



fimp Federazione Italiana Medici *Pediatri*
Sezione di Caserta

SIPPS & FIMPAGGIORNA 2012

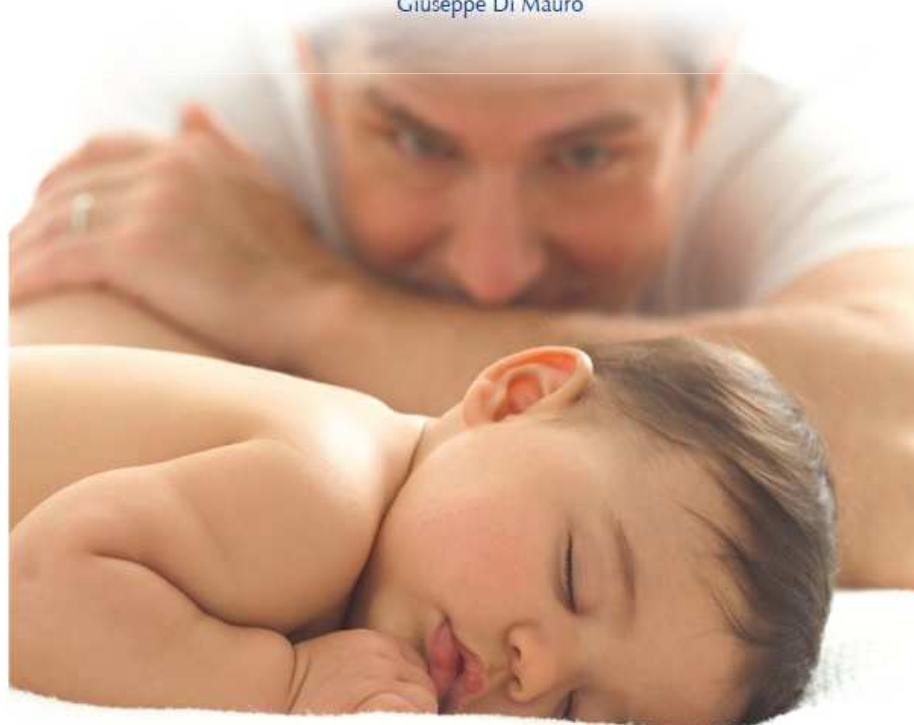
BEST PRACTICE:
la cultura del sapere e del fare in Pediatria



I corsi rientrano nel programma di Educazione Continua in Medicina del Ministero della Salute

Sede del Corso
CROWNE PLAZA HOTEL, Via Lamberti - Caserta

Coordinatore Scientifico
Giuseppe Di Mauro



Best practice nell'asma cronico

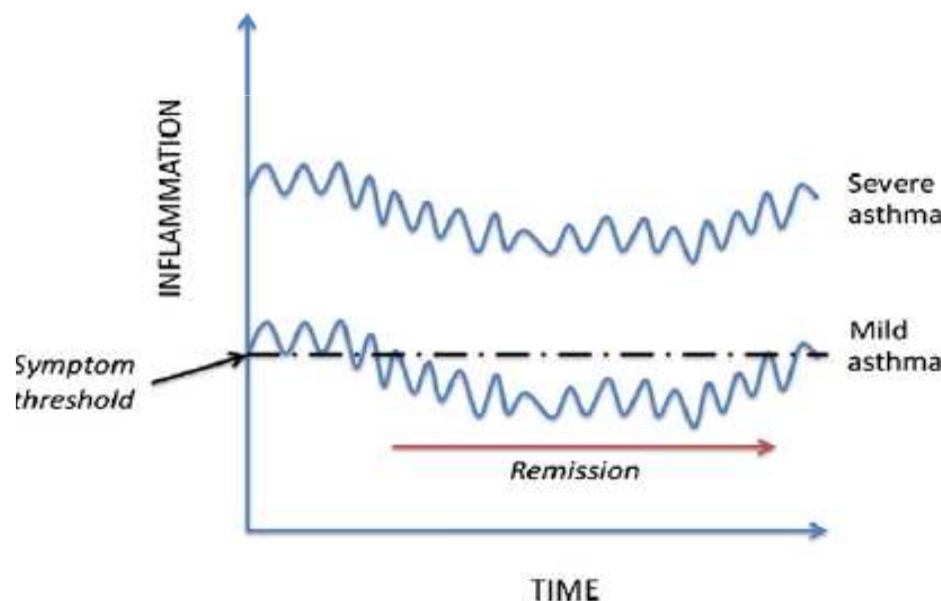
Carlo Capristo



Dipartimento di Pediatria
Seconda Università di Napoli

2011

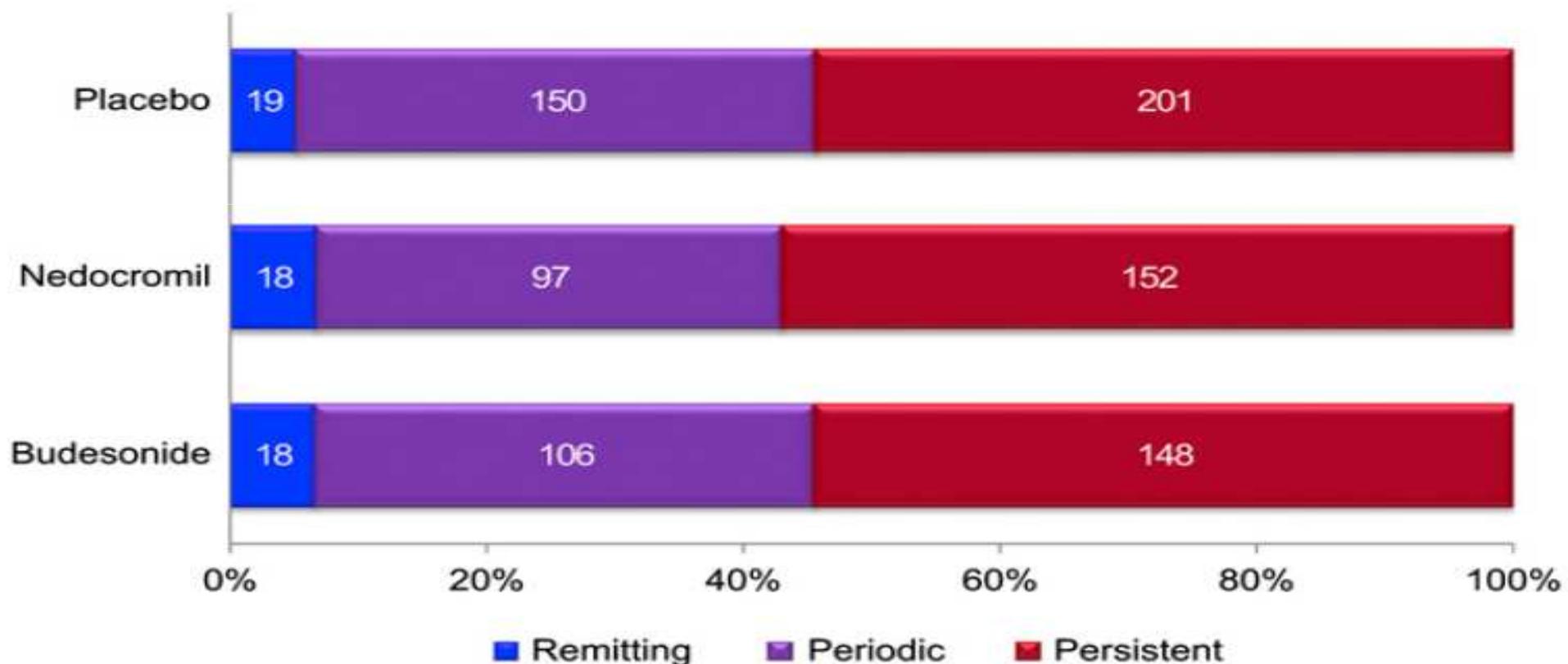
Remission of asthma: The next therapeutic frontier?



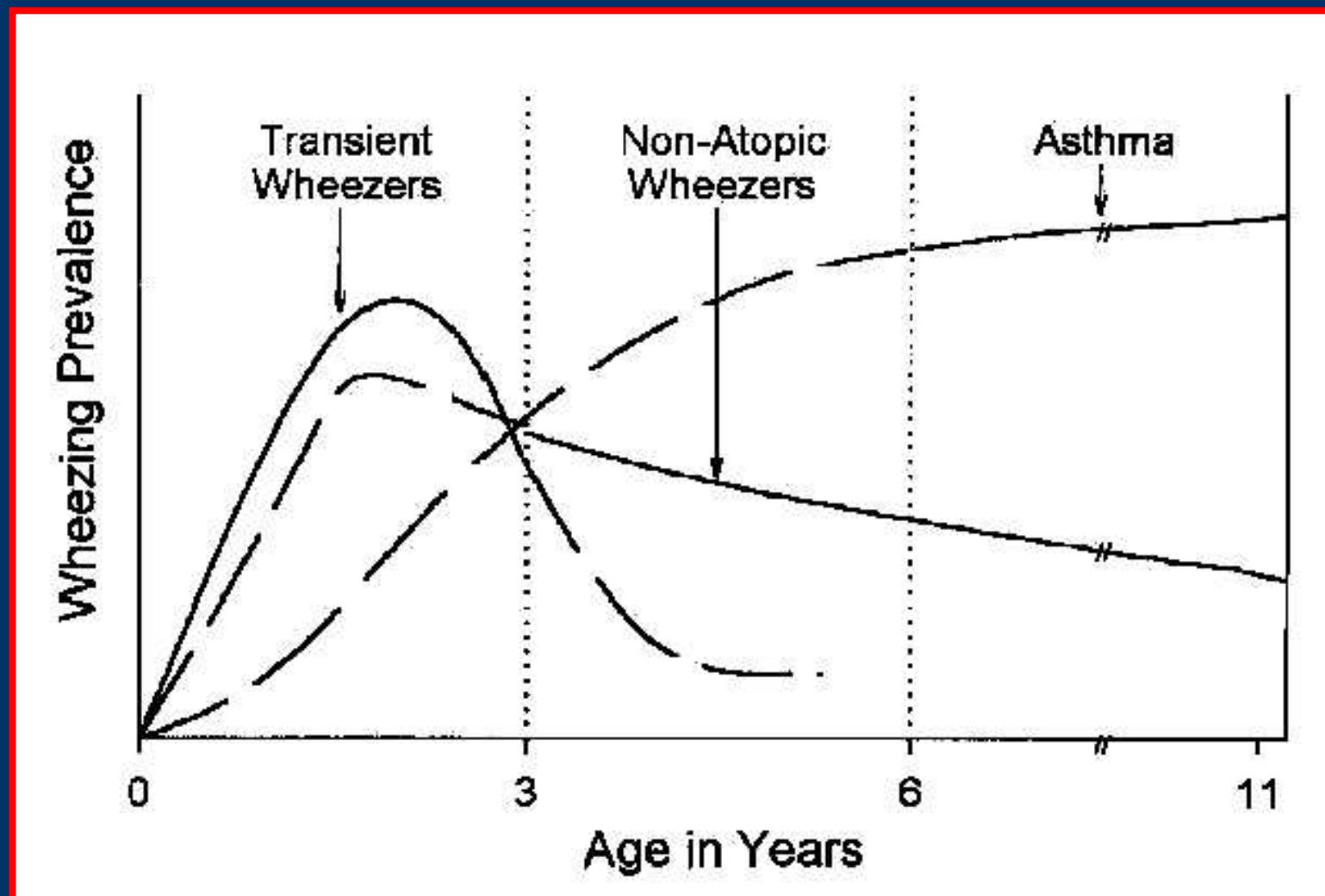
John W. Upham

Predictors of remitting, periodic, and persistent childhood asthma

Ronina A. Covar, MD,^a Robert Strunk, MD,^b Robert S. Zeiger, MD, PhD,^{c,d} Laura A. Wilson, ScM,^e Andrew H. Liu, MD,^a Scott Weiss, MD, MSc,^f James Tonascia, PhD,^e Joseph D. Spahn, MD,^a and Stanley J. Szefler, MD,^a for the Childhood Asthma Management Program Research Group *Denver, Colo, St Louis, Mo, San Diego, Calif, Baltimore, Md, and Boston, Mass*



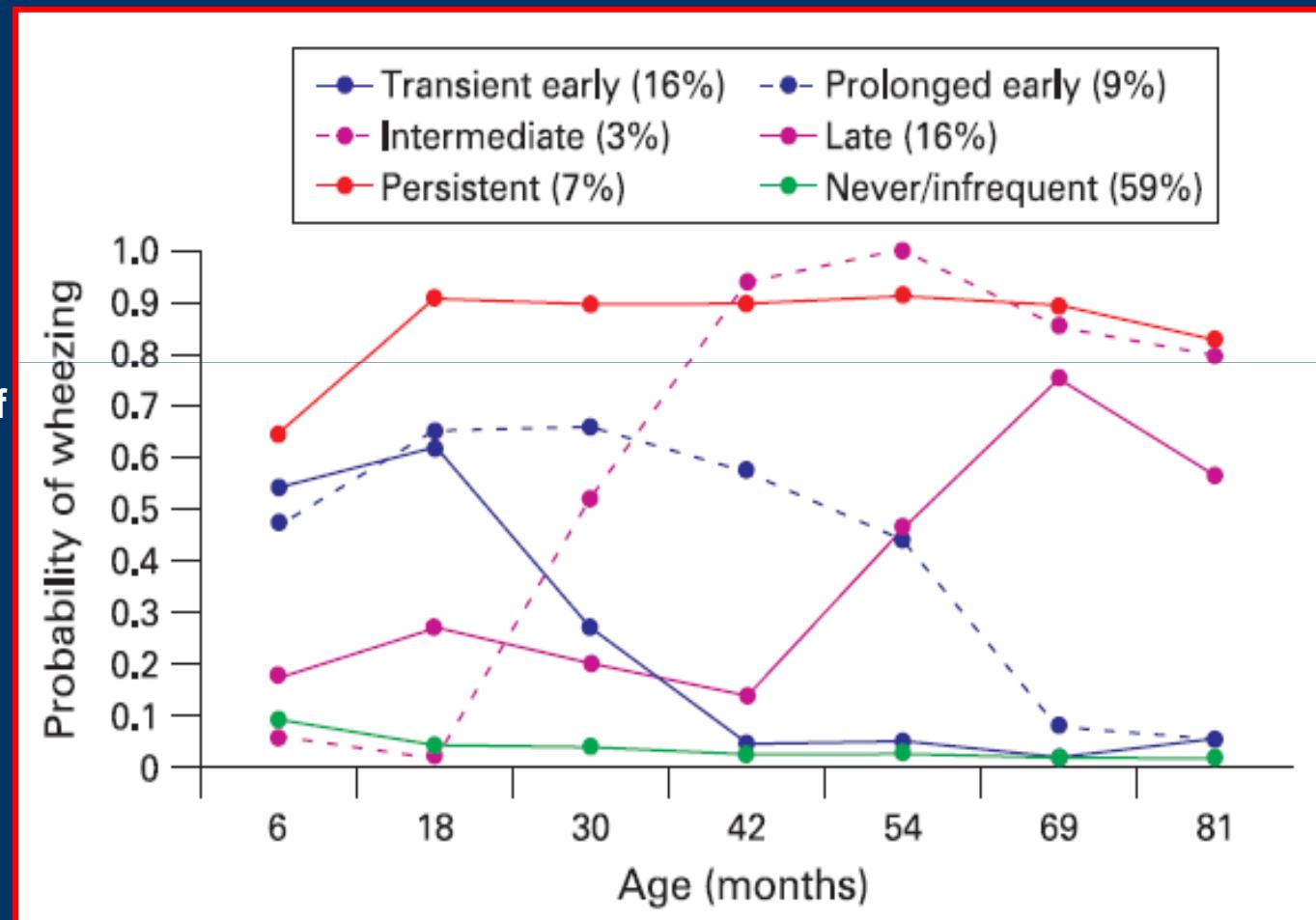
TUCSON CHILDREN'S RESPIRATORY STUDY:
1980 TO PRESENT *Taussig JACI 2003*



HYPOTHETICAL PEAK PREVALENCE BY AGE FOR THE 3 DIFFERENT WHEEZING PHENOTYPES.

Associations of wheezing phenotypes in the first 6 years of life with atopy, lung function and airway responsiveness in mid-childhood J Henderson Thorax 2008;63:974

- ✓ 6265 children in a longitudinal birth cohort (the ALSPAC)
- ✓ from birth to 7 yrs
- ✓ phenotypes based on patterns of wheezing



FENOTIPI DI ASMA DEL BAMBINO

Bacharier LB et al - JACI 2007;119:604–610

Grave wheezing intermittente

Episodi acuti non frequenti di wheezing associati con:

- Minima morbidità al di fuori del periodo di interessamento dell'apparato respiratorio
- Caratteristiche atopiche, incluso eczema, sensibilizzazione allergica ed eosinofilia ematica periferica

Fattori di rischio per asma (2-4 anni)

Guilbert - J Allergy Clin Immunol 2004; 114: 1282

≥ 3 episodi di wheezing nell'ultimo anno

PIÙ

1 criterio maggiore

- un genitore con asma
- dermatite atopica
- sensibiliz. aeroallergeni

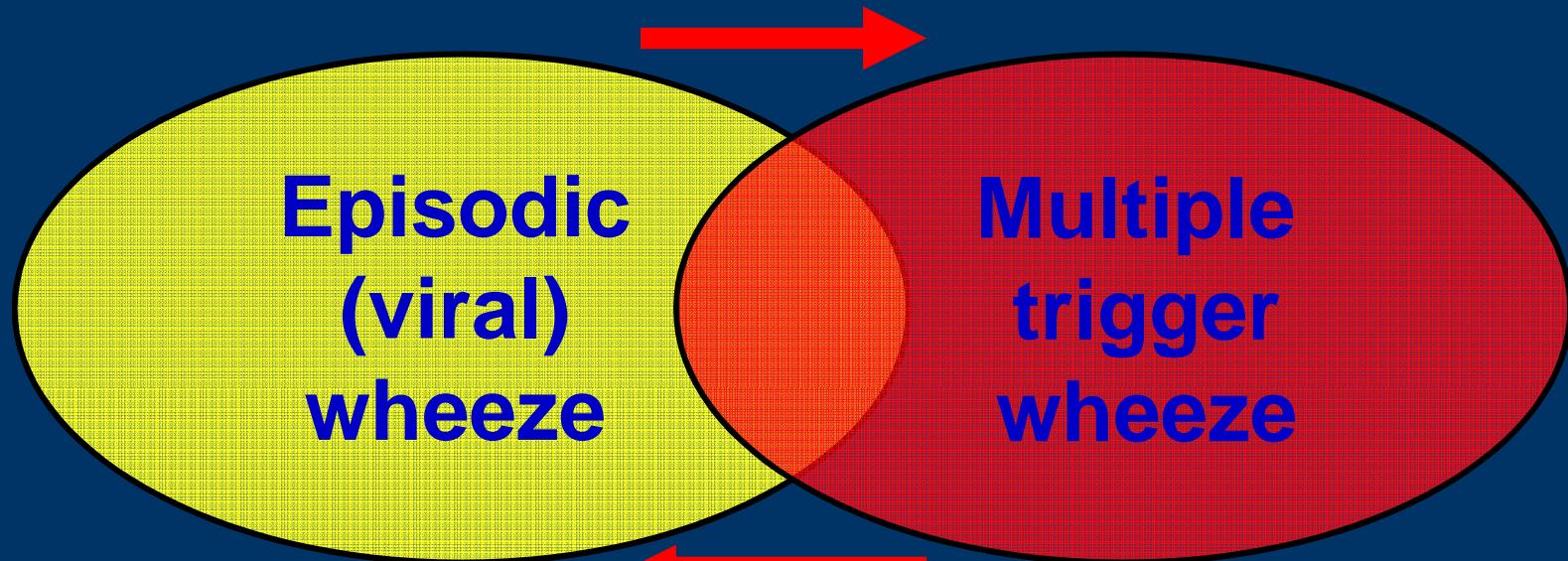
OPPURE

2 criteri minori

- sensibiliz. alimenti
- wheezing al di fuori di episodi infettivi
- eosinofilia (>4%)



