

21 MARZO 2012 • WORKSHOP
VERDE URBANO E ALLERGIE:
STRATEGIE DI PREVENZIONE
PER LA SALUTE PUBBLICA

V Giornata Nazionale del Polline dell'Associazione Italiana di Aerobiologia (AIA)
I Giornata FEDERASMA del Paziente Allergico

Utilità degli studi
aerobiologici
in allergologia

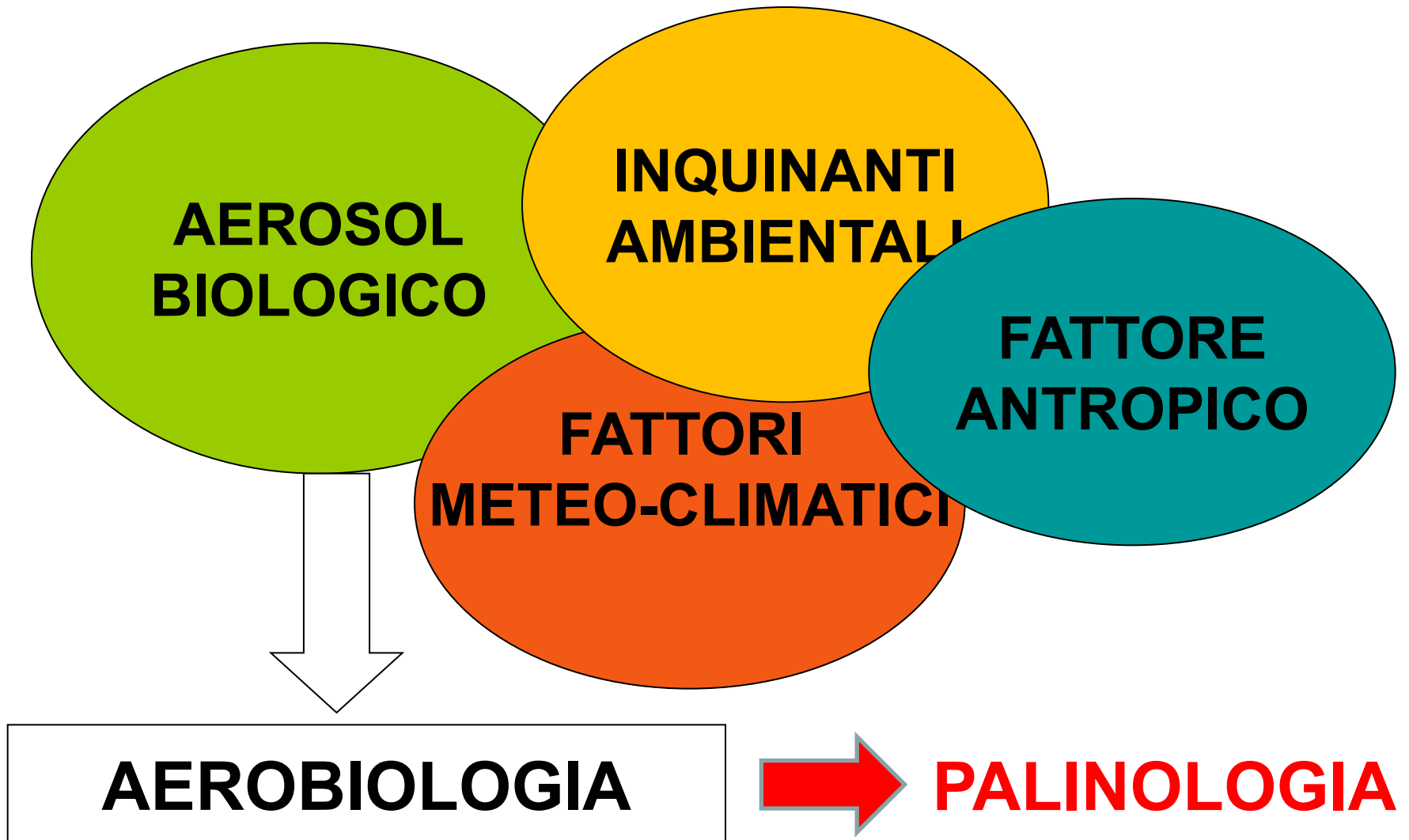


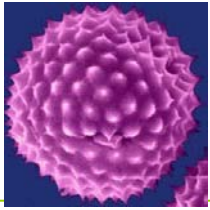
Susanna Voltolini

Unità Operativa Complessa di Allergologia
IRCCS Azienda Ospedaliera Universitaria
San Martino – IST - Genova



Ambiente e Allergie: relazione stretta e multifattoriale





LA POLLINOSI



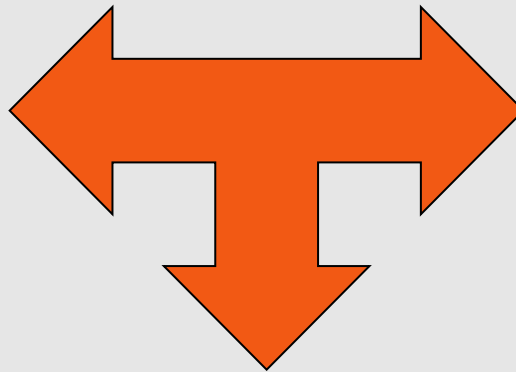
il termine *pollinosi* definisce le manifestazioni cliniche (nasali, oculari e bronchiali) che si presentano con periodicità stagionale durante la pollinazione , in soggetti sensibilizzati a specifiche famiglie di piante.

Interessa il 10-20% della popolazione

Come nasce la palinologia?

Charley Blackley . Experimental researches on the causes and nature of Catarrhus Aestivus (Hay-fever and Hay- asthma). **London, 1873.**

**PRIMO TEST
CUTANEO**



**PRIMO TEST DI
PROVOCAZIONE
NASALE**

**PRIMO CALENDARIO
POLLINICO**

Che cosa forniscono gli studi aerobiologici?

