



* Exercise-Induced Allergic Diseases

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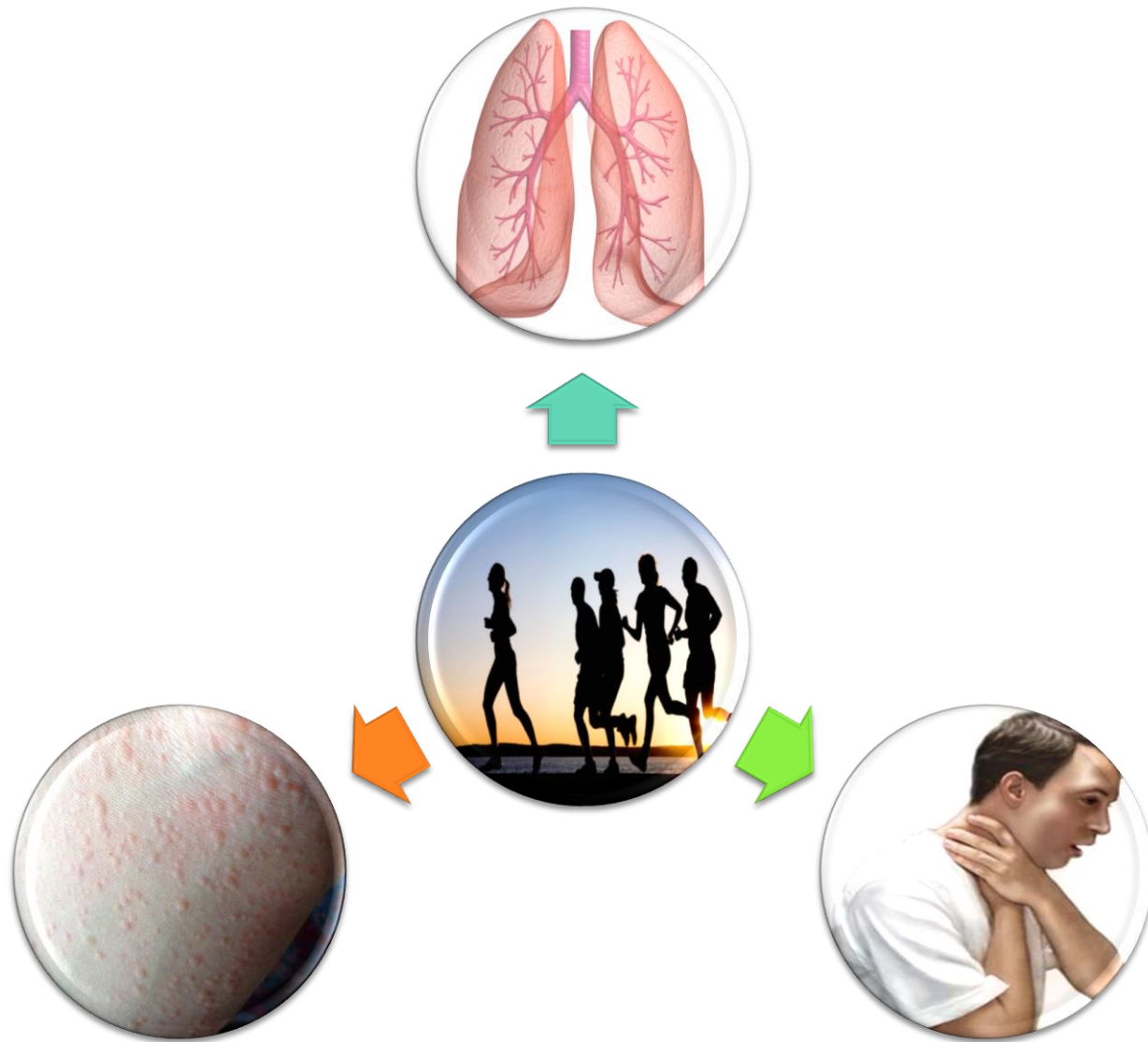
Hospital Universitari Vall d'Hebron

Barcelona, Spain

* In relation to this presentation, I declare the following, real or perceived conflicts of interest:

* ThermoFisher Scientific (Phadia)