WHEEZING IN PRE-SCHOOL CHILDREN



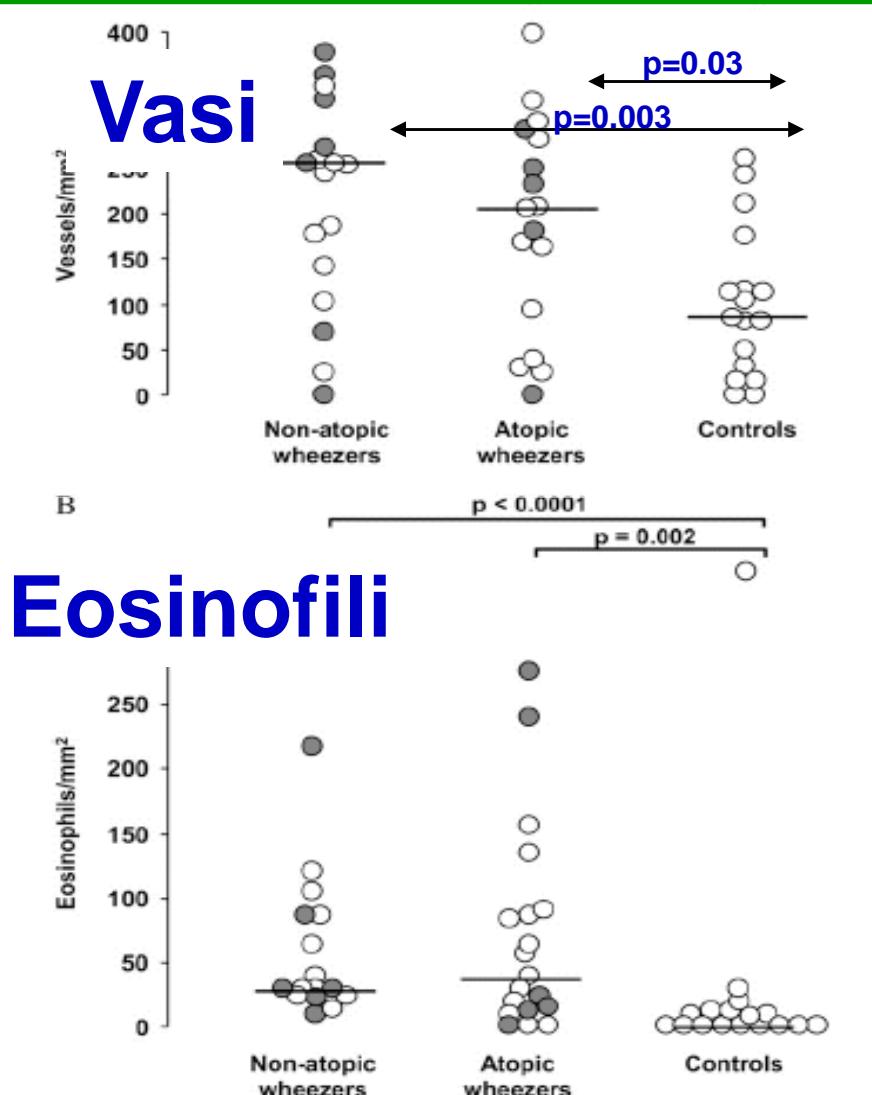
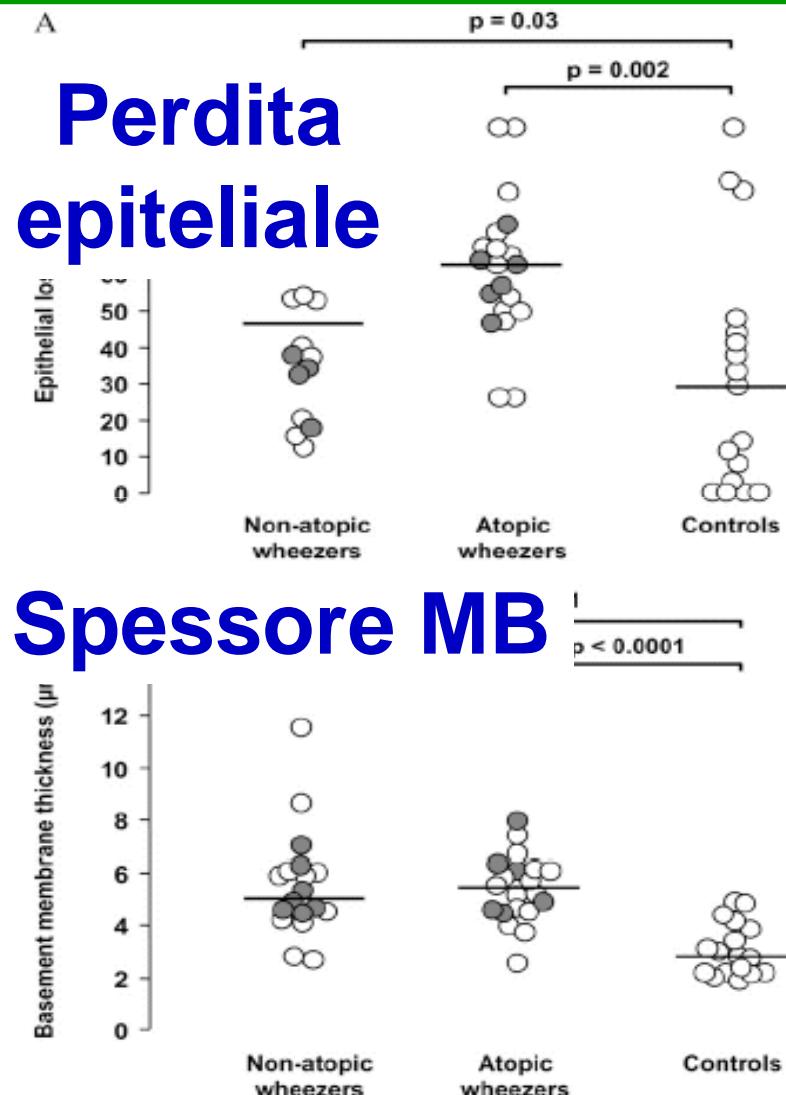
Children who wheeze intermittently and are well between episodes

Triggers: viruses

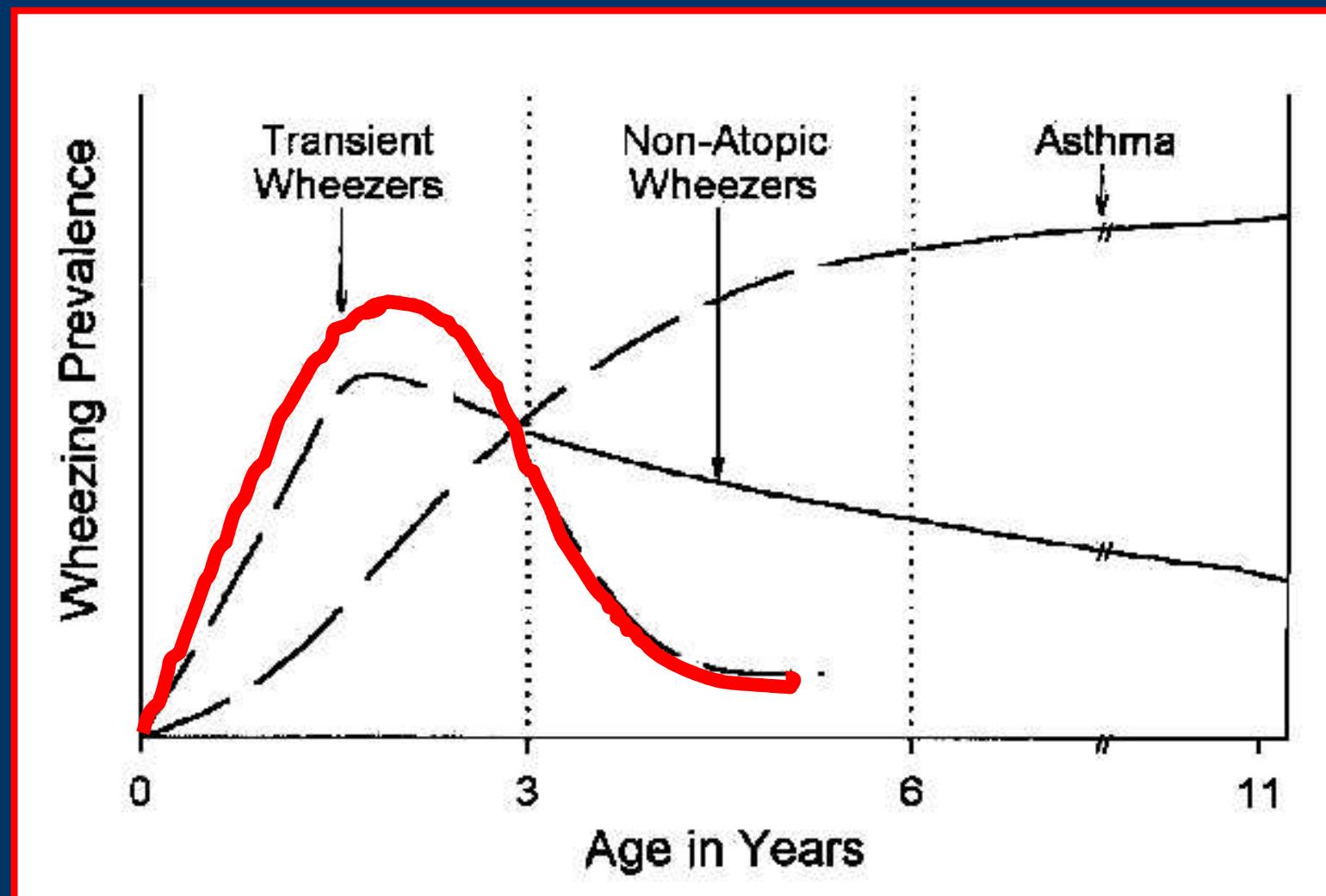
Wheeze both during and between exacerbations

Triggers: virus, smoke, allergenes, exercise

In soggetti con multi-trigger wheezing le alterazioni infiammatorie e strutturali sono simili indipendentemente dall'atopia



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1980 TO PRESENT *Taussig JACI 2003*



HYPOTHETICAL PEAK PREVALENCE BY AGE FOR THE 3 DIFFERENT WHEEZING PHENOTYPES.

The New England Journal of Medicine

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Volume 332

JANUARY 19, 1995

Number 3

ASTHMA AND WHEEZING IN THE FIRST SIX YEARS OF LIFE

FERNANDO D. MARTINEZ, M.D., ANNE L. WRIGHT, PH.D., LYNN M. TAUSSIG, M.D.,
CATHARINE J. HOLBERG, M.Sc., MARILYN HALONEN, PH.D., WAYNE J. MORGAN, M.D.,
AND THE GROUP HEALTH MEDICAL ASSOCIATES*

Table 2. Maximal Expiratory Flow at Functional Residual Capacity ($\dot{V}_{\text{max}}/\text{FRC}$) during the First Year of Life and at Six Years of Age,
According to History of Wheezing.*

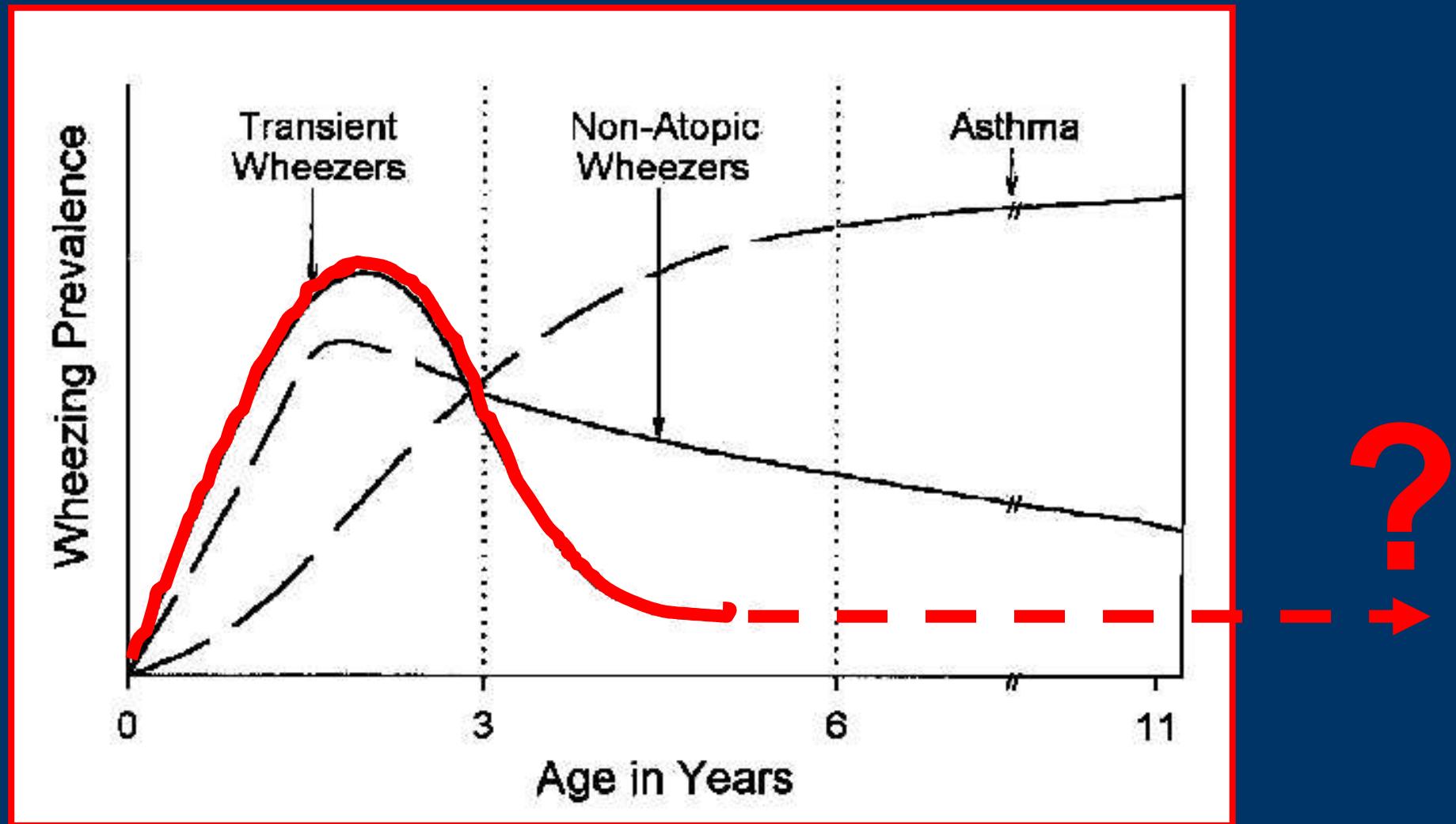
AGE	NO WHEEZING		TRANSIENT EARLY WHEEZING		LATE-ONSET WHEEZING		PERSISTENT WHEEZING		F	P VALUE
	NO.	$\dot{V}_{\text{max}}/\text{FRC}$	NO.	$\dot{V}_{\text{max}}/\text{FRC}$	NO.	$\dot{V}_{\text{max}}/\text{FRC}$	NO.	$\dot{V}_{\text{max}}/\text{FRC}$		
		ml/sec		ml/sec		ml/sec		ml/sec		
<1 year	67	123.3 (110.0–138.0)	21	70.6 (52.2–93.8)†	21	107.1 (87.5–129.6)	16	104.6 (73.6–144.5)	5.95	<0.001
6 years	260	1262.1 (1217.4–1308.1)	104	1097.7 (1034.9–1163.5)‡	81	1174.9 (1111.1–1241.1)	81	1069.7 (906.9–1146.5)‡	9.60	<0.001

*A total of 125 children underwent pulmonary-function testing during the first year of life, and 526 were tested at six years of age. Values for $\dot{V}_{\text{max}}/\text{FRC}$ are geometric means (95 percent confidence intervals). The F-test and associated P values indicate significant differences in lung function between the four groups.

†P<0.01 for the comparison with the children who never wheezed and P<0.05 for the comparisons with the children with late-onset wheezing and persistent wheezing, by Duncan's multiple-comparison test.

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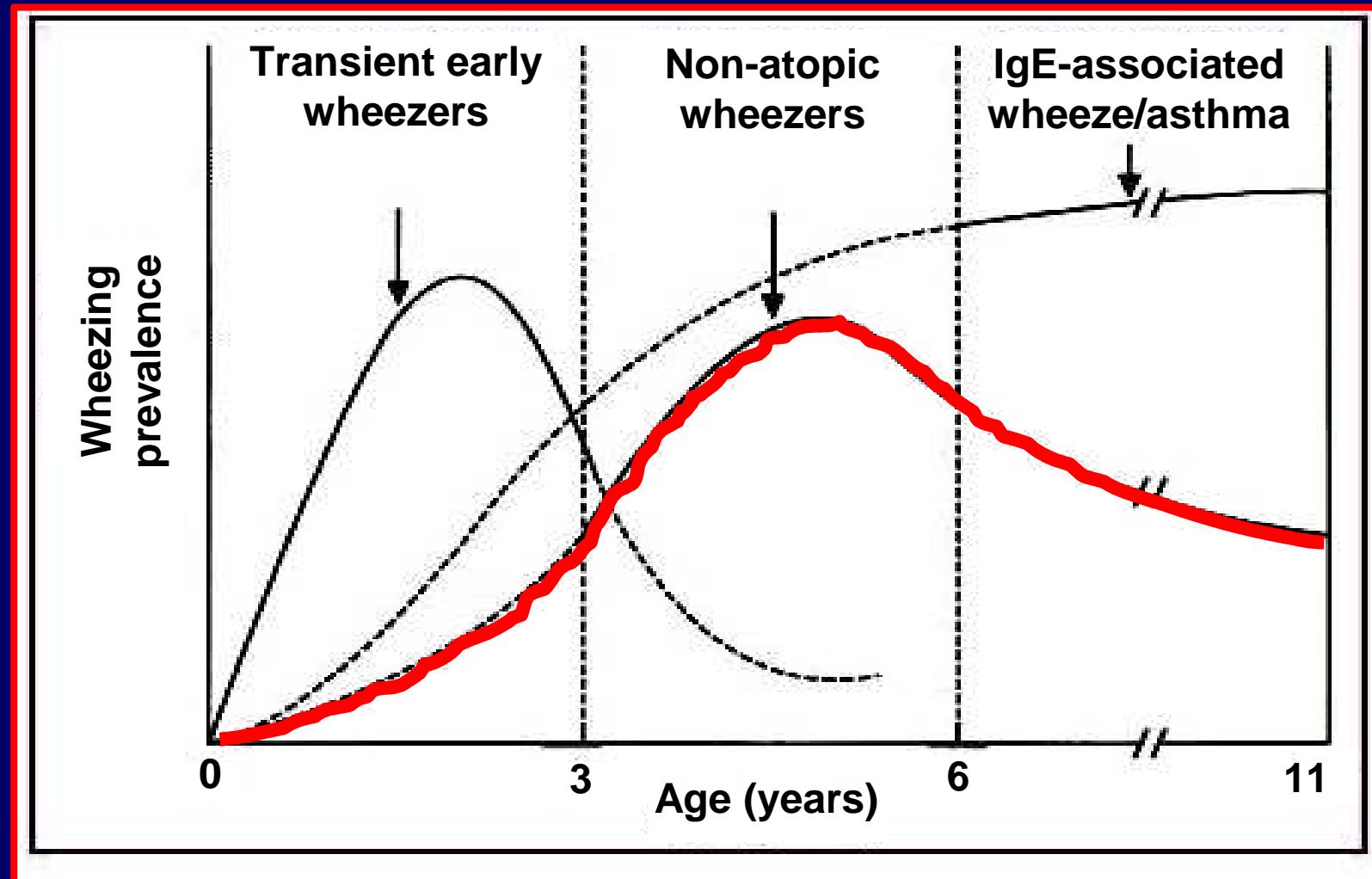
Wheezy Bronchitis in Childhood^{*} : A Distinct Clinical Entity With Lifelong Significance?

