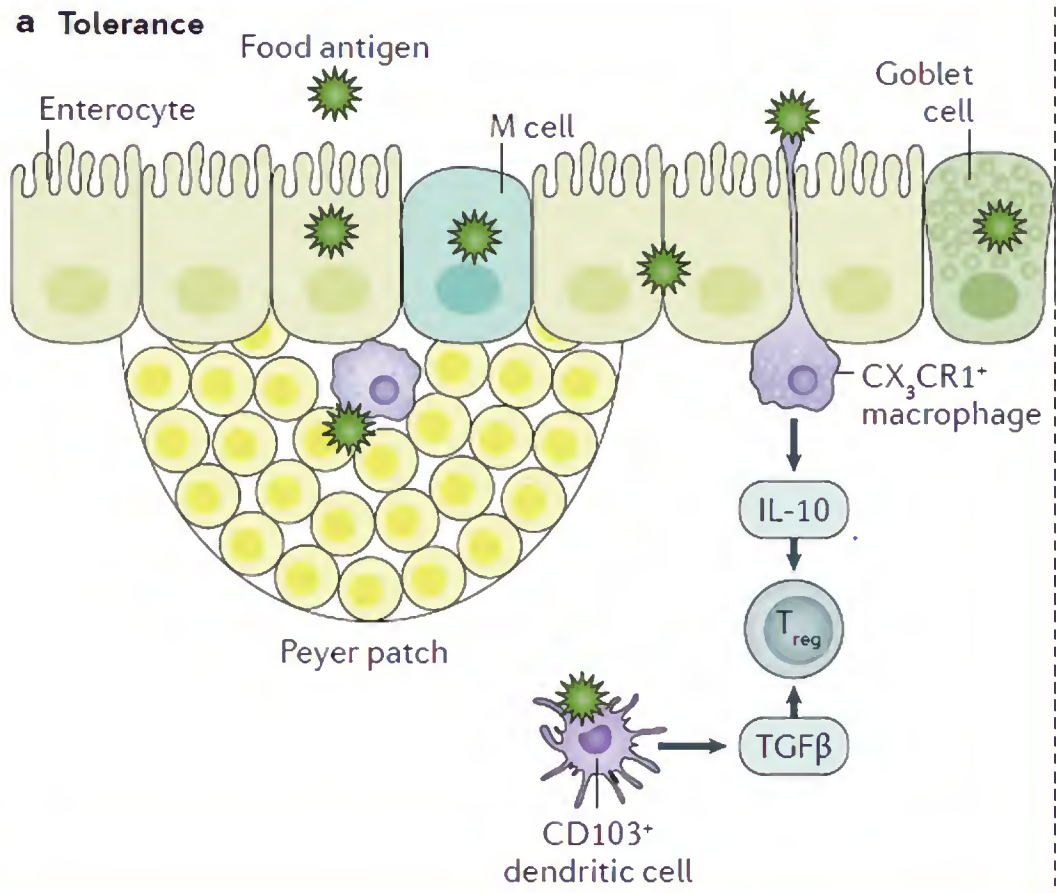


# **REAZIONI AVVERSE AGLI ALIMENTI**

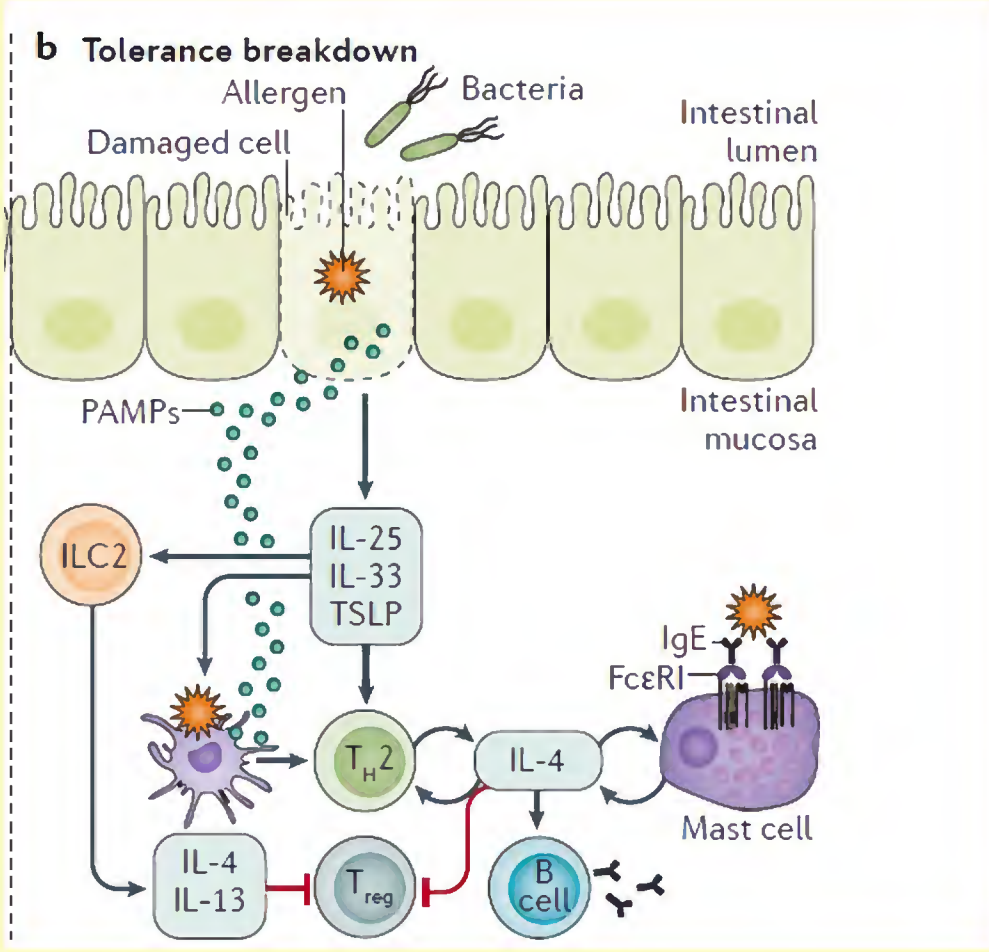
**Iride Dello Iacono**

**Benevento**

# TOLERANCE



# TOLERANCE BREAKDOWN





FOR THE DIAGNOSIS AND MANAGEMENT

**Food Allergy**

**Food Intolerances**

Adverse Food Reaction

Intolerance

Immune Mediated  
(Food Allergy and Celiac Disease)

Non-Immune Mediated  
(Primarily Food Intolerances)

IgE Mediated  
(e.g. acute urticaria, oral allergy syndrome)

Non-IgE Mediated  
(e.g. food protein-induced enteropathy, Celiac disease)

Mixed IgE and non-IgE Mediated  
(e.g. eosinophilic gastroenteritis)

Cell Mediated  
(e.g. Allergic Contact Dermatitis)

Metabolic  
(e.g. lactose intolerance)

Pharmacologic  
(e.g. caffeine)

Toxic  
(e.g. scombroid fish toxin)

Other / Idiopathic / Undefined  
(e.g. sulfites)

# FOOD ALLERGY

*The term food allergy refers to an immune response directed toward food.*

*ICON 2012*

*“Adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food.”*

*NIAID 2010*

## ICON: food allergy.

[Burks AW](#), [Tang M](#), [Sicherer S](#), [Muraro A](#), [Eigenmann PA](#), [Ebisawa M](#), [Fiocchi A](#), [Chiang W](#), [Beyer K](#), [Wood R](#), [Hourihane J](#), [Jones SM](#), [Lack G](#), [Sampson HA](#).

# IgE-mediated reactions

IgE mediated (acute onset)	Acute urticaria/angioedema	Food commonly causes acute (20%) but rarely chronic urticaria.	Primarily “major allergens” (see text)
	Contact urticaria	Direct skin contact results in lesions. Rarely this is due to direct histamine release (nonimmunologic).	Multiple
	Anaphylaxis	Rapidly progressive, multiple organ system reaction can include cardiovascular collapse.	Any but more commonly peanut, tree nuts, shellfish, fish, milk, and egg
	Food-associated, exercise-induced anaphylaxis	Food triggers anaphylaxis only if ingestion is followed temporally by exercise.	Wheat, shellfish, and celery most often described
	Oral allergy syndrome (pollen-associated food allergy syndrome)	Pruritus and mild edema are confined to oral cavity and uncommonly progress beyond the mouth (~7%) and rarely to anaphylaxis (1% to 2%). Might increase after pollen season.	Raw fruit/vegetables; cooked forms tolerated; examples of relationships: birch (apple, peach, pear, carrot), ragweed (melons)
	Immediate gastrointestinal hypersensitivity	Immediate vomiting, pain	Major allergens

## ICON: food allergy.

Burks AW, Tang M, Sicherer S, Muraro A, Eigenmann PA, Ebisawa M, Fiocchi A, Chiang W, Beyer K, Wood R, Hourihane J, Jones SM, Lack G, Sampson HA.

# Cell-mediated reactions

**In passato:  
Food  
Intolerances**

Cell mediated (delayed onset/chronic)	Food protein–induced enterocolitis syndrome	Primarily affects infants; chronic exposure: emesis, diarrhea, poor growth, lethargy; re-exposure after restriction: emesis, diarrhea, hypotension (15%) 2 hours after ingestion	Cow's milk, soy, rice, oat, meat
	Food protein–induced allergic proctocolitis	Mucus-laden, bloody stools in infants	Milk (through breast-feeding)
	Allergic contact dermatitis	Often occupational because of chemical moieties, oleoresins. Systemic contact dermatitis is a rare variant because of ingestion	Spices, fruits, vegetables
	Heiner syndrome	Pulmonary infiltrates, failure to thrive, iron deficiency anemia	Cow's milk

## ICON: food allergy.

[Burks AW](#), [Tang M](#), [Sicherer S](#), [Muraro A](#), [Eigenmann PA](#), [Ebisawa M](#), [Fiocchi A](#), [Chiang W](#), [Beyer K](#), [Wood R](#), [Hourihane J](#), [Jones SM](#), [Lack G](#), [Sampson HA](#).

# Combined IgE and cell-mediated reactions

Combined IgE and cell mediated (delayed onset/chronic)	Atopic dermatitis	Associated with food allergy in ~35% of children with moderate-to-severe rash	Major allergens, particularly egg, milk
	Eosinophilic esophagitis	Symptoms might include feeding disorders, reflux symptoms, vomiting, dysphagia, and food impaction.	Multiple
	Eosinophilic gastroenteritis	Vary on site(s)/degree of eosinophilic inflammation; might include ascites, weight loss, edema, obstruction	Multiple



# FOOD INTOLERANCES

Non-immune mediated reactions  
or food intolerances include  
metabolic, pharmacologic, toxic,  
and undefined mechanisms.

In some cases, these reactions  
may mimic reactions typical  
of an immunologic response.





### 3 In caso di sospetta allergia alimentare **NON eseguire test privi di validazione scientifica**

Per la diagnosi di allergia alimentare sono in commercio test diagnostici per i quali non è sufficientemente dimostrata l'efficacia diagnostica o, peggio, è stata già dimostrata l'inefficacia diagnostica. Rientrano tra questi test inutili:

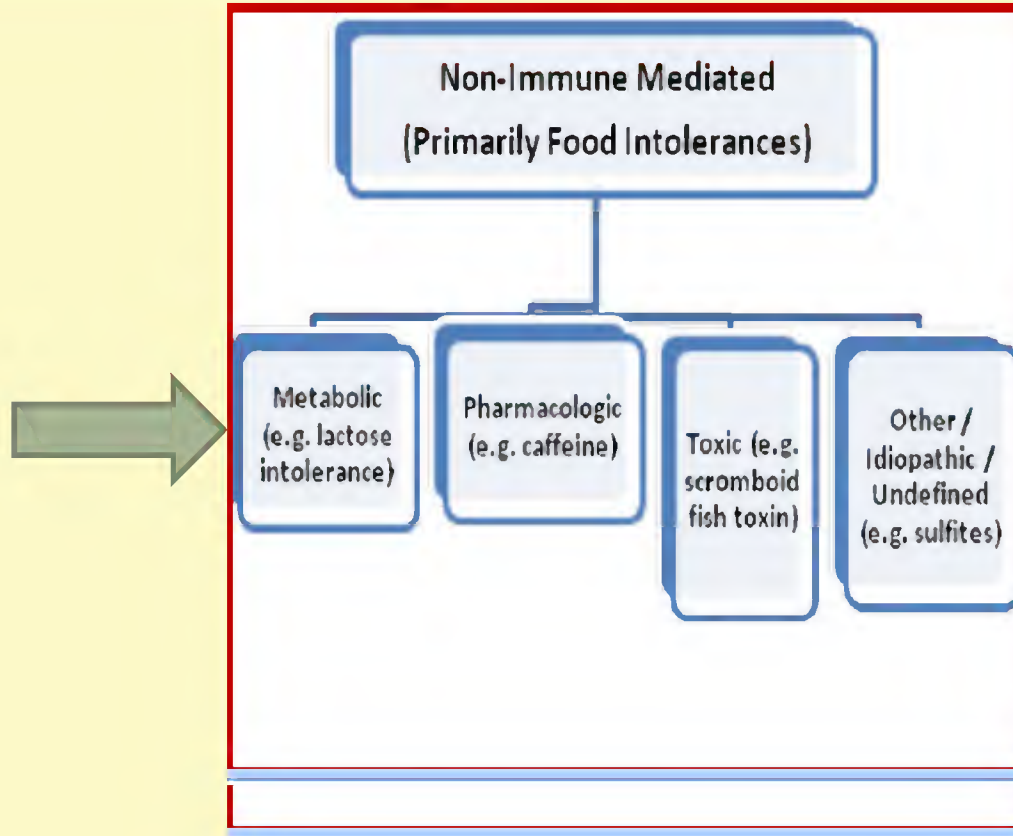
- Il test citotossico o test di Bryan;
- Il test di provocazione e neutralizzazione sublinguale o intradermico;
- La Kinesiologia applicata;
- Il test del riflesso cardio-auricolare;
- Il Pulse test;
- Il test elettrotermico o Elettroagopuntura secondo Voll;
- Il Vega Test;
- Il Sarmtest;
- Il Biostrenght test e varianti;
- La biorisonanza;
- L'analisi del capello (Hair analysis);
- Il Natrrix o FIT 184 Test.

#### Bibliografia di riferimento

Boyce et al. J Allergy Clin Immunol 2010;126:1105.  
Walsh e O'Flynn. Br J Gen Pract 2011;61:588.  
Kattan et al. Curr Allergy Asthma Rep 2013;13:58.



# FOOD INTOLERANCES



# Diagnosi Allergologica

Iter  
diagnostico

Test di provocazione

Dieta di eliminazione diagnostica

IgE s

SPT

Esame obiettivo

Anamnesi accurata



# Diagnosis

## Patient's clinical history and examination

Both a detailed medical history and a physical examination are needed to diagnose IgE-mediated, non-IgE-mediated, or mixed IgE- and non-IgE-mediated food allergy.

The medical history should capture:

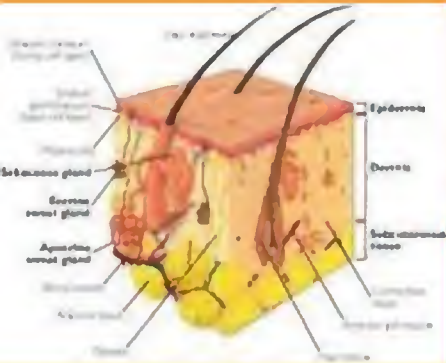
- the possible causal food or foods,
- form or forms in which ingested (raw, semicooked, cooked, or baked),
- quantity ingested,
- time course of reactions,
- nature of reactions,
- ancillary factors, such as exercise or ingestion of aspirin or alcohol.

