Società Italiana di Allergologia, Asma ed Immunologia Clinica

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FIRENZE

6/9 APRILE 2017

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SAVE THE DATE

ICON: CLINICAL CONSEQUENCES OF MITE HYPERSENSITIVITY

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CLINICA ELAVILA

WAO WORLD ALLERGY ORGANIZATION

A World Federation of Allergy, Asthma & Clinical Immunology Societies

Centro Médico Docente La Trinidad

ICON: CLINICAL CONSEQUENCES OF MITE HYPERSENSITIVITY: A GLOBAL PROBLEM

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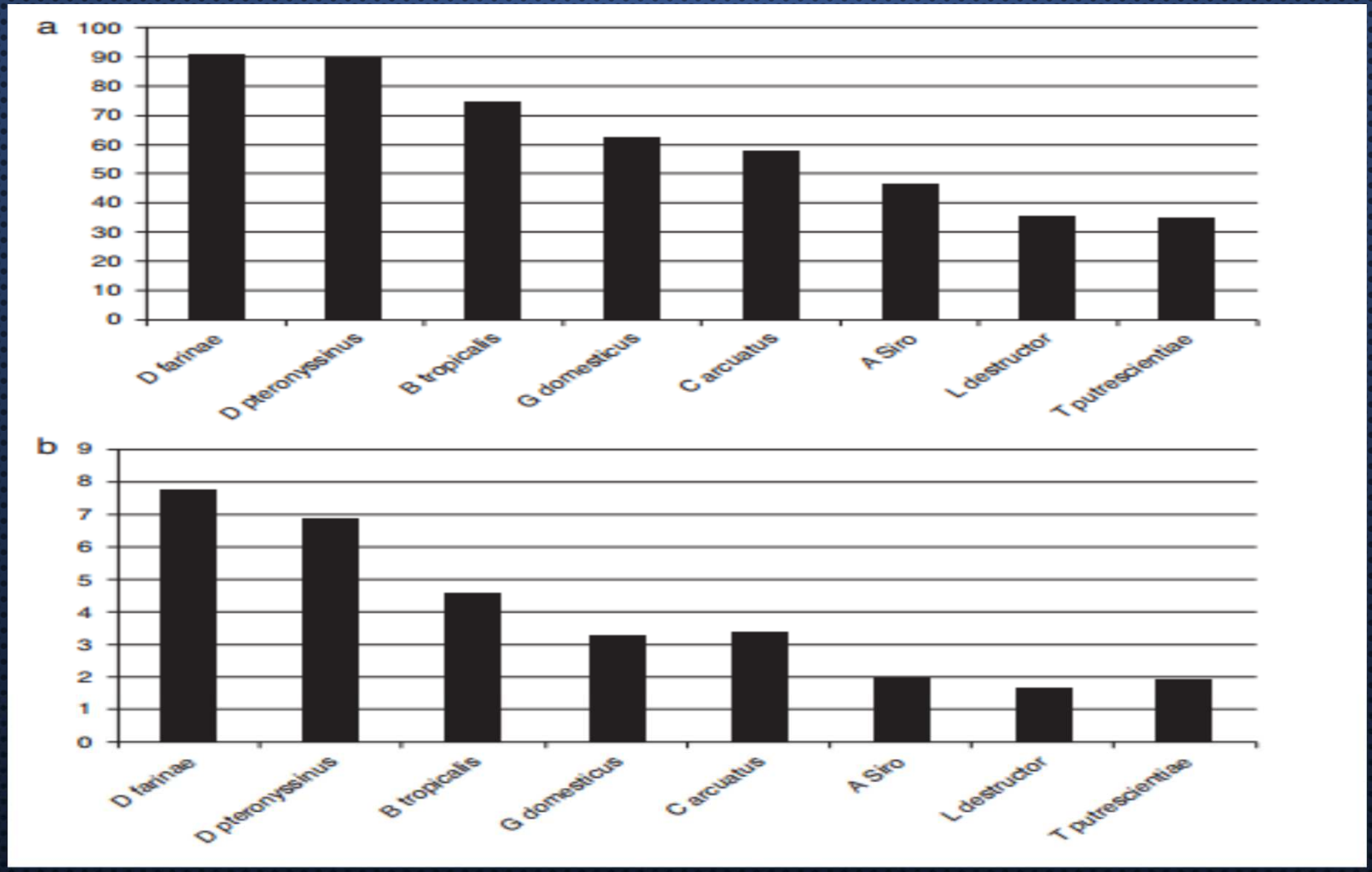
MITES AND ALLERGY: HISTORICAL PERSPECTIVE

Author	Year	Discovery
Kern	1921	The importance of house dust in allergic manifestations
Cooke	1922	The existence of allergens of unknown origin and nature in house dust. Extracts were prepared for desensitization studies
Storm Van Leeuwen	1924	Associated the dust allergy phenomenon with certain climatic circumstances
Oshima	1964	Presence in house dust of mites of the genus *Dermatophagoides farinae*
Voorhorst and Spieksma	1964	Showed that house dust contains mite species with a high allergenic power, which could be responsible for the allergenicity of house dust
Fain	1966	Identified the mite *D. pteronyssinus* as the main allergen source responsible for numerous respiratory allergies induced by the inhalation of house dust

EPIDEMIOLOGY

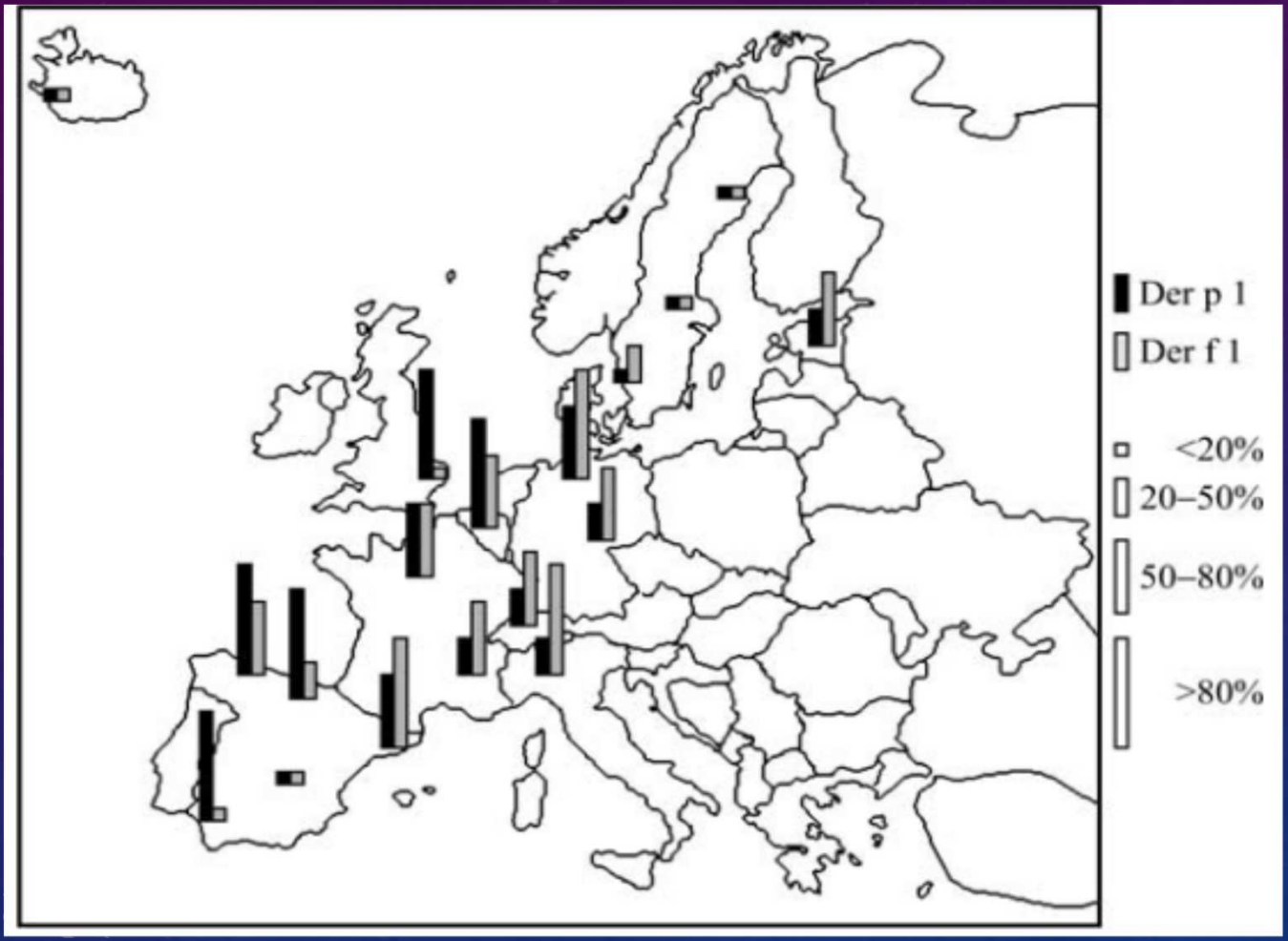
Author	Year	Population	Mite	Sensitization rate (%)
Bull WHO	1988	Asthma	HDM	45-85
Chew (Singapore)	1999	Rhinitis/asthma	*D. pteronyssinus* *D. farinae* *B. tropicalis*	93.4 92.3 96.2
Leung (Hong Kong)	2002	Asthma	HDM	>85
Sánchez-Borges (Venezuela)	2003	Rhinitis/asthma	*D. pteronyssinus* *B. tropicalis*	97.2 91.6
Davey (Ethiopia)	2005	Asthma	*D. pteronyssinus*	OR 1.21 (0.98-1.51)
Bousquet (Europe)	2007	General population in Europe	*D. pteronyssinus*	21.7