Dati sulla presenza di pollini allergizzanti aerodispersi

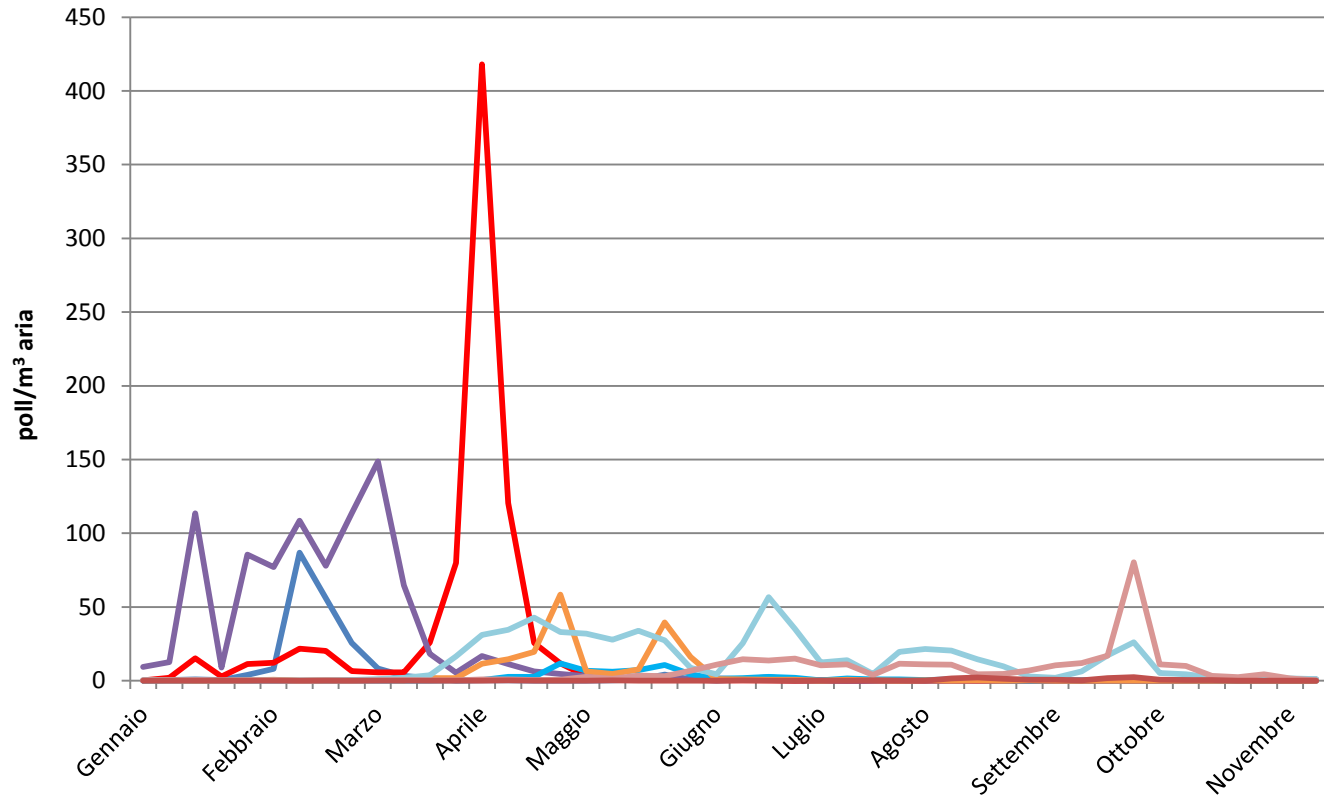
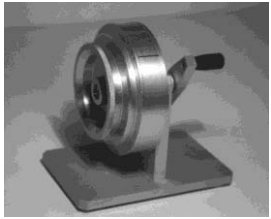
**Periodicità,
stagionalità**

**Variazioni
temporali e/o
quantitative**

**Presenza di
nuovi pollini
allergizzanti**

CALENDARI POLLINICI

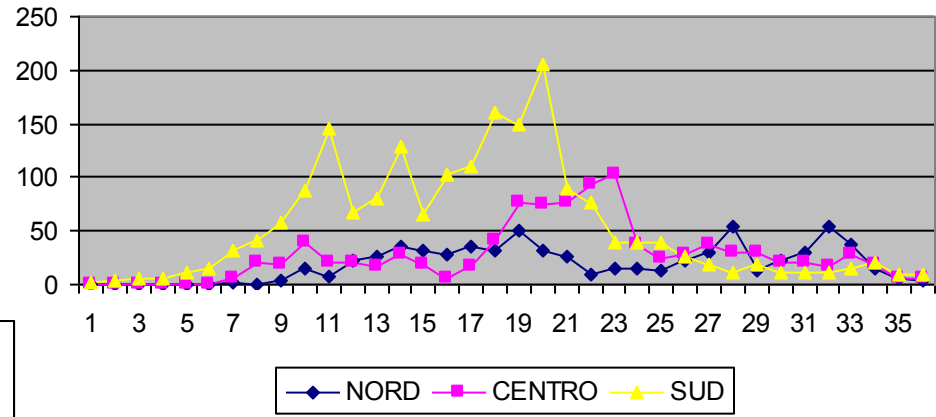
Calendario pollinico 2011 - Genova San Martino



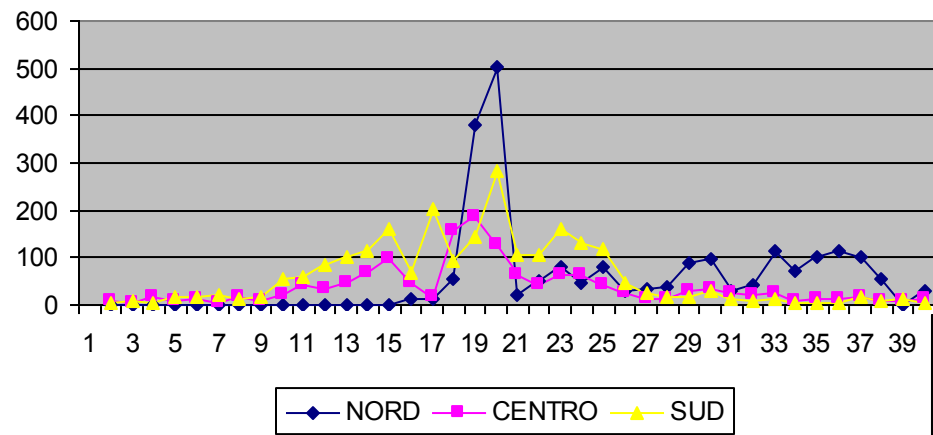
— Betulaceae — Corylaceae — Cupressaceae — Gramineae
— Oleaceae — Urticaceae — Alternaria — Compositae



