Food allergy; Issues with diagnosis

Dr Dinesh Banur

Education

2002 – **MBBS** , JJM Medical college , India
2004 – **DCH** , Bangalore medical college , India
2006- **MRCPCH** , Royal college Paediatrics and child health, UK
2012- **CCT** , London school of Paediatrics , UK
2013- **FRCPCH** , Royal college Pediatrics and child health, UK

Current Position – Consultant Paediatric Gastroenterologist, Columbia Asia Hospital, Bangalore
Publications - 3 text book chapters , 2 international posters , 2 national posters ,1 article in international Journal

Areas of interest – Cows milk allergy , Feeding disorders , Child hood constipation

Recipe of my talk

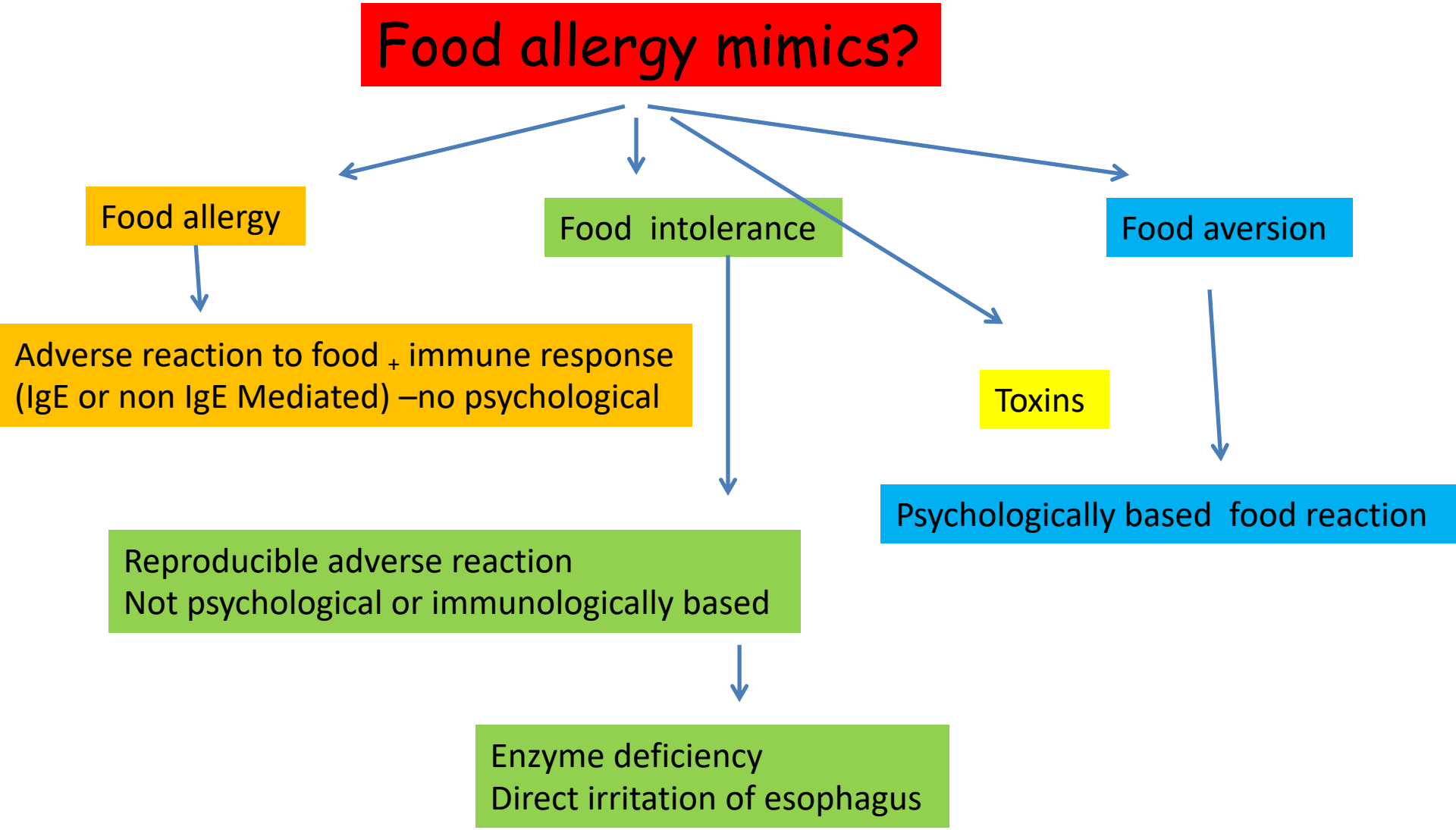
- Food allergy / mimics
- Pattern / prevalence of food allergy
- Interpretation of various test
- Prevention of food allergy

Food allergy Challenges- Indian Context

- Very little published data

Clinical experience:

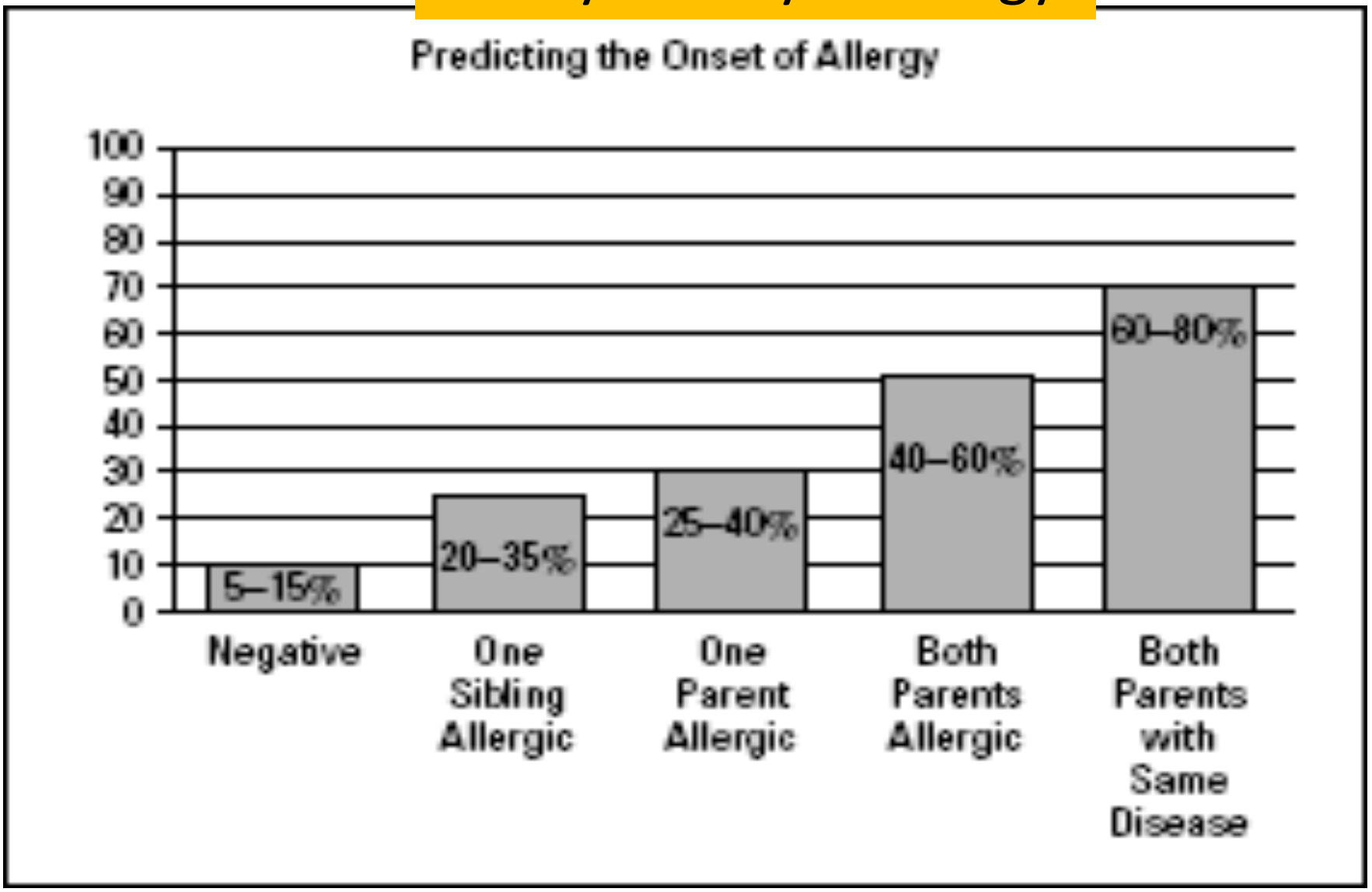
- “uncommon in general”
- Milk and egg commonly seen
- Unusual allergen: chickpeas , coconut
- Peanut allergy is rare despite heavy consumption
- Confusion between lactose intolerance and milk allergy


Food allergy mimics?
Food allergy
Food intolerance
Food aversion
Adverse reaction to food + immune response
(IgE or non IgE Mediated) –no psychological
Toxins
Psychologically based food reaction
Reproducible adverse reaction
Not psychological or immunologically based
Enzyme deficiency
Direct irritation of esophagus

How do you approach ?

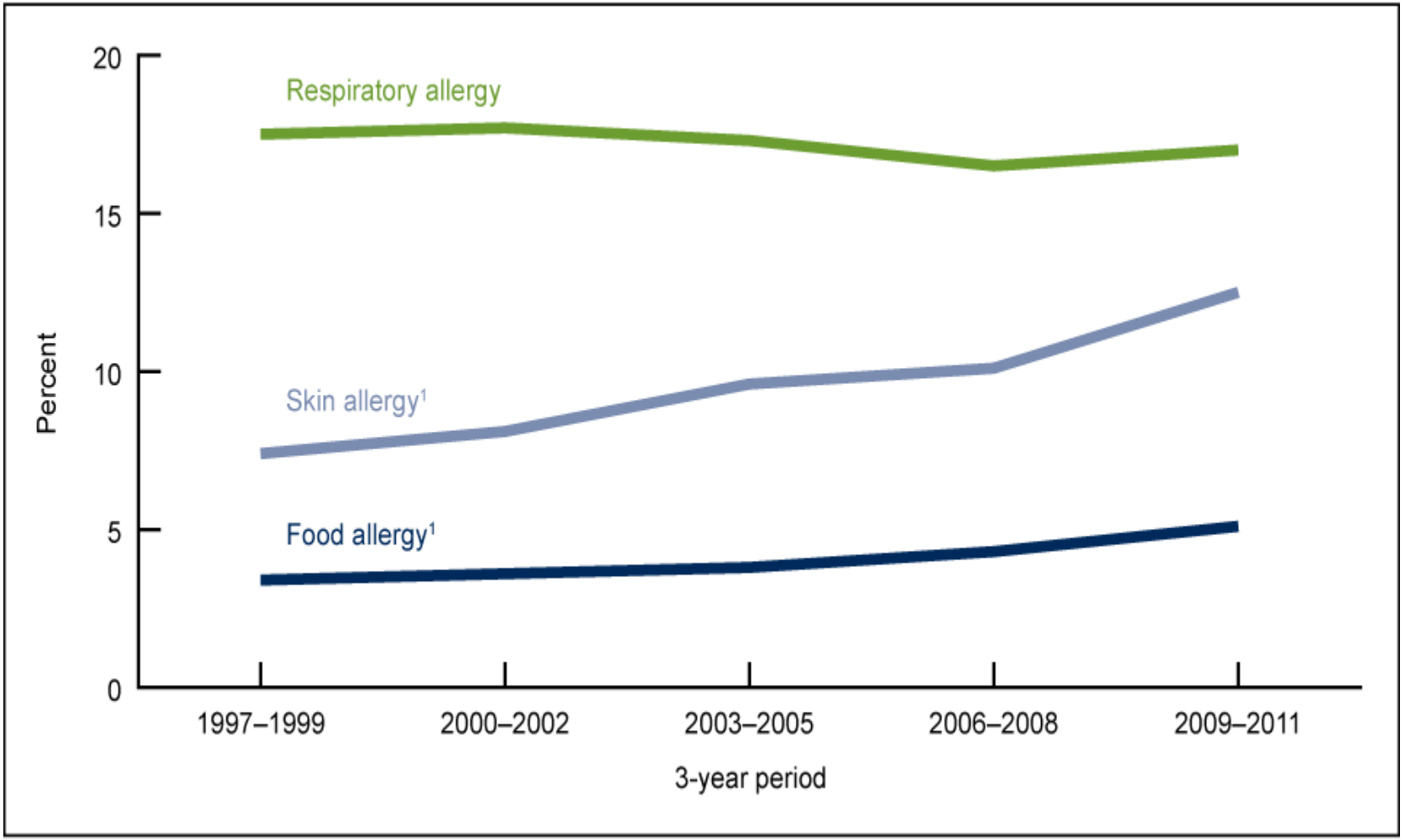
- History ……..
- History ……..
- History ……..
- Events unfolding on exposure to antigen, chronicity, symptoms, severity
- Signs, reproducibility, family history, coexisting medical other allergic diseases should be addressed

