# Changing Epidemiology of Food Allergy

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# Faculty Disclosure

There are no commercial products or services being discussed

No financial disclosures

No unlabeled use of a product is being discussed

# Agenda

1. Brief Overview of FA
2. Prevalence
3. Risk Factors
4. Natural Course

# What is food allergy?

National Institute of Allergy and Infectious Disease (NIAID):

***Food allergy*** – “adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food”

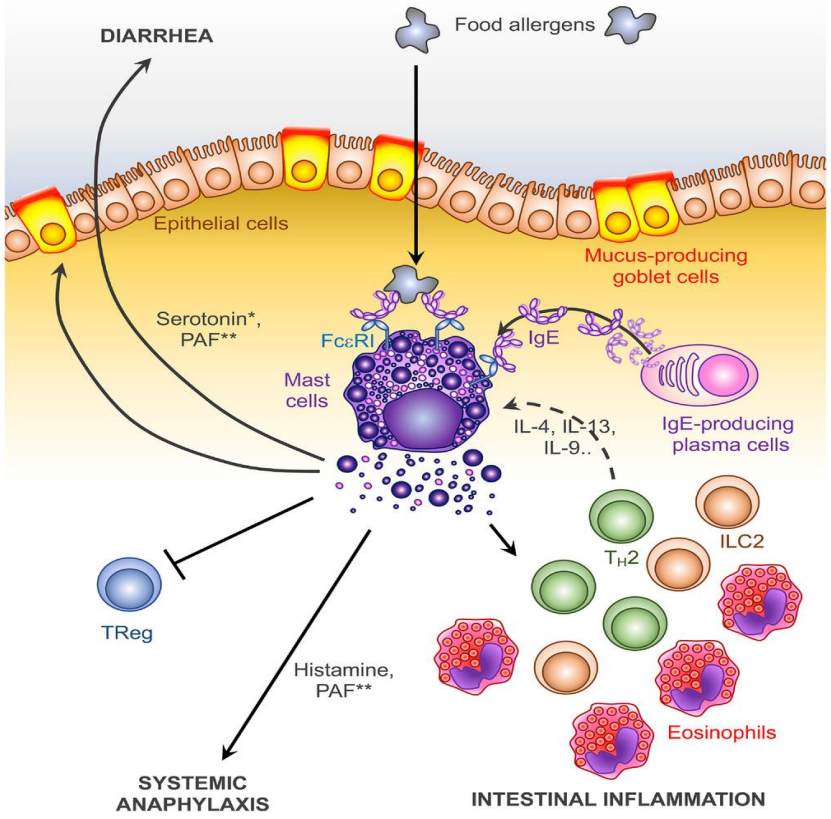
- IgE-mediated reactions: typically within minutes to 2 hours of the ingestion
- Non-IgE-mediated reactions: more subacute or chronic
  - FPAP, FPIES
- Mixed: atopic dermatitis, eosinophilic GI disorders (EGIDs)

***Food intolerance*** – nonimmune reactions that include metabolic, toxic, pharmacologic and undefined mechanisms

- GI disorders: Non-celiac gluten sensitivity, reflux, lactase deficiency, IBS
- Intolerances: caffeine, histamine-like compounds, alcohol, MSG
- Psychological reactions: food phobias and aversions

Joshua A. Boyce, et al., Guidelines for the Diagnosis and Management of Food Allergy in the United States: Summary of the NIAID-Sponsored Expert Panel Report, Journal of Allergy and Clinical Immunology, Volume 126, Issue 6, 2010, Pages 1105-1118.

# IgE in the pathophysiology of food allergy




Michelet M, Balbino B, Guilleminault L, Reber LL. IgE in the pathophysiology and therapy of food allergy. Eur J Immunol. 2021 Mar;51(3):531-543.

# Prevalence

# What we do know

Food allergies are common (5-10% affected)

Increasing in the past several decades

Disproportionately affect persons in industrialized nations

More common in children compared with adults

Relatively few foods account for the most of the disease burden

- peanut, tree nuts, fish, shellfish, egg, milk, wheat, soy, seeds

Sicherer SH, Sampson HA. Food allergy: A review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. J Allergy Clin Immunol. 2018 Jan;141(1):41-58.
Image from cofargroup.org

# Vs what we don’t know

True prevalence determination limited by multiple factors:

- different manifestations of food allergy
- different definitions of food allergy
- nature of the study
  - focus on specific populations
  - focus on different foods
  - use different methodologies

Sicherer SH, Sampson HA. Food allergy: A review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. J Allergy Clin Immunol. 2018 Jan;141(1):41-58.

# Prevalence of common food allergies by age group in the US

**TABLE 2** Prevalence of Common Food Allergies According to Age Group

| Age Group | Frequency, % (95% CI) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | All Allergens ($N$ = 3339) | Peanut ($N$ = 767) | Milk ($N$ = 702) | Shellfish ($N$ = 509) | Tree Nut ($N$ = 430) | Egg ($N$ = 304) | Fin Fish ($N$ = 188) | Strawberry ($N$ = 189) | Wheat ($N$ = 170) | Soy ($N$ = 162) |
| Prevalence among all children surveyed | | | | | | | | | | |
| All ages ($N$ = 38 480) | 8.0 (7.7–8.3) | 2.0 (1.8–2.2) | 1.7 (1.5–1.8) | 1.4 (1.2–1.5) | 1.0 (0.9–1.2) | 0.8 (0.7–0.9) | 0.5 (0.4–0.6) | 0.4 (0.4–0.5) | 0.4 (0.3–0.5) | 0.4 (0.3–0.4) |
| 0–2 y ($n$ = 5429) | 6.3 (5.6–7.0) | 1.4 (1.1–1.8) | 2.0 (1.6–2.4) | 0.5 (0.3–0.8) | 0.2 (0.2–0.5) | 1.0 (0.7–1.3) | 0.3 (0.1–0.4) | 0.5 (0.3–0.7) | 0.3 (0.1–0.5) | 0.3 (0.2–0.4) |
| 3–5 y ($n$ = 5910) | 9.2 (8.3–10.1) | 2.8 (2.3–3.4) | 2.0 (1.7–2.5) | 1.2 (0.8–1.6) | 1.3 (1.0–1.7) | 1.3 (0.9–1.7) | 0.5 (0.3–0.8) | 0.5 (0.3–0.8) | 0.5 (0.3–0.7) | 0.5 (0.3–0.7) |
| 6–10 y ($n$ = 9911) | 7.6 (7.0–8.2) | 1.9 (1.6–2.3) | 1.5 (1.2–1.8) | 1.3 (1.1–1.6) | 1.1 (0.87–1.4) | 0.8 (0.6–1,1) | 0.5 (0.3–0.7) | 0.4 (0.3–0.5) | 0.4 (0.3–0.5) | 0.3 (0.2–0.5) |
| 11–13 y ($n$ = 6716) | 8.2 (7.4–9.0) | 2.3 (1.9–2.8) | 1.4 (1.1–1.8) | 1.7 (1.3–2.1) | 1.2 (1.0–1.6) | 0.5 (0.4–0.8) | 0.6 (0.4–0.8) | 0.4 (0.3–0.6) | 0.7 (0.5–0.9) | 0.6 (0.4–0.8) |
| ≥14 y ($n$ = 10 514) | 8.6 (7.9–9.3) | 1.7 (1.4–2.1) | 1.6 (1.3–1.9) | 2.0 (1.7–2.5) | 1.2 (0.9–1.5) | 0.4 (0.2–0.5) | 0.6 (0.4–0.9) | 0.4 (0.3–0.6) | 0.3 (0.2–0.4) | 0.3 (0.2–0.4) |
| $P$ | .0000 | .0001 | .0504 | .0000 | .0000 | .0000 | .1045 | .7700 | .0089 | .0509 |

