Paradigm shifts in the management of children with food allergies

MANCHESTER 1824
The University of Manchester

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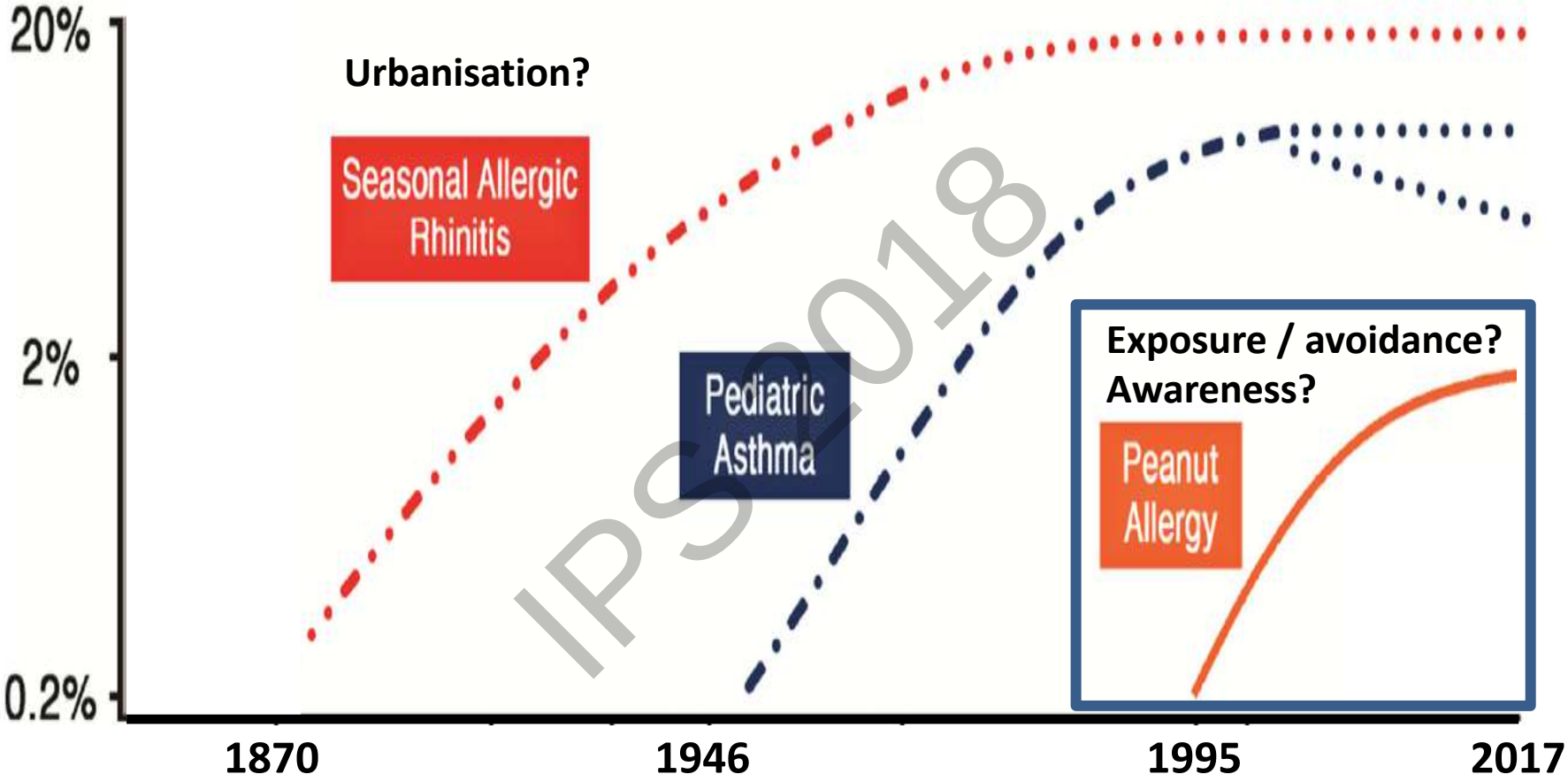
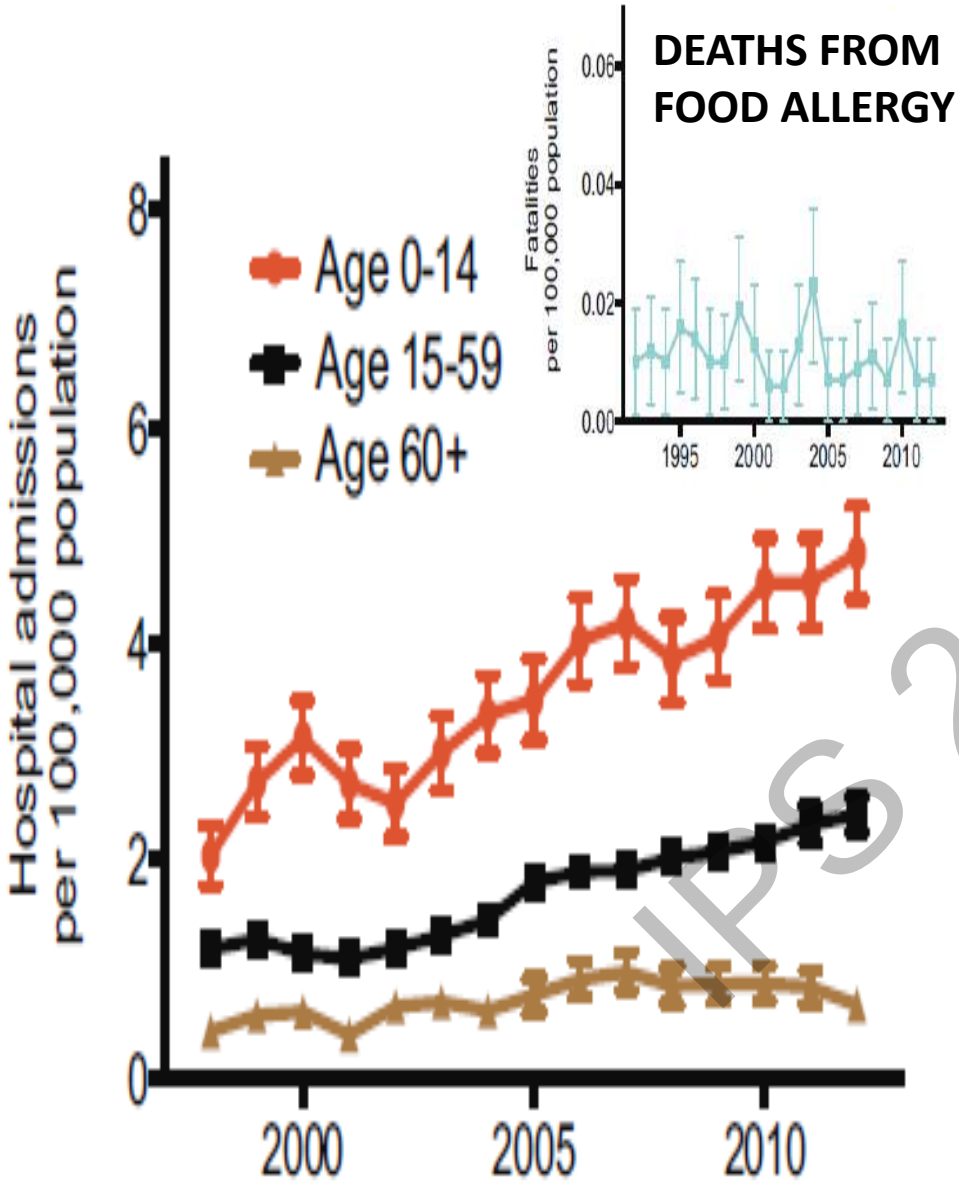
Questions to be addressed

