Cofactoren bij voedselallergie

Prof. dr. Christine Breynaert

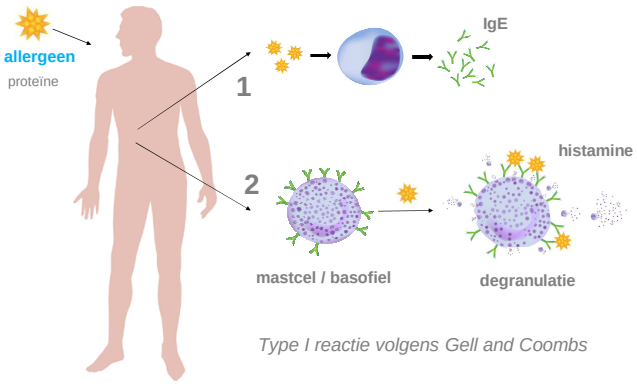
Allergie en klinische immunologie
Dienst algemene inwendige ziekten UZ Leuven

Studiedag Allergie-diëtisten
19-03-2018

UZ Leuven | Herestraat 49 B - 3000 Leuven | www.uzleuven.be tel. +32 16 33 22 11 | UNIVERSITY HOSPITALS LEUVEN

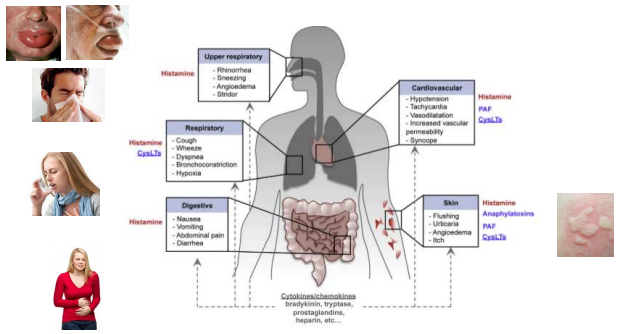
Inleiding

IgE gemedieerde voedselallergie



Type I reactie volgens Gell and Coombs

Symptomen IgE gemedieerde allergie



J Allergy Clin Immunol 2017;140:335-48.

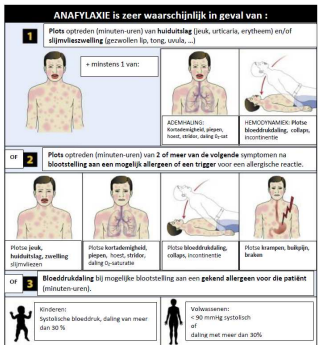
Anafylaxie

World allergy organization guidelines for the assessment and management of anaphylaxis

= Ernstige levensbedreigende gegeneraliseerde of systemische overgevoeligheidsreactie (EAACI)

Potentieel levensgevaarlijke reacties!



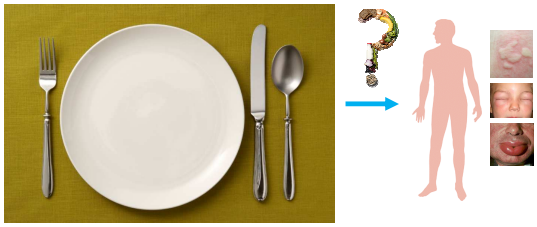


Risicofactoren voor (ernstige) reacties

Klassieke IgE gemedieerde voedselallergie



De ene keer wel... De andere keer niet...



Eerste beschrijving

1979: Maulitz et al.

Lange afstandsloper
Urticaria en angio-oedeem bovenste luchtwegen waarvoor nood aan adrenaline.

Enkel en alleen na eten van schaaldieren tot 24 uur voor de inspanning...



Exercise-induced anaphylactic reaction to shellfish

Robert M. Maulitz, M.D.,* David S. Pratt, M.D., and Alan L. Schocket, M.D.
Denver, Colo.

The syndrome of immediate type I food hypersensitivity, mediated by tissue-bound IgE antibody and mast cell histamine release, is well recorded in the medical literature. This case study represents a previously undescribed late food hypersensitivity, induced only by strenuous exercise. Identification of this new syndrome illustrates classical epidemiologic analysis, improves medical advice for the allergic and athletically inclined, and raises new questions in the areas of allergy and immunology.