Carole A. Edwards, Liesl M. Osman, David J. Godden and J. Graham Douglas

Table 5—Absolute Decline in Adjusted FEV₁ Over the 12-Year Period 1989 to 2001*

Groups	Mean Adjusted FEV ₁ Decline, L	Adjusted FEV ₁ Decline Difference, L	95% CI for Difference
Childhood no respiratory symptoms	0.59		
Childhood wheezy bronchitis	0.75	0.15	0.04–0.28†
Childhood asthma	0.75	0.15	0.05–0.27†

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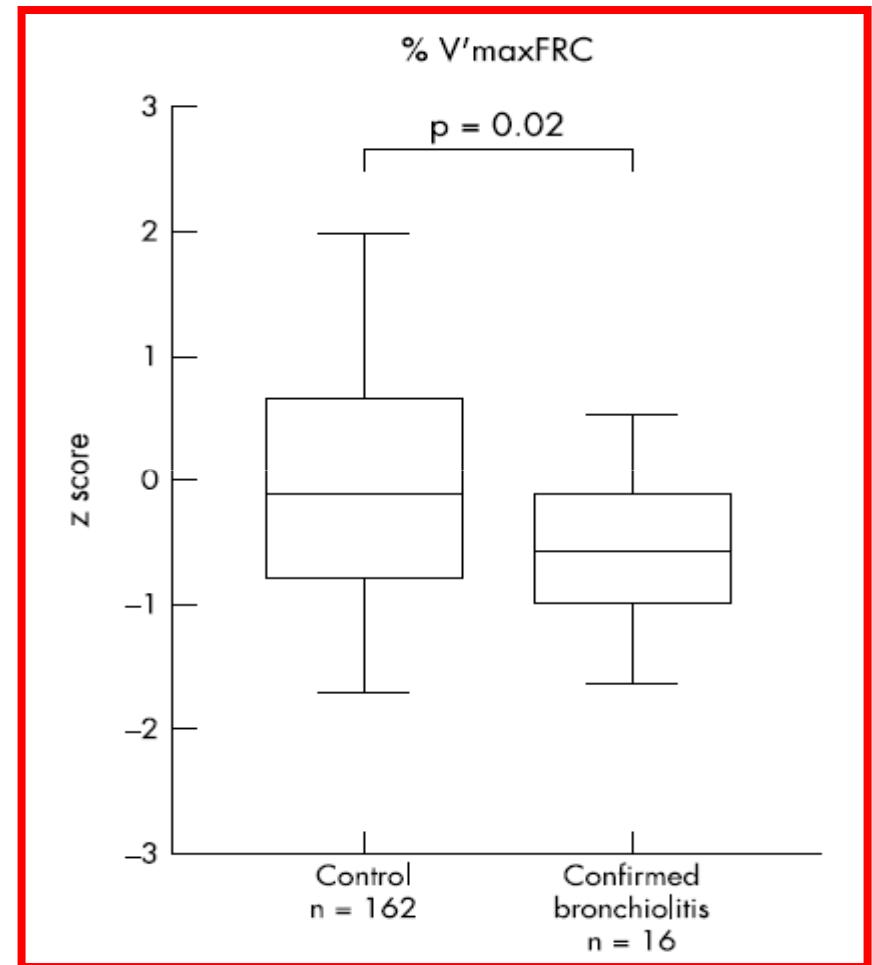
ORIGINAL ARTICLE

Reduced lung function both before bronchiolitis and at 11 years

Arch Dis Child 2002;87:417–420

S W Turner, S Young, L I Landau, P N Le Souëf

- 253 cohort members
- VmaxFRC at 1 month of age
- Individuals with bronchiolitis were prospectively identified
- At 11 years of age lung function was repeated



Box and whisker plot for z scores for % V'maxFRC at 1 month

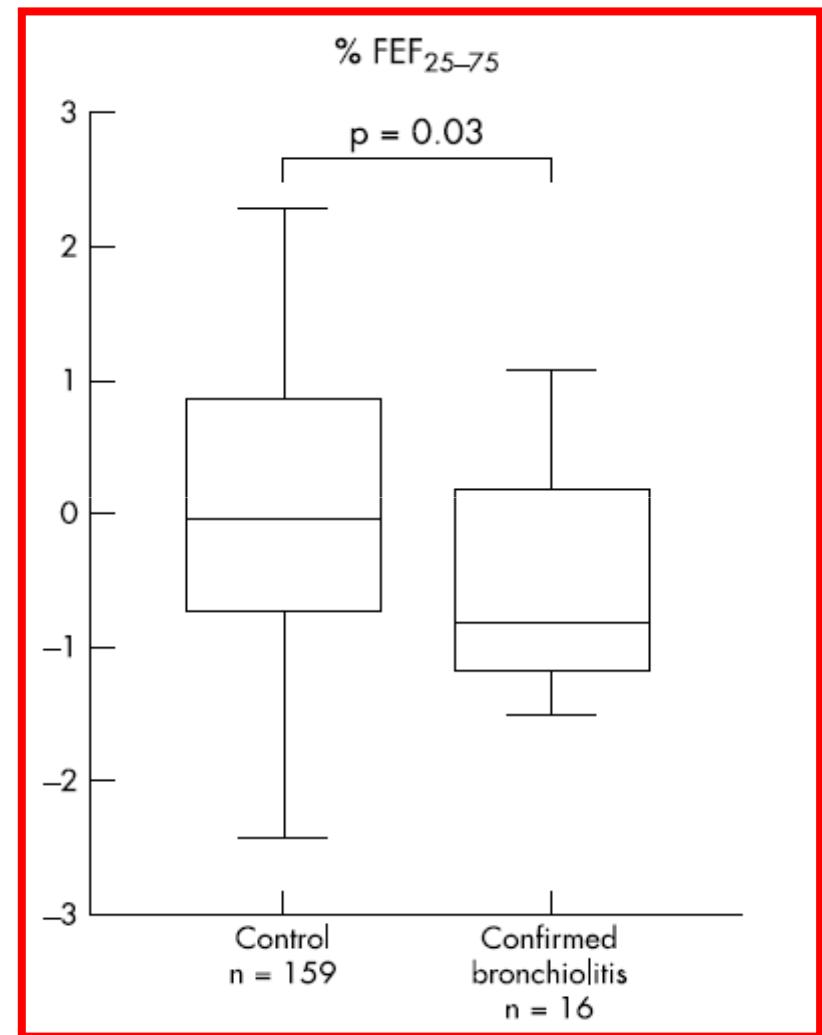
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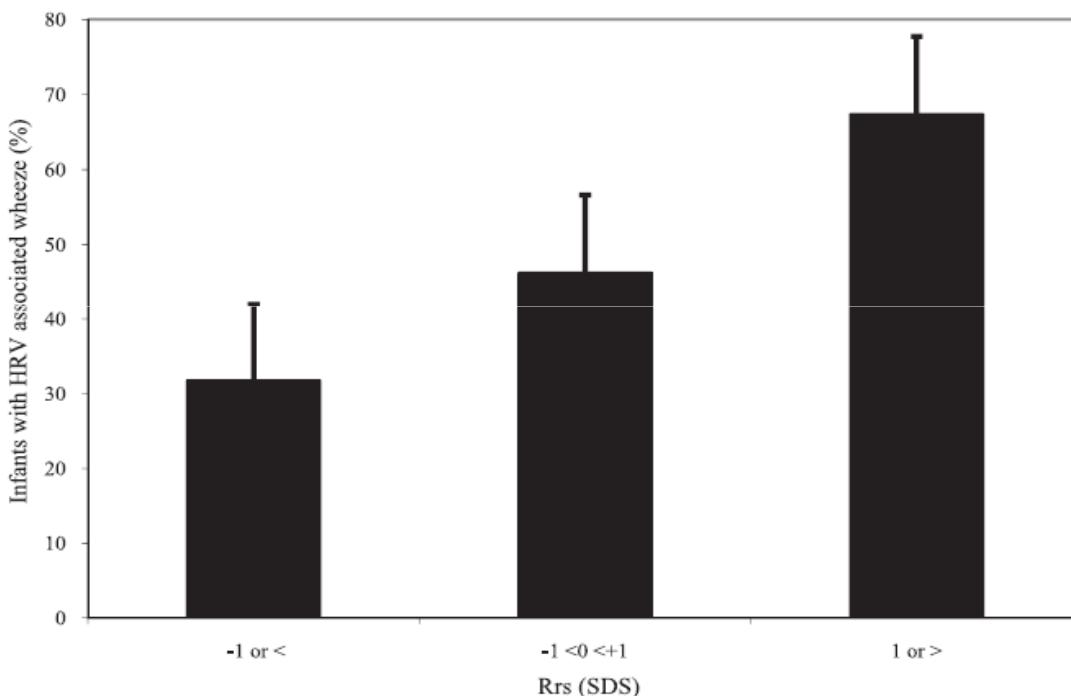
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Box and whisker plot for z scores for % FEF₂₅₋₇₅ at 11 years

The Influence of Neonatal Lung Function on Rhinovirus-associated Wheeze

Marieke M. van der Zalm¹, Cuno S. P. M. Uiterwaal², Berry Wilbrink³, Marije Koopman¹, Theo J. M. Verheij², and Cornelis K. van der Ent¹



AT A GLANCE COMMENTARY

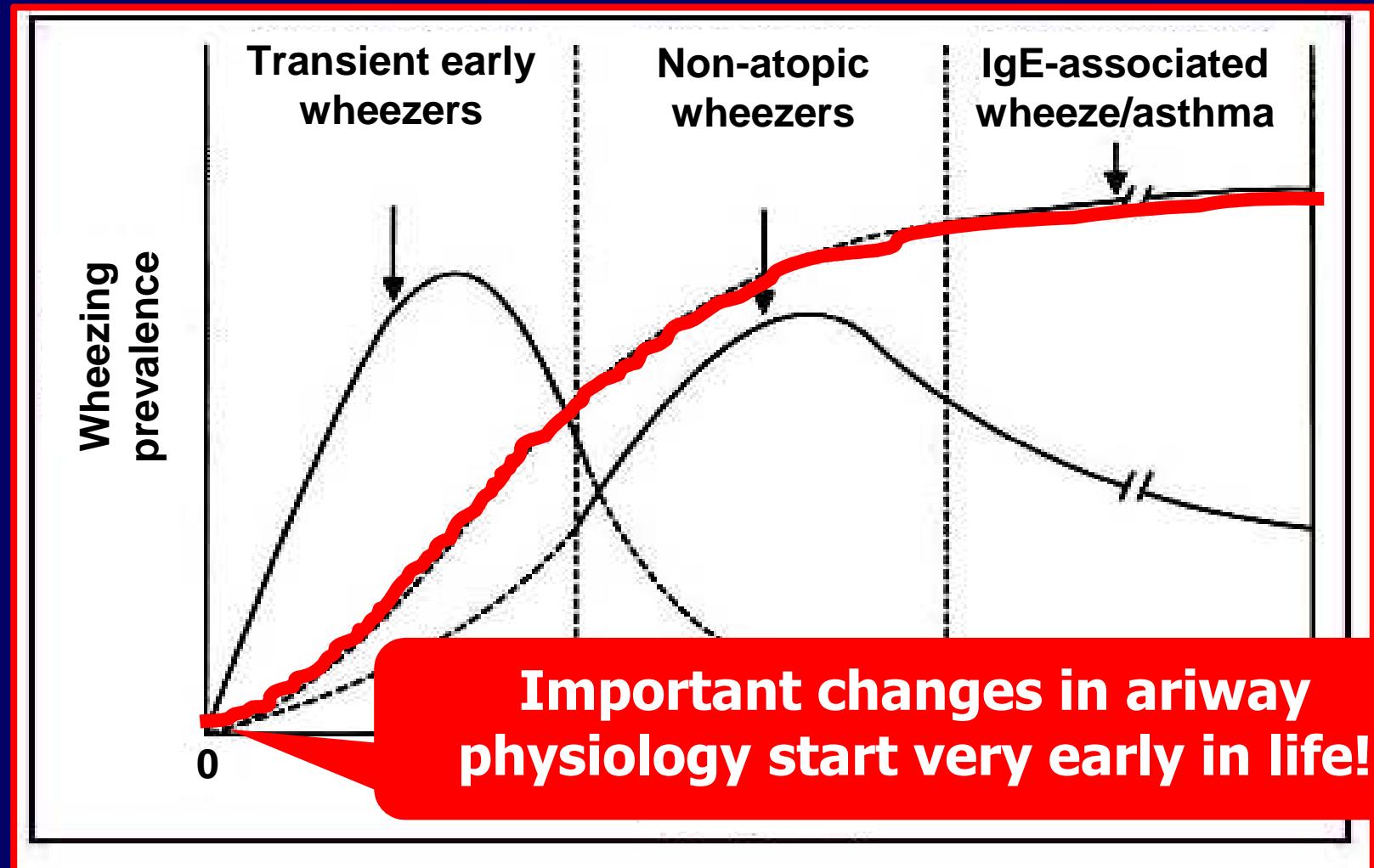
Scientific Knowledge on the Subject

It has been suggested that reduced lung function early in life predisposes infants to wheezing during viral respiratory infections, but the association between neonatal lung function and subsequent confirmed viral infections has never been investigated.

What This Study Adds to the Field

Our study shows that total lung resistance is clearly associated with polymerase chain reaction–proved human rhinovirus (HRV)-associated wheeze. Moreover, HRV-associated wheeze might be the first sign to recognize infants with increased airway resistance, which sheds new light on the role of HRV in asthma-like symptoms.

TUCSON CHILDREN'S RESPIRATORY STUDY:
1980 TO PRESENT *Taussig JACI 2003*



HYPOTHETICAL PEAK PREVALENCE BY AGE FOR THE 3 DIFFERENT WHEEZING PHENOTYPES.

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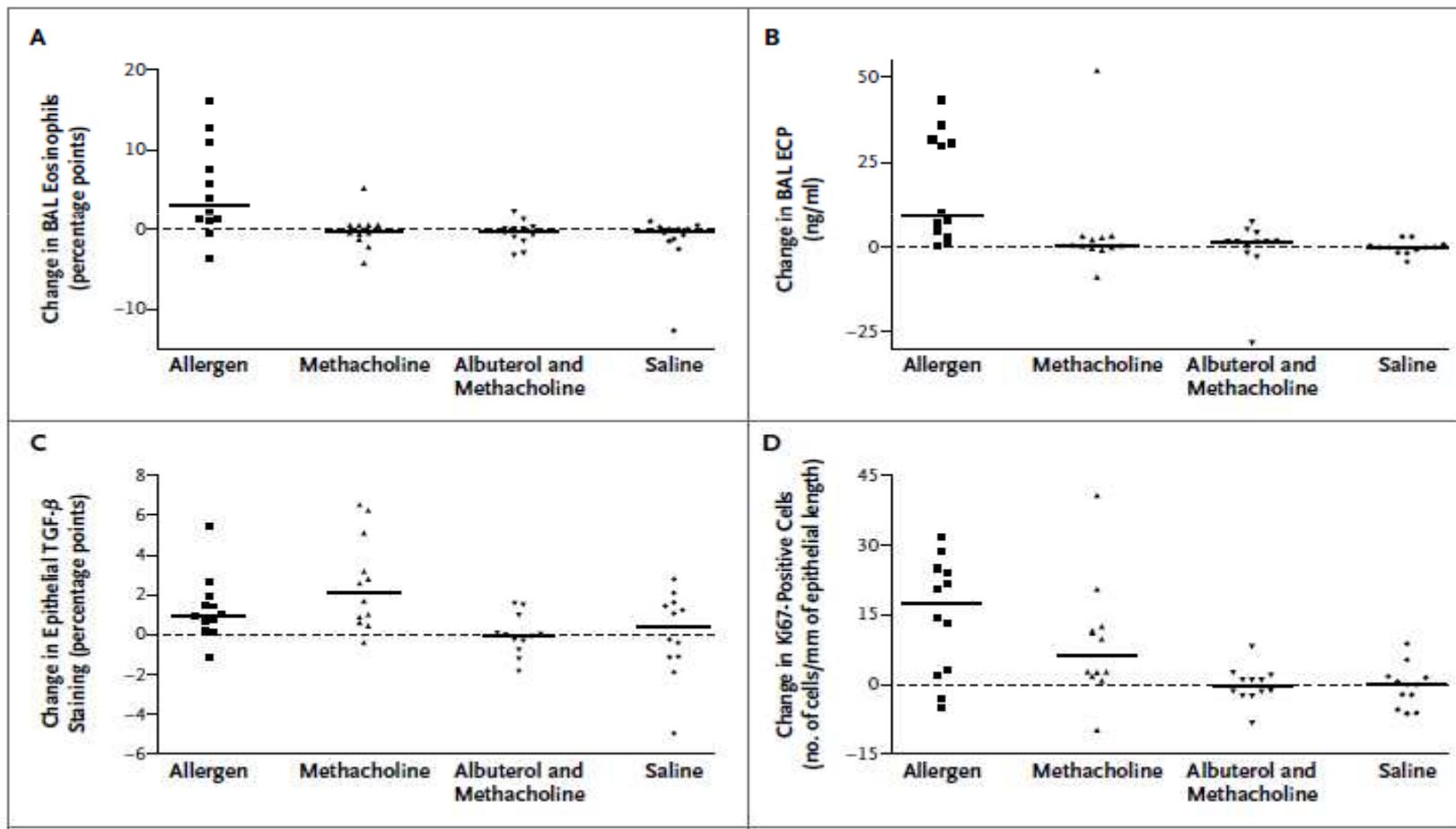
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ORIGINAL ARTICLE

Effect of Bronchoconstriction on Airway Remodeling in Asthma



L. Grainge

Developmental physiology: lung function during growth and development from birth to old age

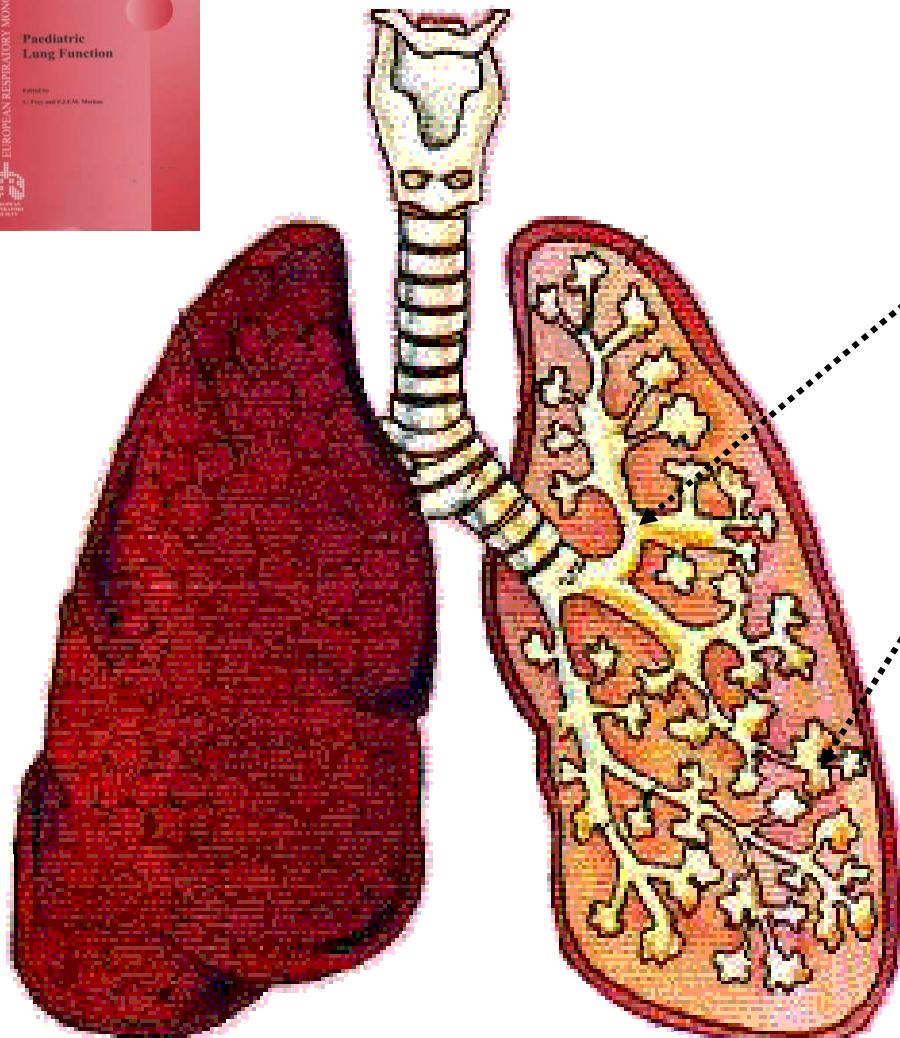
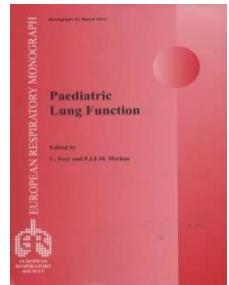
Reduced lung development is a premorbid predisposing factor for:

- 1. Transient wheezing,**
- 2. Bronchiolitis,**
- 3. Persistent atopic wheezing,**



C. Calogero, P.D. Sly Eur Respir Mon 2010

Developmental physiology: lung function during growth and development from birth to old age



Windows of susceptibility

Bronchial development complete by the 18° week

True alveoli begin to develop at 28 weeks and increase in number, size and complexity during the first 3-4 years of life.