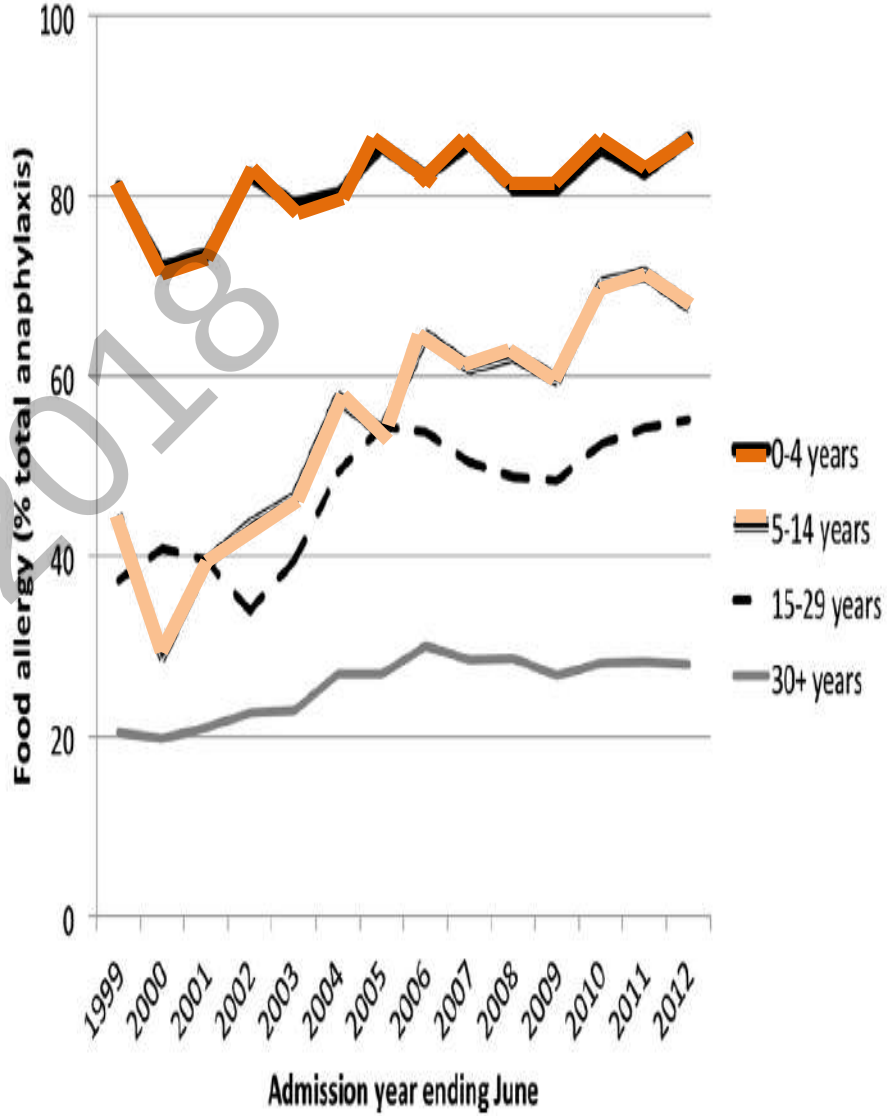
- Is there really an epidemic in food allergies?
- Do dietary restrictions prevent food allergies?
- How do children acquire tolerance to foods?
- What are the risk factors for anaphylaxis?

