

6th Jack Pepys Workshop

Asthma in the Workplace

May 13, 2016, Toronto, Canada

Theme 4: Diagnosis of occupational asthma and rhinitis:

usefulness of recombinant allergens (component resolved diagnosis), metabolomics and other new aspects.

Gianna Moscato

Usefulness of basophil Activation Test (BAT) in occupational settings

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Basophil activation test (BAT)

- Basophil activation test measures basophil response to allergen cross-linking IgE on between 150 and 2000 basophil granulocytes in <0.1 ml fresh blood. Dichotomous activation is assessed as the fraction of reacting basophils.
- In addition to clinical history, skin prick test, and specific IgE determination, BAT can be a part of the diagnostic evaluation of patients with food-, insect venom-, and drug allergy and chronic urticaria. It may be helpful in determining the clinically relevant allergen.

BAT in occupational settings

Disease	Occupation	Agent	Tests	Reference
Generalized allergic reactions at the workplace	loom tuners in a textile factory.	extracts of the elastic and the cutting dust material.	slgE + to rHev b 5, rHev b 6.01, rHev b 6.02 and rHev b 13 BAT+ HME elastic material	Lopata et al, Int Arch Allergy Immunol. 2007;144(1):64-8
Bakers asthma	Bakers	Recombinant LPT Tri a 14	slgE + to Tri a 14 BAT+ to Tri a 14	Palacin, CEA 2009 Aug; 39(8):1267-76
OA and OR	screen-printing worker	carmine red (E-120)	SPT + to carmine red SIC + to carmine red BAT+ to carmine red	Cox CE, B-ENT. 2012;8(3):229-32
OA and OR	carpenters	Obeche wood - two new purified 24 kDa putative thaumatin-like protein and a 12 kDa gamma-expansin	BAT+ to the new purified proteins	Aranda, PLoS One. 2013;8(1):e53926.
OA	carpenter	Iroko wood (<i>Chlorophora excelsa</i>) (IW)	SPT IW – SIC IW+ BAT IW+	de las Marinas, J Investig Allergol Clin Immunol 2013; 23:5124
OA	farmer with asthma in the presence of fresh flowers	<i>Limonium tataricum</i> (Lt) flowers.	SPT Lt+ NPT Lt+ BAT Lt+	Ariano, Eur Ann Allergy Clin Immunol. 2013 May;45(3):84-9
OA and OR	lactase tablets manufacturing plant	Lactase	SPT + slgE+ to lactase BAT lactase +	Stocker, Arch Environ Occup Health. 2015

INSECTS e LAR

- [Curr Opin Allergy Clin Immunol](#). 2011 Aug;11(4):332-6. doi: 10.1097/ACI.0b013e32834877ab. **Insect anaphylaxis: addressing clinical challenges.** [Tracy JM](#)¹, [Lewis EJ](#), [Demain JG](#).
- Local allergic rhinitis: BAT suggested for diagnosis (Gómez F1, Rondón C, Salas M, Campo P. Local allergic rhinitis: mechanisms, diagnosis and relevance for occupational rhinitis. *Curr Opin Allergy Clin Immunol*. 2015 Apr;15(2):111-6. doi: 10.1097/ACI.000000000000150.)

Insect anaphylaxis: addressing clinical challenges

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**Current Opinion in Allergy and Clinical
Immunology** 2011, 11:332–336

Purpose of review

Few allergic reactions are as potentially life-threatening, or frightening to the patient, as anaphylaxis. Food, medications, and insect stings are the three most common triggers of anaphylaxis, but insect allergy provides the best opportunity to understand the biology of anaphylaxis. If the physician can establish a diagnosis of insect allergy, treatment with nearly 98% effectiveness can be initiated. However, sometimes patients have a compelling history of insect sting anaphylaxis, but negative skin and blood tests. This situation presents us with a fascinating opportunity to understand the biology of insect anaphylaxis.