C. Calogero, P.D. Sly Eur Respir Mon 2010

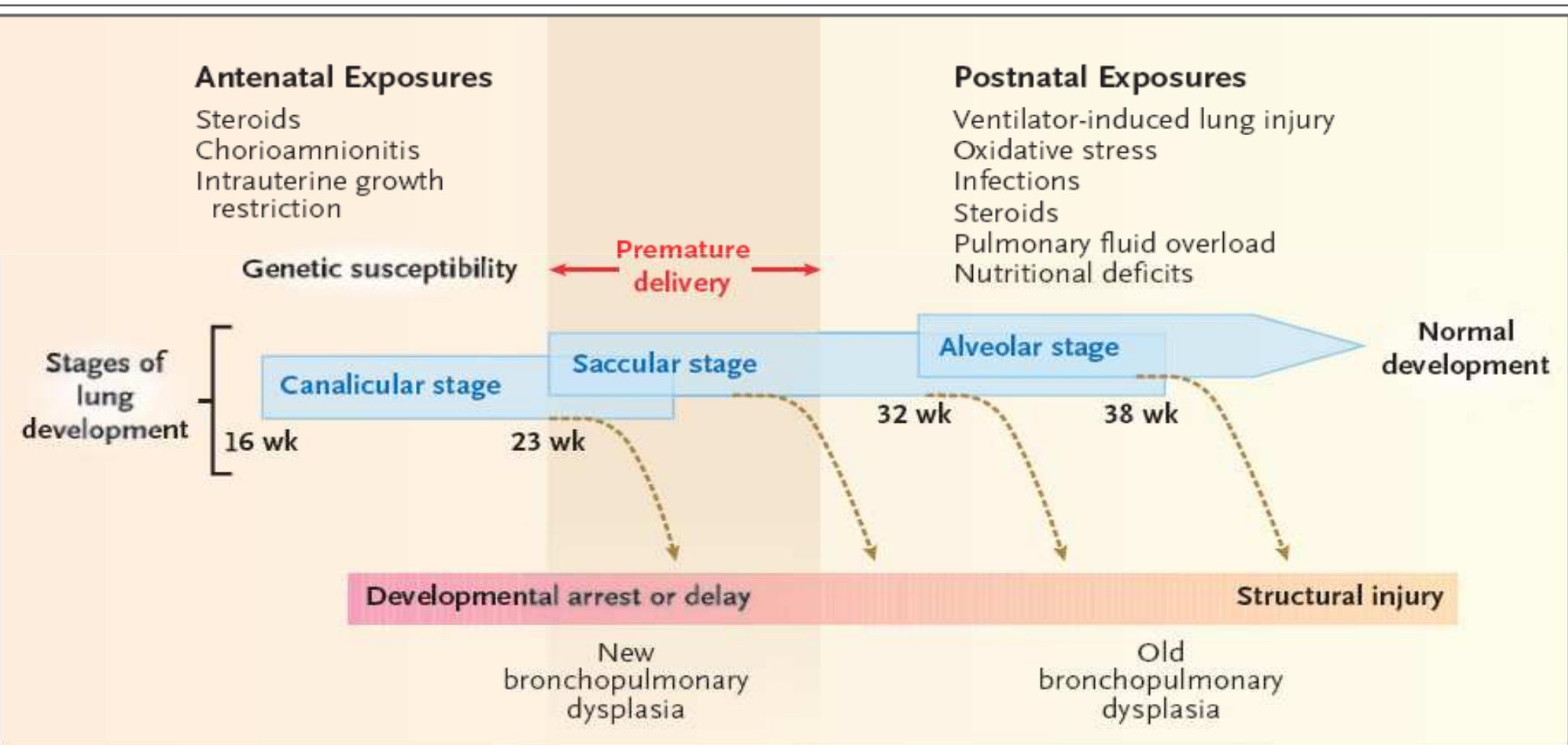
REVIEW ARTICLE

CURRENT CONCEPTS

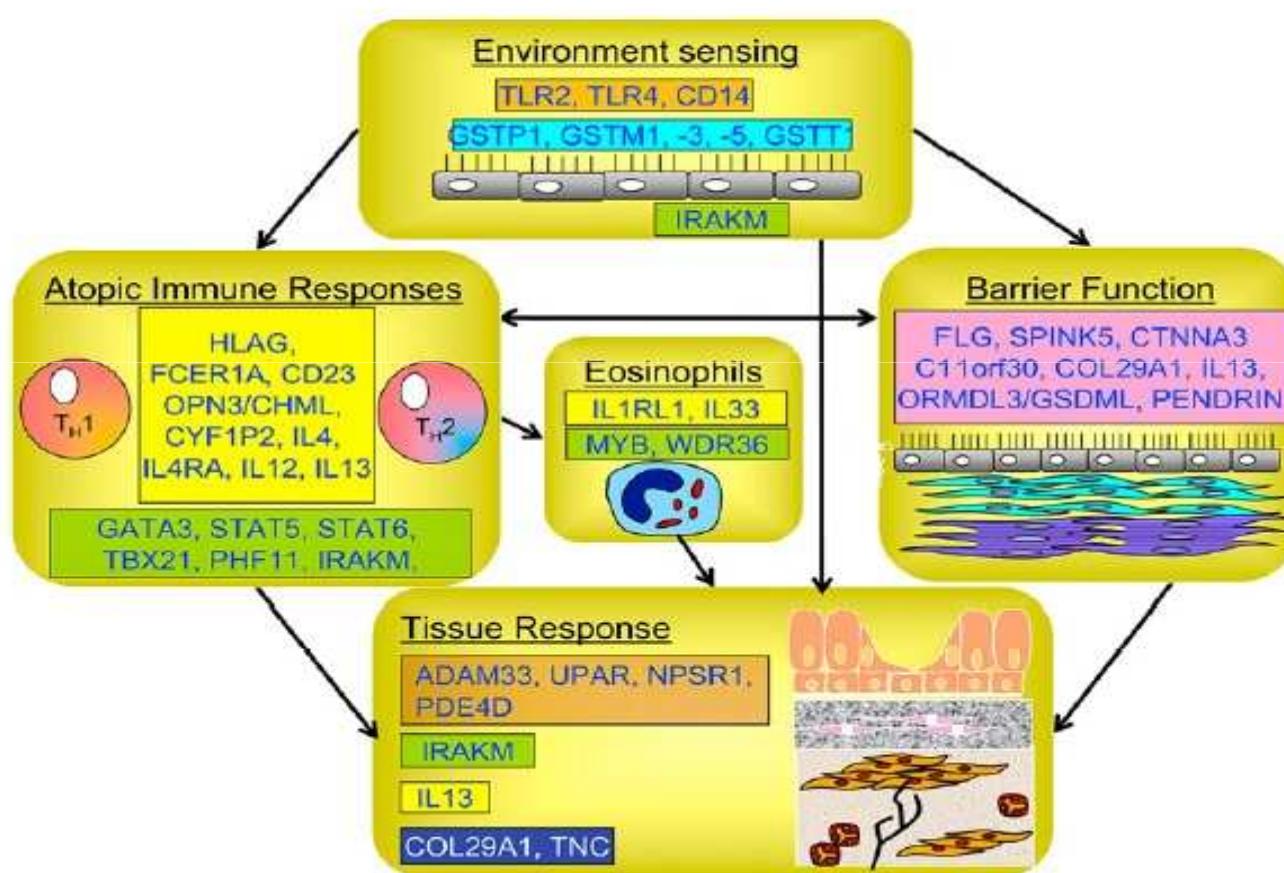
Chronic Lung Disease after Premature Birth

Eugenio Baraldi, M.D., and Marco Filippone, M.D.

2007



Genetics of allergic disease



John W. Holloway JACI 2010

The NEW ENGLAND JOURNAL of MEDICINE

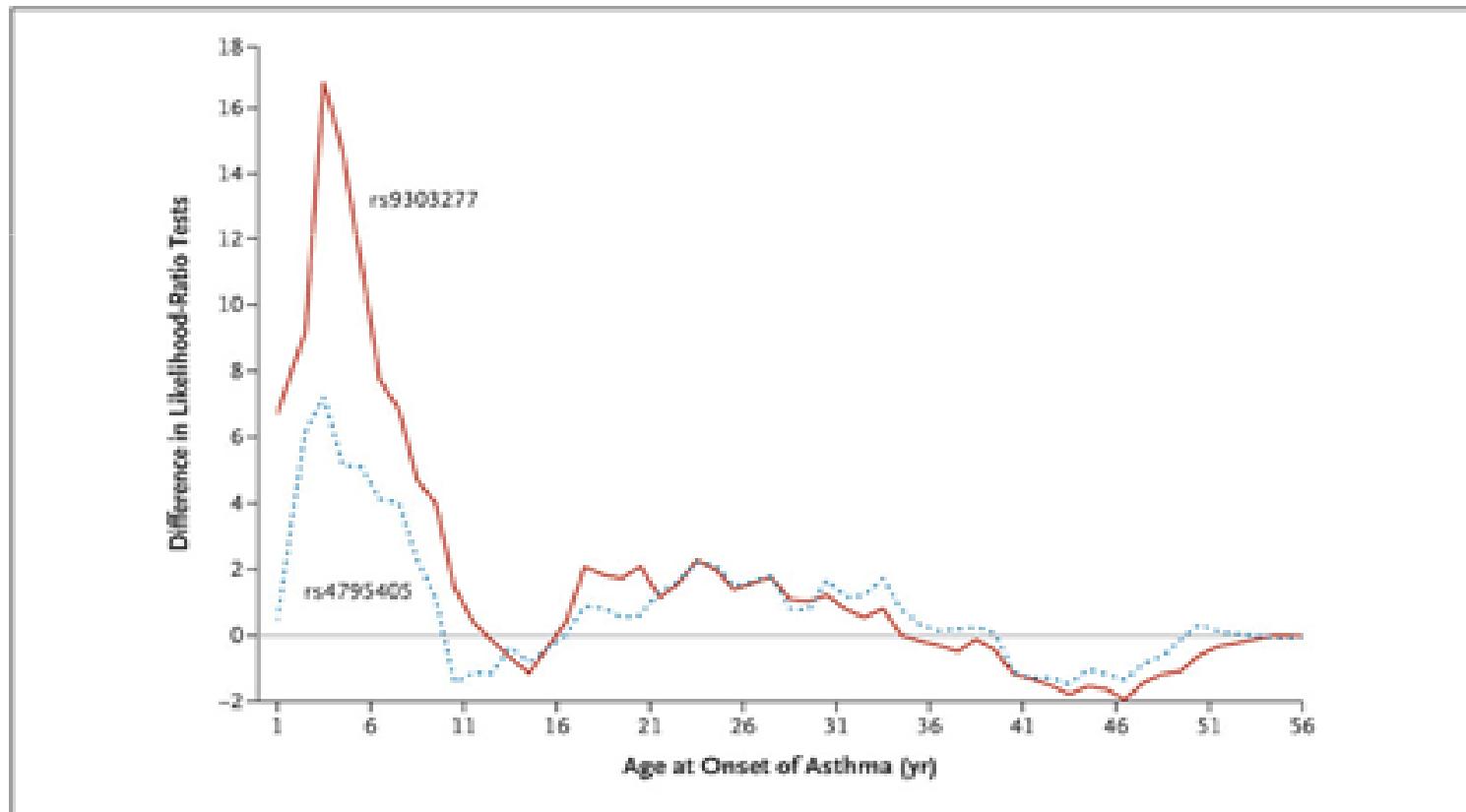
ESTABLISHED IN 1812

NOVEMBER 6, 2008

VOL. 359 NO. 19

Bouzigon E.

Effect of 17q21 Variants and Smoking Exposure in Early-Onset Asthma



Ordered-Subset Regression Analysis of Asthma with
Two Single-Nucleotide Polymorphisms (SNPs)

The NEW ENGLAND JOURNAL of MEDICINE

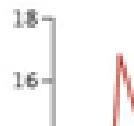
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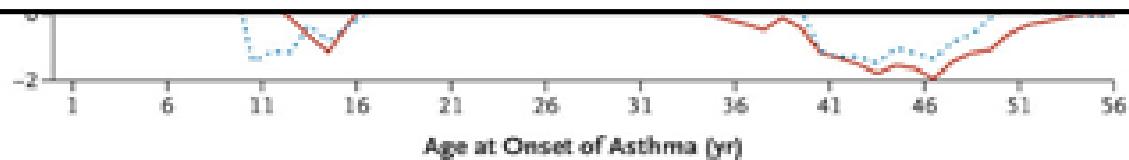
Bouzigon E.

Effect of 17q21 Variants and Smoking Exposure in Early-Onset Asthma



ORMDL3 Associated Gene Variants are Associated with
Asthma and Exacerbations but not Atopy in Early Childhood

Hans Bisgaard AJRCCM 2009



Ordered-Subset Regression Analysis of Asthma with
Two Single-Nucleotide Polymorphisms (SNPs)

ORIGINAL ARTICLE

Variants of DENND1B Associated with Asthma in Children

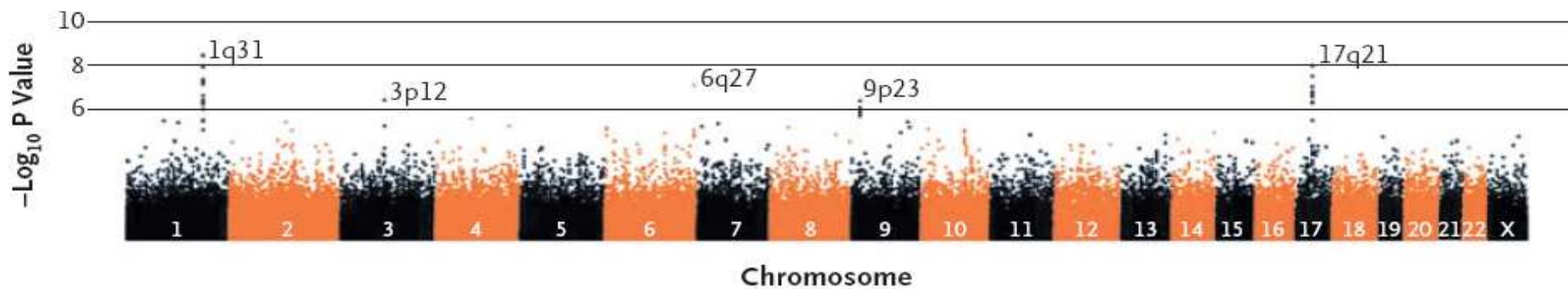
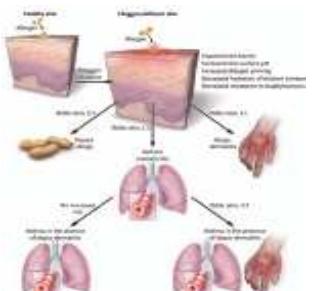


Figure 2. Manhattan Plot of the Results from the Combined Subjects of European Ancestry Who Had Asthma.

The $-\log_{10}$ P values are plotted against the physical distance. Only the two loci at chromosome 1q31 and 17q21 were significantly associated with asthma after Bonferroni correction. Individual chromosome labels are indicated in white within the Manhattan plot.

REVIEW ARTICLE

MECHANISMS OF DISEASE

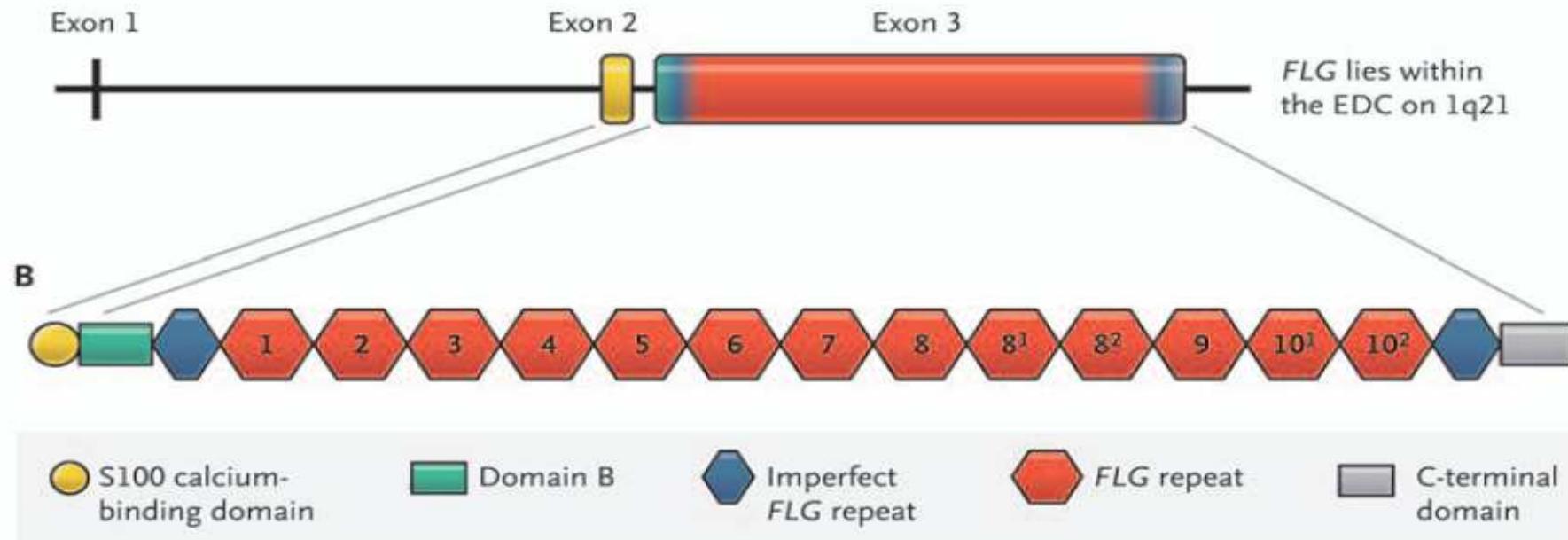


A

Filaggrin Mutations Associated with Skin and Allergic Diseases

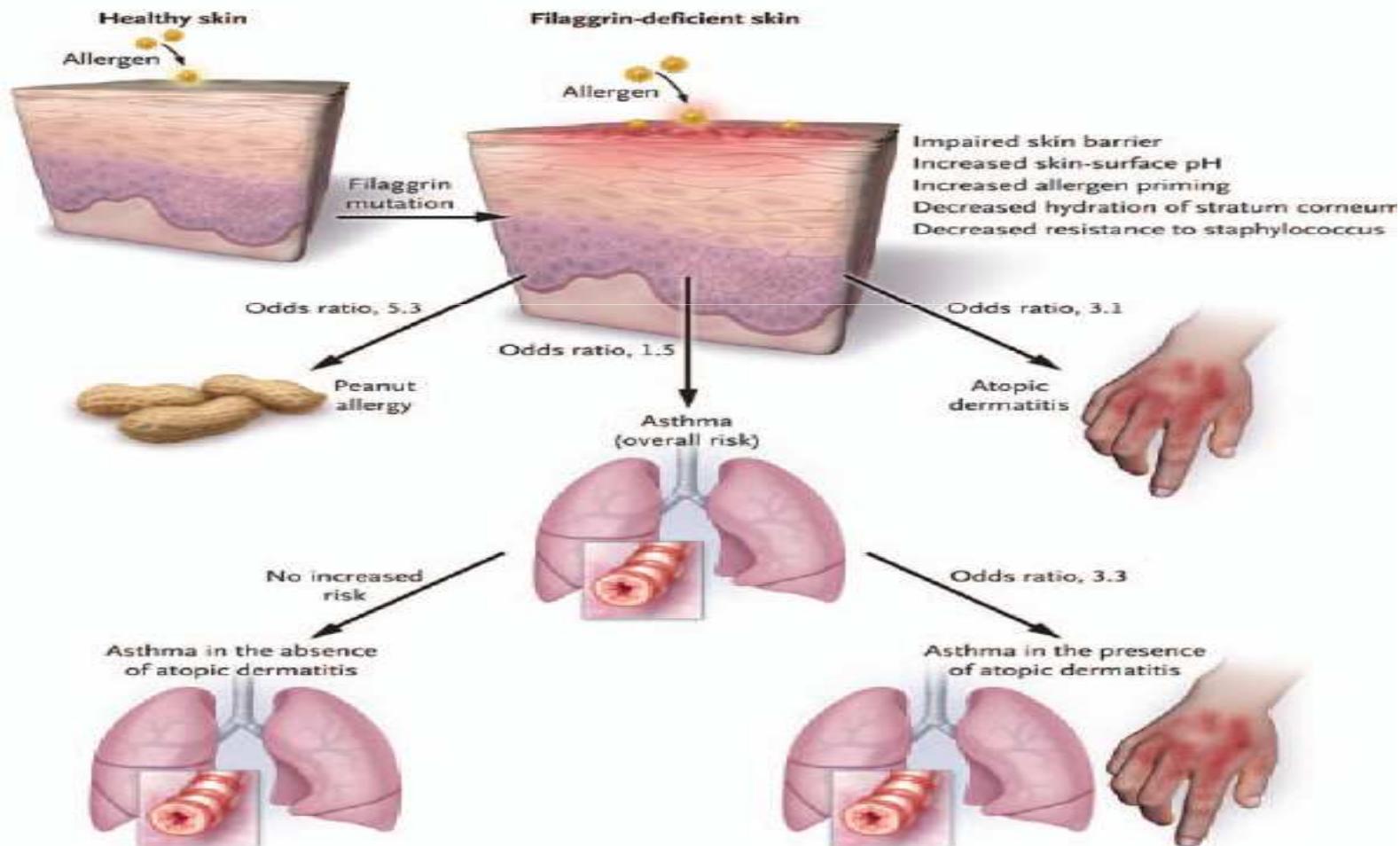
Alan D. Irvine, M.D., W.H. Irwin McLean, Ph.D., D.Sc.,

A



REVIEW ARTICLE

MECHANISMS OF DISEASE



The NEW ENGLAND JOURNAL of MEDICINE

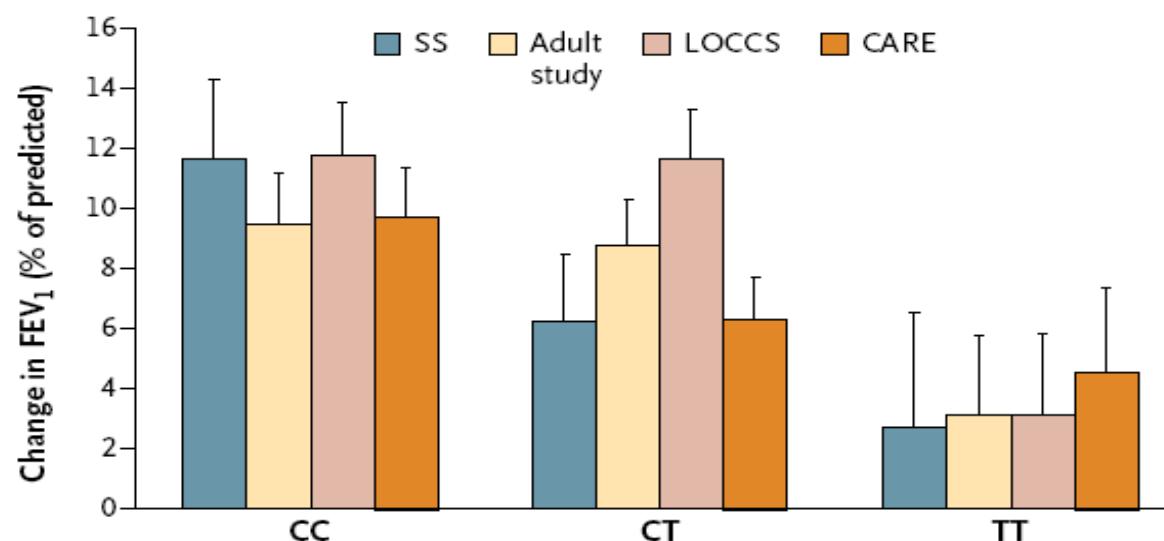
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SEPTEMBER 29, 2011

VOL. 365 NO. 13

Genomewide Association between *GLCCI1* and Response to Glucocorticoid Therapy in Asthma

Kelan G. Tantisira, M.D.



