



Come compilare e spiegare un action plan

14.9.2017

Dott. Alberto Martelli

U.O.C. Pediatria - Ospedale G. Salvini - Garbagnate Milanese

Devi avere un action plan scritto

How to treat anaphylaxis

Be prepared! Have a written anaphylaxis emergency action plan.

When anaphylaxis occurs, promptly assess the patient's airway, breathing, circulation, and skin and call for help: 911 or EMS in community settings, a resuscitation team in health care settings.

Inject epinephrine (adrenaline) IM in the mid-outer aspect of the thigh by using an EA. If needed, give a second injection 5 to 15 minutes after the first.

Place the patient on his or her back or in a position of comfort if there is respiratory distress and/or vomiting. Elevate the lower extremities. Do not allow standing, walking, or running.

Transport the patient to an emergency department, preferably by an EMS vehicle, for further assessment and monitoring. Additional treatment, including supplemental oxygen, intravenous fluids, and other interventions may be needed.

Sicherer SH, Simons FER. Section on allergy and immunology. Guidance on completing a written allergy and anaphylaxis emergency plan. Pediatrics. 2017;139(3)

Scuola: l'utilizzo dell'autoiniettore

- An individual known to be at risk of anaphylaxis may not have their own AAI immediately available (e.g. expired, broken and used but misfired).
- A second dose of adrenaline may be required before an ambulance arrives.
- A previously diagnosed individual with mild or moderate allergy who was not prescribed an AAI has anaphylaxis.
- An undiagnosed individual, not previously known to be at risk of any allergic reaction, may have their first ever episode of anaphylaxis away from home.
- General use AAIs should be considered as being *additional* to prescribed AAIs, not a substitute for prescribed AAIs.
- AAIs may be purchased from pharmacies without prescription at full price.
- An AAI brand-specific ASCIA Action Plan (general) should be stored with the AAI.
- AAIs should be replaced before their expiry date.
- The number of AAIs required will consider issues such as the number of children at risk of anaphylaxis attending offsite activity compared with the number of children remaining at school, the number of simultaneous activities, the location of out of school activities (access to emergency care, mobile phone coverage and likelihood of exposure to allergic triggers, particularly food or insect stings).

Vale S et al. ASCIA guidelines for prevention of anaphylaxis in schools, pre-schools and childcare: 2015 update. J Paediatr Child Health. 2015;51:949-54.

Piano d'azione per la reazione allergica da alimento

Nome e Cognome Mario Rossi

Data di nascita 1.1.2000

Insegnanti.....

Allergico a: frutta secca.....

Asma bronchiale **x** sì* no

* elevato rischio per reazioni severe

Fotografia del bambino

Da fare subito: guardare ed eventualmente trattare

Segni e sintomi

Terapia

Adrenalina

Antistaminico

Alimento appena assunto ma ancora nessun sintomo

- **Cavo orale:** prurito, pizzicore, e/o gonfiore delle labbra, della lingua o della bocca

- **Pelle:** prurito, rash pruriginoso, gonfiore del volto -delle estremità (mani e piedi)

- **Intestino:** nausea, dolori addominali, vomito o diarrea

- **Gola†:** gola secca, senso di ostruzione, tosse abbaiante

- **Polmone†:** respiro breve e frequente, tosse ripetuta, fischio

- **Coscienza†:** offuscamento della vista, svenimento

- **Cuore†:** polso frequente, bassa pressione arteriosa, pallore, cianosi

- **Altro :**

- **Se la reazione sta progredendo** (più sedi coinvolte)

La severità dei segni e dei sintomi può rapidamente cambiare.

† potenzialmente a rischio di vita

sì

La validazione dei pittogrammi



ADDRESSOGRAPH

Emergency Department
ANAPHYLAXIS ACTION PLAN & PRESCRIPTION Weight: _____ kg

Signs and Symptoms:

				
Skin: Hives, swelling, itching, warmth, redness, rash	Breathing: Coughing, wheezing, shortness of breath, chest pain/tightness, throat tightness, hoarse voice, trouble swallowing	Stomach: Nausea, pain/cramps, vomiting	Heart: Pale/blue colour, weak pulse, dizzy/lightheaded	

If you develop any symptoms:



- Give epinephrine at the **first sign** of a known or suspected anaphylactic reaction.
- Call 9-1-1 or local emergency medical services. Tell them the child is having a life-threatening allergic reaction.
- If the reaction continues or worsens, give a second dose of epinephrine in 5 to 15 min.
- If the child is feeling lightheaded, have them lie on their back with their knees bent.

Medications:

Epinephrine **0.15 mg** autoinjector if between 10 and 25 kg:
 Brand: Epipen Allerject Twinject Other: _____ Referral to allergist

Epinephrine **0.3 mg** autoinjector if greater than 25 kg:
 Brand: Epipen Allerject Twinject Other: _____ Medic-alert bracelet

Physician: _____ (print name) License #: _____ Signature: _____ Date: _____ (dd/mm/yyyy)

Mok G, et al. Design and validation of pictograms in a pediatric anaphylaxis action plan. *Pediatr Allergy Immunol.* 2015;26:223-33.

Apparati coinvolti

Segni e sintomi iniziali

N(%)

Tegumentario	33(60)
Respiratorio	14(25)
Gastrointestinale	3(5)
Neurologico	2(4)
Cardiovascolare	1(2)
Altri	2(4)

Segni e sintomi globali

N(%)

Tegumentario	51(93)
Respiratorio	51(93)
Cardiovascolare	14 (26)
Neurologico	14 (26)
Gastrointestinale	7(13)

I segni respiratori nell'anafilassi

Respiratory tract symptoms

Dyspnea/difficulty breathing

60 (44.8)

Tightness/fullness of the throat

57 (42.5)

Wheezing/bronchospasm

31 (23.1)

Cough

15 (11.2)

Hoarseness/raspy voice

11 (8.2)

Rhinitis

8 (6.0)

Laryngeal edema

5 (3.7)

Cyanosis

4 (3.0)

Stridor

3 (2.2)

Aphonia

3 (2.2)

Campbell RL et al. Prescriptions for self-injectable epinephrine and follow-up referral in emergency department patients presenting with anaphylaxis. *Ann Allergy Asthma Immunol* 2008;101:631-6.

Contatti familiari di emergenza:

Nome /relazione con il bambino..... Telefono # 1

Telefono # 2

NON ASPETTATE DI TROVARE IL GENITORE O PARENTE! TRATTATE SUBITO E POI PORTATE IL BAMBINO
..... AL PRONTO SOCCORSO

CHI CERCARE AL CENTRO ALLERGOLOGICO:

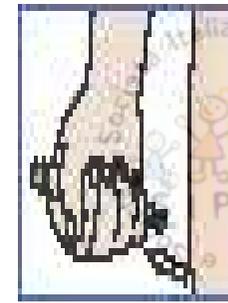
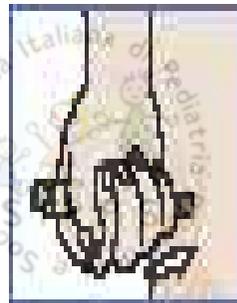
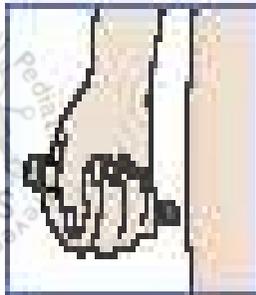
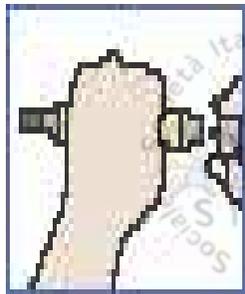
Dottor o infermiere Telefono # 1

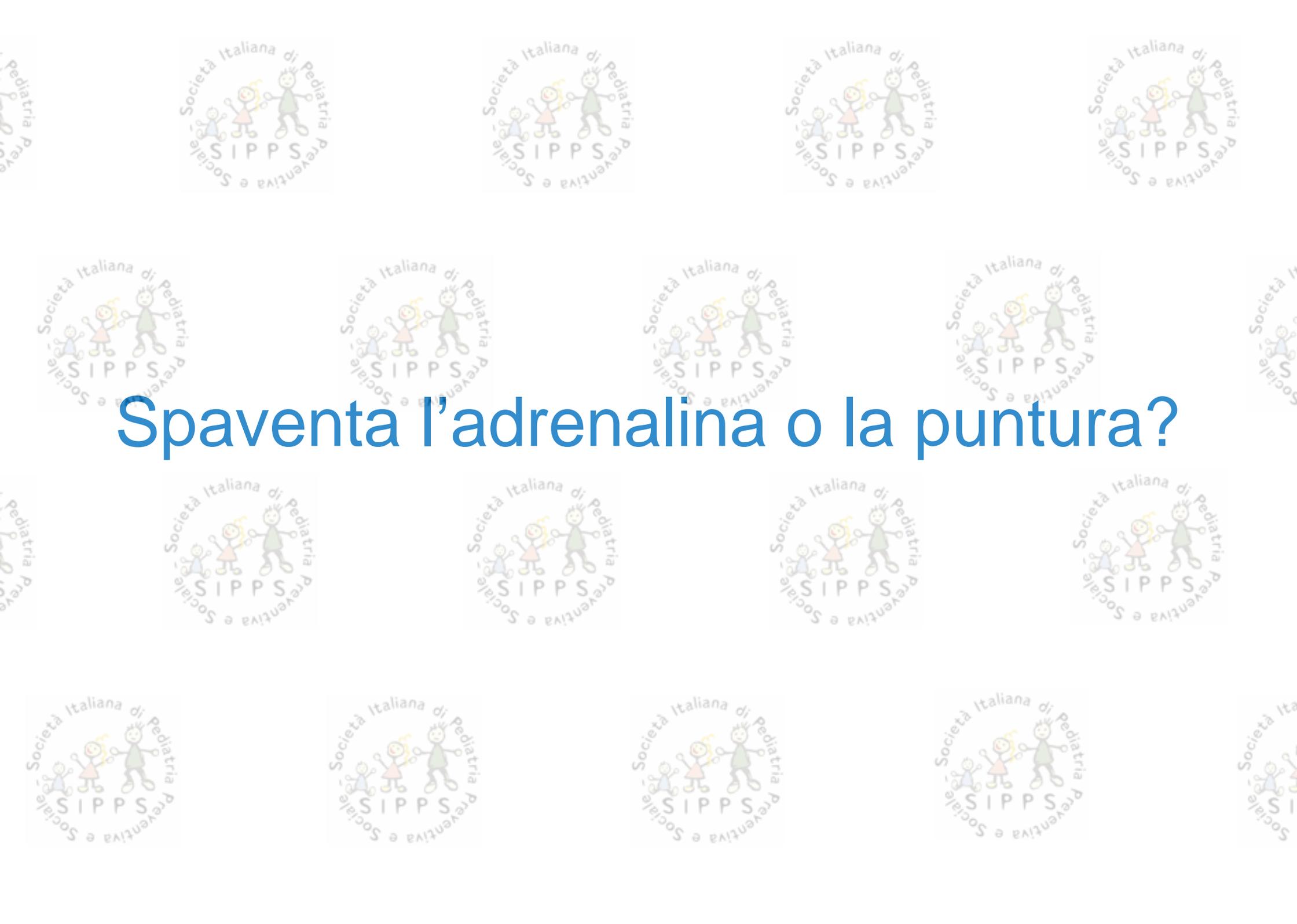
Telefono # 2

Come praticare l'adrenalina.

- 1 . Rimuovi il tappo azzurro di attivazione
- 2 . Appoggia con forza la parte arancione sulla parte laterale della coscia (sempre sulla coscia!)
- 3 . Spingi con forza finchè scatta l' auto-iniezione. Tienilo pressato e conta con calma fino a 10.
- 4 . Rimuovi Adrenalina e massaggia la zona di iniezione per 10 secondi. Porta in Pronto Soccorso anche l' Adrenalina usata. Pianifica una osservazione in Pronto Soccorso.

Per i bambini con allergie a più alimenti, considera di preparare piani di azione separati per ogni alimento.



The background of the slide is a repeating pattern of the SIPPSS logo. The logo is circular and contains the text "Società Italiana di Pediatria Preventiva e Sociale" around the top and "SIPPSS" in the center. In the middle of the logo are three stylized figures: a blue figure on the left, a yellow figure in the center, and a green figure on the right, all holding hands.

Spaventa l'adrenalina o la puntura?

Perché non viene eseguita adrenalina autoiniettiva?

- 1 failure to recognize anaphylaxis,
- 2 uncertainty about autoinjector administration technique,
- 3 uncertainty about the indication to use, and
- 4 fear of side effects.

Niggemann B et al. Adrenaline autoinjectors in food allergy: in for a cent, in for a euro? *Pediatr Allergy Immunol.* 2012;23:506-8.

Conoscenze dei Pediatri in allergia alimentare

Delaying the administration of injectable epinephrine to a child who is known to have anaphylactic reaction increases the risk..

Acidic foods such as oranges and lemons can frequently cause food allergy

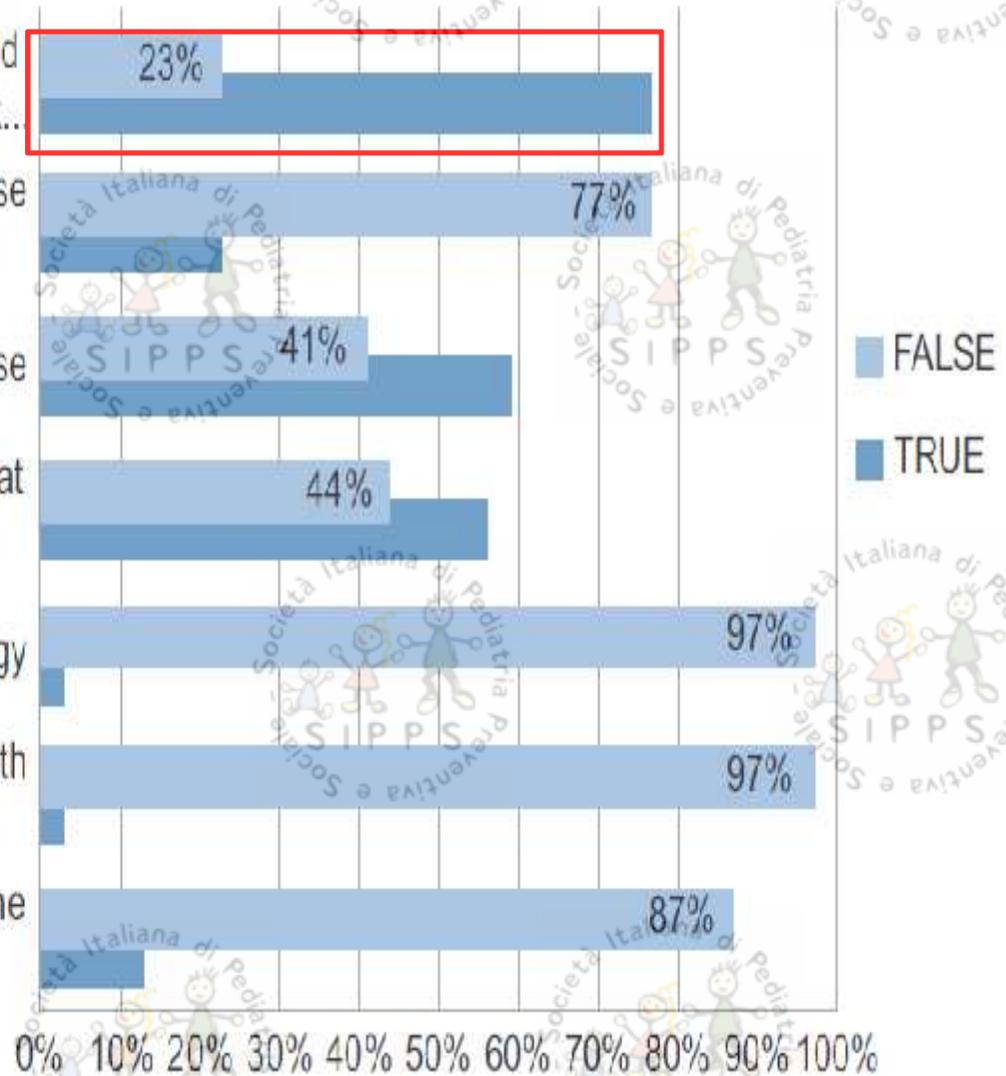
A food allergy reaction can cause demise

A peanut-free environment would be unfair to children that do not have peanut allergies

Lactose intolerance is a synonym of milk allergy

It is appropriate to dilute an allergen with water in a child with food allergy to suppress the reaction

Children with food allergy can safely eat a small amount of the food they are allergic to



Adeli M, et al. The importance of educating postgraduate pediatric physicians about food allergy. Adv Med Educ Pract. 2016;7:597-602.

Adrenalina nei casi fatali

Epinephrine was injected before cardiac arrest in only 23 % of 92 individuals who experienced a fatal anaphylaxis episode [93].

In an observational study, data confirmed the safety of IM epinephrine injection, typically given through an epinephrine auto-injector (adverse events 1 %, and no overdoses). In contrast, IV bolus injections were associated with significantly more adverse events (10 %) and overdoses (13 %) [99].

Simons FE et al. 2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines. World Allergy Organ J. 2015;8:32.

Adrenalina in film a rilascio immediato



Alayoubi A et al. Development of a fast dissolving film of epinephrine hydrochloride as a potential anaphylactic treatment for pediatrics. Pharm Dev Technol. 2016;7:1-5.

Chi non si occupa di anafilassi la conosce poco

Anaphylaxis

Allergists

Nonallergists

Common

44.3

16.4

Rare

55.4

82.2

No evidence

0.2

1.4

Martelli A. Anaphylaxis in the emergency department: a paediatric perspective. Curr Opin Allergy Clin Immunol 2008;8:321-9.