Family history & allergy



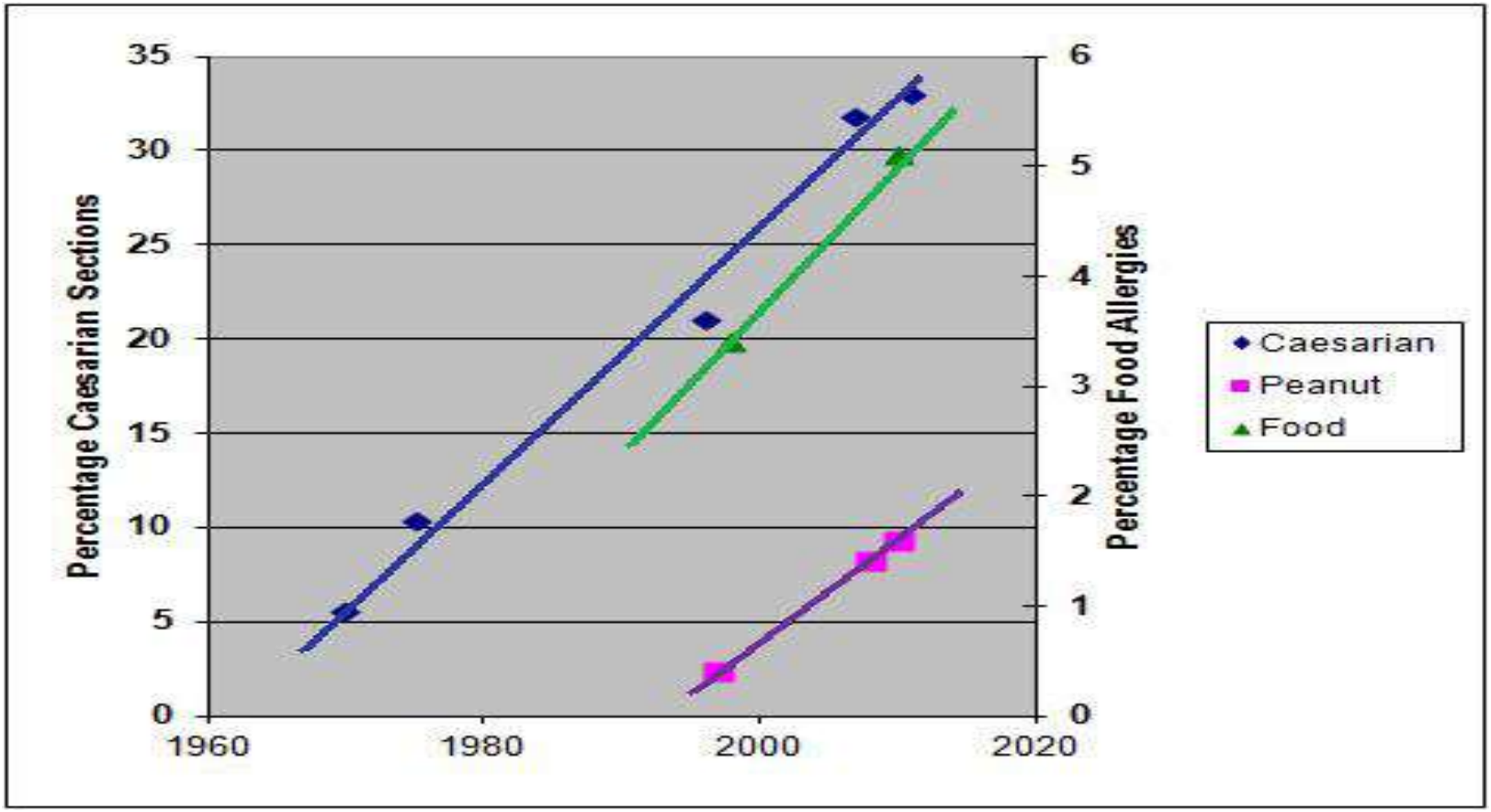
Prevalence of food allergy over the last 10 yrs –CDC data

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

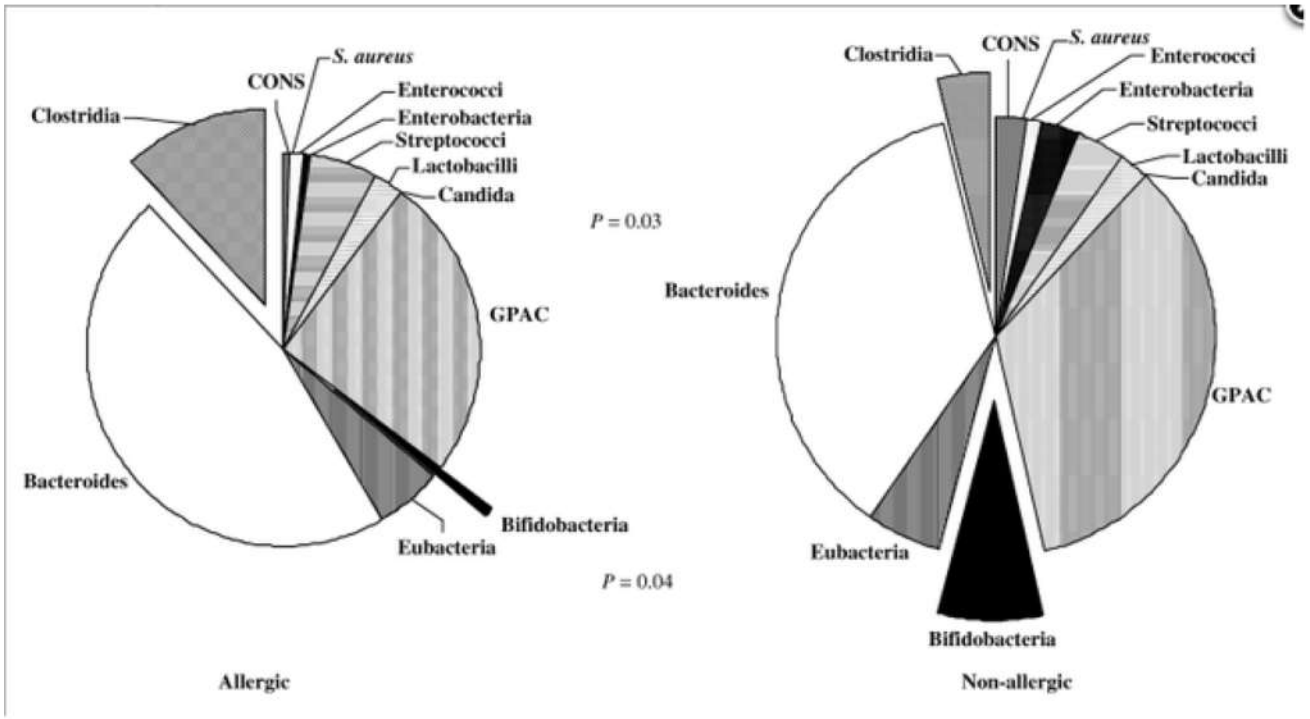


[1]Significant increasing linear trend for food and skin allergy from 1997–1999 to 2009–2011.
SOURCE: CDC/NCHS, Health Data Interactive, National Health Interview Survey.

CDC data


Percentage Caesarian Sections
Percentage Food Allergies
35
30
25
20
15
10
5
0
6
5
4
3
2
1
0
1960
1980
2000
2020
Caesarian
Peanut
Food

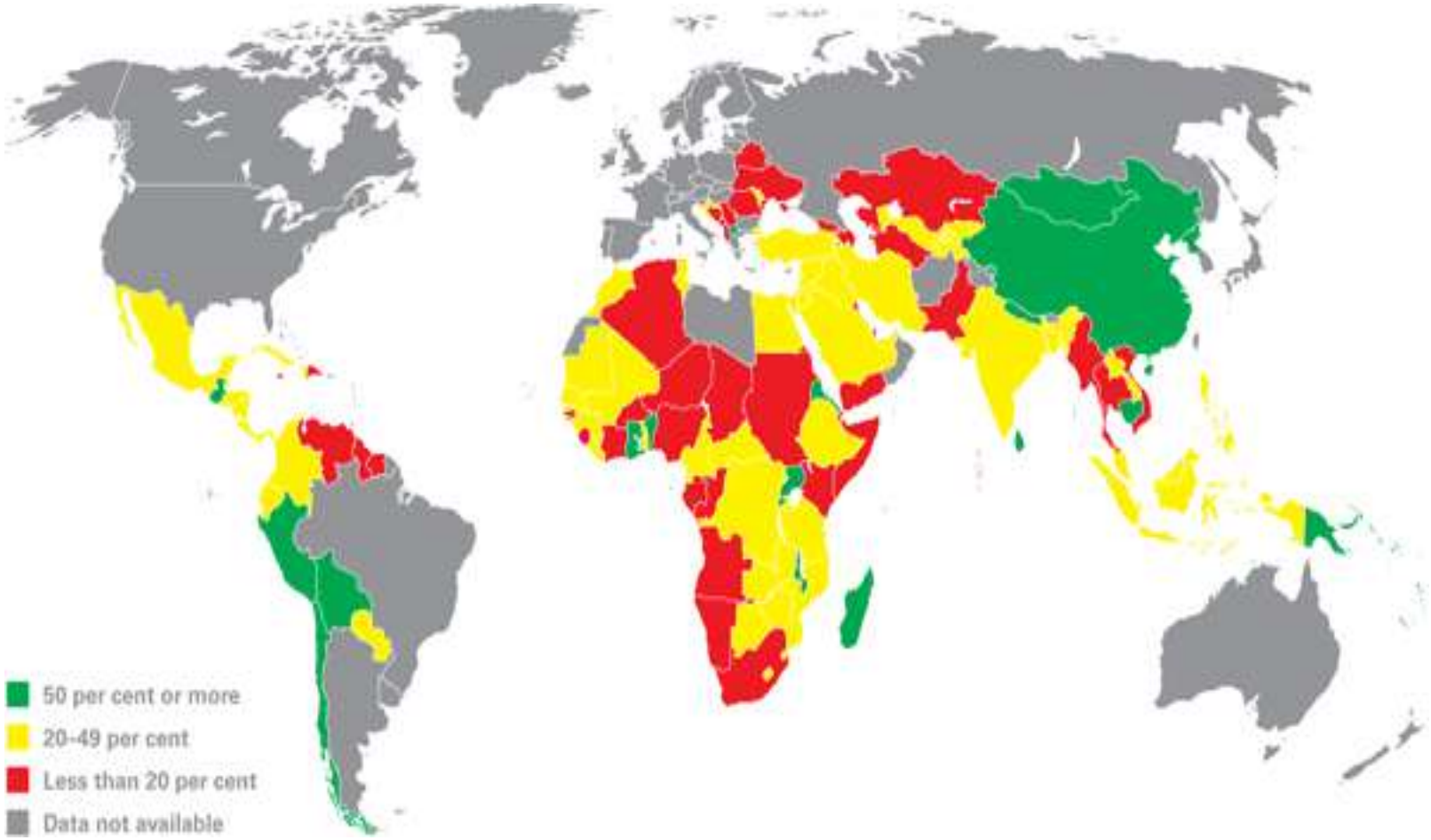
Microbiota of Gut in allergy and Non Allergy



Clinical exp Allergy , 2005:35:1141

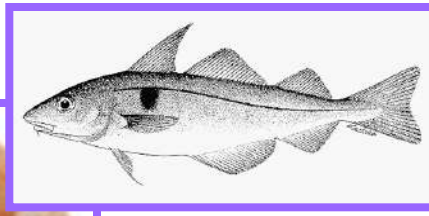
UNICEF data

Percentage of infants exclusively breastfed for the first six months of life (2000–2006)