*Food allergy: a practice parameter. Ann Allergy Asthma Immunol 2006; 96(suppl 2):S1-68.*

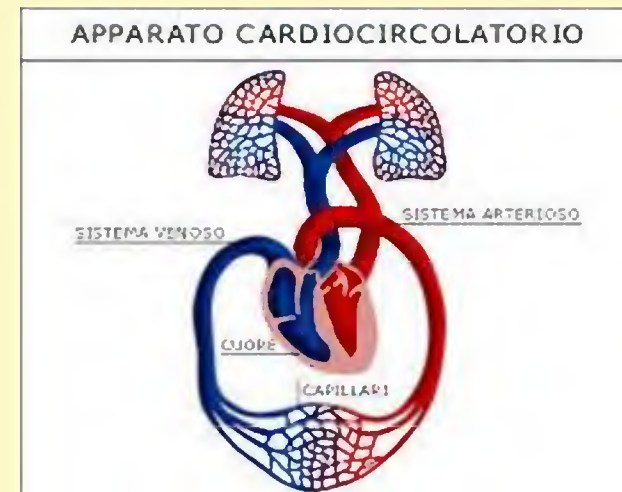
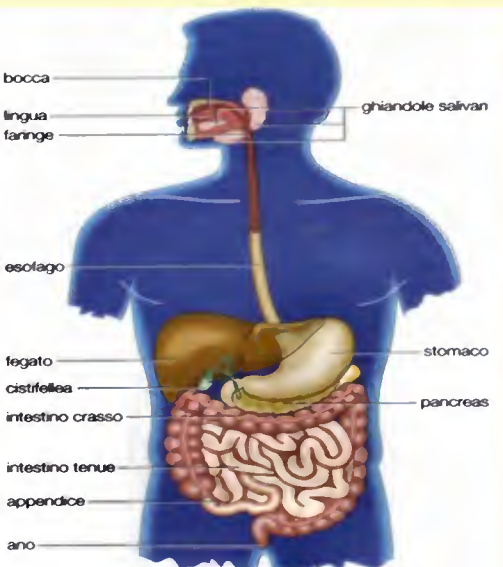
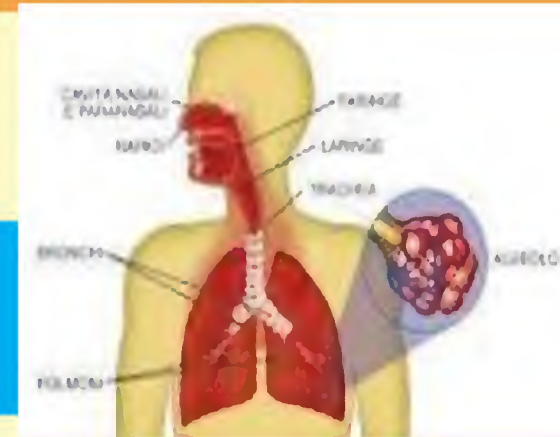
# RdM: PATIENT'S CLINICAL HISTORY

The clinical presentation of food allergy involves a large spectrum of symptoms

## IgE-mediated reactions



IgE-mediated symptoms develop within minutes to 1 to 2 hours of ingesting the food.



# IgE-mediated reactions

Test di provocazione

Dieta di eliminazione diagnostica

IgE s

SPT

Esame obiettivo

Anamnesi accurata



SENSIBILIZZAZIONE

EQUIVALE A

E' allergico  
o no?

NON





**LA RICERCA DELLA SENSIBILIZZAZIONE IN VIVO (SPT) O IN VITRO (IgEs) IN ASSENZA DI UNA STORIA CLINICA “SUGGESTIVA” CI FA CORRERE IL RISCHIO DI “INCARTARCI”**



**PERO' CI SONO .....**

**ECCEZIONI  
ALLA REGOLA**

**MICHELE GELSOMINO** — **FRANCESCO CARAMIA**

**A.S.D. FUTSAL CISTERNINO**

**SONO ATLETI DELLA SETTIMANA**

The graphic features two futsal players. On the left, Michele Gelsomino is shown in a blue jersey with white gloves, looking upwards with an open mouth. On the right, Francesco Caramia is shown in a black jersey with a red and yellow crest, looking to the left. The background is a light-colored wall with a grid pattern. The text is overlaid in bold red and black fonts.

**Risk of adverse IgE-mediate reaction at the first egg ingestion in children with atopic dermatitis. Results of a case-control study**

S. Miceli Sopo<sup>a,\*</sup>, S. Monaco<sup>a</sup>, V. Giorgio<sup>a</sup>, M. Calvani<sup>b</sup>, S. Tripodi<sup>c</sup>, R. Onesimo<sup>a</sup>

Allergol Immunopathol (Madr). 2014;42(2):96---101

**CONCLUSION:**

**A child with AD has a RR of sensitisation to egg six times higher than a child without AD, before the first known ingestion.**



**We propose to test sensitisation to egg in every child with AD who has never eaten egg, and to perform OFC in those with positive SPT in hospital setting.**

**Test di provocazione**

**Dieta di eliminazione diagnostica**

**IgE s**

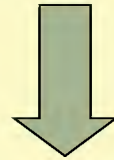
**SPT**

**Esame obiettivo**

**Anamnesi accurata**



# Alimento sospetto



**The duration of the avoidance should be no longer than necessary to achieve a significant relief of symptoms, usually 2–4 weeks for IgE-mediated symptoms** and longer for non-IgE ones [e.g., up to 6 weeks for eosinophilic esophagitis (EoE)].

# Diagnosi Allergologica

Iter  
diagnostico

Test di provocazione

Dieta di eliminazione diagnostica

IgE s

SPT

Esame obiettivo

Anamnesi accurata



# ECCEZIONE: ANAFILASSI

It would not be recommended to perform an OFC for a patient with recent anaphylaxis to the trigger food.

Novak-Wegrzyn A. et al, J Allergy Clin Immunol 2009; 124: s 365-83

Food allergy: A practice parameter update—2014

## Summary Statement 36:

.....when the history indicates that infants or children have experienced hypotensive episodes or multiple reactions to the same food, a diagnosis can be based on a convincing history and absence of symptoms when the causative food is eliminated from the diet.

## ICON: food allergy.

[Burks AW](#), [Tang M](#), [Sicherer S](#), [Muraro A](#), [Eigenmann PA](#), [Ebisawa M](#), [Fiocchi A](#), [Chiang W](#), [Beyer K](#), [Wood R](#), [Hourihane J](#), [Jones SM](#), [Lack G](#), [Sampson HA](#).

# IgE-mediated reactions

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	Immediate gastrointestinal hypersensitivity	Immediate vomiting, pain	Major allergens



POSITION PAPER

## **EAACI Food Allergy and Anaphylaxis Guidelines. Food allergy health-related quality of life measures**

A. Muraro<sup>1,†</sup>, A. E. J. Dubois<sup>2,3,†</sup>, A. DunnGalvin<sup>4</sup>, J. O'B. Hourihane<sup>5</sup>, N. W. de Jong<sup>6</sup>, R. Meyer<sup>7</sup>, S. S. Panesar<sup>8</sup>, G. Roberts<sup>9,10,11</sup>, S. Salvilla<sup>8</sup>, A. Sheikh<sup>8,12</sup>, A. Worth<sup>8</sup> & B. M. J. Flokstra-de Blok<sup>3,13</sup>

Allergy 2014; 69:845–853.

**"a severe life-threatening generalized or systemic hypersensitivity reaction"**

## POSITION PAPER

**EAACI Food Allergy and Anaphylaxis Guidelines. Food allergy health-related quality of life measures**

A. Muraro<sup>1,†</sup>, A. E. J. Dubois<sup>2,3,†</sup>, A. DunnGalvin<sup>4</sup>, J. O'B. Hourihane<sup>5</sup>, N. W. de Jong<sup>6</sup>, R. Meyer<sup>7</sup>, S. S. Panesar<sup>8</sup>, G. Roberts<sup>9,10,11</sup>, S. Salvilla<sup>8</sup>, A. Sheikh<sup>8,12</sup>, A. Worth<sup>8</sup> & B. M. J. Flokstra-de Blok<sup>3,13</sup>

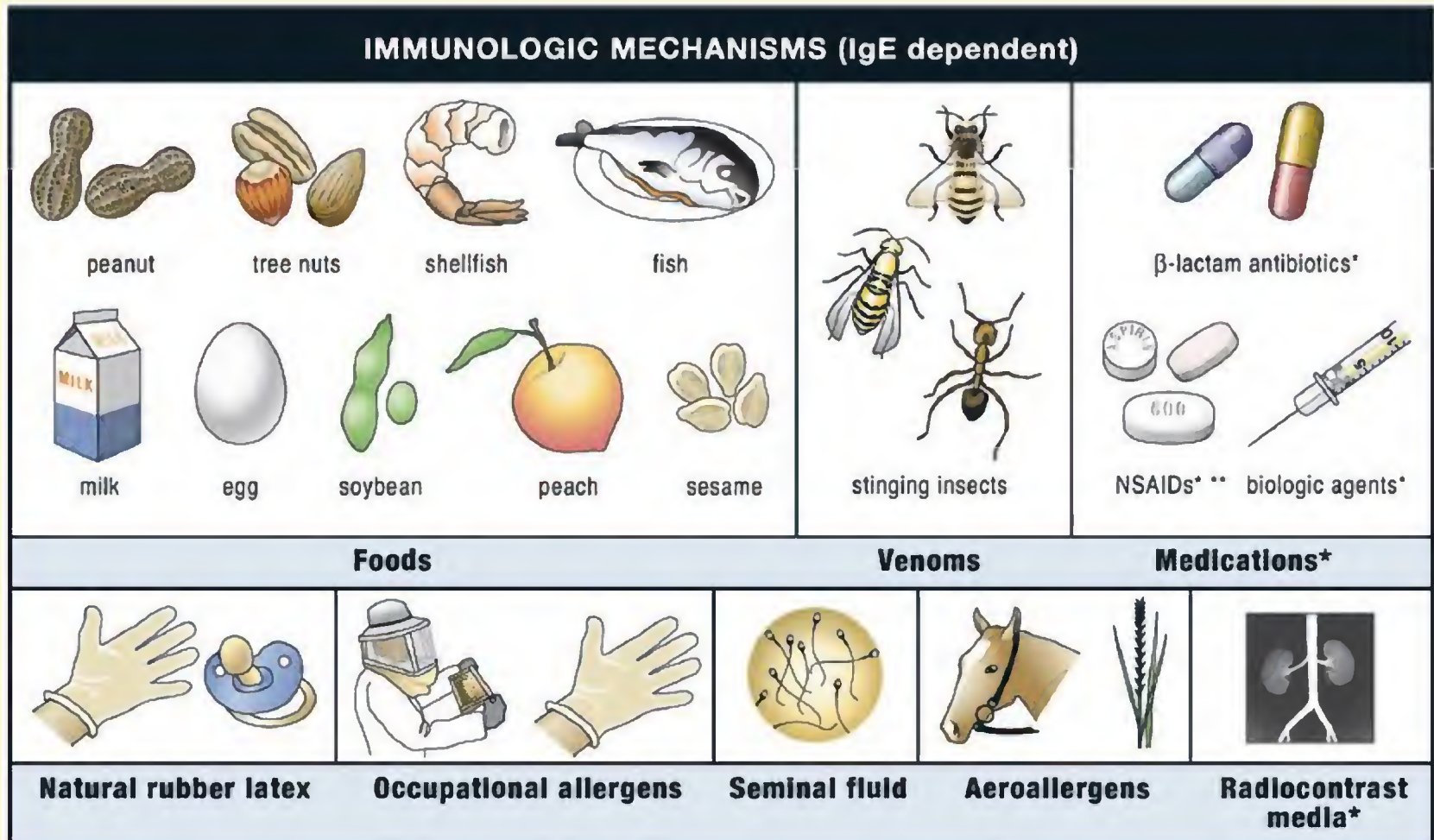
# Epidemiology

The incidence rates for all-cause anaphylaxis ranged from 1.5 to 7.9 per 100.000 person-years.

These data indicated that an estimated 0.3% (95% CI 0.1-0.5 %) of the population experience anaphylaxis at some point in their lives.

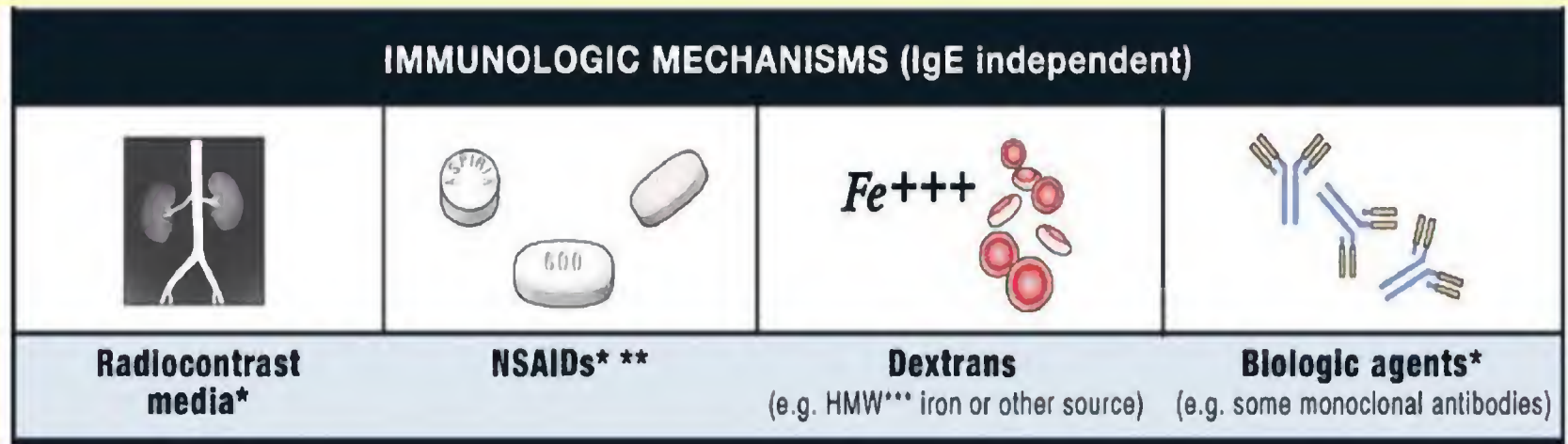
# World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis

## Anaphylaxis mechanisms and triggers



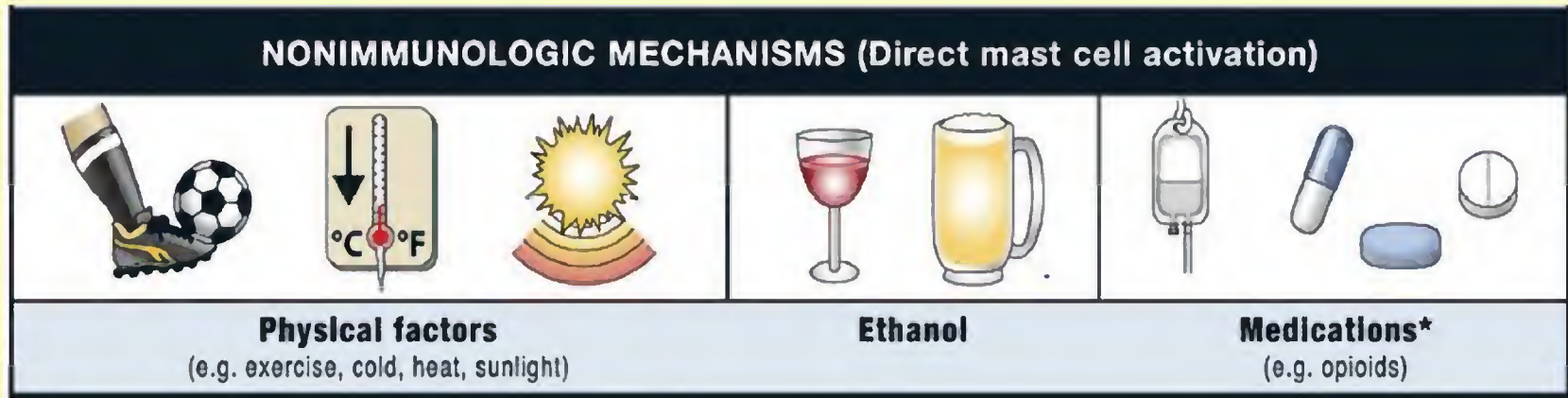
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## Anaphylaxis mechanisms and triggers




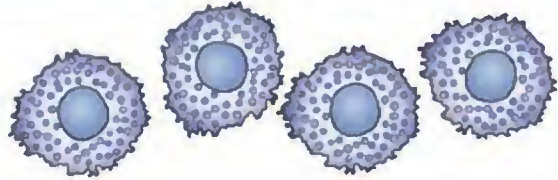
# World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis

## Anaphylaxis mechanisms and triggers



# World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis

## Anaphylaxis mechanisms and triggers

IDIOPATHIC ANAPHYLAXIS (No apparent trigger)	
	
<b>Previously unrecognized allergen?</b>	<b>Mastocytosis/clonal mast cell disorder?</b>
*Trigger anaphylaxis by more than one mechanism	**NSAIDs, non-steroidal anti-inflammatory drugs    ***HMW, high molecular weight

# World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis

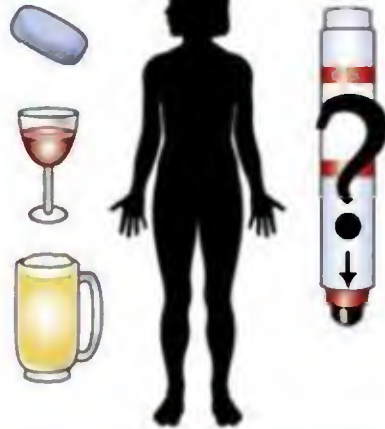
## Vulnerable patients

### AGE-RELATED FACTORS\*



#### Infants

Cannot describe their symptoms



#### Adolescents and young adults

Increased risk-taking behaviors



#### Labor and delivery

Risk from medications (e.g. antibiotic to prevent neonatal group B strep infection)



#### Elderly

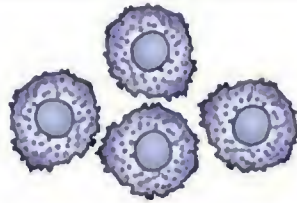
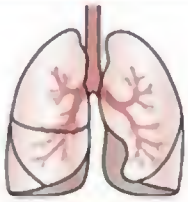
Increased risk of fatality from medication or venom-triggered anaphylaxis

\* Age-related factors, concomitant diseases, and concurrent medications potentially contribute to severe or fatal anaphylaxis. Co-factors potentially amplify anaphylaxis. Multiple factors and co-factors likely contribute to some anaphylactic episodes.

# World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis

## Vulnerable patients

### CONCOMITANT DISEASES\*



**Asthma and other respiratory diseases**

**Cardiovascular diseases**

**Mastocytosis/clonal mast cell disorders**

**Allergic rhinitis and eczema\*\***

**Psychiatric illness**  
(e.g. depression)

\* Age-related factors, concomitant diseases, and concurrent medications potentially contribute to severe or fatal anaphylaxis. Co-factors potentially amplify anaphylaxis. Multiple factors and co-factors likely contribute to some anaphylactic episodes.

\*\* Atopic diseases are a risk factor for anaphylaxis triggered by food, exercise, and latex, but not for anaphylaxis triggered by insect stings.



# World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis

## Vulnerable patients

### CONCURRENT MEDICATIONS/ETHANOL/RECREATIONAL DRUG USE\*



**$\beta$ -adrenergic blockers  
and ACE inhibitors\*\*\***



**Ethanol/sedatives/hypnotics/antidepressants/recreational drugs**  
(potentially affect recognition of anaphylaxis triggers and symptoms)

\*\*\* ACE, angiotensin-converting enzyme

# World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis

## Vulnerable patients

### CO-FACTORS THAT AMPLIFY ANAPHYLAXIS\*



**Exercise**



**Acute infection**

(e.g. a cold or fever)

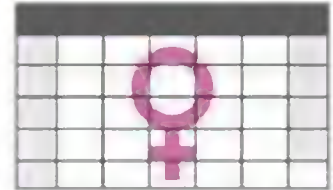


**Emotional stress**



**Disruption of routine**

(e.g. travel)



**Premenstrual status**

(females)

\* Age-related factors, concomitant diseases, and concurrent medications potentially contribute to severe or fatal anaphylaxis. Co-factors potentially amplify anaphylaxis. Multiple factors and co-factors likely contribute to some anaphylactic episodes.

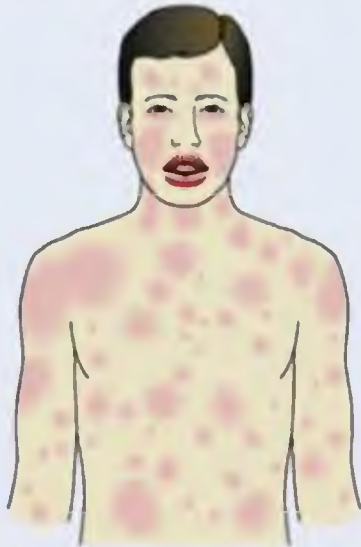
# World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis

## Clinical criteria for diagnosis

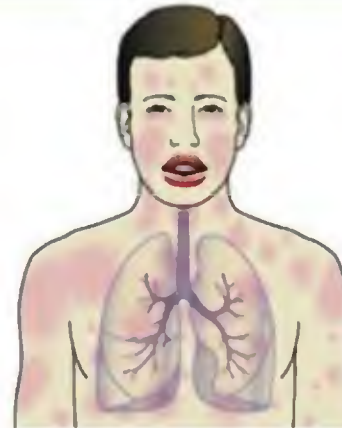
**Anaphylaxis is highly likely when any one of the following three criteria is fulfilled:**

**1**

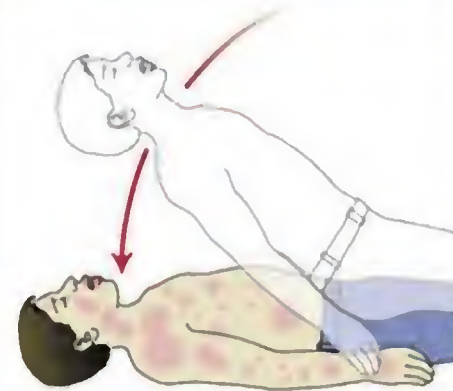
Sudden onset of an illness (minutes to several hours), with involvement of the skin, mucosal tissue, or both (e.g. generalized hives, itching or flushing, swollen lips-tongue-uvula)



**AND AT LEAST ONE  
OF THE FOLLOWING:**



**Sudden respiratory symptoms  
and signs**  
(e.g. shortness of breath, wheeze,  
cough, stridor, hypoxemia)



**Sudden reduced BP or  
symptoms of end-organ  
dysfunction** (e.g. hypotonia  
[collapse], incontinence)

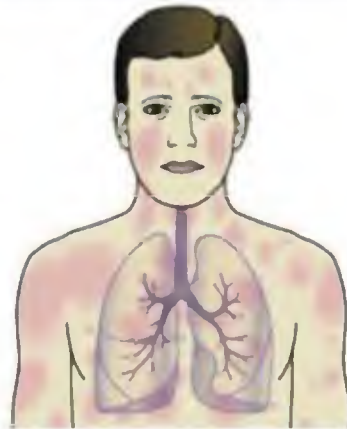
# World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis

**Anaphylaxis is highly likely when any one of the following three criteria is fulfilled:**

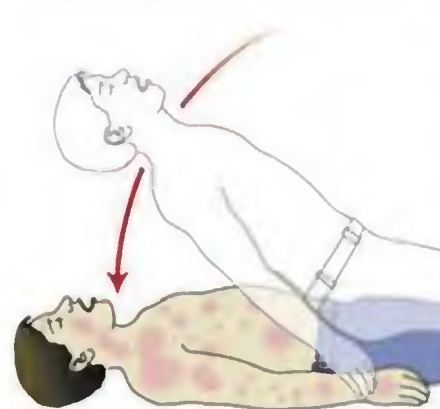
**OR 2** Two or more of the following that occur suddenly after exposure to a *likely allergen or other trigger\** for that patient (minutes to several hours):



**Sudden skin or mucosal symptoms and signs**  
(e.g. generalized hives, itch-flush, swollen lips-tongue-uvula)



**Sudden respiratory symptoms and signs**  
(e.g. shortness of breath, wheeze, cough, stridor, hypoxemia)



**Sudden reduced BP or symptoms of end-organ dysfunction** (e.g. hypotonia [collapse], incontinence)



**Sudden gastrointestinal symptoms** (e.g. crampy abdominal pain, vomiting)

\* For example, immunologic but IgE-independent, or non-immunologic (direct mast cell activation)

# World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis

**Anaphylaxis is highly likely when any one of the following three criteria is fulfilled:**

OR

**3**

Reduced blood pressure (BP) after exposure to a *known allergen\*\** for that patient (minutes to several hours):



Infants and children: low systolic BP (age-specific) or greater than 30% decrease in systolic BP\*\*\*



Adults: systolic BP of less than 90 mm Hg or greater than 30% decrease from that person's baseline

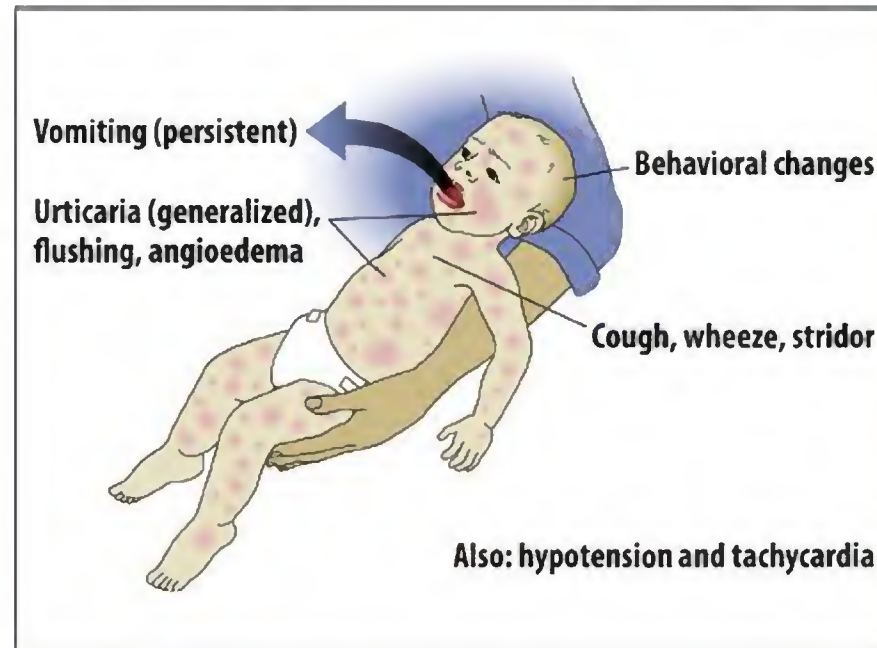
\*\* For example, after an insect sting, reduced blood pressure might be the only manifestation of anaphylaxis; or, after allergen immunotherapy, generalized hives might be the only initial manifestation of anaphylaxis.

\*\*\* Low systolic blood pressure for children is defined as less than 70 mm Hg from 1 month to 1 year, less than  $(70 \text{ mm Hg} + [2 \times \text{age}])$  from 1 to 10 years, and less than 90 mm Hg from 11 to 17 years. Normal heart rate ranges from 80-140 beats/minute at age 1-2 years; from 80-120 beats/minute at age 3 years; and from 70-115 beats/minute after age 3 years. In infants and children, respiratory compromise is more likely than hypotension or shock, and shock is more likely to be manifest initially by tachycardia than by hypotension.

# Anaphylaxis: Unique aspects of clinical diagnosis and management in infants (birth to age 2 years)

F. Estelle R. Simons, MD, FAAAAI,<sup>a</sup> and Hugh A. Sampson, MD, FAAAAI<sup>b</sup>    *Winnipeg, Manitoba, Canada, and New York, NY*

## *Anaphylaxis in infants: Potential symptoms and signs*



**FIG 1.** Clinical diagnosis of anaphylaxis in infants is based on sudden onset of characteristic symptoms and signs in 2 or more body organ systems. Typical symptoms and signs can include generalized urticaria, cough, wheeze, stridor, and/or persistent vomiting. In infants with anaphylaxis, respiratory compromise is more likely than hypotension or shock, and shock is more likely to manifest initially as tachycardia rather than hypotension.<sup>1-3</sup>

# World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis

## Role of Laboratory Tests in the Diagnosis of Anaphylaxis

Total tryptase (pro, pro', and mature forms of alpha/beta tryptases)

Obtain blood sample within 15 minutes to 3 hours of symptom onset<sup>a,b</sup>

Consider measuring levels in accurately timed serial blood samples during the anaphylactic episode

Consider comparing levels measured during the episode with a baseline level<sup>c,d</sup>

Histamine

Obtain blood sample within 15 minutes to 1 hour of symptom onset<sup>a</sup>

Special handling of the blood sample is required (use wide-bore needle, keep sample at 4°C and centrifuge it promptly, freeze plasma promptly)

Measure histamine and its metabolite *N*-methylhistamine in a 24-hour urine sample

Other<sup>e</sup>



# World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis

F. Estelle R. Simons; Ledit R.F. Arduoso; M. Beatrice Biló; Vesselin Dimov; Motohiro Ebisawa; Yehia M. El-Gamal; Dennis K. Ledford; Richard F. Lockey; Johannes Ring; Mario Sanchez-Borges; Gian Enrico Senna; Aziz Sheikh; Bernard Y. Thong; Margitta Worm

Posted: 07/16/2012; Curr Opin Allergy Clin Immunol. 2012;12(4):389-399. © 2012 Lippincott Williams & Wilkins

**1**

Have a written emergency protocol for recognition and treatment of anaphylaxis and rehearse it regularly.

**2**

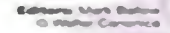
Remove exposure to the trigger if possible, eg. discontinue an intravenous diagnostic or therapeutic agent that seems to be triggering symptoms.

**3**



Assess the patient's circulation, airway, breathing, mental status, skin, and body weight (mass).