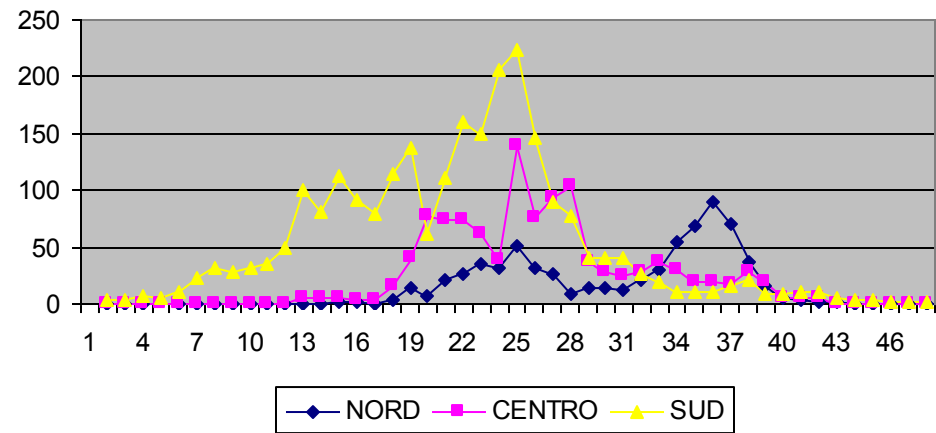
PARIETARIA 2002



PARIETARIA 2003



PARIETARIA 2004





A.I.A.

Associazione Italiana di Aerobiologia

Associazione di ricercatori biologi e medici nata nel 1985

Gestisce la **prima Rete Italiana di Monitoraggio degli Aeroallergeni**

collegata alla **European Aeroallergen Network (EAN)**

informazioni aerobiologiche



ITALIA

www.ilpolline.it

EUROPA

www.polleninfo.org

Review article

Allergenic pollen and pollen allergy in Europe

The allergenic content of the atmosphere varies according to climate, geography and vegetation. Data on the presence and prevalence of allergenic airborne pollens, obtained from both aerobiological studies and allergological investigations, make it possible to design pollen calendars with the approximate flowering period of the plants in the sampling area. In this way, even though pollen production and dispersal from year to year depend on the patterns of pre-season weather and on the conditions prevailing at the time of anthesis, it is usually possible to forecast the chances of encountering high atmospheric allergenic pollen concentrations in different areas. Aerobiological and allergological studies show that the pollen map of Europe is changing also as a result of cultural factors (for example, importation of plants such as birch and cypress for urban parklands), greater international travel (e.g. colonization by ragweed in France, northern Italy, Austria, Hungary etc.) and climate change. In this regard, the higher frequency of weather extremes, like thunderstorms, and increasing episodes of long range transport of allergenic pollen represent new challenges for researchers. Furthermore, in the last few years, experimental data on pollen and subpollen-particles structure, the pathogenetic role of pollen and the interaction between pollen and air pollutants, gave new insights into the mechanisms of respiratory allergic diseases.

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S. Bonini^{4,5,**}, **C. Nunes**^{6,*},
I. Annesi-Maesano^{7,8}, **H.**
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²Interdepartmental Centre of Bioclimatology, University of Florence, Florence, Italy; ³Allergy Clinic, Azienda Sanitaria 10 Firenze, Florence, Italy; ⁴Second University of Naples, Naples, Italy; ⁵Institute of Neurobiology and Molecular Medicine National Research Council, ARTOV, Rome, Italy; ⁶Centro de Imunoalergia do Algarve, Portimao, Portugal;

⁷INSERM, UMR S 707: EPAR, Paris, France;

⁸Université Pierre et Marie Curie – Paris 6, UMR S 707: EPAR, Paris, France; ⁹Division of Environmental Dermatology and Allergy GSF/TUM, Technical University, Munich, Germany; ¹⁰Clinical Centre of Allergology, Medical University, Sofia, Bulgaria;

¹¹Department of Oto-Rhino-Laryngology, University Hospital Gent, Belgium

Distribuzione delle piante allergeniche in Europa per aree vegetazionali (da D'Amato G. 2007).

Aree vegetazionali	Piante allergeniche
Artica	<i>betulla</i>
Centrale	<i>foresta decidua, betulla, graminacee</i>
Orientale	<i>graminacee, composite (ambrosia, artemisia)</i>
Montuosa	<i>alberi, graminacee (con pollinazione ritardata di 3-4 settimane rispetto al livello del mare)</i>
Mediterranea	<i>parietaria, olivo, graminacee, cipresso</i>

Transition from a Botanical to a Molecular Classification in Tree Pollen Allergy: Implications for Diagnosis and Therapy

Nadine Mothes^a Friedrich Horak^b Rudolf Valenta^a

Center for Physiology and Pathophysiology, ^aDepartment of Pathophysiology and ^bDepartment of Otorhinolaryngology, Vienna General Hospital, Medical University of Vienna, Vienna, Austria

Plant species	Allergen	kDa	Allergen biological function
<i>Fagales</i>			
Birch (<i>Betula verrucosa</i>)	Bet v 1	17	Pathogenesis-related protein (PRP) RNase Plant steroid carrier Nucleotide-binding protein
	Bet v 2	14	Profilin
Alder (<i>Alnus glutinosa</i>)	Aln g 1	17	PRP
	Aln g 4		Ca ²⁺ -binding protein
Hazel (<i>Corylus avellana</i>)	Cor a 1		PRP
	Cor a 2	14	Profilin
	Cor a 8	9	Lipid transfer protein
	Cor a 10	70	Luminal-binding protein
Hornbeam (<i>Carpinus betulus</i>)	Car b 1	17	PRP
White oak (<i>Quercus alba</i>)	Que a 1	17	PRP
Chestnut (<i>Castanea sativa</i>)	Cas s 1	22	PRP
	Cas s 5		Chitinase
	Cas s 8	9.7	Lipid transfer protein

Allergologia e aerobiologia: a chi è utile ?