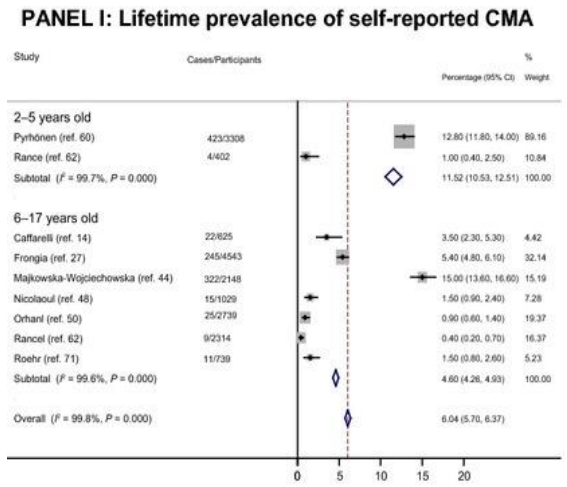
8% of children have food allergy, with peanut most common overall

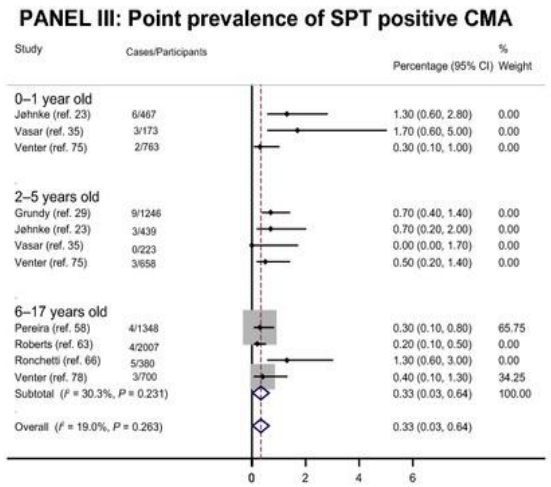
2.4% have multiple food allergies (or 30.4% of children with food allergy)

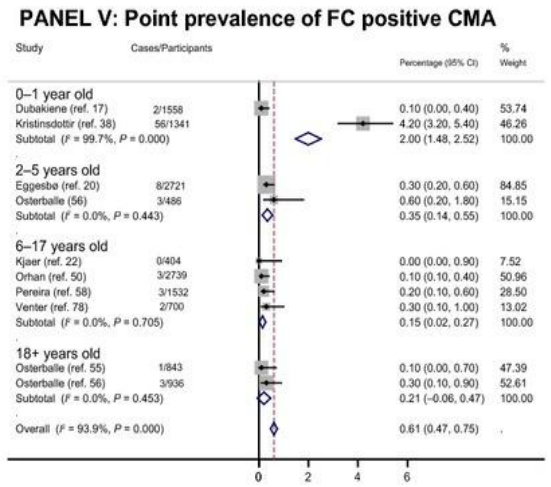
3.1% experience severe reactions (or 38.7% of children with food allergy)

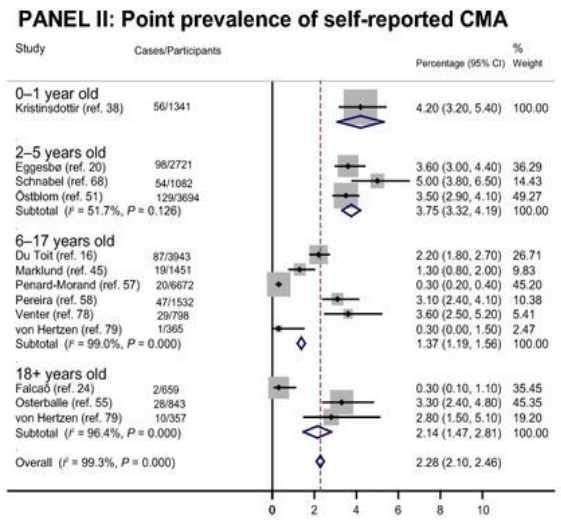
Gupta RS, Springston EE, Warrier MR, Smith B, Kumar R, Pongracic J, et al. The prevalence, severity, and distribution of childhood food allergy in the United States. Pediatrics 2011; 128:e9-17.