OPINIONS IN ALLERGY

Non-atopic intrinsic asthma and the 'family tree' of chronic respiratory disease syndromes

P. G. Holt and P. D. Sly

Clinical & Experimental Allergy

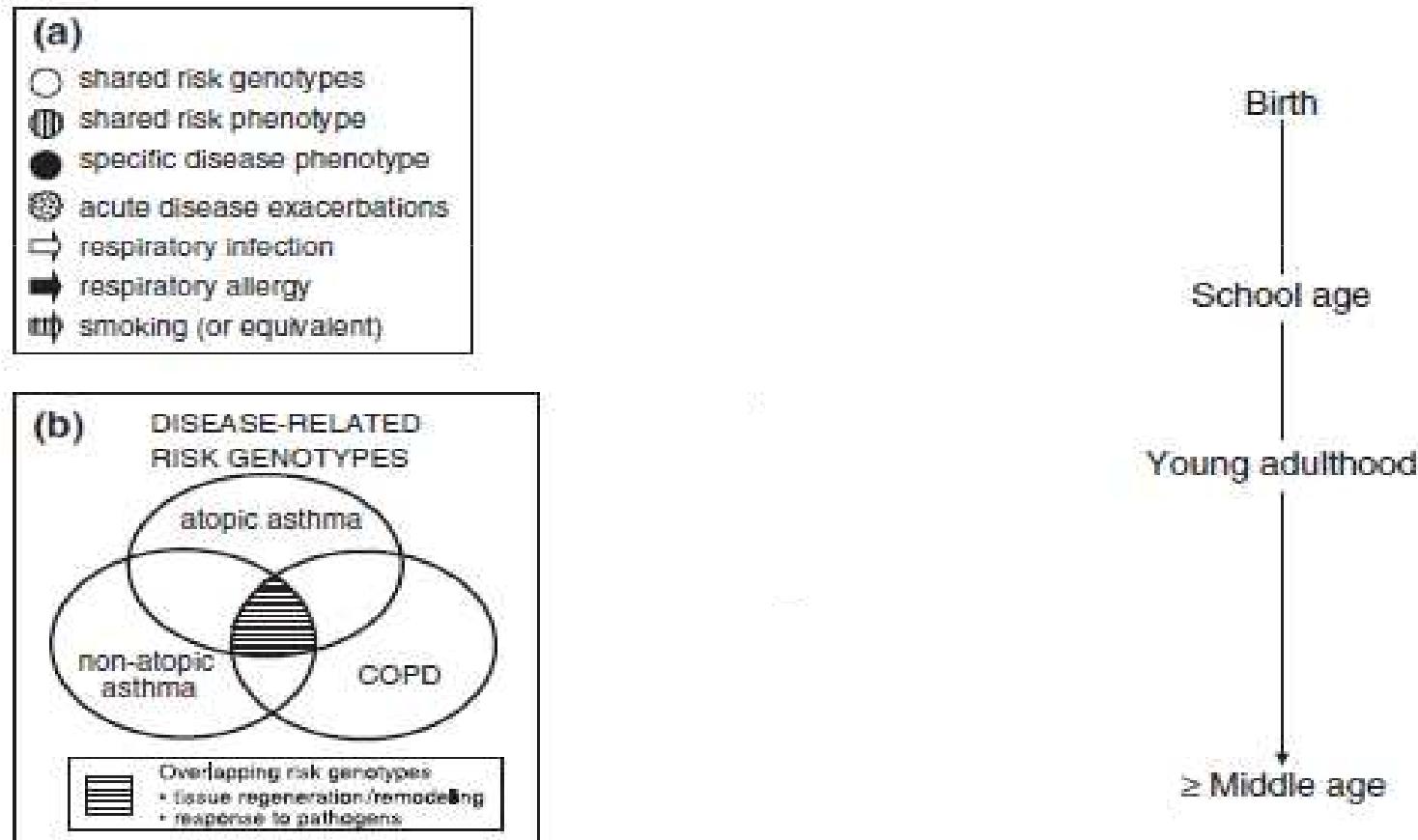
Correspondence:

P. G. Holt, Telethon Institute for Child Health Research, and Centre for Child Health Research, Faculty of Medicine and Dentistry, University of Western Australia, Perth, Australia.

E-mail: patrick@ichr.uwa.edu.au

Cite this as: P. G. Holt and P. D. Sly,

Clinical & Experimental Allergy, 2009
(39) 807–811.



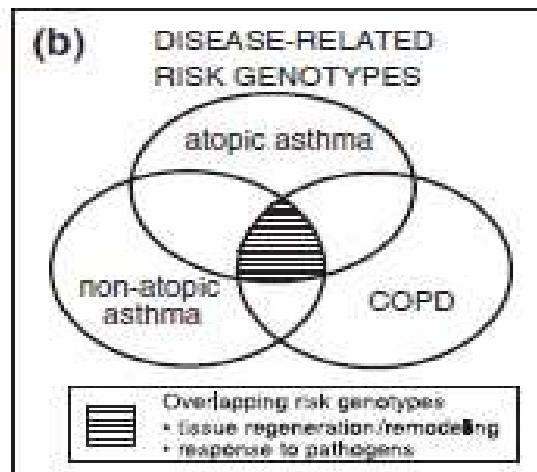
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- (a)
- shared risk genotypes
 - ◐ shared risk phenotype
 - specific disease phenotype
 - ◎ acute disease exacerbations
 - ↔ respiratory infection
 - respiratory allergy
 - smoking (or equivalent)



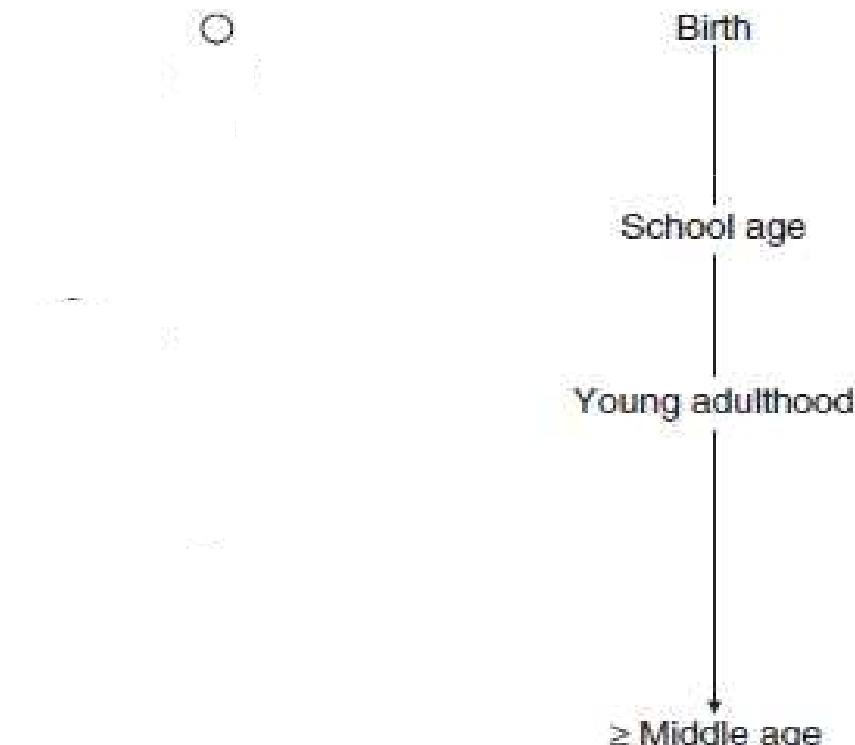
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P. G. Holt, Telethon Institute for Child Health Research, and Centre for Child Health Research, Faculty of Medicine and Dentistry, University of Western Australia, Perth, Australia.

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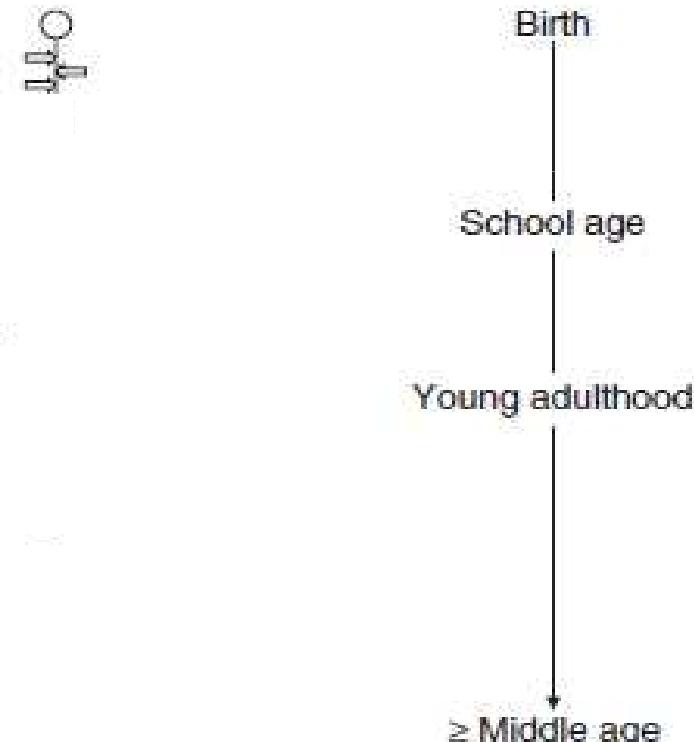
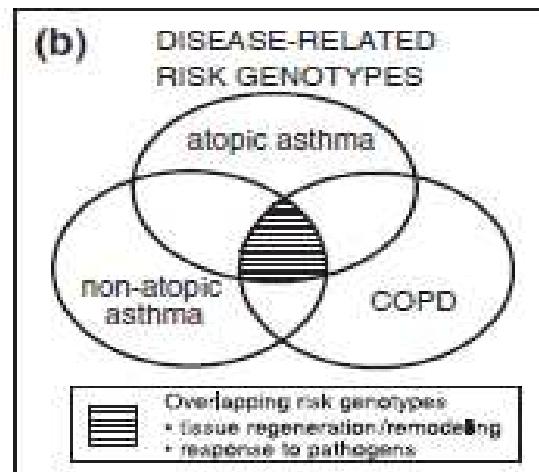
P. G. Holt, Telethon Institute for Child Health Research, and Centre for Child Health Research, Faculty of Medicine and Dentistry, University of Western Australia, Perth, Australia.

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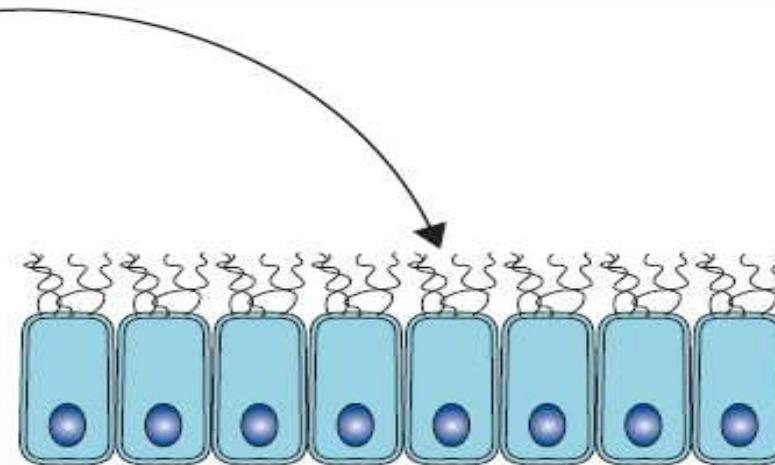
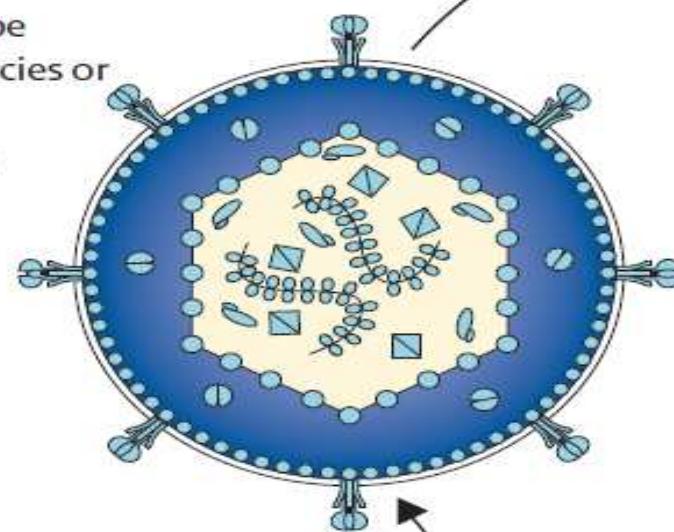
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- (a)
- shared risk genotypes
 - ◐ shared risk phenotype
 - specific disease phenotype
 - ◎ acute disease exacerbations
 - ↔ respiratory infection
 - respiratory allergy
 - smoking (or equivalent)



Infectious agent

- Virus type
- HRV species or strain
- (class C)
- Load

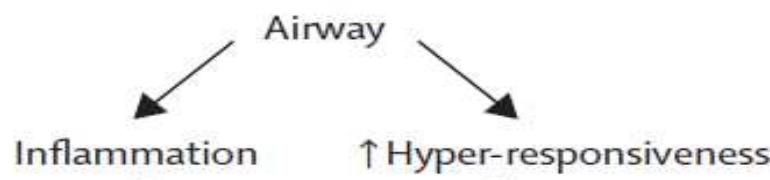


Patient

- Inflammation
- Eosinophils
- Neutrophils
- Allergies
- Immune response
 - innate
 - adaptive

+

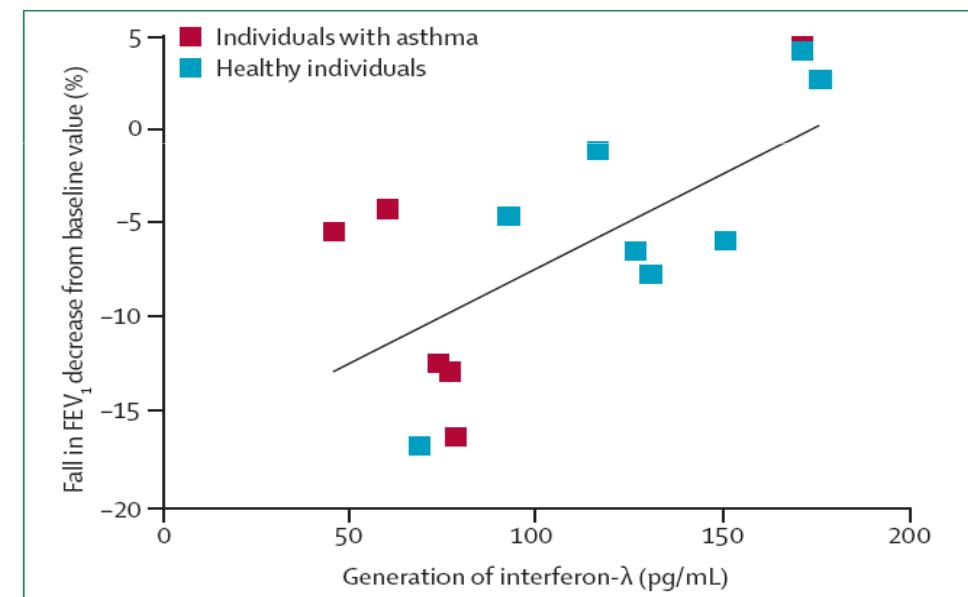
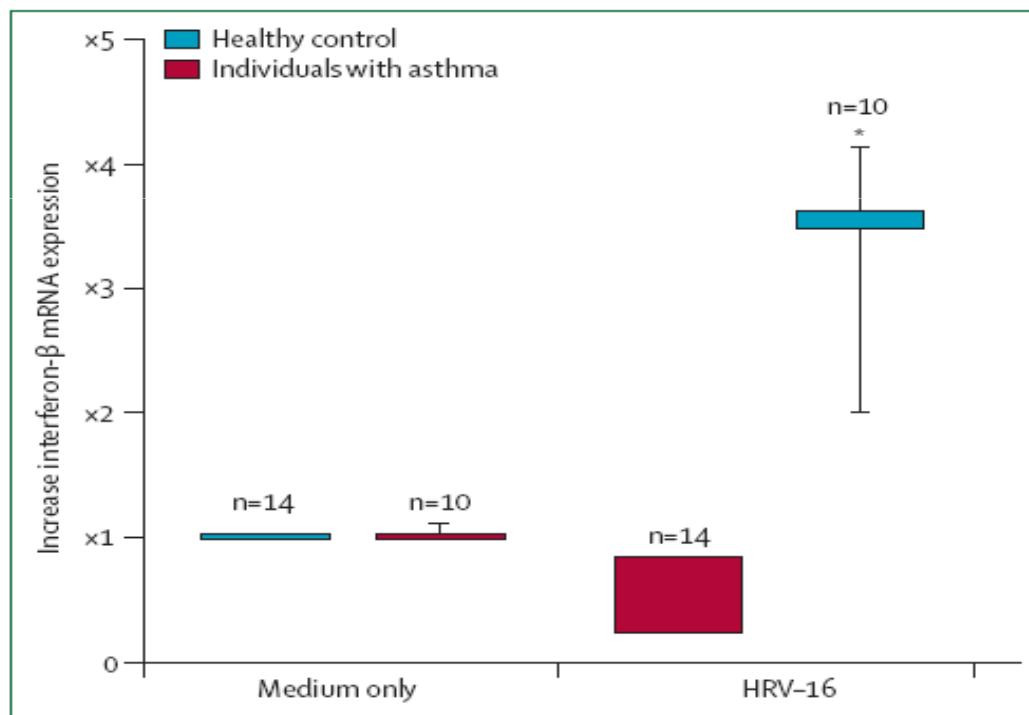
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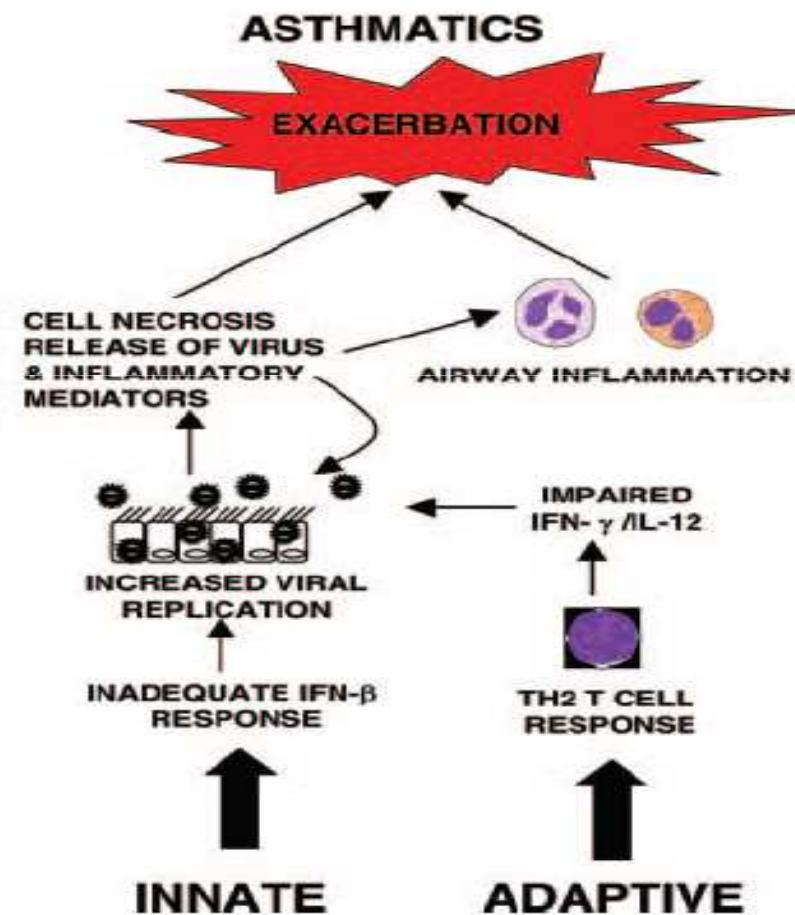
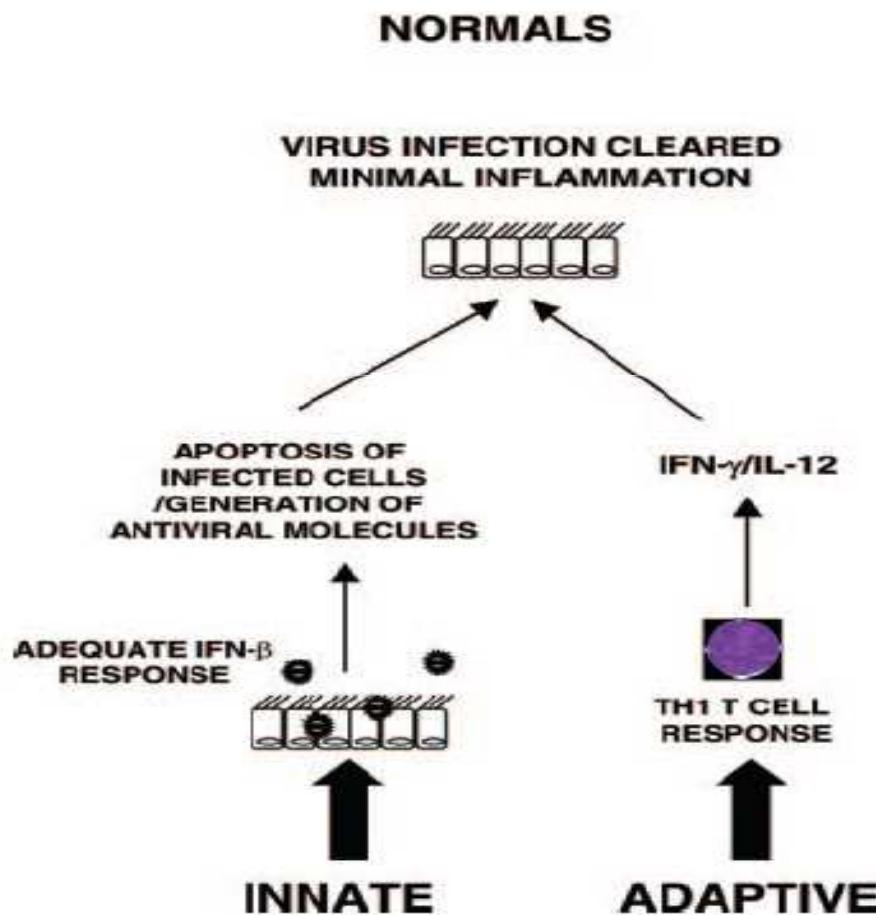
Fattori che influiscono sulla patogenesi dell'asma da infezioni respiratorie
Busse et al. Lancet 2010