# World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis

F. Estelle R. Simons; Ledit R.F. Arduso; M. Beatrice Biló; Vesselin Dimov; Motohiro Ebisawa; Yehia M. El-Gamal; Dennis K. Ledford; Richard F. Lockey; Johannes Ring; Mario Sanchez-Borges; Gian Enrico Senna; Aziz Sheikh; Bernard Y. Thong; Margitta Worm

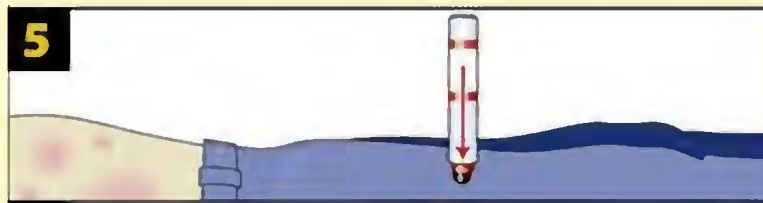
Posted: 07/16/2012; Curr Opin Allergy Clin Immunol. 2012;12(4):389-399. © 2012 Lippincott Williams & Wilkins

**Promptly and simultaneously,  
perform steps 4, 5 and 6.**

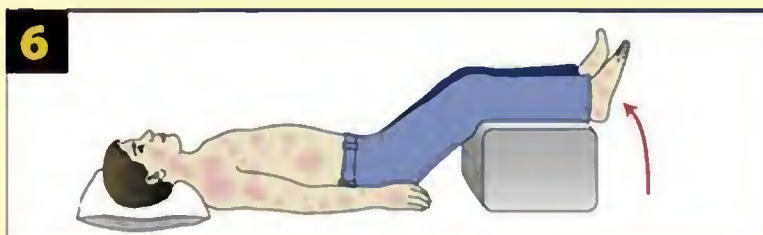
**Call for help:** resuscitation team (hospital) or emergency medical services (community) if available.



**Call for help:** resuscitation team (hospital) or emergency medical services (community) if available.



**Inject epinephrine** (adrenaline) intramuscularly in the mid-antrolateral aspect of the thigh, 0.01 mg/kg of a 1:1 000 (1 mg/mL) solution, maximum of 0.5 mg (adult) or 0.3 mg (child); **record the time of the dose and repeat it in 5-15 minutes**, if needed. Most patients respond to 1 or 2 doses.



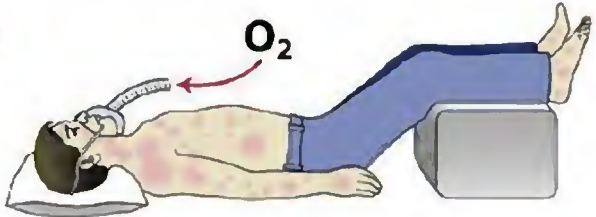
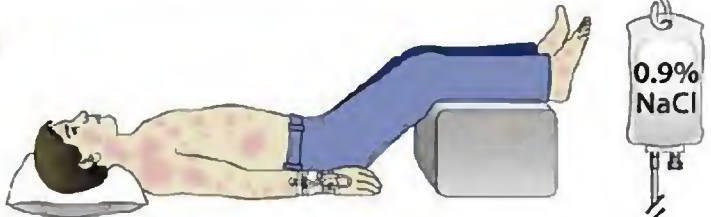

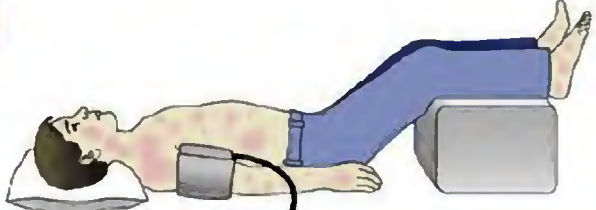
**Place patient on the back** or in a position of comfort if there is respiratory distress and/or vomiting; **elevate the lower extremities**; fatality can occur within seconds if patient stands or sits suddenly.



# World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis

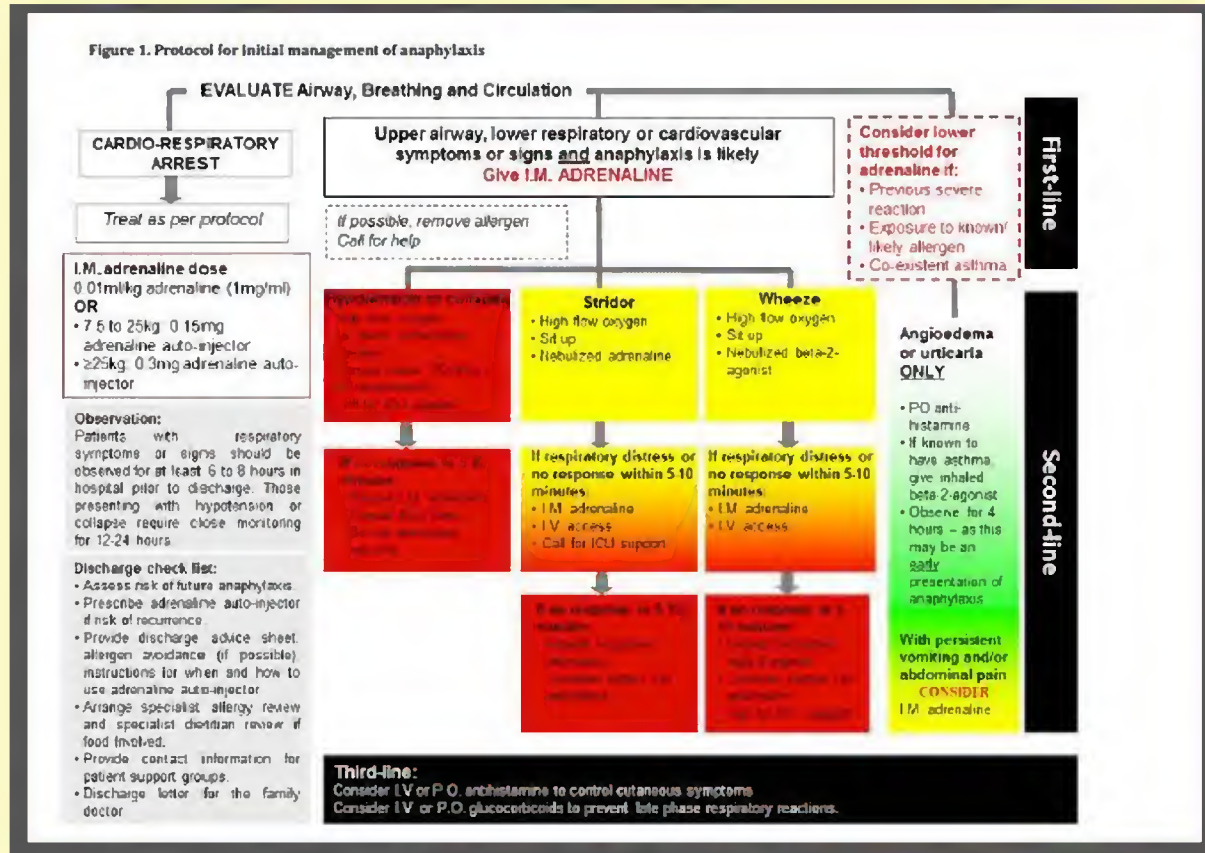
F. Estelle R. Simons; Ledit R.F. Arduso; M. Beatrice Biló; Vesselin Dimov; Motohiro Ebisawa; Yehia M. El-Gamal; Dennis K. Ledford; Richard F. Lockey; Johannes Ring; Mario Sanchez-Borges; Gian Enrico Senna; Aziz Sheikh; Bernard Y. Thong; Margitta Worm

Posted: 07/16/2012; Curr Opin Allergy Clin Immunol. 2012;12(4):389-399. © 2012 Lippincott Williams & Wilkins

<p><b>7</b></p> 	<p>When indicated, give high-flow supplemental oxygen (6-8 L/minute), by face mask or oropharyngeal airway.</p>
<p><b>8</b></p> 	<p>Establish intravenous access using needles or catheters with wide-bore cannulae (14 - 16 gauge). When indicated, give 1-2 litres of 0.9% (isotonic) saline rapidly (e.g. 5-10 mL/kg in the first 5-10 minutes to an adult; 10 mL/kg to a child).</p>
<p><b>9</b></p> 	<p>When indicated at any time, perform cardiopulmonary resuscitation with continuous chest compressions.</p>
<p><b>10</b></p> 	<p><b>In addition,</b></p> <p>At frequent, regular intervals, monitor patient's blood pressure, cardiac rate and function, respiratory status, and oxygenation (monitor continuously, if possible).</p>

# Recognition and first-line treatment of anaphylaxis.

Lieberman PL<sup>1</sup>.



Epinephrine is the only first-line treatment of anaphylaxis; it is the sole effective treatment for an acute reaction.

# AUVI-Q



# World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis

## ***Epinephrine Dosing and Route of Administration***

Epinephrine should be injected by the intramuscular route in the mid-anterolateral thigh as soon as anaphylaxis is diagnosed or strongly suspected, in a dose of 0.01 mg/kg of a 1:1,000 (1 mg/mL) solution, to a maximum of 0.5 mg in adults (0.3 mg in children).

This achieves peak plasma and tissue concentrations rapidly. Depending on the severity of the episode and the response to the initial injection, the dose can be repeated every 5–15 minutes, as needed.

Most patients respond to 1 or 2 doses of epinephrine injected intramuscularly promptly; however, more than 2 doses are occasionally required.

Somministrazione dell'adrenalina con siringhe da tubercolina

## OCCORRENTE SEMPRE PRONTO



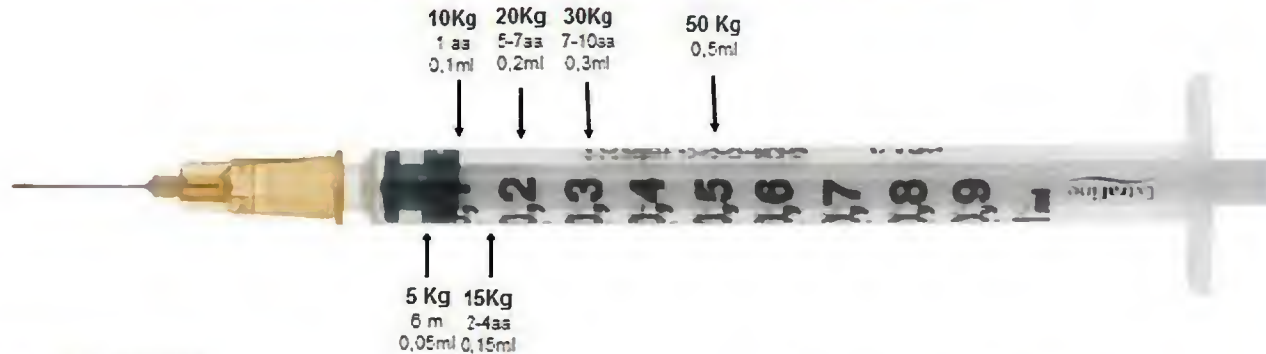
1) adrenalina 1ml=1mg  
(0,01 mg/ kg)  
NON DILUIRE

2) siringa tubercolina tacche in ml  
ago estraibile

3) ago IM



**Prima cambia l'ago, poi aspira l'adrenalina**



Oppure: **fastjekt**  
165 mcgr - meno di 30 Kg  
330 mcgr - piu'di 30 Kg



in una busta "anafilassi"  
tenere pronto l'occorrente



SI



NI



NO

## FASTJEKT

### *Somministrare Adrenalina*

- 1) Prendere la Adrenalina auto-iniettabile e togliere il tappo



- 2) Puntarlo contro il muscolo anterolaterale della coscia



- 3) Premere con forza fino a che non si sente un click e mantenerlo premuto per almeno 10 secondi



- 4) Estrarre la siringa e massaggiare la sede della iniezione per almeno 10 secondi. Mantenere sdraiato il bambino. Chiamare il 118 o portarlo ad un Pronto Soccorso



165 – 330 mcg

## CHENPEN

150 – 300 mcg



JEXT



REVIEW

Open Access

# CSACI position statement: epinephrine auto-injectors and children < 15 kg



Michelle Halbrich<sup>1\*</sup>, Douglas P. Mack<sup>2</sup>, Stuart Carr<sup>3</sup>, Wade Watson<sup>4</sup> and Harold Kim<sup>5,6</sup>

The Canadian Society of Allergy and Immunology (CSACI) therefore recommends, for the child weighing less than 15 kg, given the lack of a suitable alternative, prescribing the 0.15 mg epinephrine autoinjector.

Adverse effects of an epinephrine dose of 0.15 mg given intramuscularly in infants or children weighing less than 15 kg **are expected to be mild and transient** at the plasma epinephrine concentrations achieved; therefore, these effects need to be measured against **the consequences of not receiving epinephrine at all, which can include fatality.**



## ICON: food allergy.

[Burks AW](#), [Tang M](#), [Sicherer S](#), [Muraro A](#), [Eigenmann PA](#), [Ebisawa M](#), [Fiocchi A](#), [Chiang W](#), [Beyer K](#), [Wood R](#), [Hourihane J](#), [Jones SM](#), [Lack G](#), [Sampson HA](#).

# Cell-mediated reactions

Cell mediated (delayed onset/chronic)	Food protein–induced enterocolitis syndrome	Primarily affects infants; chronic exposure: emesis, diarrhea, poor growth, lethargy; re-exposure after restriction: emesis, diarrhea, hypotension (15%) 2 hours after ingestion	Cow's milk, soy, rice, oat, meat
	Food protein–induced allergic proctocolitis	Mucus-laden, bloody stools in infants	Milk (through breast-feeding)
	Allergic contact dermatitis	Often occupational because of chemical moieties, oleoresins. Systemic contact dermatitis is a rare variant because of ingestion	Spices, fruits, vegetables
	Heiner syndrome	Pulmonary infiltrates, failure to thrive, iron deficiency anemia	Cow's milk

# Non-IgE-mediated gastrointestinal food allergies in children

Jean-Christoph Caubet<sup>1,2</sup>, Hania Szajewska<sup>3</sup>, Raanan Shamir<sup>4</sup> & Anna Nowak-Węgrzyn<sup>1</sup>

PAI 2016

**Table 1** Clinical characteristics of non-IgE-mediated gastrointestinal food allergies

	FPIES	FPIAP	FPE
Typical age of onset	Days to 1 year	Days to 6 months	2–24 months
Symptoms			
Emesis	Prominent	No	Intermittent
Diarrhea	Severe	No	Moderate
Bloody stools	Severe	Moderate	Rare
Edema	Acute, severe	No	Moderate
Shock	15–20%	No	No
Failure to thrive	Moderate	No	Moderate
Allergy evaluation			
Food prick skin test	Negative*	Negative	Negative
Serum food-specific IgE	Negative*	Negative	Negative
Total IgE	Normal	Normal	Normal
Peripheral blood eosinophilia	No	Occasional	No
Biopsy findings			
Villous injury	Patchy, variable	No	Variable, crypt length
Colitis	Prominent	Focal	No
Mucosal erosions	Occasional	Occasional, linear	No
Lymph nodular hyperplasia	No	Common	No
Eosinophils	Prominent	Prominent	Few
Food challenge	Vomiting in 4–6 h; diarrhea in 5–8 h	Rectal bleeding in 6–72 h	Vomiting, diarrhea, or both in 40–72 h

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**International consensus guidelines for the diagnosis and management of food protein–induced enterocolitis syndrome: Executive summary—Workgroup Report of the Adverse Reactions to Foods Committee, American Academy of Allergy, Asthma & Immunology**

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J Allergy Clin Immunol 2017;139:1111-26

Food protein–induced enterocolitis (FPIES) is a **non-IgE cell mediated food allergy** that can be severe and lead to shock. Despite the potential seriousness of reactions, awareness of FPIES is low; high-quality studies providing insight into pathophysiology, diagnosis, and management are lacking; and clinical outcomes are poorly established.