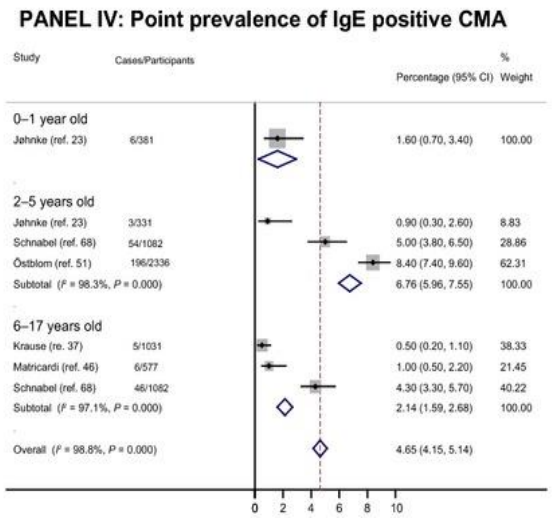
# Limitations of self report

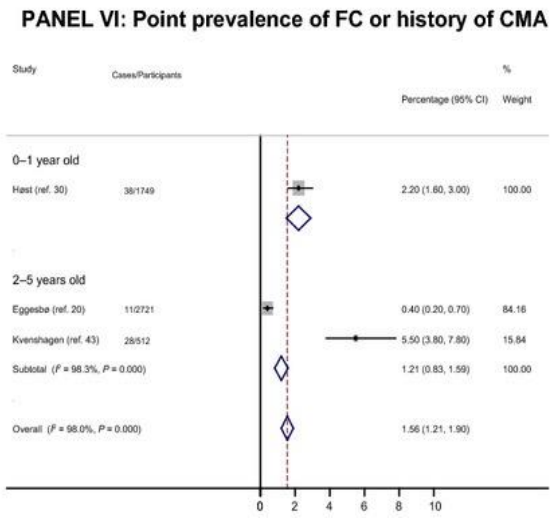


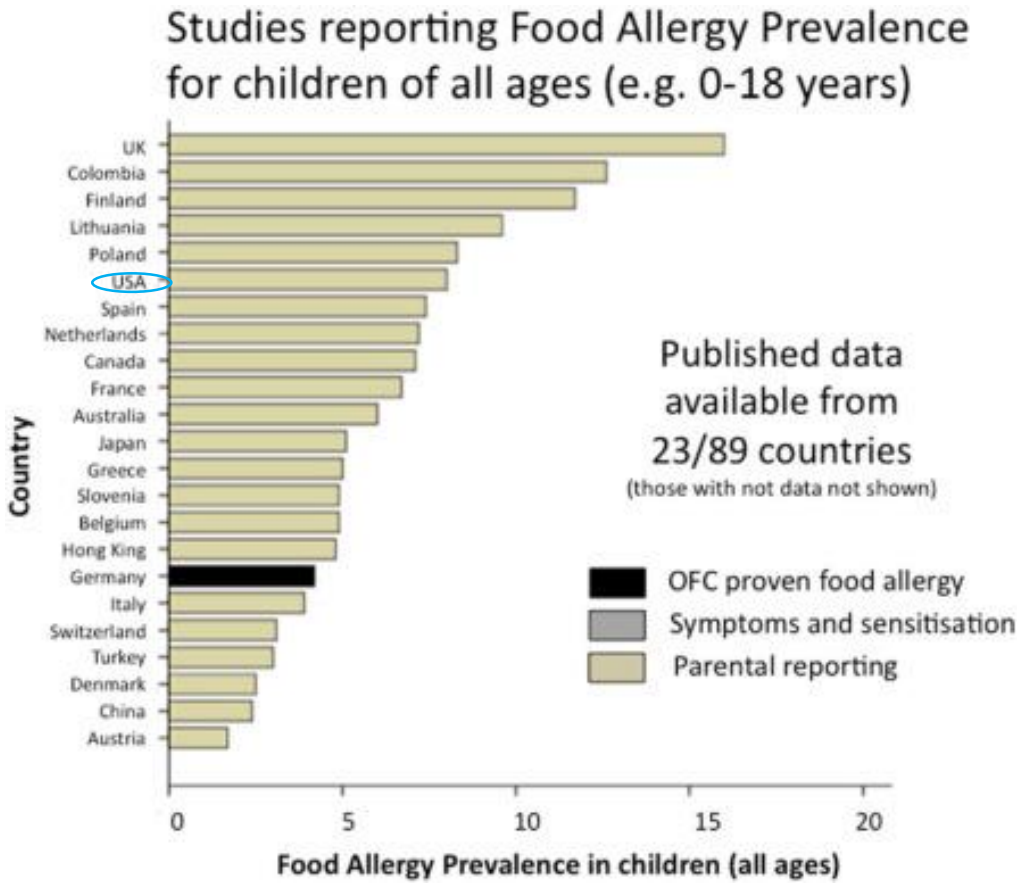




Nwaru BI et al. Prevalence of common food allergies in Europe: A systematic review and meta-analysis. Allergy 2014; 69: 992-1007.

# Global food allergy disease burden


Prescott SL et al. A global survey of changing patterns of food allergy burden in children. World Allergy Organization Journal, Vol6, 2013: 21.

# Increase in food allergy in recent decades

In Sweden, the frequency of positive peanut-specific IgE increased by 32% in 5 years (1994-1998) despite no concomitant increase in peanut national consumption

In the UK, reviewing data from 4-year-old children on the Isle of Wight, a 3-fold increase in both peanut sensitization and peanut clinical allergy from a group of 4-year-olds six years earlier

In Canada, peanut allergy in young children was increased by 36% within a 5-year period

In NY state, a study from 1990-2006 revealed a 4-fold increase in the anaphylaxis hospitalization rate

Self-reported tree nut allergy increased from 0.2% in 1997 to 1.1% in 2008

Van Odijk J, et al. Specific IgE Antibodies to peanut in western Sweden. Allergy. 2011 June; 56:573-577.
Grundy J, Matthews S, Bateman B, et al. Rising Prevalence of allergy to peanut in children: data from 2 sequential cohorts. J Allergy Clin Immunol. 2002 Nov; 110(5):784-789.
Ben-Shoshan M, Kagan RS, Alizadehfar R, et al. Us the prevalence of peanut allergy increasing? A 5-year follow-up studty in children in Montreal. J Allergy Clin Immunolo. 2009 Apr; 123(4):783-789.
Sicherer SH, Muñoz-Furlong A, Godbold JH, Sampson HA. US prevalence of self-reported peanut, tree nut, and sesame allergy: 11-year follow-up. J Allergy Clin Immunol. 2010 Jun;125(6):1322-6,

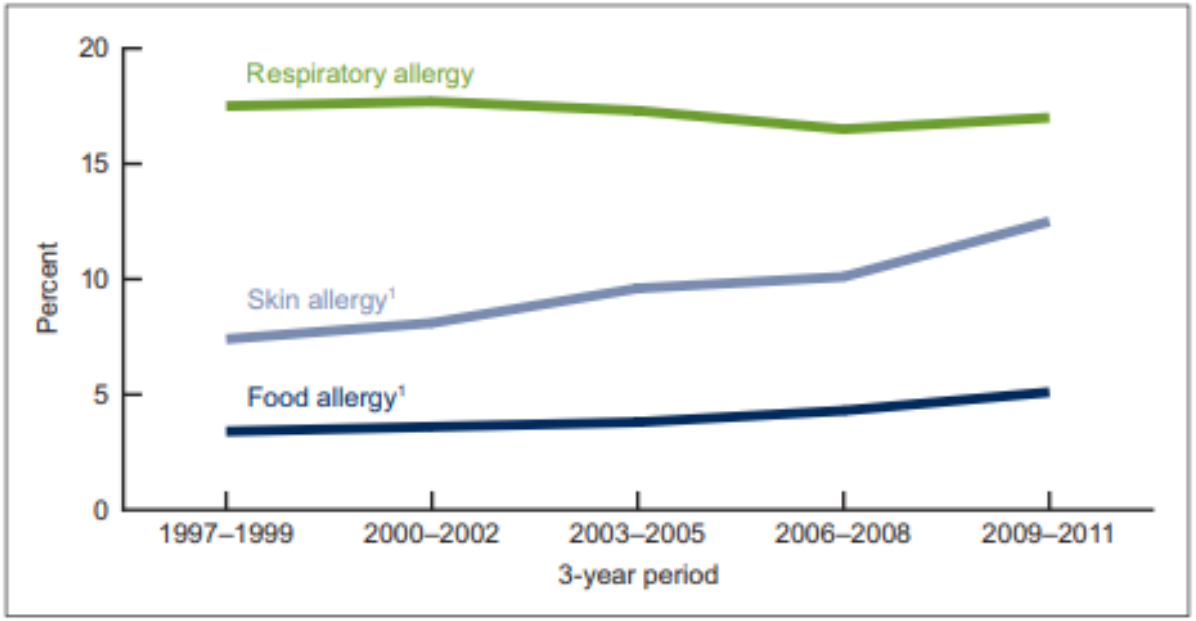
# Increase in Prevalence

US National Health Interview Survey

- 3.4% in 1997 to 1999
- 5.1% in 2009 to 2011
- 6.2% in 2016

**The prevalence of food and skin allergies increased in children aged 0–17 years from 1997–2011.**

Figure 1. Percentage of children aged 0–17 years with a reported allergic condition in the past 12 months: United States, 1997–2011