Results of skin tests with eight mite allergens in 157 patients with allergic rhinitis or rhinosinusitis



Sánchez-Borges M et al. Allergol Immunopathol (Madr). 2014;42(2):120-126

Distribution of Der p 1 and Der f 1 allergens in Europe

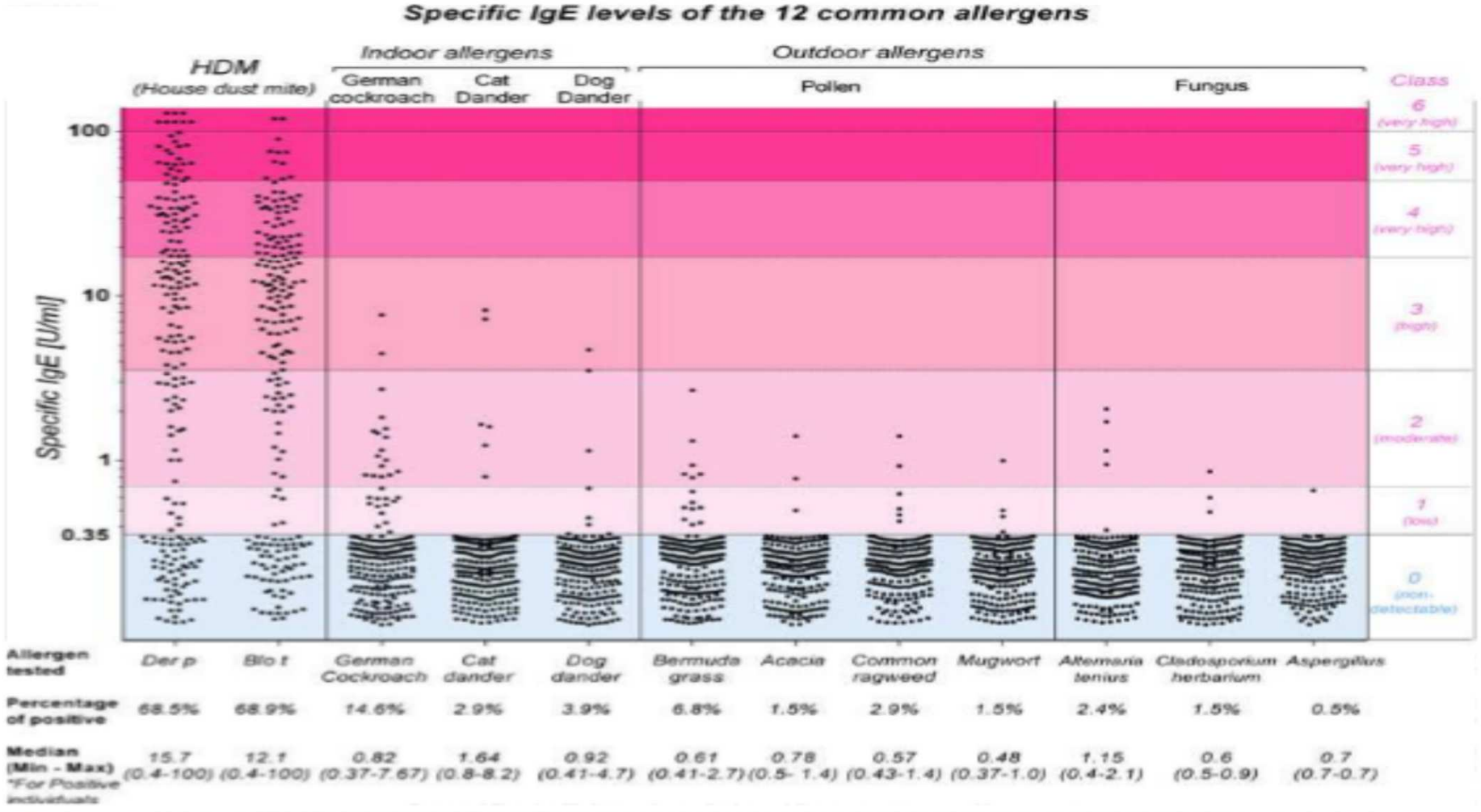


Low winter temperatures reduced Der p 1 rather than Der f 1. Important risk factors for high allergen levels included an older mattress, a lower floor level of the bedroom, limited ventilation of the bedroom, and dampness for Der p 1 but not for Der f1. Mite allergen exposure may be reduced by replacing the mattress regularly and increasing ventilation of the bedroom, particularly in winter.

Zock J et al. J Allergy Clin Immunol 2006;118:682-90

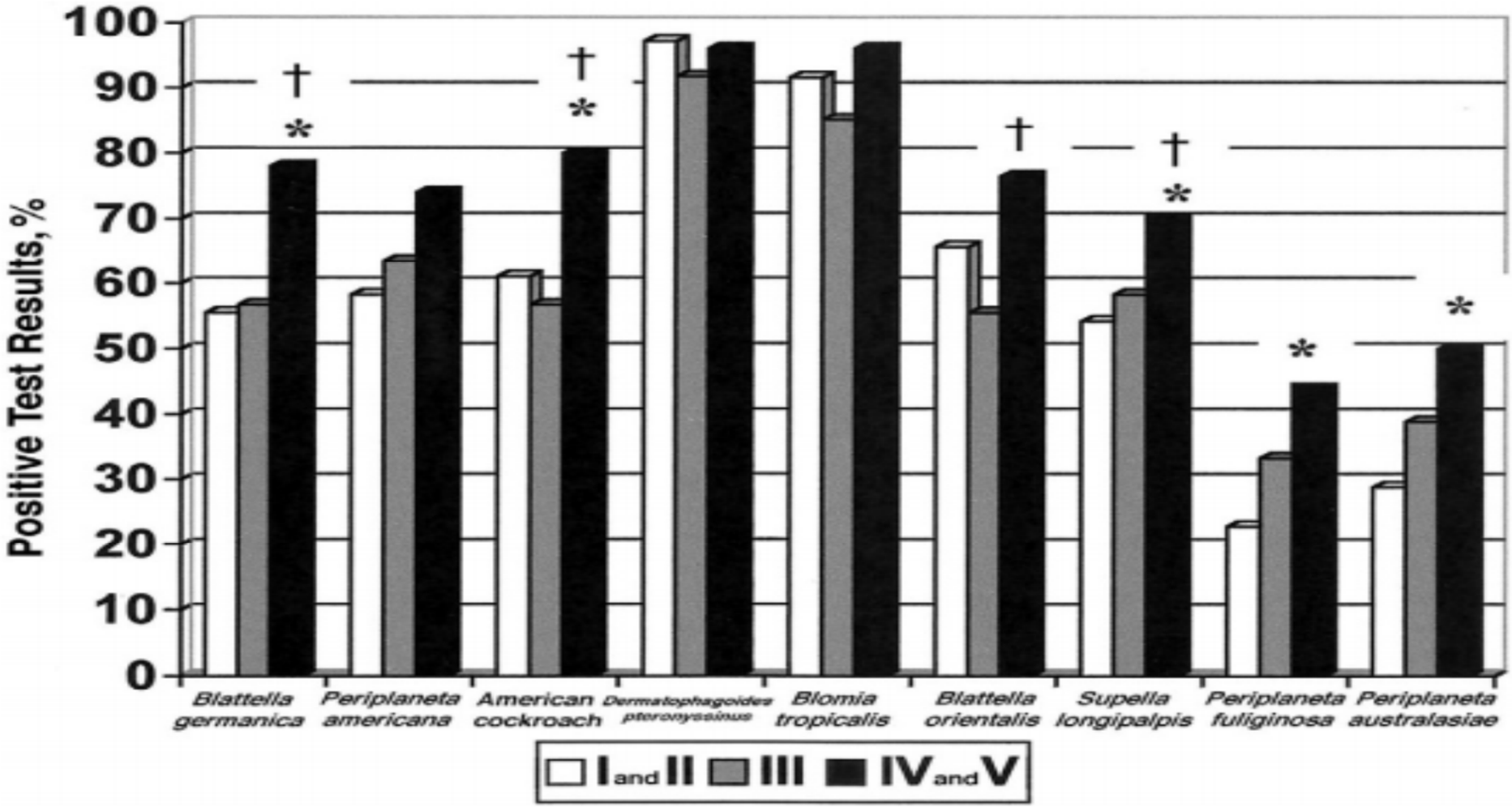
Allergic airway diseases in a tropical urban environment are driven by dominant mono-specific sensitization against house dust mites