* **Disclosure**



* **Exercise-induced allergic diseases**



ARTÍCULO ESPECIAL

Enfermedad de riesgo vital en el deporte de origen respiratorio o alérgico

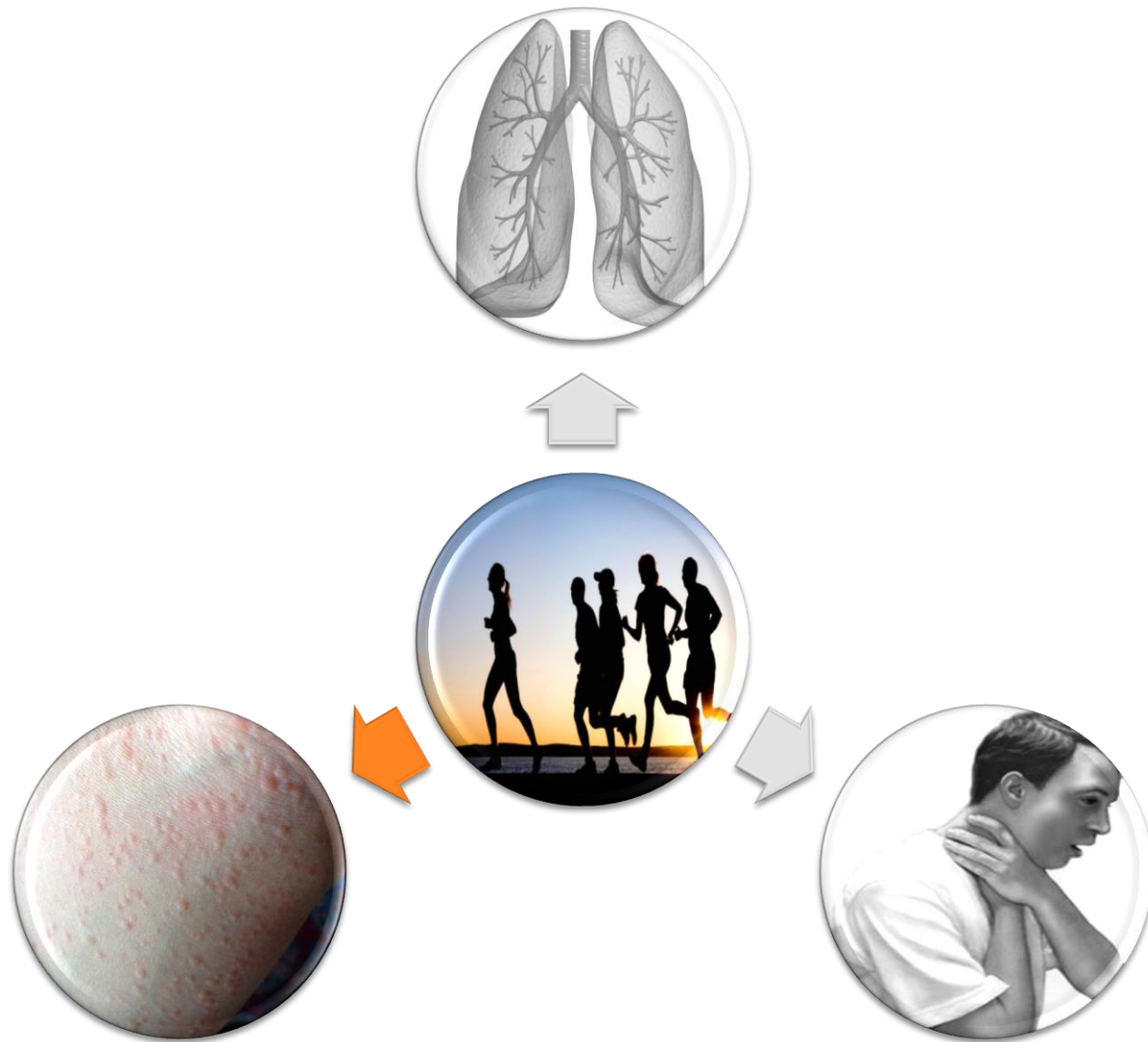
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* Exercise-induced allergic diseases

- * Pinpoint size, highly pruritic wheals, subside rapidly
- * Increased body core temperature
- * Impaired QoL, especially sporting & sexual activities

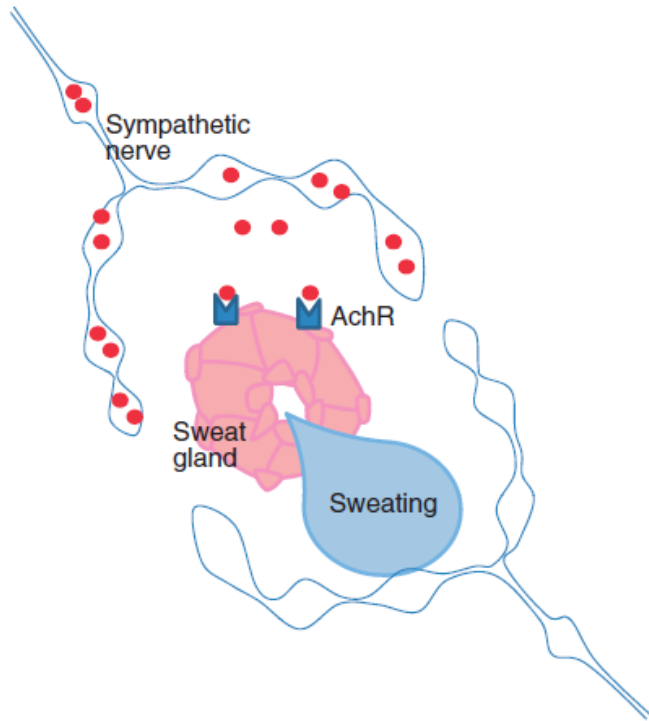


* Cholinergic urticaria

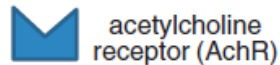
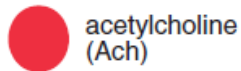
Subtype	Sweat allergy	Anhidrosis/ hypohidrosis	Intradermal test with acetylcholine	Pathology	Treatment
Sweat hypersensitivity	Positive	None	Positive	Infiltrate of lymphocytes around sweat glands	Antihistamines Desensitization?
Anhidrosis or hypohidrosis	Mostly negative	Necessary, mosaic	Partial positive	Normal	Systemic steroid
Idiopathic	Negative	None	Negative	Normal	Antihistamines