Audiovisivi per fare educazione sanitaria per l'utilizzo dell'adrenalina



Rosen J, et al. Creation and validation of web-based food allergy audiovisual educational materials for caregivers. *Allergy Asthma Proc* 2014;35:178-84.

Dosaggio:

Adrenalina: iniezione intramuscolare nella coscia

Adrenalina adulti

Antistaminico: somministra.....

farmaco, dose, via di somministrazione

Altro: somministra.....

farmaco, dose, via di somministrazione

Subito dopo il trattamento: chi chiamare

Chiamare il 112

- Dite che c'è una reazione allergica grave in un bambino, e che è già in corso il trattamento

Firma dei genitori..... Firma del medico.....



Allergy and Anaphylaxis Emergency Plan

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™



Child's name: _____ Date of plan: _____

Date of birth: ____/____/____ Age ____ Weight: ____ kg

Child has allergy to: _____

- Child has asthma. Yes No (If yes, higher chance severe reaction)
 Child has had anaphylaxis. Yes No
 Child may carry medicine. Yes No
 Child may give him/herself medicine. Yes No (If child refuses/is unable to self-treat, an adult must give medicine)



IMPORTANT REMINDER

Anaphylaxis is a potentially life-threatening, severe allergic reaction. If in doubt, give epinephrine.

<p>For Severe Allergy and Anaphylaxis What to look for</p> <p>If child has ANY of these severe symptoms after eating the food or having a sting, give epinephrine.</p> <ul style="list-style-type: none"> • Shortness of breath, wheezing, or coughing • Skin color is pale or has a bluish color • Weak pulse • Fainting or dizziness • Tight or hoarse throat • Trouble breathing or swallowing • Swelling of lips or tongue that bother breathing • Vomiting or diarrhea (if severe or combined with other symptoms) • Many hives or redness over body • Feeling of "doom," confusion, altered consciousness, or agitation <p><input type="checkbox"/> SPECIAL SITUATION: If this box is checked, child has an extremely severe allergy to an insect sting or the following food(s): _____. Even if child has MILD symptoms after a sting or eating these foods, give epinephrine.</p>	<p>Give epinephrine! What to do</p> <ol style="list-style-type: none"> 1. Inject epinephrine right away! Note time when epinephrine was given. 2. Call 911. <ul style="list-style-type: none"> • Ask for ambulance with epinephrine. • Tell rescue squad when epinephrine was given. 3. Stay with child and: <ul style="list-style-type: none"> • Call parents and child's doctor. • Give a second dose of epinephrine, if symptoms get worse, continue, or do not get better in 5 minutes. • Keep child lying on back. If the child vomits or has trouble breathing, keep child lying on his or her side. 4. Give other medicine, if prescribed. Do not use other medicine in place of epinephrine. <ul style="list-style-type: none"> • Antihistamine • Inhaler/bronchodilator
<p>For Mild Allergic Reaction What to look for</p> <p>If child has had any mild symptoms, monitor child.</p> <p>Symptoms may include:</p> <ul style="list-style-type: none"> • Itchy nose, sneezing, itchy mouth • A few hives • Mild stomach nausea or discomfort 	<p>Monitor child What to do</p> <p>Stay with child and:</p> <ul style="list-style-type: none"> • Watch child closely. • Give antihistamine (if prescribed). • Call parents and child's doctor. • If symptoms of severe allergy/anaphylaxis develop, use epinephrine. (See "For Severe Allergy and Anaphylaxis.")

Medicines/Doses

Epinephrine, intramuscular (list type): _____ Dose: 0.15 mg 0.30 mg (weight more than 25 kg)

Antihistamine, by mouth (type and dose): _____

Other (for example, inhaler/bronchodilator if child has asthma): _____

Parent/Guardian Authorization Signature _____

Date _____

Physician/HCP Authorization Signature _____

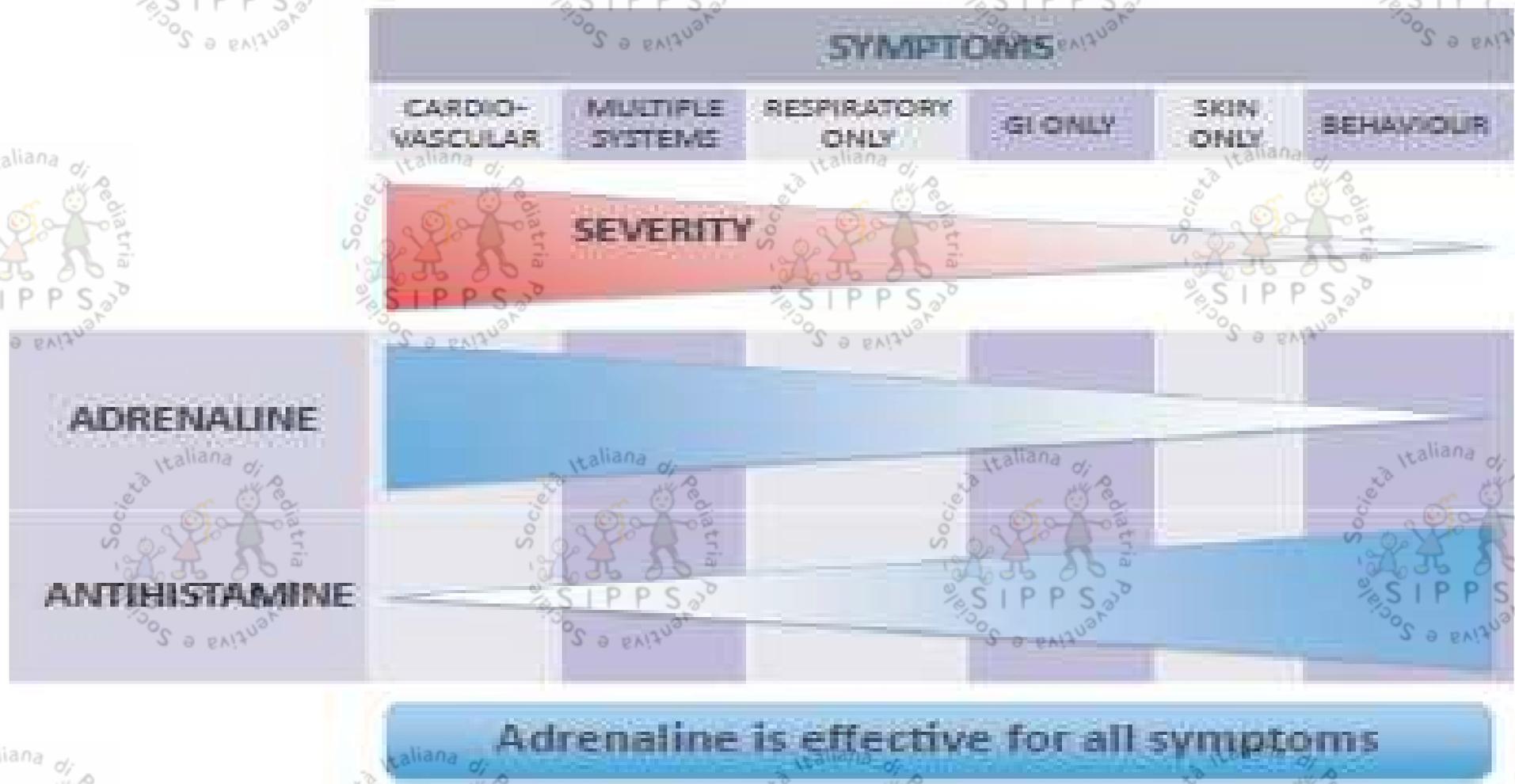
Date _____

© 2017 American Academy of Pediatrics. All rights reserved. Your child's doctor will tell you to do what's best for your child. This information should not take the place of talking with your child's doctor. Page 1 of 2.

FIGURE 1
AAP Allergy and Anaphylaxis plan

Wang J, Sicherer SH; Section on allergy and immunology. Guidance on completing a written allergy and anaphylaxis emergency plan. Pediatrics. 2017;139(3)

Cortisone non considerato



Muraro A et al. EAACI Food Allergy and Anaphylaxis Guidelines Group. Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. *Allergy*. 2014;69:1026-45.

Più il cortisone dell'adrenalina

	Total number	Percentage
Content of emergency kits: corticosteroids	37	69.8 %
Content of emergency kits: antihistamines	33	62.3 %
Content of emergency kits: β 2-agonists	20	37.7 %
Content of emergency kits: adrenaline auto-injector	14	26.4 %

Kilger M et al. Acute and preventive management of anaphylaxis in German primary school and kindergarten children. BMC Pediatr. 2015;15:159.

Anafilassi indotta da alimento

Not associated with exercise	88.3 (78.5,94.2)	92.9 (79.4,98.1)
Mild reaction	21.9 (14.1,31.8)	17.8 (8.5,32.5)
Moderate reaction	63.0 (52.3,72.7)	73.3 (57.8,84.9)
Severe reaction	15.2 (8.8, 24.6)	8.9 (2.9,22.1)
Received epinephrine outside the hospital	52.2 (41.6,62.6)	57.8 (42.2,72.0)
Received antihistamines outside the hospital	50.0 (39.9,60.0)	51.1(35.9,66.0)
Received steroids outside the hospital	3.3 (0.8,9.9)	0

De Schryver S et al. Food-induced anaphylaxis to a known food allergen in children often occurs despite adult supervision. *Pediatr Allergy Immunol.* 2017 Aug 8.

Indicazioni assolute/relative per l'adrenalina

Absolute indications:

- Previous cardiovascular or respiratory reaction to a food, insect sting or latex.
- Exercise induced anaphylaxis.
- Idiopathic anaphylaxis.
- Child with food allergy and co-existent persistent asthma*.

Relative indications:

- Any reaction to small amounts of a food (e.g. airborne food allergen or contact only via skin).
- History of only a previous mild reaction to peanut or a tree nut.
- Remoteness of home from medical facilities.
- Food allergic reaction in a teenager.

Simons FER et al. World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis. J Allergy Clin Immunol 2011;127:593.e1- e22

Più fra i teenagers

Clinical implications: Acceleration in the rate of increase in food-related anaphylaxis in older children and teenagers has implications for management of EA in these age groups, who are at greatest risk of fatal anaphylaxis.

Mullins RJ et al. Time trends in Australian hospital anaphylaxis admissions in 1998-1999 to 2011-2012. J Allergy Clin Immunol. 2015;136:367-75.

La ragazza del censimento

- Reazione da inalazione di vapori di latte vaccino
- Non aveva adrenalina con sé
- E' andata a casa a prenderla
- Forse si sarebbe salvata se l'avesse avuta con sé

Barbi E et al. Fatal allergy as a possible consequence of long-term elimination diet. *Allergy* 2004;59:668-9.

Meglio avere sempre con sé l'adrenalina



Ballardini N, et al. Anaphylactic Reactions to Novel Foods: Case Report of a Child With Severe Crocodile Meat Allergy. Pediatrics. 2017 Mar 8.

Minuti fra I e II adrenalina

How to treat anaphylaxis

Be prepared! Have a written anaphylaxis emergency action plan.

When anaphylaxis occurs, promptly assess the patient's airway, breathing, circulation, and skin and call for help: 911 or EMS in community settings, a resuscitation team in health care settings.

Inject epinephrine (adrenaline) IM in the mid-outer aspect of the thigh by using an EA. If needed, give a second injection **5 to 15 minutes** after the first.

Place the patient on his or her back or in a position of comfort if there is respiratory distress and/or vomiting. Elevate the lower extremities. Do not allow standing, walking, or running.

Transport the patient to an emergency department, preferably by an EMS vehicle, for further assessment and monitoring. Additional treatment, including supplemental oxygen, intravenous fluids, and other interventions may be needed.

Sicherer SH et al. SECTION ON ALLERGY AND IMMUNOLOGY. Epinephrine for First-aid Management of Anaphylaxis. Pediatrics. 2017 Feb 13

Quando prescriverne più di 1?

- 1 high body weight requiring a higher dose than delivered by one device, especially with the relatively low maximum dose of 300 µg available in most countries,
- 2 fear of a possible miss-firing,
- 3 a location without promptly available professional medical help,
- 4 concern that the first shot may not help sufficiently or for long enough,
- 5 protracted or recurrent clinical reactions in the past, and
- 6 persistent bronchial asthma.

Niggemann B et al. Adrenaline autoinjectors in food allergy: in for a cent, in for a euro? *Pediatr Allergy Immunol.* 2012;23:506-8.

Circa 25%: 2 o + adrenaline

Number of doses of epinephrine received	Number of patients	Place of Epinephrine Administration (Number of patients)
	104	—
1	77	Home (31) EMS* (3) ED [±] (71)
2	25	Home and ED [±] (2) EMS* and ED [±] (1) ED [±] (22)
3	2	1 dose at Home and 2 in the ED [±] (1) 2 doses by the EMS* and 1 in the ED [±] (1)

Manivannan V et al. Factors associated with repeated use of epinephrine for the treatment of anaphylaxis. Ann Allergy Asthma Immunol. 2009;103:395-400.



One out of three people may
have a reaction severe enough
to require a second dose.

Shock anafilattico da PLV in neonato



Demirdöven M et al. Anaphylactic Shock Due to Cow's Milk Allergy in the Neonatal Period. Breastfeed Med. 2015;10:341.

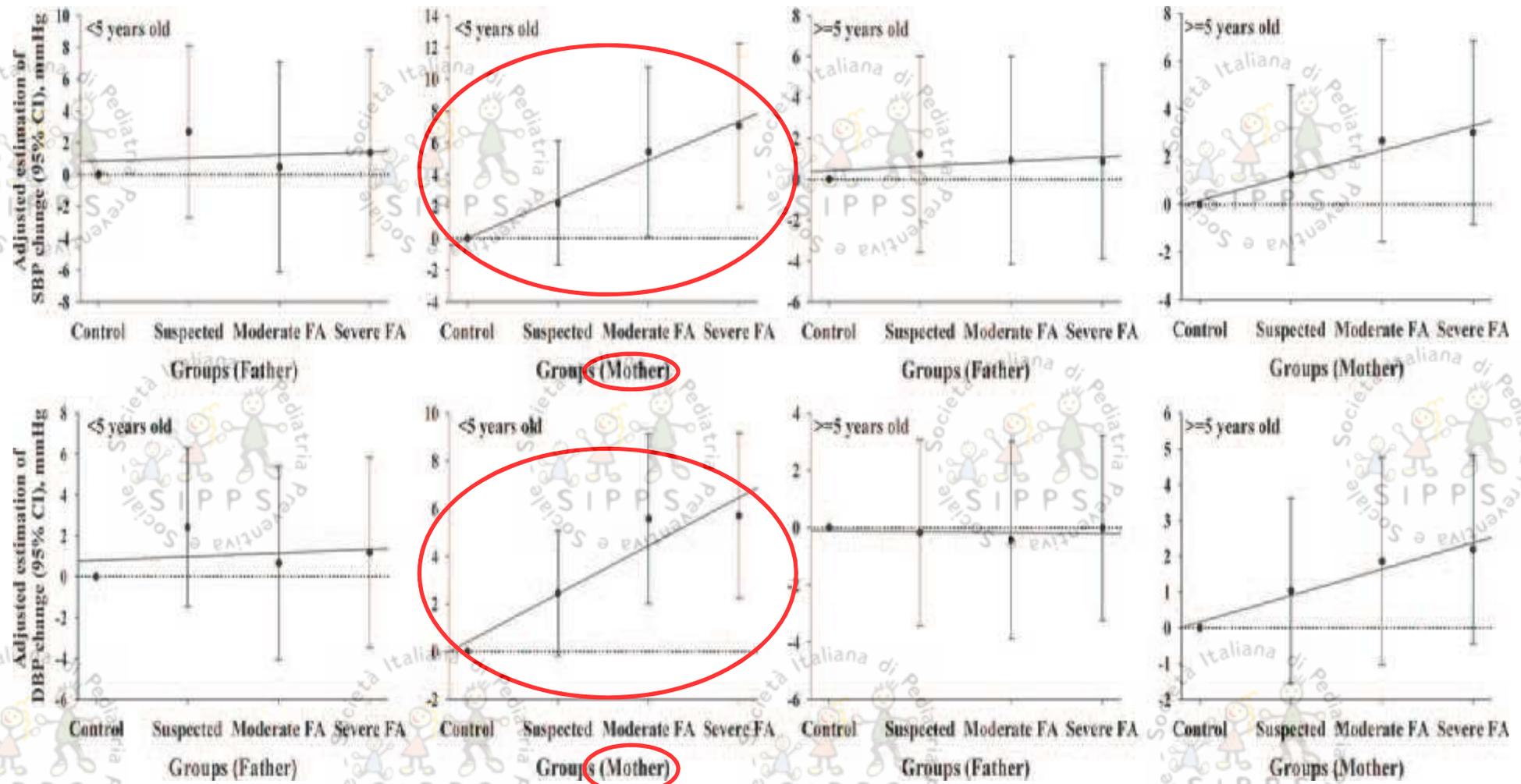
Come preparare adrenalina ad un lattante?

- Usare siringa di vetro
- Preparate voi, da una fiala di Adrenalina (1 mg = 1 ml) tenuta in frigorifero, dose corretta (0,01 mg/kg)
- Preparare con la stessa diluizione in fisiologica dell'Al
- Porre la stagnola intorno alla siringa e mettere il tutto in un porta spazzolino
- Porre il tutto in frigorifero
- Trasportarla con borsa refrigerata
- Adeguare spesso il dosaggio in base al peso

Non è così facile...

