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XLI Congress of the Brazilian Association of Allergy and Immunology (ASBAI)

Practical Course
Allergen Immunotherapy (AIT)
How to be effective

Michel Dracoulakis

HSPE-"FMO" – São Paulo-SP – Brazil

Allergen immunotherapy - beginning

- Dunbar – almost died with first inoculation
- 1911 – Noon and Freeman published first work
  - Became standard treatment for asthma/hay fever
  - Diverse build up schemes and duration
- Indiscriminate use made the specialty untrustworthy
- 1963 – Lowell and Franklin – first placebo controlled study

Studies over Allergen Immunotherapy

- Venom Anaphylaxis
  - Up 98% efficacy (bee and wasp)
- Rhinitis
  - Sublingual IT (SLIT) better than anti-H1 and placebo/similar to nasal steroids
  - Subcutaneous (SCIT) and SLIT better than placebo
- Asthma
  - Meta-analysis confirms efficacy for children an adults
- Atopic Dermatitis
  - Trend for efficacy - need better studies

J Allergy Clin Immunol 2005; 115; 439-47
BMC Medicine 2014, 12:71
Cochrane Database Syst Rev. 2010;(8):CD001186
Curr Opin Allergy Clin Immunol. 2012 Aug;12(4):427-33

Efficacy of AIT

- Children – carry over effect of 12 years
- Reduces progression to asthma
- Reduces new sensitizations
- SLIT – carry over of 2 years documented in adults
- Long-lasting effect – 15 years after 4 years of SLIT

- Preventive SLIT – asymptomatic children
  - Safe / *in vitro* effects

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Indication of AIT

- Identified allergen
- IgE mediated disorders
- Exposure correlate with symptoms
- Good extract available?
  - Allergen standardization

Bousquet J, Lockey R, Malling HJ. ; J Allergy Clin Immunol. 1998 Oct;102(4 Pt 1):558-62
Allergen immunotherapy: A practice parameter third update Cox *et al*; J Allergy Clin Immunol. 2011
Persistent rhinitis – allergic or nonallergic? – Allergy 2004: 59 (Suppl. 76): 11–15

Indication of AIT

- Patient selection
  - Patient adherence
  - Symptoms intensity
  - Monosensitized x polysensitized
  - Seasonal x perennial
  - How much allergic is the symptom?
    - Rhinitis – allergic x non-allergic = 3:1
    - Mixed rhinitis – 44-87%
    - Atopic Dermatitis – intrinsic, food allergy...
    - Geriatric population – perception / co-morbidities

J Allergy Clin Immunol 2008;122:S1-84.
Int Forum Allergy Rhinol. 2014 Oct;4(10):796-801

Efficacy of AIT – practical issues

- SLIT x SCIT – SCIT better
- Up dosing protocol
  - Conventional
    - Time consuming - more dropouts
  - Cluster
    - Zhang *et al.* – safe as conventional (HDM)
    - Feng *et al.* – meta-analysis – efficacy in RQLQ
  - Rush
    - Safer in Venom AIT
- Pre-medication – Anti-histamines/Omalizumab

Int Arch Allergy Immunol 2009;148:161–169
PLoS One. 2014 Jan 28;9(1):e86529
J Allergy Clin Immunol 2012;130:1097-107

Efficacy of AIT – practical issues

- Maintenance
  - Missed doses
    - Patient evaluation – Peak-Expiratory Flow
    - Flexibility – dose interval?
  - How much time
    - 3-5 years
    - Venom IT
  - Dose?

Optimal duration of allergen immunotherapy in children with dust mite respiratory allergy - doi: 10.1111/pai.12296
Bousquet J, Lockey R, Malling HJ. ; J Allergy Clin Immunol. 1998 Oct;102(4 Pt 1):558-62

Efficacy of AIT – the allergens

- Choice of allergens
  - Multiple allergens AIT
  - Single allergen AIT
- Bystander effect?

Bousquet J, Lockey R, Malling HJ. ; J Allergy Clin Immunol. 1998 Oct;102(4 Pt 1):558-62

Mixing allergens

- Dose
  - Cross-reactive allergens – increased dose
  - Too many allergens – insufficient dose
- Enzymatic activity
- Time between mixing and applying
  - Greater dilution = lower shelf life

Bousquet J, Lockey R, Malling HJ. ; J Allergy Clin Immunol. 1998 Oct;102(4 Pt 1):558-62
Allergen immunotherapy: A practice parameter third update Cox *et al*; J Allergy Clin Immunol. 2011

Tailoring AIT

- Recommended doses – flexibility
  - Venom AIT – 100 μcg
- Modifying AIT
  - Adverse reactions
    - Large Local reactions
    - Systemic reactions
  - Lack of response – 1 year
    - Non-allergic component
    - Missed main triggers
    - Continued exposure to allergen

Optimal duration of allergen immunotherapy in children with dust mite respiratory allergy - doi: 10.1111/pai.12296
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Monitoring AIT

- Clinical response
  - Symptoms
  - Medications

- Cutaneous late responses (intradermal test)
- IgG4/serum inhibitory activity for IgE-allergen complex binding to B cells
- Basophil histamine release
- Basophil expression of diamine oxidase

J Allergy Clin Immunol 2012;130:918-24
J Allergy Clin Immunol. 2014 Nov 22 pii: S0091-6749(14)01477-8. doi: 10.1016/j.jaci.2014.09.049. [Epub ahead of print]

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For questions or commentaries please contact

mdracoulakis@gmail.com