Bito T et al. Allergol Int. 2012 Dec;61(4):539-44

* Clinical subtypes of cholinergic urticaria

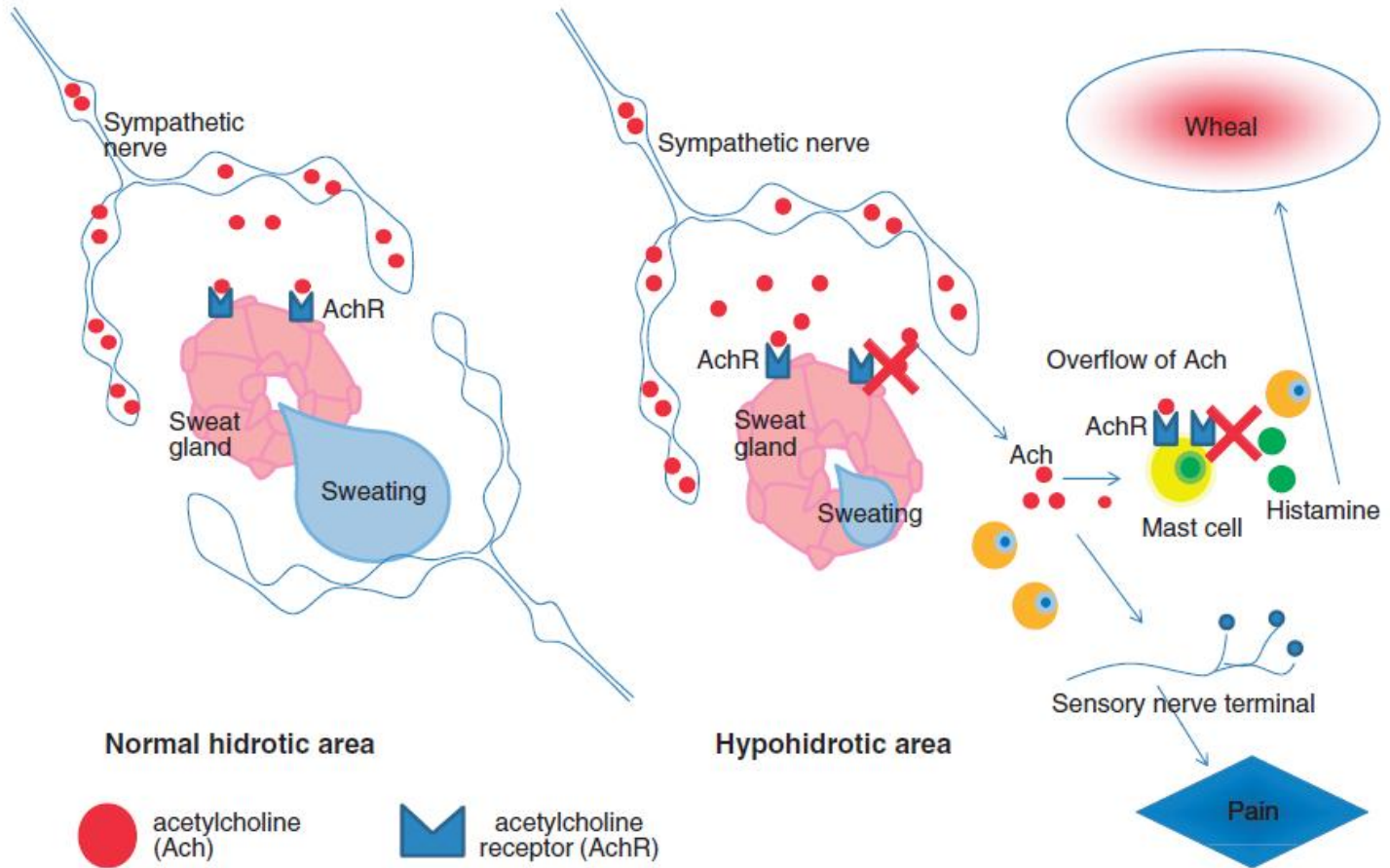


Normal hidrotic area



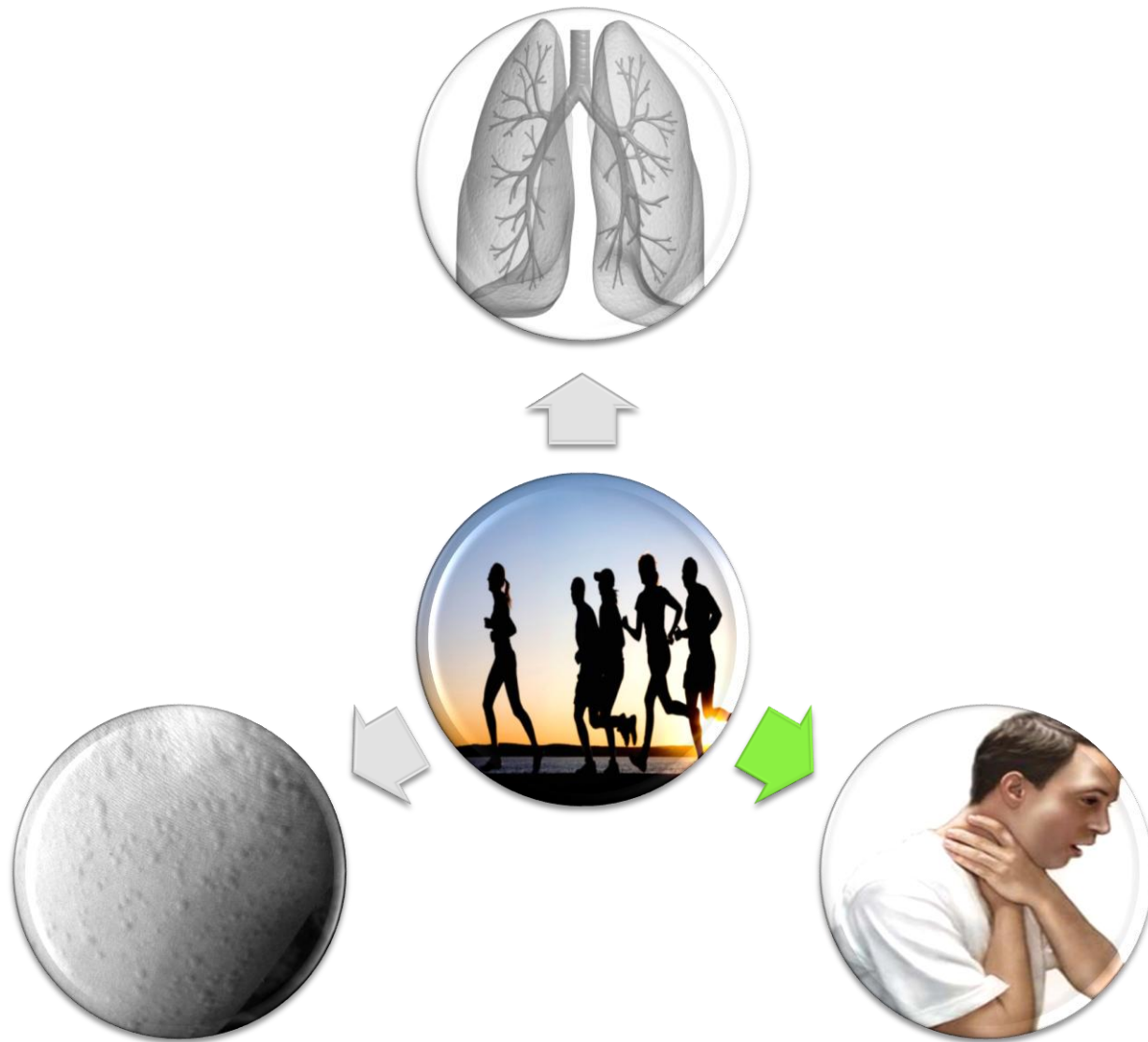
Bito T et al. Allergol Int. 2012 Dec;61(4):539-44