# International consensus guidelines for the diagnosis and management of food protein–induced enterocolitis syndrome: Executive summary—Workgroup Report of the Adverse Reactions to Foods Committee, American Academy of Allergy, Asthma & Immunology



J Allergy Clin Immunol 2017;139:1111-26

TABLE I. Proposed defining features for clinical phenotyping of FPIES

FPIES subtypes	Defining features
Age of onset	
Early	Younger than age 9 mo
Late	Older than age 9 mo
Severity	
Mild-to-moderate	Repetitive emesis with or without diarrhea, pallor, mild lethargy
Severe	Repetitive projectile emesis with or without diarrhea, pallor, lethargy, dehydration, hypotension, shock, methemoglobinemia, metabolic acidosis
Timing and duration of symptoms	
Acute	Occurs with intermittent food exposures, emesis starts usually within 1-4 h, accompanied by lethargy and pallor; diarrhea can follow within 24 hours, with usual onset of 5-10 h. Usual resolution of symptoms within 24 h after elimination of the food from the diet. Growth is normal, and child is asymptomatic during food trigger elimination.
Chronic	Occurs with daily ingestion of the food (eg, feeding with CM- or soy-based formula in an infant); symptoms include intermittent emesis, chronic diarrhea, poor weight gain, or FTT. Infants with chronic FPIES usually return to their usual state of health within 3-10 d of switching to a hypoallergenic formula, although in severe cases temporary bowel rest and intravenous fluids might be necessary. Subsequent feeding of the offending food after a period of avoidance results in acute symptoms.
IgE positivity	
Classic	Food specific, IgE negative
Atypical	Food specific, IgE positive

# International consensus guidelines for the diagnosis and management of food protein–induced enterocolitis syndrome: Executive summary—Workgroup Report of the Adverse Reactions to Foods Committee, American Academy of Allergy, Asthma & Immunology



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J Allergy Clin Immunol 2017;139:1111-26

TABLE II. Proposed defining features of mild and severe acute FPIES

	Mild-to-moderate acute FPIES	Severe acute FPIES
Clinical features	<p><b>Required</b></p> <ul style="list-style-type: none"> <li>● Vomiting (onset usually 1-4 h, can range from 30 min to 6 h): few episodes of intermittent vomiting (1-3), can be bilious</li> <li>● Decreased activity level</li> <li>● Pallor</li> <li>● Self-resolving; the child is able to tolerate oral rehydration at home</li> </ul> <p><b>Optional</b></p> <ul style="list-style-type: none"> <li>● Mild watery diarrhea, onset usually within 24 hours, can be bloody (occasionally)</li> </ul>	<p><b>Required</b></p> <ul style="list-style-type: none"> <li>● Vomiting (onset usually at 1-4 h, can range from 30 min to 6 h): projectile (forceful), repetitive (<math>\geq 4</math>), bilious and dry heaving</li> <li>● Altered behavior ranging from decreased activity to lethargy</li> <li>● Pallor</li> <li>● Dehydration</li> <li>● Requires intravenous hydration</li> </ul> <p><b>Optional</b></p> <ul style="list-style-type: none"> <li>● Hypotension</li> <li>● Abdominal distention</li> <li>● Hypothermia</li> <li>● Diarrhea, onset usually within 24 hours, can be bloody</li> <li>● Hospitalization</li> </ul>
Laboratory features (optional, when available)	<ul style="list-style-type: none"> <li>● Increased white blood cell count with neutrophilia</li> <li>● Thrombocytosis</li> <li>● Stool might be positive for leukocytes, eosinophils, or increased carbohydrate content</li> </ul>	<ul style="list-style-type: none"> <li>● Increased white blood cell count with neutrophilia</li> <li>● Thrombocytosis</li> <li>● Metabolic acidosis</li> <li>● Methemoglobinemia</li> <li>● Stool might be positive for leukocytes, eosinophils, or increased carbohydrate content</li> </ul>



**International consensus guidelines for the diagnosis and management of food protein–induced enterocolitis syndrome: Executive summary—Workgroup Report of the Adverse Reactions to Foods Committee, American Academy of Allergy, Asthma & Immunology**



J Allergy Clin Immunol 2017;139:1111-26

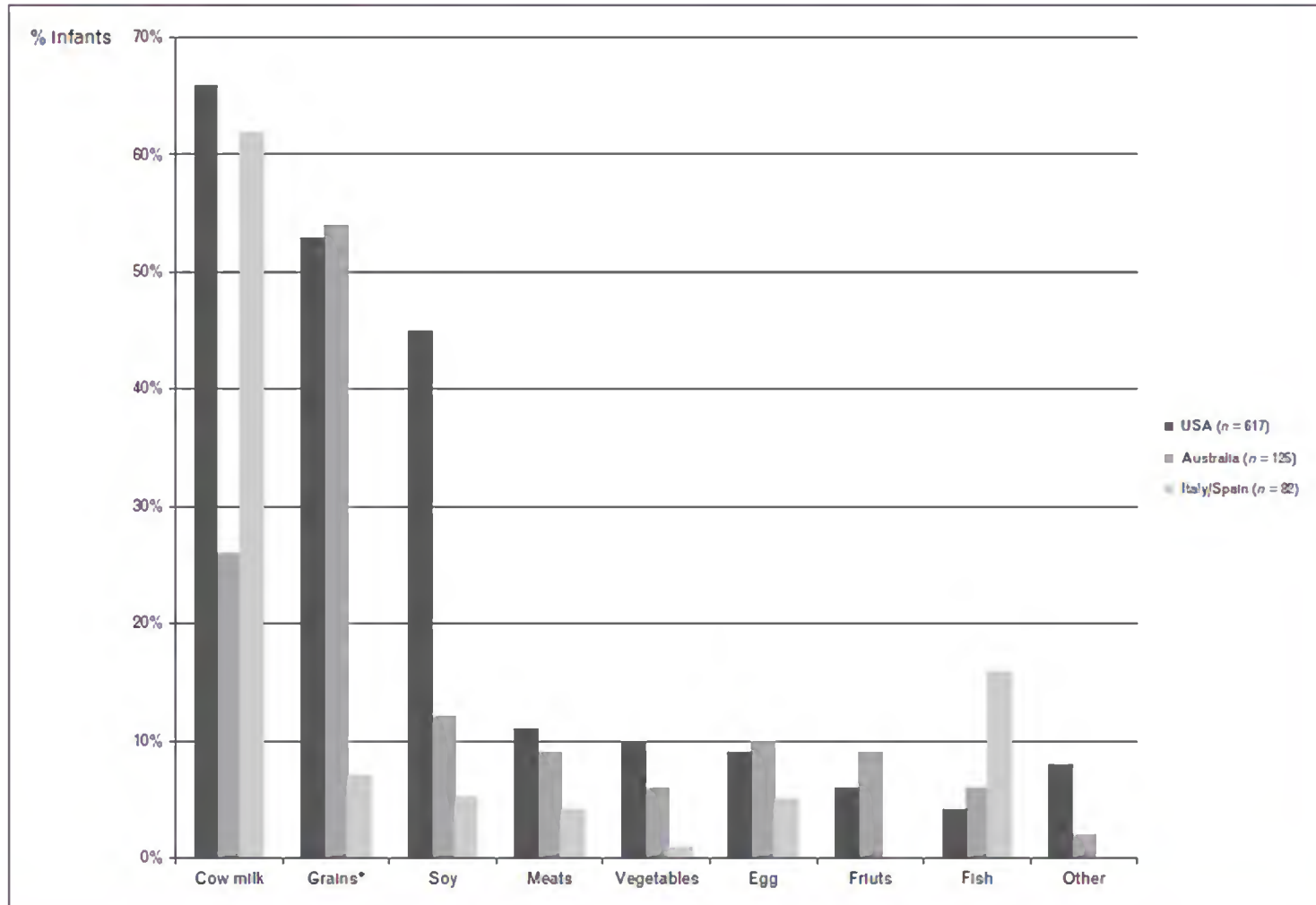
TABLE IV. Diagnostic criteria for patients presenting with possible FPIES

Acute FPIES	
Major criterion: Vomiting in the 1- to 4-h period after ingestion of the suspect food and absence of classic IgE-mediated allergic skin or respiratory symptoms	Minor criteria: <ol style="list-style-type: none"><li>1. A second (or more) episode of repetitive vomiting after eating the same suspect food</li><li>2. Repetitive vomiting episode 1-4 h after eating a different food</li><li>3. Extreme lethargy with any suspected reaction</li><li>4. Marked pallor with any suspected reaction</li><li>5. Need for emergency department visit with any suspected reaction</li><li>6. Need for intravenous fluid support with any suspected reaction</li><li>7. Diarrhea in 24 h (usually 5-10 h)</li><li>8. Hypotension</li><li>9. Hypothermia</li></ol>

The diagnosis of FPIES requires that a patient meets the major criterion and  $\geq 3$  minor criteria. If only a single episode has occurred, a diagnostic OFC should be strongly considered to confirm the diagnosis, especially because viral gastroenteritis is so common in this age group. Furthermore, although not a criteria for diagnosis, it is important to recognize that acute FPIES reactions will typically completely resolve over a matter of hours compared with the usual several-day time course of gastroenteritis. The patient should be asymptomatic and growing normally when the offending food is eliminated from the diet.

# Epidemiology of food protein-induced enterocolitis syndrome

Sam Mehr<sup>a</sup>, Katie Frith<sup>b</sup>, and Dianne E. Campbell<sup>a,c</sup>



# LA TERAPIA DELLE AA

J ALLERGY CLIN IMMUNOL  
VOLUME 126, NUMBER 6

BOYCE ET AL 55

**Guidelines for the Diagnosis and Management of Food Allergy in the United States: Report of the NIAID-Sponsored Expert Panel**

**JAMA**

Diagnosing and Managing Common Food Allergies: A Systematic Review

REVIEW ARTICLE

World Allergy Organization (WAO) Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA) Guidelines

Issue date: February 2011

**Food allergy in children and young people**

Diagnosis and assessment of food allergy in children and young people in primary care and community settings

POSITION PAPER

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

doi: 10.1111/cea.12302

*Clinical & Experimental Allergy*, 44, 642-672

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**BSACI GUIDELINES**

BSACI guideline for the diagnosis and management of cow's milk allergy

D. Luyt<sup>1</sup>, H. Ball<sup>1</sup>, N. Makwana<sup>2</sup>, M. R. Green<sup>3</sup>, K. Bravin<sup>3</sup>, S. M. Nasser<sup>3</sup> and A. T. Clark<sup>3</sup>

<sup>1</sup>University Hospitals of Leicester NHS Trust, Leicester, UK; <sup>2</sup>Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, UK and <sup>3</sup>Cambridge University Hospital NHS Foundation Trust, Cambridge, UK

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## ICON: Food allergy

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A. Wesley Burks, MD,<sup>a</sup> Mimi Tang, MBBS, PhD,<sup>b</sup> Scott Sicherer, MD,<sup>c</sup> Antonella Muraro, MD, PhD,<sup>d</sup> Philippe A. Eigenmann, MD,<sup>e</sup> Motohiro Ebisawa, MD, PhD,<sup>f</sup> Alessandro Fiocchi, MD,<sup>g</sup> Wen Chiang, MBBS, MRCPCH,<sup>h</sup> Kirsten Beyer, MD,<sup>i</sup> Robert Wood, MD,<sup>j</sup> Jonathan Hourihane, MB, DM, MRCPI, FRCPHC,<sup>k</sup> Stacie M. Jones, MD,<sup>l</sup> Gideon Lack, FRCPCH,<sup>m</sup> and Hugh A. Sampson, MD<sup>c</sup> *Chapel Hill, NC, Parkville, Australia, New York, NY, Padua, Italy, Geneva, Switzerland, Kanagawa, Japan, Milan, Italy, Singapore, Berlin, Germany, Baltimore, Md, Cork, Ireland, Little Rock, Ark, and London, United Kingdom*

### J Allergy Clin Immunol 2012

**[\\*The primary therapy for food allergy is strict avoidance of the causal food or foods.](#)**

**\*This is true for IgE-mediated, non-IgE-mediated, and mixed IgE- and non-IgE-mediated food allergy syndromes.**

**GRADE****World Allergy Organization (WAO)  
Diagnosis and Rationale for Action against  
Cow's Milk Allergy (DRACMA) Guidelines**

Treating cow's milk allergy (CMA) entails a nutritional risk, as milk is a staple food in particular for children less than 2 years of age. When a replacement formula is needed, the allergist can avail themselves with different types of formula:

1. Amino acid formula (AAF)
2. Extensively hydrolyzed formula of cow's milk proteins (eHF)
3. Soy formula (SF)
4. Rice extensively hydrolyzed formula (RHF)
5. Soy hydrolyzed formula (SHE)
6. Other mammal's milks.

**2010**

## APLV IgE-mediata: fenotipi clinici

# WAO (WAO) Diagnosis and Rationale for Action (DRA) for Cow's Milk Allergy (DRACMA) Guidelines

Alfonso Di Lorenzo, Jan Brozek, Holger Schünemann, (Chair), Sami L. Bahna, Andrea von Berg, Kees van Halbeek, Martin Bozzola, Julia Bradsher, Enrico Compalati, Motohiro Ebisawa, Maria Antonietta Tronchetti, Haiqi Li, Ralf G. Heine, Paul Keith, Gideon Lack, Massimo Landi, Alberto Martelli, Francesco Rancé, Hugh Sampson, Airton Stein, Luigi Terracciano, and Stefan Vieths

WAO Journal - April 2010

### Clinical Recommendations

**In children with IgE-mediated CMA at high risk of anaphylactic reactions** (prior history of anaphylaxis and currently not using extensively hydrolyzed milk formula), we suggest amino acid formula rather than extensively hydrolyzed milk formula (conditional recommendation/very low quality evidence).

**In children with IgE-mediated CMA at low risk of anaphylactic reactions** (no prior history of anaphylaxis or currently on extensively hydrolyzed milk formula), we suggest extensively hydrolyzed milk formula over amino acid formula (conditional recommendation/very low quality evidence).