Recent findings



Local allergic rhinitis: mechanisms, diagnosis and relevance for occupational rhinitis

Francisca Gómez, Carmen Rondón, María Salas, and Paloma Campo

Curr Opin Allergy Clin Immunol 2015, 15:111–116

BAT in occupational settings

Our experience

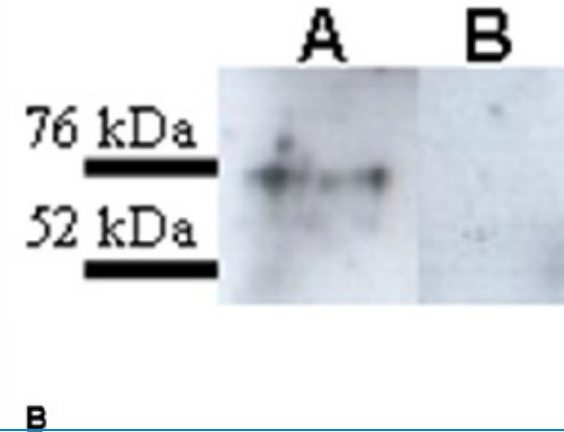
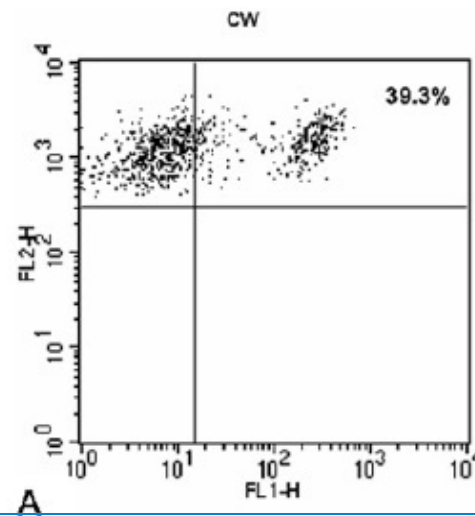
Disease	Occupation	Agent	Other tests	Reference
OA and OR	parquet floor layer	Cabreuva wood (CW)	SIC CW + SPT CW- BAT CW+	<i>Pala</i> , Ann Allergy Asthma Immunol 2010
OA and OR	cereal stocker	Ephestia kuehniella (cereal pest)	SIC EK + SPT EK+ BAT EK +	<i>Pala</i> , EAACI 2010, DOI: 10.1594/ eaacinet2010/CR/ 1-070410
Occupational NAEB	baker	Storage mites	SPT mites+ BAT storage mites+	<i>Pala G</i> , Allergy 2010
OA	Employed in a food processing factory	Lima bean (<i>Phaseolus lunatus</i>)	SIC LB (home made extract-HME) + SPT LB (HME) + BAT LB (HME) +	Tonini 2012
Contact urticaria	cook	crustaceans	SPT crust (HME) + BAT crust (HME) +	<i>Pala</i> , J Investig Allergol Clin Immunol 2012; Vol. 22(2): 133-153

OCCUPATIONAL RHINITIS AND ASTHMA DUE TO CABREUVA WOOD DUST

ANNALS OF ALLERGY, ASTHMA & IMMUNOLOGY

VOLUME 104, MARCH, 2010

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-Parquet floor layer, symptoms of rhinitis and asthma when handling *Cabreuva* wood(CW)
-SPT with CW extract → negative



BAT positive for CW extract

BAT with other wood extracts → negative

BAT with CW extract negative in 2 atopic and in 2 non atopic controls

SIC with wood extract → positive

BAT was useful in confirming sensitization

BAT with homemade extracts

Occupational asthma induced by exposure to lima bean (*Phaseolus lunatus*)

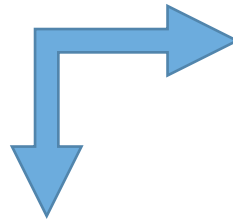
Ann Allergy Asthma Immunol 108 (2012) 60–67

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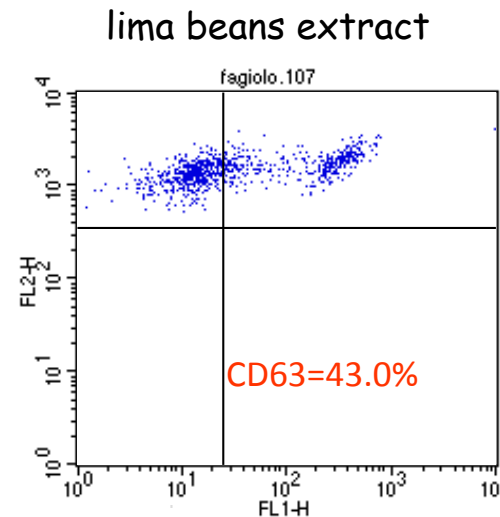
Extract from cooked beans (taken directly in the factory) was prepared.