Role of viral respiratory infections in asthma and asthma exacerbations

William W Busse, Robert F Lemanske Jr, James E Gern



How Viral Infections Cause Exacerbation of Airway Diseases



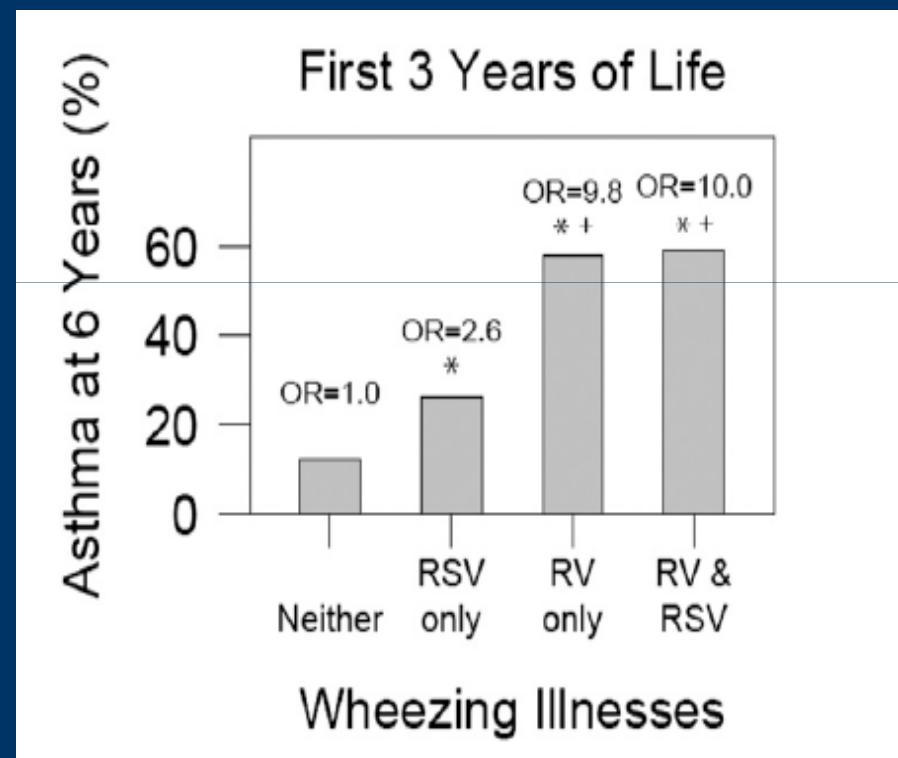
Wheezing Rhinovirus Illnesses in Early Life Predict Asthma Development in High-Risk Children

259 bambini seguiti dalla nascita fino all'età di 6 anni

Lavaggi nasali, colture e PCR durante gli episodi di wheezing

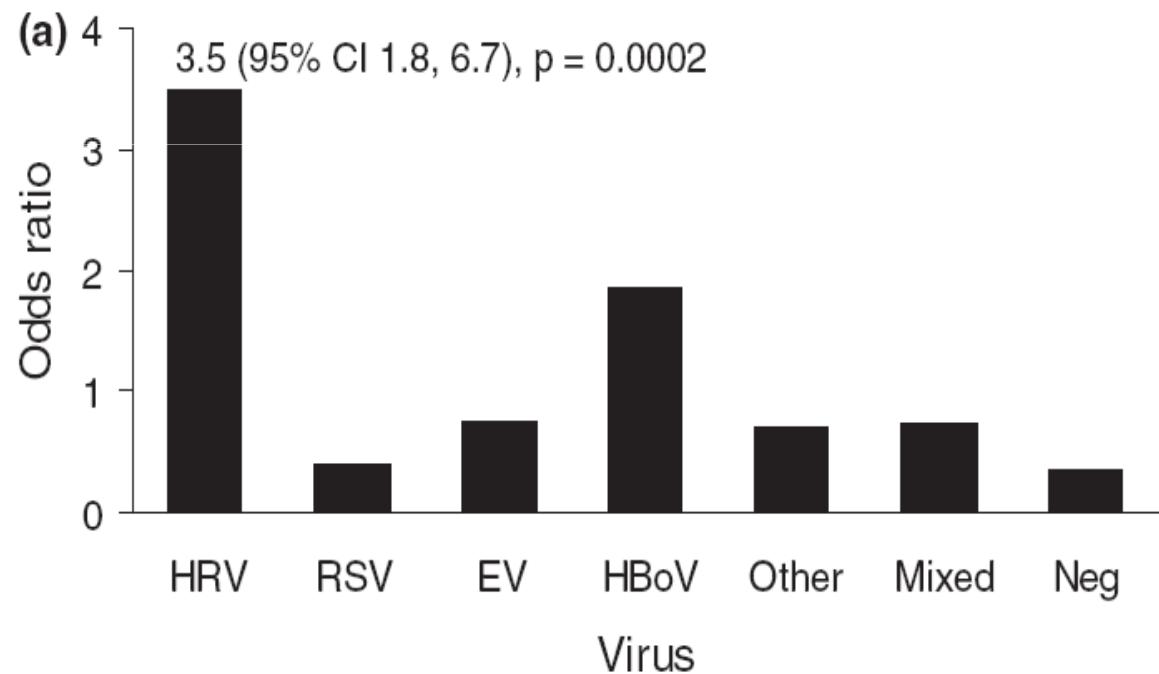
Episodi di wheezing tra 0 a 3 anni indotti da RSV (OR: 2,6), RV (OR: 9,8) o entrambi (OR: 10) sono correlati ad un maggiore rischio di asma a 6 anni

Dall' età di 3 anni, il wheezing indotto da RV è maggiormente correlato (OR 25,6) ad asma all'età di 6 anni rispetto alla sensibilizzazione verso pneumo allergeni (OR 3.4).



Jackson Am J Respir Crit Care Med Vol 2008

Allergic sensitization is associated with rhinovirus-, but not other virus-, induced wheezing in children



T. Jartti¹, H. Kuusipalo¹, T. Vuorinen²,
M. Söderlund-Venermo³, T. Allander⁴,
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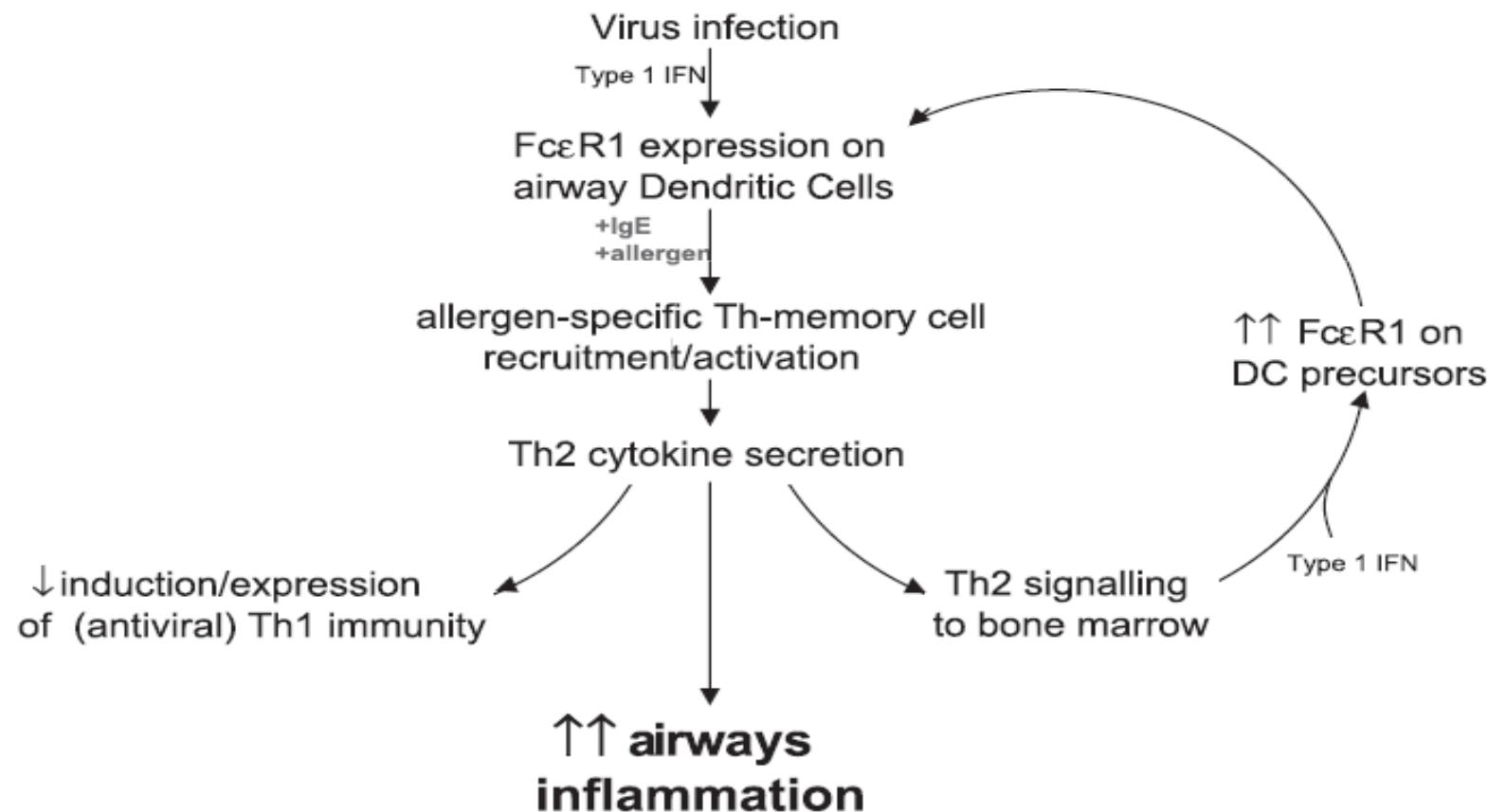
Key words: asthma; atopy; rhinovirus; respiratory syncytial virus; virus; wheezing

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Accepted 15 March 2010

Interaction Between Adaptive and Innate Immune Pathways in the Pathogenesis of Atopic Asthma : Operation of a Lung/Bone Marrow Axis



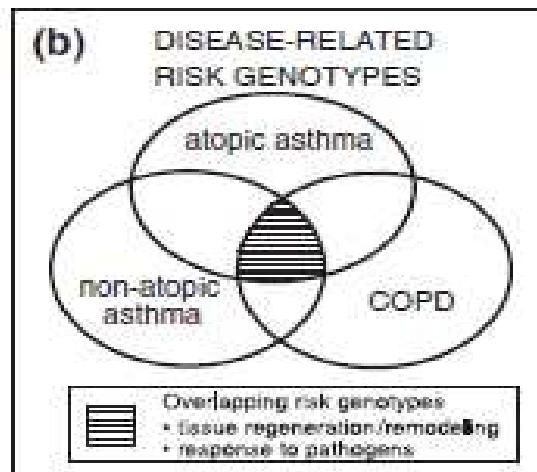
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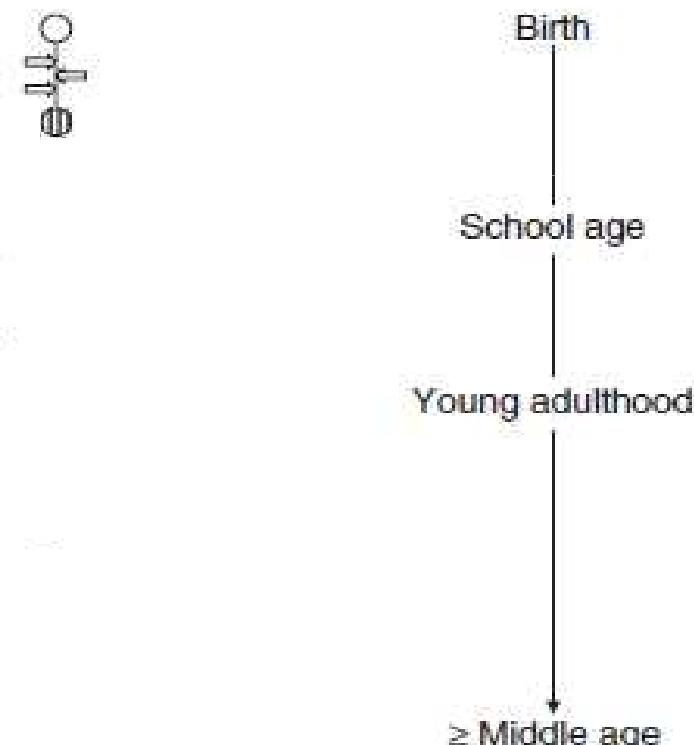
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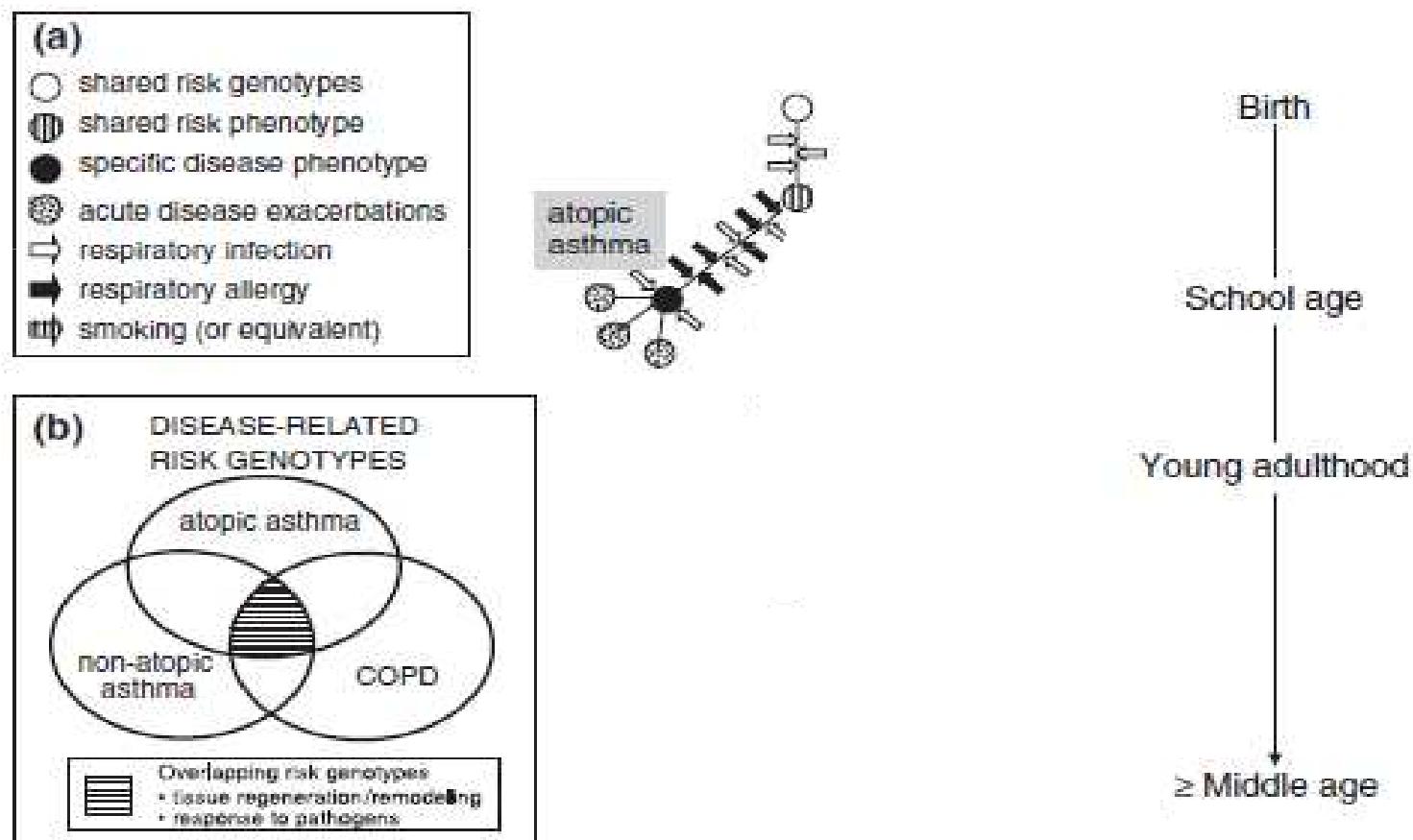