Allergy Epidemics



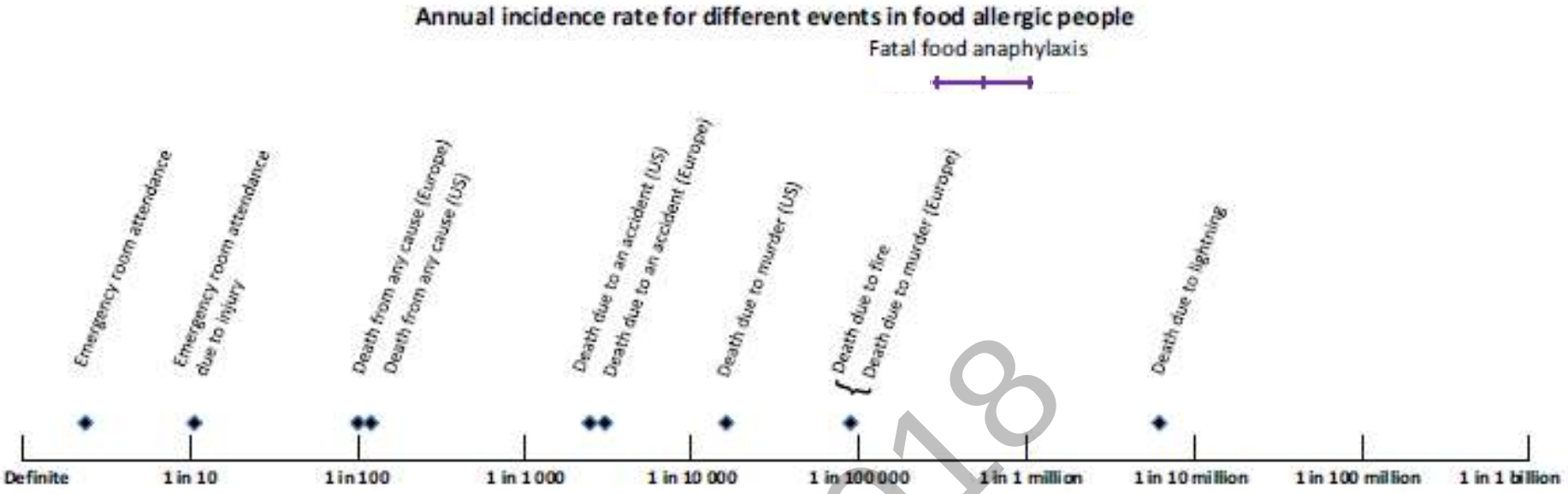
Platts-Mills T. *JACI*, 2015

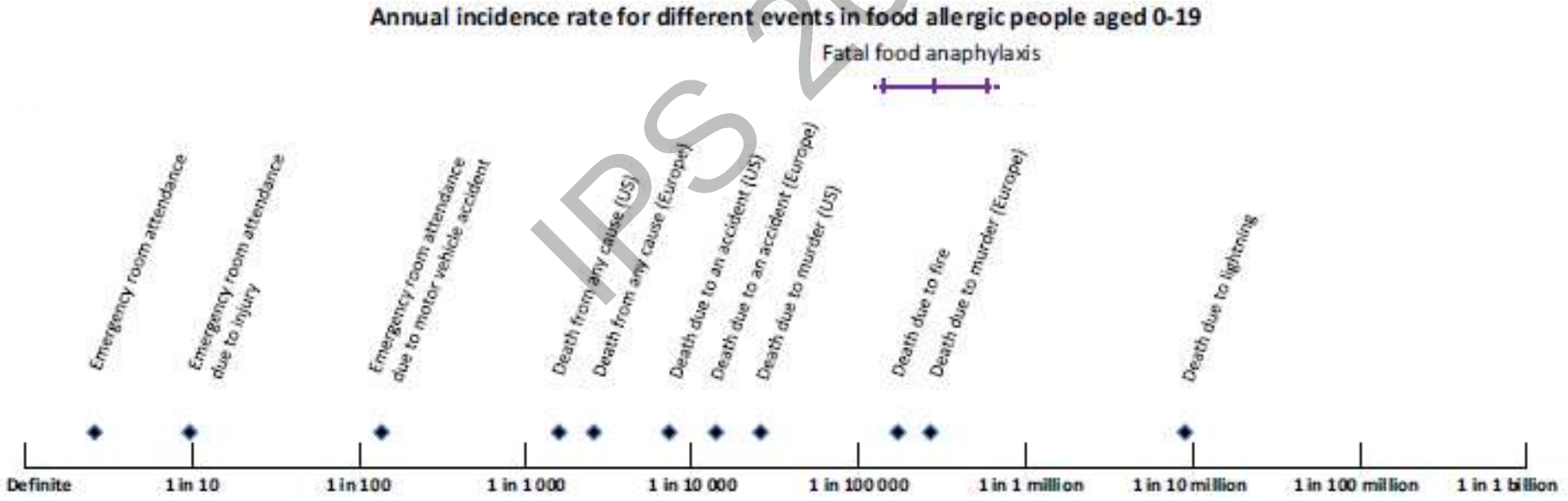




Turner PJ, *et al. JACI*, 2015 *England & Wales*

Mullins RJ, *et al. JACI*, 2015 Australia





Umasunthan T *et al. Clin Exp Allergy*, 2013

Question 1

Are the trends in food allergy real or is this hype?

Labelling patients with allergies

- clinical history: acute/delayed/both
- allergy tests: specific IgE, skin prick tests
- formal challenge (gold standard)

Doctor-supervised food challenges

City	Trial size	Outcome	Reference
New York	701, 0–21y	19% positive	Lieberman JA *et al, JACI*, 2011
Denver	125, 1–19y	11% positive	Fleischer DM *et al, J Pediatr*, 2011

Manchester, UK
130, 0 – 18y
"peanut allergy"
32% +ve

Answer

- 10 – 20% of children labelled with food allergy have clinical disease

- risk of death from food-induced anaphylaxis is 1/100,000 to 1/million

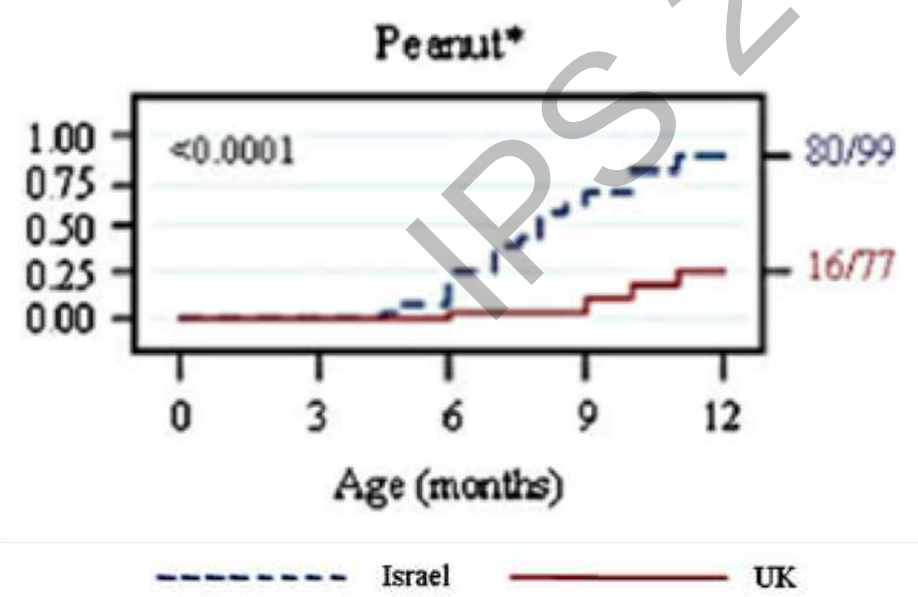
Question 2

Do dietary restrictions prevent food allergies?

Background

Infants	UK (n=5,171)	Israel (n=5,615)
Peanut allergy† 4 – 12y	2.05%	0.12%
Peanut consumption* 4 – 12y	0g / month	7.1g / month 8X / month

*Roasted peanut butter introduced at weaning
†OR 9.8 (95% CI, 3.1-30.5) in primary school children



De Toit *et al. JACI*, 2008

Hypothesis

Unnecessary avoidance of foods (peanuts) in infancy promotes rather than prevents allergy

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Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy

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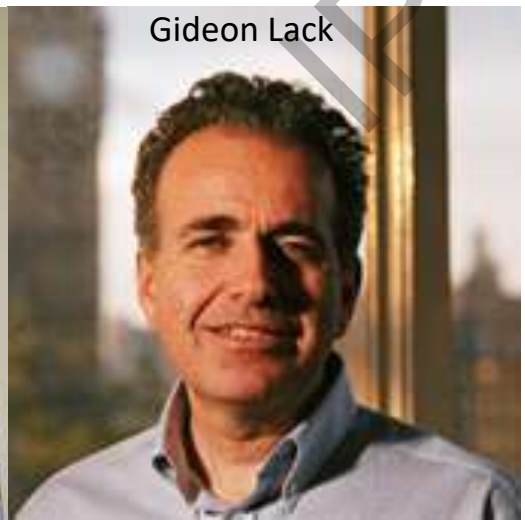
George Du Toit



