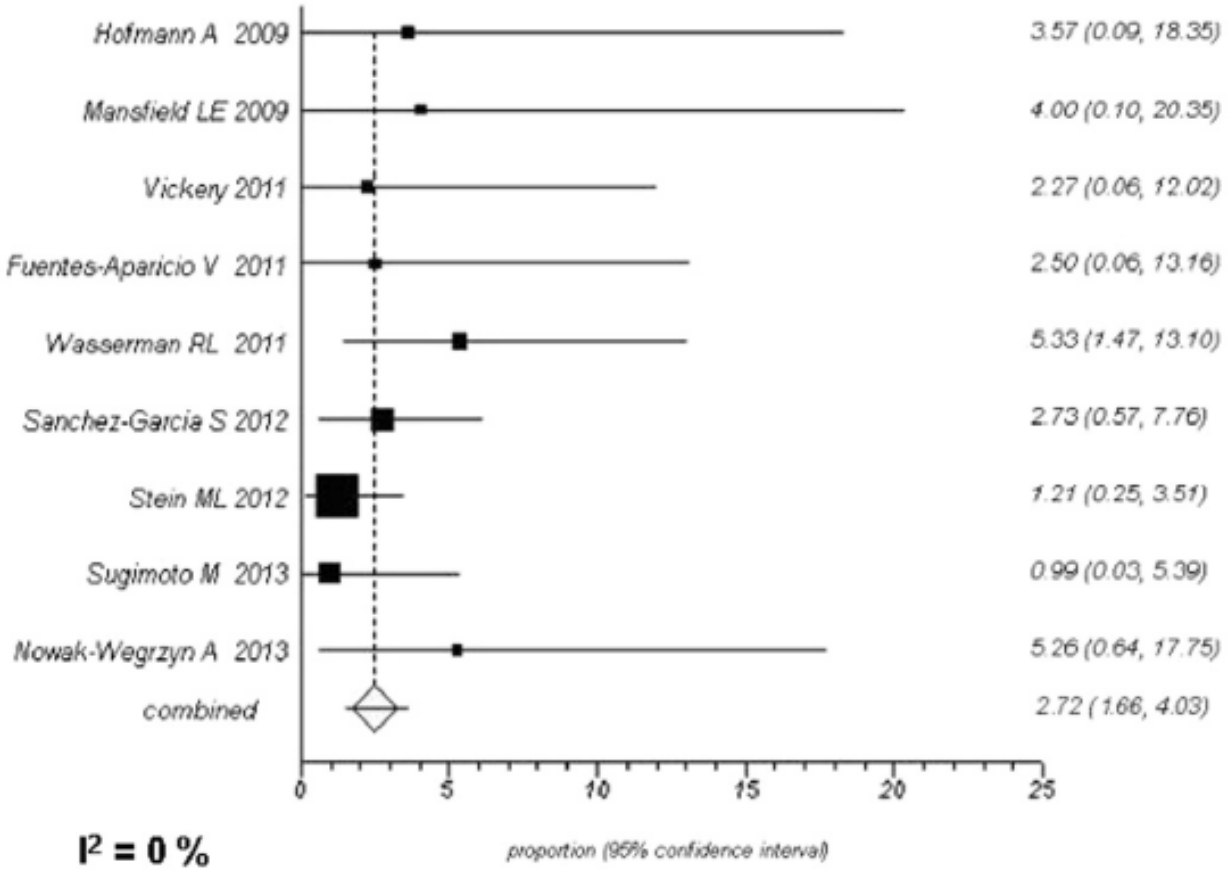
Thus the role of the immunologist decreased…

But…When one door closes, another opens up…

Oral Immunotherapy (OIT)