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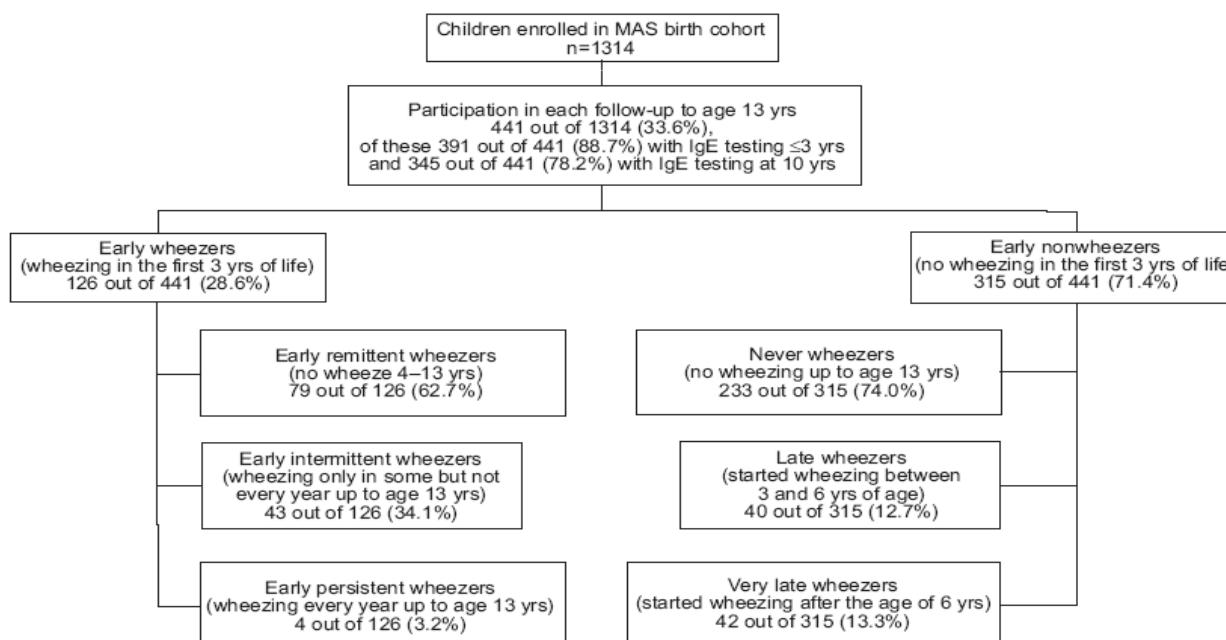
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Wheezing in childhood: incidence, longitudinal patterns and factors predicting persistence

P.M. Matricardi*, S. Illi#, C. Grüber*, T. Keil†, R. Nickel*,
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Wheezing in childhood: incidence, longitudinal patterns and factors predicting persistence

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U. Wahn* and S. Lau*

TABLE 2 Parental atopy, sex and atopy in children with different longitudinal patterns of wheezing from birth to age 13 yrs

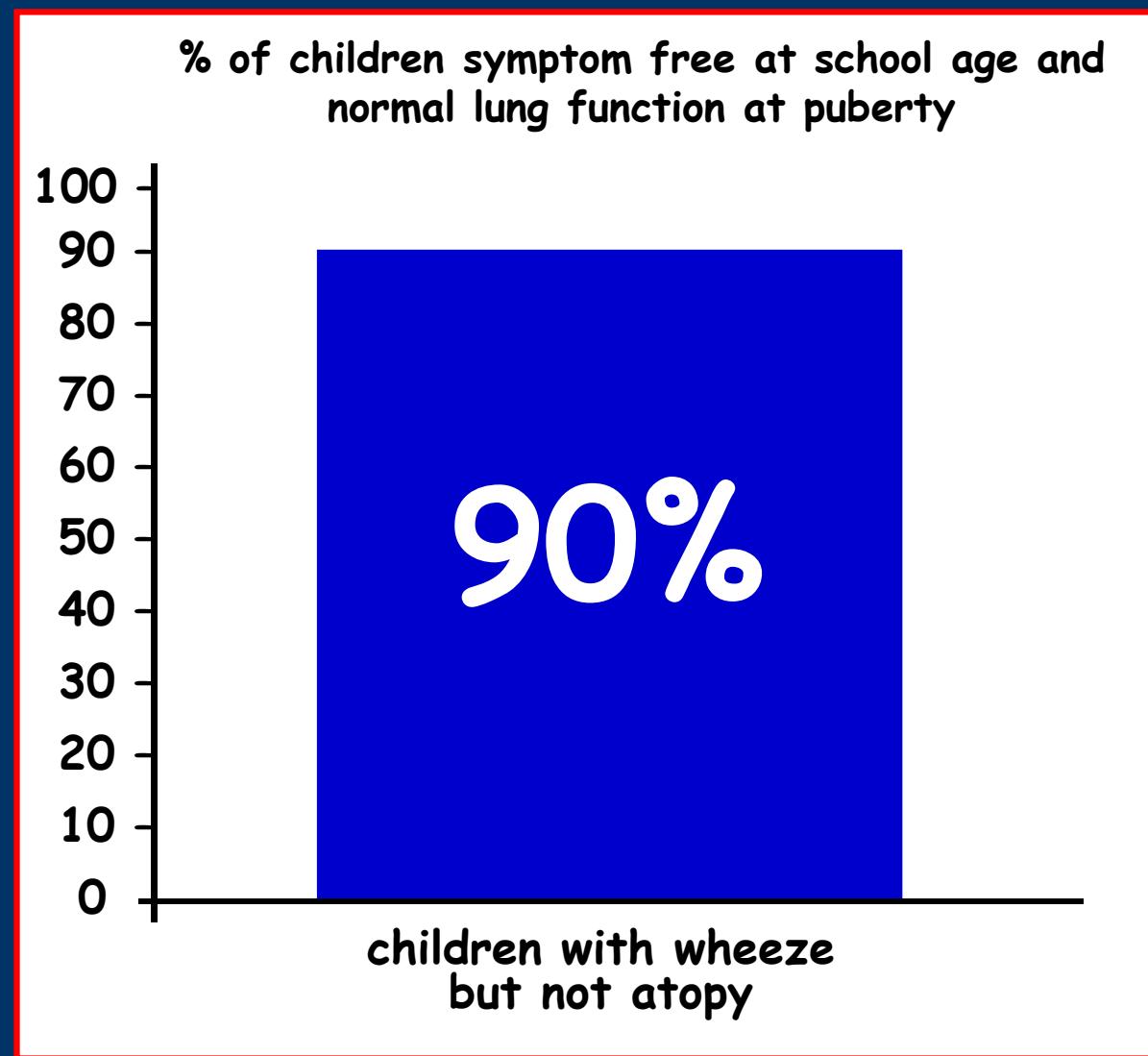
	Total subjects n	Parental atopy	Male sex	Atopy ≤ 3 yrs	Atopy 10 yrs
Early wheezers					
All	126	77/125 (61.6)	74/126 (58.7)	31/116 (26.7)	47/103 (45.6)
Remittent	79	41/78 (52.6)	48/79 (60.8)	14/73 (19.2)	19/63 (30.2)
Intermittent	43	32/43 (74.4)	23/43 (53.5)	14/39 (35.9)	25/36 (69.4)
Persistent	4	4/4 (100.0)	3/4 (75.0)	3/4 (75.0)	3/4 (75.0)
Late wheezers					
Very late wheezers	40	24/40 (60.0)	23/40 (57.5)	11/34 (32.3)	15/33 (45.4)
Never wheezers	42	28/42 (66.7)	19/42 (45.2)	6/32 (18.7)	17/32 (53.1)

Data are presented as n/n total (%), unless otherwise stated.

PERENNIAL ALLERGEN SENSITISATION EARLY IN LIFE AND CHRONIC ASTHMA IN CHILDREN: A BIRTH COHORT STUDY

Illi *Lancet* 2006; 368: 763

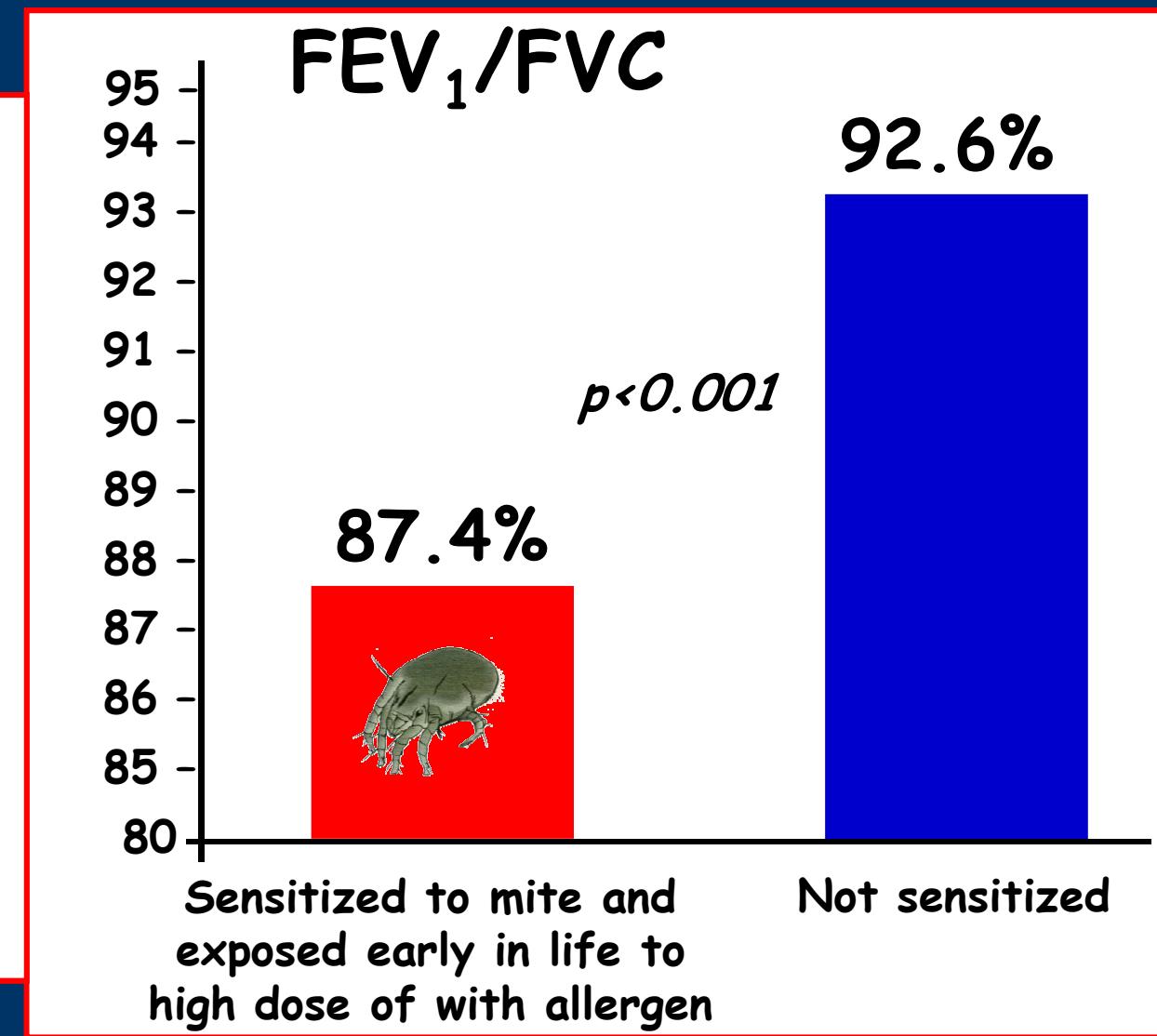
- 1314 children from birth to 13 years of age (MAS study)
- Allergen exposure at age 6 months, 18 months, and at 3, 4, and 5 yrs
- Lung function at 7, 10, and 13 yrs



PERENNIAL ALLERGEN SENSITISATION EARLY IN LIFE AND CHRONIC ASTHMA IN CHILDREN: A BIRTH COHORT STUDY

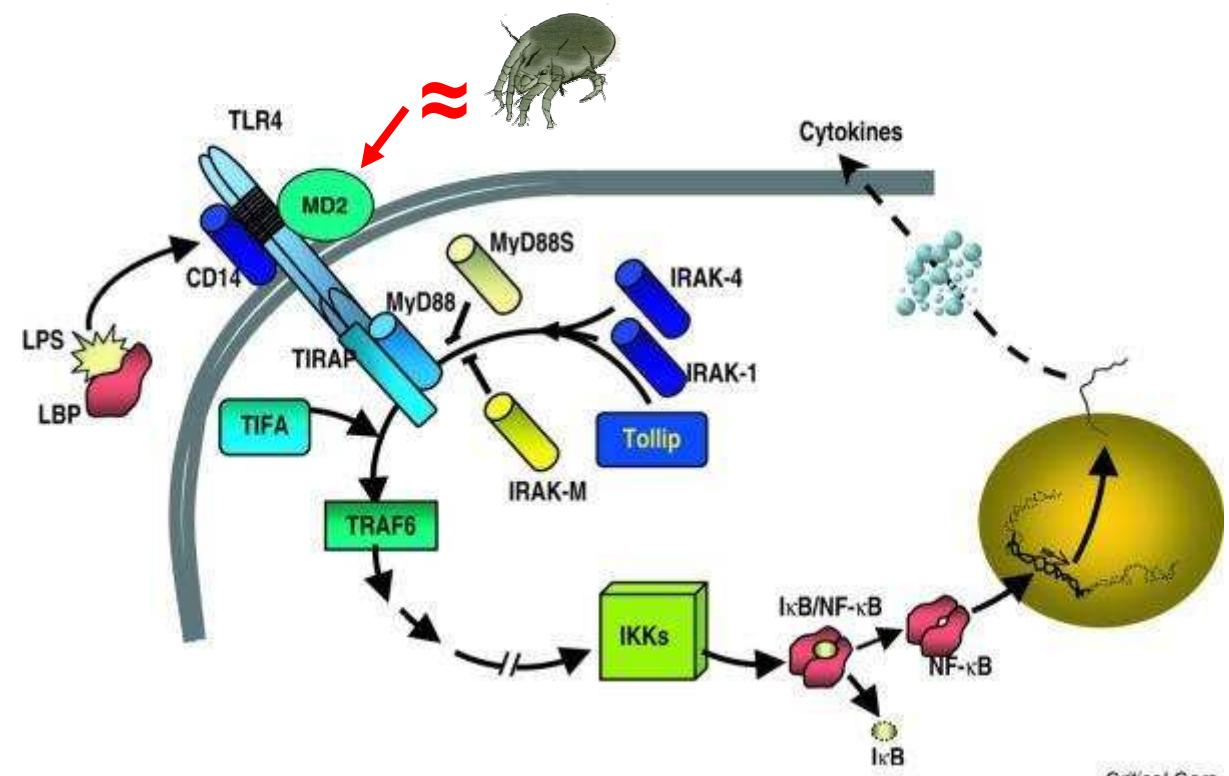
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Allergenicity resulting from functional mimicry of a Toll-like receptor complex protein

- The main house-dust-mite allergen, Der p 2, has structural homology with MD-2 (also known as LY96), the lipopolysaccharide (LPS)-binding component of the Toll-like receptor (TLR) 4 signalling complex.
- Here we show that Der p 2 also has functional homology, facilitating signalling through direct interactions with the TLR4 complex, and reconstituting LPS-driven TLR4 signalling in the absence of MD-2.



Trompette, Nature 2009



Wheezing and bronchial hyper-responsiveness in early childhood as predictors of newly diagnosed asthma in early adulthood: a longitudinal birth-cohort study

Debra A Stern, Wayne J Morgan, Marilyn Halonen, Anne L Wright, Fernando D Martinez

	Inactive		Newly diagnosed		Chronic	
	M-OR† (95% CI)	p	M-OR (95% CI)	p	M-OR (95% CI)	p
Parental asthma	2.0 (1.1-3.6)	0.030	2.7 (1.4-5.2)	0.004	3.2 (1.9-5.4)	<0.0001
Physician diagnosed eczema by 2 years	3.8 (1.9-7.8)	0.0002	1.1 (0.4-3.3)	0.9	2.0 (1.0-4.1)	0.047
Early wheezing phenotype						
Transient early	1.6 (0.7-3.5)	0.3	2.0 (0.8-4.8)	0.14	1.4 (0.7-2.9)	0.3
Late onset	5.4 (2.5-11)	<0.0001	4.6 (1.7-12)	0.003	7.4 (3.9-14.0)	<0.0001
Persistent	8.9 (4.0-20)	<0.0001	4.0 (1.2-14)	0.027	14.0 (6.8-28)	<0.0001
Alternaria skin-test positive at 6 years	2.0 (1.0-4.0)	0.067	0.6 (0.2-2.2)	0.4	3.6 (2.1-6.4)	<0.0001
CA-BHR at 6 years	2.4 (0.9-6.5)	0.083	6.9 (2.3-21.0)	0.0006	4.5 (1.9-10.0)	0.0006
Lowest V'maxFRC quartile at 6 years	1.1 (0.5-2.4)	0.8	2.8 (1.1-6.9)	0.029	2.1 (1.1-3.9)	0.021

Multinomial odds ratio (M-OR) estimated with multinomial logistic regression with all risk factors listed in the table included in the model with the no asthma group as the reference group. Models were additionally adjusted for ethnicity, sex, and current smoking at age 22 years. CA-BHR=bronchial hyperresponsiveness to cold air challenge at age 6 years. V'maxFRC=lowest quartile compared to upper three quartiles combined.

Table 5: Multinomial odds ratio for asthma groups at age 22 years by different risk factors in early life

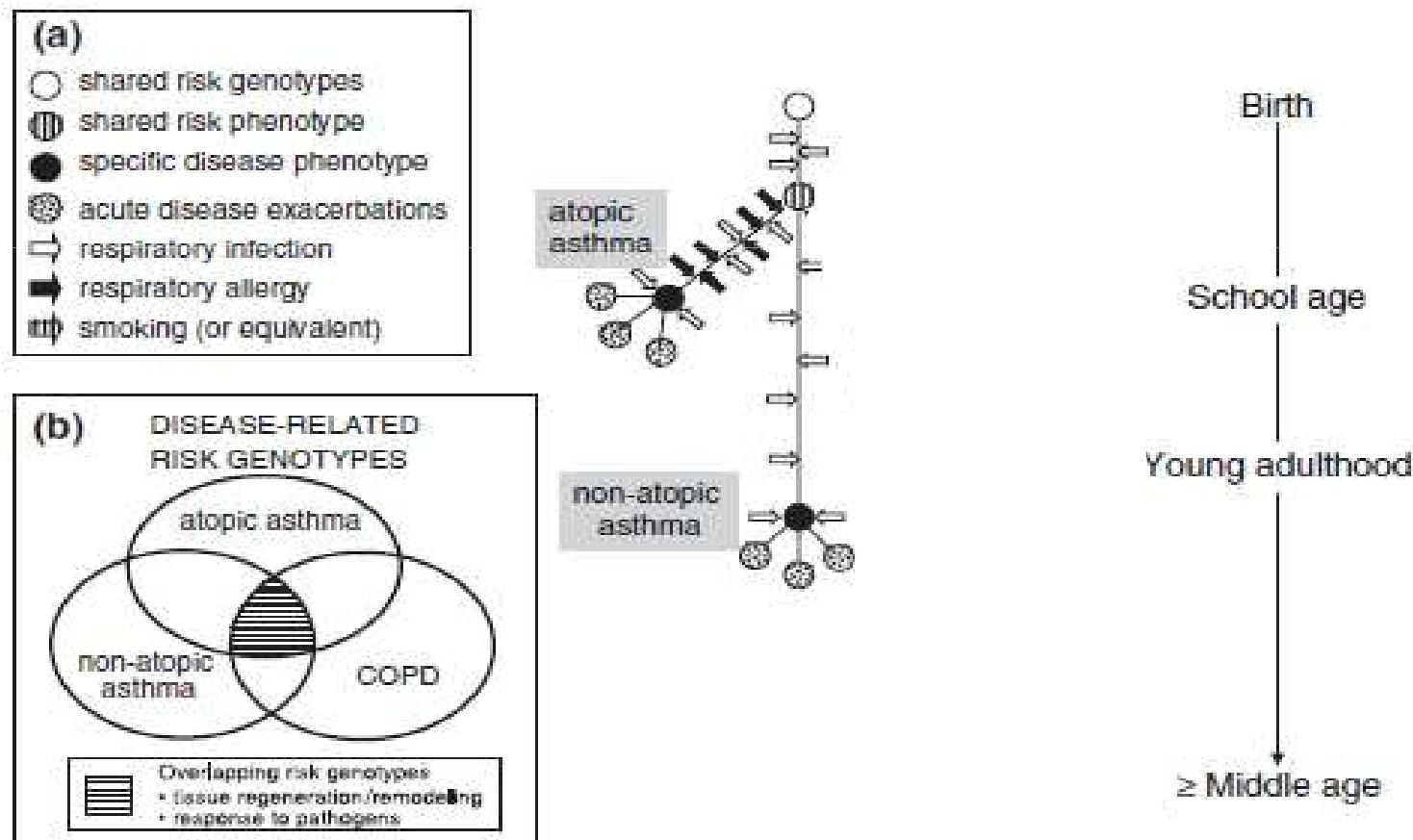
Lancet 2008; 372: 1058-64

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TWO NOVEL SEVERE ASTHMA PHENOTYPES IDENTIFIED DURING CHILDHOOD USING A CLUSTERING APPROACH

Three independent clusters of asthma were identified.