* **Cholinergic urticaria with hypohidrosis**



Bito T et al. Allergol Int. 2012 Dec;61(4):539-44

* Cholinergic urticaria with hypohidrosis



* Exercise-induced allergic diseases

EXERCISE-INDUCED ALLERGIC DISEASES

 **Exercise induced
anaphylaxis**

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Ver

Marathon Runner Won't Let Allergy to Exercise Hold Her Back

Oct 15, 2014, 11:31 AM ET
By SYDNEY LUPKIN via GOOD MORNING AMERICA

468

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52

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2

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21 Comments



The first one happened when she was 18 and went out for a morning run before breakfast. Because she hadn't eaten anything and didn't test positive for any **food allergies**, doctors eventually diagnosed her with exercise-induced anaphylaxis.

468
Like
101
share
52
Tweet
2
8+
21 Comments



PHOTO: At left, Mary Johnson on the way to the ER, and at right, Johnson in the Intensive Care Unit

WAO ANAPHYLAXIS GUIDELINES: 2011

PATIENTS AT ↑ RISK OF SEVERE OR FATAL ANAPHYLAXIS

CONCOMITANT DISEASES*

				
Asthma and other respiratory diseases	Cardiovascular diseases	Mastocytosis/clonal mast cell disorders	Allergic rhinitis and eczema**	Psychiatric illness (e.g. depression)

CONCURRENT MEDICATIONS/ETHANOL/RECREATIONAL DRUG USE*

		
β-adrenergic blockers and ACE inhibitors***	Ethanol/sedatives/hypnotics/antidepressants/recreational drugs (potentially affect recognition of anaphylaxis triggers and symptoms)	

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)

Simons FER et al for the WAO. *J Allergy Clin Immunol* 2011;127:587-593e22

Risk factors for anaphylactic reactions



Augmenting factors

= Factors, which lower the reaction threshold or which make symptoms more severe by directly influencing the immunological mechanism of type I allergy

e.g. physical exercise, menstruation, NSAID, alcohol, body temperature, infections, antacids



Concomitant diseases

= Co-existing diseases, which jeopardize patients or which increase mortality

e.g. bronchial asthma, cardiac diseases, mastocytosis



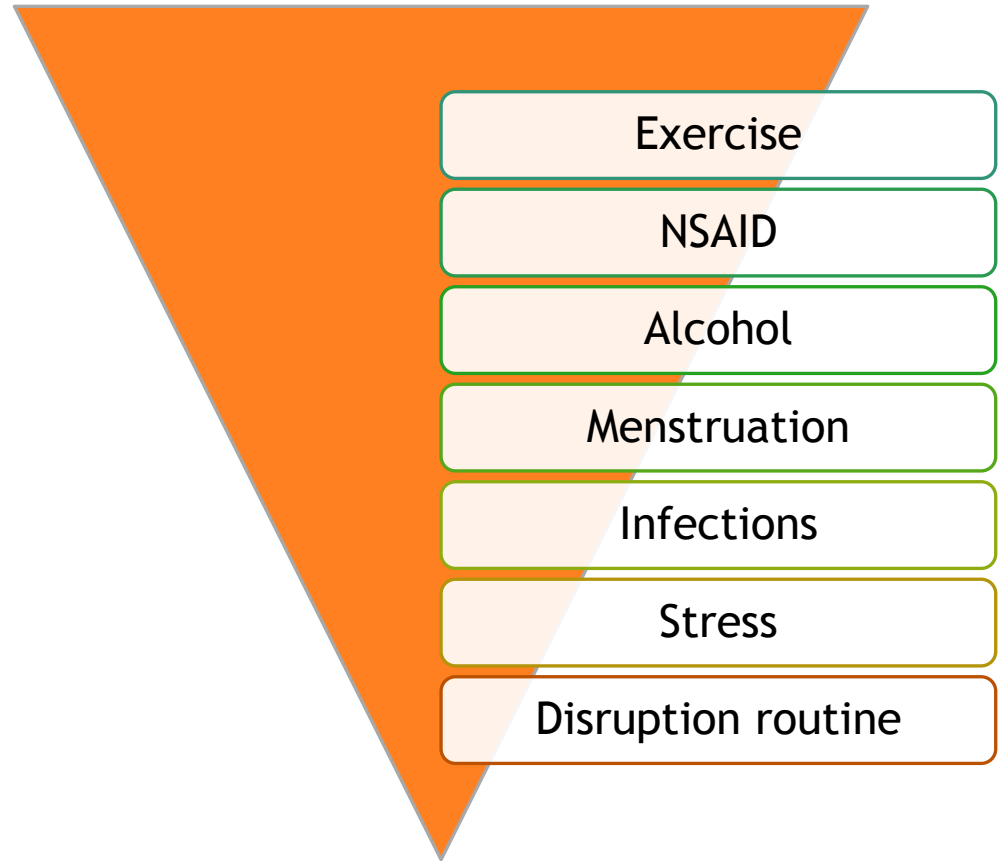
Co-factors

(= a subgroup of risk factors, not acting on an immunological basis themselves)