- Non ci sono osservazioni controllate in merito
- Impossibile ottenere la sterilità perché viene preparata non in cappa
- Le siringhe sono monouso e non preparate per contenere farmaci per lunghi periodi.
- La siringa potrebbe rilasciare sostanze nel farmaco
- Potrebbe verificarsi un vero collasso della plastica della siringa

Le mamme, l'età < 5 anni e la PA

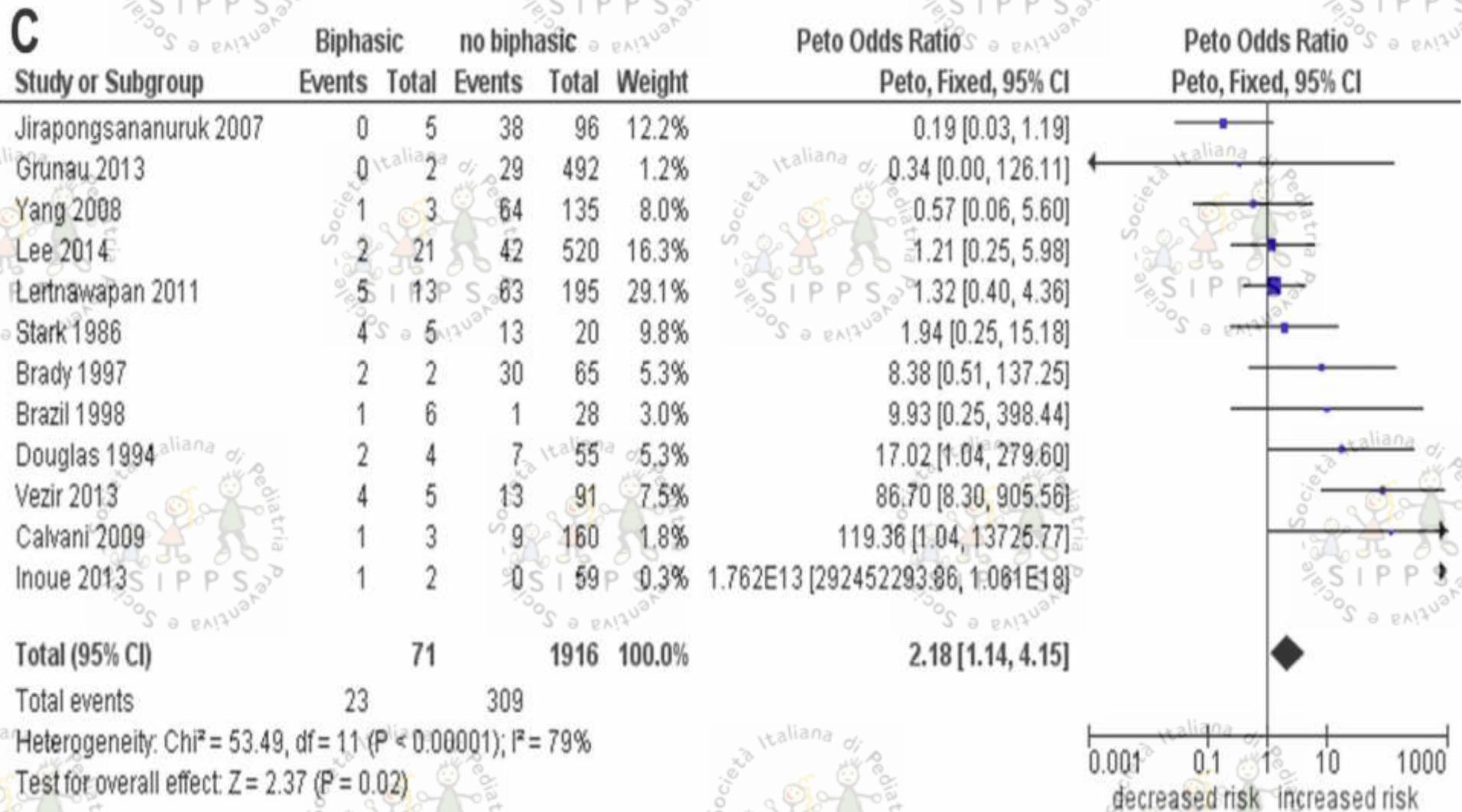


Walker SO et al. Cardiovascular Risk Factors in Parents of Food-Allergic Children. *Medicine (Baltimore)*. 2016;95:e3156.

Conclusioni

- L'ation plan deve essere correttamente compilato e spiegato a genitori, nonni, insegnanti e a tutte le persone che possono assistere il bambino.
- Fate incontri con gli insegnanti
- Devono essere periodicamente ripetute e ripassate tali indicazioni
- Sempre tre cose con il bambino: action plan, adrenalina e antistaminico
- Bisogna continuare a fare educazione sanitaria per ridurre il rischio che l'adrenalina non venga iniettata quando occorre

Ipotensione e rischio di reazione bifasica



Lee S, et al. Time of Onset and Predictors of Biphasic Anaphylactic Reactions: A Systematic Review and Meta-analysis. *J Allergy Clin Immunol Pract.* 2015;3:408-16.



GAZZETTA UFFICIALE

(GU Parte Seconda n.123 del 15-10-2016)

Parte del testo della Gazzetta Ufficiale

Codice Pratica N.: N1B/2016/1898 conclusa in data 14/09/2016 con
esito regolare.

Medicinale: FASTJEKT

Confezioni e numero di AIC:

"330 microgrammi soluzione iniettabile per uso intramuscolare". 1
iniettore preriempito da 2,05 ml AIC n° 028505016

"330 microgrammi soluzione iniettabile per uso intramuscolare" 2
iniettori preriempiti da 2,05 ml AIC n° 028505030

"165 microgrammi soluzione iniettabile per uso intramuscolare" 1
iniettore preriempito da 2,05 ml A.I.C. n. 028505028

"165 microgrammi soluzione iniettabile per uso intramuscolare" 2
iniettori preriempiti da 2,05 ml AIC n° 028505042

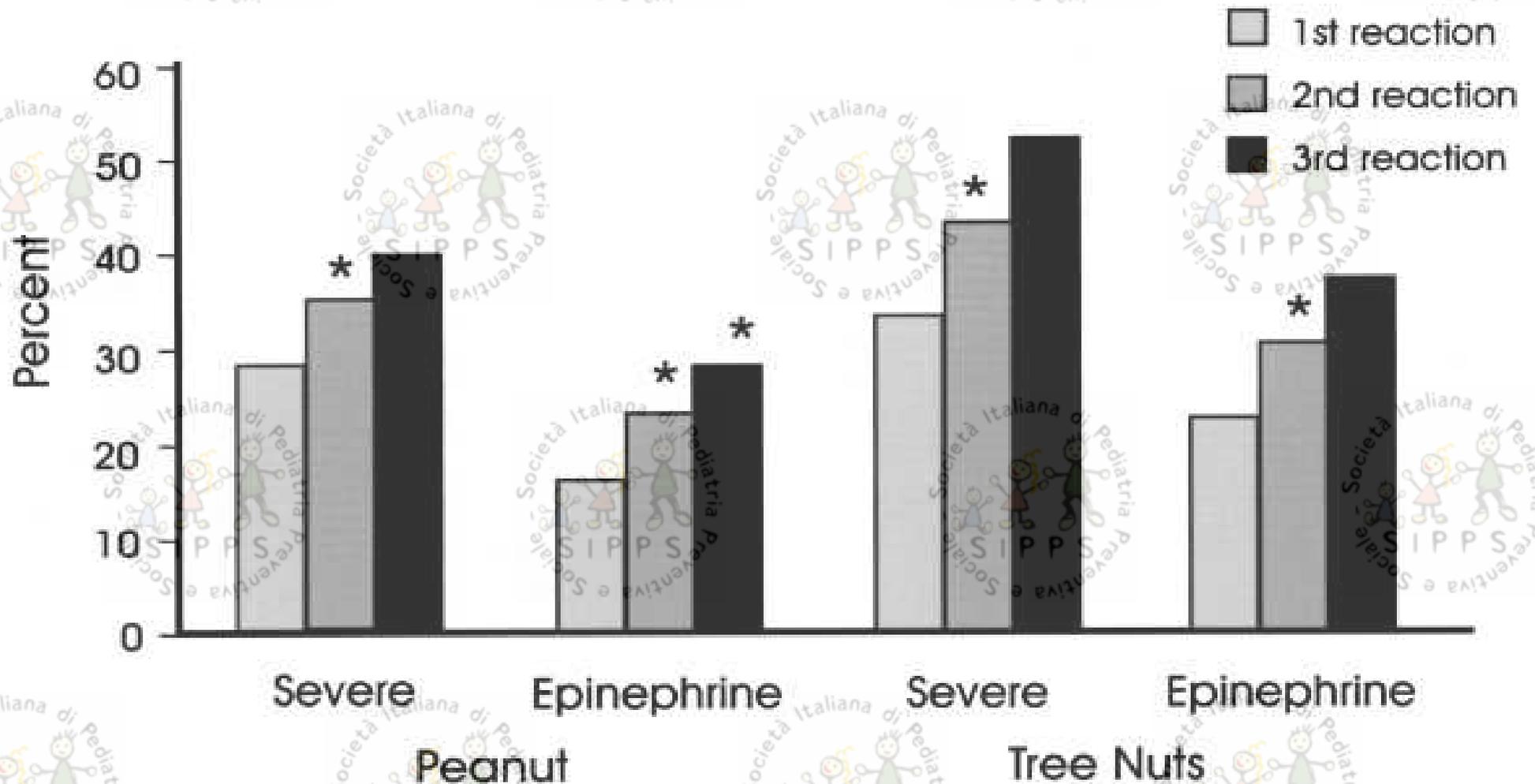
Tipologia variazione oggetto della modifica: IB.A.2.b)

Modifica apportata: Modifica della denominazione della specialita'
medicinale da FASTJEKT a EPIPEN.

Cosa diremo

- Quando prescrivere l'adrenalina
- Come presentare alla famiglia "allargata" l'action plan
- **Quando usare due adrenaline**
- Lo scarso utilizzo
- Cosa fare se si tratta di un piccolo lattante

Anafilassi lieve non sempre resta tale



Simons FER. First-aid treatment of anaphylaxis to food: focus on epinephrine. J Allergy Clin Immunol 2004;113:837-844.

Cosa diremo

- Quando prescrivere l'adrenalina
- Come presentare alla famiglia "allargata" l'action plan
- Quando usare due adrenaline
- Lo scarso utilizzo
- Cosa fare se si tratta di un piccolo lattante

Grado		Cute	Gastro intestinale	Respiratorio	Cardio-vascolare	Neurologica
LIEVE	1	Prurito Orticaria Angioedema localizzato	Prurito orale Lieve edema delle labbra	-	-	-
	2	Prurito Orticaria Angioedema generalizzato	Idem + dolori addominali e/o nausea e/o vomito	Congestione nasale o starnuti	-	Variazione nel livello di attività
MODERATA	3	Come 2	Come 2 + vomito ripetuto o edema della lingua	Rinorrea, marcata congestione, sensazione di prurito o edema della gola	Tachicardia (FC > 15 ') pallore	Variazione nel livello di attività, ansia
	4	Come 2	Come 3 + diarrea	Come 3 + raucedine, tosse abbaiante, difficoltà nel deglutire, o nel respirare, asma, cianosi	Come 3 + lieve disritmie o ipotensione	Confusione mentale e/o sensazione di morte imminente
GRAVE	5	Come 2	Come 4 + perdita di controllo dell'intestino	Come 4 + arresto respiratorio	Severa bradicardia e/o ipotensione o arresto cardiaco	Perdita di coscienza

Sampson HA. Anaphylaxis and emergency treatment. Pediatrics 2003;111:1601-8.

Definizione d'ipotensione arteriosa sistolica

- Fino all'anno : < 70 mm Hg
- Da 1 a 10 anni: < 70 mm Hg + (2 x età)
- Dagli 11 ai 17 anni: < 90 mm Hg

Sampson H.A. et al. Second symposium on the definition and management of anaphylaxis: Summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. J Allergy Clin Immunol 2006; 117: 391-397.

TABLE I. Clinical criteria for diagnosing anaphylaxis

Anaphylaxis is highly likely when any one of the following 3 criteria are fulfilled:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula)

AND AT LEAST ONE OF THE FOLLOWING

- a. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)
 - b. Reduced BP or associated symptoms of end-organ dysfunction (eg, hypotonia [collapse], syncope, incontinence)
2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):
 - a. Involvement of the skin-mucosal tissue (eg, generalized hives, itch-flush, swollen lips-tongue-uvula)
 - b. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)
 - c. Reduced BP or associated symptoms (eg, hypotonia [collapse], syncope, incontinence)
 - d. Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)
 3. Reduced BP after exposure to known allergen for that patient (minutes to several hours):
 - a. Infants and children: low systolic BP (age specific) or greater than 30% decrease in systolic BP*
 - b. Adults: systolic BP of less than 90 mm Hg or greater than 30% decrease from that person's baseline

PEF, Peak expiratory flow; BP, blood pressure.

*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.

Scarso uso dell'adrenalina

Reference	Study design	Auto-injector prescription	Used an auto-injector during follow-up*	Reactions where initial intramuscular adrenaline dose was followed by additional doses**
(61)	Retrospective clinic population	All	4% (41/969) over a 12-month period	32% (13/41)
(88)	Retrospective clinic population	All	22% (15/68) over a 20-month period	15% (2/13)
(89)	Prospective clinic population	Not all	3% (23/785) over an average of 48 months	0% (0/23)
(84)	Prospective clinic population	Not all	19% (78/413) over an average of 24 months	19% (18/95)
(15)	Patient survey	Not all	27% (500/1885)	18% (90/500)
(83)	Patient survey	Not all	35% (22/63)	18% (4/22)

Notes

*Refers to individual patients.

**Refers to individual allergic reactions (often more than one per patient). Additional doses were usually given by a healthcare professional.

Muraro A et al. EAACI Food Allergy and Anaphylaxis Guidelines Group. Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. *Allergy*. 2014;69:1026-45.



Parents' education, affect, and possession of an epinephrine autoinjector were associated with a heightened perceived risk of future anaphylaxis.

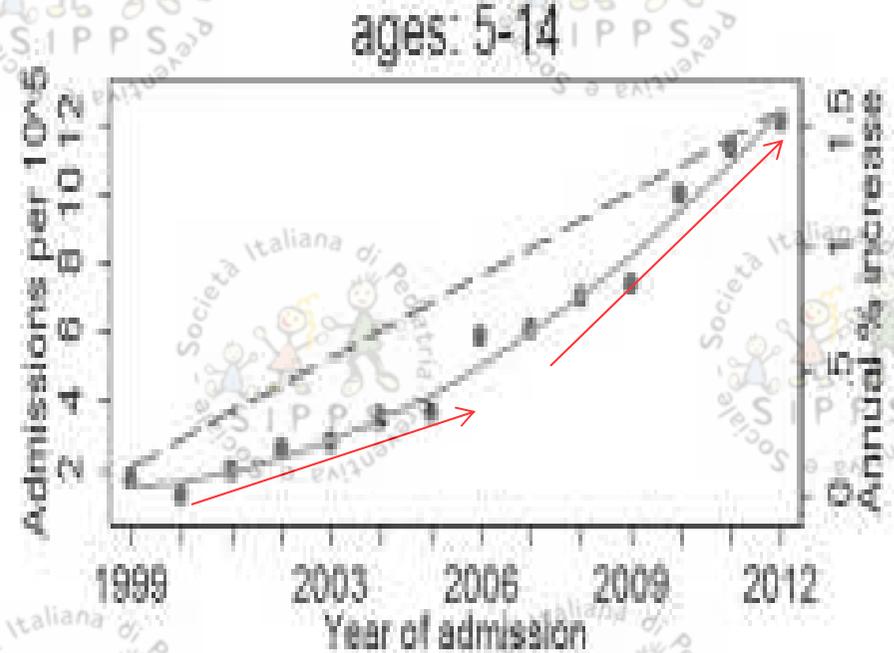
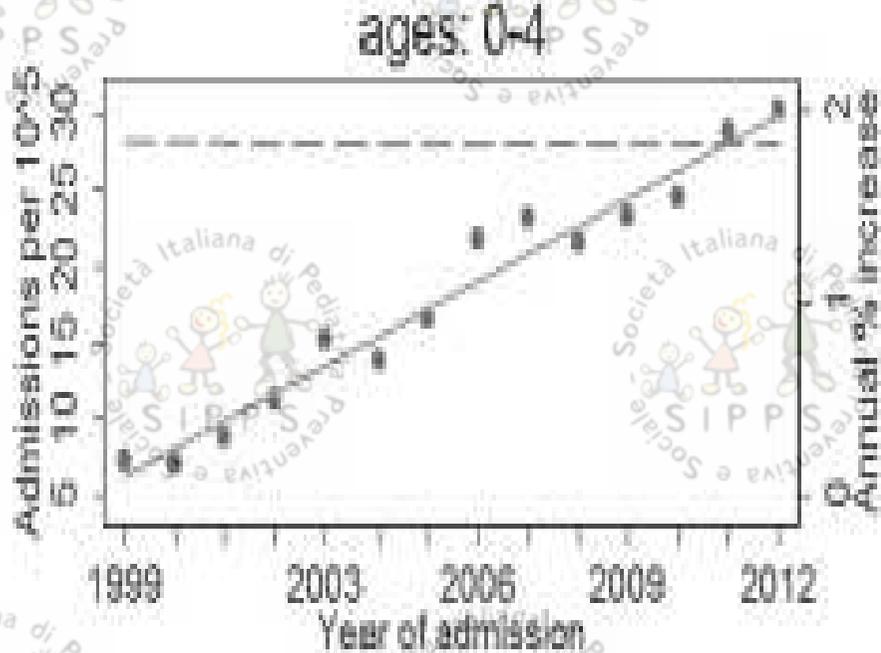
Clinicians should consider not only the child's needs but should also provide counseling for parents, particularly those who possess autoinjectors. Parents of children with multiple food allergies may need additional education and training to help them cope with future reactions.

Ogg J, Factors that determine parents' perception of their child's risk of life-threatening food-induced anaphylaxis. Allergy Asthma Proc. 2017 Jan 1;38(1):44-53.