Singapore



Andiappan AK et al. Allergy 2014; 69: 501–509

Percentages of positive skin prick test results according to socioeconomic level (I, II, III, IV, or V). *P 0.05 vs I and II. †P 0.05 vs III.

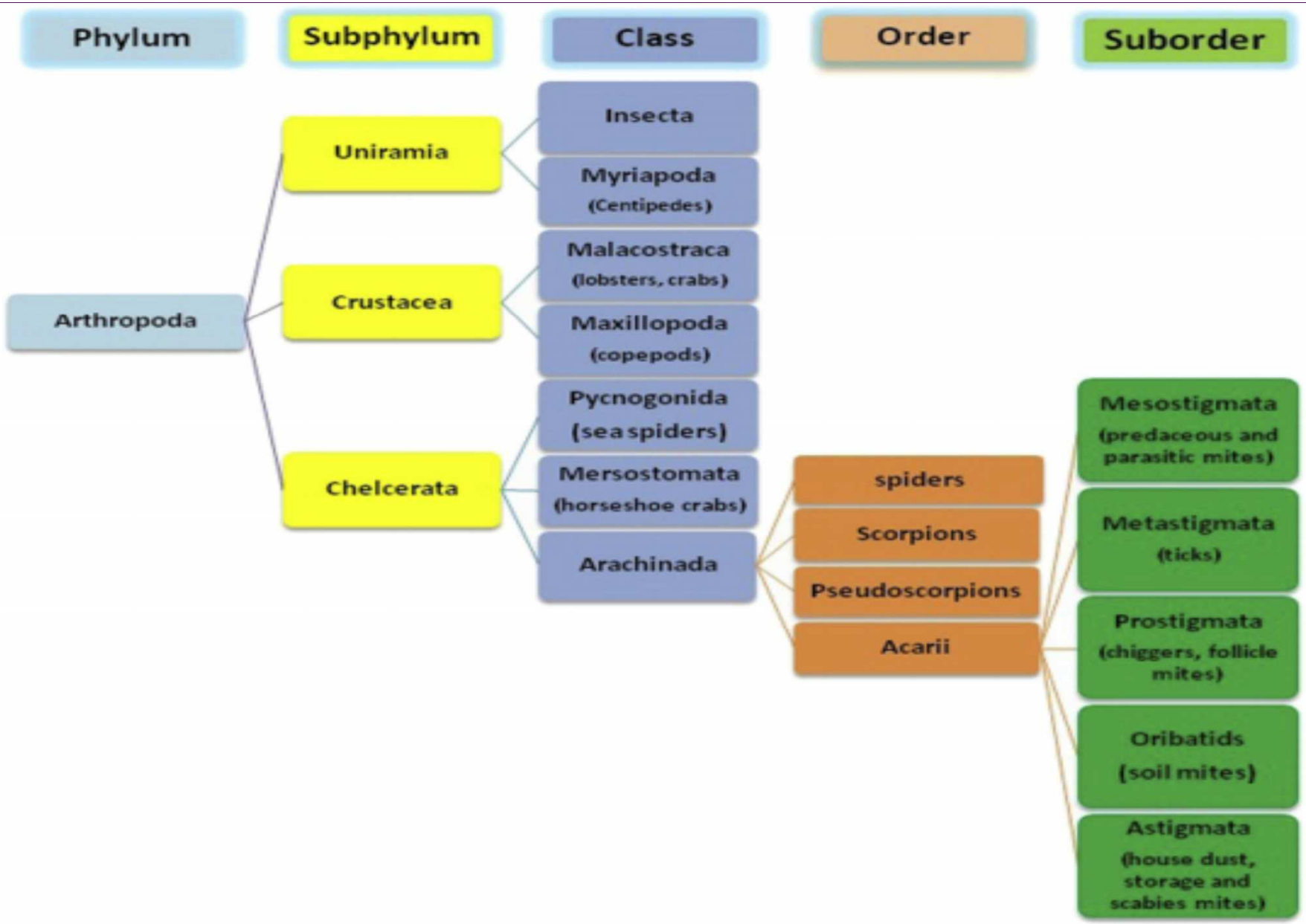


Sánchez-Borges M et al. Ann Allergy Asthma Immunol. 2003;90:664– 668.

Levels and distribution of Der p 1 and Der f 1 in Pavia, Italy

	Mattress	Living-room f17loor
Der p 1 (µg/g) (median, 1st-3rd quartile)	0.34 (0.17-0.65)	0.15 (0.11-0.21)
Der p 1 (µg/m2) (median, 1st-3rd quartile)	0.02 (0.014-0.06)	0.006 (0.003-0.009)
Der f 1 (µg/g) (median, 1st-3rd quartile	7.76 (5.5-13.75)	0.83 (0.33-1.94)
Der f 1 (µg/m2) (median, 1st-3rd quartile)	0.73 (0.32-1.11)	0.03 (0.01-0.09)
Homes (n,%) with **Der p 1 >2µg/g** **> 10 µg/g**	5 (11.4) 0 (0)	0 (0) 0 (0)
Homes (n,%) with **Der f 1 >2µg/g** **> 10 µg/g**	3.8 (86.4) 17 (38.6)	10 (22.7) 0 (0)

Moscato G et al. Allergy 2000: 55: 873-87


Phylum
Subphylum
Class
Order
Suborder
Arthropoda
Uniramia
Crustacea
Chelcerata
Insecta
Myriapoda
(Centipedes)
Malacostraca
(lobsters, crabs)
Maxillopoda
(copepods)
Pycnogonida
(sea spiders)
Mersostomata
(horseshoe crabs)
Arachinada
spiders
Scorpions
Pseudoscorpions
Acarii
Mesostigmata
(predaceous and parasitic mites)
Metastigmata
(ticks)
Prostigmata
(chiggers, follicle mites)
Oribatids
(soil mites)
Astigmata
(house dust, storage and scabies mites)

MITE SPECIES IN TROPICAL AND TEMPLATE REGIONS

TEMPLATE

Domestic

- *D. pteronyssinus*
- *D. farinae*
- *D. microceras*
- *E.maynei*
- *Hirstia domicola*

Storage

- *Blomia spp.*
- *Acarus spp.*
- *Tyrophagus spp.*
- *Suidasia spp.*
- *Glycyphagus spp.*
- *Lepidoglyphus spp.*
- *Chortoglyphus arcuatus*
- *Cheyletus spp.*

TROPICAL

Domestic

- *D. pteronyssinus*
- *D. farinae*
- *D. neotropicalis*
- *E. maynei*
- *Hirstia domicola*
- *D. siboney*
- *Pyroglyphus africanus*

Storage

- *Blomia tropicalis*
- *Acarus spp.*
- *Tyrophagus spp.*
- *Suidasia spp.*
- *Glycyphagus spp.*
- *Lepidoglyphus spp.*
- *Chortoglyphus arcuatus*
- *Cheyletus spp.*
- *Tropilichus aframericanus*

Fernández-Caldas E, Lockey R. ACI News 1995; 7: 39-42

ALLERGENS FROM *Dermatophagoides* SPECIES

Table 1 Dermatophagoides spp.