e.g. certain allergens, adolescence, beta-blocker, ACE-inhibitors, psyche

Niggemann B, Beyer K. Allergy. 2014 Dec;69(12):1582-7

* **Factors augmenting allergic reactions**



* Co-factor enhanced food allergy (CEFA)

Wheat proteins

Albumins

Globulins

Glutens

Gliadins

Glutenins

α -gliadin

β -gliadin

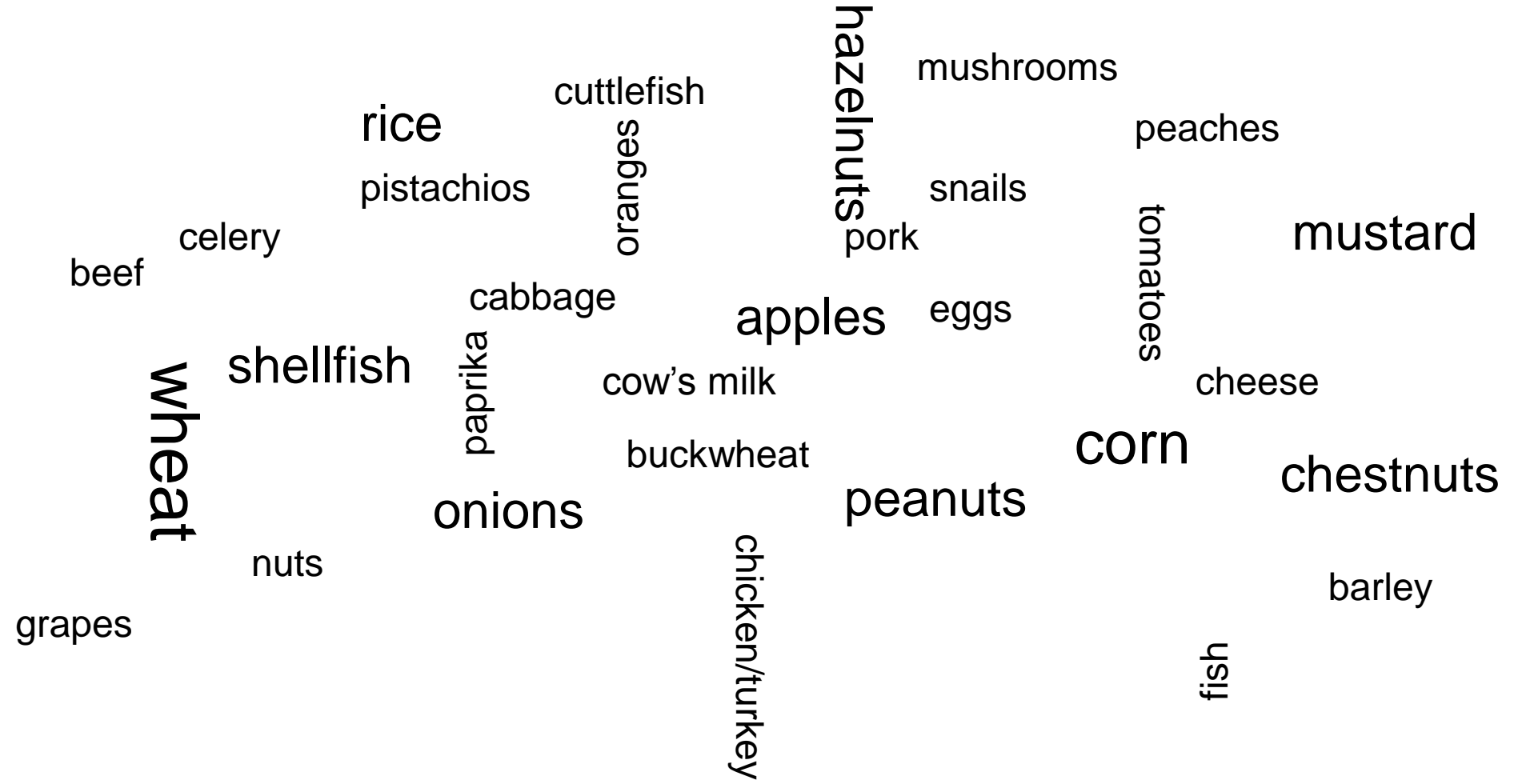
γ -gliadin

ω -gliadin
(Tri a 19)



+





*** Foods implicated in CEFA**

BRIEF COMMUNICATION

Co-factor-enhanced food allergy

V. Cardona^{1,2}, O. Luengo^{1,2}, T. Garriga^{1,2}, M. Labrador-Horrillo^{1,2}, A. Sala-Cunill^{1,2}, A. Izquierdo^{1,2},
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To cite this article: Cardona V, Luengo O, Garriga T, Labrador-Horrillo M, Sala-Cunill A, Izquierdo A, Soto L, Guilarte M. Co-factor-enhanced food allergy. *Allergy* 2012; **67**: 1316–1318.