# DRACMA one year after: Which changes have occurred in diagnosis and treatment of CMA in Italy?

2011

## CLINICAL RECOMMENDATIONS

Clinical presentation	1st choice	2nd choice	3rd choice
Anaphylaxis	AAF <sup>+</sup>	eHF <sup>#5</sup>	SF
Acute urticaria or angioedema	eHF <sup>5b</sup>	AAF <sup>^</sup> /SF <sup>°</sup>	
Atopic dermatitis	eHF <sup>5b</sup>	AAF <sup>^</sup> /SF <sup>°</sup>	
Immediate gastrointestinal allergy	eHF <sup>5b</sup>	AAF <sup>^</sup> /SF <sup>°</sup>	
Allergic eosinophilic oesophagitis	AAF		
Gastroesophageal reflux disease (GERD)	eHF <sup>b</sup>	AAF	
Cow's milk protein-induced enteropathy	eHF <sup>5b</sup>	AAF	
Food protein-induced enterocolitis syndrome (FPIES)	eHF <sup>*</sup>	AAF	
CM protein-induced gastroenteritis and proctocolitis	eHF <sup>p</sup>	AAF	
Severe irritability (colic)	eHF <sup>b</sup>	AAF	
Constipation	eHF <sup>b</sup>	AAF	Donkey milk <sup>x</sup>
Milk-induced chronic pulmonary disease (Heiner's syndrome) **	AAF <sup>^</sup>	eHF	SF

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

## (B1) Elimination diet

A sufficient elimination diet should be based on a formal allergy diagnosis identifying the food allergen(s) responsible of the patient's symptoms/reactions. The indications should be re-evaluated at appropriate intervals

Appropriate dietary avoidance is the key treatment in the management of food allergy

Patients with food allergy who are on long-term elimination diets should have access to appropriate dietetic counseling, ideally by a dietitian with competencies in food allergy, and regular monitoring of growth (in children)

Extensively hydrolyzed cow's milk formulas with documented hypoallergenicity can be recommended as first choice for the treatment of cow's milk allergy, especially in infants and young children. Amino acid formulas can also be recommended especially for the subgroup of patients with more severe symptoms

Soy formulas should not be recommended before 6 months of age and at any age in the presence of gastrointestinal symptoms. From 6 to 12 months, it can be considered on a case-by-case basis

mula (67) or meat-based formula (68). In summary, it is recommended that the choice of an appropriate cow's milk substitute should be assessed carefully balancing the following factors: age, type of food allergy (IgE/non-IgE), coexistence of gastrointestinal symptoms, history of life-threatening reactions, and nutritional requirements as well as cost-effectiveness.

Fenotipi immunologici e clinici

IV  
III  
D

A

I B

2014



# BSACI GUIDELINES

## BSACI guideline for the diagnosis and management of cow's milk allergy

D. Luyt<sup>1</sup>, H. Ball<sup>1</sup>, N. Makwana<sup>2</sup>, M. R. Green<sup>1</sup>, K. Bravin<sup>1</sup>, S. M. Nasser<sup>3</sup> and A. T. Clark<sup>3</sup>

<sup>1</sup>University Hospitals of Leicester NHS Trust, Leicester, UK, <sup>2</sup>Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, UK and <sup>3</sup>Cambridge University Hospital NHS Foundation Trust, Cambridge, UK

- **A hypoallergenic formula is one that meets the defined criterion of 90% clinical tolerance (with 95% confidence limits) in infants with proven cow's milk allergy.**
- **Only amino acid and extensively hydrolysed formulas meet this criterion and are the formulas of choice for the treatment of cow's milk allergy.**
- **Some individuals highly sensitized to cow's milk may react to residual cow's milk proteins in extensively hydrolysed formulas (EHFs) and will thus require an amino acid formula (AAF)**

2014

## BSACI guideline for the diagnosis and management of cow's milk allergy

D. Luyt<sup>1</sup>, H. Ball<sup>1</sup>, N. Makwana<sup>2</sup>, M. R. Green<sup>1</sup>, K. Bravin<sup>1</sup>, S. M. Nasser<sup>3</sup> and A. T. Clark<sup>3</sup>

<sup>1</sup>University Hospitals of Leicester NHS Trust, Leicester, UK, <sup>2</sup>Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, UK and <sup>3</sup>Cambridge University Hospital NHS Foundation Trust, Cambridge, UK

# Extensively hydrolysed formulas

There are differences between brands

- The protein source
- The size of peptides under 1000 Daltons
- Palatability

# Cow's milk allergy: evidence-based diagnosis and management for the practitioner

Carlos Lifschitz · Hania Szajewska

## Which formula and to whom

### Extensively hydrolyzed formulas

The American Academy of Pediatrics defines as “extensively hydrolyzed formula” those containing only oligopeptides that have a molecular weight <3.000 Da

# FORMULE IDROLISATE

## Secondo il grado di idrolisi :

- Idrolisi parziale (pHF o HA) (“lowdegree”)
- Idrolisi estensiva (eHF) (“extensive” or “high degree”)

## Secondo le proteine utilizzate:

- Idrolisati di caseina (eHF-C)
- Idrolisati di sieroproteine (eHF-W)

## ***Formule a base di AA:***

***costruite dal “basso” con l’aggiunta di AA***

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

### (B1) Elimination diet

A sufficient elimination diet should be based on a formal allergy diagnosis identifying the food allergen(s) responsible of the patient's symptoms/reactions. The indications should be re-evaluated at appropriate intervals	IV	D
Appropriate dietary avoidance is the key treatment in the management of food allergy	IV	D
Patients with food allergy who are on long-term elimination diets should have access to appropriate dietetic counseling, ideally by a dietitian with competencies in food allergy, and regular monitoring of growth (in children)	IV	D
Extensively hydrolyzed cow's milk formulas with documented hypoallergenicity can be recommended as first choice for the treatment of cow's milk allergy, especially in infants and young children. Amino acid formulas can also be recommended especially for the subgroup of patients with more severe symptoms	I	A
Soy formulas should not be recommended before 6 months of age and at any age in the presence of gastrointestinal symptoms. From 6 to 12 months, it can be considered on a case-by-case basis	I	B

mula (67) or meat-based formula (68). In summary, it is recommended that the choice of an appropriate cow's milk substitute should be assessed carefully balancing the following factors: age, type of food allergy (IgE/non-IgE), coexistence of gastrointestinal symptoms, history of life-threatening reactions, and nutritional requirements as well as cost-effectiveness.

# Safety and tolerance of a new extensively hydrolyzed rice protein-based formula in the management of infants with cow's milk protein allergy

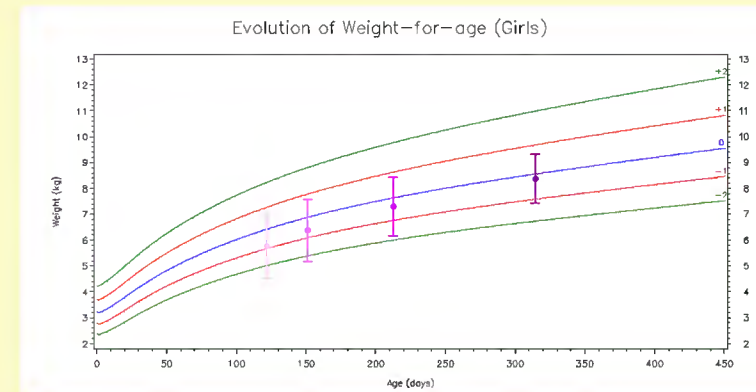
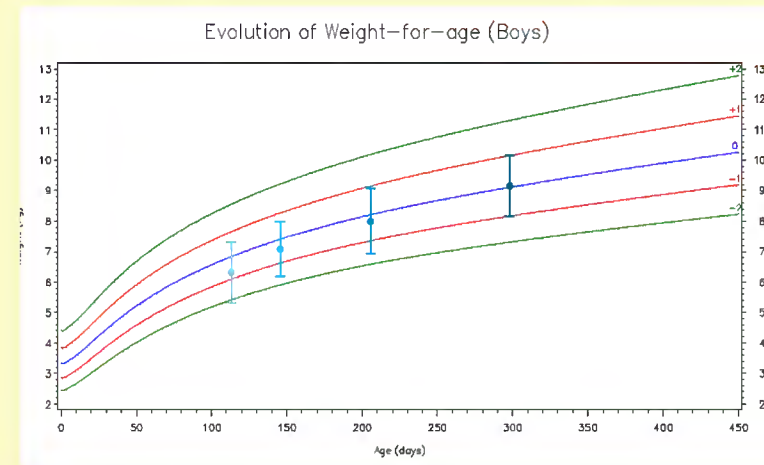
Vandenplas 2014

**A prospective trial** was performed to evaluate the hypo-allergenicity and safety of a new eRHF in infants with a confirmed CMPA. Patients were fed the study formula for **6 months**. Clinical tolerance of the eRHF was evaluated with a symptom-based score (SBS) and growth (weight and length) was monitored.

**Forty infants (mean age, 3.4 months; range, 1–6 months) with CMPA confirmed by a food challenge were enrolled.**

**Conclusion:** In accordance with current guidelines, this eRHF was tolerated by more than 90 % of children with proven CMPA with a 95 % confidence interval.

**This eRHF is an adequate and safe alternative to cow milk-based eHF.**



# Management of food allergy

J ALLERGY CLIN IMMUNOL  
VOLUME 126, NUMBER 6

BOYCE ET AL S5

**Guidelines for the Diagnosis and Management of Food Allergy in the United States: Report of the NIAID-Sponsored Expert Panel**

**JAMA**<sup>®</sup>

Online article and related content  
current as of May 12, 2010.

**Diagnosing and Managing Common Food Allergies: A Systematic Review**

Jennifer J. Schneider Chafen; Sydne J. Newberry; Marc A. Riedl; et al.

JAMA. 2010;303(18):1848-1856 (doi:10.1001/jama.2010.582)

<http://jama.ama-assn.org/cgi/content/full/303/18/1848>

REVIEW ARTICLE

***Until now, the cornerstones of the clinical management of food allergies have been the identification and complete avoidance of the responsible food allergen(s) and, in those who have had severe reactions, the carriage and use of self-injectable epinephrine (adrenaline). This management strategy is challenging, requiring considerable vigilance to avoid accidental exposure.***

A. Muraro<sup>1,\*</sup>, T. Werfel<sup>2,\*</sup>, K. Hoffmann-Sommergruber<sup>3,\*</sup>, G. Roberts<sup>4,5,6</sup>, K. Beyer<sup>7</sup>,  
C. Bindslev-Jensen<sup>8</sup>, V. Cardona<sup>9</sup>, A. Dubois<sup>10</sup>, G. duToit<sup>11,12</sup>, P. Eigenmann<sup>13</sup>, M. Fernandez Rivas<sup>14</sup>,  
S. Halken<sup>15</sup>, L. Hickstein<sup>16</sup>, A. Høst<sup>14</sup>, E. Knol<sup>17</sup>, G. Lack<sup>11,12</sup>, M. J. Marchisotto<sup>17</sup>, B. Niggemann<sup>7</sup>,  
B. I. Nwaru<sup>18</sup>, N. G. Papadopoulos<sup>19,20</sup>, L. K. Poulsen<sup>21</sup>, A. F. Santos<sup>11,22,23</sup>, I. Skypala<sup>24</sup>,  
A. Schoepfer<sup>25</sup>, R. Van Ree<sup>26</sup>, C. Venter<sup>4</sup>, M. Worm<sup>7</sup>, B. Vlieg-Boerstra<sup>27</sup>, S. Panesar<sup>28</sup>, D. de Silva<sup>29</sup>,  
K. Soares-Weiser<sup>30</sup>, A. Sheikh<sup>28,31</sup>, B. K. Ballmer-Weber<sup>32</sup>, C. Nilsson<sup>33</sup>, N. W. de Jong<sup>34</sup>,  
& C. A. Akdis<sup>35,36</sup> on behalf of the EAACI Food Allergy and Anaphylaxis Guidelines Group

# The rapidly changing world of food allergy in children

Katherine Anagnostou<sup>1</sup>, Rosan Meyer<sup>2</sup>, Adam Fox<sup>1</sup> and Neil Shah<sup>2,3\*</sup>

2015

Recent evidence relating to new strategies to induce tolerance development has emerged.





1) the role of desensitization to food

2) the role of baked egg and milk introduction in children with milk or egg allergies



# 1) the role of desensitization to food

# EAACI Guidelines on allergen immunotherapy: IgE-mediated food allergy

G. B. Pajno<sup>1</sup> | M. Fernandez-Rivas<sup>2</sup> | S. Arasi<sup>1,3</sup>  | G. Roberts<sup>4,5,6</sup>  | C. A. Akdis<sup>7</sup> | M. Alvaro-Lozano<sup>8</sup> | K. Beyer<sup>9,10</sup> | C. Bindslev-Jensen<sup>11</sup> | W. Burks<sup>12</sup> | M. Ebisawa<sup>13</sup> | P. Eigenmann<sup>14</sup> | E. Knol<sup>15</sup> | K. C. Nadeau<sup>16</sup>  | L. K. Poulsen<sup>17</sup> | R. van Ree<sup>18</sup> | A. F. Santos<sup>19,20,21</sup> | G. du Toit<sup>19,20,21</sup> | S. Dhimi<sup>22</sup>  | U. Nurmatov<sup>23</sup> | Y. Boloh<sup>24</sup> | M. Makela<sup>25</sup> | L. O'Mahony<sup>7</sup> | N. Papadopoulos<sup>26</sup> | C. Sackesen<sup>27</sup> | I. Agache<sup>28</sup> | E. Angier<sup>29</sup> | S. Halken<sup>30</sup> | M. Jutel<sup>31,32</sup> | S. Lau<sup>3</sup> | O. Pfaar<sup>33,34</sup> | D. Ryan<sup>35</sup> | G. Sturm<sup>36,37</sup> | E.-M. Varga<sup>38</sup> | R. G. van Wijk<sup>39</sup> | A. Sheikh<sup>35</sup> | A. Muraro<sup>40</sup> | on behalf of EAACI Allergen Immunotherapy Guidelines Group

EAACI Guidelines on allergen immunotherapy: IgE-mediated food allergy

Immunotherapy relies on the delivery of gradually increasing doses of specific allergen to increase the threshold of reaction while on therapy (also known as desensitization) and ultimately to achieve post-discontinuation effectiveness (also known as tolerance or sustained unresponsiveness).

The time period required to establish true post discontinuation effectiveness is not yet defined.