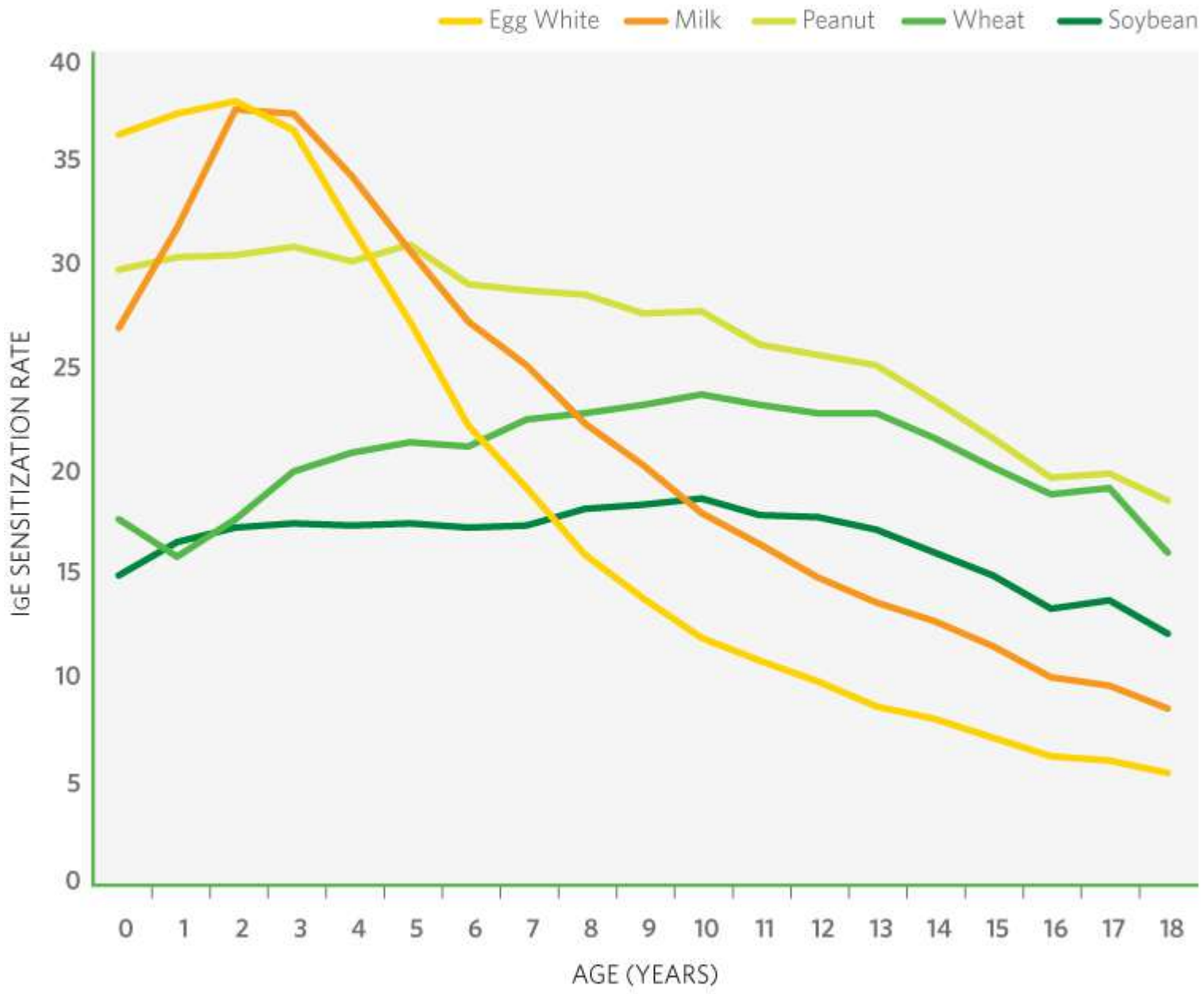


Food Allergies

Big 8



IGE SENSITIZATION RATE FOR FOOD ALLERGIES IN CHILDHOOD



Source: Quest Diagnostics Health Trends™

Pooled prevalence of food allergy in Europe – Sep 2000- Sep 2012

	Life time prevalence (self report)	Point time prevalence (self report)	Sensitized to one food	Symptoms + sensitization to one food	Convincing clinical history or positive food challenge
Children 0-17 yrs	17.4 %	6.9%	12.2 / 3.0 %	3.6/ 1.5%	2.6 %
Western Europe	23%				
Eastern Europe	41%				

Reported Point prevalence 6 times more than challenge proven food allergy

Muraro et al , EAACI , 2014

Parents and physicians often overestimate allergy

Epidemiology of Food Allergy in India Results from Europrevall

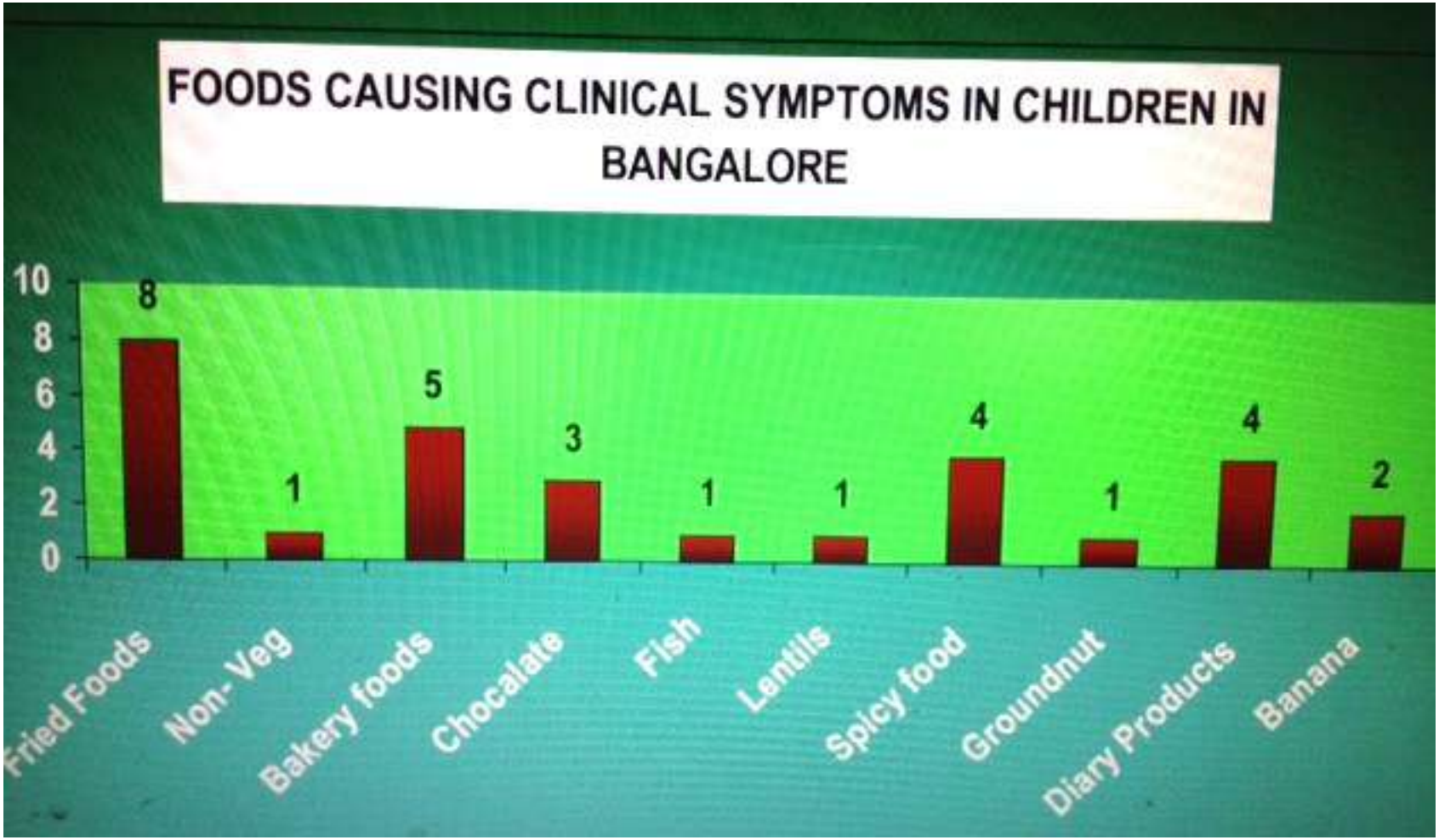
- First population based study according to proper epidemiological methods in India
- Aim to fill the gap in providing reliable information about food allergy in India in both adults and children