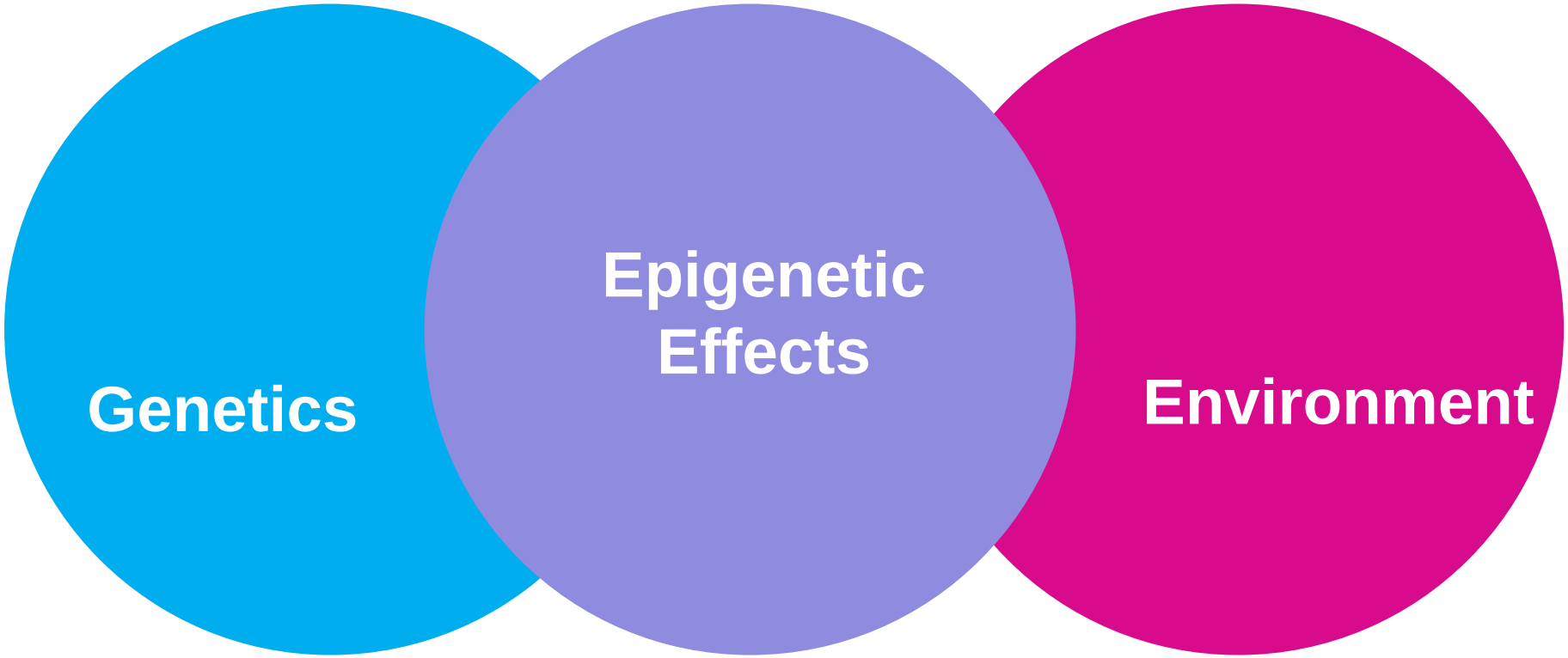



[1]Significant increasing linear trend for food and skin allergy from 1997–1999 to 2009–2011.
SOURCE: CDC/NCHS, Health Data Interactive, National Health Interview Survey.

Jackson, Kristen D., LaJeana D. Howie, and Omolara Jean Akinbami. *Trends in allergic conditions among children: United States, 1997-2011*. No. 121. US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, 2013.

# Risk factors

# Complex interplay of risk factors



# What is to blame?

Race and ethnicity

Obesity

Male sex

Specific genes

Microbiome

Comorbid eczema

Timing and route of food exposure

Increased hygiene

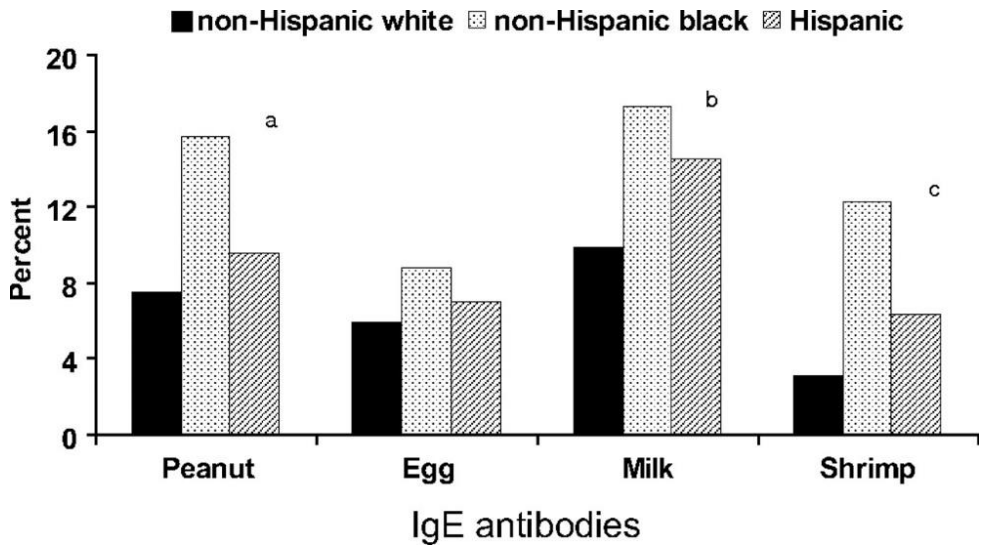
HLA

Familial associations

Reduced consumption of omega-3s

VITAMIN D INSUFFICIENCY

# Proportion of children with detectable levels of IgE antibodies




Branum AM, Lukacs SL, Food allergy among children in the United States. Pediatrics. 2009; 124 (6): 1549-1555.

# Racial and Ethnic Differences

One large systematic review evaluated 20 studies to identify disparities

Study limitations precluded a definitive disparity

However:

- Six studies noted higher odds of food sensitization (sIgE) among black than white children
  - did not determine whether ingestion produced an allergic reaction
- Four studies noted a higher parent-reported rate of FA in self-identified blacks than whites
  - did not report whether these patients were actually sensitized
- One study noted lower race-based odds of being able to identify signs of FA or to identify a FA trigger
  - limited by self report

Matthew Greenhawt, Christopher Weiss, Marisa L. Conte, Marlie Doucet, Amy Engler, Carlos A. Camargo, Racial and Ethnic Disparity in Food Allergy in the United States: A Systematic Review, The Journal of Allergy and Clinical Immunology: In Practice, Volume 1, Issue 4, 2013.