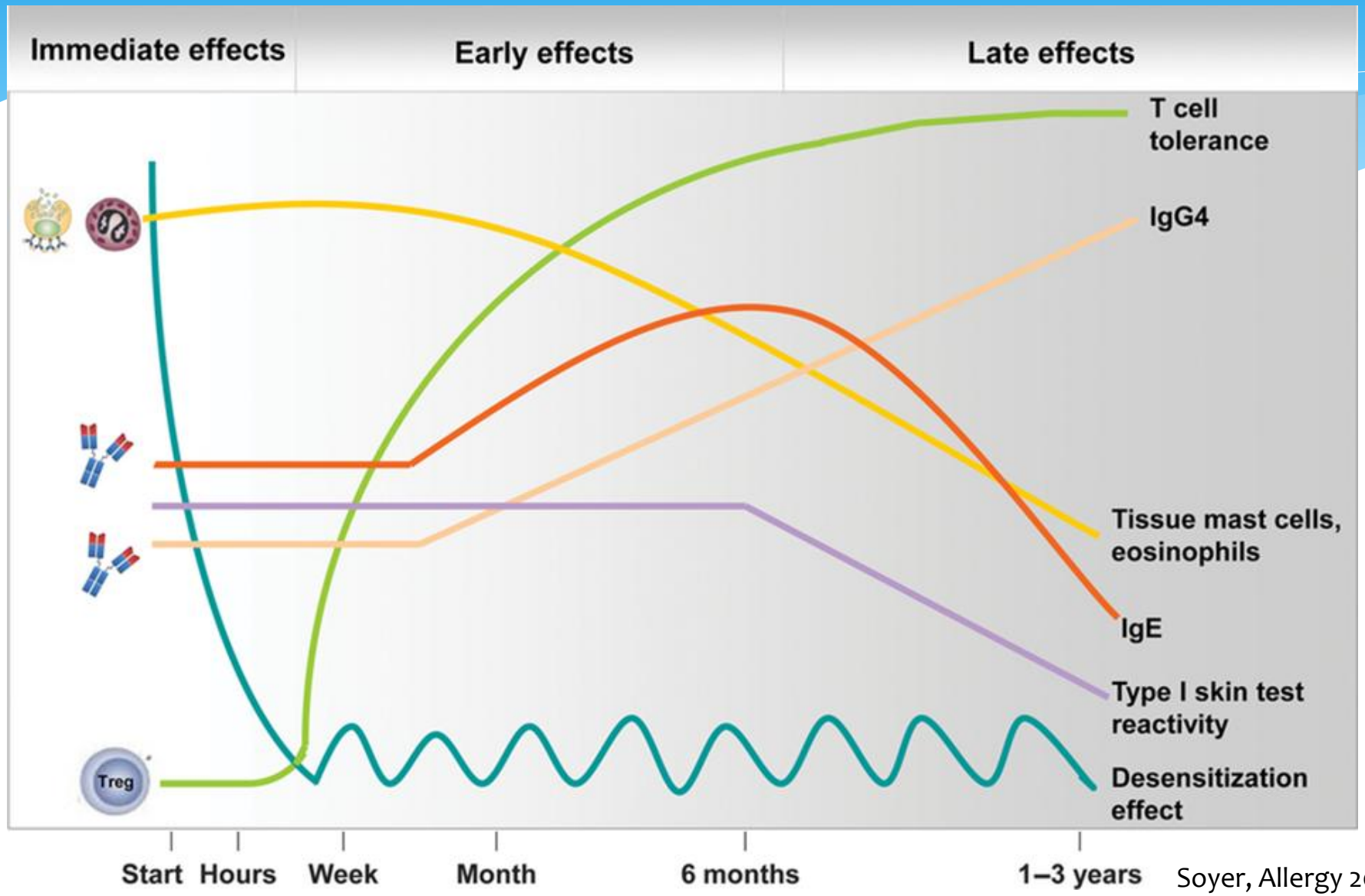


Oral immuno-therapy and EoE



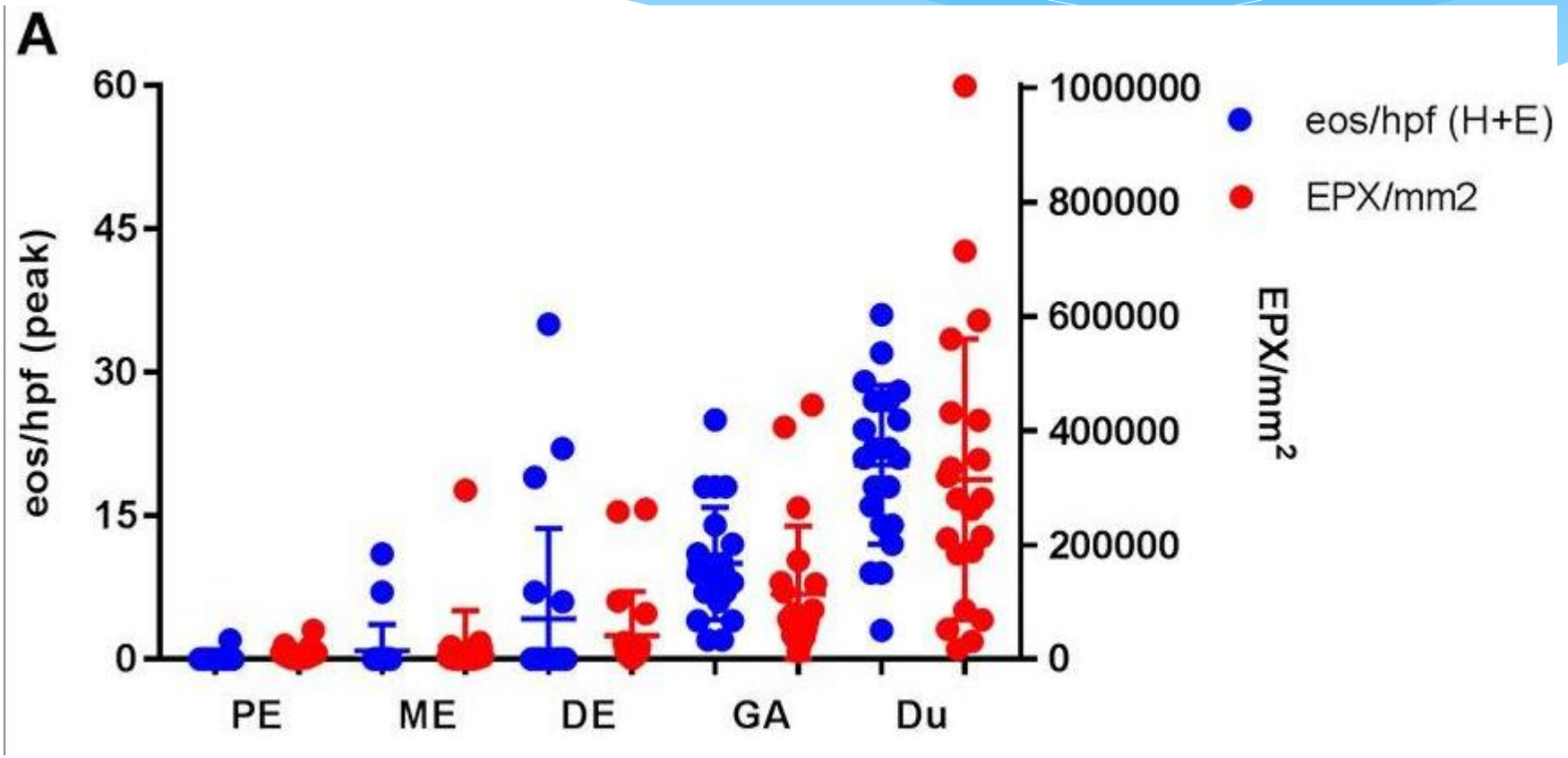
Lucendo et al Ann Allergy Asthma Immunol 2014

Changes occurring during immunotherapy



Soyer, Allergy 2012

But….Esophageal Eos present prior to OIT



Wright et al *Front Immunol* 2018

Role for Food Specific IgG4 in EoE?

* High sIgG4 to Cow's milk protein was associated with EoE. Schuyler et al *JACI* 2018
* Food Specific IgG4 are elevated in plasma and esophageal tissue in EoE patients compared to Controls . Wright *JACI* 2016
* IgG4/IgE may be better predictors.

The problem with a seesaw is you're always off balance.

IgE reactions post food elimination

* Patients without IgE associated allergy, developed IgE dependent reactions following dietary elimination and then re-introduction.