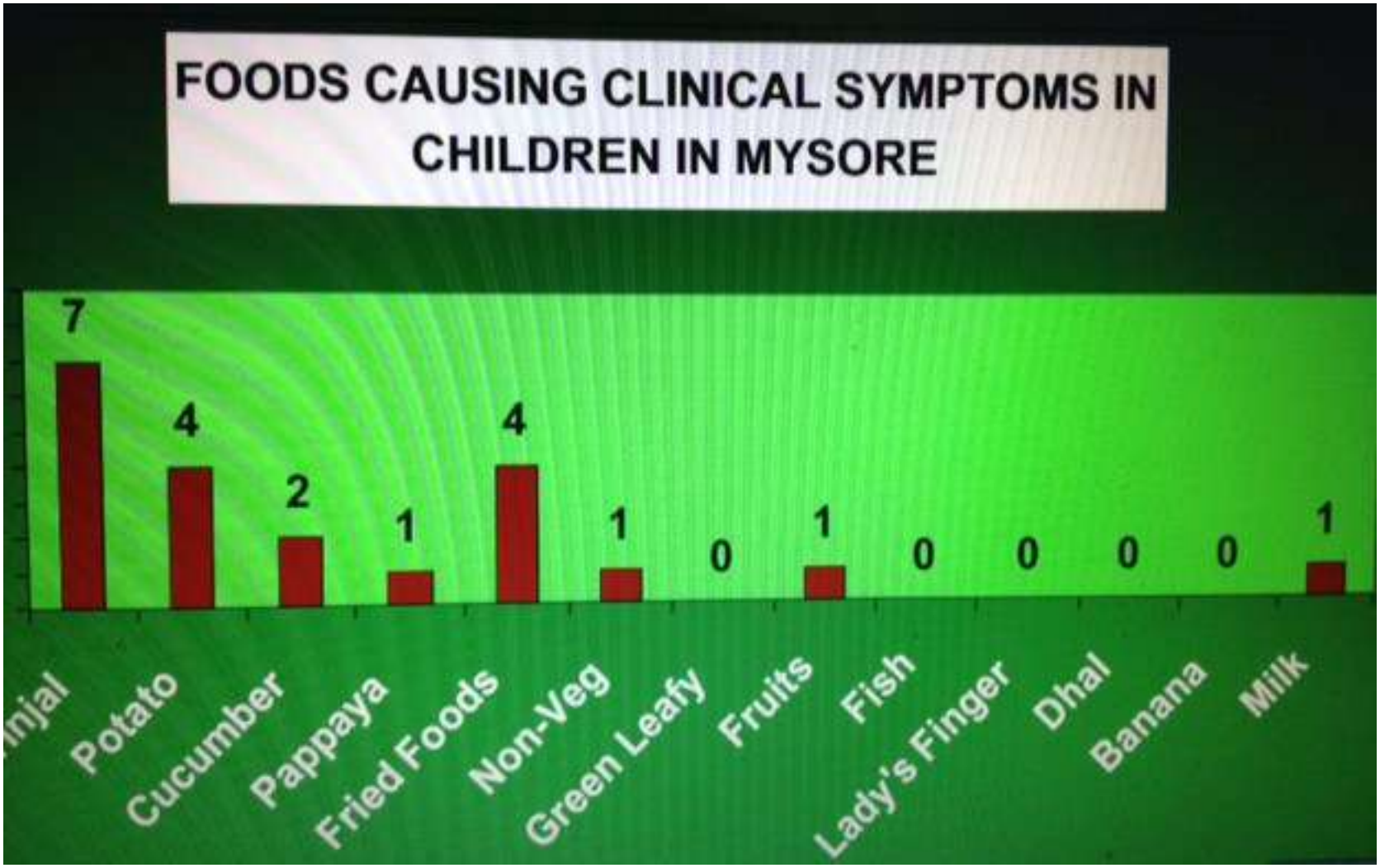
Europreval study

30 clusters 90 house holds , school going children

	Bangalore	Mysore
n	2021	1.8%
Prevalence	1386	1.7%

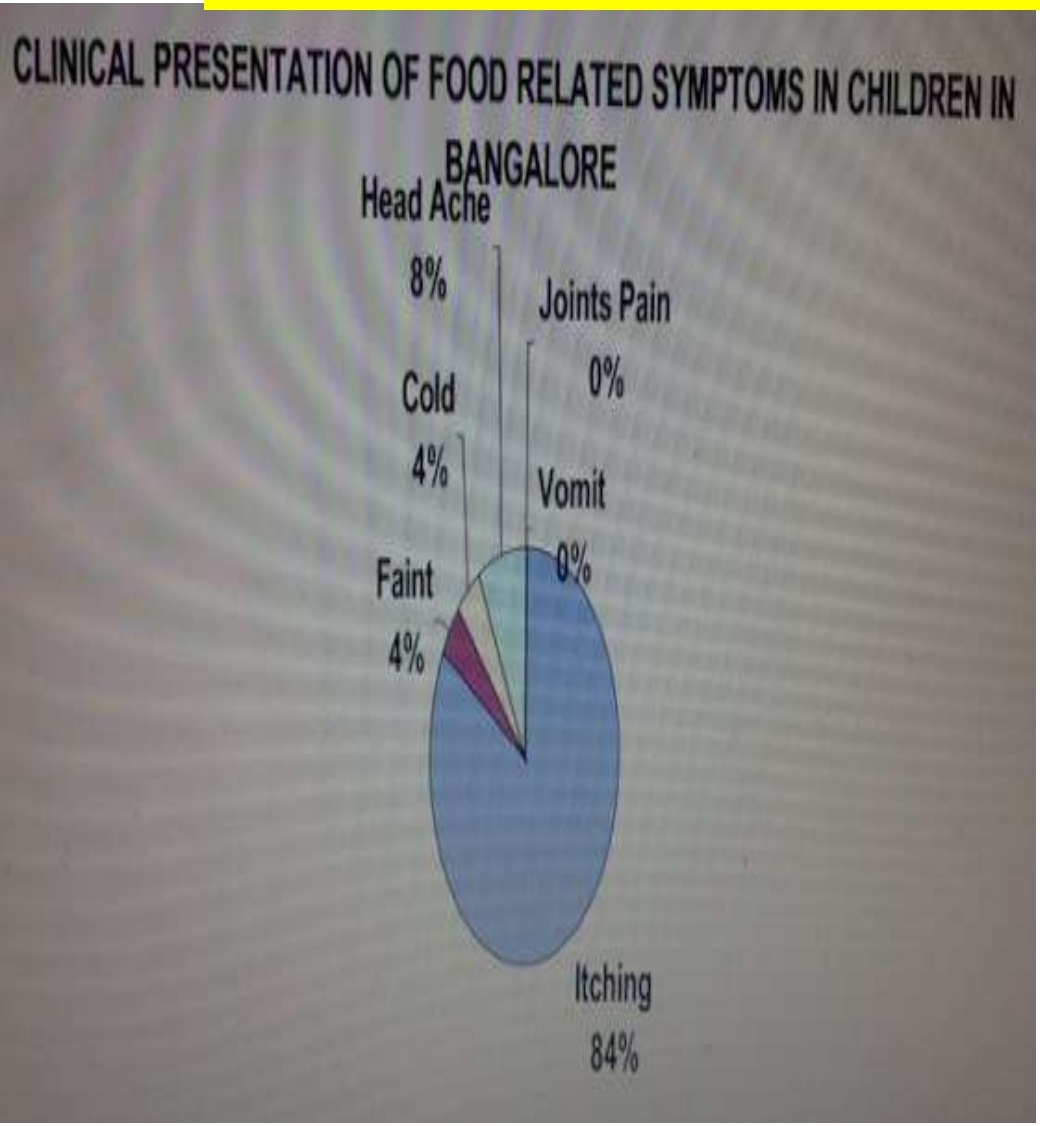
No difference between male and female

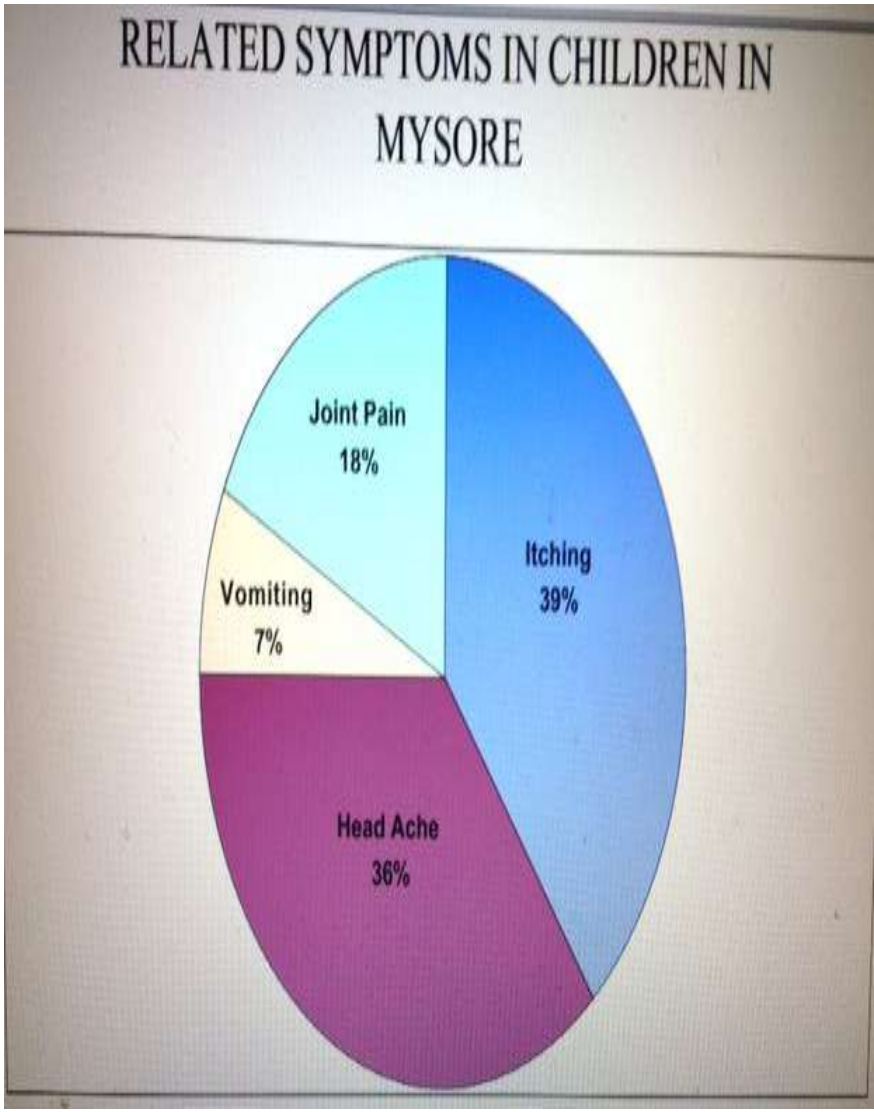

FOODS CAUSING CLINICAL SYMPTOMS IN CHILDREN IN BANGALORE
10
8
6
4
2
0
8
1
5
3
1
1
4
1
4
2
Fried Foods
Non- Veg
Bakery foods
Chocalate
Fish
Lentils
Spicy food
Groundnut
Diary Products
Banana



Variation in the nature of allergy between urban and semi-urban population

Symptoms of food allergy in urban and semi-urban population





Results

- The differences in prevalence of food allergies in India in different wards
- Almost 45 fold differences are noted within the same city
- Lessons to be learnt
- Why some areas have such low prevalence as 0.2% and some as high as 9.6%?
- What factors are playing a role?
- What are modifiable?

Europreval study Chinese and Indian children

	HK	BJ City	BJ rural	India
N	6194	5948	4274	7429
Adverse reaction to food Once	3.6%	4.5%	4%	0.3%

"Prevalence of allergic disease in Asia is likely to increase to similar levels to those seen in the West."

Alessandro Fiocchi, *Asian Pac J Allergy Immunol 2012;30:S6-8*

from 9.9% to 18.0% (p =0.02).7

Asian Pac J Allergy Immunol 2012;30:S6-8

Classification of food allergy

Skin			
	Urticaria Angioedema	Atopic dermatitis	
Respiratory			
	Asthma Rhinitis		Heiner's Syndrome
Gastrointestinal			
	Oral allergy	Eosinophilic oesophagitis	Enterocolitis Enteropathy Proctocolitis
Systemic			
	Anaphylaxis or GI Food-associated, exercise-induced anaphylaxis		

Difference b/w Skin prick test and sIgE

Skin prick test

- Widely available / not expensive/ older infants
- Affected by recent antihistamine
- Unable to perform in severe/recent anaphylaxis Severe eczema
- Results available in 15 min
- Large wheal = more like hood of allergy

Specific IgE antibodies in the serum.

- Not Widely available / expensive/ any age
- Not Affected by recent antihistamine
- Can be performed in severe/recent anaphylaxis ,Severe eczema
- Results available 1 week
- Higher conc = more like hood of allergy

Both test will not predict severity of reaction ,

Both have Sensitivity (70-100%) and specificity (40-60%) s

Interpretations of test

sIgE test results

- Egg, 7 kUA/L (2 kUA/L for children less than two years of age)
- Milk, 15 kUA/L (5 kUA/L for children less than two years of age)
- Peanut, 14 kUA/L
- Tree nuts, approximately 15 kUA/L
- Fish, 20 kUA/L
- Shrimp , cod , salmon, chicken , pork +ve

Interpretations

- **Geographic location, diet pattern**
- **Sensitization**  **allergy**
- **Negative SPT or sIgE - in non IgE allergy**
- **Serum Hyper IgE – False positive results**
- Presenting features and the magnitude of results are taken into account

SPT - Wheal size > 8mm for > 2 yrs >6 mm < 2 yrs

SPT & SIgE TEST

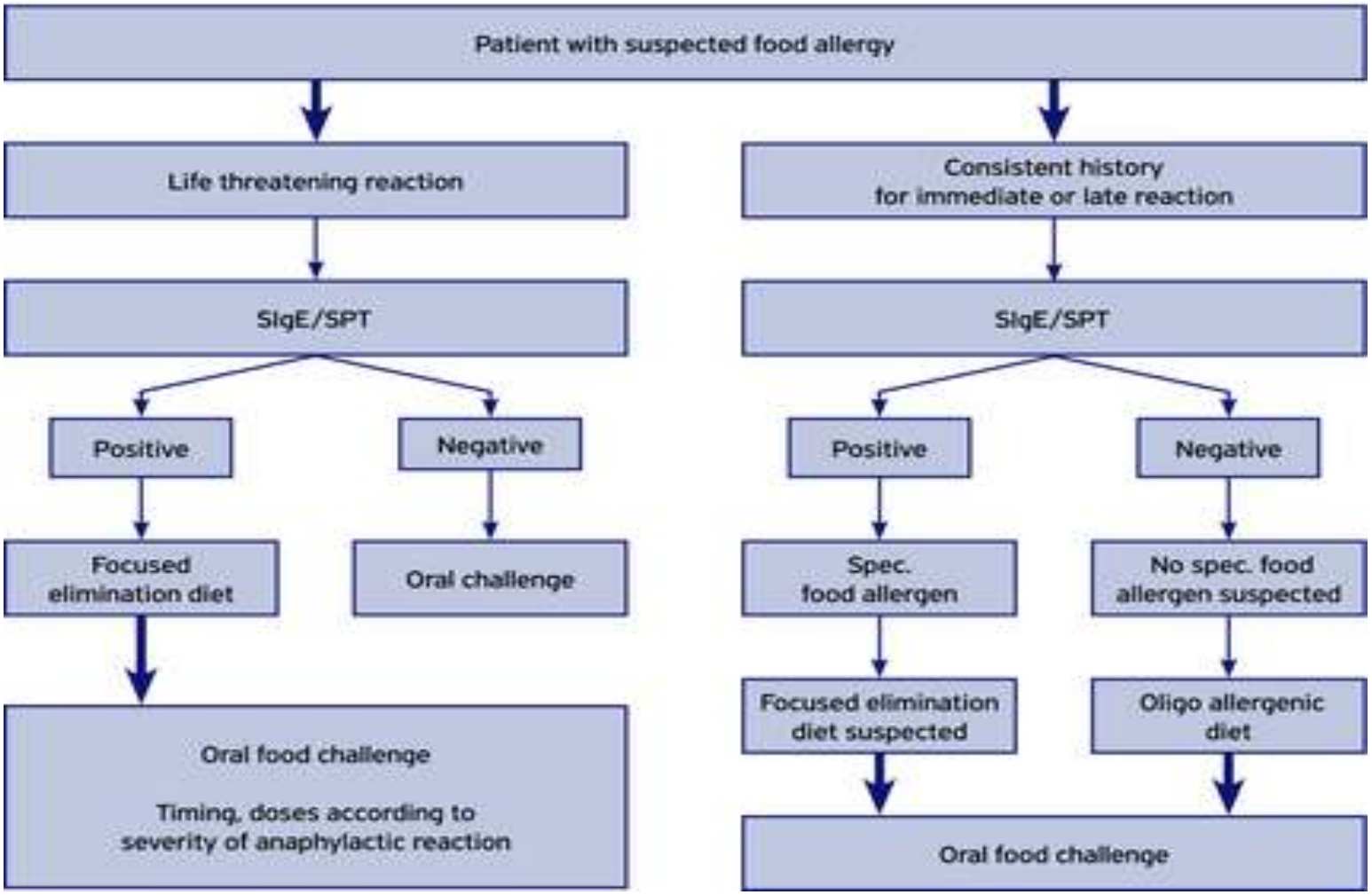
Advantages

- Avoid unnecessary food challenge – cost factors
- Avoid adverse anaphylaxis reaction
- Skin prick has a more negative predictive value

- Disadvantages
- Low specificity – should not be used as a screening tool
- False negative 2-4%- miss diagnosis , unnecessary investigation
- False positive- 5-6%- unnecessary food avoidance