The clinical syndrome of immediate type I food hypersensitivity to shellfish is well described in the medical literature.[1–3] The clinical presentation can include urticaria, angioedema, hives, pruritus, conjunctivitis, wheezing, and hypotension. The allergic event is mediated by IgE antibody activity and mediator release from mast cells. Allergic manifestations usually appear rapidly after ingestion of the known antigenic agent. The present case illustrates a previously undescribed late reaction to shellfish precipitated only by strenuous exercise.

CASE REPORT

A 31-year-old vigorous male long-distance runner (50 to 130 km/wk with races from 5,000 m to marathon distance) was initially seen because of approximately 10 bouts over 3 yr of transient facial flushing and edema, diffuse urticaria, and intense pruritus occurring immediately following exercise. The patient had an atopic history with an allergy to penicillin and a history of seasonal hay fever. Shellfish were a staple of his diet and routinely caused no systemic allergic reaction. Two bouts of the postexercise urticaria within 4 days with almost complete upper airway closure, requiring epinephrine and antihistamines, brought him to our attention.

A detailed epidemiologic history including dietary intake revealed shellfish intake 5 and 24 hr prior to the two exercise-related events. Eight boiled shrimp with ketchup preceded the first bout of urticaria and 1 can (100 gm) of smoked oysters was eaten prior to the second reaction. Similar data were not available for previous episodes. Two runs of 10 k on intervening days between the bouts of urticaria were not preceded by shellfish and did not result in allergic reaction.

The patient initially avoided shellfish due to strong suspicion generated after first medical evaluation. Because of the near total airway closure during the reactions and for safety, he carried an Ana-Kit (Center Labs., Port Washington, N. Y.) accompanied the patient on all workouts during the subsequent 30-day period, carrying appropriate epinephrine and antihistamines. At least 30 opportunities from 10 to 15 k in distance over the 30-day period did not induce an allergic episode. However, an inadvertent self-challenge with shellfish (100 gm smoked oysters) 20 hr prior to running 1 month later resulted in the described reaction immediately following exercise. The young athlete now assiduously avoids shellfish and has had no further reactions.

Cutaneous allergy testing showed positive prick tests to clams, oysters, shrimp, crabs (all 1/20 w/v), peanuts (1/20 w/v), trees, grass, and weeds (all 20,000 protein nitrogen units/ml (Dorsi Labs., Lenexa, N. C.).

DISCUSSION

The patient developed severe systemic allergic reactions which were induced by the ingestion of a specific food (shellfish) followed by exercise. Although the patient has specific IgE to the food, systemic allergic reactions were not produced by ingestion alone. Likewise, no reaction occurred following prolonged exercise without prior ingestion of the allergen. In addition, since the reactions occurred in the

From the Divisions of Pulmonary Sciences and Clinical Immunology, Department of Medicine, University of Colorado Medical Center.
Received for publication Sept. 8, 1978.
Accepted for publication Jan. 15, 1979.
Reprint requests to: Robert M. Maulitz, M.D., University of Colorado Medical Center, Box C-272, 4200 E. 9th Ave., Denver, CO 80262.
*Supported in part by National Heart, Lung and Blood Institute Training Grant No. HL 07005.

0091-6749/79/063433–10$00.20/0 © 1979 The C. V. Mosby Co. Vol. 63, No. 6, pp. 433-434

J Allergy Clin Immunol. 1979 Jun;63(6):433-4.

Cofactor-dependente anafylaxie

Uitlokken van anafylaxie enkel in aanwezigheid van een **co-factor**

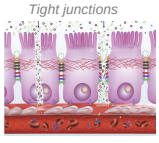


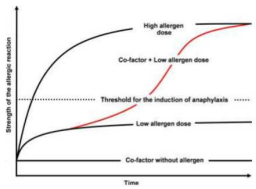
Mechanisme cofactordependente reacties

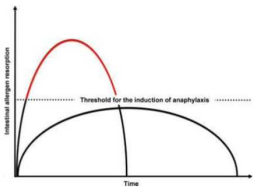


Inspanning
Aspirine
Alcohol

Tight junctions







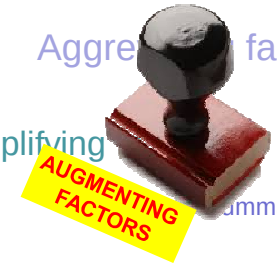
Allergy. 2013 Sep;68(9):1085-92.