Medico curante e specialista

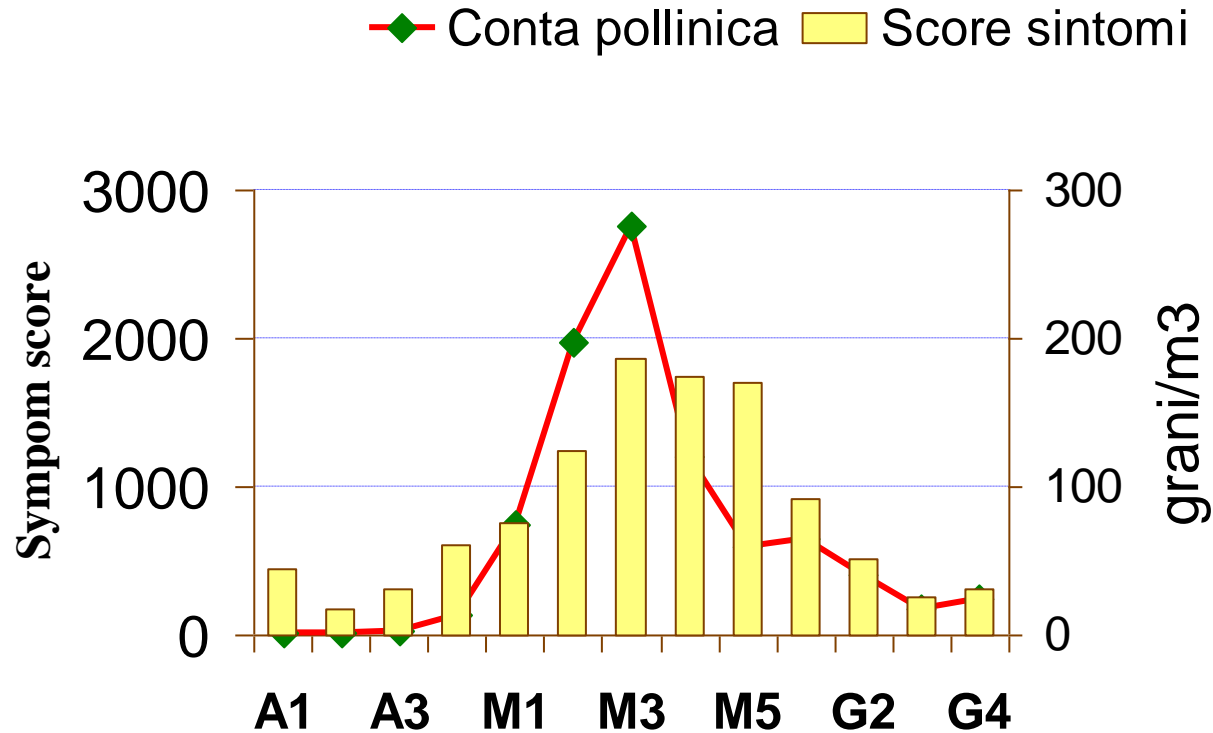
E' interessato:

- A stabilire la rilevanza clinica di una sensibilizzazione dimostrata in un soggetto
- A monitorare i sintomi
- Alla somministrazione di immunoterapia Specifica
- A prescrivere una terapia farmacologica "mirata"
- Ad individuare aeroallergeni "emergenti"

**IMPORTANZA DELL'USO
DI DIARI CLINICI**

Relazione tra sintomi di rinocongiuntivite e concentrazione di pollini aerodispersi

GRAMINACEAE



Allergologia e aerobiologia: a chi è utile ?

Il paziente

E' interessato:

- ✘ All'inizio della stagione pollinica, ai picchi di concentrazione e alla durata del periodo critico**
- ✘ Alle variazioni per area geografica anche in rapporto ad eventuali spostamenti**

Norman P.S.

«Allergic rhinitis»

JACI 1985

Studi sperimentali sulla rinite allergica:
variabilità della quantità minima scatenante
di polline da 10 a 5000 granuli **in differenti**
pazienti!

Confronto tra valori di soglia clinica per i pollini studiati

polline	Soglia minima p/m3	Soglia media p/m3	Soglia massima p/m3
graminacee	10	25	50
betulla	10	20	80
Parietaria	10	15	80
Ambrosia	1-3	10	50

Variabili nella relazione pollini-sintomi

Individuali

- **livello di IgE totali e specifiche**
- **patologie associate**
- **sensibilità d'organo, variabile a seconda della stagione**

Ambientali

- **fattori meteo-climatici**
(temperatura, umidità, vento, variazioni improvvise, temporali)
- **inquinamento atmosferico**

Urban Air Pollution and Climate Change as Environmental Risk Factors of Respiratory Allergy: An Update

G D'Amato,¹ L Cecchi,^{2,3} M D'Amato,⁴ G Liccardi¹ *J Investig Allergol Clin Immunol* 2010; Vol. 20(2): 95-102

Table 1. Possible Relationship Between Components of Air Pollution and Allergens in Inducing respiratory Allergy

Air pollution may be responsible for the following:

- Interaction with pollen grains, leading to increased release of allergens characterized by modified antigenicity.
 - Interaction with microscopic allergen-carrying particles released by plants. These particles are able to reach the lower airways in inhaled air, inducing asthma in predisposed individuals.
 - An inflammatory effect on the airways of susceptible individuals, with increased epithelial permeability, easier penetration of pollen allergens in the mucosa, and easier interaction with cells of the immune system. There is also evidence that predisposed individuals have increased airway reactivity induced by air pollution and increased bronchial responsiveness to inhaled pollen allergens.
 - An adjuvant immunologic effect on IgE synthesis in atopic individuals, as already shown with diesel exhaust particles.
-

INQUINANTI AMBIENTALI

MUCOSE

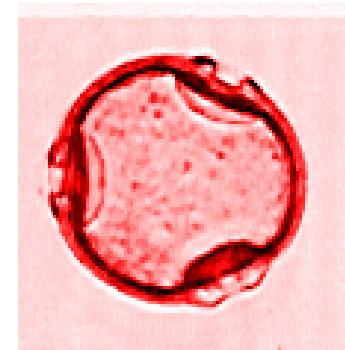
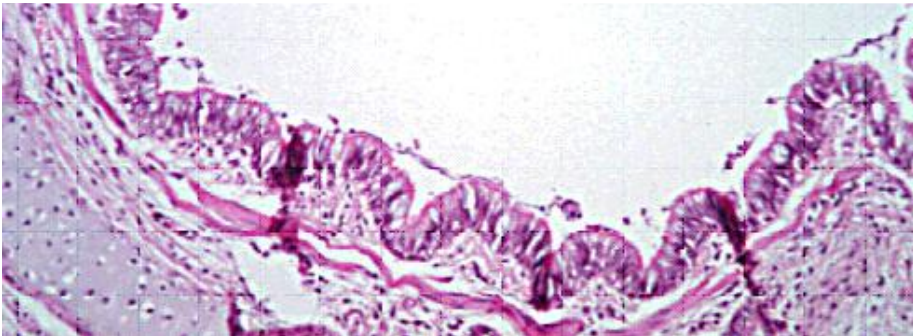
POLLINI