Di cosa parleremo

- Perché è importante parlare di anafilassi in età pediatrica
- La definizione di anafilassi
- Indicazioni assolute e relative alla prescrizione di adrenalina
- Novità

Ricoveri in H per anafilassi da alimento Aumentano nel bambino e nel teenager



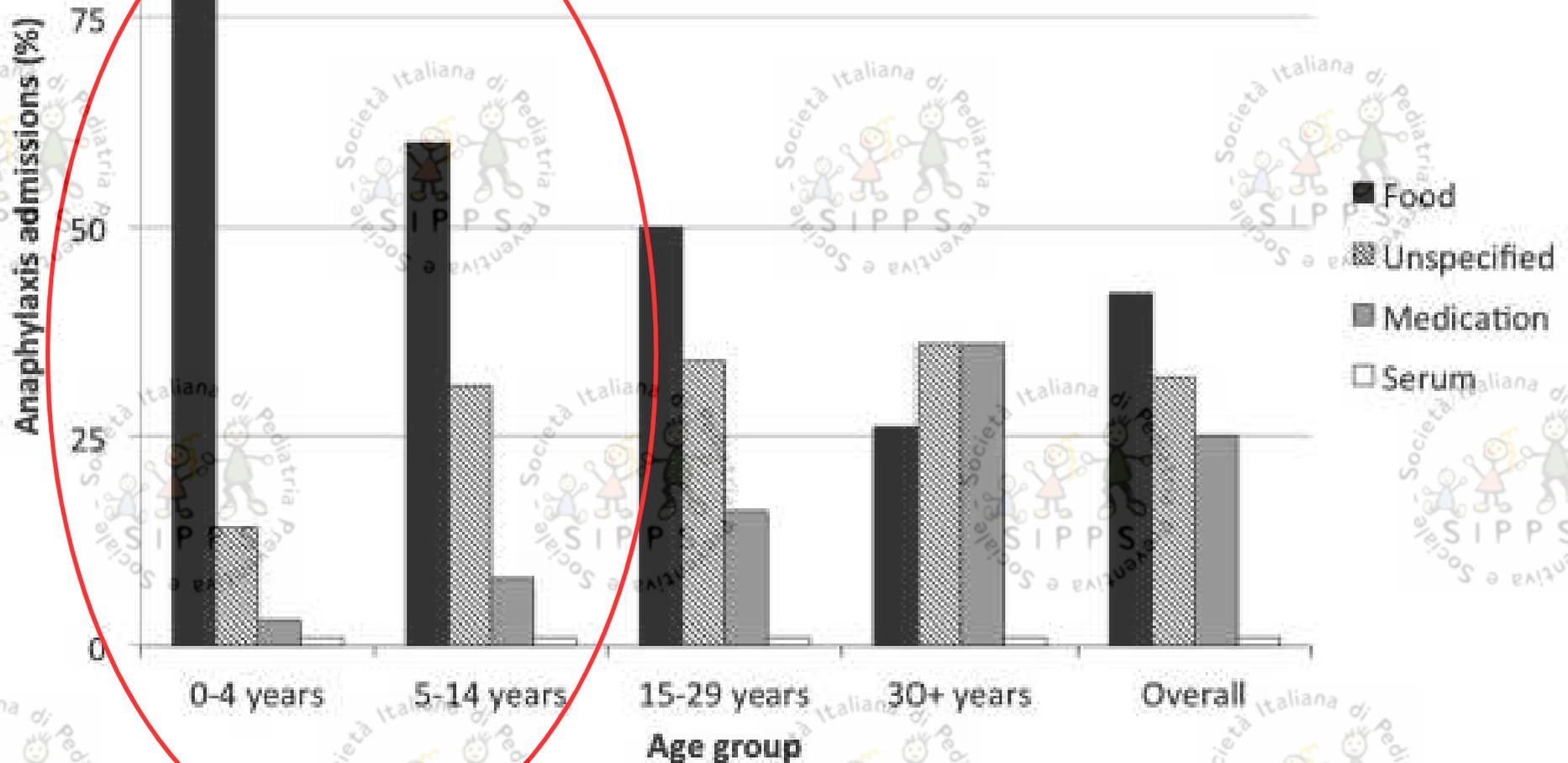
Mullins RJ et al. Time trends in Australian hospital anaphylaxis admissions in 1998-1999 to 2011-2012. J Allergy Clin Immunol. 2015;136:367-75.

Più del 10%: > 2 adrenaline

Variables	Patients receiving no epinephrine N=104	%	Patients receiving 1 dose of epinephrine N=77	%	Patients receiving ≥2 doses of epinephrine N=27	%
Demographics						
Race and ethnicity						
Caucasian	89	85.6	67	87	19	70.4
Black	5	2.8	0	0	15	3.7
Hispanic	1	4.8	0	0	0	0
Asian-Pacific Islander	2	1.9	4	5.2	1	3.7
Other	0	0	1	1.3	0	0
Unknown	7	6.7	5	6.5	6	22.2
Age (Years)						
Median	30.5		31.2		18.9	
Interquartile Range	15 to 43		14 to 40		10 to 34	
Female Gender	67	64.4 ^W	36	46.8	13	48.2
Inciting Agent						
Food	32	30.8	28	36.4	8	29.6
Insect	20	19.2	16	20.8	3	11.1
Medications	12	11.5	11	14.3	6	22.2
Other	11	10.6	6	7.8	2	7.4
Unknown	29	27.9	16	20.8	8	29.6
Hospital Admission						
Hospital Admission	10	10.3 ^W	17	22.4 [^]	13	48.2 ^W
History of Asthma						
History of Asthma	23	22.6	21	27.6	10	37
Prescription of SIE						
Prescription of SIE	26	28.6 ^W	38	60.3	15	71.4
Allergist Referral						
Allergist Referral	40	38.8	33	43.4	14	51.9

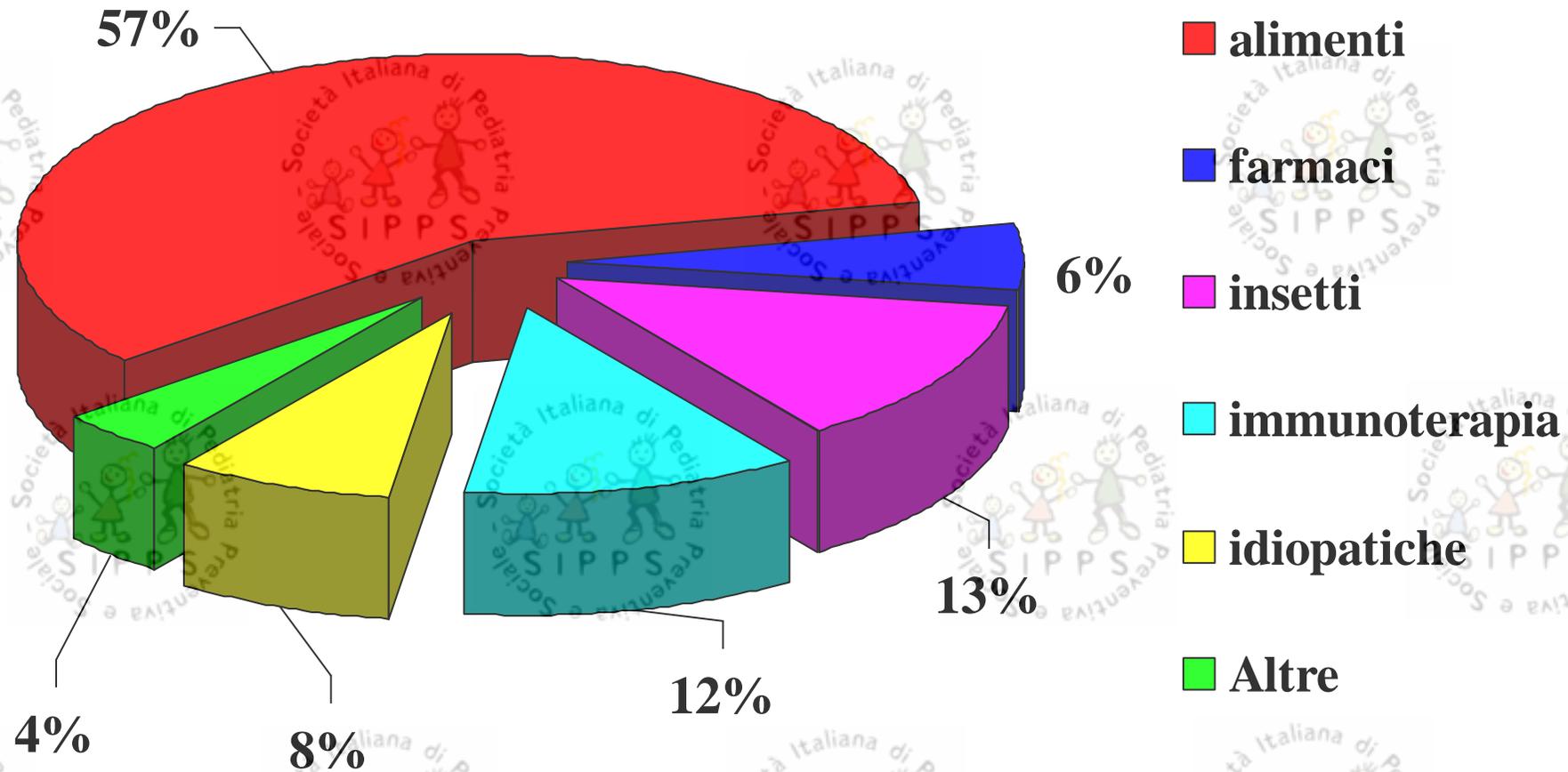
Manivannan V et al. Factors associated with repeated use of epinephrine for the treatment of anaphylaxis. Ann Allergy Asthma Immunol. 2009;103:395-400.

Ricoveri in H per anafilassi in Australia



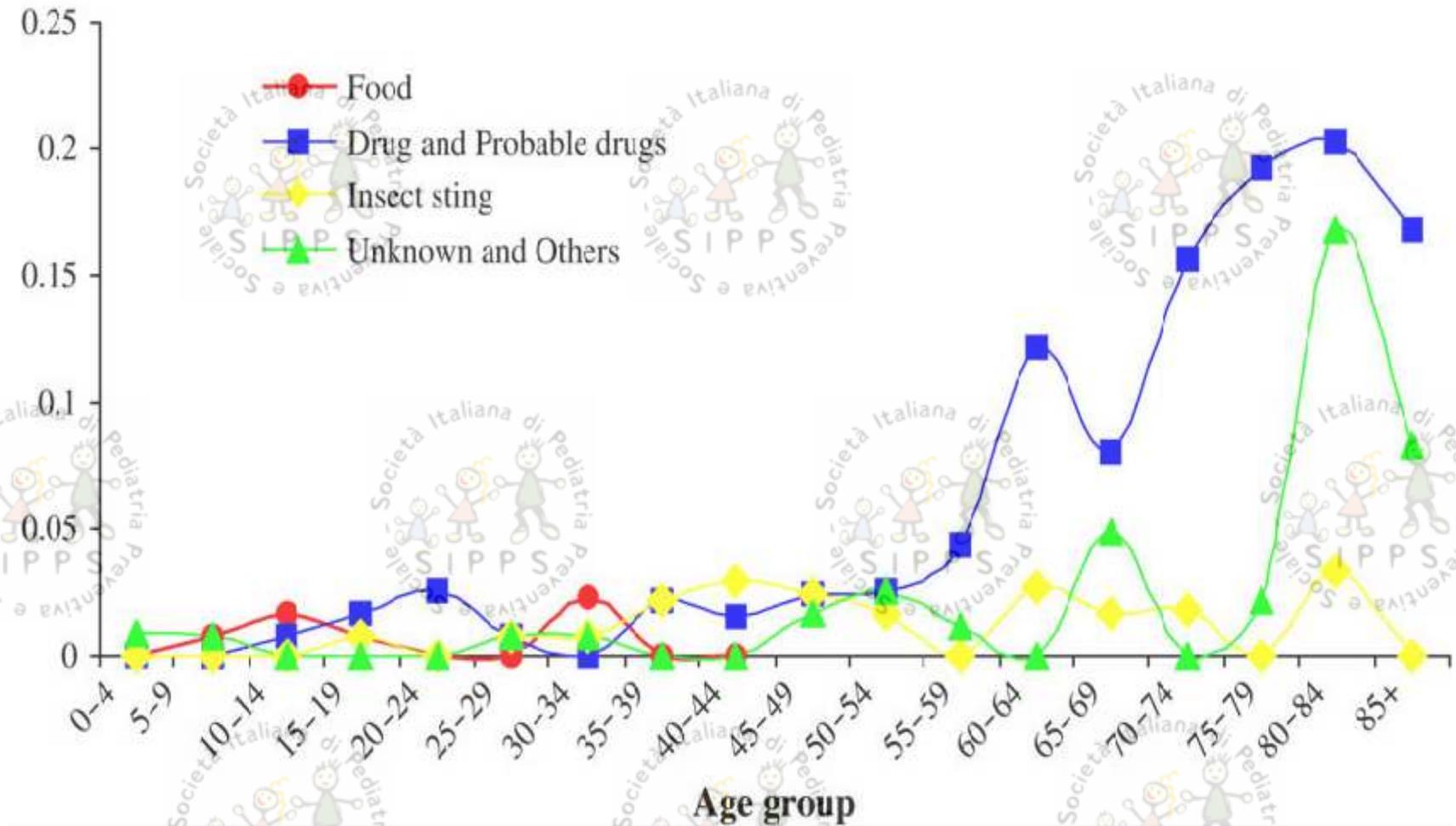
Mullins RJ et al. Time trends in Australian hospital anaphylaxis admissions in 1998-1999 to 2011-2012. J Allergy Clin Immunol. 2015;136:367-75.

Eziologia anafilassi (103 episodi)



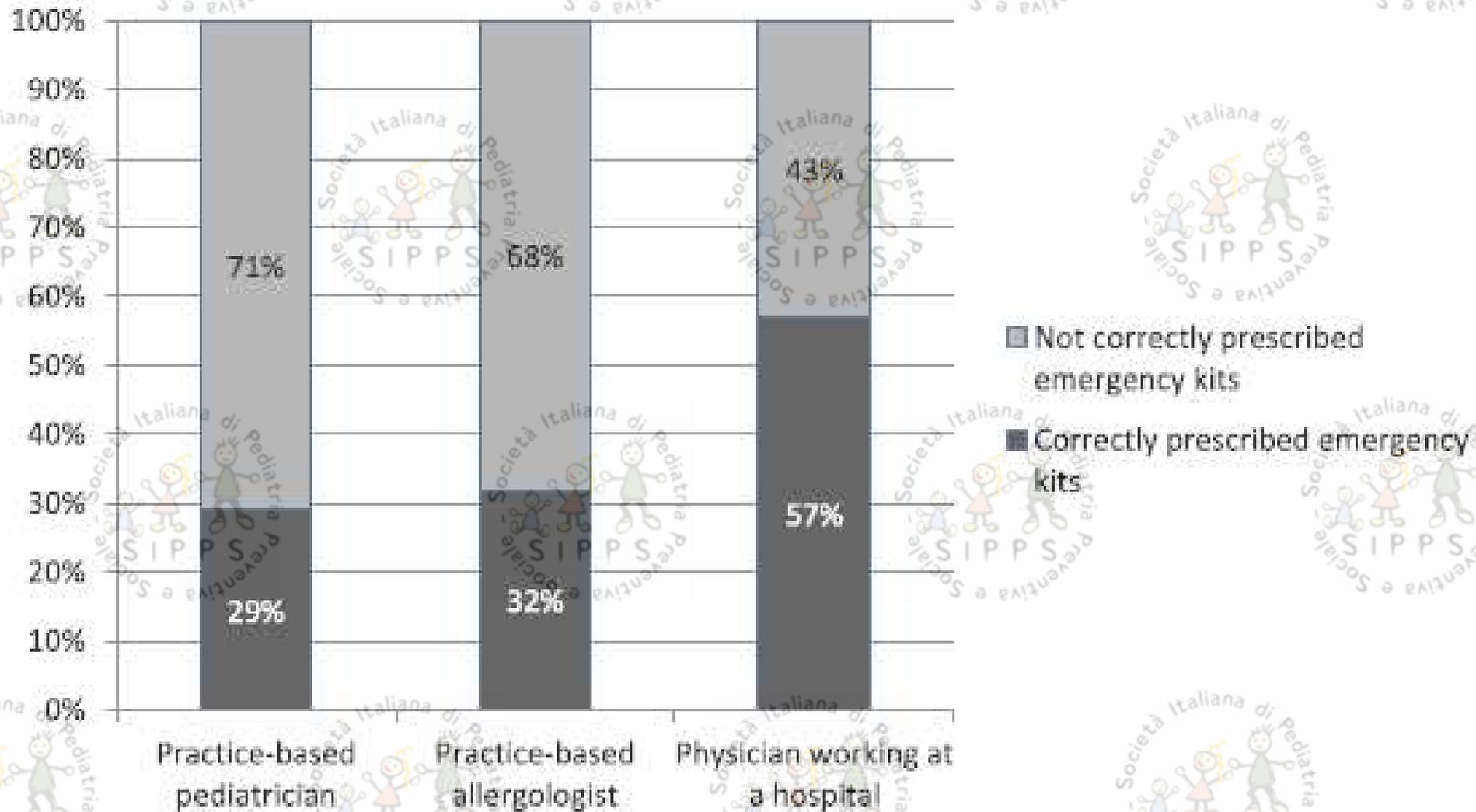
Mehl A et al. Anaphylactic reactions in children--a questionnaire-based survey in Germany. Allergy 2005;60:1440-5.