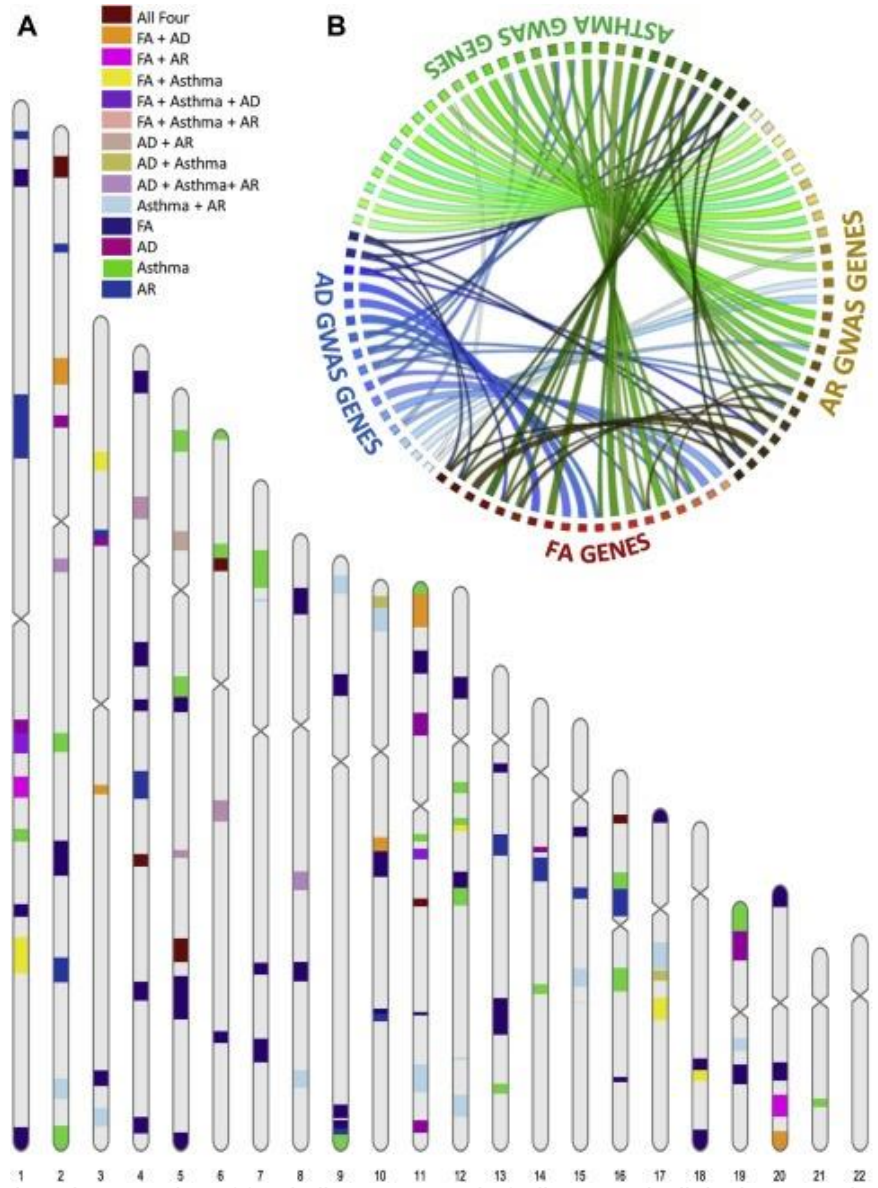
# Genetics of food allergy

Genetic loci and genes associated with food allergy come from several main functional categories:

- Skin barrier integrity (FLG)
- Vascular and endothelial cell factors
- Innate immunity
- Adaptive immunity
- Immune modulation and regulation

Sibling risk in food allergy:

- Food sensitized ~67%
- Clinically reactive ~13%



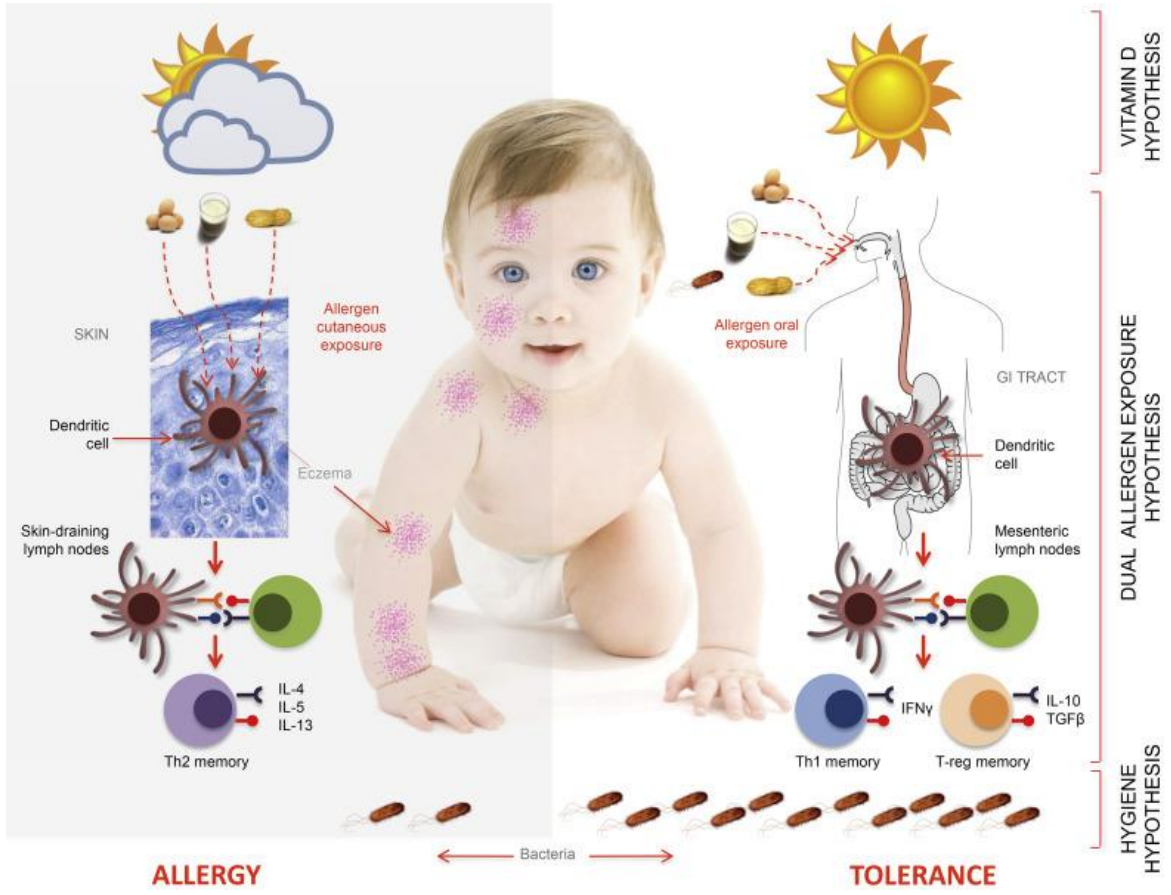

Kanika Kanchan, Selene Clay, Haritz Irizar, Supinda Bunyavanich, Rasika A. Mathias, Current insights into the genetics of food allergy, Journal of Allergy and Clinical Immunology, Volume147, Issue 1, 2021, Pages 15-28,
Ruchi S. Gupta, Madeline M. Walkner, Matthew Greenhawt, Claudia H. Lau, Deanna Caruso, Xiaobin Wang, Jacqueline A. Pongracic, Bridget Smith, Food Allergy Sensitization and Presentation in Siblings of Food Allergic Children, The Journal of Allergy and Clinical Immunology: In Practice, Volume 4, Issue 5, 2016, Pages 956-962