Immunodominant		Mid-tier		Minor		Unknown	
1	Cysteine protease	4	Alpha amylase	3	Trypsin	14	Large lipid transfer protein
2	ML domain protein	5	Unknown coiled coil bundle	6	Chymotrypsin	22	ML domain protein
23	Peritrophin homologue	7	LPS binding protein homologue	8	Glutathione-S-transferase	24	Cytochrome c reductase binding protein
		21	Group 5 homologue	9	Collagen serine protease	25	Triosephosphate isomerase
				10	Tropomyosin	26	Myosin alkali light chain
				11	Paramyosin	27	Serpin
				13	Fatty acid binding	28	Heat shock protein
				16	Gelsolin	29	Cyclophilin
				17	Unknown EF hand protein	30	Ferritin
						31	Cofilin
						32	Pyrophosphatase
						33	Alpha tubulin

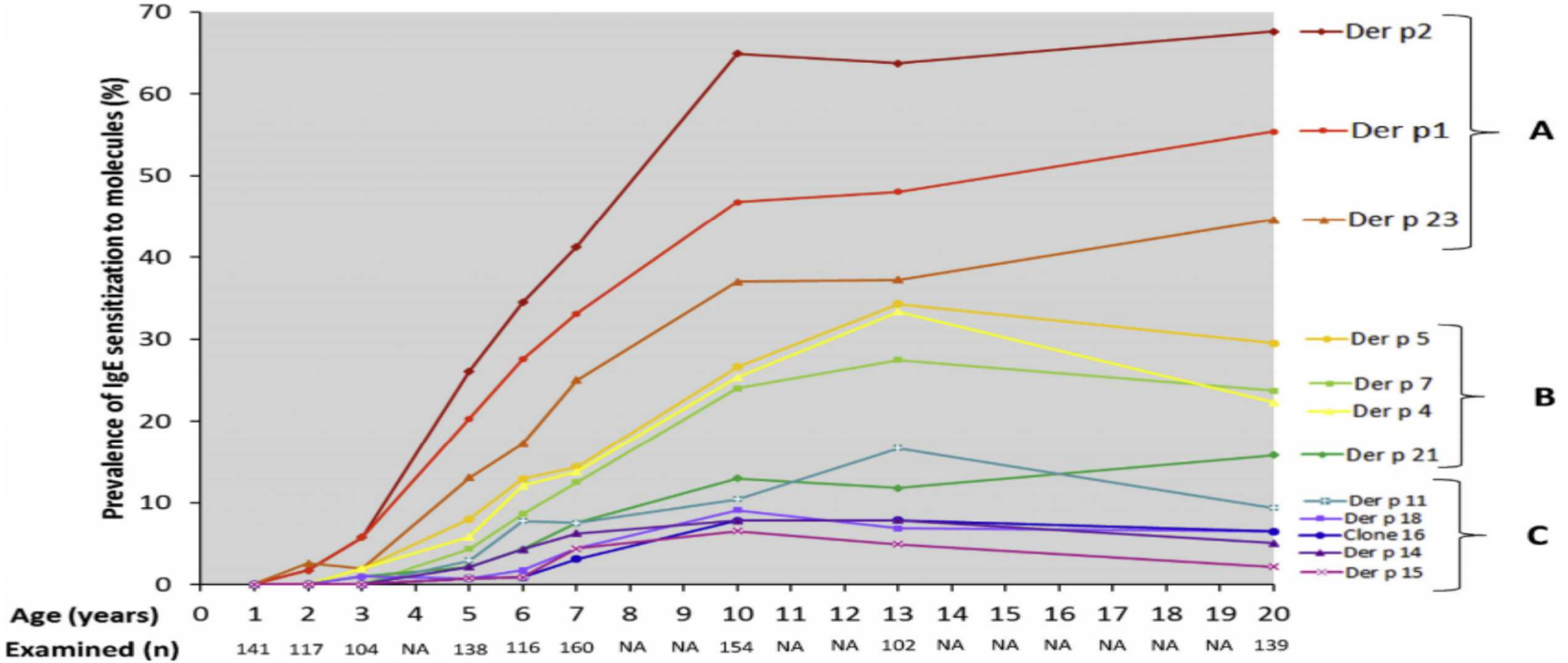
Notes

(1) Group 12 and 19 allergens have not been found for *Dermatophagoides* spp.

(2) No quantitative assessments of IgE binding have been reported for the Unknown groups due to the tests used or the nature of the allergen preparations.

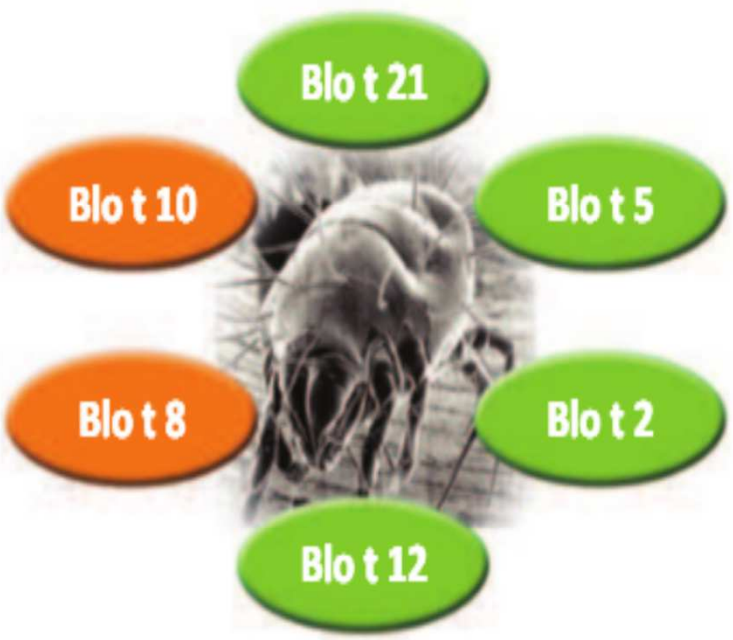
Evolution of IgE responses to 12 D pteronyssinus molecules from birth to age 20 years

Posa D et al. JACI 2017;139:541-9.

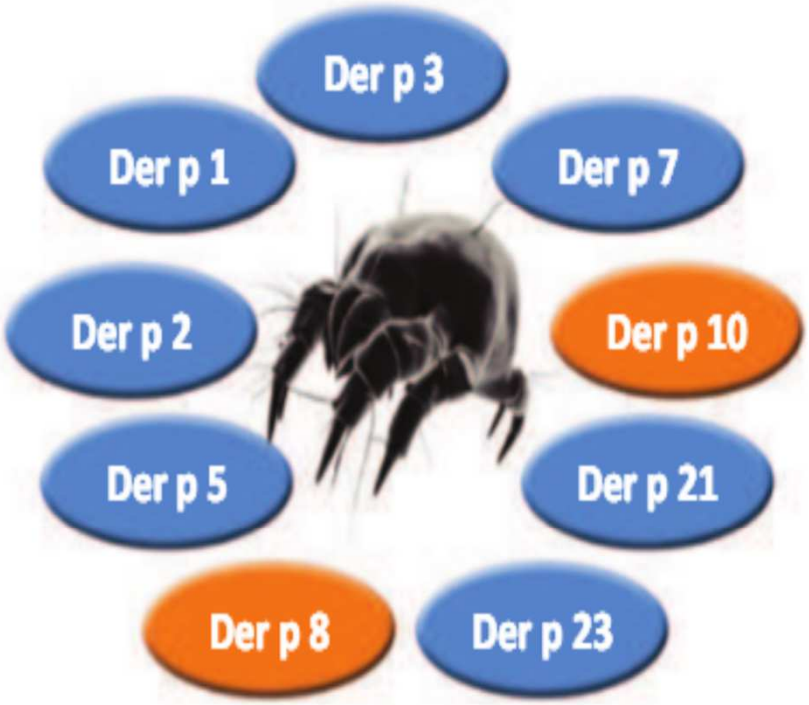


Clinical implications: Parental hay fever, higher mite allergen exposure in infancy, and early IgE sensitization predict a broader IgE response to D pteronyssinus molecules, which in turn predicts current Mite AR and current and future asthma.