Cause di morte per anafilassi per età



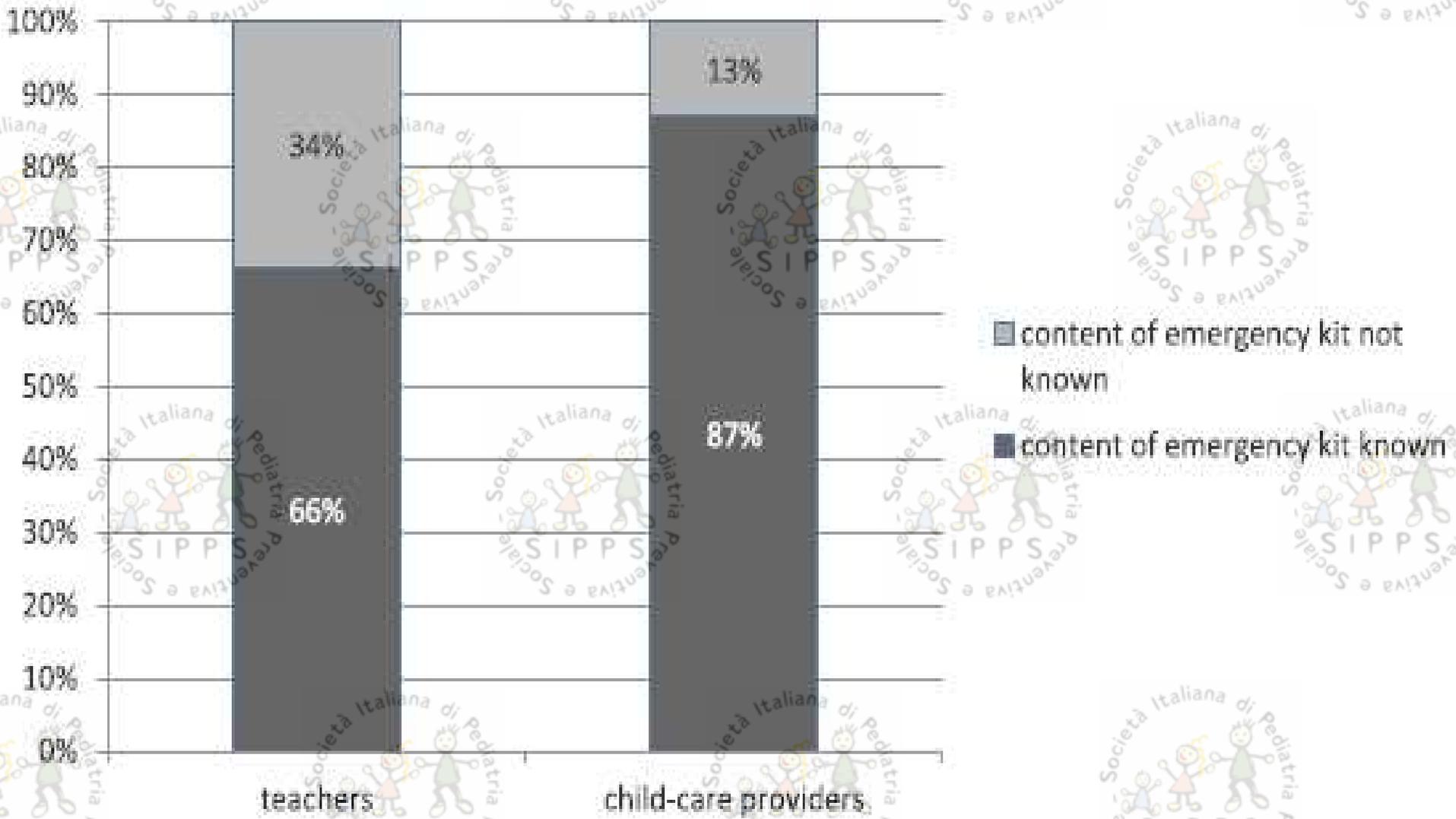
Liew WK. J Allergy Clin Immunol 2009;123:434-42.

Il doppio dei Medici in H prescrive correttamente



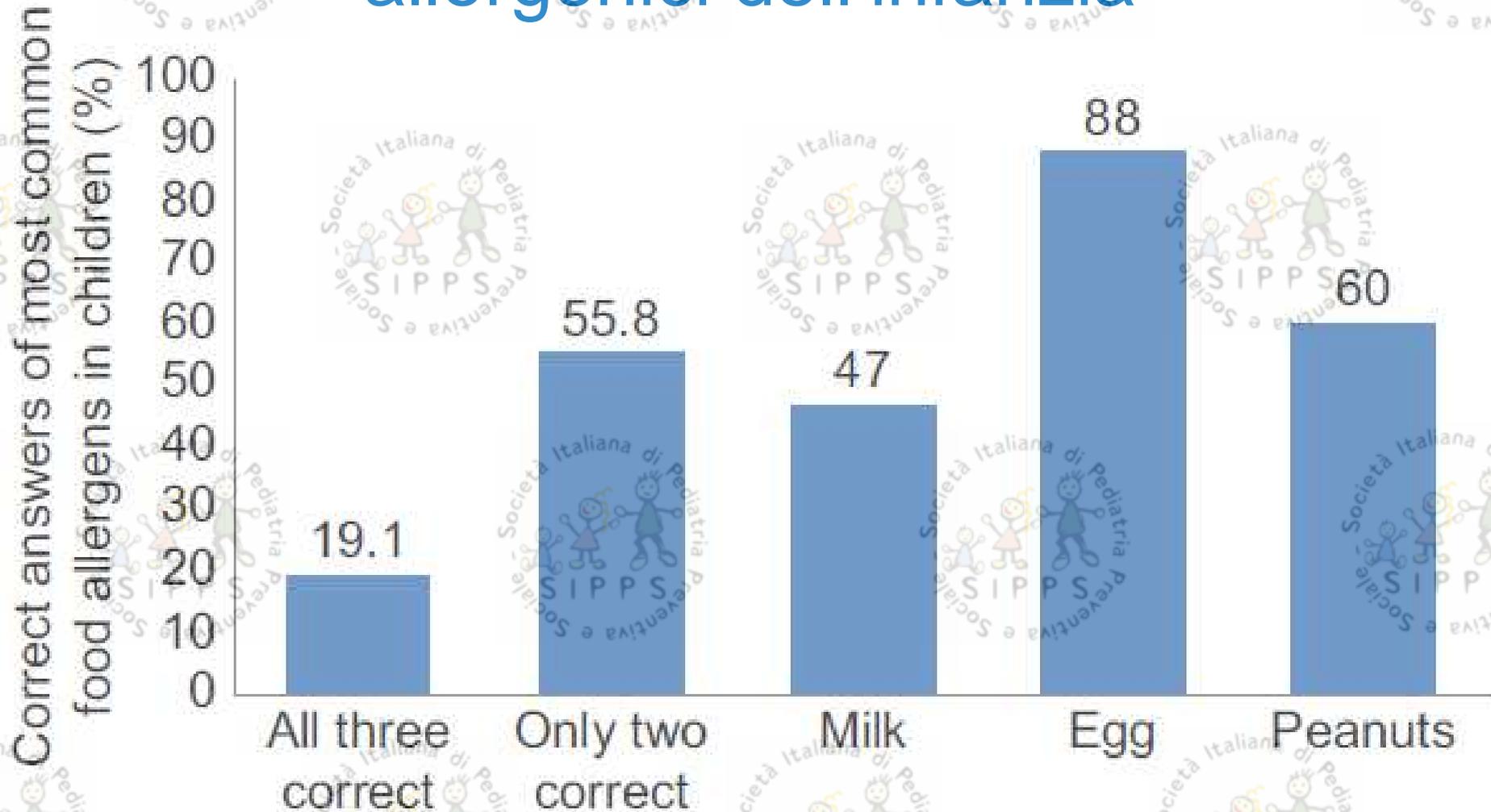
Kilger M et al. Acute and preventive management of anaphylaxis in German primary school and kindergarten children. BMC Pediatr. 2015;15:159.

Gli insegnanti sanno poco del kit



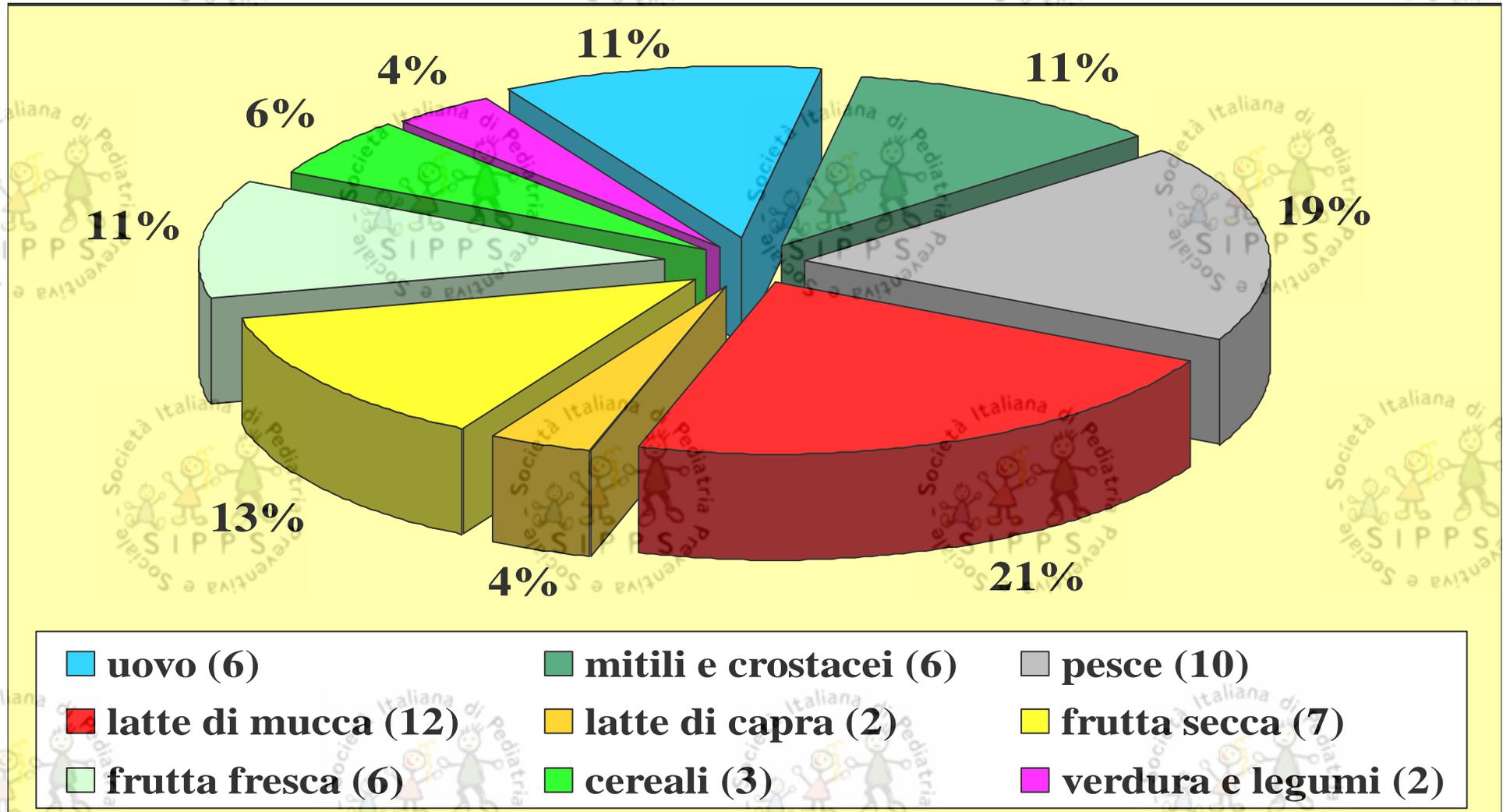
Kilger M et al. Acute and preventive management of anaphylaxis in German primary school and kindergarten children. BMC Pediatr. 2015;15:159.

Risposte dei Pediatri sui 3 alimenti più allergenici dell'infanzia



Adeli M, et al. The importance of educating postgraduate pediatric physicians about food allergy. *Adv Med Educ Pract.* 2016;7:597-602.

Cause di anafilassi alimentare

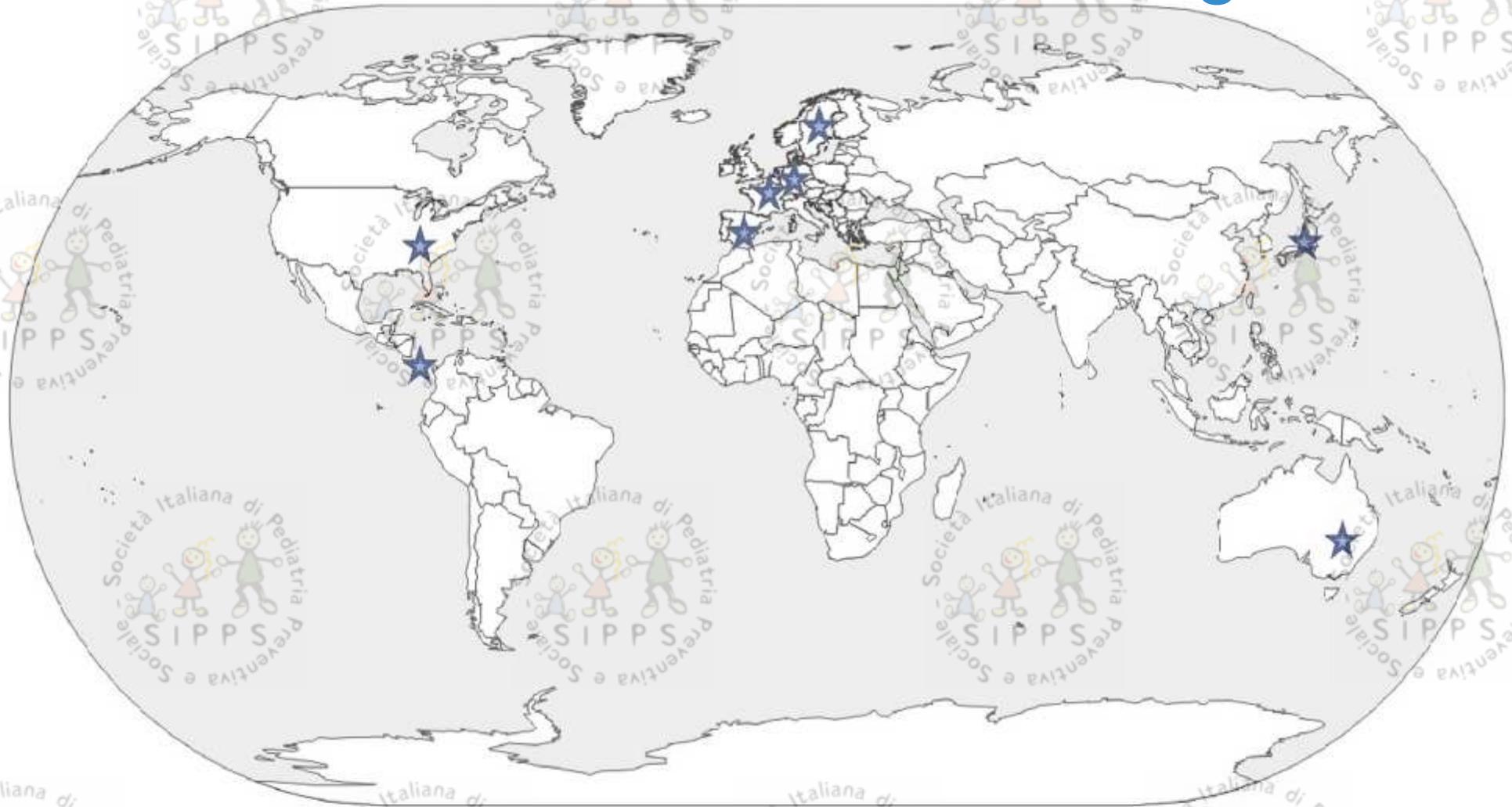


Novembre E. Anaphylaxis in children: clinical and allergologic features.
Pediatrics. 1998; 101:E8

Di cosa parleremo

- Perché è importante parlare di anafilassi in età pediatrica
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- Novità

Planisfero con i casi alfa-gal



★ = Location of published reports of mammalian meat allergy due to sIgE to galactose-alpha-1,3-galactose detailed in Table I

Commins SP et al. Delayed anaphylaxis to alpha-gal, an oligosaccharide in mammalian meat. *Allergol Int.* 2016;65:16-20.

I tempi della reazione

Country	Suspected tick species	Timing of reactions	Implicated foods	Reference
Australia	<i>Ixodes holocyclus</i>	1–6 h	N-PMM, kangaroo, horse, gelatin	16,17
France		0.5–5 h	N-PMM, pork kidney, horse	8,9
Germany	<i>Ixodes ricinus</i>	0.25–5 h	N-PMM, pork kidney, gelatin	12,13
Japan		>2 h	N-PMM	11
Panama	<i>Amblyomma cajennense</i>	1.5–6 h	N-PMM	15
Spain	<i>Ixodes ricinus</i>	2–6 h	N-PMM	10
Sweden	<i>Ixodes ricinus</i>	1.5–6 h	N-PMM, moose	14,26
United States	<i>Amblyomma americanum</i>	2–6 h	N-PMM, squirrel, gelatin	6,7,22,24

N-PMM, non-primate mammalian meat = e.g., beef, pork, lamb, goat, venison, rabbit.

Commins SP et al. Delayed anaphylaxis to alpha-gal, an oligosaccharide in mammalian meat. *Allergol Int.* 2016;65:16-20.