Gideon Lack

KING'S HEALTH PARTNERS

KING'S College LONDON

NHS National Institute for Health Research

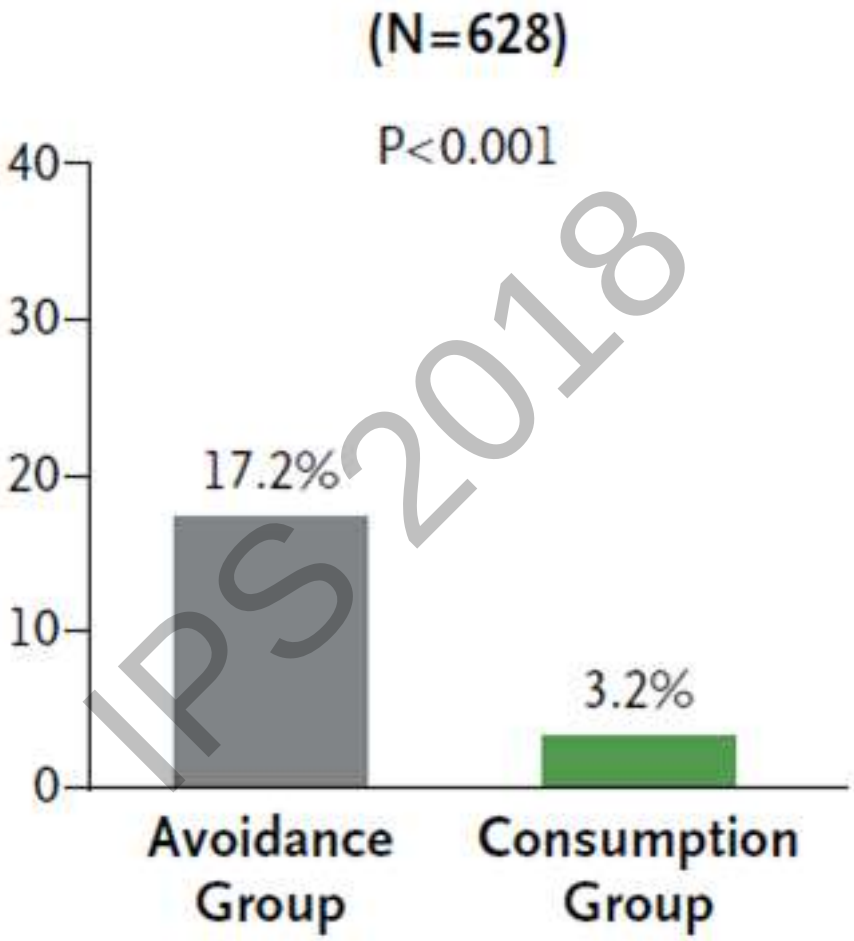
Guy's and St Thomas' NHS
NHS Foundation Trust

Methods

- 640 4–10 month old infants, randomised, single-centre trial
- inclusion: eczema / egg allergy

  exclusion: SPT>4mm, positive challenge
- 321 avoided vs 319 consumed 6g peanut (Bamba) (3 meals/week) until 5 years old
- primary outcome: blinded 9g peanut challenge at 5y
- 98% of patients followed up

Primary outcome
failed oral peanut challenge at 5 years old



80% reduction in allergy

Adverse events

- 57 had positive challenge, 14 anaphylaxis (9 given IM adrenaline)
- no significant differences between groups

Conclusions

- eating peanuts by infants with eczema/egg allergy in early childhood reduced the risk of peanut allergy by 70-90%
- follow-on studies
  - LEAP-On study* (all children told to avoid peanuts for 12 months) no significant change in positive challenge in treatment group 4% → 5%
  - Nutritional impact† no difference in breast feeding, anthropometry or nutritional intake

*De Toit *et al, NEJM*, 2016
†Feeney M *et al, JACI*, 2016

EAT study

(Enquiring About Tolerance)

- 1,303 exclusively breast fed 3 month old infants
- randomised to early introduction of foods* or avoidance until 6 months
- primary outcome ≥1 food allergy between 1 – 3 years old

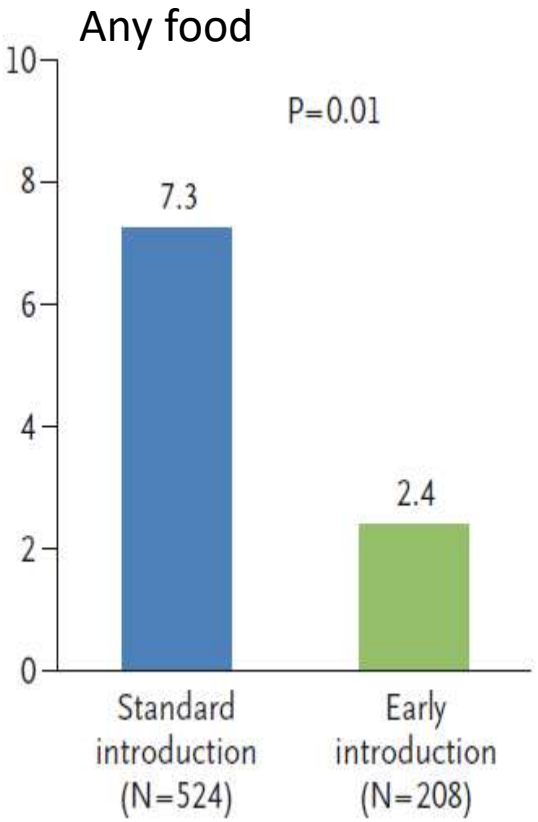
Perkins MR *et al, NEJM*, 2016

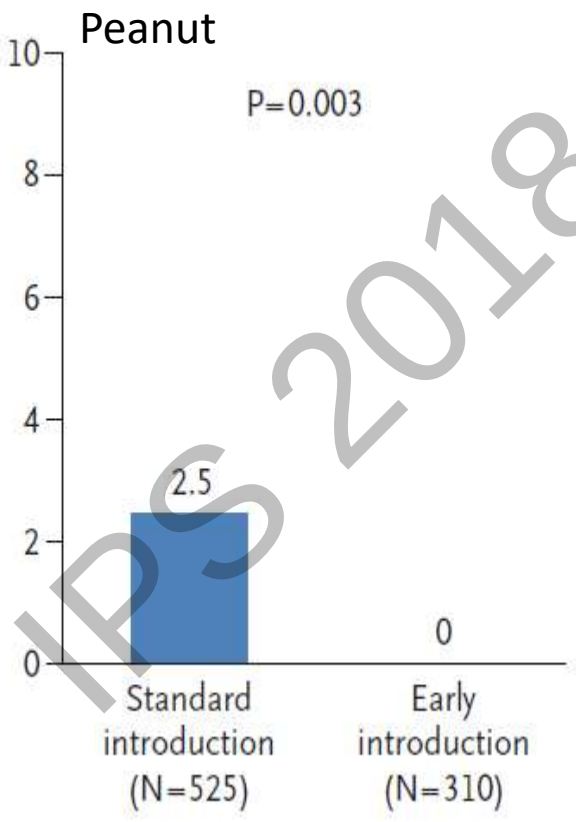
*cow's milk (first), egg, fish, peanut, sesame, wheat (last) aiming for 2g each food per week

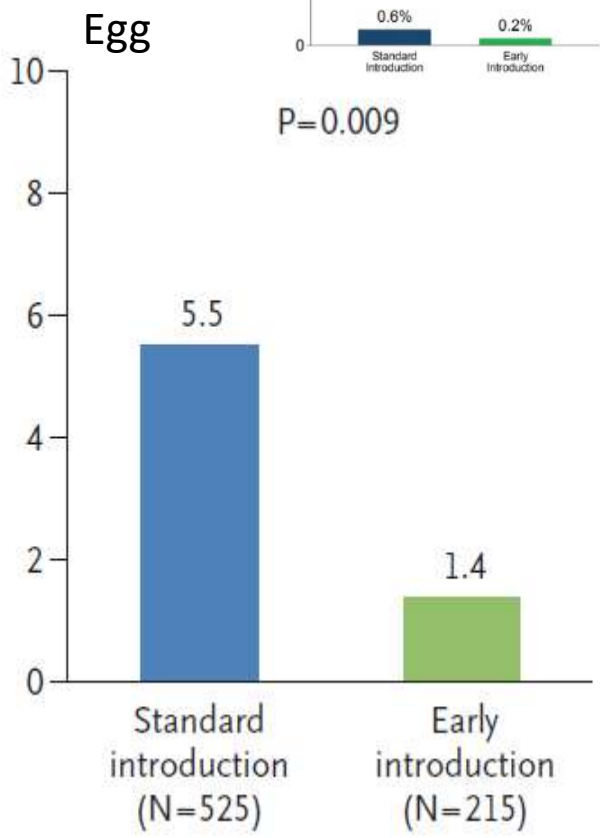
EAT study

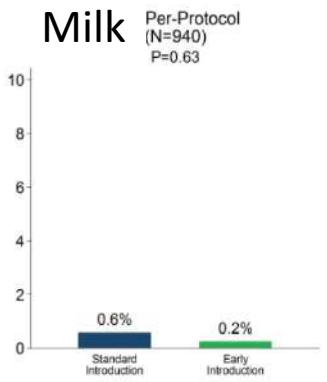
per protocol results

(63% of all participants, 42% in early introduction group)