Clinically relevant mite allergens (Cross-reactivity in orange)

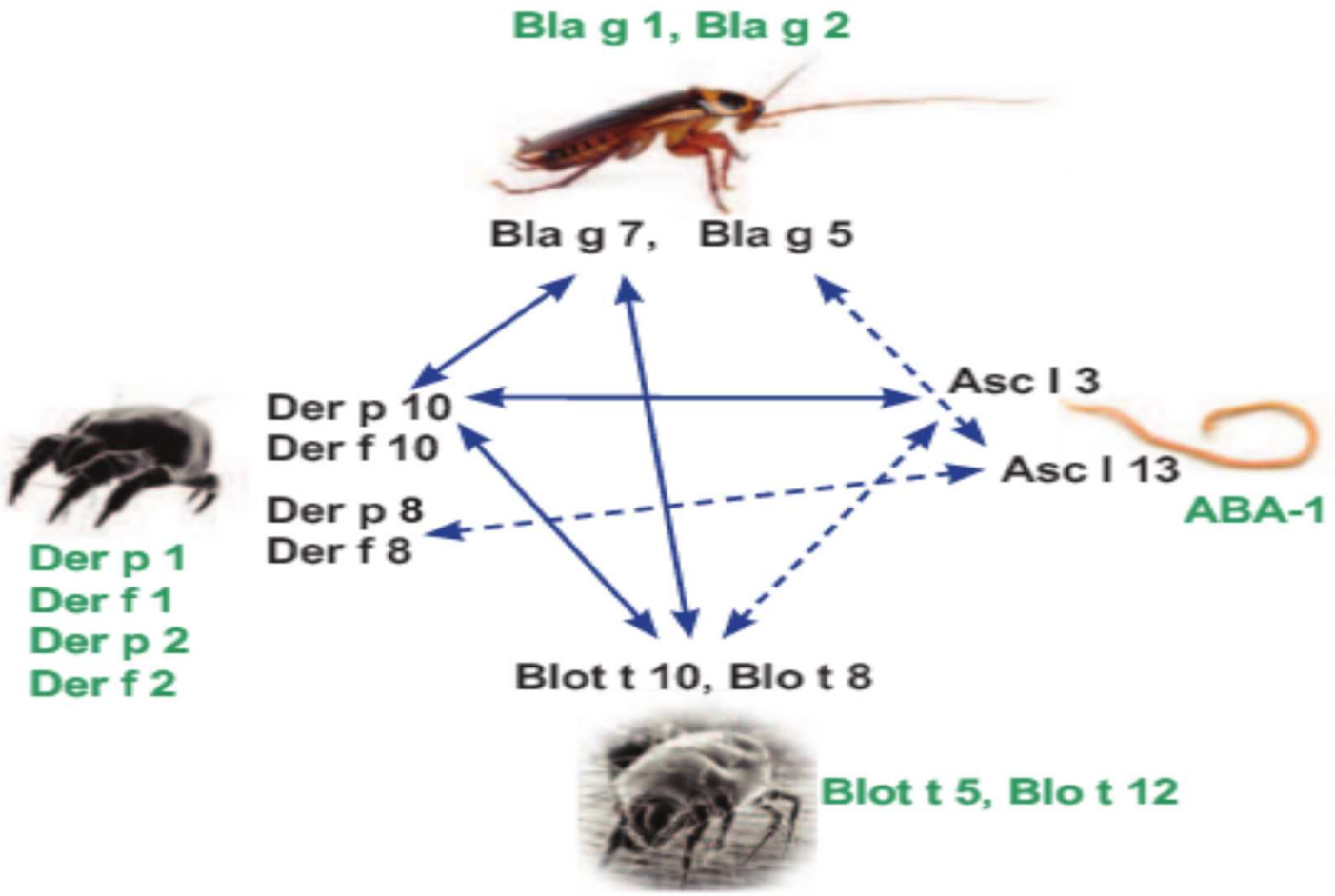


Blomia tropicalis

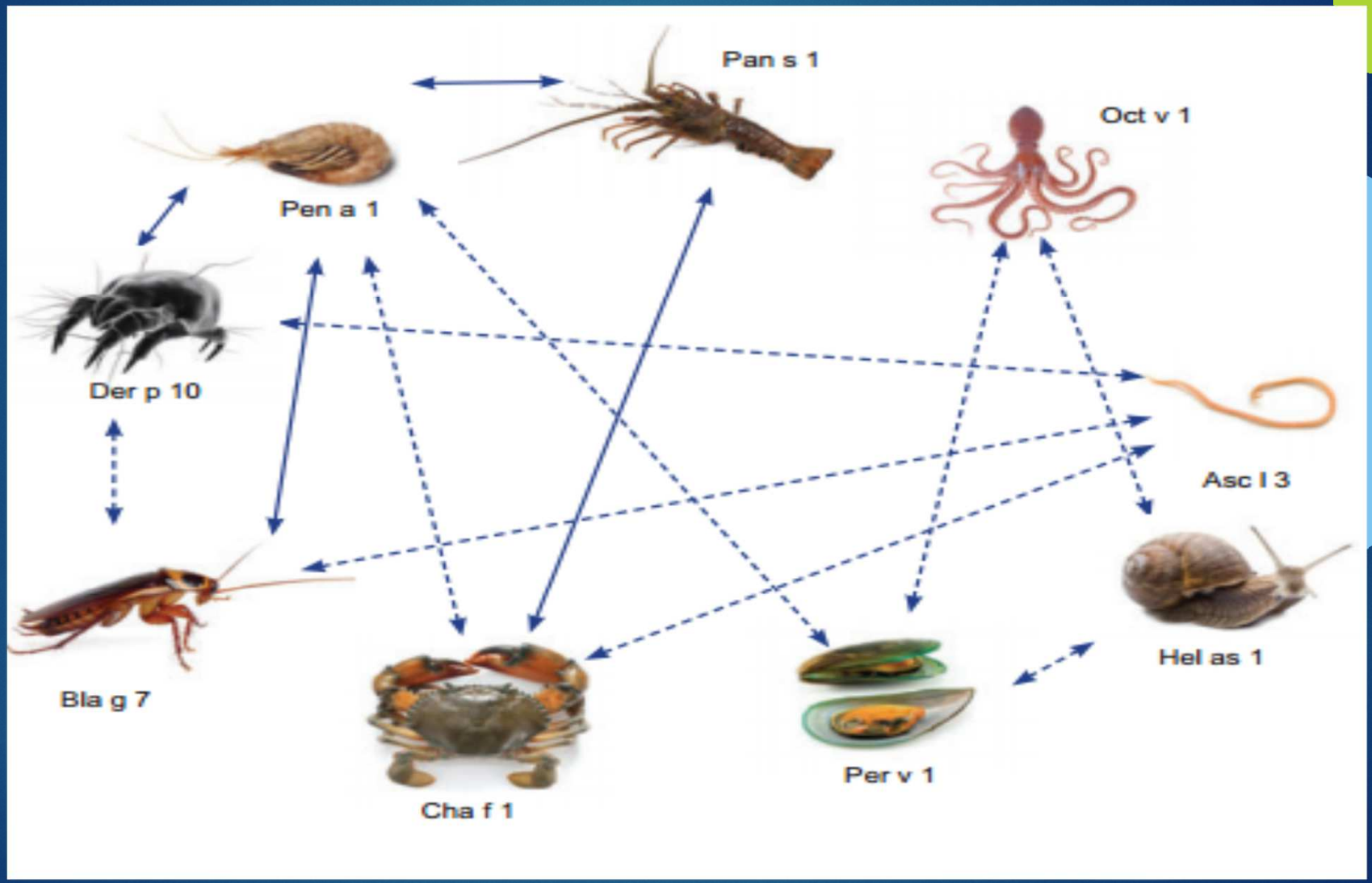


Dermatophagoides pteronyssinus

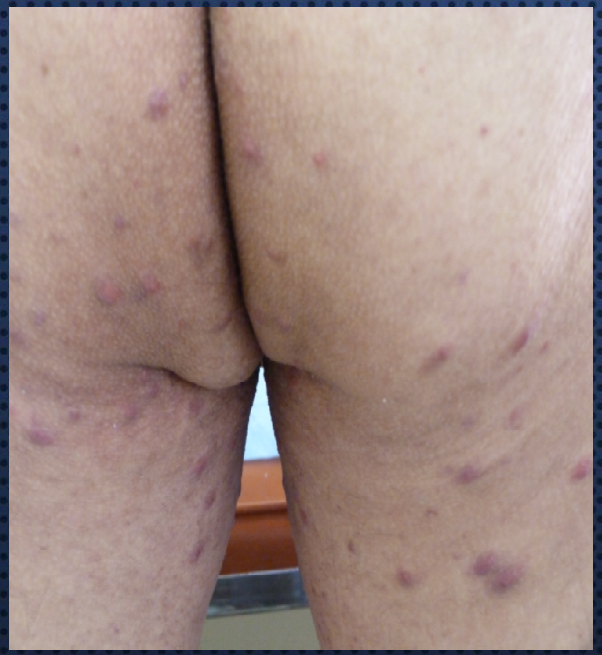
Clinically relevant cross-reactivity of mite allergens
(Species-specific components in green)



Cross-reactivity between allergenic tropomyosins



CRUSTED (Norwegian) SCABIES



Sarcoptes scabiei var humanus

Sánchez-Borges M et al, 2017 (submitted)

RELEVANCE OF SCABIES TO ALLERGY DIAGNOSIS

- S. scabiei mite produces a number of allergens homologous of HDM allergens, among them: Group 11 (paramyosin), group 14 (apolipoprotein), group 8 (glutathione S-transferase), group 3 (serine protease), and group 1 (cysteine protease)
- Positive immediate-type skin tests performed with HDM allergen extracts are observed in patients with past or current scabies infestation, which may be due to cross-reactive antibodies to Der p 4 and Der p 20
- Scabies represents a major confounder in the diagnosis of HDM sensitization because scabies-infested or exposed subjects have high-titre IgE binding to Der p 4 (amylase) and Der p 20 (arginine kinase) with the anti-Der p 4 persisting in previously exposed subjects.

