Exercise-Induced Allergic Diseases

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

* ThermoFisher Scientific (Phadia)
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
<table>
<thead>
<tr>
<th>Subtype</th>
<th>Sweat allergy</th>
<th>Anhidrosis/ hypohidrosis</th>
<th>Intradermal test with acetylcholine</th>
<th>Pathology</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweat hypersensitivity</td>
<td>Positive</td>
<td>None</td>
<td>Positive</td>
<td>Infiltrate of lymphocytes around sweat glands</td>
<td>Antihistamines Desensitization?</td>
</tr>
<tr>
<td>Anhidrosis or hypohidrosis</td>
<td>Mostly negative</td>
<td>Necessary, mosaic</td>
<td>Partial positive</td>
<td>Normal</td>
<td>Systemic steroid</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>Negative</td>
<td>None</td>
<td>Negative</td>
<td>Normal</td>
<td>Antihistamines</td>
</tr>
</tbody>
</table>

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

*Cholinergic urticaria with hypohidrosis*
Cholinergic urticaria with hypohidrosis

Bito T et al. Allergol Int. 2012 Dec;61(4):539-44
Exercise-induced allergic diseases
Exercise induced anaphylaxis
Marathon Runner Won't Let Allergy to Exercise Hold Her Back


By SYDNEY LUPKIN via GOOD MORNING AMERICA

Mary Johnson, 27, is a marathoner. She’s also allergic to exercise — literally.

Courtesy Mary Johnson
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.

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*
Factors augmenting allergic reactions

Niggemann B, Beyer K. Allergy. 2014 Dec;69(12):1582-7
Exercise
NSAID
Alcohol
Menstruation
Infections
Stress
Disruption routine

*Co-factor enhanced food allergy (CEFA)*
Wheat proteins

- Albumins
- Globulins
- Glutens
  - Gliadins
    - α-gliadin
    - β-gliadin
    - γ-gliadin
  - Glutenins
    - ω-gliadin (Tri a 19)

+ Sandwich

+ Cycling race
*Foods implicated in CEFA*
BRIEF COMMUNICATION

Co-factor-enhanced food allergy

V. Cardona\textsuperscript{1,2}, O. Luengo\textsuperscript{1,2}, T. Garriga\textsuperscript{1,2}, M. Labrador-Horrillo\textsuperscript{1,2}, A. Sala-Cunill\textsuperscript{1,2}, A. Izquierdo\textsuperscript{1,2}, L. Soto\textsuperscript{1,2} & M. Guilarte\textsuperscript{1,2}

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* 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)
*1859 reports
*74 cases included:
  * age 34.5 y IQR(27.4-42.4)
  * ♀/♂: 1:1
  * 87% sensitised to inhalant allergens

*CEFA: results
*82% had experienced previous food allergy reactions

![Bar chart showing percentages of OAS, Urticaria, and Anaphylaxis.][1]

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*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

Wheat: 18
Oats: 2
Barley: 1

Beans: 4
Soja: 1
Lupin: 1

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

Apple: 8
Peach: 3

Large VEGETABLES and FRUITS:

*CEFA: results*
* ISAC in 60/74 patients:

<table>
<thead>
<tr>
<th>Prüfstoff</th>
<th>Anteil (%)</th>
<th>Anzahl (in Klammern)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pru p 3 (LTP)</td>
<td>91,7% (55/60)</td>
<td></td>
</tr>
<tr>
<td>ω-5-gliadin (Tri a19)</td>
<td>6,7% (4/60)</td>
<td></td>
</tr>
<tr>
<td>Act d 2</td>
<td>8,3% (5/60)</td>
<td></td>
</tr>
</tbody>
</table>

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

A. Romano¹,², E. Scala³, G. Rumi¹, F. Gaceta¹, 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
* Sequence of exposure is varied

* In some cases, several cofactors are needed, even in food challenge
  Fujii H et al. Allergol Int. 2008 Mar;57(1):97-8
  Nakamura K et 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

* Special aspects of CEFA

- +
- ?
<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Mode of action</th>
</tr>
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<tbody>
<tr>
<td>Increased gastrointestinal permeability</td>
<td>Has been described for alcohol, exercise, NSAID, stress</td>
</tr>
<tr>
<td>Increased mast cell activation</td>
<td>Lower threshold for mast cell activation and increased mediator release</td>
</tr>
<tr>
<td>“Neo-antigen” formation or allergenicity increase</td>
<td>Has been described with omega-5-gliadine cross-linking to tissue transglutaminase</td>
</tr>
<tr>
<td>Non-specific increase of mediator release</td>
<td>NSAID, through cyclooxigenase inhibition, enhances mediator release, such as LT</td>
</tr>
<tr>
<td>Other</td>
<td>Blood flow redistribution, increased osmolality, increased endogenous endorphin release, alterations in plasma pH</td>
</tr>
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Brockow K et al. J Allergy Clin Immunol. 2014 (in print)

*Increased intestinal permeability*
**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


*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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