PIU' RECETTIVE

PIU' AGGRESSIVI

- azione adiuvante sulla produzione di IgE e sulla flogosi
- * > broncoreattività
- * > permeabilità delle vie aeree

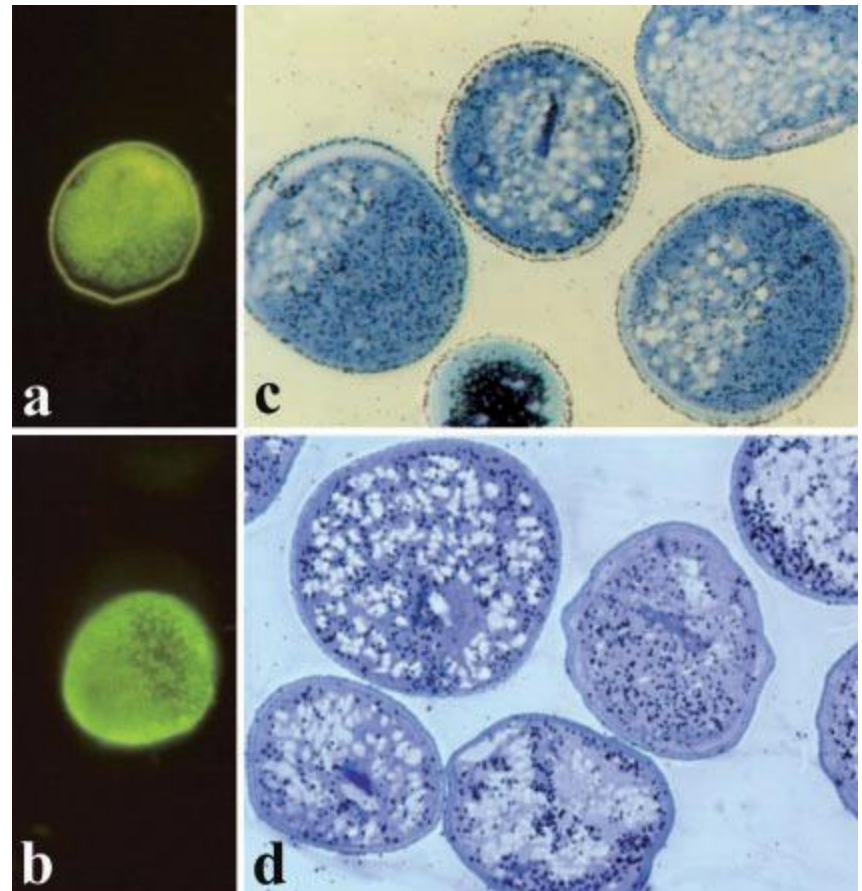
- * Modificata allergenicità
- * > Liberazione di allergeni e di eicosanoidi
- * Veicolamento da parte dei fattori inquinanti.



“Timothy grass (*Phleum pratense* L.) pollen as allergen carriers and initiators of an allergic response”

Behrendt H et al. Int Arch Allergy Immunol 1999

- **Differenze nel contenuto di allergene maggiore tra pollini raccolti in aree a differente traffico**
- **Differente rilascio di allergene e proteine**
- **Pollini in grado di rilasciare eicosanoidi: PGD2 e LKT B4**



Ozone affects pollen viability and NAD(P)H oxidase release from *Ambrosia artemisiifolia* pollen

Stefania Pasqualini^{a,*}, Emma Tedeschini^a, Giuseppe Frenguelli^a, Nicole Wopfner^b, Fatima Ferreira^b, Gennaro D'Amato^c, and Luisa Ederli^a

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^cDivision of Respiratory and Allergic Diseases, 'A. Cardarelli' High Speciality Hospital, Naples, Italy

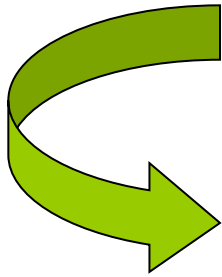
Variabili «Polliniche»

- **tipo di polline**
- **dimensione**
- **velocità e modalità di rilascio del polline**
- **contenuto di allergene e suo rilascio nell'aria** (Behrendt 1999, Buters, 2008)
- **rilascio allergene nelle mucose**

aggressività

biodisponibilità

I pazienti piu' sensibili accusano sintomi anche prima che il polline sia catturato dai campionatori



Esistenza di particelle submicroniche rilasciate da parti delle piante diverse dai pollini (es. foglie), dotate di allergene

Hyde 1972; Marsh 1975, Davies 1975, Busse WW, 1972, Solomon WR, 1983
Spieksma FT, 1990, D'Amato G, 1991

“Airborne paucimicronic allergen-carrying particles and seasonal respiratory allergy”

G D'Amato, *Allergy*, 56,12:1109–1111, 2001

Nuove metodiche di campionamento aerobiologico

- La semplice conta dei pollini può non essere rappresentativa della reale esposizione allergenica.
- Sono in corso studi di monitoraggio in contemporanea della concentrazione dei pollini al microscopio ottico e di allergeni ricombinanti rappresentativi, determinati in aria con metodiche immunoenzimatiche



The combination of airborne pollen and allergen quantification to reliably assess the real pollinosis risk in different bioclimatic areas

F. Javier Rodríguez-Rajo · Victoria Jato · Zulima González-Parrado · Belén Elvira-Rendueles · Stella Moreno-Grau · Ana Vega-Maray · Delia Fernández-González · Juan A. Asturias · María Suárez-Cervera

Received: 10 March 2010 / Accepted: 13 May 2010
© Springer Science+Business Media B.V. 2010

Abstract Exposure to allergens represents a key factor among the environmental determinants of asthma. The most common information available for pollinosis patients is the concentration of pollen grains in the bioaerosol and their temporal distribution. However, in recent years, discordance between pollen concentrations and allergic symptoms has been detected. The purpose of this research is to evaluate the relationship between pollen counts and the atmospheric aeroallergen concentrations in different Spanish bioclimatic areas. For the monitoring of allergen content in the air, a quantitative antigen–antibody

technique combined with the Cyclone sampling methodology was used. The study was conducted during 2007 by considering some of the most common allergens that induce pollinosis in each area: *Platanus* and Urticaceae in Ourense and Cartagena, and Poaceae in Ourense and León. In Ourense, pollen counts and aeroallergen concentrations coincided for the three pollen types studied, and the pollen and allergen data associated with the meteorological factors were highly significant for the pollen counts. In Cartagena (for *Platanus* and Urticaceae) and León (for Poaceae), the low correlations between pollen counts and allergen concentrations obtained could be due to the specific bioclimatic conditions. In contrast, the higher allergen concentrations found in the atmosphere in Cartagena and León compared to Ourense could be related to the existing pollutant levels there, inducing a higher expression of plant pathogenesis-related proteins in the plants of polluted cities. The combination of pollen counts and allergen quantification must be assessed to reliably estimate exposure of allergic people to allergens in different bioclimatic areas.