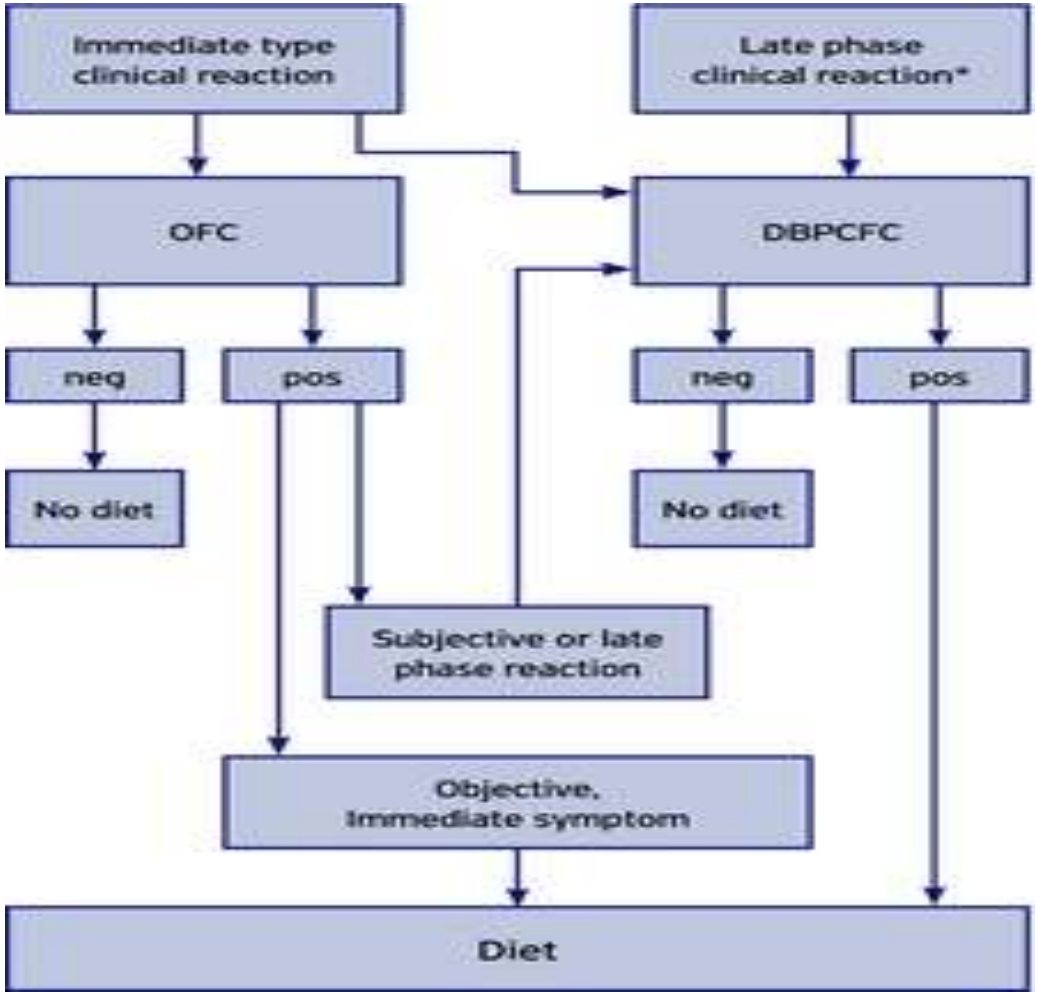
Where facilities available , oral food challenge should be considered

EAACI Food Allergy and Anaphylaxis Guidelines: diagnosis and management of food allergy



Allergy
9 JUN 2014 DOI: 10.1111/all.12429
http://onlinelibrary.wiley.com/doi/10.1111/all.12429/full#all12429-fig-0001

EAACI Food Allergy and Anaphylaxis Guidelines: diagnosis and management of food allergy

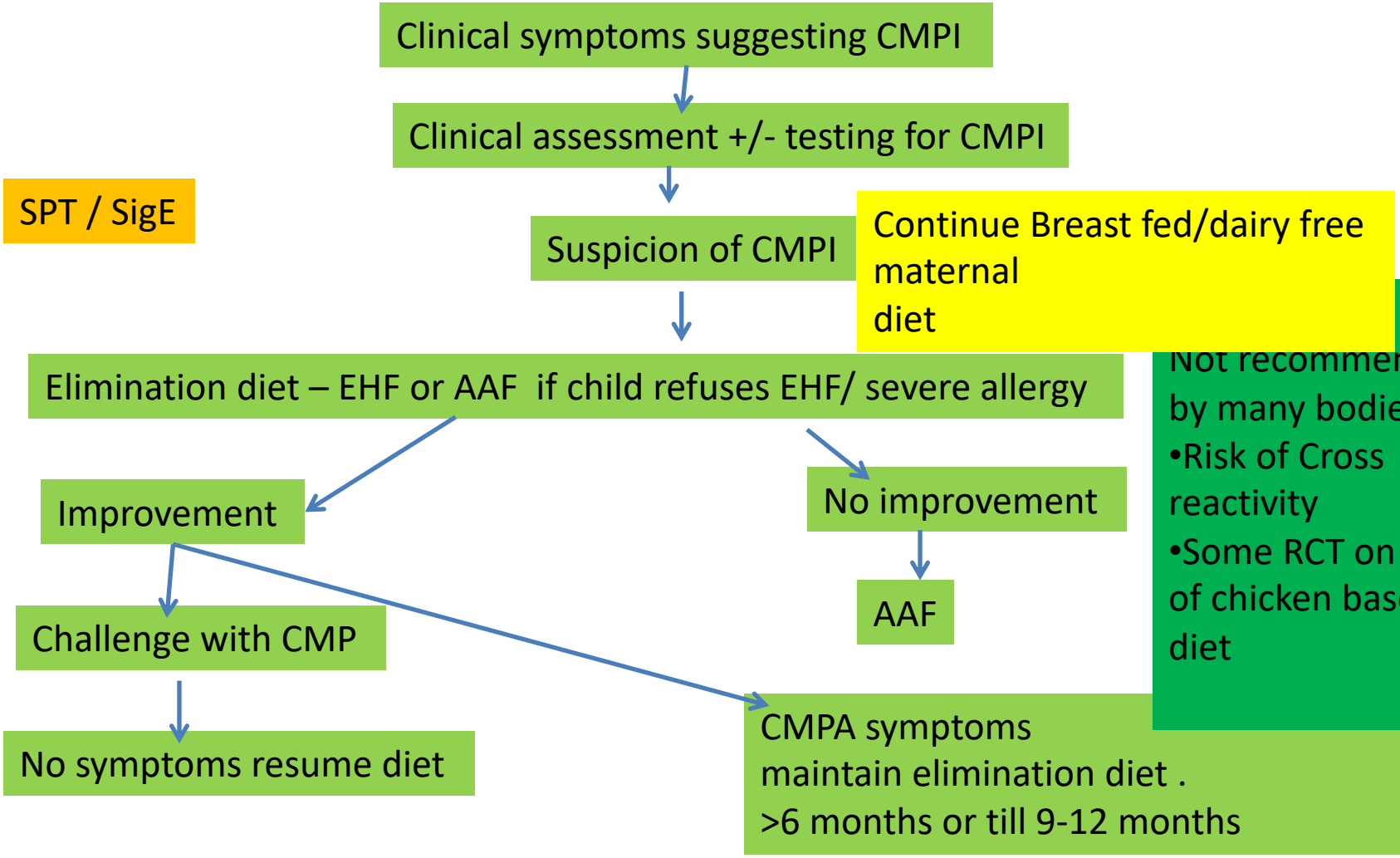


- Food given at dose increment at set interval
- Dose ranges from 3 mg to 3 g of food protein seem sufficient in clinical practice
- Food allergy challenges are usually stopped if objective clinical reactions are observed
- Demonstrate allergy/ tolerance/
- Regularly re evaluate for development of tolerance , 6-12 months for milk And egg, early for nuts

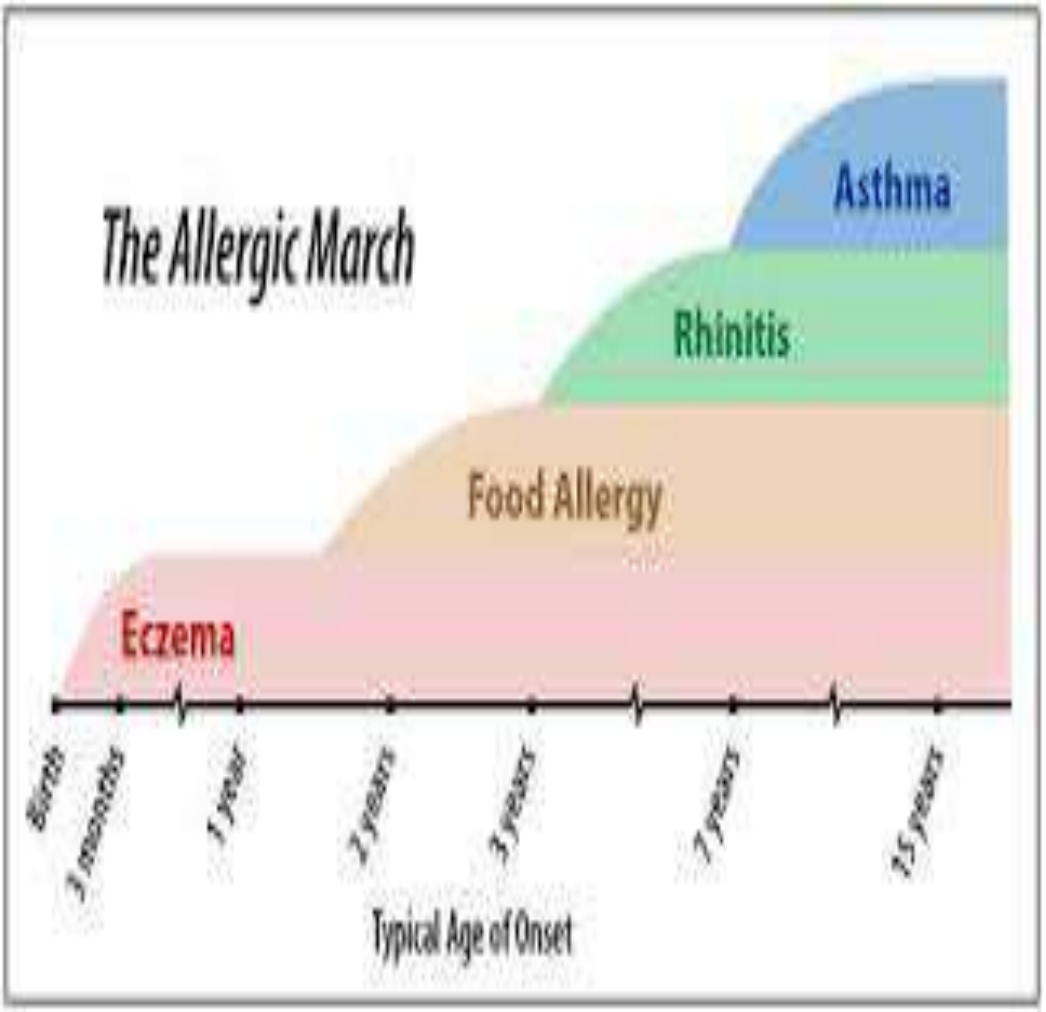
OFC – Oral food challenge
DBPCFC- Double blind placebo controlled food challenge

Allergy
9 JUN 2014 DOI: 10.1111/all.12429
http://onlinelibrary.wiley.com/doi/10.1111/all.12429/full#all12429-fig-0002

Decision tree Cows milk protein allergy –Non IgE



EHF – Extensively hydrolized formula, AAF –Amino acid based formula



Allergy prevention

If early forms of disease can be prevented
there is a potential sustained
Long term benefits and reduction of other forms of allergic disease in later life

Burgess et al, J Asthma 2009;46;429-36

World allergy organization 2011

Timing of introduction of allergenic food

Early exposure to solid food in infancy has been associated with development of allergic disease

	Solid food	Cows mik	eggs	Peanuts	Fish
AAP 2000	>4 mon	> 12 mon	> 24 mo	>36 mo	>36 mo
ASCIA 2005	> 4-6 mon			Optional	Optional
ACAAI 2006		> 12 mon	> 24 mon	> 36 mon	> 36 mon

Recommendations for weaning

Many recommendations agree ,

No convincing scientific evidence that avoidance

Or delayed introduction of potentially allergenic food beyond 4-6 months reduce allergy

Ref	Age of weaning
EAACI 2014	4 to 6 months
AAAI 2013	4 to 6 months
US NIAID 2010	4 to 6 months
AAP	4 To 6 months
ESPGHAN	After 17 weeks , but not later than 26 wks
CSACI 2013	4 to 6 months

Ongoing research

- **EAT study** – (RCT of early introduction of 6 allerginic food vs current recommendations)
- **LEAP study** – RCT of early vs delayed exposure of peanuts in at risk infants
- **QUEST** reastfeeding mothe velopment in infants
- **STEP study** - **Timing of egg introduction into the diets of infants to prevent egg allergy.**

Results are expected 2014-2015

Probiotics in prevention of allergy Current recommendations

AAP 2010

- The results of some studies support the prophylactic, use of probiotics during pregnancy and lactation and during the first 6 months of life in infants who are risk of atopic disorders

World allergy organization 2012

- Probiotics do not have a established role in the prevention and treatment of allergy

Further studies are needed

Other interventions in food allergy

Intervention	Effect	Reference
N3 PUFA	During pregnancy better than lactation	No recommendations
Antioxidants &folate	No interventional studies , role unclear	
Vitamin D	No	ESPGHAN 2013
Avoidance Maternal Cigarette smoking	Strong evidence	EAACI

Exclusive breast feeding at least for 3 months reduces atopic dermatitis

Partially hydrolyzed formula meta-analysis of all studies – compared to standard formula reduced the Risk of allergic diseases , particularly cumulative incidence of atopic dermatitis among children with high risk

Organization	Risk	Recommendations (if not breast fed)
US NIAID 2010	At risk	Hydrolyzed formula
EAACI 2008	At risk	Formula with documented reduced allergenicty > 4 months
AAP 2008	At risk	Hydrolyzed formula Not all HF provide same degree of protective benefit
French society for paediatrics 2008	At risk Unknown	PHF exclusively for 6 months PHF with proven efficacy till family history known

For prevention of atopic eczema EH casein and PH whey can be cost effective and even cost saving

Newer Test and Newer therapy

Molecular component resolved diagnostic test (CRD)	**antibodies against individual allergenic molecules**	**Improved sensitivity and specificity Promising test , further RCT required**
Basophil activation tests (BAT)		Higher specificity and NPV Limited to research
Atopic patch test/specific IgG testing		Not recommended