Risk factor

Facilitator

Aggre factor

Amplifying



ummation factor

Cofactor

Risicofactoren voor ernstige reacties

ERNST ALLERGISCHE REACTIE

- *Fysieke activiteit*
- *Oestrogenen*
- *Alcohol*
- *Lichaamstemperatuur*
- *Infectie/ziekte*
- *NSAIDs*
- *PPI*
- *Statines*

→ **Augmenting factors**

- *β-blokkers*
- *ACE-I*

→ **Co-factoren**

- *Astma*
- *Cardiovasculair lijden*
- *Mastocytose*
- *...*

→ **Concommitante aandoeningen**

Allergy. 2013 Sep;68(9):1085-92. Allergy. 2014 Dec;69(12):1582-7.

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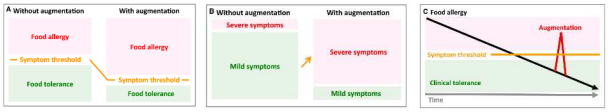
Augmenting factors

- *Fysieke activiteit*
- *Oestrogenen*
- *Alcohol*
- *Lichaamstemperatuur*
- *Infectie/ziekte*
- *NSAIDs*
- *PPI*
- *Statines*

Beïnvloeden op directe manier het immunologische mechanisme van de type 1 allergie

→ **Augmenting factors**

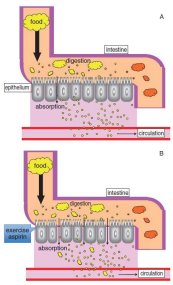
Verlagen drempel | **Verhogen ernst** | **Omkeren tolerantie**



Allergy. 2013 Sep;68(9):1085-92. Allergy. 2014 Dec;69(12):1582-7.

Inspanning



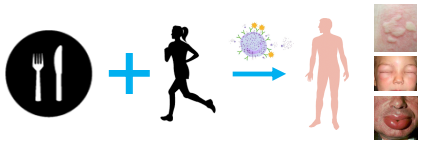


- Verhoogde permeabiliteit
- Activatie immuuncellen
- Toegenomen bloedflow visceraal: redistributie bloedflow
- Verandering serum osmolaliteit weefsels

Allergy 2015; 70:1212-1221. Immunol Allergy Clin N Am 2015; 35:261-275.

Inspanning

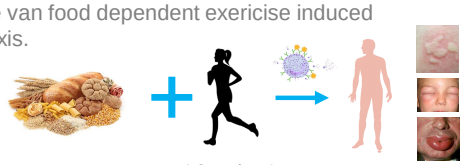
- **Food dependent exercise induced anaphylaxis (FDEIA)**
- Enkel **combinatie** van voedselingestie en fysieke activiteit leidt tot anafylaxie.
- Zowel inspanning als voeding worden onafhankelijk van elkaar getolereerd.



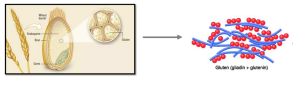
Clin Exp Allergy. 2012 Nov;42(11):1643-53. J Allergy Clin Immunol. 1979 Jun;63(6):433-4. Allergy. 2013 Sep;68(9):1085-92.

Wheat dependent exercise induced anaphylaxis (WDEIA)

- Prototype van food dependent exericise induced anaphylaxis.



4-6 uur later!



Tri a19
Omega-5-gliadine

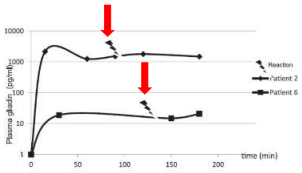
Delayed hypersensitivity: uitgestelde allergische reactie!

Clin Exp Allergy. 2012 Nov;42(11):1643-53.J Allergy Clin Immunol. 1979 Jun;63(6):433-4. Allergy. 2013 Sep;68(9):1085-92.

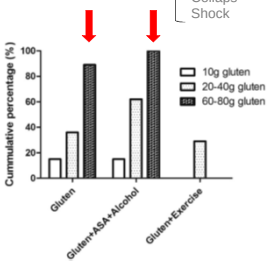
Augmentation-factor triggered anaphylaxis

Tarwe ingestie + augmenting factor → **reactie**

- Urticaria
- Angio-oedeem
- Dyspneu
- Hypotensie
- Collaps
- Shock



Drempel verschillend!