Employed in a food processing factory
Symptoms of asthma when handling lima bean

Positive BAT



Skin prick test → positive
Specific inhalation test → positive



**BAT was useful in confirming the results of other tests →
could SIC be avoided?**



AN UNCOMMON CASE OF OCCUPATIONAL RHINITIS AND ASTHMA

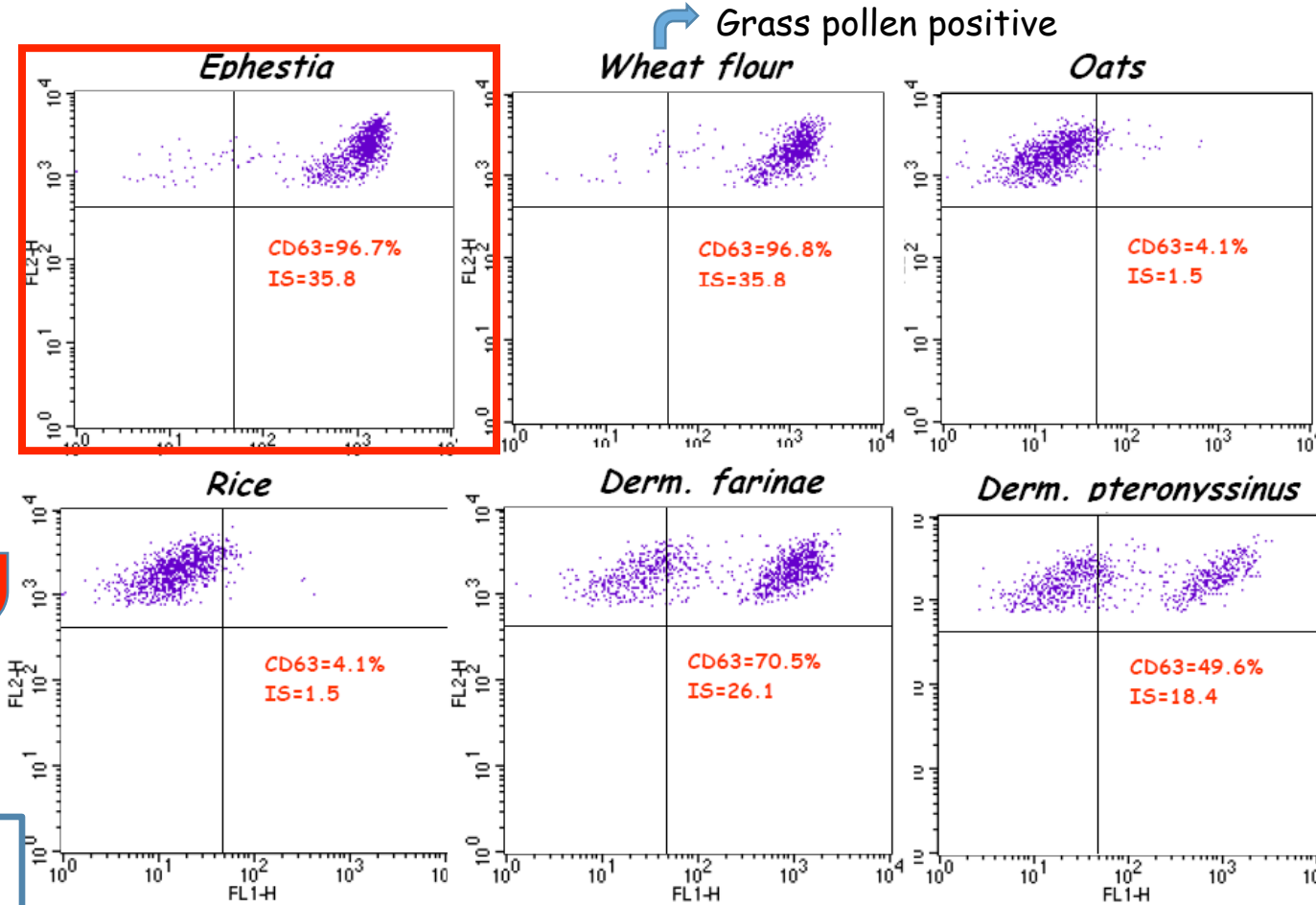
Pala G^{a,b}, Pignatti P^{a,b}, Perfetti L^a, Caminati M^c, Moscato G^{a,b}

EAACI 2010, DOI: 10.1594/eaacinet2010/CR/1-070410

- A 30-year-old atopic man with work-related respiratory symptoms.
- Cereal stocker
- Onset of symptoms when handling various types of stored cereal seeds
- SPT + for grass, mites, cereals, *Ephestia kuehniella* (cereal pest, never described as cause of OA)