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Keywords Acrobiologia · Aeroallergens ·
Cyclone sampler · Lol p 1 · Par j 1–2 · Pla a 1

1 Introduction

Nowadays, Type I pollen allergy disorders caused by airborne pollen proteins are on the rise and have a

Utilità degli studi aerobiologici nella ricerca clinica

- **Studi epidemiologici** sulla pollinosi
- Valutazione della risposta a **nuovi farmaci** o a **terapia iposensibilizzante**
- **Confronto tra soggetti** residenti in aree geografiche differenti
- Valutazione di **trend di esposizione** e di conseguente patologia

General Trends in Airborne Pollen Production and Pollination Periods at a Mediterranean Site (Badajoz, Southwest Spain)

R Tormo-Molina,¹ MA Gonzalo-Garijo,² I Silva-Palacios,³ AF Muñoz-Rodríguez⁴

J Investig Allergol Clin Immunol 2010; Vol. 20(7): 567-574

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³School of Agrarian Engineering, University of Extremadura, Badajoz, Spain

⁴Faculty of Biology, University of Huelva, Spain

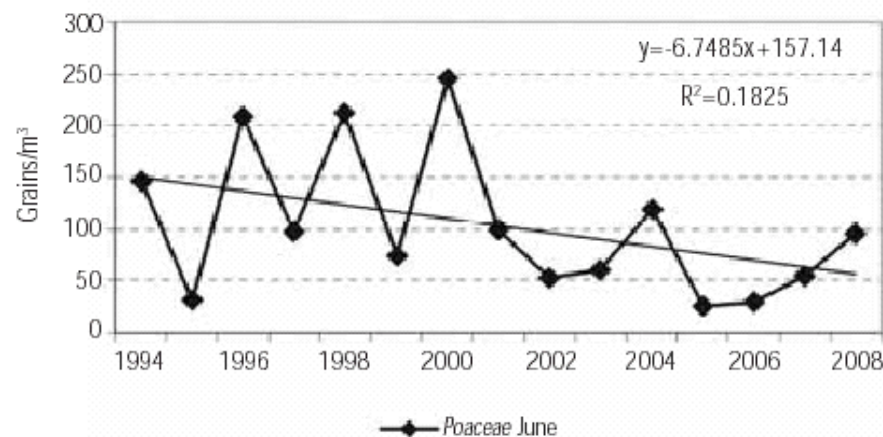
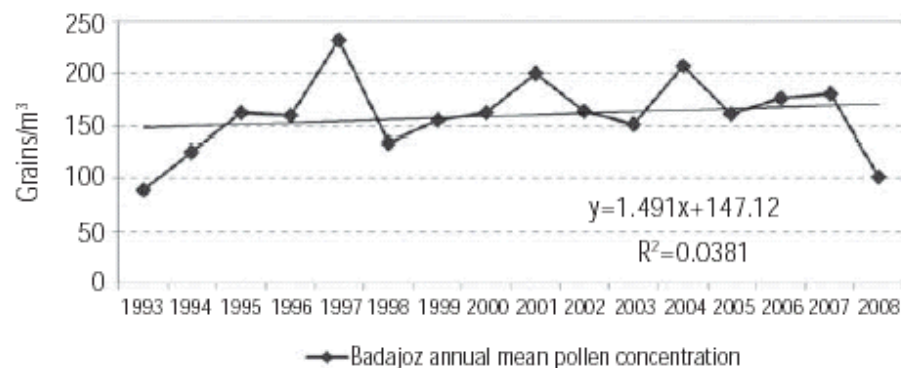


Figure 2. Annual mean of the total airborne pollen concentration during 1994-2008.

POLLINOSI “EMERGENTI”

“An epidemiological survey on the allergological importance of some emerging pollens in Italy” Corsico R, Falagiani P., Ariano R. et al. Invest Allergol Clin Immunol, 2000; 10:155-61

**RICERCA CONDOTTA DA 21 CENTRI ALLERGOLOGICI ITALIANI:
28 % DEI PAZIENTI CON ALLERGIA RESPIRATORIA
PRESENTAVANO POSITIVITA' VERSO I POLLINI
“EMERGENTI” :**

- CIPRESSO
- AMBROSIA
- BETULLA
- NOCCIOLO
- ONTANO
- CARPINO NERO

Allergy to **ragweed** in northern Italy and prevention strategies.

Zanon P, Chiodini E, Berra D.

Monaldi Arch Chest Dis. 2002 Apr;57(2):144-6



Long distance transport of **ragweed** pollen as a potential cause of allergy in central Italy.

Cecchi L, Morabito M, Paola Domeneghetti M, Crisci A, Onorari M, Orlandini S.

Ann Allergy Asthma Immunol. 2006 Jan;96(1):86-91.



2002, vol 12, N. 4



**Prevalenza
della Pollinosi da
Cupressacee
In Italia= 18,4 %**

AN EPIDEMIOLOGICAL SURVEY OF THE CUPRESSACEAE POLLINOSIS IN ITALY.

**R. Ariano 1, A. Antico 2, G. Di Lorenzo 3, M.C. Artesani 4, G. Bagnato 5, P. Bonadonna 6,
Bossi 7 , E. Bucher 8, R. Calabrese 9, P. Campi 10, R. Corsico 11, A. Dama 6, S. Del Giacco 12,
M.P. Domeneghetti 13, S. Gangemi 5, S. Isola 5, G. Piu 14, S. Pugliese 15,
F. Purello D'Ambrosio 5, C. Pronzato 11, M. Manfredi 10, G. Moscato 7,
M. Onorari 13, Romano A. 4, G. Senna 6, C. Troise 16, F. Vannucci 17, F. Vinciguerra 15,
A. Venuti 4, S. Voltolini 16.**

Troise C, Voltolini S, Delbono G, Negrini AC.

Allergy to pollens from Betulaceae and Corylaceae in a Mediterranean area (Genoa, Italy)--a ten-year retrospective study.

J Investig Allergol Clin Immunol. 1992 Nov-Dec;2(6):313-7.