- * Retrospective study of cases (January 2007-July 2011):
 - * Key words: food allergy, NSAID, exercise, alcohol, anaphylaxis
- * Inclusion of suspected CEFA cases:
 - * Exercise, alcohol or NSAID 2h before up to 4h after intake of sensitising food
- * Data: demographic, clinical reaction, sensitisations (SPT & sIgE), culprit food, coF, tolerance to the culprit food & coF after the reaction, time-frame
- * CRD (ImmunoISAC or ImmunoCAP, ThermofisherScientific)

* **CEFA: methods**

* 1859 reports

* 74 cases included:

* age 34.5 y IQR(27.4-42.4)

* ♀/♂: 1:1

* 87% sensitised to inhalant allergens

68%



50%

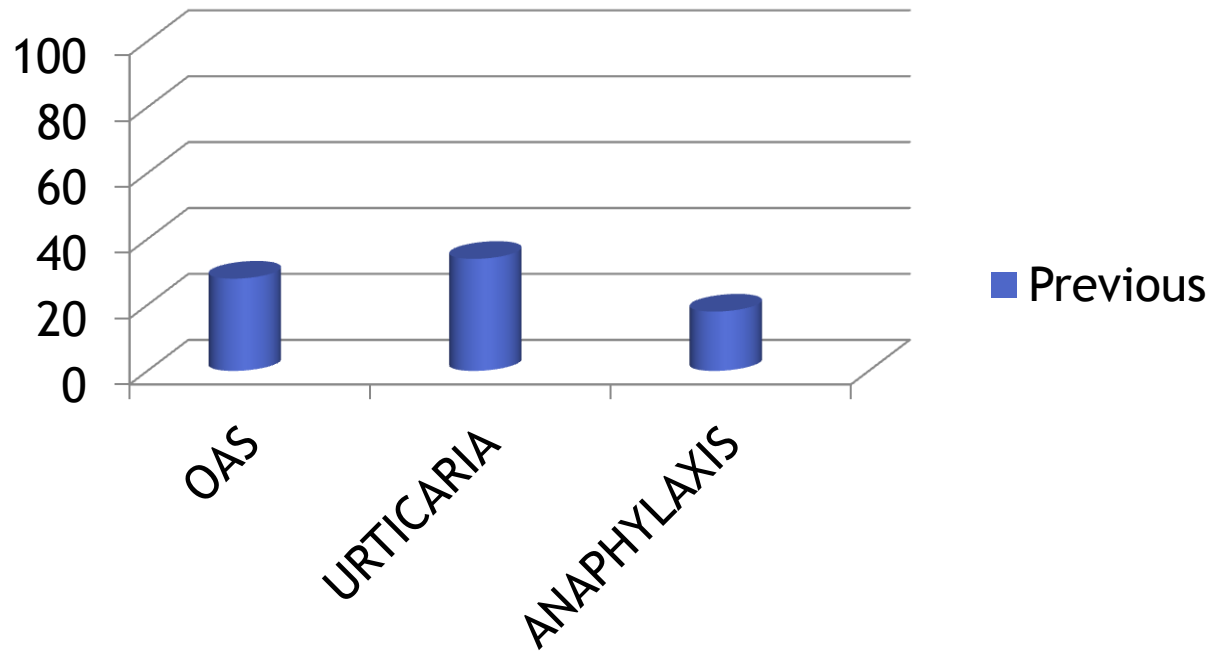


43%



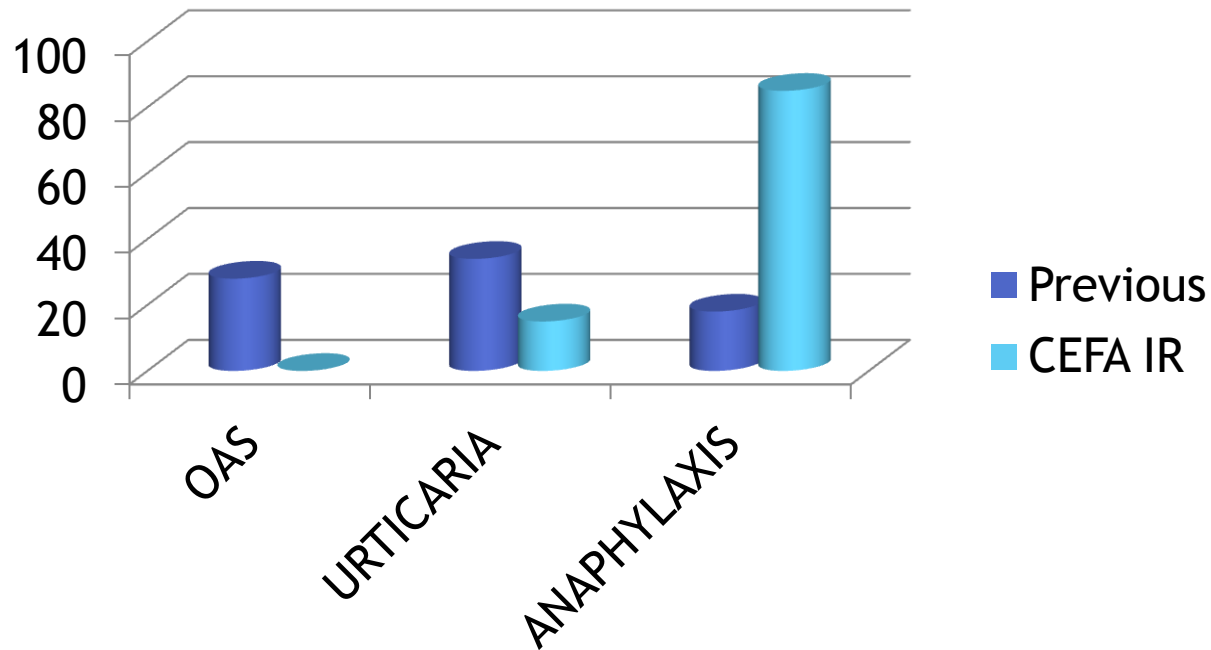
* **CEFA: results**

*82% had experienced previous food allergy reactions



* **CEFA: results**

* **82%** had experienced **previous food allergy** reactions



* 40% had experienced several CEFA reactions with the same or related foods (mean 3 reactions)