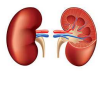
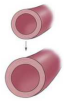


J Allergy Clin Immunol. 2015 Apr;135(4):977-84.e4.

Alcohol



- **Tot 15,2% van de reacties**
  (J Clin Exp Allergy 2005;35:746-750)
- **Fysiologische effecten van alcohol**

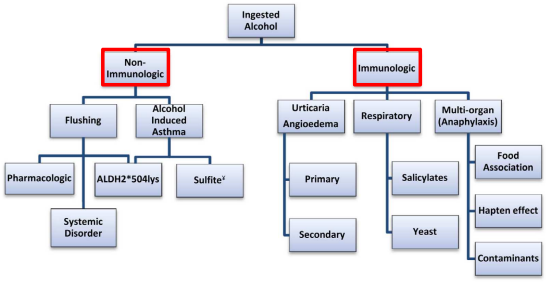
Perifere vasodilatatie
Direct effect: ↑ NO synthetase activiteit
- Centrale effecten
- Symptomen: flushing, rhinitis, ↑ BLW weerstand

- **Effecten van alcohol op anafylaxie?**
  - Hogere IgE waarden bij alcoholici
  - Augmenting factor ?
  - Reacties op ingredienten van alcoholische dranken

Ann Allergy Asthma Immunol 111 (2013) 439e445

Alcohol





Ann Allergy Asthma Immunol 111 (2013) 439e445

Anafylaxie op alcohol



R Hicks. **Ethanol, a possible allergen.** Ann Allergy, 26 (**1968**), pp. 641-643

Fatal anaphylaxis after alcohol consumption

Am J Forensic Med Pathol. 1996 Mar;16(1):45-7.

Death caused by an allergic reaction to ethanol.

McCormick GM 2nd[1], Young DR.

Author information

Abstract

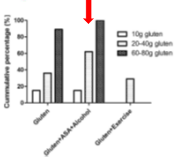
Death as a result of anaphylaxis remains rare and is only occasionally related to ingestion of common substances. This article reports a death due to an allergic reaction to ethanol, as well as a review of the reported deaths in the literature attributed to ethanol. This report emphasizes the importance of awareness of such obscure allergies by forensic pathologists, the significance of antemortem testing, and the value of gathering accurate medical information, both antemortem and postmortem.

PMID: 7771382

Medicatie

- **NSAIDs**: onstekingsremmers, aspirine
  1,2-4,7% van de reacties
  Mechanismen:
  - Effect op intestinale permeabiliteit
  - Effect op mastcellen/basofielen
  - Idiosynchrasie (niet-immunologische reactie)
  - Anafylaxie op NSAIDs





- **PPI:** maagzuurremmers
  Mechanismen:
  - Reactie op molecule zelf
  - Verandering pH maag



- **Statines**



Allergy. 2013 Sep;68(9):1085-92. Allergy. 2014 Dec;69(12):1582-7.
J Allergy Clin Immunol. 2015 Apr;135(4):977-84.e4.

Oestrogenen

- **Catameniale anafylaxie**

Ziekte/lichaamstemperatuur

- Warme versus koude omgeving

UZ LEUVEN

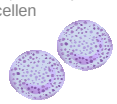
Cofactoren

- *β-blokkers*
- *ACE-I*
- *Emotionele factoren*
- *Ontwikkeling*

Subgroep van risico-factoren die geen invloed hebben op de immunologische IgE-gemedieerde reactie zelf

Co-factoren

ACE-inhibitoren en β-blokkers
- Wisselende gegevens
- Gecombineerde inname: ↑ risico op ernstige anafylaxie
- Directe invloed op mastcellen



Allergy. 2013 Sep;68(9):1085-92. Allergy. 2014 Dec;69(12):1582-7.