TABLE I. Clinical criteria for diagnosing anaphylaxis

Anaphylaxis is highly likely when any one of the following 3 criteria are fulfilled:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula)

AND AT LEAST ONE OF THE FOLLOWING

- a. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)
 - b. Reduced BP or associated symptoms of end-organ dysfunction (eg, hypotonia [collapse], syncope, incontinence)
2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):
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Apparati coinvolti

Segni e sintomi iniziali

N(%)

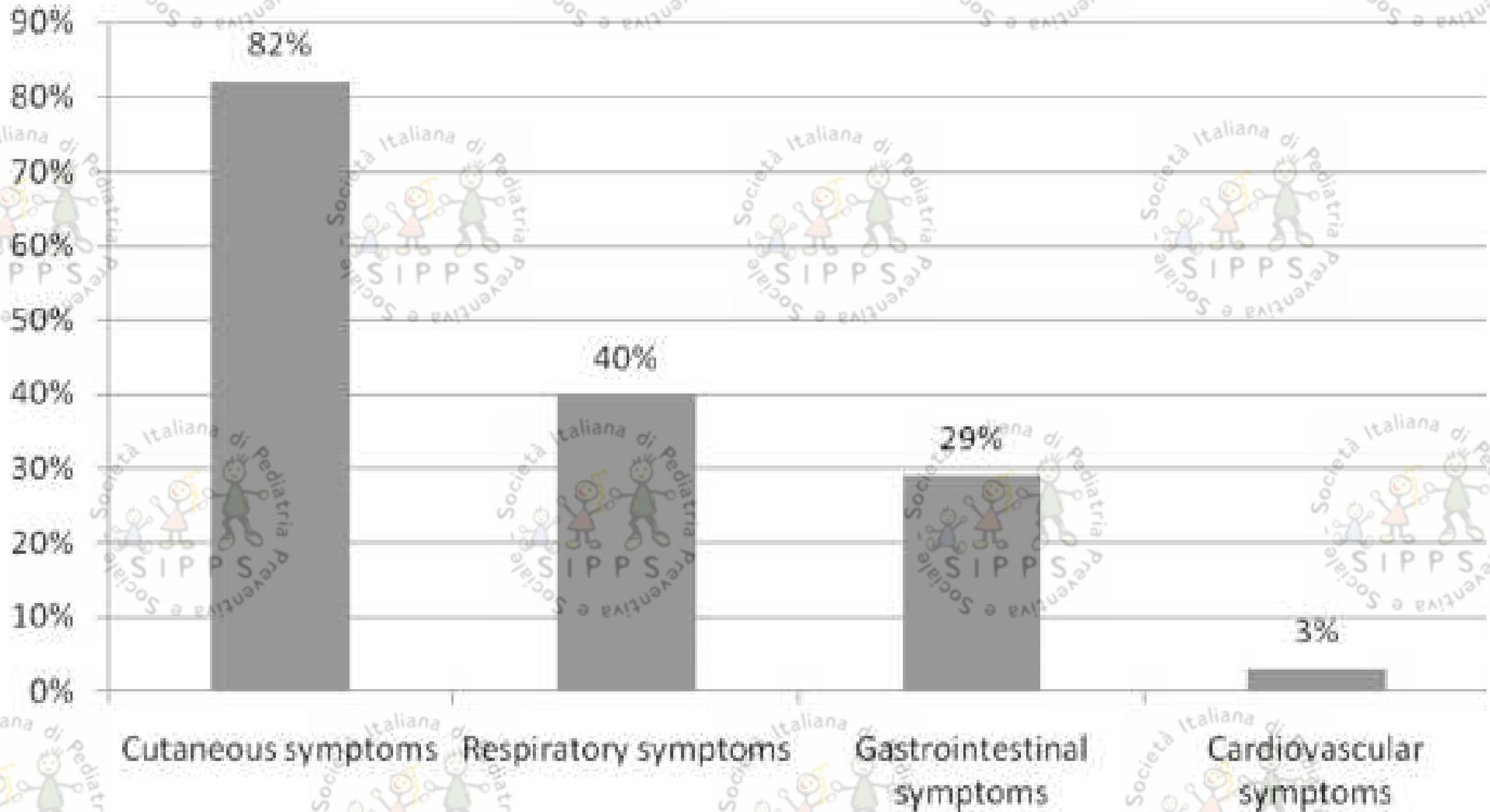
Tegumentario	33(60)
Respiratorio	14(25)
Gastrointestinale	3(5)
Neurologico	2(4)
Cardiovascolare	1(2)
Altri	2(4)

Segni e sintomi globali

N(%)

Tegumentario	51(93)
Respiratorio	51(93)
Cardiovascolare	14(26)
Neurologico	14(26)
Gastrointestinale	7(13)

Meno segni respiratori



Kilger M et al. Acute and preventive management of anaphylaxis in German primary school and kindergarten children. BMC Pediatr. 2015;15:159.

Asma e asma severo

Topic	Clinical or basic research concerns	Advances and observations
Food allergy	Epidemiology	<ul style="list-style-type: none"> Childhood peanut allergy appears to have increased and exceeds a prevalence of 1%. Delayed introductions of milk and egg are associated with increased risk of atopic outcomes. Maternal ingestion of peanut during pregnancy was associated with increased risk of infant peanut sensitization among a cohort of atopic infants.
	Pathophysiology	<ul style="list-style-type: none"> Allergen-induced <i>IL4</i> expression was related to milk allergy in the absence of <i>GATA3</i> expression.
	Diagnostic testing	<ul style="list-style-type: none"> Binding to Ara h 2 provided the best peanut allergy diagnostic discrimination in a population-based cohort. Studies of epitope binding provide insights on the prognosis, severity, and phenotypic expression of milk allergy.
	Treatment/management	<ul style="list-style-type: none"> Oral immunotherapy shows promise for the treatment of peanut allergy. A preliminary study of epicutaneous immunotherapy with milk protein shows a trend toward efficacy.
Anaphylaxis	Epidemiology	<ul style="list-style-type: none"> A database of >1 million person-years shows increased risk for anaphylaxis among persons with asthma, particularly severe asthma.

Sicherer SH et al. Advances in allergic skin disease, anaphylaxis, and hypersensitivity reactions to foods, drugs, and insects in 2010. *J Allergy Clin Immunol* 2011;127:326-35.

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Cosa vuol dire “likely allergen”?

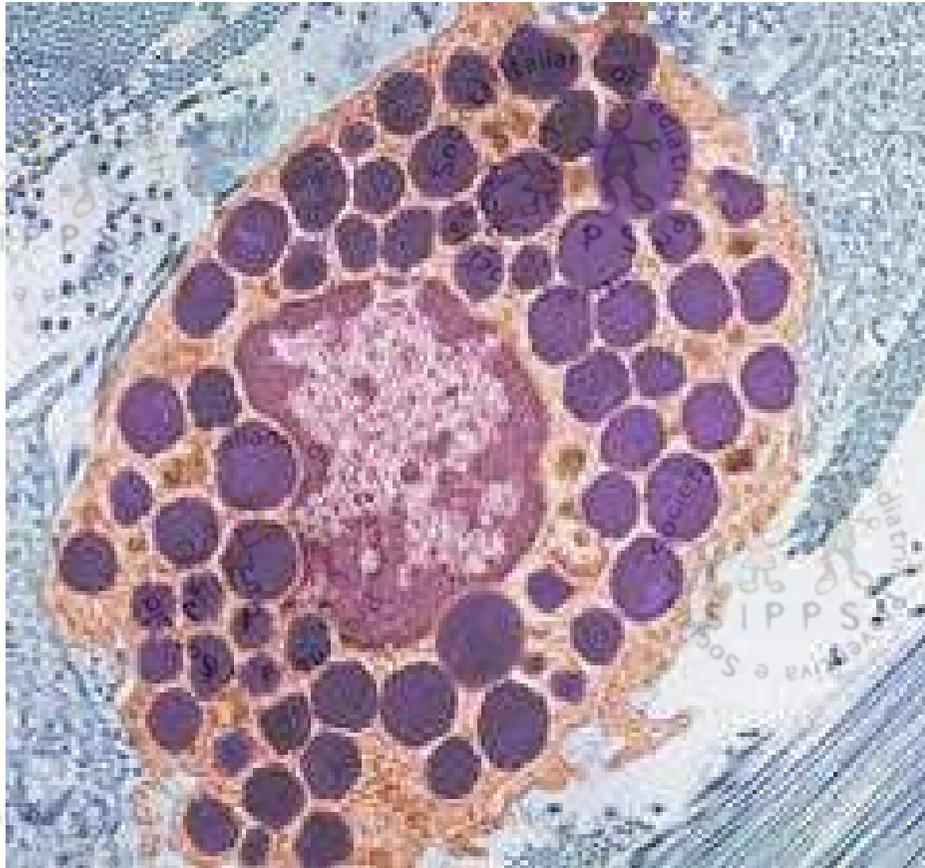
Allergene probabile

- Che ha un intervallo temporale breve
- La reazione si è ripetuta per lo stesso alimento senza ancora aver fatto diagnosi
- Reazione che si è verificata per un nuovo alimento probabilmente cross-reattivo con l'alimento indice
- Si tratta di un alimento introdotto per la prima volta, ma molto allergizzante (frutta secca, pesce ecc.)

Di cosa parleremo

- Perché è importante parlare di anafilassi in età pediatrica
- La definizione di anafilassi
- **Indicazioni assolute e relative alla prescrizione di adrenalina**
- **Novità**

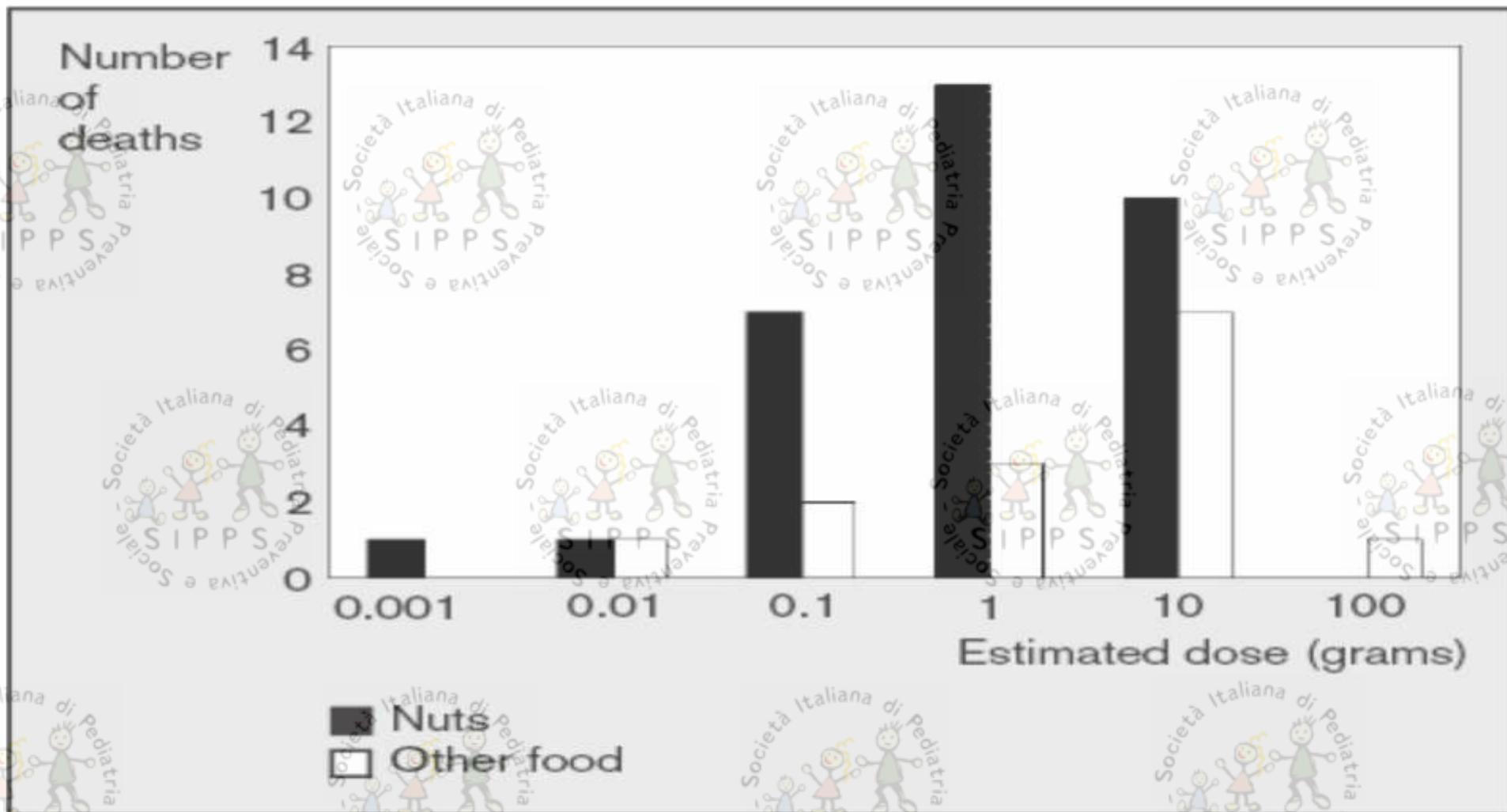
La mastocitosi



In children, increased risk is limited to those with extensive skin involvement and high tryptase.

Schuch A et al. Mastocytosis and Anaphylaxis. Immunol Allergy Clin North Am. 2017;37:153-164.

Anafilassi fatale: dose stimata di alimento come causa di morte



Pumphrey. Anaphylaxis: can we tell who is at risk of a fatal reaction? Curr Opin Allergy Clin Immunol 2004;4:285-290



Abril-Gil M et al. Effect of a cocoa-enriched diet on immune response and anaphylaxis in a food allergy model in Brown Norway rats. J Nutr Biochem. 2016;27:317-26.

Anafilassi da carne rossa

TIPO DI ALLERGIA	CARATTERISTICHE
allergia alla carne	IgE mediata. allergeni: sieroalbumine bovine/ovine.
pork-cat syndrome	cross-reattività carne di maiale & epitelio del gatto. allergene: sieroalbumina.
milk-beef syndrome	cross-reattività latte & carne di manzo. allergene: sieroalbumina bovina.
FDEIA food-dependent exercise-induced anaphylaxis	anafilassi da carne dopo esercizio fisico. allergeni: proteine della carne.
anafilassi ritardata da carne di mammifero	anafilassi ritardata (3-7 h) dopo assunzione di carni di mammiferi (carni bovine, suine, ovine). allergene: α-gal

Si ripetono: la necessità di parlarne ai parenti

Ratio Boys/Girls	50/37	57.5%/42.5%
Average age (in years) of children affected	7	
Children with a single episode of anaphylaxis	30	34.5%
Children with 2 to 5 episodes of anaphylaxis	41	47.1%
Children with more than 5 episodes of anaphylaxis	12	13.8%
Missing data concerning episodes of anaphylaxis	4	4.6%
Occurrence of the anaphylactic reaction: 6 months ago	9	10.3%
Occurrence of the anaphylactic reaction: 12 months ago	10	11.5%
Occurrence of the anaphylactic reaction: 18 months ago	9	10.3%
Occurrence of the anaphylactic reaction: more than 24 months ago	56	64.4%
Occurrence of the anaphylactic reaction: missing data	3	3.5%
Site of occurrence of anaphylactic reaction: child's home	58	66.7%
Site of occurrence of anaphylactic reaction: school or kindergarten	23	26.4%
Site of occurrence of anaphylactic reaction: relative's/friend's house	19	21.8%
Site of occurrence of anaphylactic reaction: on holiday	15	17.2%

Kilger M et al. Acute and preventive management of anaphylaxis in German primary school and kindergarten children. BMC Pediatr. 2015;15:159.

Frutta secca e cross reattività

Food allergen	Potential clinical cross-reactivity
Peanut	<p>Legumes (soy, lentils, chickpeas)</p> <p>High rate of cross-sensitization, but clinical cross-reactivity uncommon (5%)</p> <p>Multiple legume allergy may be associated with sensitization to lentil and chickpea</p>
Tree nuts	<p>Tree nuts</p> <p>Approximately one-third of patients with peanut allergy report clinical reactivity to tree nuts (not evaluated by DBPCFC)</p> <p>Significant cross-reactivity between peanut and certain tree nut epitopes (almond, walnut, pecan, hazelnut, Brazil nut)</p>
Seeds	<p>Seeds</p> <p>Co-sensitization is common, but clinical cross-reactivity unknown</p>
Tree nuts	<p>Other tree nuts</p> <p>Clinical reactivity to multiple tree nuts reported in up to one-third of patients (37%)</p>
Seeds	<p>Seeds</p> <p>Co-sensitization is common, but clinical cross-reactivity unknown</p>
Walnut	<p>Peanut (see above)</p> <p>Pecan – clinical cross-reactivity</p>
Cashew	<p>Coconut – homologous but clinical cross-reactivity rare</p> <p>Pistachio – clinical cross-reactivity</p>

Lomas JM et al. Managing nut-induced anaphylaxis: challenges and solutions. J Asthma Allergy. 2015;8:115-123.

Evidenze per l'action plan

Recommendation	Evidence level	Grade
Anaphylaxis management plan An anaphylaxis management plan should be used from the time of diagnosis to prevent future reactions, and aid recognition and treatment of any further reactions	III	C
Venom immunotherapy Subcutaneous venom immunotherapy is recommended in venom-allergic patients with a previous episode of anaphylaxis and adults with systemic cutaneous reactions	I	A
Training Training in the recognition and management of anaphylaxis should be offered to all patients and caregivers of children at risk of anaphylaxis ideally from the time of diagnosis	V	D
Training in the recognition and management of anaphylaxis, including the use of adrenaline auto-injectors, should be offered to all professionals dealing with patients at risk of anaphylaxis	IV	C
Training packages should be developed with the target groups	V	D
Training should cover allergen avoidance, symptoms of allergic reactions, when and how to use an adrenaline auto-injector, and what other measures are needed within the context of an anaphylaxis management plan	V	D
Training may involve more than one session to allow revision, an interactive scenario-based approach, a standardized program with manual and educational material and simulation tools. Content and language should be tailored to be understood and memorized	V	D
Psychological interventions Educational interventions should ideally incorporate psychological principles and methods to address anxiety so that children and families may function well at home, at school/work, and socially despite their risk of future reactions and should ideally be part of their educational training. This can be done in a group format. Some patients, with severe anxiety of ongoing duration, may need more in-depth one-to-one psychological intervention	V	D

Muraro A et al. EAACI Food Allergy and Anaphylaxis Guidelines Group. Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. *Allergy*. 2014;69:1026-45.