* **CEFA: results**



Lettuce: 14
 Tomato: 5
 Onion: 1
 Artichoke: 1

21 (28,4%)



Mixed 2
 Walnut: 2
 Peanut: 2
 Almond: 2
 Hazelnut: 1
 Sunflower seeds 1

12 (16,2%)



Wheat: 18
 Oats: 2
 Barley: 1

21 (28,4%)

Apple: 8
 Peach: 3



11 (14,9%)



Beans: 4
 Soja: 1
 Lupin: 1

6 (8,1%)

*** CEFA: results**

* ISAC in 60/74 patients:

Pru p 3 (LTP)
91,7%
(55/60)

ω -5-gliadin (Tri a19)
6,7%
(4/60)

Act d 2
8,3%
(5/60)

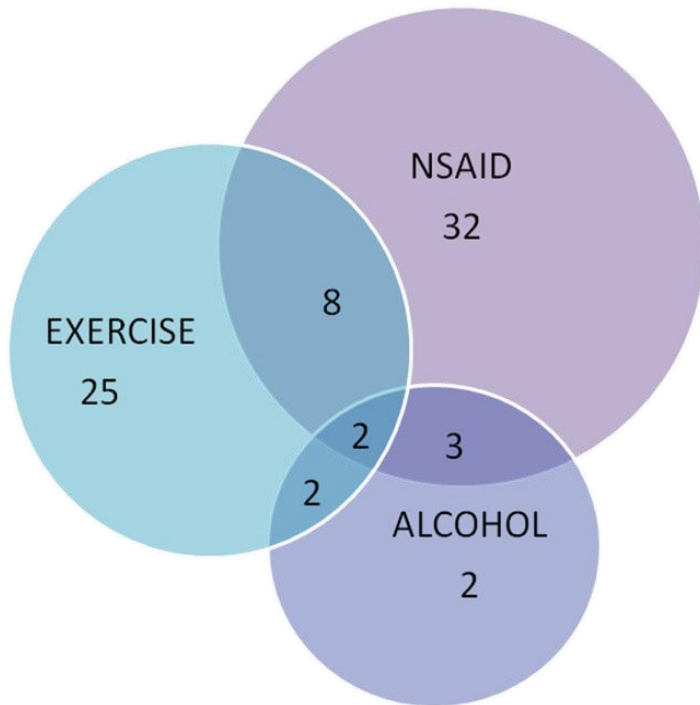
* 21 cereal allergic patients (ISAC or sIgE rTria a 19):

* 11/21 (52,4%): ω -5-gliadin

* 9/21 (42,8%): Pru p 3 (Tri a 14??)

* 1/21 (4,7%): ω -5-gliadin + Pru p 3

* CEFA: results



* 89% tolerated food without the coF (11% OAS):

- * Current consumption in 66%
- * Food challenge in 54%



* 34 NSAID challenges: 100% good tolerance

All patients improved upon avoidance of combining the food+coF

* CEFA: results

ORIGINAL ARTICLE Allergens

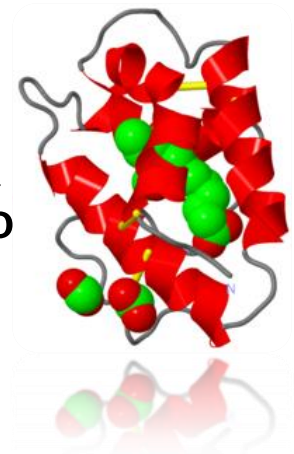
Lipid transfer proteins: the most frequent sensitizer in Italian subjects with food-dependent exercise-induced anaphylaxis

A. Romano^{1,2}, E. Scala³, G. Rumi¹, F. Gaeta¹, C. Caruso¹, C. Alonzi¹, M. Maggioletti¹, R. Ferrara³, P. Palazzo³, V. Palmieri⁴, P. Zeppilli⁴ and A. Mari³

¹Allergy Unit, Complesso Integrato Columbus, Rome, ²IRCCS Oasi Maria S.S., Troina, ³Center for Molecular Allergology, IDI-IRCCS and ⁴Department of Internal Medicine and Geriatrics, UCSC – Sports Medicine Unit, Rome, Italy



78%



*Sequence of exposure is varied

Wolańczyk-Medrala A et al. Ann Agric Environ Med. 2010 Dec;17(2):315-7

*In some cases, several cofactors are needed, even in food challenge

Fujii H et al. Allergol Int. 2008 Mar;57(1):97-8

Nakamura Ket al. Arerugi. 2010 Dec;59(12):1634-41

Brockow K et al. J Allergy Clin Immunol. 2014 (in print)