Perkins MR *et al, NEJM*, 2016

*cow's milk, wheat, fish, sesame no significant differences (≤0.5% allergic)

60-80% were eating each food group

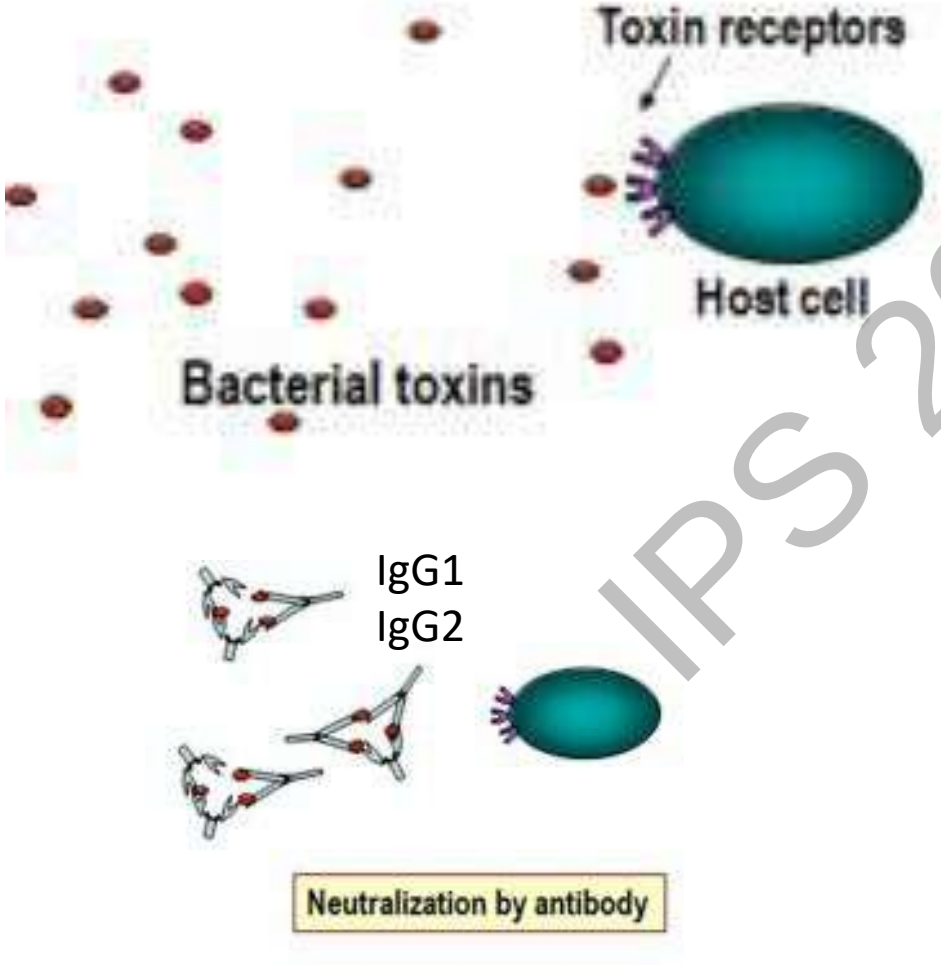
Answer

- avoidance of egg and peanut by infants, particularly those with eczema can increase the risk of allergy 4-5 fold
- for milk, wheat, fish and sesame further studies are required
- evidence suggests that previous expert opinion may have promoted the current food allergy epidemic

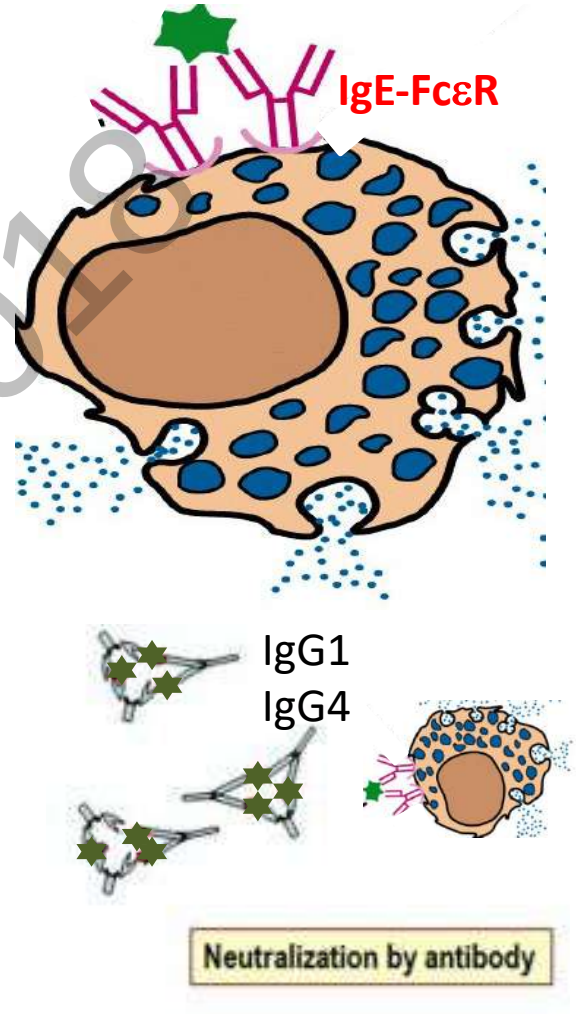
Question 3

How do children acquired tolerance to foods?