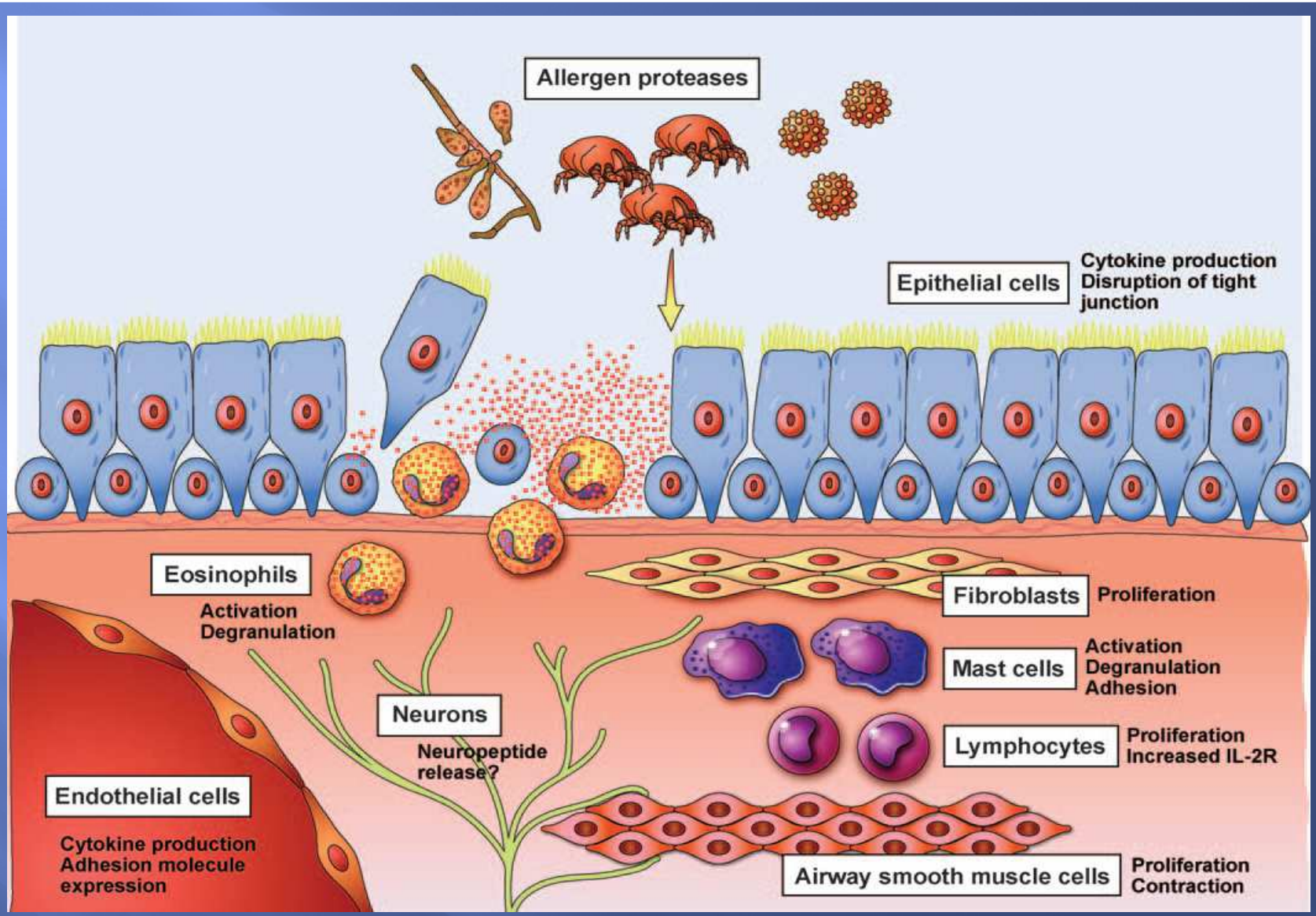
CLINICAL APPLICATIONS OF PURIFIED MITE ALLERGENS AND ASSAYS

- Improved allergen standardization and formulation.
- Development of formulations of purified allergens for molecular diagnostics with useful discrimination and quantitation of IgE antibody levels and to enable the measurement of allergen-specific IgG antibodies as potential prognostic markers for diagnosis.
- Environmental exposure assessments to improve patient education about mite allergen exposure and asthma. To develop objective assessments of allergen control procedures, methods and devices. To understand the aerodynamics and distribution of mite allergens.
- Improve the formulation, reproducibility and potency of mite allergen immunotherapeutics and to develop new strategies for immunotherapy and true prophylactic vaccines.

Component-Based Allergen-Microarray: Der p 2 and Der f 2 Dust Mite Sensitization Is More Common in Patients With Severe Asthma

Characteristics	Groups According to Asthma Severity			Total	*P* Value[b]
	Intermittent (n=39)	Mild to Moderate (n=42)	Severe (n=45)	Population (n=126)	
Mean age, y	34.7	37.5	47.9	40.4	<.0001
Range	18-66	18-68	21-74	18-74	
SD	12.8	12.6	15.7	14.9	
Sex, No. (%)					
Men	18 (46.2)	14 (33.3)	20 (44.4)	52 (41.3)	.436
Women	21 (53.8)	28 (66.7)	25 (56.6)	74 (58.7)	
FEV_1, % (range)	98.8 (75-128)	82.85 (57-111)	70.69 (28-124)		
Missing values, No.	27	22	19		
Rhinitis, No. (%)	35 (89.7)	36 (85.7)	26 (57.8)	97 (77.0)	.0006
Conjunctivitis, No. (%)	33 (84.6)	24 (57.1)	8 (17.8)	65 (51.6)	<.0001
Treatment, No. (%)					
Inhaled corticosteroid	10 (25.6)	42 (100.0)	45 (100.0)	97 (77.0)	
β_2-agonist (long-acting)	18 (46.2)	30 (71.4)	42 (93.3)	90 (71.4)	
Results					
Skin prick test sensitization, No. (%)					
Dust mite allergen	19 (48.7)	23 (54.8)	29 (65.9)	71 (56.8)	.273
Birch pollen	21 (53.9)	17 (40.5)	7 (15.9)	45 (36.0)	.001
ImmunoCAP ISAC, No. (%)					
Dust mite allergen	17 (43.6)	17 (40.5)	29 (64.4)	63 (50.0)	.052
Birch pollen	25 (64.1)	17 (40.5)	13 (28.9)	55 (43.7)	.005
Sensitization to Der p 2, No. (%) (ImmunoCAP ISAC)	14 (35.9)	14 (33.3)	26 (57.8)	54 (42.9)	.040
Sensitization to Der f 2, No. (%) (ImmunoCAP ISAC)	14 (35.9)	14 (33.3)	28 (62.2)	54 (44.4)	.011

Sylvestre L et al. J Investig Allergol Clin Immunol. 2016;26(2):141-3



Reed CE, Kita H. The role of protease activation of inflammation in allergic respiratory diseases. J Allergy Clin Immunol. 2004 Nov;114(5):997-1008.

DUST MITE SENSITIZATION AND ASTHMA

- Celedon et al reported that increased HDM exposure (≥10 mg/g) in early life was associated with increased risk for asthma at 7 years old (OR 3.0). Other studies did not find an association between exposure in infancy and asthma at 3, 6–7 or 8 years of age
- The effects of HDM on asthma exacerbations and whether interventions aimed at exposure reduction can significantly improve symptoms are also controversial
- One recent study looked at different levels of exposure to dust mites in different locations to identify the major sources and settings of exposure. The highest average exposure (1117 pg/m3, 95% CI: 289-4314) occurred on public transport and the lowest overnight in bed (45 pg/m3, 95% CI: 17-117), which contributed only 9.8% (95% I: 4.4%-15.1%) of total daily exposure

DUST MITE SENSITIZATION AND RHINITIS/RHINOSINUSITIS

- HDM induced allergic rhinitis typically is perennial with seasonal exacerbations
- The diagnosis is likely if all of the following signs are present; the diagnosis is possible if any of these signs is absent:

* symptoms are perennial with seasonal exacerbations (Spring, Fall)
* symptoms improve in altitude (>1500 m)
* it is aggravated by contact with household dust and domestic/indoors activities
* skin prick test to house dust mites extract is positive

- Consider comorbidities, especially asthma and allergic conjunctivitis

DUST MITE SENSITIZATION AND ATOPIC DERMATITIS

- The role of sensitization to inhalant allergens in atopic dermatitis is uncertain. Total serum IgE levels are elevated but seem to be more elevated in AD patients with filaggrin mutations

1- The rate of IgE–mediated sensitization to foods and inhalant allergens is high.