Voltolini S, Modena P, Minale P, Bignardi D, Troise C, Puccinelli P, Parmiani S.

Sublingual immunotherapy in tree pollen allergy. Double-blind, placebo-controlled study with a biologically standardised extract of three pollens (alder, birch and hazel) administered by a rush schedule.

Allergol Immunopathol (Madr). 2001 Jul-Aug;29(4):103-10.



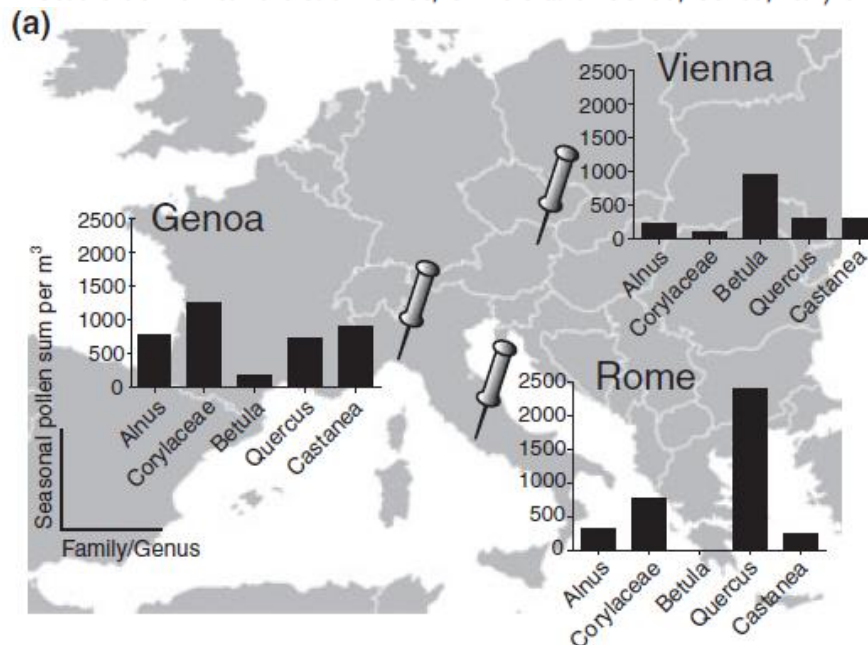
Bet v 1-like pollen allergens of multiple *Fagales* species can sensitize atopic individuals

M. Hauser^{1,*}, C. Asam^{1,*}, M. Himly¹, P. Palazzo², S. Voltolini³, C. Montanari⁴, P. Briza⁵, M. L. Bernardi², A. Mari², F. Ferreira¹ and M. Wallner¹

¹Christian Doppler Laboratory for Allergy Diagnosis and Therapy, Department of Molecular Biology, University of Salzburg, Salzburg, Austria, ²Center for Molecular Allergology, IDI-IRCCS, Rome, Italy, ³UOC Allergologia, Azienda Ospedaliera Universitaria San Martino, Genoa, Italy, ⁴Dipartimento per lo Studio del Territorio e sue Risorse, Università di Genoa, Genoa, Italy and ⁵Department of Molecular Biology, University of Salzburg, Salzburg, Austria

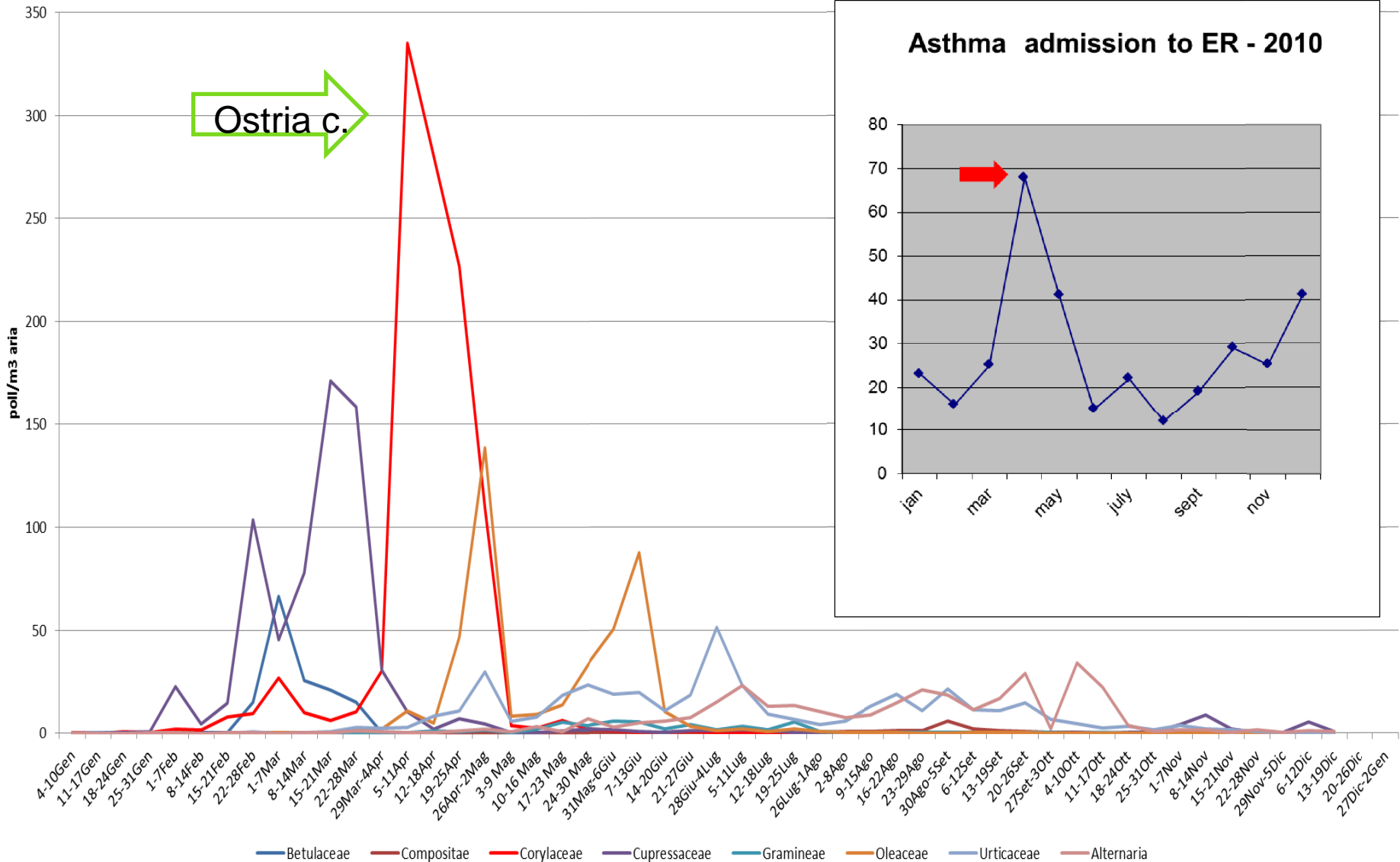
Clinical & Experimental Allergy, 1–11

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Conclusions and Clinical Relevance The data suggest that Bet v 1-like allergens of the *Betuloideae* and *Coryloideae* subfamily might have the potential to induce IgE antibodies with different specificities, while allergic reactions towards *Fagaceae* allergens are the result of IgE cross-reactivity.