*Food sensitisation is necessary, sometimes low or difficult to assess



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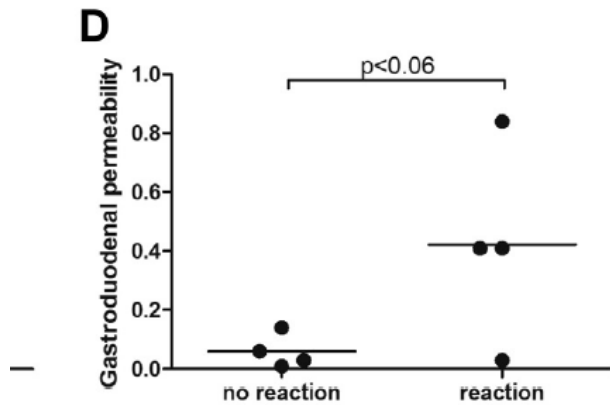
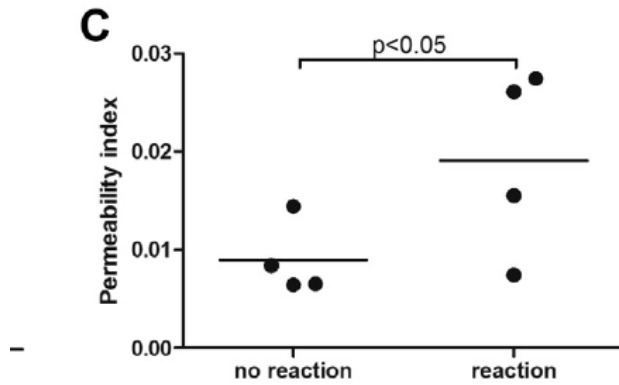


?

*Special aspects of
CEFA

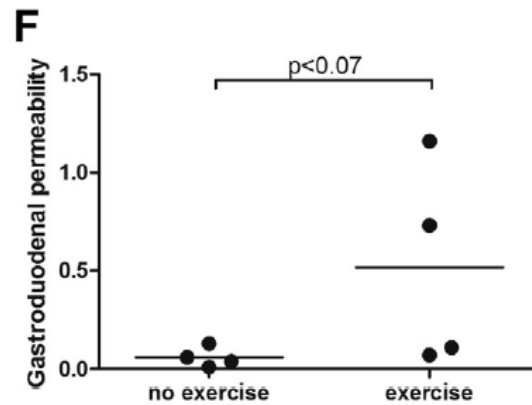
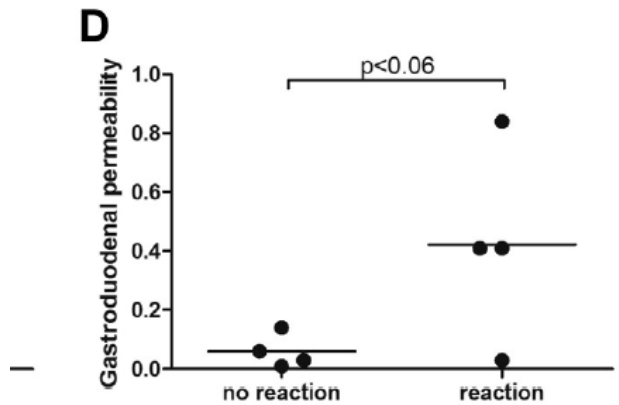
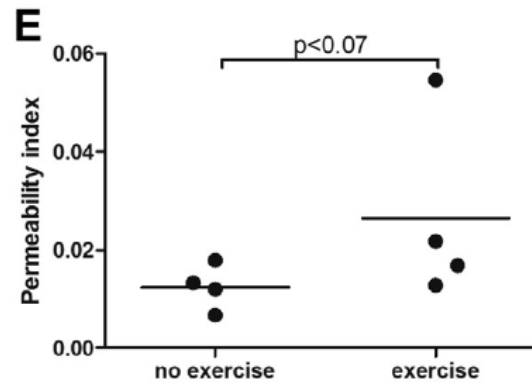
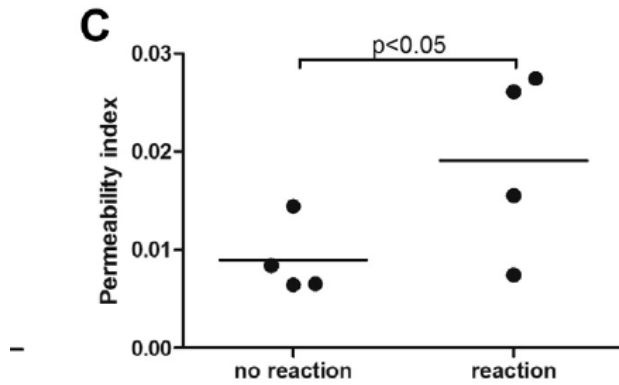
Mechanism	Mode of action
Increased gastrointestinal permeability	Has been described for alcohol, exercise, NSAID, stress
Increased mast cell activation	Lower threshold for mast cell activation and increased mediator release
“Neo-antigen” formation or allergenicity increase	Has been described with omega-5-gliadine cross-linking to tissue transglutaminase
Non-specific increase of mediator release	NSAID, through cyclooxygenase inhibition, enhances mediator release, such as LT
Other	Blood flow redistribution, increased osmolality, increased endogenous endorphin release, alterations in plasma pH

* Pathophysiology of CEFA



Brockow K et al. J Allergy Clin Immunol. 2014 (in print)

* **Increased intestinal permeability**



Brockow K et al. J Allergy Clin Immunol. 2014 (in print)

* **Increased intestinal permeability**

In vivo:

- Increased skin sensitivity after ASA intake

In vitro:

- Increased allergen induced basophil activation (BAT) + L-ASA

Inhibition by chromoglycate, ketotifen

Aihara M, et al. Br J Dermatol 2002, 146:466–472.

Bartra J et al. J Allergy Clin Immunol 2011 127: 185



Increased mast cell reactivity



- * High clinical suspicion needed for diagnosis
- * LTP is a relevant allergen in CEFA in Barcelona, but what happens in other areas?
- * Other allergen molecules, other than ω -5-gliadin, are involved in CEFA
- * Currently we always test for foods when patient consults because of exercise or NSAID reaction, and we always ask about enhancers in food allergies!
- * Mechanisms not fully understood

* **Take home messages...**

Thank you for your attention!

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Allergy and Clinical Immunology
6 – 10 June 2015
Barcelona, Spain



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Abstract
Submission
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2015**

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