Prophylactic administration of antihistamines	**Not recommended**
Food allergen-specific immunotherapy/Anti-IgE	Not recommended

EAACI Food Allergy Guidelines, 2014

Thank you

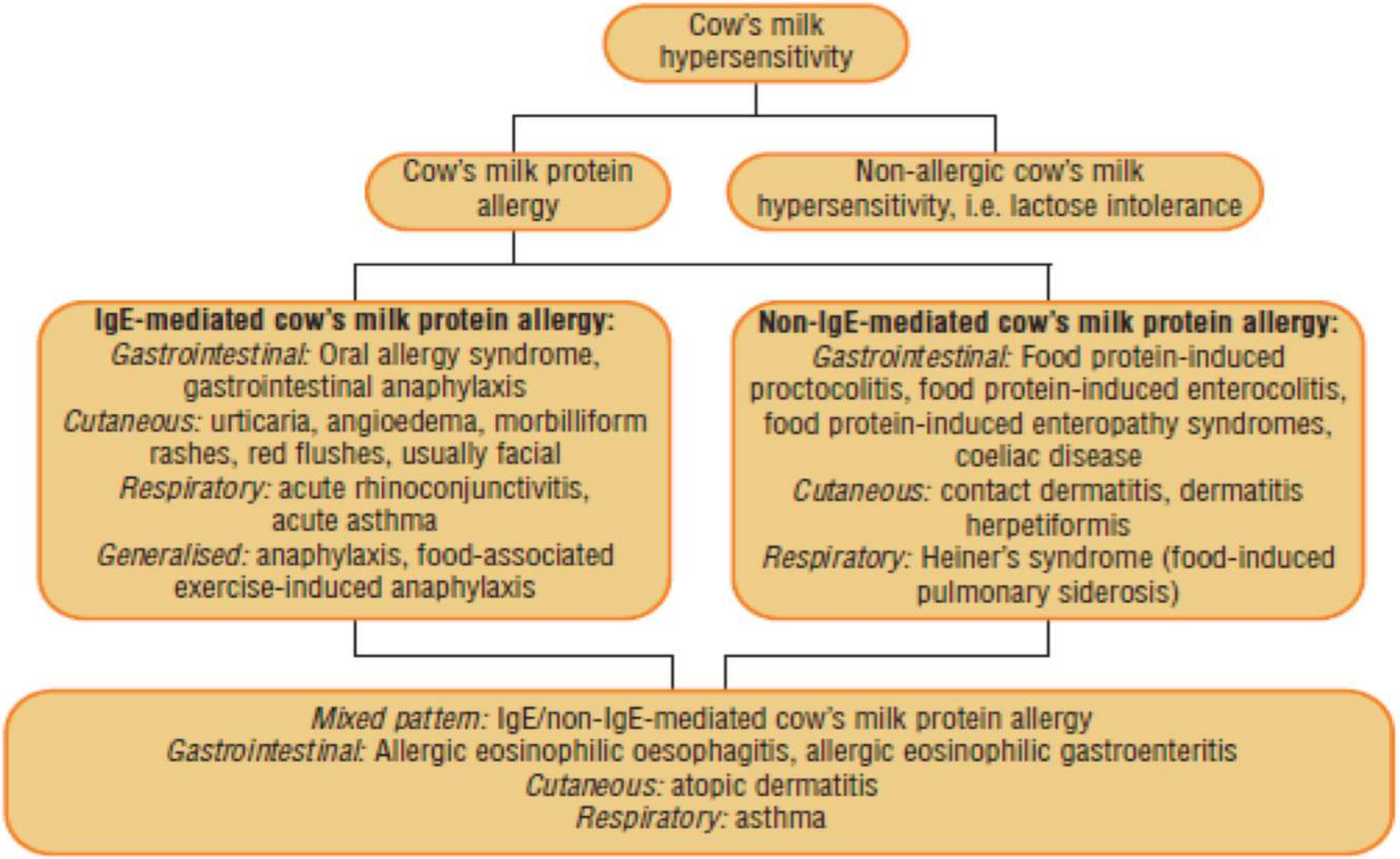
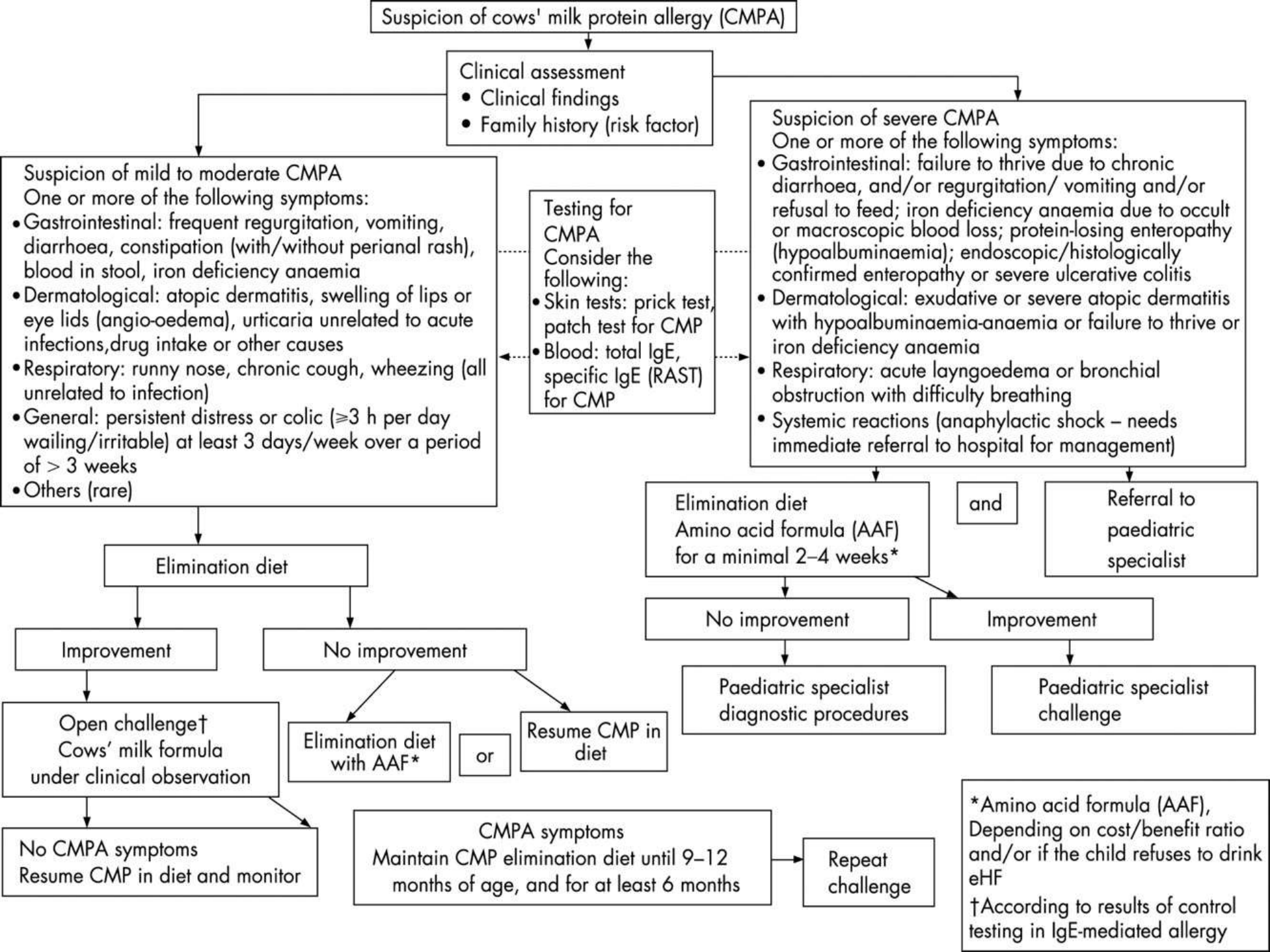


Figure 1: Definition of cow's milk protein allergy (adapted from Venter[3])


Suspicion of cows' milk protein allergy (CMPA)
Clinical assessment
• Clinical findings
• Family history (risk factor)
Suspicion of mild to moderate CMPA
One or more of the following symptoms:
• Gastrointestinal: frequent regurgitation, vomiting, diarrhoea, constipation (with/without perianal rash), blood in stool, iron deficiency anaemia
• Dermatological: atopic dermatitis, swelling of lips or eye lids (angio-oedema), urticaria unrelated to acute infections,drug intake or other causes
• Respiratory: runny nose, chronic cough, wheezing (all unrelated to infection)
• General: persistent distress or colic (≥3 h per day wailing/irritable) at least 3 days/week over a period of > 3 weeks
• Others (rare)
Testing for CMPA
Consider the following:
• Skin tests: prick test, patch test for CMP
• Blood: total IgE, specific IgE (RAST) for CMP
Suspicion of severe CMPA
One or more of the following symptoms:
• Gastrointestinal: failure to thrive due to chronic diarrhoea, and/or regurgitation/ vomiting and/or refusal to feed; iron deficiency anaemia due to occult or macroscopic blood loss; protein-losing enteropathy (hypoalbuminaemia); endoscopic/histologically confirmed enteropathy or severe ulcerative colitis
• Dermatological: exudative or severe atopic dermatitis with hypoalbuminaemia-anaemia or failure to thrive or iron deficiency anaemia
• Respiratory: acute laryngoedema or bronchial obstruction with difficulty breathing
• Systemic reactions (anaphylactic shock – needs immediate referral to hospital for management)
Elimination diet
Amino acid formula (AAF) for a minimal 2–4 weeks*
and
Referral to paediatric specialist
No improvement
Improvement
Paediatric specialist diagnostic procedures
Paediatric specialist challenge
Elimination diet
Improvement
No improvement
Open challenge†
Cows' milk formula under clinical observation
Elimination diet with AAF*
or
Resume CMP in diet
No CMPA symptoms
Resume CMP in diet and monitor
CMPA symptoms
Maintain CMP elimination diet until 9–12 months of age, and for at least 6 months
Repeat challenge
*Amino acid formula (AAF), Depending on cost/benefit ratio and/or if the child refuses to drink eHF
†According to results of control testing in IgE-mediated allergy

Food intolerance

- Prevalence ~ 2-20%*.
- Food proteins are recognised as “foreign”.
- Food specific IgG production and formation of antigen/antibody complexes.
- Complexes are deposited in tissues and activate complement & macrophages: Inflammation.
- Delayed reaction and may last for days.

Allergy	Intolerance
Obvious symptoms	Subtle symptoms
Immediate reaction – within one hour	Delayed reaction – 12 hrs to days
Rapid onset of symptoms & often reaction magnifies with each exposure	Slow onset & often slow magnification of symptoms, even after the often long delay
Often triggered by minute amount of food	Not predominantly affected by food quantity
Involves IgE	Involves IgG
Not common	Very common
Generally non-reversible	Reversible
Well recognized by medical science	Just beginning to be recognized by medical science

- Enzyme deficiencies: Lactose, Gluten intolerance
- Sensitivity to food additives (antioxidants, flavourings, colourings, preservatives, sweeteners, thickeners): Sulfites used to preserve dried fruit, canned goods
- Digestive diseases: Irritable bowel syndrome
- Recurring stress or psychological factors
- Disturbance in normal microbial flora of intestine due to use of oral antibiotics
- Toxins produced by bacterial and fungal infection