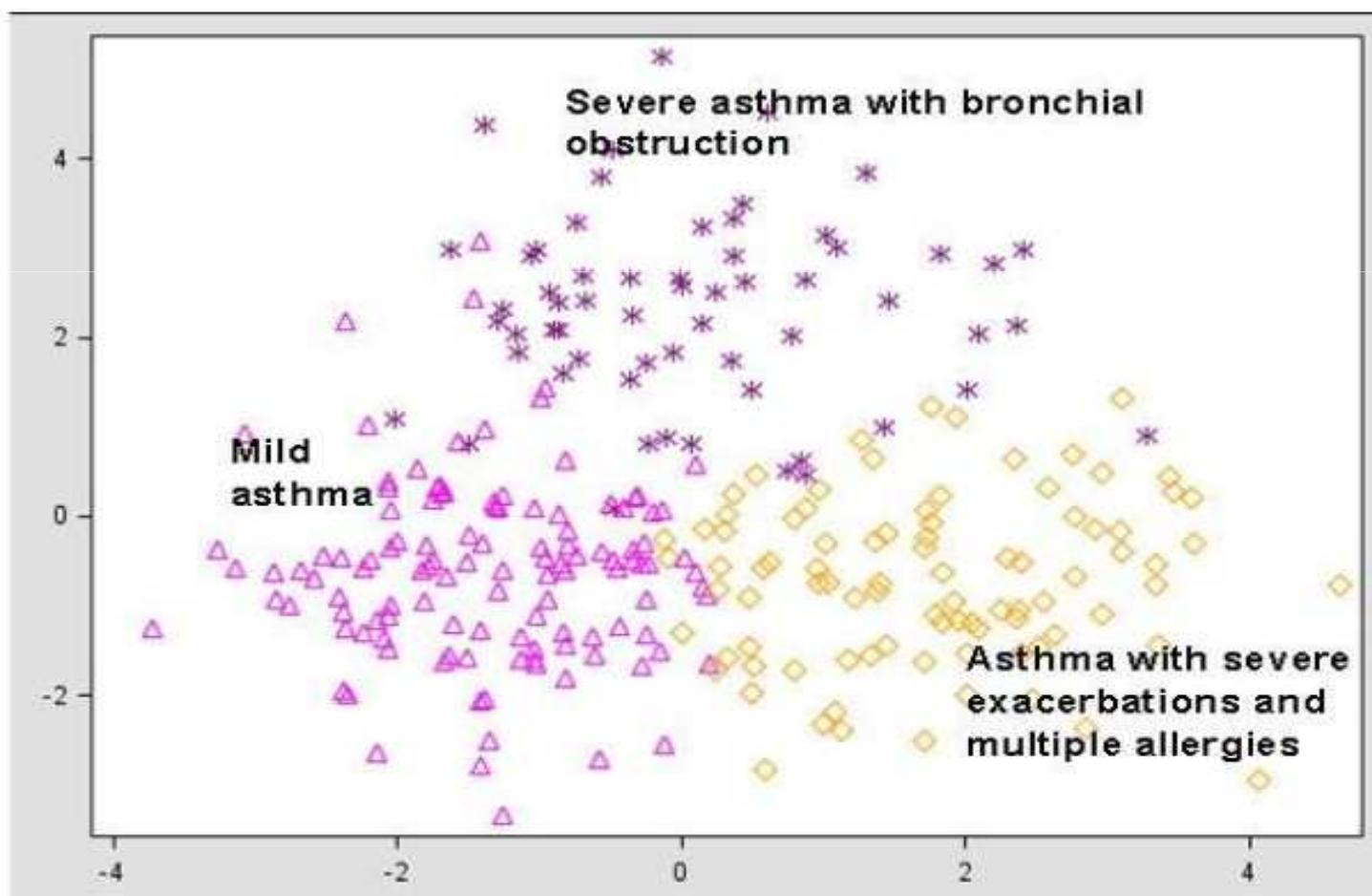


Table II: Features of children according to cluster analysis in the entire population (n=315)

	Cluster 1 "Asthma with severe exacerbations and multiple allergies" (n=103)	Cluster 2 "Severe asthma with bronchial obstruction" (n=72)	Cluster 3 "Mild asthma" (n=140)	p value*
Age (y)	8.8 (8.5;9.2)	10.3 (10.0;10.6)	8.3 (8.0;8.5)	<.0001
BMI (Kg/m ²)	17.1 (16.6;17.5)	20.0 (19.1;21.0)	16.7 (16.3;17.0)	<.0001
Maternal asthma (%)	25 (33)	8 (13)	16 (13)	<.001
Paternal asthma (%)	25 (29)	11 (18)	11 (9)	.001
Number of sensitizations to food allergens, median (range)	0.3 (0.2;0.5)	0.0 (0.0; 0.0)	0.1 (0.0;0.1)	<.0001
Number of sensitizations to inhaled allergens, median (range)	3.0 (2.6;3.5)	1.9 (1.5;2.3)	1.2 (1.0;1.5)	<.0001
Total IgE (kU/L), median (range)	805 (657;952)	485 (365;605)	450 (323;577)	<.0001
IgG (g/L), median (range)	9.9 (9.6;10.4)	11.7 (11.2;12.3)	8.6 (8.1;9.0)	<.0001
IgA (g/L), median (range)	1.3 (1.2;1.4)	1.8 (1.6;1.9)	1.1 (1.0;1.2)	<.0001
IgM (g/L), median (range)	1.1 (1.0;1.2)	1.3 (1.1;1.4)	0.9 (0.9;1.0)	.001
Blood eosinophils (/mm ³)	734 (650;817)	514 (421;607)	454 (395;515)	<.0001
Blood basophils (/mm ³)	42 (34;50)	3 (4;14)	24 (18;23)	<.0001
Blood lymphocytes (/mm ³)	3036 (2889;3182)	3030 (2852;3208)	2691 (2561;2820)	<.001
Blood neutrophils (/mm ³)	2767 (2540;2993)	3423 (3082;3765)	3250 (3009;3492)	.001
Blood monocytes (/mm ³)	505 (474;536)	550 (511;588)	515 (483;541)	.08
Baseline FEV ₁ (% predicted)	89 (86;92)	82 (78;86)	97 (95;100)	<.0001
Asthma duration ≥ 5y (%)	91 (88)	49 (68)	93 (66)	<.001
≥ 1 hospitalization for asthma exacerbation (%)	67 (65)	7 (10)	20 (14)	<.0001

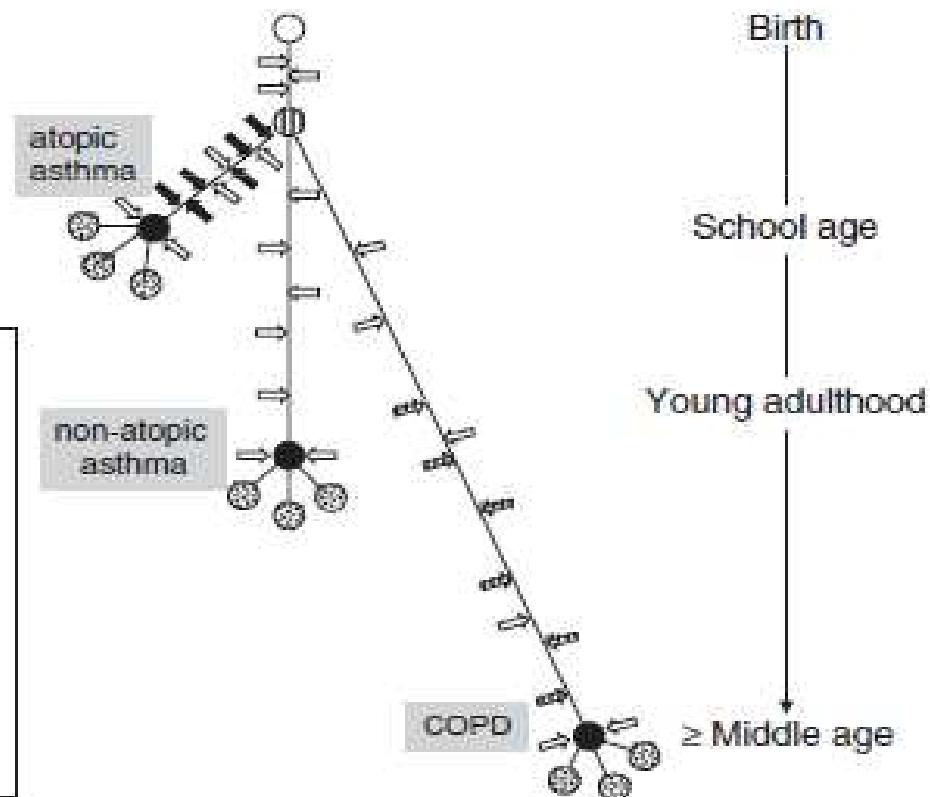
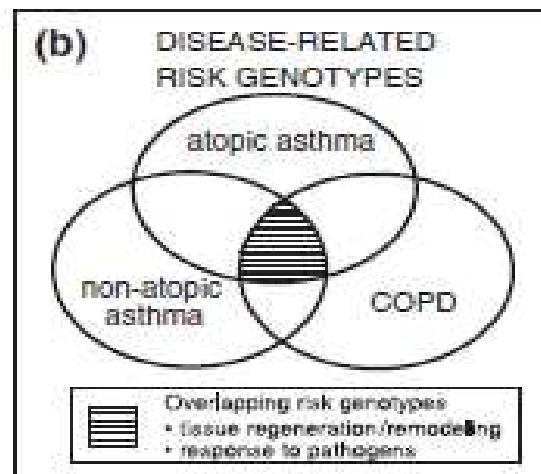
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Early life origins of chronic obstructive pulmonary disease

Thorax 2010

C Svanes,^{1,2} J Sunyer,^{2,3} E Plana,² S Dharmage,⁴ J Heinrich,⁵ D Jarvis,⁶ R de Marco,⁷ D Norbäck,⁸ C Raherison,⁹ S Villani,¹⁰ M Wijst,⁵ K Svanes,¹¹ J M Antó^{2,3}

Childhood disadvantage factors

- European Community Respiratory Health Survey participants aged 20–45 years randomly selected from general populations.
- Spirometry in 1991–3 (n=13,359) and 9 years later (n=7,738).

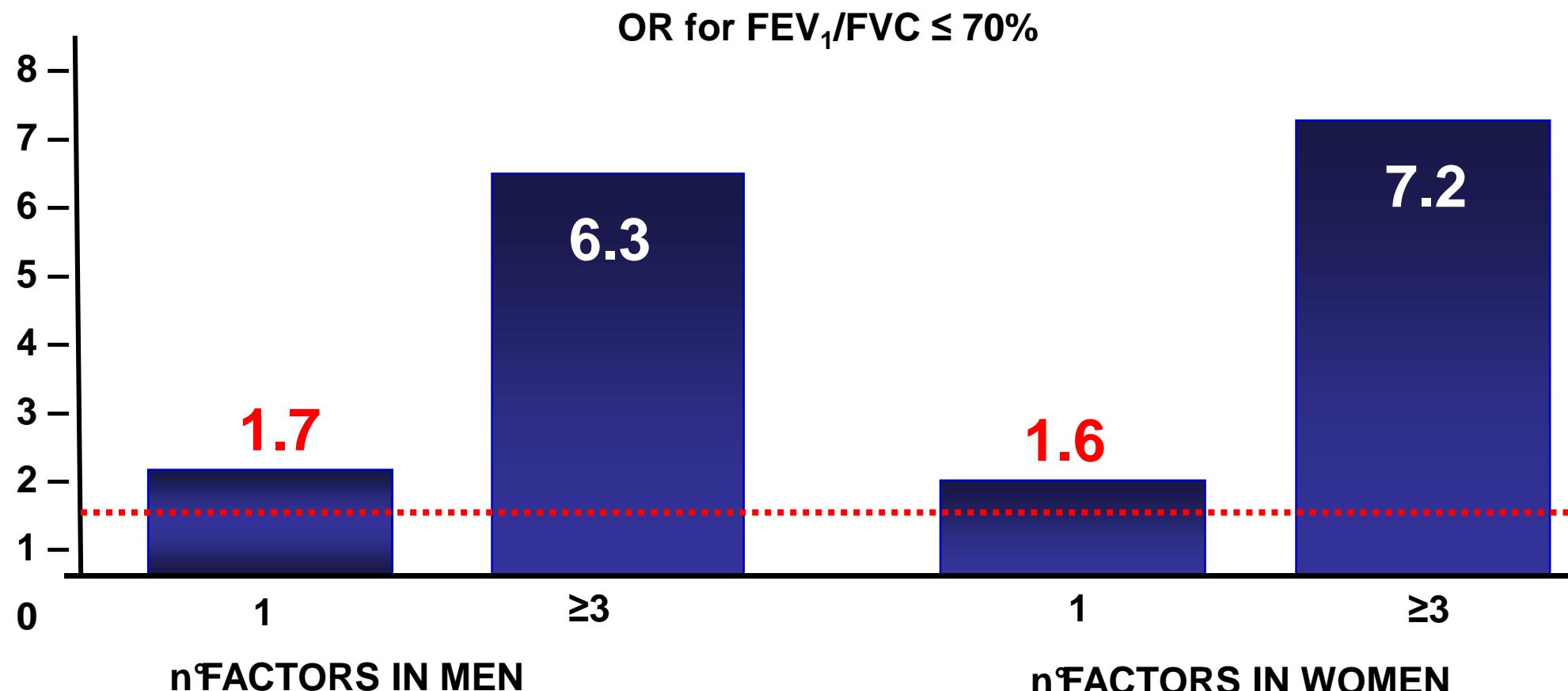
- Maternal asthma,
- Paternal asthma,
- Childhood asthma,
- Maternal smoking and
- Childhood respiratory infections



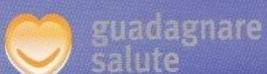
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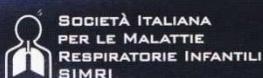
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I danni dell'esposizione al fumo di sigaretta: fisiopatogenesi, implicazioni cliniche, strategie di intervento in Pediatria



rendere facili le scelte salutari



Carlo Capristo
Dipartimento di Pediatria S.U.N.

Danni da fumo passivo

Il fumo passivo è quello che viene inalato involontariamente dalle persone che si trovano a contatto con uno o più fumatori attivi e rappresenta il principale inquinante degli ambienti chiusi. Esso è la risultanza del fumo espirato dal fumatore attivo (corrente terzaria) sommato al fumo prodotto dalla combustione lenta e imperfetta della sigaretta lasciata bruciare nel portacenere o in mano fra un tiro e l'altro (corrente secondaria). Si ammette che il fumo passivo sia costituito per 6/7 dalla corrente secondaria e per 1/7 dalla corrente terzaria. Si definisce anche fumo laterale (*sidestream smoke*) per distinguerlo dal fumo centrale (*mainstream smoke*) che rappresenta invece il fumo attivo.

Negli Stati Uniti si stima che il 60% dei bambini tra 3 e 11 anni siano esposti ad inquinamento ambientale da tabacco (*environmental tobacco smoke, ETS*) e che per il 90% questa esposizione avvenga in casa [1].

L'esposizione all'ETS è associata ad un aumentato rischio di sindrome da morte improvvisa del neonato (SIDS), infezioni respiratorie e otiti medie; rappresenta un importante fattore di rischio per asma ed è fortemente correlato, nei soggetti asmatici, ad uno scarso controllo dei sintomi e ad una riduzione della funzionalità respiratoria. In uno studio recentemente pubblicato si dimostra un'associazione statisticamente significativa tra riduzione dell'esposizione all'ETS e riduzione degli episodi di asma non controllato, incluse le visite mediche, le ospedalizzazioni e le assenze scolastiche [2]. È accertata la correlazione del fumo materno durante la gravidanza con la riduzione della funzione respiratoria e la comparsa di *wheezing* nell'infanzia precoce e successivamente di asma. I neonati esposti in utero al fumo materno presentano vie aeree con calibro ridotto, pareti ispessite, meno elastiche ed ipertono della muscolatura liscia bronchiale [3].

Diversi studi associano l'esposizione al fumo di tabacco nell'ambiente domestico a sintomi respiratori, quali tosse e respiro sibilante, ad un incremento delle assenze scolastiche per malattie respiratorie e alle cure mediche che ne conseguono [4, 5].

I principali costituenti del fumo di tabacco che colpiscono l'apparato respiratorio comprendono elementi gassosi, quali monossido di carbonio, ossidi d'azoto, formaldeide, cianuro d'idrogeno, diossido di zolfo e

nitrosammime, e particolati, come nicotina, metalli pesanti (piombo, cadmio, nichel) e benzopirene. I loro effetti sono mediati da diversi meccanismi che includono effetti irritanti diretti, meccanismi immunologici e mutagenesi [6].

L'esposizione al fumo di tabacco determina una soppressione della difesa immunitaria innata a livello dell'epitelio polmonare, altera la *clearance* mucociliare, favorisce l'adesione e la colonizzazione batterica, influenza la funzione delle cellule immunitarie [7].

L'immunità innata rappresenta la prima linea di difesa del polmone e i peptidi antimicrobici (AMPs) sono le principali molecole effettive di questo sistema. A livello del tratto respiratorio sono principalmente espresse le β -defensine e le catepsine. In particolare le β -defensine vengono prodotte e secrete dalle cellule epiteliali della mucosa respiratoria in seguito all'induzione da parte di prodotti batterici mediatori infiammatori. Il fumo di tabacco sopprime questa induzione, tant'è che nelle secrezioni di soggetti fumatori sono state evidenziate in corso di polmoniti basse concentrazione di β -defensine. Il fumo si pensa influenzzi diversi *pathway* proinflammatori (MAP chinasi, ERK1/2, JNK, NF- κ B). In particolare l'acroleina, maggiore prodotto della combustione organica, inibisce l'attivazione del nuclear factor kappa B (NF- κ B) attraverso l'interazione con complesso inhibitore delle chinasi (IKK), inibendo così l'espressione di citochine infiammatorie come l'IL-8. Inoltre, il fumo inibisce la produzione di citochine infiammatorie indotte dal liposaccaride batterico, sopprimendo l'attivazione della activator protein-1 (AP-1) nelle cellule epiteliali bronchiali. Anche la *downregulation* dei recettori toll-like (TLRs), in particolare di TLR4, nelle cellule epiteliali può contribuire all'effetto del fumo sull'espressione delle β -defensine.

La soppressione dell'immunità innata determina un aumento della carica batterica, favorendo così la suscettibilità alle infezioni. La combinazione di questo con i danni diretti dal fumo alla barriera epiteliale sfocia in un circolo vizioso di infiammazione, danno strutturale, infezione.

Il fumo di tabacco danneggia profondamente l'epitelio ciliato della mucosa respiratoria. Nei soggetti fumatori si determinano delle tipiche alterazioni istologiche che

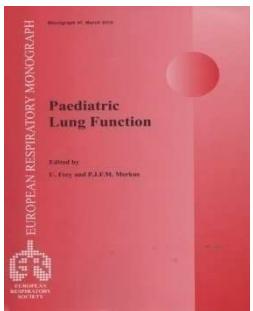


- Anamnesi ed insieme dei sintomi
- Esame obiettivo
- Prove di funzionalità respiratoria
 - Spirometria
 - Test di reversibilità
 - Test di provocazione bronchiale aspecifico
- Indagini per identificare i fattori di rischio
- Altre indagini

Developmental physiology: lung function during growth and development from birth to old age

Exposures accelerating decline in lung function in adults

When spirometry is used to measure lung function, a decline is seen with advancing age [11]. This decline is greater over the age of 50 yrs and is slightly greater in males than in females [11, 78]. A more rapid decline in FEV₁ is also seen in smokers [79], asthmatics [79] and in those with chronic mucus hypersecretion [79]. Chronic exposure to higher levels of air pollution is associated with lower lung function in adults [80]. Exposure to indoor air pollutants, including ETS, PM from burning biomass fuel and bioaerosols have also been associated with lower lung function and more rapid decline in FEV₁ [80].



C. Calogero, P.D. Sly Eur Respir Mon 2010





**GRAZIE PER
L'ATTENZIONE**



Thesis 2012

PERCORSI INTERATTIVI E FORMATIVI PEDIATRICI

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