Il termine anafilassi

The term anaphylaxis stems from the Greek words *ana* (against) and *utkaniv* phylaxis (protection)

Was first coined by Professor Charles Robert Richet in 1902, Nobel Prize Winner for Medicine and Physiology, and by Dr Portier to describe a set of symptoms that was the opposite of immunity.

Portier MM, Richet C. De l'action anaphylactique de certains venims. *Comptes Rendus des Seances Mem Soc Biol* 1902;54:170–172.

Ben-Shoshan M et al. Anaphylaxis: past, present and future. *Allergy* 2011;66:1-14.

Anafilassi da Ranitidina e.v.



Mori F, et al. Anaphylaxis to Intravenous Ranitidine in a Child. Pharmacology. 2015;95:240-242.

Anafilassi durante desensibilizzazione orale alla rifampicina



Syrigou E et al. Anaphylaxis during rapid oral desensitization to rifampicin. J Allergy Clin Immunol Pract. 2015 Oct 23.

Anche gli agenti biologici



Puxeddu I et al. Hypersensitivity reactions during treatment with biological agents. Clin Exp Rheumatol. 2016 Jan 9.



Delayed diagnosis of anaphylaxis secondary to ondansetron

A case report



Preeti Goyal, Kaggere Paramesh, Sarang Puranik, Mark Proctor
and Mihir Sanghvi



Goyal P et al. Eur J Anaesthesiol. 2016 Feb;33(2):146-7.

Cosa diremo

- Quando prescrivere l'adrenalina
- Come presentare alla famiglia "allargata" l'action plan
- Quando usare due adrenaline
- **Lo scarso utilizzo**
- Cosa fare se si tratta di un piccolo lattante

Fatal Anaphylactic Shock Ceftriaxone-Induced in a 4-Year-Old Child

Gioacchino Calapai, MD, Selene Imbesi, MD,† Elvira Ventura-Spagnolo, MD,‡ Viviana Cafeo, MD,*
Livio Milone, MD,‡ Michele Navarra, PharmD,§|| and Sebastiano Gangemi, MD†¶*

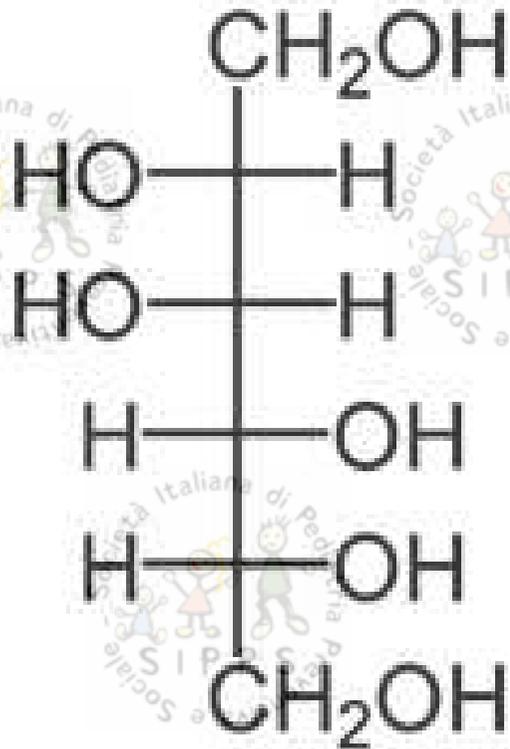
- Breve intervallo fra assunzione e anafilassi
- Pregressa esposizione a stessa cefalosporina e probabile sensibilizzazione
- Congestione poliviscerale e intensa eosinofilia all'esame istologico

6 casi di anafilassi con shock

- **Beta-methasone**
- Methylprednisolone
- Prednisolone
- Triamcinolone

Caduff C et al. Immediate hypersensitivity reactions to parenteral glucocorticoids? Analysis of 14 cases. Schweiz Med Wochenschr 2000 1;130:977-83.

Anafilassi a farmaco e.v. già assunto per os: è un problema di eccipienti



D-MANNITOLO



MANNA (linfa estratta dalla corteccia del frassino opportunamente incisa)

Jain SS et al. Anaphylaxis following intravenous paracetamol: the problem is the solution. *Anaesth Intensive Care*. 2015;43:779-81.

Effetti antiedemigeni cerebrali



Lightner DD et al. A case of mannitol hypersensitivity. J Pediatr Hematol Oncol. 2013;35:e274-5.



The background of the slide is a repeating pattern of the SIPPSS logo. Each logo is circular and contains the text 'Società Italiana di Pediatria Preventiva e Sociale' around the perimeter and 'SIPPSS' in the center. In the middle of the logo is a colorful illustration of three stylized children holding hands.

Diagnosi 2016

La spettrometria di massa



Poli C et al. Comparison of two enzymatic immunoassays, high resolution mass spectrometry method and radioimmunoassay for the quantification of human plasma histamine. J Pharm Biomed Anal. 2016;118:307-14.

Laboratory tests to be considered in the differential diagnosis of anaphylaxis

- **Serum tryptase levels**

peak 60-90 minutes after the onset of anaphylaxis and persists to six hours.

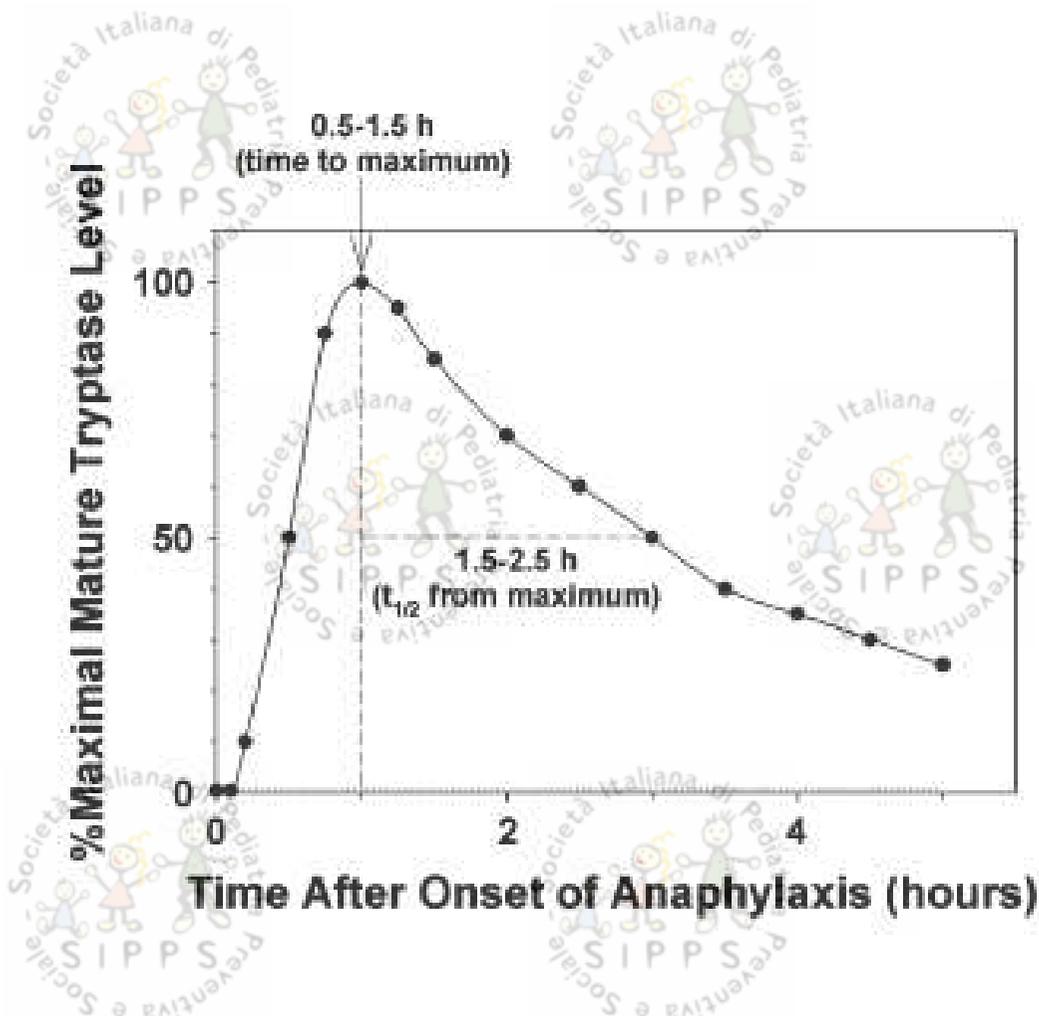
- **Plasma histamine levels**

begin to rise within 5-10 minutes and remain elevated only for 30-60 minutes.

- **24-hour urinary histamine (methyl histamine) and its metabolites**

are elevated for a longer period of time – up to 24 hours.

Andamento dei livelli ematici di triptasi: prelievo da 1 a 3 h dopo esordio





- Porcine angiotensin I converting enzyme (ACE I)
- Aminopeptidase N (AP-N).

Hilger C et al. Two galactose- -1,3-galactose carrying peptidases from pork kidney mediate anaphylactogenic responses in delayed meat allergy. Allergy. 2016 Jan 5.

The background of the slide is a repeating pattern of the SIPPSS logo. Each logo is circular and contains the text 'Società Italiana di Pediatria Preventiva e Sociale' around the perimeter and 'SIPPSS' in the center. In the middle of the logo is a colorful illustration of three stylized children holding hands.

Terapia 2016

Adrenalina in film a rilascio immediato



Alayoubi A et al. Development of a fast dissolving film of epinephrine hydrochloride as a potential anaphylactic treatment for pediatrics. Pharm Dev Technol. 2016;7:1-5.



Abril-Gil M et al. Effect of a cocoa-enriched diet on immune response and anaphylaxis in a food allergy model in Brown Norway rats. J Nutr Biochem. 2016;27:317-26.

Conclusioni

- L'anafilassi deve essere correttamente riconosciuta in base ai criteri internazionali di classificazione.
- La prescrizione dell'autoiniettore di Adrenalina è assoluta in alcuni casi ben specificati
- Solo in casi particolari può essere fatta una doppia prescrizione
- Bisogna continuare a fare educazione sanitaria per ridurre il rischio che l'adrenalina non venga iniettata quando occorre

Prescrizione per autoiniettore

Recommendation	Evidence level	Grade	Key references
Absolute indications for at least one adrenaline auto-injector			
Previous anaphylaxis triggered by food, latex, or aeroallergens	IV	C	(127, 128)
Previous exercise-induced anaphylaxis	IV	C	(58)
Previous idiopathic anaphylaxis	IV	C	(61)
Co-existing unstable or moderate to severe, persistent asthma and a food allergy*	IV	C	(15, 83–86)
Venom allergy in adults with previous systemic reactions (not receiving maintenance VIT) and children with more than cutaneous/mucosal systemic reactions	IV	C	(56, 129, 130)
Underlying mast cell disorders or elevated baseline serum tryptase concentrations together with any previous systemic allergic reactions to insect stings, even in VIT-treated patients	IV	C	(52, 56, 103, 130)
Consider prescribing at least one adrenaline auto-injector with any of the following additional factors (especially if more than one is present)			
Previous mild-to-moderate allergic reaction* to peanut and/or tree nut	IV	C	(51, 79)
Teenager or young adult with a food allergy*	IV	C	(22, 45, 46, 63, 131)
Remote from medical help and previous mild-to-moderate allergic reaction to a food, venom, latex, or aeroallergens	V	D	(131); Expert consensus
Previous mild-to-moderate allergic reaction to traces of food*	V	D	(22, 45, 46, 63, 131)

Notes

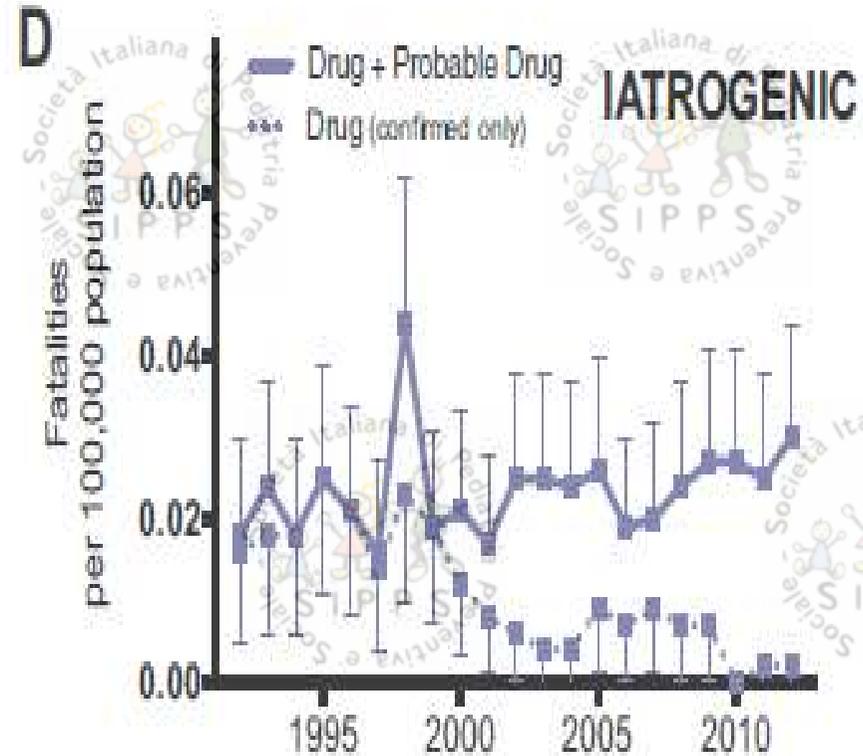
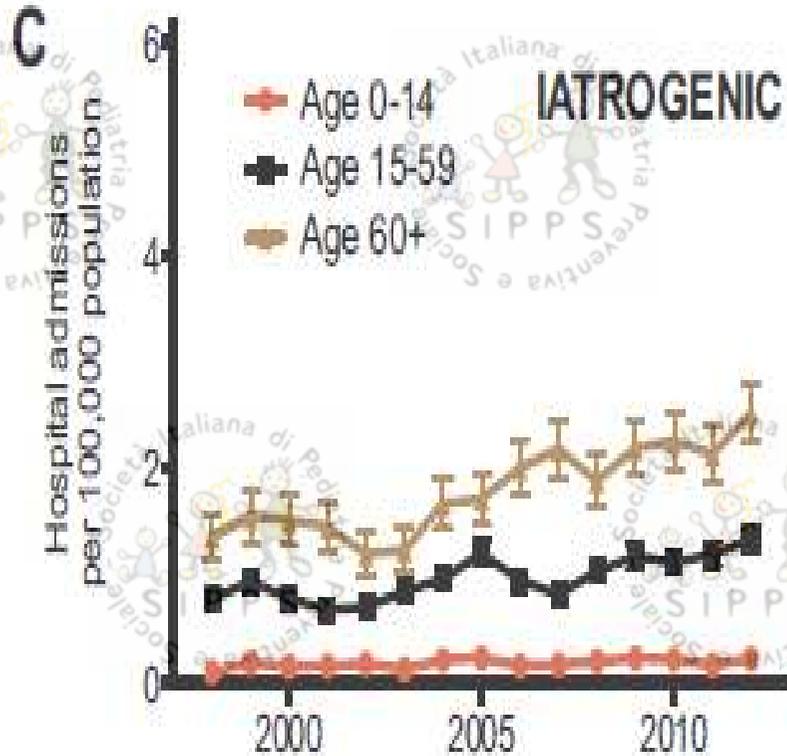
*Excluding pollen food syndrome (oral allergy syndrome).

Muraro A et al. EAACI Food Allergy and Anaphylaxis Guidelines Group. Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. *Allergy*. 2014;69:1026-45.