UZ LEUVEN

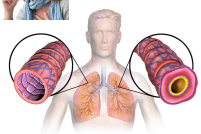
Concommitante aandoeningen

- *Astma*
- *Cardiovasculair lijden*
- *Mastocytose*
- *...*

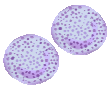
Concommitante aandoeningen bij patiënt die beperken of mortaliteit verhogen

Concommitante aandoeningen





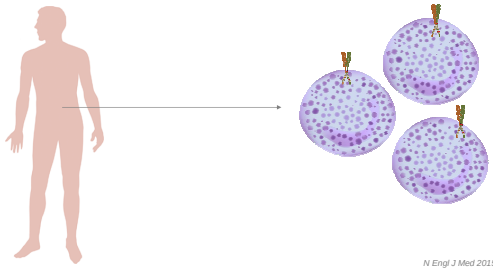




Mastocytose

MASTeL
MASTcelaandoeningen Leuven

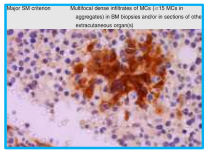
= heterogene groep van aandoeningen die gekenmerkt worden door de expansie en accumulatie van **monoclonale mastcellen** in één of meerdere organen

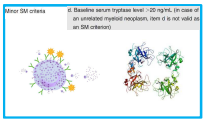


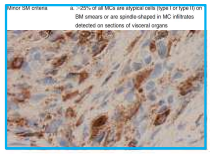
N Engl J Med 2015;373:163-72

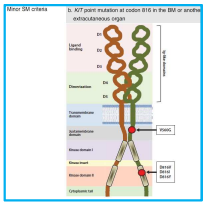
WHO criteria voor diagnose van SM

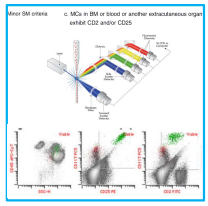
Annu.Rev.Pathol.Mech.Dis.2017;12:487-514
Blood 2017;129:1420-1427.
J Intern Med. 2016 Mar;279(3):211-28.











Mastocytose en anafylaxie

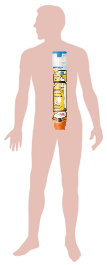
Cumulatieve prevalentie 22% - 43% - 49%

Prevalentie van anafylaxie in geval van mastocytose:

100 x hoger

In vergelijking met de gewone bevolking

Lifetime risk 1,6% - Prevalentie 0,3% - incidentie 5/100 000 personen jaren

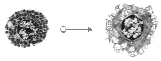


Indolente systeemmastocytose (zonder huidaantasting) > Cutane mastocytose





Anafylaxie = symptoom dat meestal leidt tot diagnose

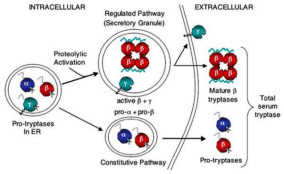


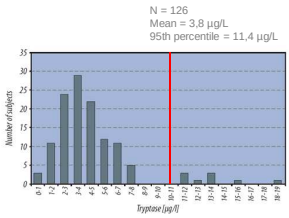
CAVE aspecifieke mastceldegranulatie: schaaldieren, alcohol, tomatenconcentraten,...

Immunol Allergy Clin North Am. ***2017*** *Feb;37(1):153-164.*

Verhoogd basaal serum tryptase

= verhoogd mastcel aantal of mastcel releasibility

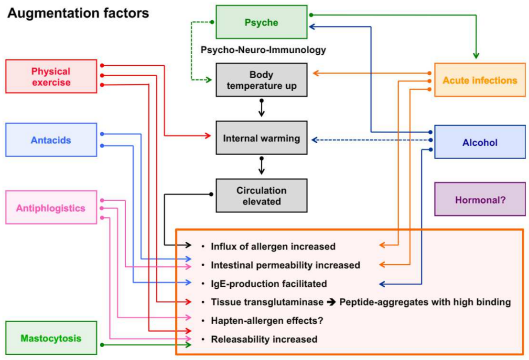




J Allergy Clin Immunol. 2006 Jun;117(6):1411-4.

UZ LEUVEN

Take home messages



Allergy. 2014 Dec;69(12):1582-7.

Take home message

- Uitgebreide anamnese
- **Dagboek**: goede documentatie van de omstandigheden (voeding tot 12 uur voordien, medicatie, inspanning, ziekte, alcohol, cyclus).
- Denk aan cofactoren/augmenting factors/concommitante aandoeningen die de ernst van een reactie kunnen beinvloeden



UZ LEUVEN



Dank voor uw aandacht!

Prof. dr. Christine Breynaert

Adjunct kliniekhoofd - Allergie en klinische immunologie
Dienst algemene inwendige ziekten UZ Leuven
Assistant professor – Laboratorium voor Klinische Immunologie – KU Leuven