Classical antigen



Allergen



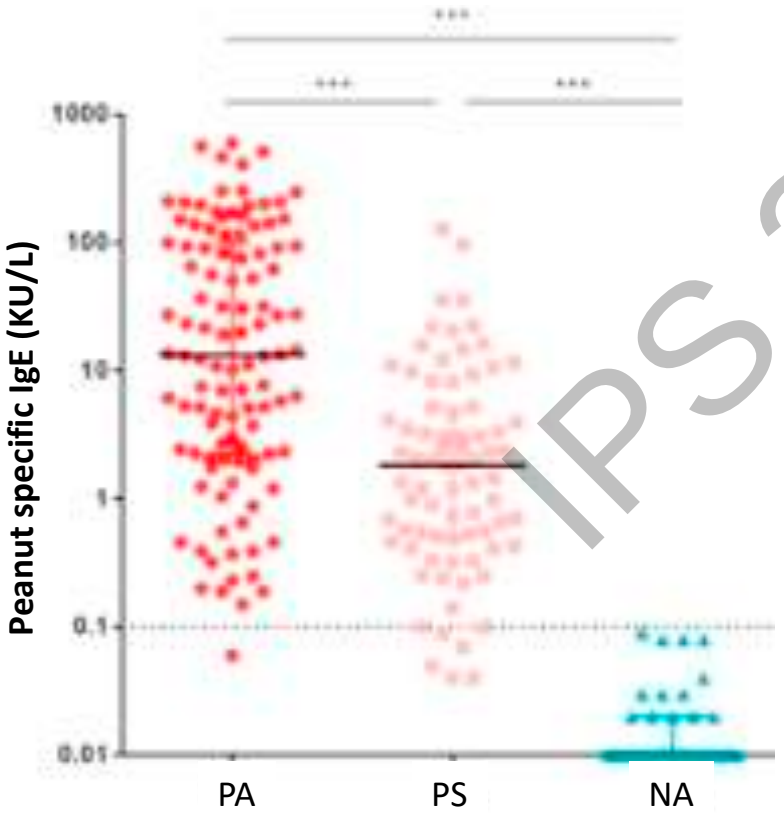
MAAS peanut study

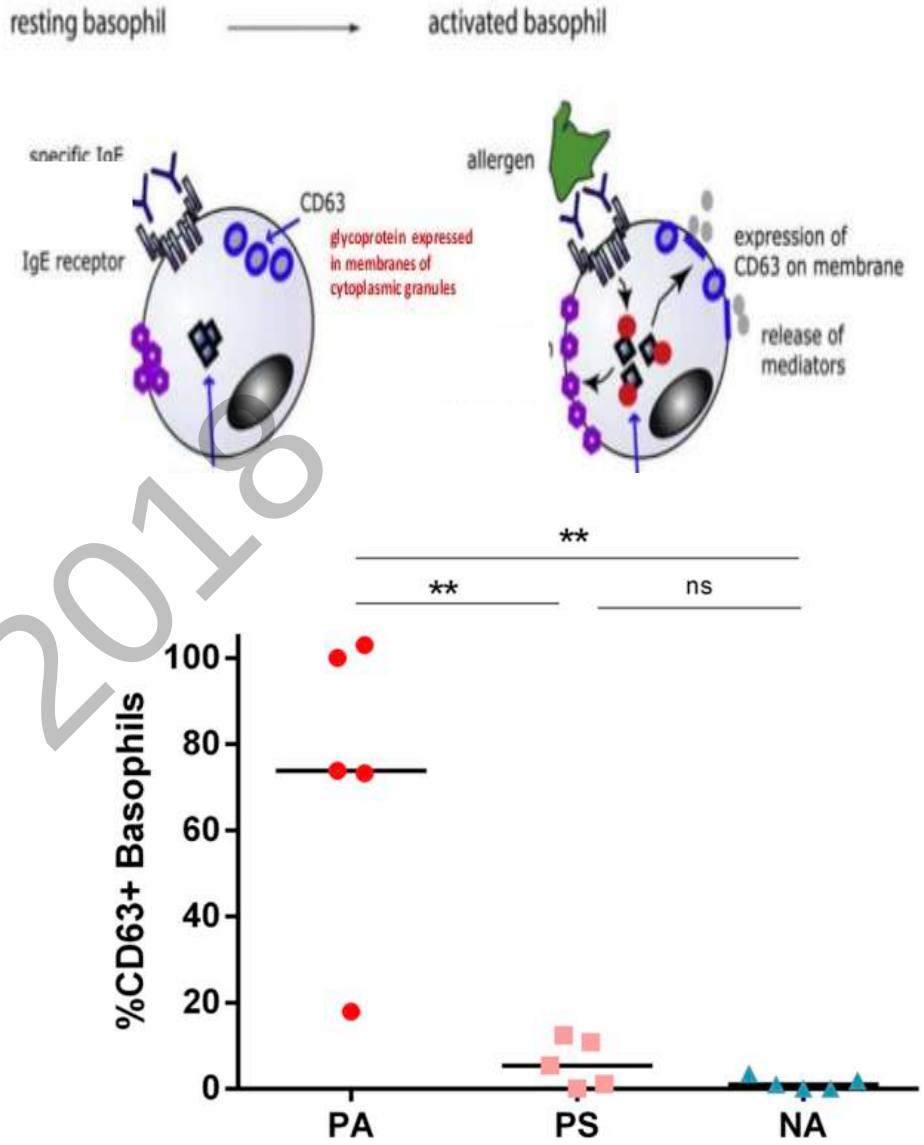
unselected Manchester birth cohort

- 79 eight year old children
- no history of clinical reactions to peanuts but evidence of IgE sensitisation (sIgE / SPT)
- oral peanut challenge – 13 reacted (17%)
- >80% of children with positive allergy tests but no history of clinical reactions are not peanut allergic