Agaricus arvensis e Agaricus campestris

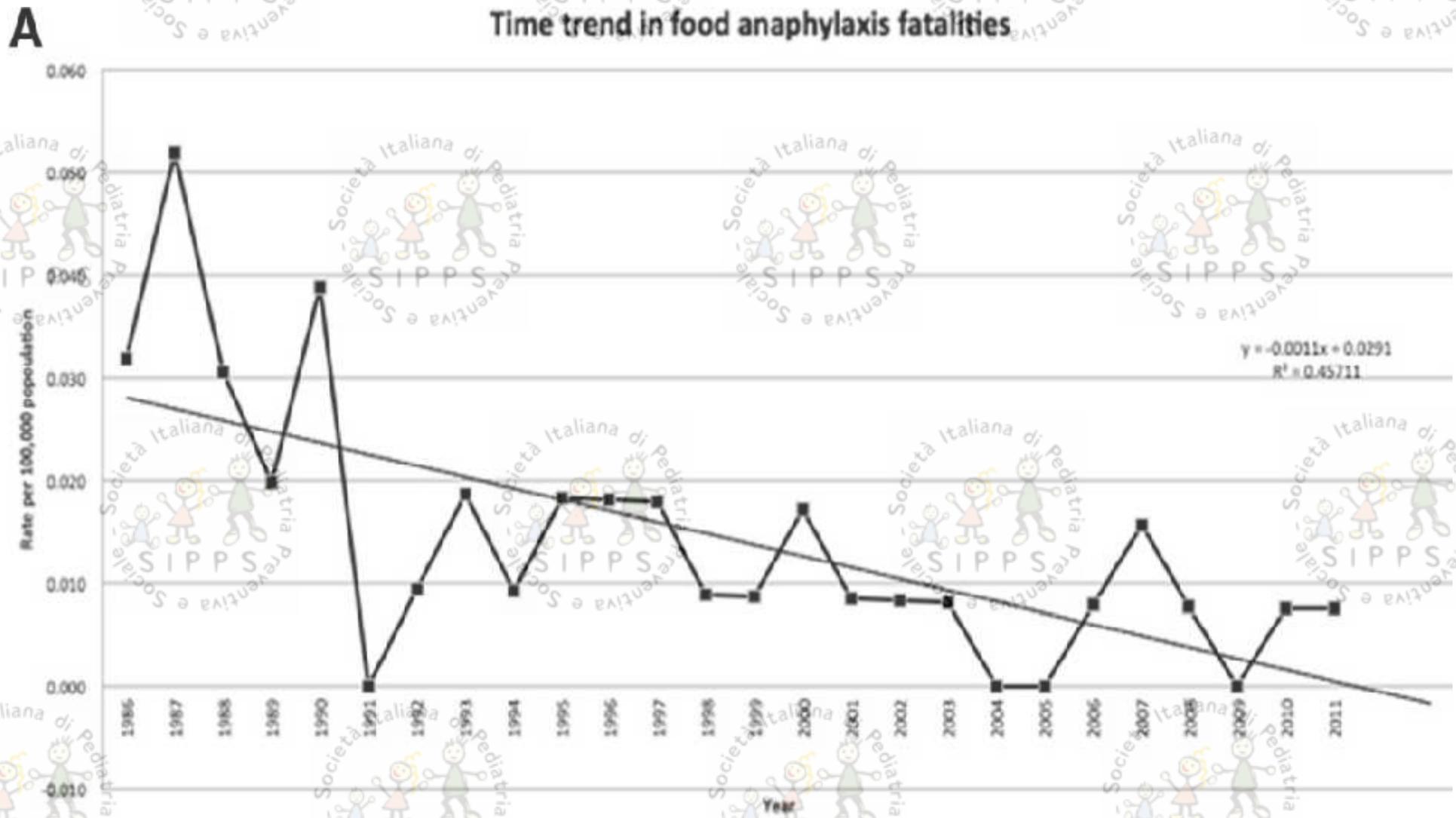


Ricoveri e decessi per anafilassi da farmaco. Quando la diagnostica migliora i casi calano



Turner PJ et al. Increase in anaphylaxis-related hospitalizations but no increase in fatalities: an analysis of United Kingdom national anaphylaxis data, 1992-2012. *J Allergy Clin Immunol.* 2015 Apr;135(4):956-63.e1.

Ontario: cause di eventi fatali da alimento



Xu YS et al. Anaphylaxis-related deaths in Ontario: a retrospective review of cases from 1986 to 2011. Allergy Asthma Clin Immunol. 2014;10:38.

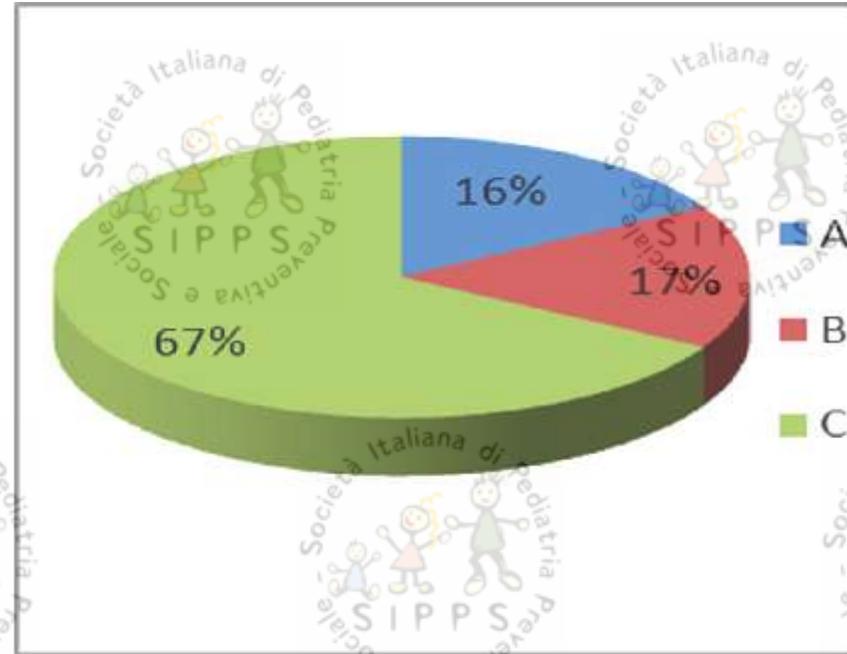


Quali sono le caratteristiche del paziente ideale?

A. Anafilattici per tracce o per dosi molto basse

B. Soggetti con una tolleranza parziale

C. Entrambi



A	B	C
4	4	16

Meglio P. et al. The oral food desensitization in the Italian allergy centres. Eur Ann Allergy Clin Immunol 2015;47:68-76.

OR e fallimento precoce o tardivo della SOTI in APLV: non viene mai fatta

Background variable	6-month OIT induction phase OR (95% CI, p-value)	2 years after induction phase OR (95% CI, p-value)
Sex (male)	1.0 (0.2–5.7, p = 0.93)	1.2 (0.3–4.7, p = 0.80)
Asthma	13.7 (1.1–170, p = 0.041)	0.7 (0.2–3.1, p = 0.66)
Allergy to eggs and/or wheat	0.1 (0.03–0.77, p = 0.024)	0.6 (0.1–2.4, p = 0.46)
History of the use of <u>epinephrine</u> due to milk allergy	1.1 (0.2–6.2, p = 0.91)	1.6 (0.4–6.0, p = 0.47)
Age	1.0 (0.8–1.3, p = 0.96)	0.9 (0.7–1.1, p = 0.29)
Milk-specific IgE < 10 IU/L (before OIT)	1	1
Milk-specific IgE 10–100 IU/L (before OIT)	0.9 (0.1–7.1, p = 0.90)	2.0 (0.5–8.3, p = 0.33)
Milk-specific IgE > 100 IU/L (before OIT)	15.7 (1.8–137, p = 0.013)	4.7 (0.6–36.4, p = 0.14)

Kivistö JE et al. Half of the children who received oral immunotherapy for a cows' milk allergy consumed milk freely after 2.5 years. Acta Paediatr 2015;104:1164-8

Bene a 7 anni

Symptoms and rescue treatments	Questionnaire at three years (n = 20)	Questionnaire at four years (n = 17)	Questionnaire at five years (n = 13)	Questionnaire at seven years (n = 16)
Symptoms				
Intestinal	4	3	1	2
Oral	4	4	4	0
Dermal	8	5	3	1
Angioedema	1	0	2	0
Asthma	3	0	2	0
Conjunctival	1	0	0	0
Nasal	0	0	1	0
No symptoms	10 (50.0%)	10 (58.8%)	8 (61.5%)	13 (81.3%)
Treatment for symptoms				
Oral antihistamine	5	5	5	3
Oral corticosteroid	2	1	2	1
Adrenalin injection	1	0	0	0
No treatment for symptoms	15 (75.0%)	12 (70.6%)	8 (61.5%)	13 (81.3%)

Paassilta M et al. Children who were treated with oral immunotherapy for cows' milk allergy showed long-term desensitisation seven years later. Acta Paediatr. 2015 Oct 27.

Carne – -Gal

Triggers

- Le reazioni di tipo ritardato avvengono dopo l'ingestione di carne rossa o frattaglie, cioè manzo, maiale, montone, vitello, cavallo, coniglio, cinghiale, lingua, fegato, rene, intestino, ma non pollo, tacchino o pesce
- I pazienti sono spesso in grado di tollerare piccole quantità di carne senza reazioni; quantità elevate come un doppio hamburger o 2 salsicce (86 g) possono indurre reazioni gravi
- Più la carne è grassa maggiore è il rischio
- Il rene è molto ricco in -Gal e può indurre reazioni anche con minime quantità e talvolta non ritardate
- Sia la carne cruda che cotta può causare reazioni
- Molti pazienti allergici alla carne sono sensibilizzati alla **gelatina** (contiene -Gal) che rappresenta quindi un rischio (presente in caramelle, addensanti alimentari, gelati, maionese, yogurt, salame, salsicce)
- -Gal è contenuta anche nel frammento Fab dell'anticorpo monoclonale **Cetuximab**. È quindi consigliata la verifica di assenza di positività prima della somministrazione
- I co-fattori come le infezioni, l'esercizio fisico, l'alcol, i FANS, possono diminuire la dose di allergene necessaria per scatenare i sintomi



Ricoveri in H per anafilassi in Australia

Mullins RJ et al. Time trends in Australian hospital anaphylaxis admissions in 1998-1999 to 2011-2012. J Allergy Clin Immunol. 2015;136:367-75.

Ricoveri in H per anafilassi in Australia

Anafilassi
totali

Anafilassi
da
alimento

Mullins RJ et al. Time trends in Australian hospital anaphylaxis admissions in 1998-1999 to 2011-2012. J Allergy Clin Immunol. 2015;136:367-75.

Pancake anaphylaxis

Adachi YS et al. A case of mite-ingestion-associated exercise-induced anaphylaxis mimicking wheat-dependent exercise-induced anaphylaxis. *Int Arch Allergy Immunol* 2013;162:181-3.

Indicazioni assolute

- Farmaci?
- Idiopatiche in generale o perché non capiamo noi?
- Asma persistente

Caso fatale a Messina

Tryptase can even be measured from a blood sample taken from any person who has died of the anaphylactic shock.

In the normal condition, the level of **tryptase** circulating in serum is at or close to zero.

Calapai G et al. Fatal Anaphylactic Shock Ceftriaxone-Induced in a 4-Year-Old Child. *Pediatr Emerg Care.* 2016;32:32-3.

Riduzione rischio di esposizione in FA

Vale S et al. ASCIA guidelines for prevention of anaphylaxis in schools, pre-schools and childcare: 2015 update. J Paediatr Child Health. 2015;51:949-54.

Multiplex CRD nell'anafilassi idiopatica?



Luengo O et al. Component resolved diagnosis: when should it be used?
Clin Transitional Allergy 2014;4:28

Le considerazioni

- Several hours: anafilassi tardiva alla carne rossa
- Orticaria + edema dell'ugola: un solo apparato
- Compromissione respiratoria: deve esserci una sintomatologia severa
- SNC ipotonia e rilascio degli sfinteri
- I disturbi gastrointestinali sono persistenti

La diagnosi differenziale

Simons FER et al. World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis. J Allergy Clin Immunol 2011;127:593.e1- e22



Anaphylaxis is a under recognized disease

- First episode
 - Trigger not apparent, hidden or not previously recognized
 - Idiopathic anaphylaxis
-
- Failure to recognize (by patient or caregiver) because of:
 - Cognitive, visual or auditory impairment
 - Neurologic, psychiatric, or psychologic problems
 - Use of medications, including sedating H₁ antihistamines or recreational drugs, or use of ethanol
 - Failure to diagnose (by health care professional) because of:
 - Absence of skin symptoms and signs
 - Patient not undressed or fully examined
 - Vulnerable person: infant, elderly
 - Patient who cannot describe subjective symptoms because of being:
 - Aphonic or disphonic
 - Dyspneic
 - Unconscious
 - Reporting of serious or fatal anaphylactic events is not mandatory

Simons FE. J Allergy Clin Immunol 2008;122:1166-8.

Overdiagnosis of anaphylaxis

- Subjective symptoms only
 - Nonspecific signs
 - Diagnostic error
 - Hyperventilation
 - Anxiety

Panic attack (difficulty breathing)

Vasovagal episode (faint)

Munchausen syndrome or by proxy (in children)

Scombroidosis

Anisakiasis

Simons FE. J Allergy Clin Immunol 2008;122:1166-8.



Administration of epinephrine for life - threatening allergic reactions in school settings

In 24% of the cases, the individual was not known to have a life-threatening allergy.

McIntyre CL. Pediatrics 2005;116:1134-40.



Definizione di anafilassi idiopatica

- L'anafilassi idiopatica è un'anafilassi non spiegata da una causa comprovata o presunta.
- Diventa una diagnosi di esclusione, dopo aver eliminato altre cause come ad esempio alimenti, farmaci, esercizio fisico, alimento + esercizio fisico, punture di insetti, mastocitosi, e deficit o ipoattività del C1 inibitore

La classificazione dell'anafilassi idiopatica



Greenberger PA. Idiopathic anaphylaxis. Immunol Allergy Clin North Am. 2007; 27:273-93.

L'identikit del paziente con anafilassi idiopatica

- Circa 10-60% di tutti i casi di anafilassi (rara nel bambino)
- Rapp. F/M 2:1
- Nel 35% dei casi notturna
- Sintomi cutanei presenti in 0 100% dei casi
- Alta incidenza di associazione con anafilassi da causa nota e OC idiop.
- Recidive frequenti
- Frequente remissione spontanea entro alcuni anni
- Rari coinvolgimento cardiovascolare e fatalità
- Generalmente responsiva ai glucocorticoidi
- D.D. con molte patologie (in primis mastocitosi)

Ditto, AAI 1996;77:285

Ditto, JACI 1997;100:320

Tejedor-Alonso, AAI 2002;88:313

Greenberger, JACI Pract 2014;2:243

Tryptase levels

□ **β tryptase precursors** seem to be continuously secreted by human mast-cells, with their levels in blood typically reflecting the burden or number of mast-cells.

- Mature tryptase (β - tryptase) is stored in in secretory granules and is secreted only during granule exocytosis, reflecting mast-cell activation.



[Red rectangular box highlighting a logo instance]



Tanner A et al. Epinephrine Policies and Protocols Guidance for Schools:
Equipping School Nurses to Save Lives. NASN Sch Nurse. 2016;31(1):13-22.

Dal lavoro di Ondansentron



Errori nel follow-up

- 60 scolari delle scuole elementari con prescrizione di adrenalina per pregresso episodio di anafilassi
- I kit di adrenalina vengono spesso usati a sproposito o non usati quando sarebbe il caso
- Prescrizioni approssimative
- Non accompagnate da esaurienti istruzioni scritte
- Esagerazione nel numero di confezioni
- Insufficiente follow-up dei bambini

Blyth TP, Sundrum R. Adrenaline autoinjectors and schoolchildren: a community-based study. Arch Dis Child 2002;86:26-27.

Classificazione: rappresentazione grafica

Manivannan V et al. Visual representation of National Institute of Allergy and Infectious Disease and Food Allergy and Anaphylaxis Network criteria for anaphylaxis. Int J Emerg Med. 2009;2:3-5.

TABLE I. Clinical criteria for diagnosing anaphylaxis

Anaphylaxis is highly likely when any one of the following 3 criteria are fulfilled:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula)

AND AT LEAST ONE OF THE FOLLOWING

- a. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)
 - b. Reduced BP or associated symptoms of end-organ dysfunction (eg, hypotonia [collapse], syncope, incontinence)
2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):
 - a. Involvement of the skin-mucosal tissue (eg, generalized hives, itch-flush, swollen lips-tongue-uvula)
 - b. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)
 - c. Reduced BP or associated symptoms (eg, hypotonia [collapse], syncope, incontinence)
 - d. Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)
 3. Reduced BP after exposure to known allergen for that patient (minutes to several hours):
 - a. Infants and children: low systolic BP (age specific) or greater than 30% decrease in systolic BP*
 - b. Adults: systolic BP of less than 90 mm Hg or greater than 30% decrease from that person's baseline

PEF, Peak expiratory flow; BP, blood pressure.

*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.

Prurito orale predittore di segni obiettivi durante DBPCFC per PLV

Kok EE et al. Oropharyngeal symptoms predict objective symptoms in double-blind, placebo-controlled food challenges to cow's milk. Allergy 2009;64:1226-7

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Apparati coinvolti

Segni e sintomi iniziali

N(%)

Tegumentario	33(60)
Respiratorio	14(25)
Gastrointestinale	3(5)
Neurologico	2(4)
Cardiovascolare	1(2)
Altri	2(4)

Segni e sintomi globali

N(%)

Tegumentario	51(93)
Respiratorio	51(93)
Cardiovascolare	14(26)
Neurologico	14(26)
Gastrointestinale	7(13)

Il release

Blank U. et al. Vesicular trafficking and signaling for cytokine and chemokine secretion in mast cells. *Front Immunol.* 2014;5:453.



Rachid O, Simons FE, Rawas-Qalaji M, Lewis S, Simons KJ. Epinephrine autoinjectors: does freezing or refrigeration affect epinephrine dose delivery and enantiomeric purity? *J Allergy Clin Immunol Pract.* 2015 Mar-Apr;3(2):294-6.



Concomitanti mastocitosi o malattie cardiovascolari

Simons FE et al. International consensus on (ICON) anaphylaxis. World Allergy Organ J. 2014;7:9.

Cosa diremo

- Quando prescrivere l'adrenalina
- Come presentare alla famiglia "allargata" l'action plan
- Quando usare due adrenaline
- Lo scarso utilizzo
- Cosa fare se si tratta di un piccolo lattante

Proposte per la prescrizione di Adrenalina in AA

Niggemann B et al. Adrenaline autoinjectors in food allergy: in for a cent, in for a euro? *Pediatr Allergy Immunol.* 2012;23:506-8.

Indicazioni relative

- Ogni reazione a piccola dose? Dipende dall'alimento. Se ad esempio è il kiwi diventa difficile venire a contatto anche con piccole dosi.
- Reazione lieve, non moderata, a frutta secca. Le reazioni successive possono essere più marcate?
- Due fattori relativi fanno sempre uno assoluto?
- Airborne food allergy. E' la stessa cosa per cute e respiratorio?
- Per un teenager può bastare per la prescrizione solo una reazione all'alimento senza anafilassi?