WISC 2014

WAO International Scientific Conference 2014 and
the XLI Congress of the Brazilian Association of Allergy and Immunology (ASBAI)

Advancing the Borders of Allergy:
From Treatment to Prevention by Targeting the Environment, Infections and the Susceptible Patient

A meeting of WAO World Allergy Organization — A World Federation of Allergy, Asthma & Clinical Immunology Societies in collaboration with ASBAI Associação Brasileira de Alergia e Imunologia

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ADVERSE REACTIONS TO IMMUNOTHERAPY

José Carlos Perini , MD

ASBAI - BRAZIL

ADVERSE REACTION

WHO, Definitions (1972)

'A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease or for the modifications of physiological function'

Speaking the same language: The World Allergy Organization Subcutaneous Immunotherapy Systemic Reaction Grading System

Linda Cox, MD,[a] Desiree Larenas-Linnemann, MD,[b] Richard F. Lockey, MD,[c] and Giovanni Passalacqua, MD[d], Editors
Davie and Tampa, Fla, Mexico City, Mexico, and Genoa, Italy

- Subcutaneous allergen immunotherapy (SCIT) is an effective treatment for allergic rhinitis, asthma and venom hypersensitivity and has the potential of producing serious life-threatening anaphylaxis.
- New indications of Immunotherapy
  - Atopic Dermatitis
  - VIT for LLRS (large local reaction) (Immunotherapy Practice Parameters - 3rd edition)

World Allergy Organization Subcutaneous Immunotherapy Systemic Reaction Grading System (see text)				
Grade 1	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
Symptom(s)/ sign(s) of one organ system present[i] **Cutaneous** Generalized pruritus, urticaria, flushing or sensation of heat or warmth[ii] **or** Angioedema (not laryngeal, tongue or uvular) **or** **Upper respiratory** Rhinitis (e.g., sneezing, rhinorrhea, nasal pruritus and/or nasal congestion) **or** Throat-clearing (itchy throat) **or** Cough perceived to come from the upper airway, not the lung, larynx, or trachea **or** **Conjunctival** Conjunctival erythema, pruritus or tearing **Other** Nausea, metallic taste, or headache	*Symptom(s)/ sign(s) of more than one organ system present* **or** **Lower respiratory** Asthma: cough, wheezing, shortness of breath (e.g., less than 40% PEF or FEV1 drop, responding to an inhaled bronchodilator) **or** **Gastrointestinal** Abdominal cramps, vomiting, or diarrhea or **Other** Uterine cramps	**Lower respiratory** Asthma (e.g., 40% PEF or FEV1 drop, NOT responding to an inhaled bronchodilator) **or** **Upper respiratory** Laryngeal, uvula or tongue edema with or without stridor	**Lower or Upper respiratory** Respiratory failure with or without loss of consciousness **or** **Cardiovascular** Hypotension with or without loss of consciousness	Death

From Cox L, Larenas-Linnemann D, Lockey RF, et al. J Allergy Clin Immunol 125:569-574, e567;

ADVERSE REACTIONS: SUMMARY

- Local Reactions
- Generalized Pruritus
- Rhinitis
- Angioedema
- Itchy throat
- Cough
- Conjunctival symptons
- Nausea

ADVERSE REACTIONS: SUMMARY

- Asthma
- Abdominal cramps
- Uterine cramps
- Laringeal,uveal and tongue edema
- Respiratory failure
- Hypotension
- Death

FATAL REACTIONS TO IMMUNOTHERAPY(SCIT) IN THE USA

- 1973
  - 18 deaths
- 1984
  - 17 deaths
- 1989
  - 41 deaths
- 2001
  - 6 deaths
- 2007
  - 0 (zero) deaths
- 2011
  - Locker et all JACI 1987, Reid et al JACI 1993, Bernstein Jaci 2004 Jaci 2010

Why deaths are decreasing in immunotherapy?