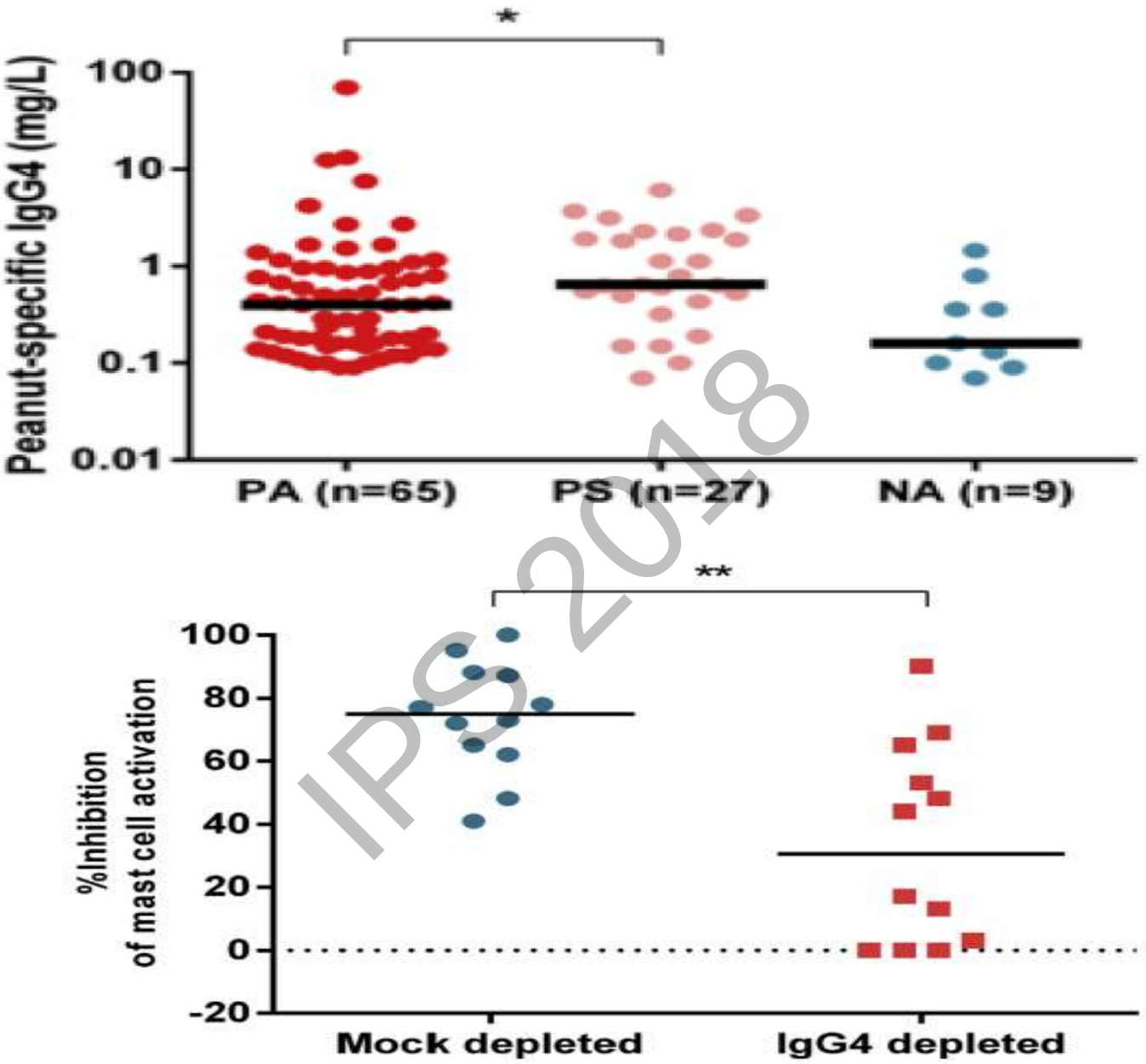
Nicolaou N *et al, JACI*, 2010

reactions: 1mg X3, 10mg X4, 100mg X2, 1g X1, 5g X3





Santos A *et al, JACI*, 2015



Santos A *et al, JACI*, 2015

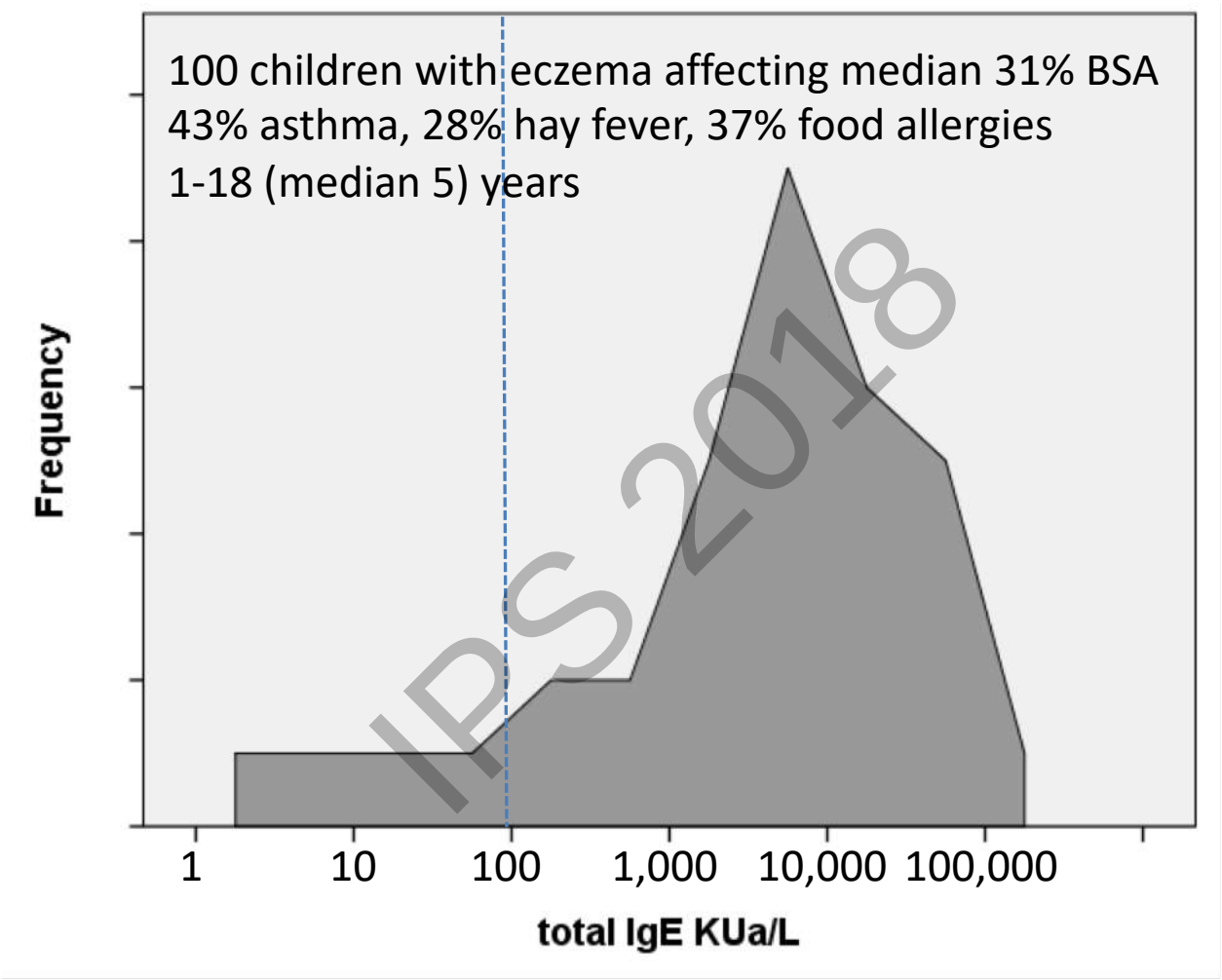
Answer

- **IgE** specifically links allergens to mast cells, triggering acute allergy/anaphylaxis
- **IgG** (IgG4) can neutralise allergen in the same way that it neutralised classical microbial antigens
- induction of allergen-specific IgG in IgE sensitised/allergic patients promotes tolerance

Question 3b

What practical strategies can doctors use to prevent allergies and promote tolerance?