# “The Dual Allergen Exposure Hypothesis”

Low dose *cutaneous* sensitization to food may lead to food sensitivity

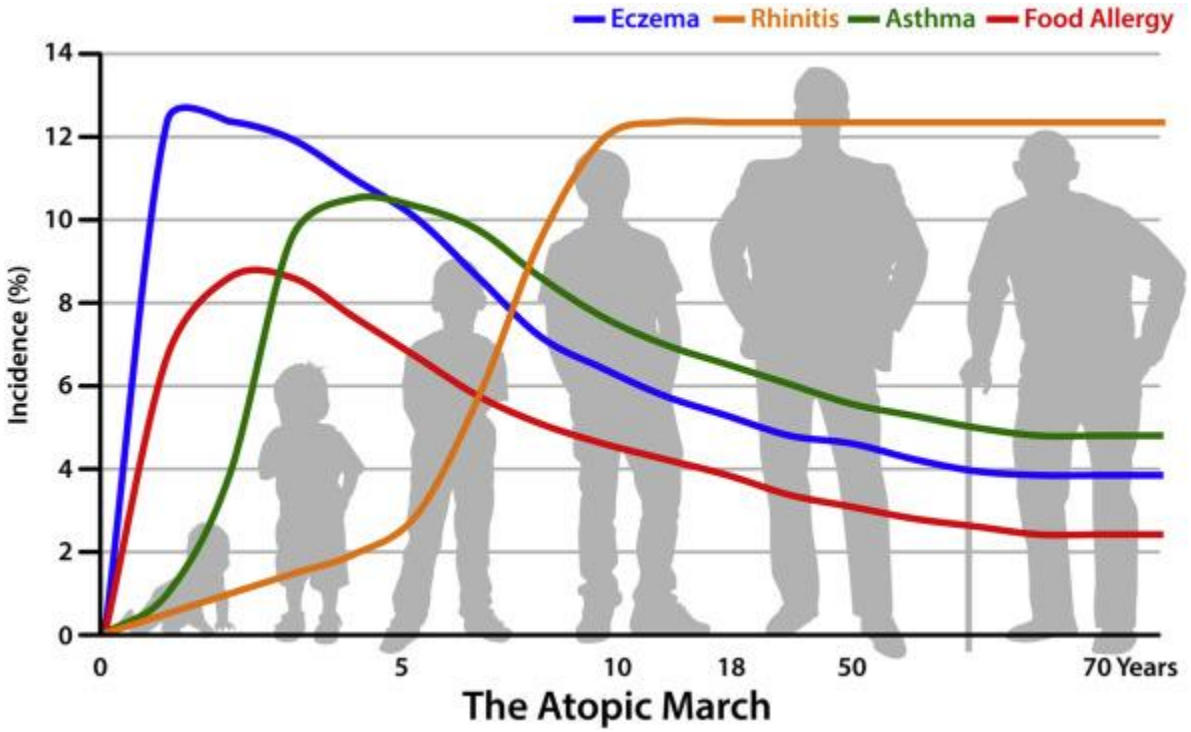
Early consumption of food may induce tolerance

This theory supports the idea that an impaired skin barrier plays a role in sensitization as a first step toward food allergy




du Toit G, Tsakok T, Lack S, Lack G. Prevention of food allergy. J Allergy Clin Immunol. 2016 Apr;137(4):998-1010.