# Food allergen immunotherapy: Current status and prospects for the future



Robert A. Wood, MD *Baltimore, Md*

J Allergy Clin Immunol 2016;137:973-82

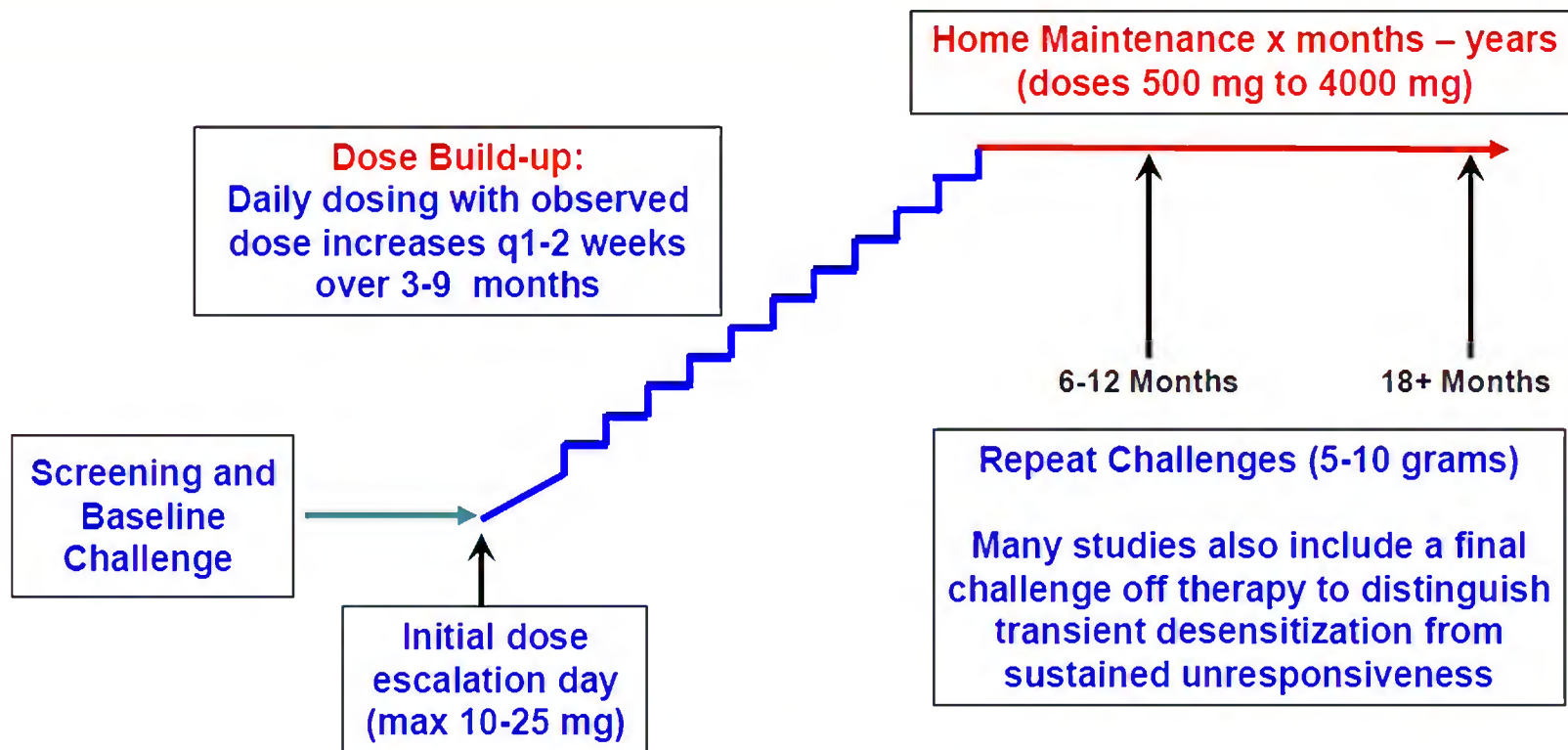
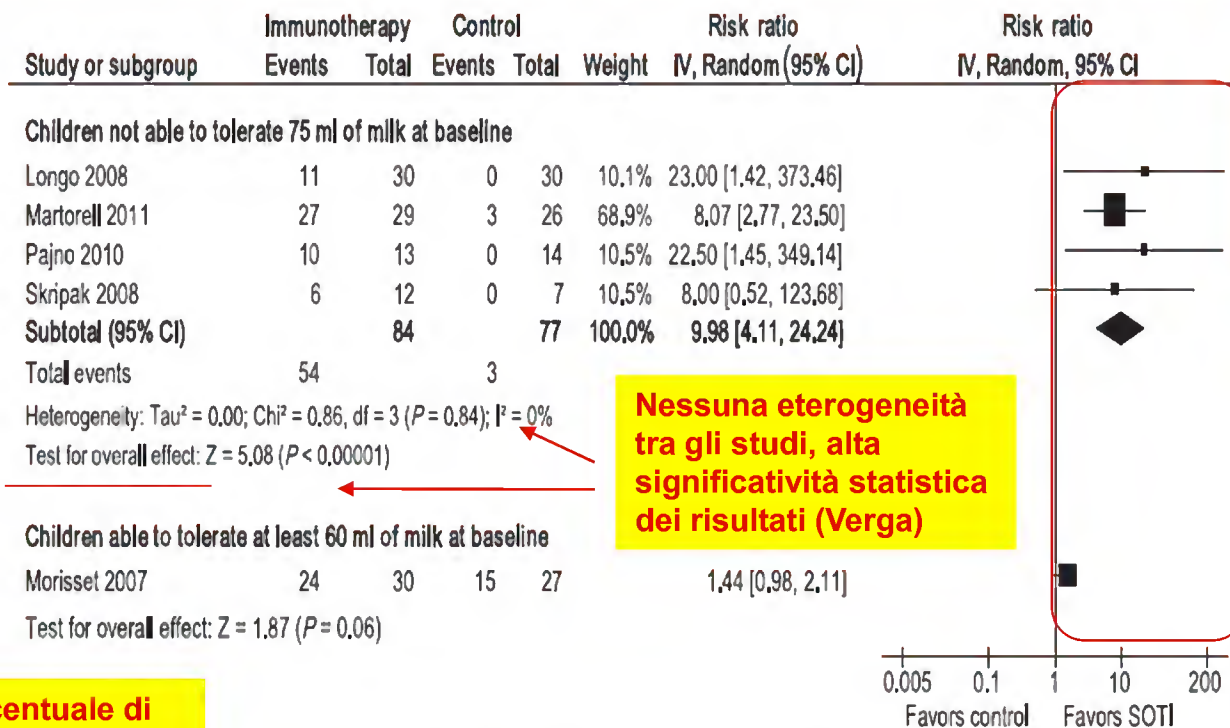


FIG 1. Schematic representation of the typical approach to OIT. For SLIT, the overall scheme is similar, with far lower goal doses and a somewhat more rapid dose build-up.

# COCHRANE META-ANALYSIS IN ALLERGY

## Oral immunotherapy for IgE-mediated cow's milk allergy: a systematic review and meta-analysis

J. L. Brożek<sup>1</sup>, L. Terracciano<sup>2</sup>, J. Hsu<sup>3</sup>, J. Kreis<sup>4,5</sup>, E. Compalati<sup>6</sup>, N. Santesso<sup>5</sup>, A. Fiocchi<sup>2</sup> and H. J. Schünemann<sup>1</sup>



IC tutti contenuti nella parte dx del forest plot, a favore del trattamento (Verga)

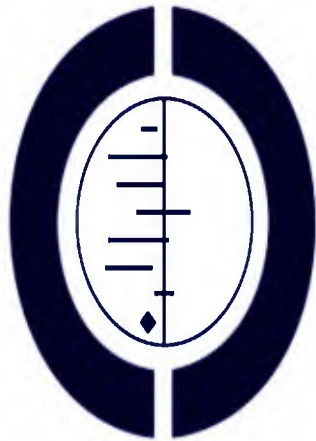
Nessuna eterogeneità tra gli studi, alta significatività statistica dei risultati (Verga)

RR= 9.98 La percentuale di pazienti che acquisiscono la tolleranza totale è, nei trattati, 10 volte superiore rispetto ai controlli (Verga)

Fig. 1. Probability of achieving full tolerance of cow's milk (i.e. being able to tolerate ≥ 150 mL of milk and eat dairy products with no problems) with oral immunotherapy, compared to placebo or elimination diet, in patients with CMA.

# Oral and sublingual immunotherapy for egg allergy (Review)

Romantsik O, Bruschetti M, Tosca MA, Zappettini S, Della Casa Alberighi O, Calevo MG



**THE COCHRANE  
COLLABORATION®**

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2014, Issue 11

<http://www.thecochranelibrary.com>

Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study

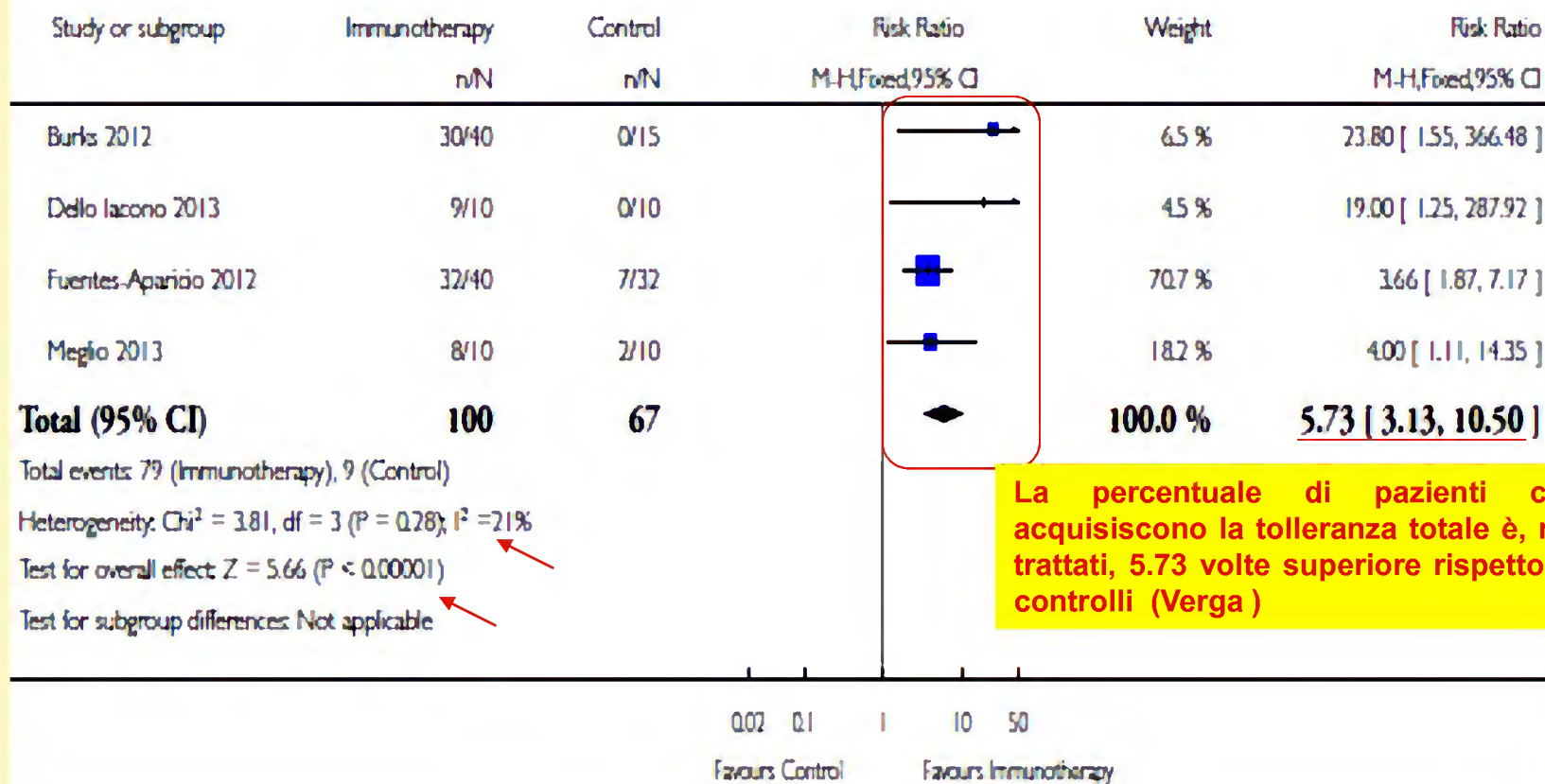
	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
Burks 2012	+	+	-	-	+	+
Dello Iacono 2013	+	+	-	-	+	+
Fuentes-Aparicio 2012	?	?	-	-	+	?
Meglio 2013	+	+	-	-	+	?

## Analysis I.I. Comparison I Oral and sublingual Immunotherapy versus no therapy for egg allergy, Outcome I Increase in the amount of egg that can be tolerated.

Review: Oral and sublingual immunotherapy for egg allergy

Comparison: I Oral and sublingual immunotherapy versus no therapy for egg allergy

Outcome: I increase in the amount of egg that can be tolerated



La percentuale di pazienti che acquisiscono la tolleranza totale è, nei trattati, 5.73 volte superiore rispetto ai controlli (Verga)

Robert A. Wood, MD *Baltimore, Md*

## Long-term efficacy

There are a paucity of long-term follow-up studies, and those that have been done indicate that even patients who appear to be completely desensitized can lose protection over time



## EAACI Guidelines on allergen immunotherapy: IgE-mediated food allergy

### Long-term safety

Long-term safety is not addressed in trials; these predominantly focus on efficacy and short-term safety. The development of EoE after OIT has been reported.

In a SR, new-onset EoE was found in 2.7% (95% CI 1.7, 4.0). All the studies analyzed were retrospective with significant publication bias suggested by funnel plot analysis.

It is therefore recommended to monitor patients for symptoms of new-onset EoE which may appear in the course of FA OIT (Grade A).

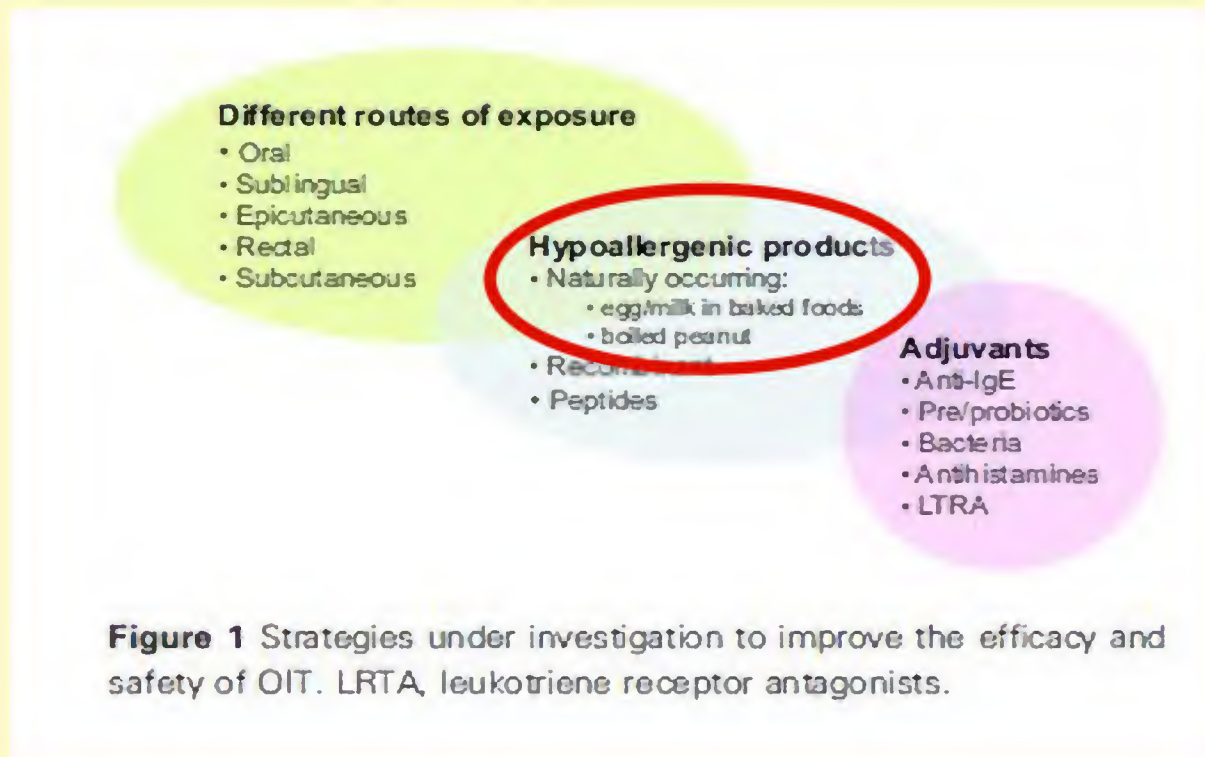
**EAACI Guidelines on allergen immunotherapy: IgE-mediated food allergy**

Allergen immunotherapy (AIT) is potentially a curative therapy.

FA-AIT should only be performed in research centers or in clinical centers with an extensive experience in FA-AIT.

Patients and their families should be provided with information about the use of FA-AIT for IgE-mediated food allergy to allow them to make an informed decision about the therapy.