Inducing IgE



Skin exposure → allergy

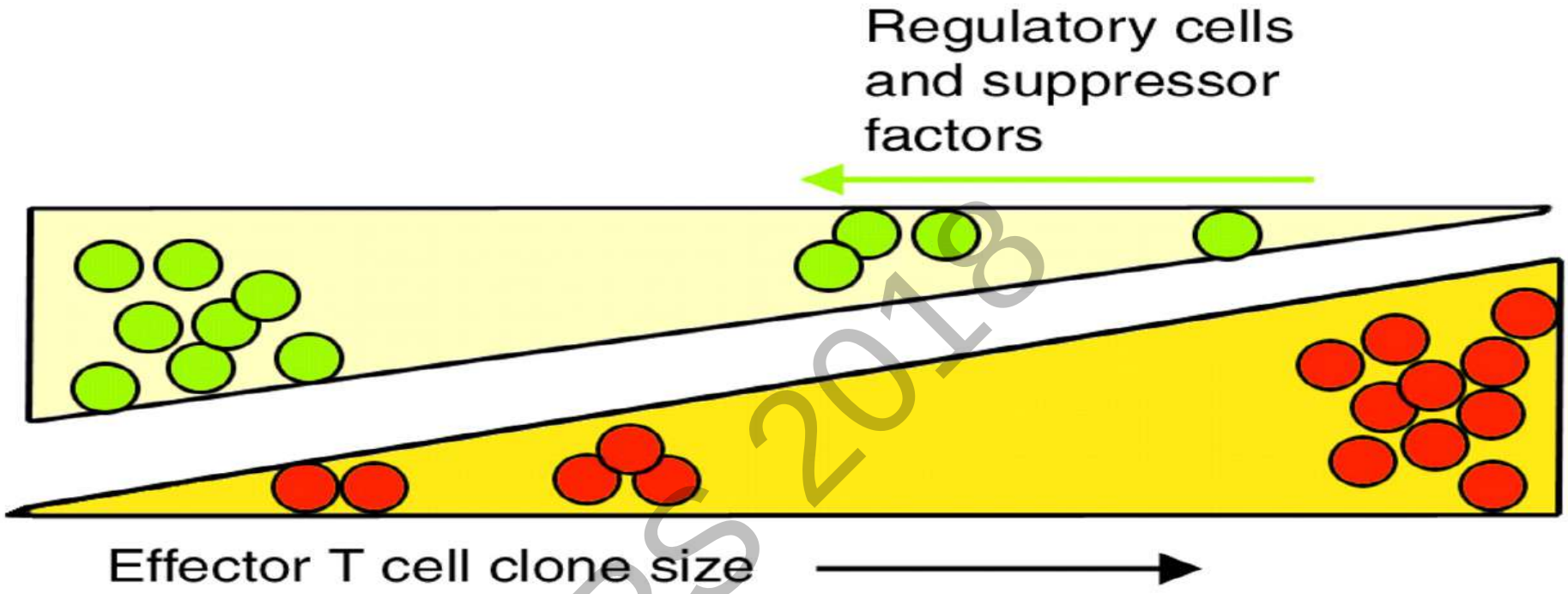
Peanut allergy

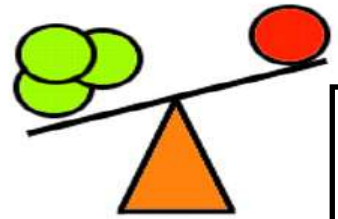
Avon longitudinal study
13,971 pre-school children
23 confirmed peanut allergy

<u>Correlates (OR (95%CI):</u>

Nuts during pregnancy	0.8 (0.5 – 2.0)
Eczema first 6 months	
nil-mild	1
moderate	4 (0.4 – 37)
severe	44 (6 – 388)
Use of peanut oil preps	7 (1.4 – 33)

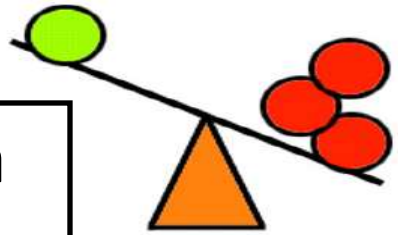
Lack G *et al*. *New Engl J Med,* 2003





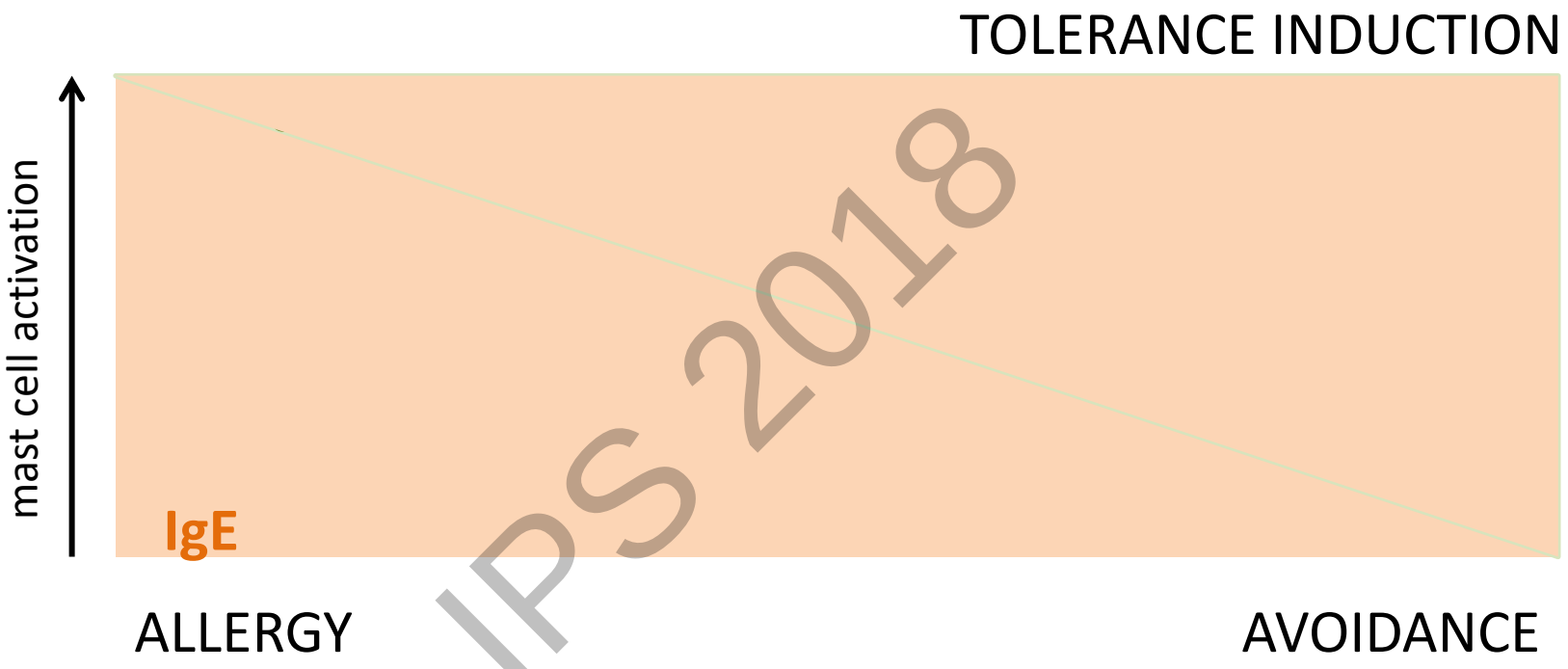
Tolerance

Exposure via **GUT**	Exposure via **SKIN**
more Tregs/IgG4	**more allergy/IgE**



Allergy

Avoidance vs Desensitisation



Answer

antigen exposure through inflamed skin promotes allergic / IgE mediated response

antigen exposure by ingestion promotes tolerance

dietary restrictions, particularly in children with eczema will promote allergies

Question 4

What are the risk factors for anaphylaxis – respiratory compromise with allergic reactions?

MARD study
risk of anaphylaxis

- 1,940 patients (76% children) with nut allergy
- 35% **bronchospasm** with acute reactions
  - risk 3X if asthma with no hospital admissions
  - risk 7X if asthma with hospital admissions
- 43% **pharyngeal edema** with acute reactions
  - risk 2X with hay fever controlled with std meds
  - risk 4X with hay fever not controlled with meds

Summer C *et al, JACI*, 2008

Take home messages

- There is a food allergy epidemic, but there is a much larger problem with false labelling of children with allergies
- Dietary restrictions, particularly in children with eczema are associated with an increased risk of food allergies (particularly to egg and peanuts)
- Immune tolerance is usually acquired by eating the food, not avoiding it
- Doctors should promote early weaning at 3 – 10 months with ongoing breast feeding
- Treating the eczema can prevent food allergies
- Controlling asthma & hay fever can reduce the risk of anaphylaxis