# Genetics of food allergy

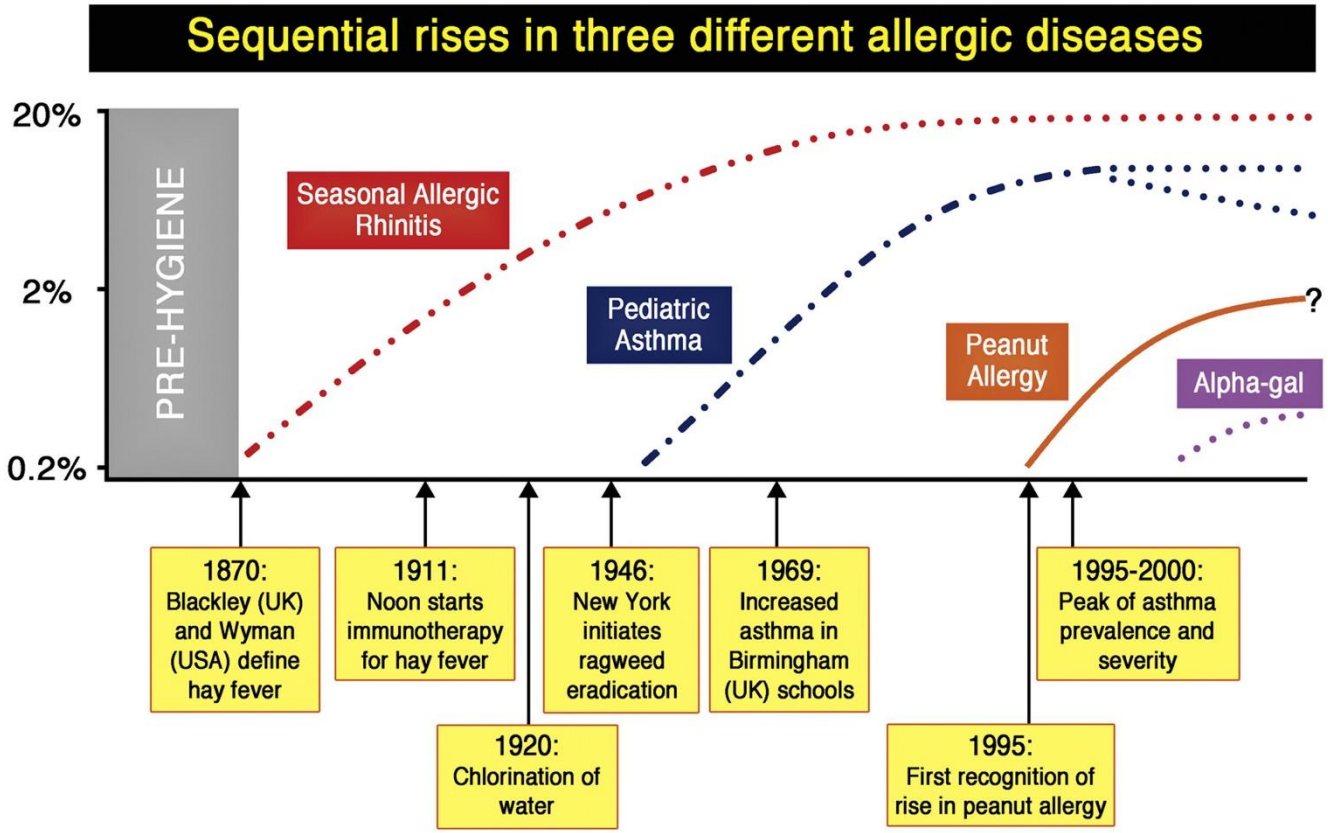



| Locus | Genes | FA | AD | Asthma | AR |
|---|---|---|---|---|---|
| 4q27 | IL2 \| IL21 | | | | |
| 5q31.1 | IL13 \| KIF3A | | | | |
| 6p21.32 | HLA | | | | |
| 11q13.5 | C11ORF30/EMSY \| LRRC32 \| LOC101928813 | | | | |
| 16p13.13 | CLEC16A | | | | |
| 1q21.3 | FLG | | | | |
| 11q13.1 | OVOL1 | | | | |
| 2p25.1 | LINC00299 | | | | |
| 9q13.2 | CCDC80 | | | | |
| 10q21.2 | ZNF365 | | | | |
| 11p15.4 | OR10A3 \| NLRP10 | | | | |
| 20q13.33 | TNFRSF6B | | | | |
| 3p22.3 | GLB1 | | | | |
| 5q22.1 | SLC25A46 \| TSLP | | | | |
| 12q13.3 | STAT6 | | | | |
| 17q21.33 | ZNF652 | | | | |
| 18q21.33 | SERPINB7 | | | | |
| 4p14 | TLR1 \| TLR10 | | | | |
| 5q22.1 | WDR36 | | | | |
| 2q12.1 | IL18L1 | | | | |
| 8q21.13 | ZBTB10 | | | | |
| 5p13.2 | CAPSL \| IL7R | | | | |
| 5q31.1 | RAD50 | | | | |
| 2p25.1 | RNF144A \| ID2 | | | | |
| 3q28 | LPP | | | | |
| 6q15 | BACH2 | | | | |
| 7p15.1 | JAZF1 | | | | |
| 8q24.21 | MYC \| TMEM75 | | | | |
| 9p24.1 | IL33 \| RANBP6 | | | | |
| 10p14 | CELF2 \| GATA3 | | | | |
| 11q23.3 | CXCR5 \| DDX6 | | | | |
| 12q24.12 | ATXN2 | | | | |
| 12q24.31 | SPPL3 | | | | |
| 15q22.2 | RORA | | | | |
| 15q23.33 | SMAD3 | | | | |
| 17q12 | GSDMB | | | | |
| 19q13.11 | CEBPA | | | | |


Wendy F. Davidson et al. Report from the National Institute of Allergy and Infectious Diseases workshop on “Atopic dermatitis and the atopic march: Mechanisms and interventions”, Journal of Allergy and Clinical Immunology, Volume 143, Issue 3, 2019,

Kanika Kanchan, Selene Clay, Haritz Irizar, Supinda Bunyavanich, Rasika A. Mathias, Current insights into the genetics of food allergy, Journal of Allergy and Clinical Immunology, Volume147, Issue 1, 2021, Pages 15-28,

# Hygiene Hypothesis




Thomas A.E. Platts-Mills, The allergy epidemics: 1870-2010, Journal of Allergy and Clinical Immunology, Volume 136, Issue 1, 2015, Pages 3-13.

# Natural course

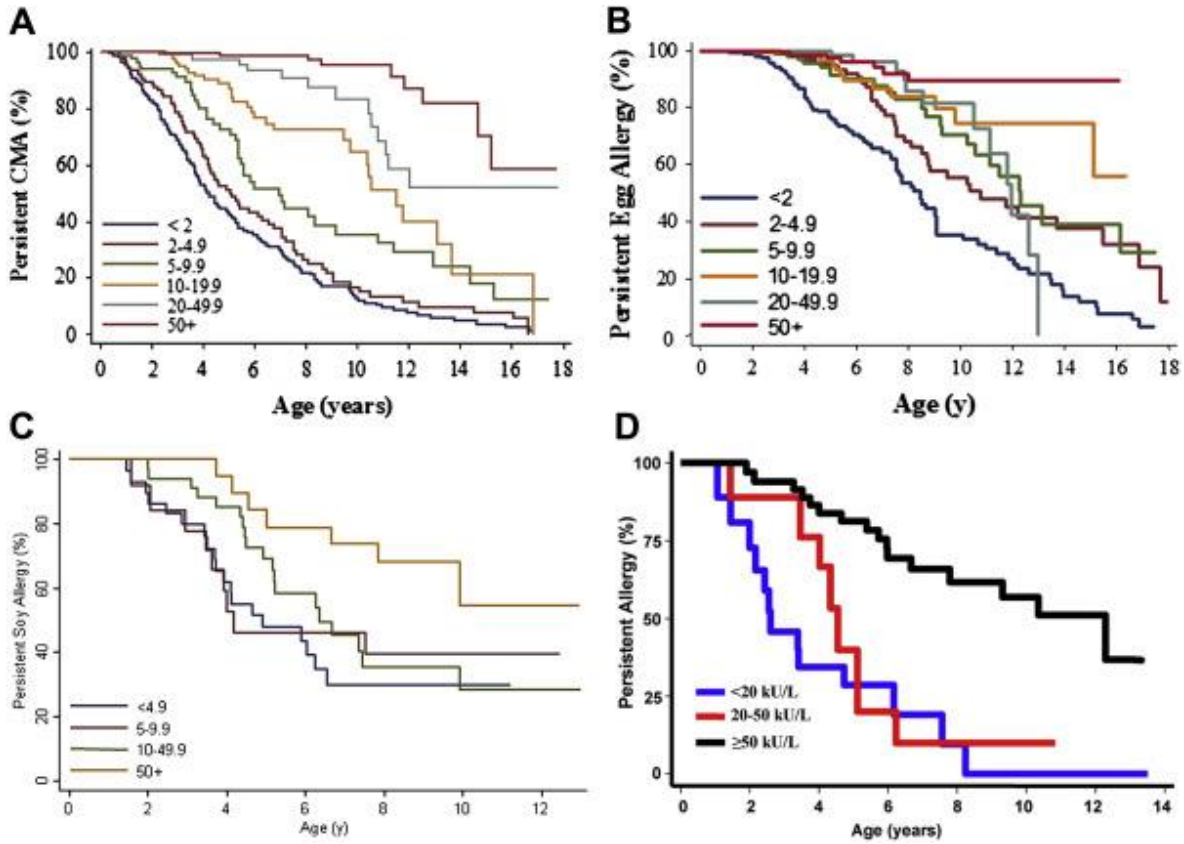
# Natural course is variable for different foods

Some foods have a high rate of resolution in childhood

- milk: >50% by age 5-10 years
- egg: ~50% by age 2-9 years
- wheat: 50% by age 7 years
- soy: 45% by age 6 years

While others tend to persist

- peanut: around 20% resolution by age 4 years
- tree nuts: ~10% resolution
- fish, shellfish, seeds less common