## REVIEW ARTICLE

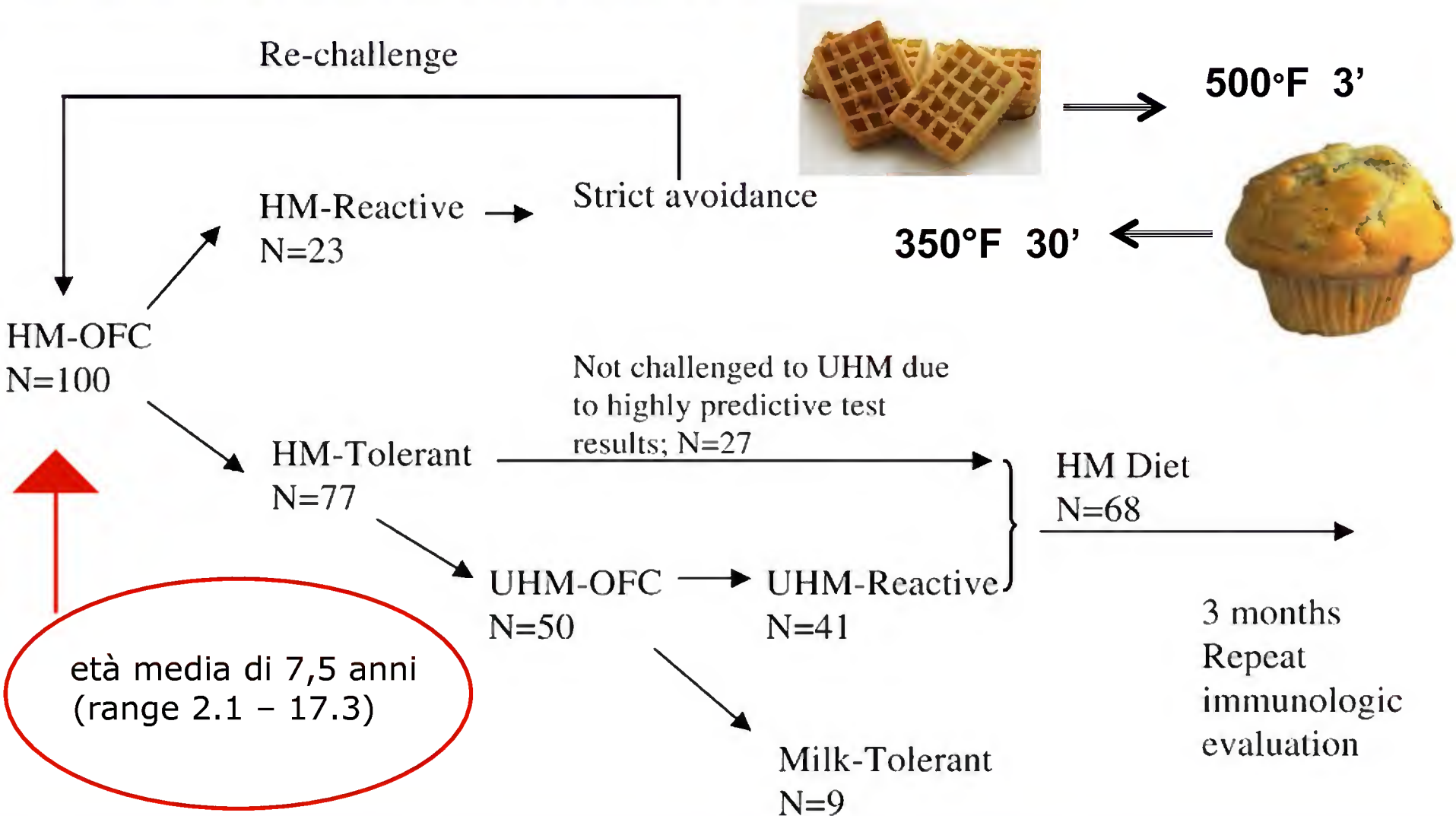
**Improving the safety of oral immunotherapy for food allergy**Marta Vazquez-Ortiz<sup>1</sup> & Paul J. Turner<sup>1,2</sup><sup>1</sup>Section of Paediatrics, Imperial College London, London, UK; <sup>2</sup>Discipline of Paediatrics and Child Health, School of Medicine, University of Sydney, Sydney, NSW, Australia**To cite this article:** Vazquez-Ortiz M, Turner PJ. Improving the safety of oral immunotherapy for food allergy. *Pediatr Allergy Immunol* 2016; **27**: 117–125.

**2) the role of baked egg and  
milk introduction in children  
with milk or egg allergies**

# Tolerance to extensively heated milk in children with cow's milk allergy

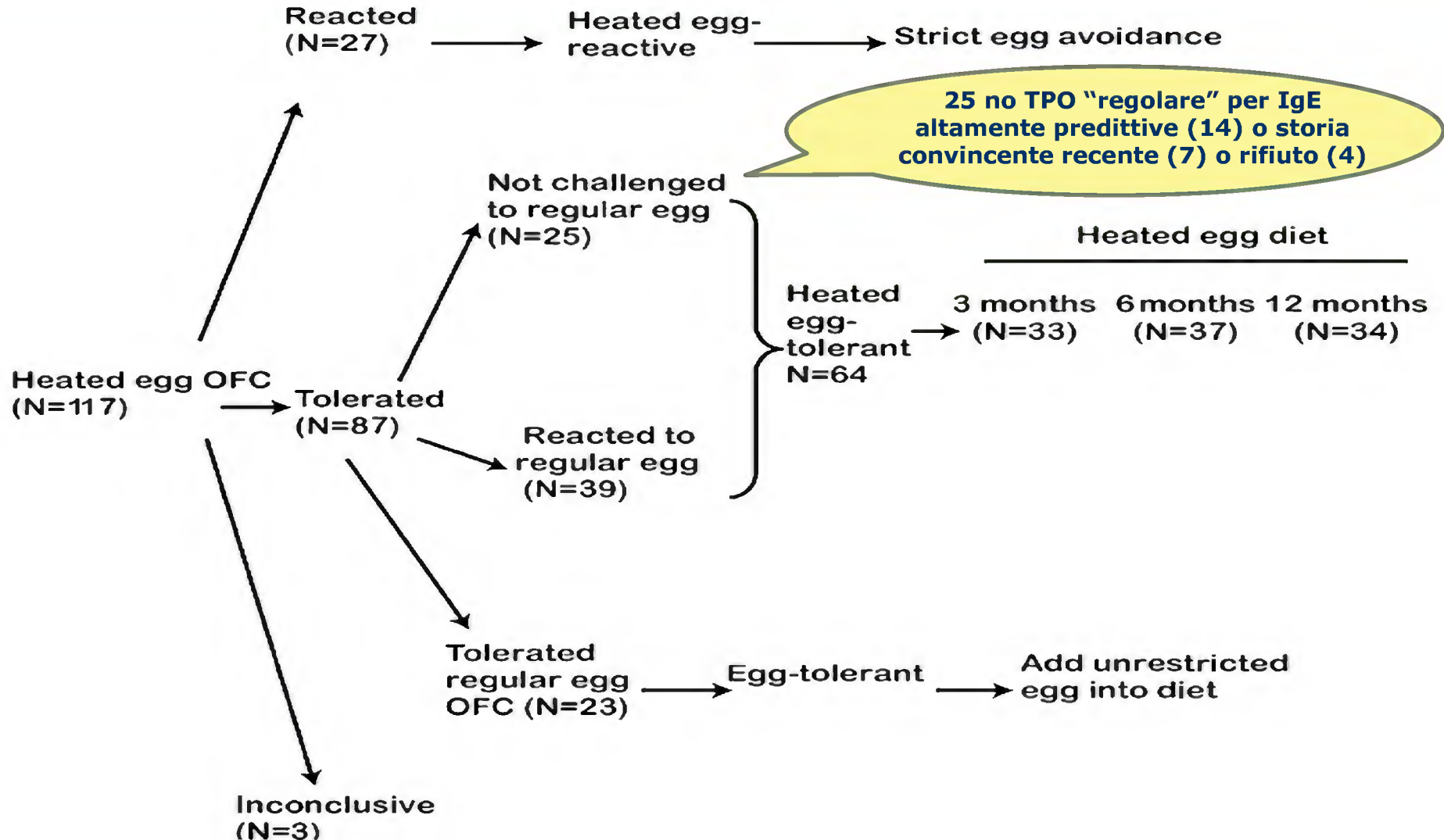
2008

Anna Nowak-Wegrzyn, MD, Katherine A. Bloom, MD, Scott. H. Sicherer, MD, Wayne G. Shreffler, MD, PhD, Sally Noone, RN, Niya Wanich, MD, and Hugh A. Sampson, MD *New York, NY*



# Heather Lemon-Mulè et al

## Immunologic changes in children with egg allergy ingesting extensively heated egg JACI 2008



# Dietary baked milk accelerates the resolution of cow's milk allergy in children

Jennifer S. Kim, MD,\* Anna Nowak-Węgrzyn, MD,\* Scott H. Sicherer, MD, Sally Noone, RN, Erin L. Moshier, MS, and Hugh A. Sampson, MD *New York, NY*

[J Allergy Clin Immunol.](#) 2011 Jul;128(1):125-131.e2. Epub 2011 May 23

Tolerance of baked milk is a marker of transient IgE-mediated cow's milk allergy, whereas reactivity to baked milk portends a more persistent phenotype. The addition of baked milk to the diet of children tolerating such foods appears to accelerate the development of unheated milk tolerance compared with strict avoidance

0 6 12 18 24 30 36 42 48 54 60

Months Following First Visit

75%

33%

# Dietary baked egg accelerates resolution of egg allergy in children

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Stephanie A. Leonard, MD,<sup>a\*</sup> Hugh A. Sampson, MD,<sup>a</sup> Scott H. Sicherer, MD,<sup>a</sup> Sally Noone, RN,<sup>a</sup> Erin L. Moshier, MS,<sup>b</sup> James Godbold, PhD,<sup>b</sup> and Anna Nowak-Węgrzyn, MD<sup>a</sup> *New York, NY*

J Allergy Clin Immunol 2012;130:473-80



**Initiation of a baked egg diet accelerates the development of regular egg tolerance compared with strict avoidance.**



**NON ESISTE SOLO IL BIANCO ED IL NERO**

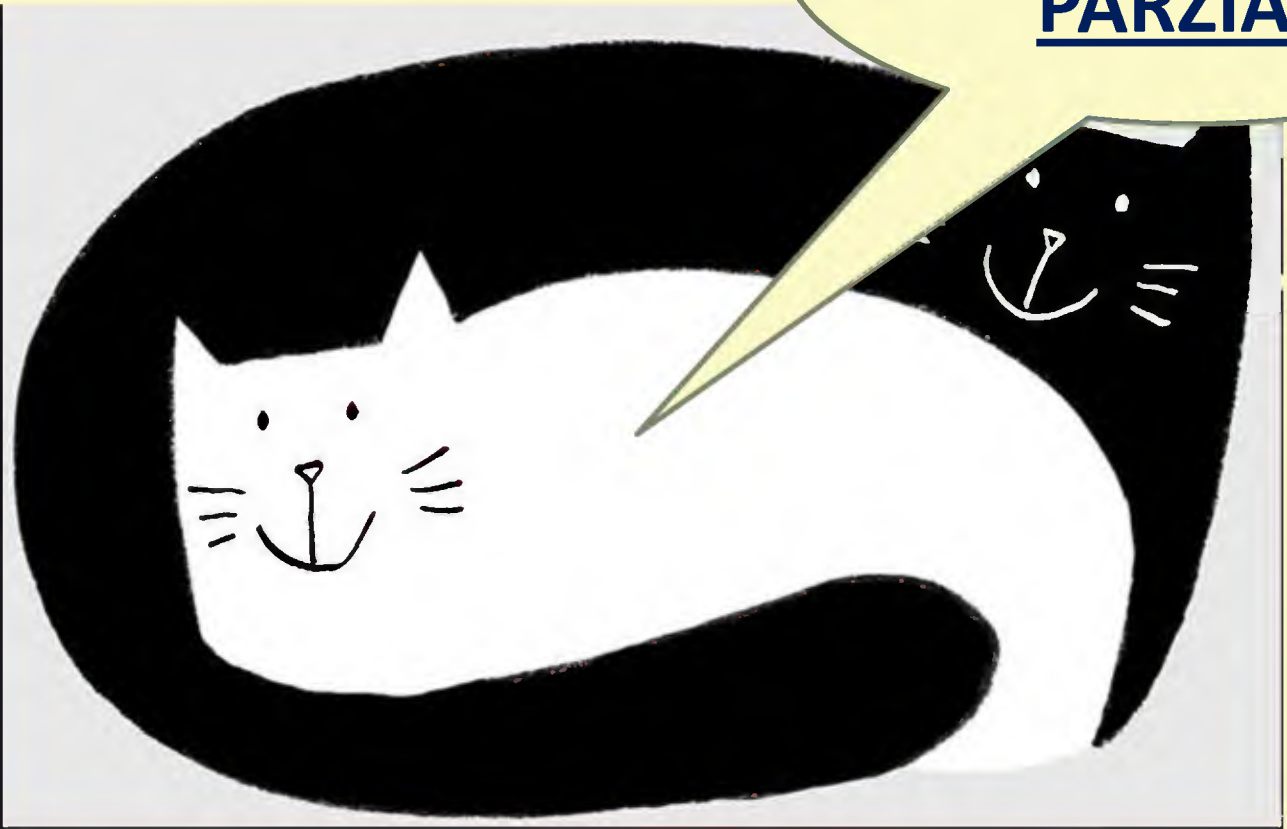
**ALLERGICI**

**TOLLERANTI**



**MA.....**

**TOLLERANTI**  
**PARZIALI**



# Food allergy: A practice parameter update—2014

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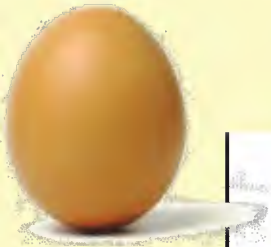
Hugh A. Sampson, MD, Seema Aceves, MD, PhD, S. Allan Bock, MD, John James, MD, Stacie Jones, MD, David Lang, MD, Kari Nadeau, MD, PhD, Anna Nowak-Wegrzyn, MD, John Oppenheimer, MD, Tamara T. Perry, MD, Christopher Randolph, MD, Scott H. Sicherer, MD, Ronald A. Simon, MD, Brian P. Vickery, MD, and Robert Wood, MD

**J Allergy Clin Immunol 2014;134:1016-25**

Although a strict avoidance diet of all allergic foods is typically recommended, recent studies indicate that regular exposure of heat-modified egg and milk protein in allergic patients is not only well tolerated in up to 70% of allergic patients but might be clinically beneficial.

Recent data suggest that introduction of these foods also accelerates development of tolerance.

# UN TPO TAGLIATO SU MISURA



# TAKE MESSAGES

- La terapia universalmente accettata delle Allergie Alimentari è, tuttora, rappresentata dall'evitamento dell'allergene offending**
- Numerosi studi hanno dimostrato che il rigido evitamento dell'alimento offending, per ogni fenotipo di paziente con allergia alimentare, rappresenta un dogma ormai superato**
- La tolleranza agli alimenti non è un fenomeno del tutto o nulla; esiste una TOLLERANZA PARZIALE che permette l'assunzione di quantità ridotte di allergene o anche di quantità normali di alimento ad allergenicità ridotta dalla cottura**

# TAKE MESSAGES

- Le metanalisi sulla OIT ne dimostrano l'efficacia ma la via è percorribile solo in setting altamente specializzati e dopo opportuna analisi del rapporto costi-benefici con il paziente e la sua famiglia**
- L'introduzione di latte ed uovo estesamente cotto nella stragrande maggioranza dei pazienti allergici a tale alimento costituisce una opzione percorribile e potrebbe rappresentare una via di più facile acquisizione della tolleranza anche verso gli alimenti crudi**



***GRAZIE***