2- Most AD patients have elevated levels of serum IgE antibodies specific to HDM allergens; biopsy specimens of AD lesional skin have been shown to be infiltrated with T lymphocytes that recognize Der p

3- Group 1 mite allergens may facilitate its entry into the skin by enzymatically breaking down the epidermal barrier. Mite allergens can activate keratinocytes and induce them to produce and secrete pro-inflammatory cytokines.

4- Allergens may sensitize infants with AD via the skin. The proliferation of lymphocytes stimulated with HDM allergens shows significantly higher responses in AD infants than in controls

DUST MITE SENSITIZATION AND ATOPIC DERMATITIS

5- RESPIRATORY ALLERGIC DISEASES DUE TO INHALANT ALLERGENS ARE FREQUENT AMONG AD PATIENTS

6- PATIENTS WITH AD SHOWED A HIGHER PREVALENCE OF MITES ON THEIR SKIN THAN DID HEALTHY INDIVIDUALS

7- HDM AVOIDANCE MEASURES MAY REDUCE THE ECZEMA

8- EPICUTANEOUS APPLICATION OF HDM (ALLERGEN PATCH TEST, APT) INDUCES AD IN NONLESIONAL SKIN OF 50% OF AD PATIENTS

9- TSLP PLAYS AN IMPORTANT ROLE IN THE PATHOGENESIS OF AD

MITES AND ANAPHYLAXIS

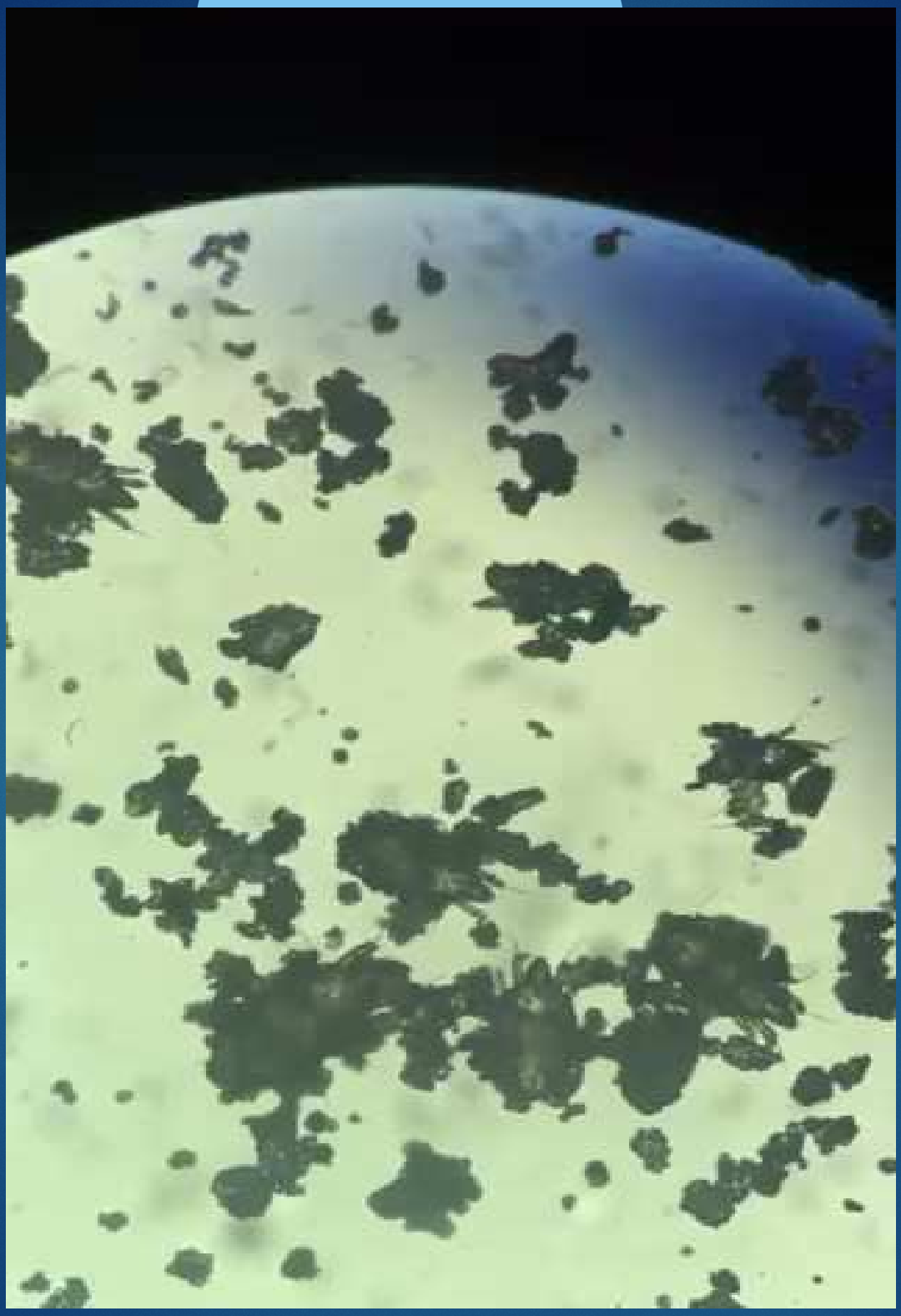
- Heavy mite exposure in the environment can induce allergic systemic reactions.
- More recently, the induction of anaphylaxis through ingestion of mite-contaminated foods has been described.
- Pancake anaphylaxis, also called oral mite anaphylaxis (OMA), is a relatively new syndrome characterized by severe allergic symptoms occurring immediately after eating foods, especially containing flours, contaminated with mites.

- *Erben AM et al. J Allergy Clin Immunol 1993; 92: 846-9*
- *Spiegel WA et al. Ann Allergy 1994; 72: 56*

ORAL MITE ANAPHYLAXIS: DEMOGRAPHICS

Number of cases	171
Age range	6-71 years
Gender: Female/Male	99/72
Location	Spain 59 Venezuela 47 Japan 40 USA 7 Brazil 2 Singapore 2 Belgium 2 Taiwan 1 Panama 10 Thailand 1
Foods	Pancakes, beignets, pizza dough, sponge cake, cupcakes, okonomi-yaki, tako-yaki, tempura, polenta, scones, grits, steak and chicken parmigiana , chorizo, cured ham
NSAID hypersensitivity	75/170 (44.1 %)

Sánchez-Borges M, Fernández-Caldas E. Curr Opin Allergy Immunol 2015, Sánchez-Borges M et al. J Allergy Clin Immunol 2013; 131: 31-5. . Sánchez-Borges M et al. Cutis 1997; 59: 311-14



Oral Mite Anaphylaxis Mimicking Acute Asthma

Maria Eugenia Garcia, Mario Sánchez-Borges, Arnaldo Capriles-Hulett, Enrique Fernandez-Caldas