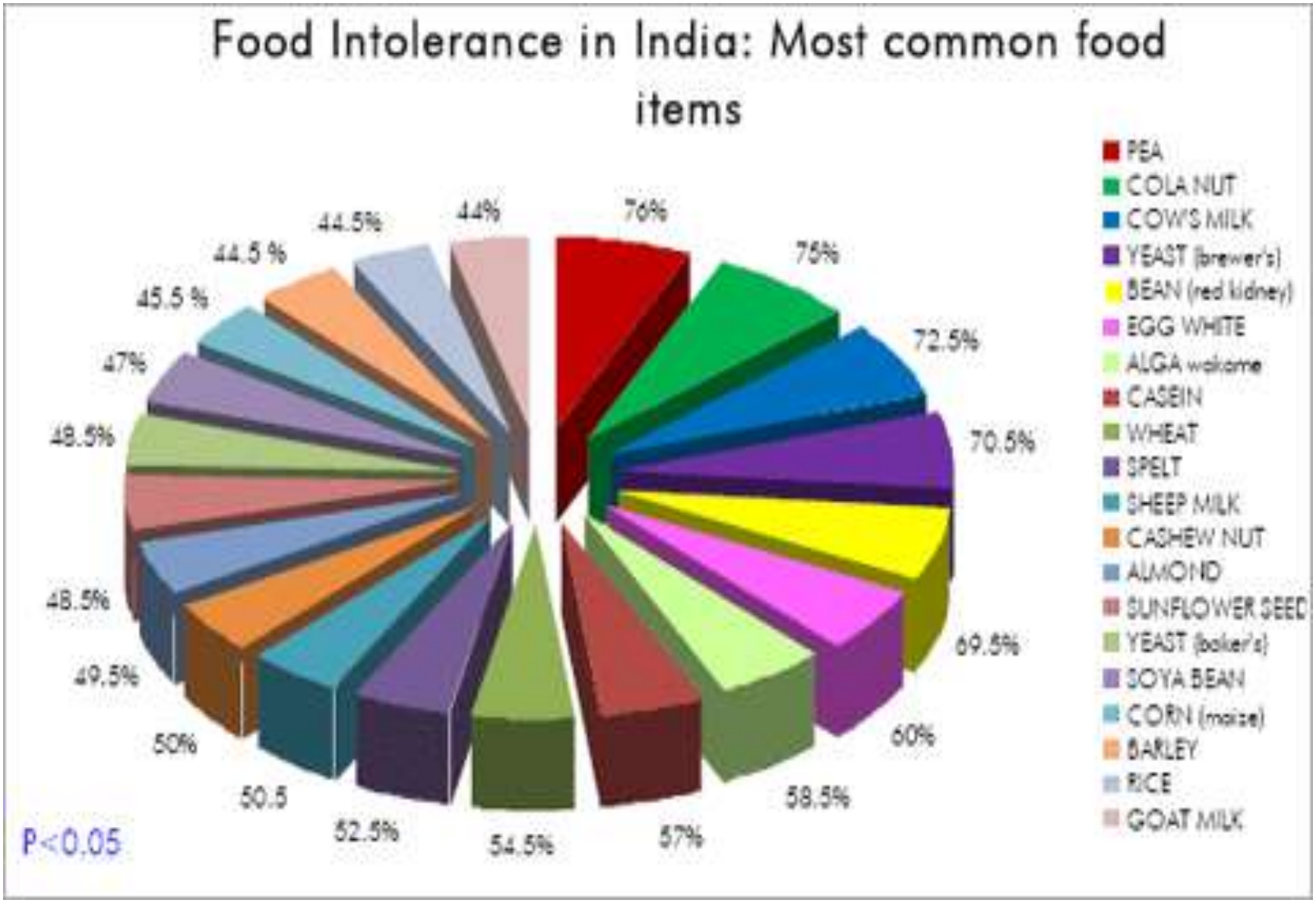
Symptoms of food intolerance

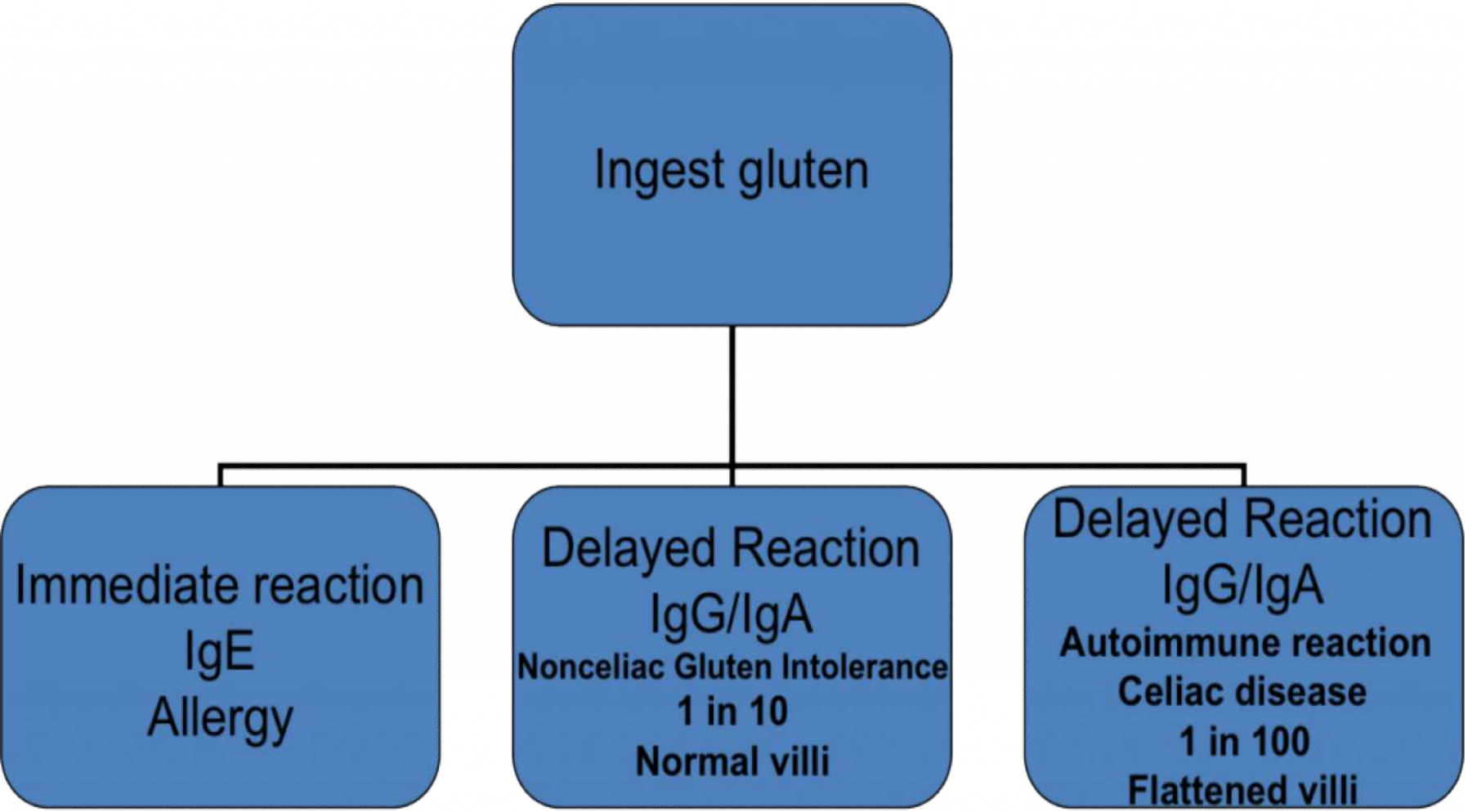
- Frequent Stomach and bowel upsets
- Bloating
- Headaches
- Wheezing and a runny nose
- Joint aches
- Skin rashes

Oral Allergy Syndrome

- Symptoms
  - Pruritis and/or tingling
  - lip, tongue, palate, & throat
  - Edema of the lips tongue
- Association with Fresh Fruits and Vegetables
  - Peaches, Apricot, Cherry and Plum
  - Carrots, Broccoli, Tomato and Celery
- Association with pollens
  - Ragweed, Banana, Melons
  - Birch, Carrot ,Celery, Potato, Apple, Hazelnut, Kiwi

Food Intolerance in India: Most common food items



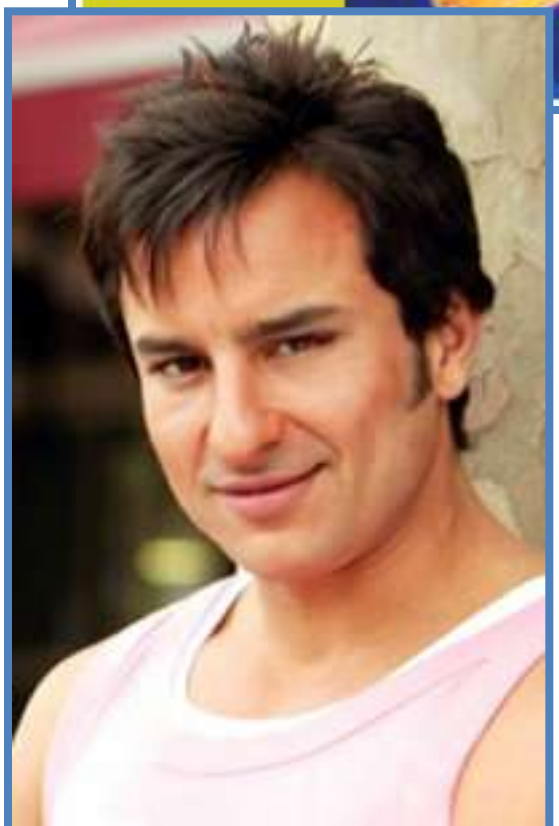

Ingest gluten
Immediate reaction
IgE
Allergy
Delayed Reaction
IgG/IgA
Nonceliac Gluten Intolerance
1 in 10
Normal villi
Delayed Reaction
IgG/IgA
Autoimmune reaction
Celiac disease
1 in 100
Flattened villi

Challenges in allergy avoidance

- Contamination of food in products with advisory statement.
- Low level of knowledge regarding food allergy in hotel staff
- 42% ready to eat allergenic food

Allergen	Main nutrients provided
Milk	Calcium, Vitamin D, Phosphorus, Vitamin A, Vitamin B12, Riboflavin, Pantothenic acid
Soy	Thiamin, Riboflavin, Folate, Magnesium, Phosphorus
Eggs	Vitamin B12, Folate, Riboflavin, Selenium
Wheat	Thiamin, Riboflavin, Niacin, Iron, Folic Acid


Lay's
Magic Masala




Sunfeast
Strawberry Cream Biscuits
Spread The Smile
Now with Jagmag
Sunfeast
DREAM CREAM
STRAWBERRY

When to introduce cows milk ?

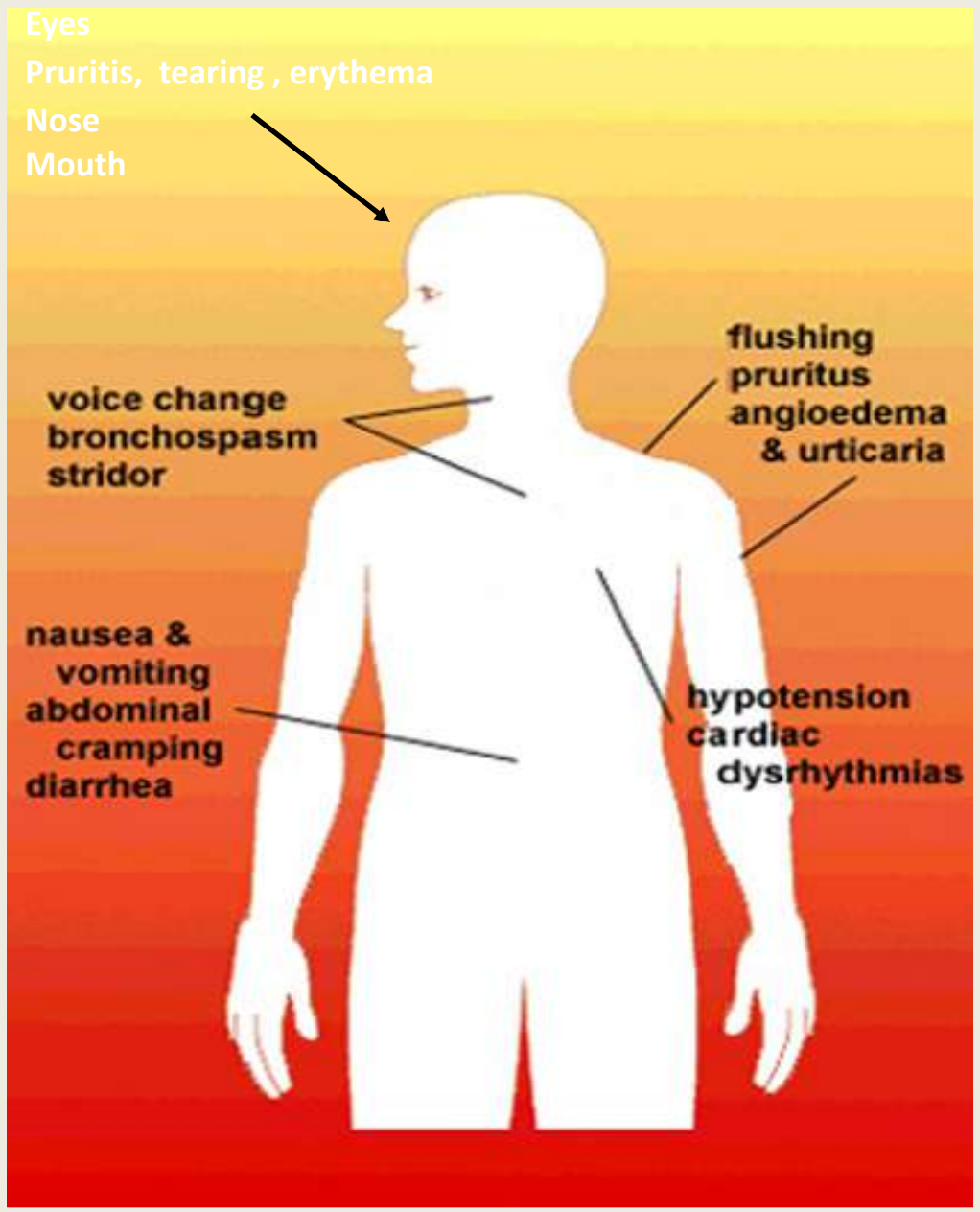
- Difference of opinion in regarding introduction in industrial countries
- Most countries advise wait till 6 months
- Canada, Sweden , Denmark – 9-10 months