- Better quality and standarized antigens
- Awareness of the risks
- Increased prophylatic measures
- Adequated facilities for delivering immunotherapy
- Guidelines on Immunotherapy
- Guidelines on Anaphylaxis
- Better trained allergy specialists

Survey of fatalities from skin testing and immunotherapy 1985-1989

Michael J. Reid, MD, Richard F. Lackey, MD, Paul C. Turkeltaub, MD, and
Thomas A. E. Platts-Mills, MD, PhD San Francisco, Cal& Tampa, Fla.,
Bethesda, Md., and Charlottesville, Va.
J ALLERGY CLIN IMMUNOL VOLUME 95, NUMBER 1, PART 1

- 17 deaths from anaphylaxis after allergen injection occurred from 1985 through 1989.
- Only one patient received house mite antigens injections. All the others received different polen antigens mixtures
- Most of the deaths occurred due to :
  - New vial, overdose,
  - personal agravating circunstances like obesity, asthma ,
  - multiuple extracts,
  - use antigen in the middle of the polen season.
- Only one patient was using the extract at home

Twelve-year survey of fatal reactions to allergen injections and skin testing: 1990-2001

David I. Bernstein, MD et al
The Immunotherapy Committee of the American Academy of Allergy, Asthma and Immunology
Journal of Allergy and Clinical Immunology
Volume 113, Issue 6, Pages 1129–1136, June 2004

- **Dosing errors and β-blockers were not major contributing factors, as in previous surveys.[6]**
- Delay or failure to administer adequate doses of epinephrine is a common feature of fatal reactions.
- This highlights the need to prohibit injection therapy in any clinic that is not fully equipped and staffed to treat severe anaphylaxis
- ***OUR COMMENT: all patients were on polen extracts. Some also received house mite ag . All of the them received multiple antigens injections. It seems pollens antigens may be a risk factor***

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- **273 incidents of near fatal reactions**
- **5,4 events per 1000 000 injections**
  - 46% occured during the height of the allergy season(Pollen season in USA)
  - 25% were due to dose errors
  - 4 out 5 near fatal reactions were asthma patients
  - FEV1 < 70% in 4 out 7 near fatal patients who had asthma

RISK FACTOR FOR ADVERSE REACTIONS

- Severe asthma specially with FEV1 <70%
- B blockers and ECA inhibitors
- Polen season
- Route of delivery (SCIT more than SLIT)
- Patients sensibility to the allergen
- Dose of the allergen
- Non standarized antigen
- New vial
- Rush and cluster immunotherapy

WHAT TO DO ABOUT IMMUNOTHERAPY IN CASE OF ADVERSE REACTIONS?

- Previous local reactions are not a indicative of future more severe reactions BUT
  - Review the causes of adverse reactions
  - Review the antigen concentration
  - It there is a suspicion switch the vial for a new one
  - Keep the patient under observation for a longer period (1h) next time

COMPLICATIONS MOSTLY OCCUR DUE TO:

- Delay in recognizing the severity or potencial severity of the inicial reaction
- Delay in the use of Epinephrine
- Asthma
- Lack of resources of life support
- Untrained professional

PROPHYILAXIS MEASURES

- **Antihistamines** decrease local reactions in cluster and rush immunotherapy
- **Antileucotriens** have a protective effect on rush protocol
- **An assessment of patients health**
- **Peak flow, Blood pressure** level measurement
- **Local life support resources** avaiable such as:
  - Drugs: epinephrine, antihistaminic, corticosteroids betaadrenergics, oxygen, dopamine, atropine, Glucagon
  - ACLS training or equivalent training for professionals
- **Reliable antigens** in standarized vials, individualized for the patient
- Check for usage of **prohibited drugs** such as betablockers and ECA inhibitors
- Keep **patient under observation** for at least 30 min

New forms of allergy immunotherapy for rhinitis and asthma

Harold S. Nelson, M.D. Allergy & Asthma Proceedings July/Aug 2014 – Vol 35 # 4

INCREASED SAFETY AND/OR EFFICACY WITH CURRENTLY AVAILABLE EXTRACTS

- Delayed absorption
  - Aluminum
  - Tyrosine
- Reduced levels of IgE
  - Omalizumab
- Alternative routes of delivery
  - Oral
  - Bronchial
  - Nasal
  - Epicutaneous
  - Intralymphatic
  - Intradermal
  - Sublingual

THE FUTURE

Molecular allergology, the science that describes the detailed structure of the molecules that cause allergies, is expected to take the field to the next step, as the components of treatment will be defined to precision in quality and quantity. (EAACI)

ASBAI2015

XLII Congresso Brasileiro de Alergia e Imunologia

De 03 a 06 de outubro - Centro de Convenções Vitória - ES

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