Allergol Immunopathol 2016, in press

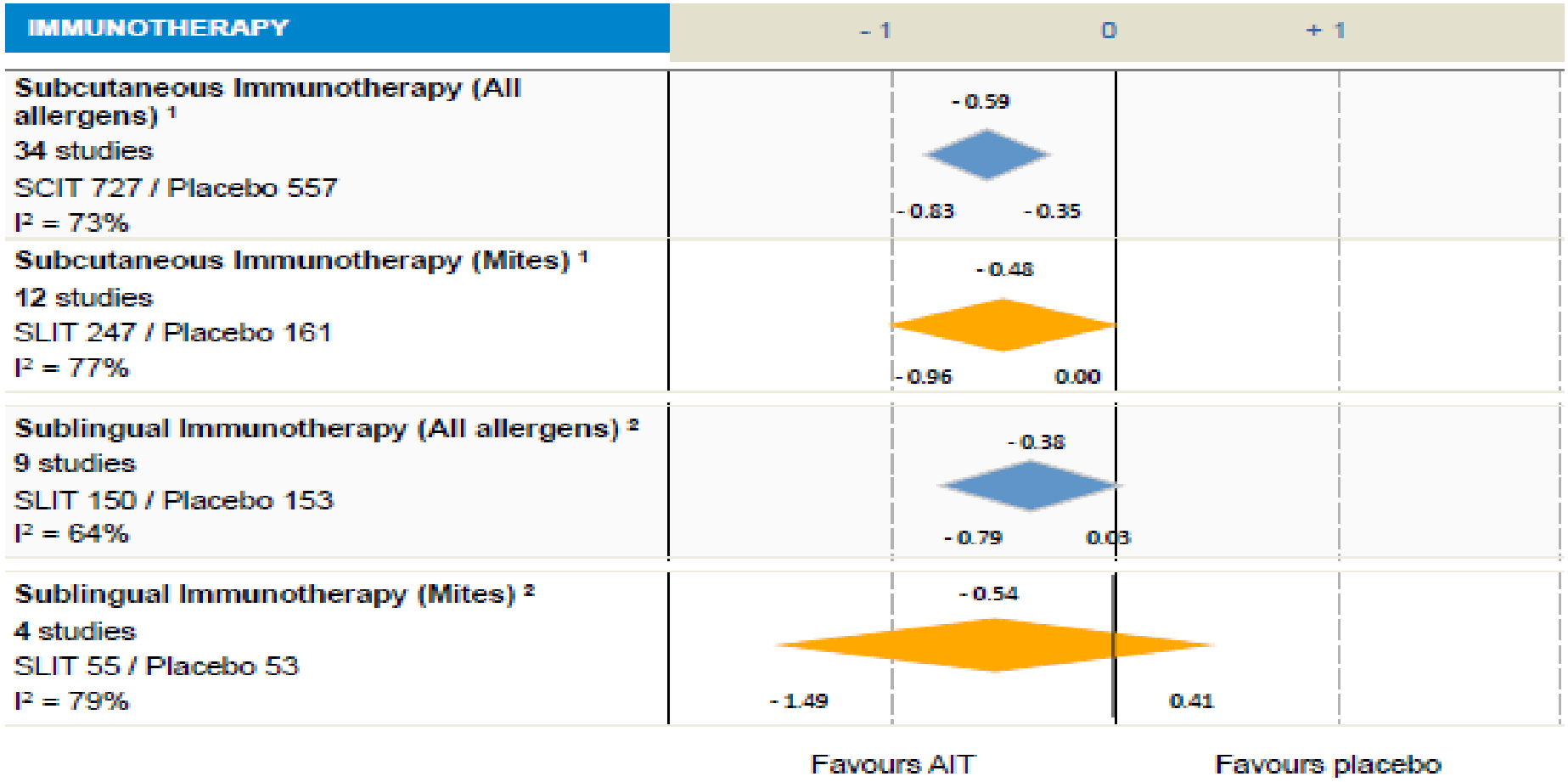
Respiratory allergy caused by house dust mites: What do we really know?

- A recent review article by Calderon et al states that "sensitization can be both systemic and localized. Inhalation of HDM aeroallergens can elicit eczematous lesions".
- Deposition of an allergen in one organ (the respiratory tract) causes symptom flare-ups in another organ.
- Local allergen-dependent mechanisms can theoretically cause concomitant reactions elsewhere in the body, with the most severe form being a systemic anaphylactic reaction.

- Our case report highlights the possibility of induction of bronchial obstruction through the exposure to mite allergens via the GI tract

Calderon MA et al. J Allergy Clin Immunol 2015; 136: 38-48

ALLERGEN IMMUNOTHERAPY FOR ASTHMA

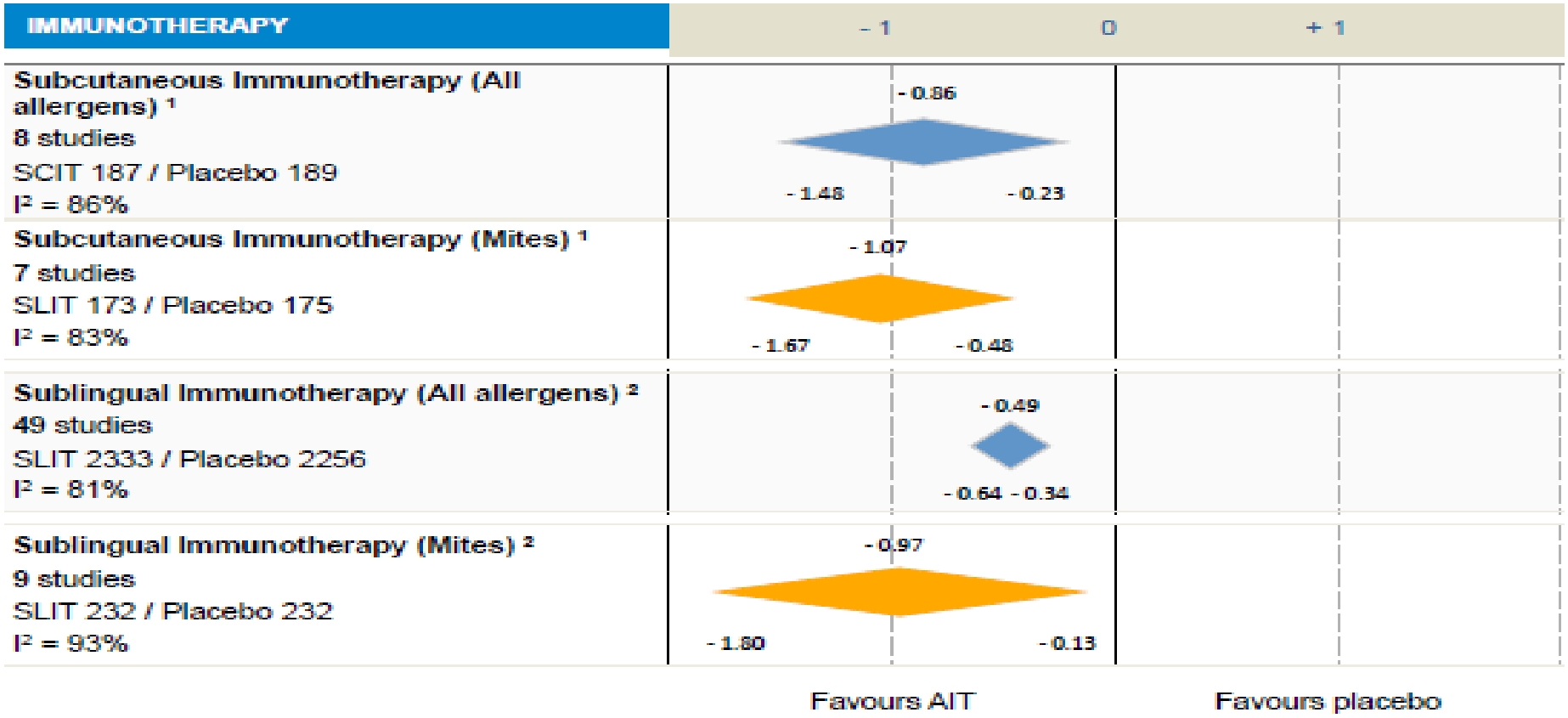


Calderon MA et al. J Allergy Clin Immunol In Practice 2015; 3: 843-55.

[1] Abramson MJ et al. Cochrane Database Syst Rev. 2010 Aug 4; (8): CD001186.

[2] Calamita Z et al. Allergy 2006; 61: 1162-72.

ALLERGEN IMMUNOTHERAPY FOR RHINITIS



Calderon MA et al. J Allergy Clin Immunol In Practice 2015; 3: 843-55.
[1]Calderon MA et al. Cochrane Database of Systematic Reviews 2013, No.: CD007163 [*In press*]
[2] Radulovic S et al. Cochrane Database Syst Rev. 2010 Dec 8;(12):CD002893.

IMMUNOTHERAPY FOR MITE ALLERGY

- SLIT induces effects from 14 weeks onward
- Decrease of symptom and medication scores
- Decrease combined RC score
- Improvement of QoL
- Reduction of corticosteroid use and asthma exacerbations
- Sustained benefits for up to 7 years
- SLIT and SCIT are equipotent
- Choice according to local availability and patient preference

Marogna M et al. J Allergy clin Immunol 2010; 126: 969-75
Mosbech H et al. J Allergy Clin Immunol 2014; 134: 568-75
Durham SR and Penagos M. J Allergy Clin Immunol 2016; 137: 339-44
Canonica GW et al. Expert Rev Clin Immunol. 2016; 12: 805-15

THANK YOU !!!