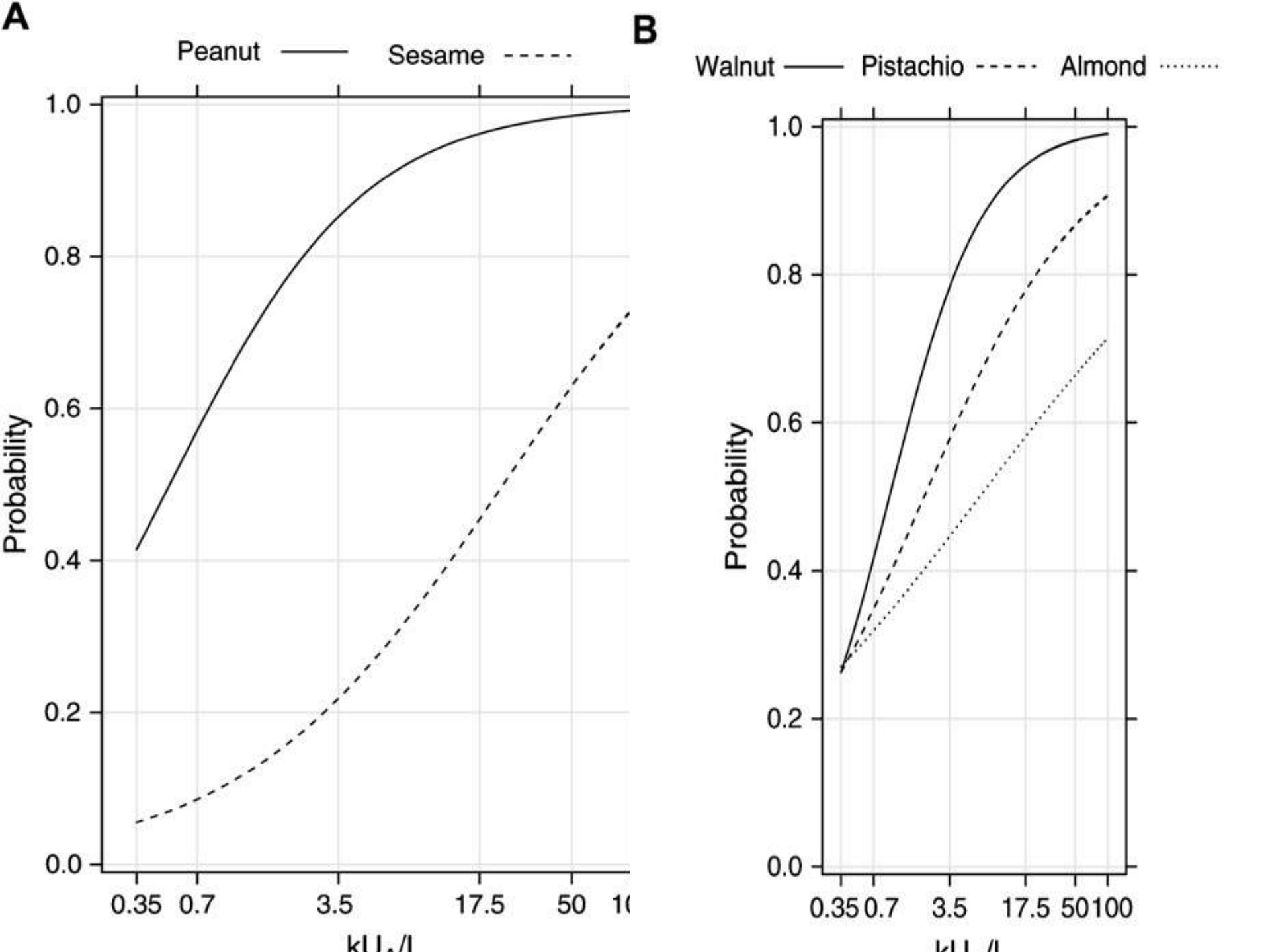
ESPGHAN
Milk can be introduced taking into consideration of traditional and feeding practices , and intake of iron rich diet

Allergy prevention

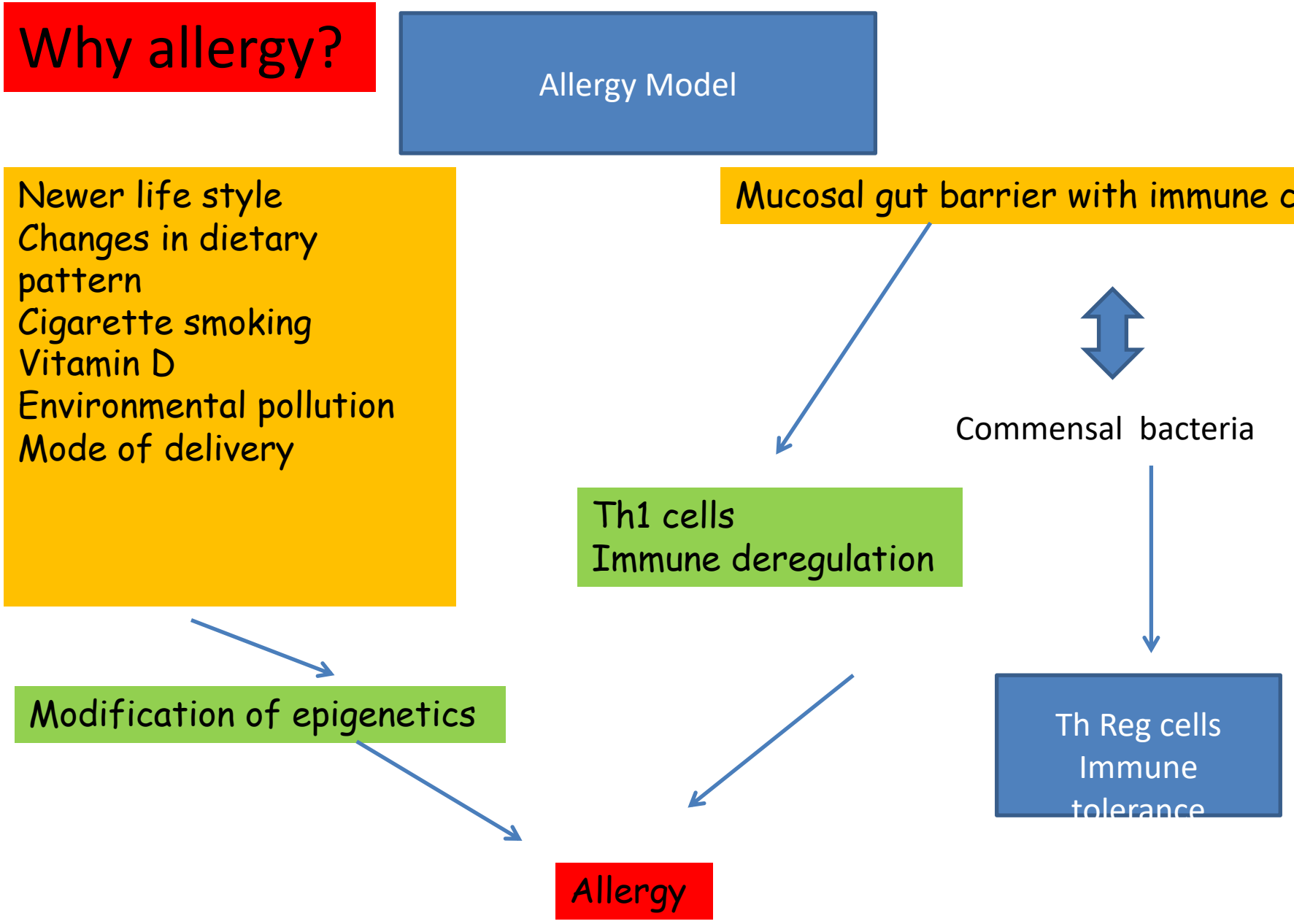
Intervention period	Method of intervention	Evidence
Pregnancy	Stop Cigarette smoking	Strong evidence
	3 PUFA	Likely to be of benefit , no recommendations
	Vitamin D	Sound basis, further RCT needed
	Probiotics	L- Rhamnosus, Cochrane
Prenatal + 1 st year	Breast feeding for 6 months	Protective , recommended
	Introduction of solid food at 6 months	Many bodies agree and recommend Report of further trails awaited
	Pro and prebiotics	Likely to be benefit , no recommendations
	Partially hydrolyzed milk in atopic individual	Recommended by many bodies

Anaphylaxis




A
Peanut
Sesame
1.0
0.8
0.6
0.4
0.2
0.0
Probability
0.35
0.7
3.5
17.5
50
B
Walnut
Pistachio
Almond
1.0
0.8
0.6
0.4
0.2
0.0
Probability
0.35
0.7
3.5
17.5
50
100

Why allergy?


Allergy Model
Newer life style
Changes in dietary pattern
Cigarette smoking
Vitamin D
Environmental pollution
Mode of delivery
Mucosal gut barrier with immune cells
Commensal bacteria
Th1 cells
Immune deregulation
Modification of epigenetics
Th Reg cells
Immune tolerance
Allergy

How much would you recollect, 24 hrs later after listening to a talk?

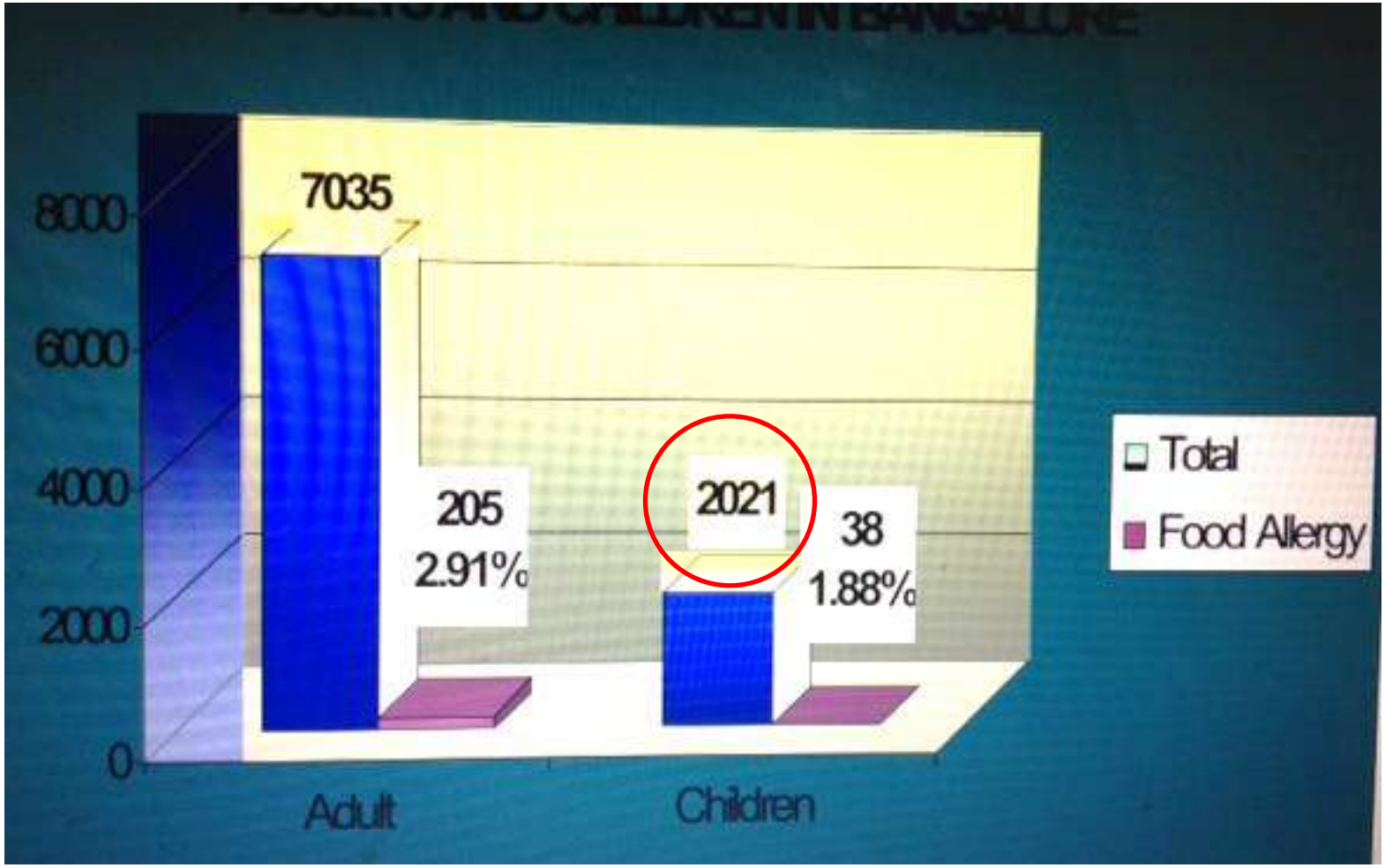
- 5% Listening
- 50% Discuss
- 90% Teach
- 100 % , I am a super human!

Story of Adbhut

- 8 month old , previously well, mother introduced formula milk 2 day ago, h/o of vomiting two times , tummy rumbling and gassy, now refuses to feed .

Mother thinks “A” is allergic to milk and she is worried !

Prevalence of food related symptoms in adults and children in Bangalore



Prevalence of food related symptoms in adults and children in Mysore

Oral Immunotherapy for milk allergy

- Meta-anaylsis of MOIT protocol

-Quality of evidence is generally low

-Desensitization in the majority of individuals with IMCMA

-Development of long-term tolerance has not been established

-Major drawback of MOIT is the frequency of adverse effects