Challenge with
Ephestia k. extract

Rhinorrhea, nasal obstruction and a 26% FEV₁ fall 5 min after the end of exposure



BAT was helpful in determining the clinically relevant allergen

BAT in occupational settings

- Promising tool in diagnosis of OA and OR
- Especially useful in the case of:
 - a high clinical suspicion of an occupational disease and other *in vivo* or *in vitro* tests negative or equivocal
 - evidence of increased airway inflammation after work but other tests negative or equivocal
 - can confirm results of other *in vivo* or *in vitro* tests and helps confirming sensitization
 - may be helpful in determining the clinically relevant allergen
- Allows to test very reactive substances not available for *in vivo* test.
 - Drugs → drug company workers.
- Allows to test homemade extracts
 - Wood extracts
 - Food extracts
 - Etc...

Studies are needed to evaluate sensitivity and specificity in diagnosing OA and OR

When is SIC necessary?????

Wheat Monika Curr Opin

- A total of 70 different IgE-binding protein spots in wheat flour have been identified by means of high-resolution two-dimensional gel electrophoresis and immunoblotting.
- A panel of allergens from Tri a was approved by the International Union of Immunological Societies (IUIS) Allergen Nomenclature Subcommittee (www.allergene.org) (Table 1)[9&&,10&&], not only with respect to baker's asthma but also for ingested food allergens.
- The use of different detection methods (single-ex vs multiplex) may be the reason of the different results on the panel of allergen sensitization may be the it cannot not be excluded that the most important sensitizing wheat flour allergens differ per country with impact for the diagnosis.
- The highest frequencies of IgE binding were found for Tri a 27 and Tri a 28. Although a combination of IgE tests to five components Tri a 27, Tri a 28, Tri a 29.02, Tri a 39, and Tri a 32 produced a good test performance, the authors concluded that **the allergen-specific IgE tests with the whole wheat flour extracts remain mandatory because of superior diagnostic sensitivity.**

WHEAT Summary

- Several studies have shown that for baker's asthma no major wheat allergen can be identified and the IgE-sensitization profile of each baker showed great interindividual variation.
- Although the combination of IgE test to five wheat allergens produced a promising test performance the **recommendation for routine diagnosis of baker's asthma is still the assessment of allergen-specific IgE with whole wheat (and/or rye) flour extract.**



Is SIC necessary????

LATEX

- currently 15 allergens identified from NRL *Hevea brasiliensis* have been included in the nomenclature list of the International Nomenclature Committee of Allergens (WHO/IUIS) and assigned official numbers (Hev b1–15; <http://www.allergen.org>) (Table 2).
- five of them (rHev 1, 3, 5, 6.01 and 8) are on the ISAC,
- → **Specific IgE measurement with NRL extract** is an important method **to diagnose latex sensitization** and could be significantly improved by **addition of the major allergen rHev b 5** as a stable recombinant protein to the NRL extract preparation [17].
- patients with spina bifida and occupational latex exposed healthcare workers are sensitized by different NRL allergens
- In healthcare workers suffering from occupational latex allergy, the most important NRL allergens are Hev b 5 and Hev 6.01 or Hev b 6.02
- the conventional ImmunoCAP k82 showed a superior sensitivity than ISAC with respect to detection of NRL sensitization (Seyfarth)

LATEX Summary

- → **Specific IgE measurement with NRL extract** is an important method to **diagnose latex sensitization** and could be significantly improved by **addition of the major allergen rHev b 5** as a stable recombinant protein to the NRL extract preparation [17].
- The conventional ImmunoCAP k82 shows a superior sensitivity than ISAC with respect to detection of NRL sensitization (Seyfarth 2014)
- In healthcare workers suffering from occupational latex allergy, the most important NRL allergens are Hev b 5 and Hev 6.01 or Hev b 6.02
- **In suspected OA, high levels of sIgE against rHev b 5 combined with rHev b 6.01 or 6.02 are the most efficient predictors of a bronchial response to NRL (Vandenplas, Allergy 2016).** Since 'classical' diagnostic latex extracts for SPT are no longer readily available (different manufacturers removed latex extracts from distribution) and powdered gloves for bronchial challenge test are no longer commercially available, these results are quite important for the diagnosis of occupational latex allergy

Can SIC be avoided?