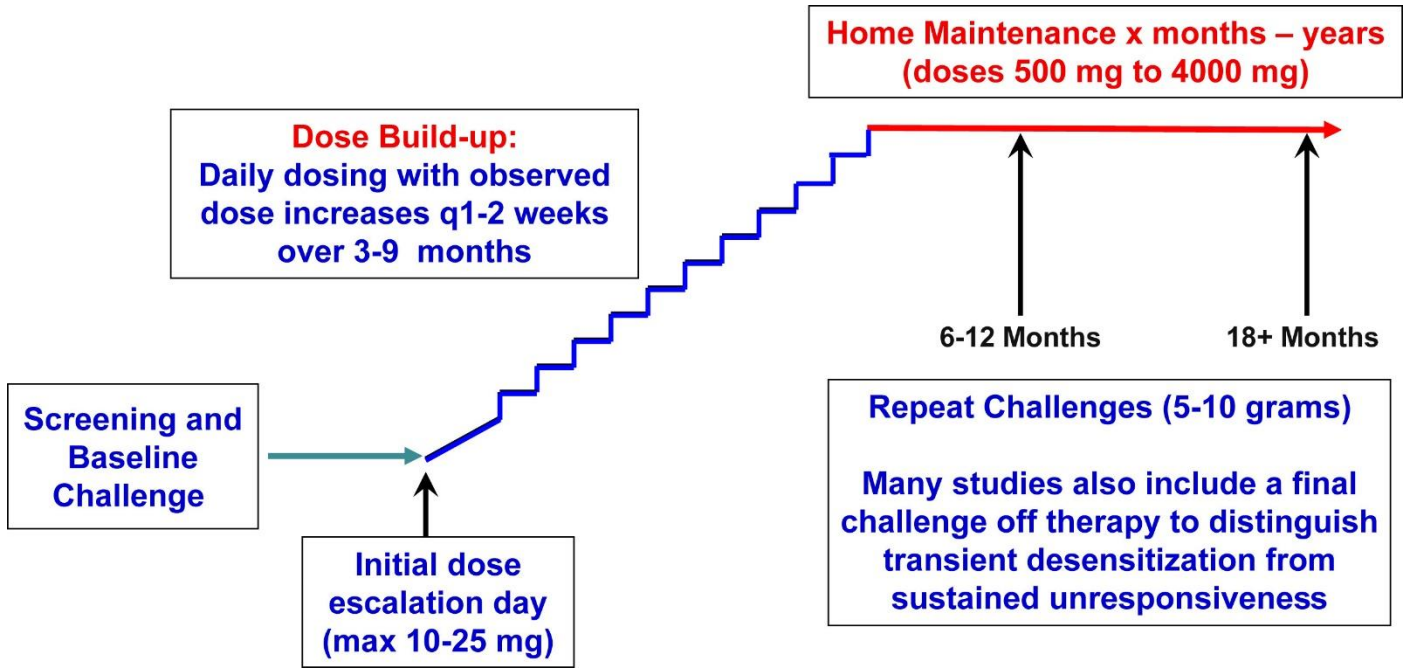



Jessica Savage, Scott Sicherer, Robert Wood, The Natural History of Food Allergy, The Journal of Allergy and Clinical Immunology: In Practice, Volume 4, Issue 2, 2016.

# Where do we go from here?

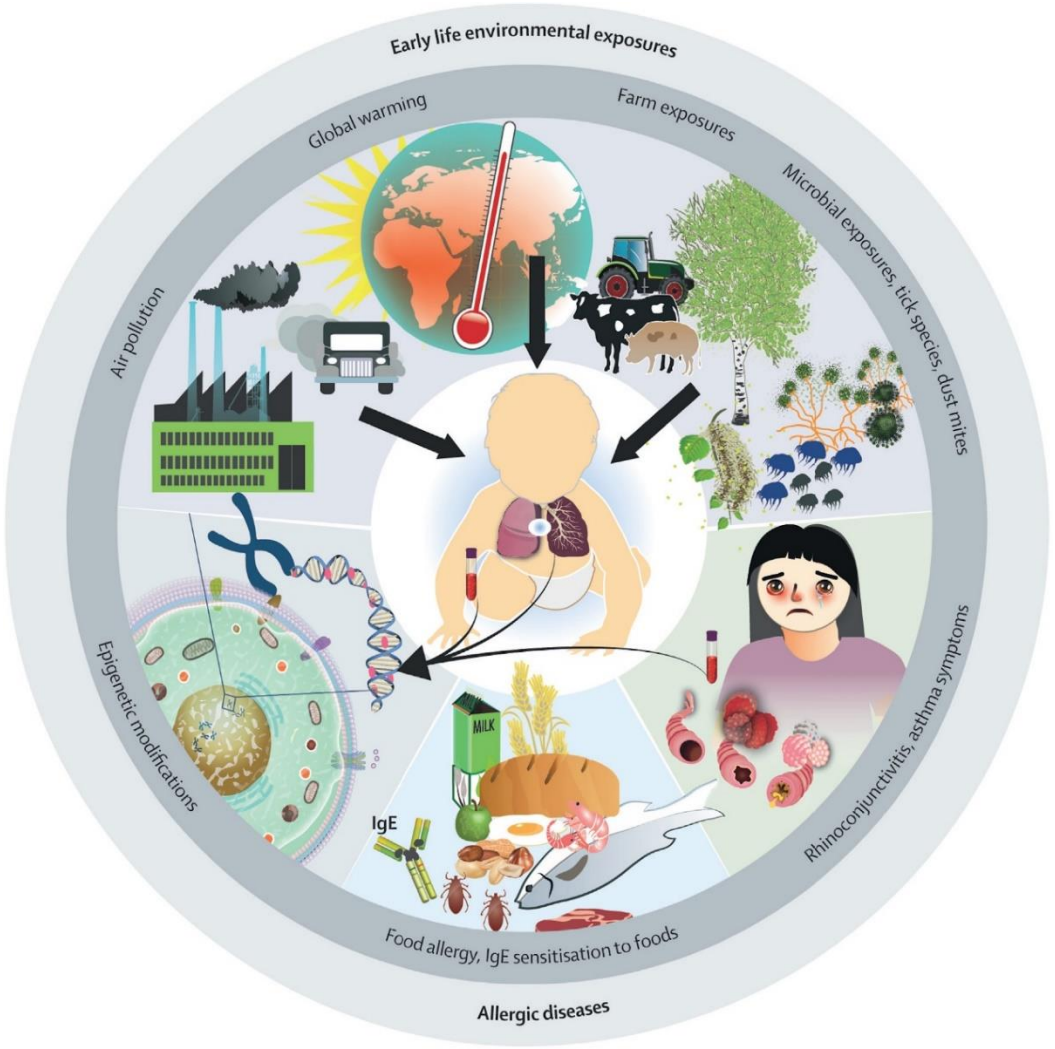
# The new landscape of OIT

Long standing management has been avoidance and administration of emergency medications on accidental exposure




Robert A. Wood, Food allergen immunotherapy: Current status and prospects for the future, Journal of Allergy and Clinical Immunology, Volume 137, Issue 4, 2016.

# Global Environmental Changes




Erik Melén, Gerard H Koppelman, Ana Maria Vicedo-Cabrera, Zorana Jovanovic Andersen, Supinda Bunyavanich, Allergies to food and airborne allergens in children and adolescents: role of epigenetics in a changing environment, The Lancet Child & Adolescent Health, Volume 6, Issue 11, 2022, Pages 810-819.

# Thank You!

Mount Sinai

*Kravis Children's Hospital*