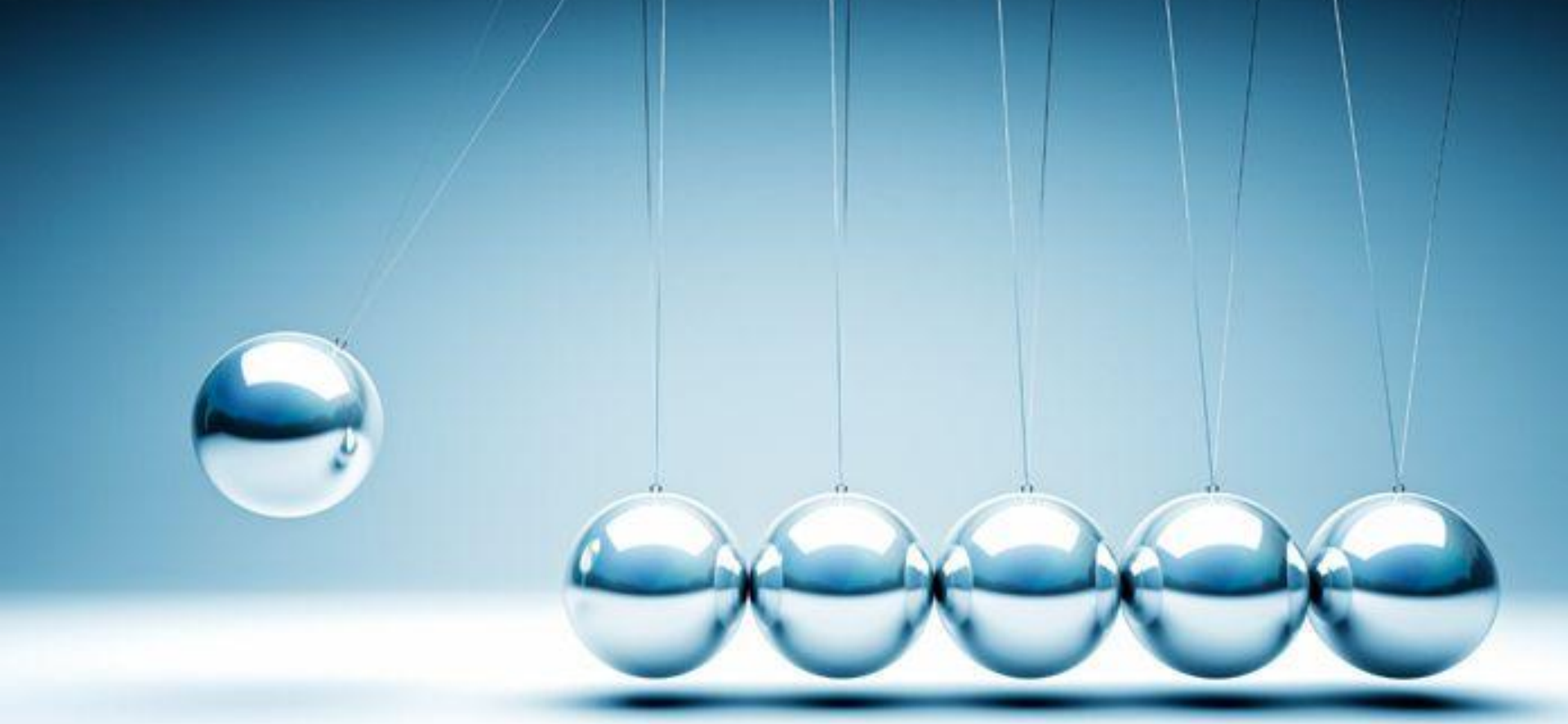
Gottlieb et al Ann Allergy Asthma Immunol 2019

Ho et al *JACI in Pract* 2018

* This is a currently rare but worrysome scenario.

So what may be the future role of immunologists in the treatment of EoE?

* Current
  * Assess for sensitization to foods
    * Prior to elimination diet
    * Prior to reintroduction - to assess risk and need for observed reintroduction of antigens
* Future – collaborative studies
  * Study the role of EoE in oral immune tolerance
  * Assess for risk of EoE following acquisition of tolerance to foods
  * Assessment of food specific IgG4 (in peripheral blood to tissue) to assess for its prognostic value.



We must remain aware that each action we take may cause a reaction somewhere unexpected. Learn to expect this, and work together with