VALUTAZIONE DEL POSSIBILE RUOLO DEI POLLINI DI *OSTRYA CARPINIFOLIA* COME CAUSA DI ASMA STAGIONALE



ORIGINAL RESEARCH

Short-term effects of airborne pollens on asthma attacks as seen by general practitioners in the Greater Paris area, 2003-2007

Bich Tram Huynh^a, Séverine Tual^a, Clément Turbelin^b, Camille Pelat^b, Lorenzo Cecchi^c, Gennaro D'Amato^d, Thierry Blanchon^b, *Isabella Annesi-Maesano^a

^a INSERM and UPMC Paris VI EPAR, Medical School Saint-Antoine, Paris, France

^b INSERM and UPMC Paris VI, Paris, France

^c University of Florence, Florence, Italy

^d Ospedale Cardarelli, Naples, Italy

Table 3. Adjusted relative risks (RR) and 95% confidence intervals (CI) for GP consultations for asthma attacks for an inter-quartile range (IQR) increase in pollen counts, Paris and surrounding area, 2003-7.

	IQR (grains/m ³)	Model with one pollen			Model adjusted for all types of pollens		
		RR	IC	p value	RR	IC	p value
<i>Betula</i>	16.3	1.073	1.038-1.109	<0.0001	1.037	1.002-1.073	0.0396
<i>Fraxinus</i>	7.1	1.054	1.008-1.102	0.0195	0.987	0.944-1.032	0.5738
<i>Poaceae</i>	17.6	1.700	1.469-1.968	<0.0001	1.540	1.331-1.790	<0.0001

Review article

Thunderstorm-asthma and pollen allergy

which can penetrate deep into lower airways. In other words, there is evidence that under wet conditions or during thunderstorms, pollen grains may, after rupture by osmotic shock, release into the atmosphere part of their content, including respirable, allergen-carrying cytoplasmic starch granules (0.5–2.5 μm) or other paucimicronic components that can reach lower airways inducing asthma reactions in pollinosis patients. The thunderstorm-asthma outbreaks are



Figure 1. *Parietaria* pollen bursting under osmotic shock with release of cytoplasmic fragments carrying allergens.

Thunderstorm-related asthma epidemic owing to *Olea Europaea* pollen sensitization

L. Losappio, E. Heffler, F. Contento, C. Cannito, G. Rolla

Allergy, Volume 66, Issue 11, November 2011

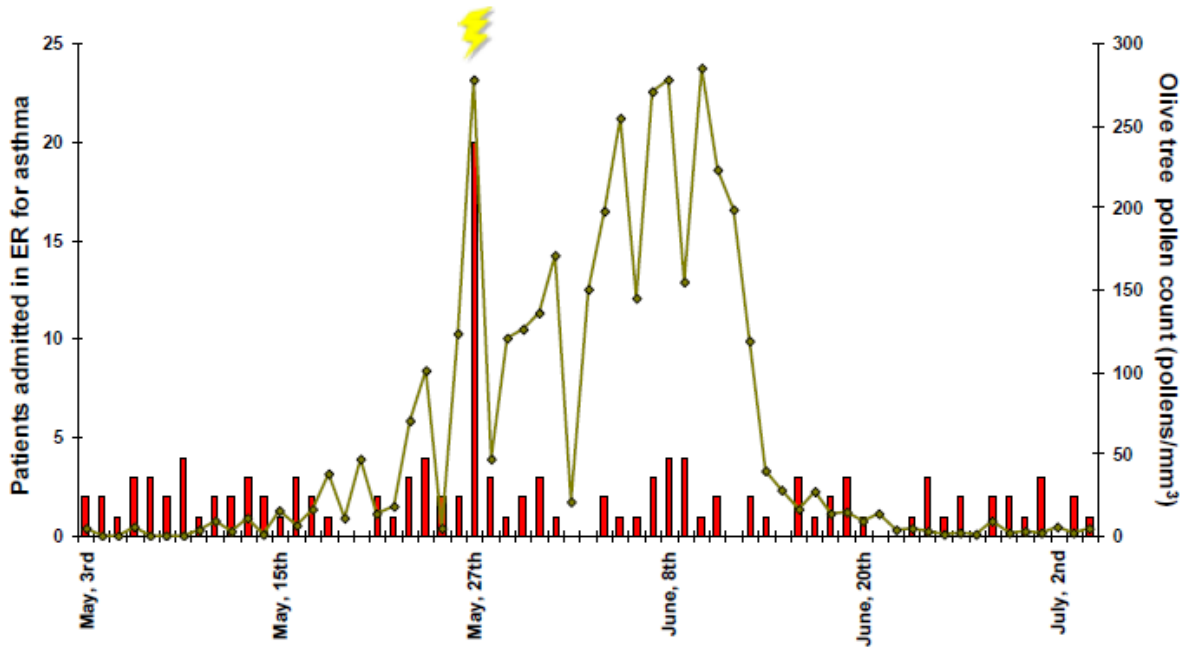


Figure 1 number of patients admitted to emergency department for asthma between 3 May and 4 July 2010 and olive tree pollen count in the same period. The thunderbolt-arrow indicates the day of thunderstorm.

This is the first report of thunderstorm-related asthma owing to olive tree pollen sensitization. Allergic patients should be informed of the risk of severe asthma attack during thunderstorms.

The seasonal symptoms of hyposensitized and untreated hay fever patients in relation to birch pollen counts: correlations with nasal sensitivity, prick tests and RAST

M. VIANDER and A. KOIVIKKO

Clinical Allergy, 1978, Volume 8, pages 387-396

*Departments of Medical Microbiology and Pediatrics,
University of Turku, Turku, Finland*

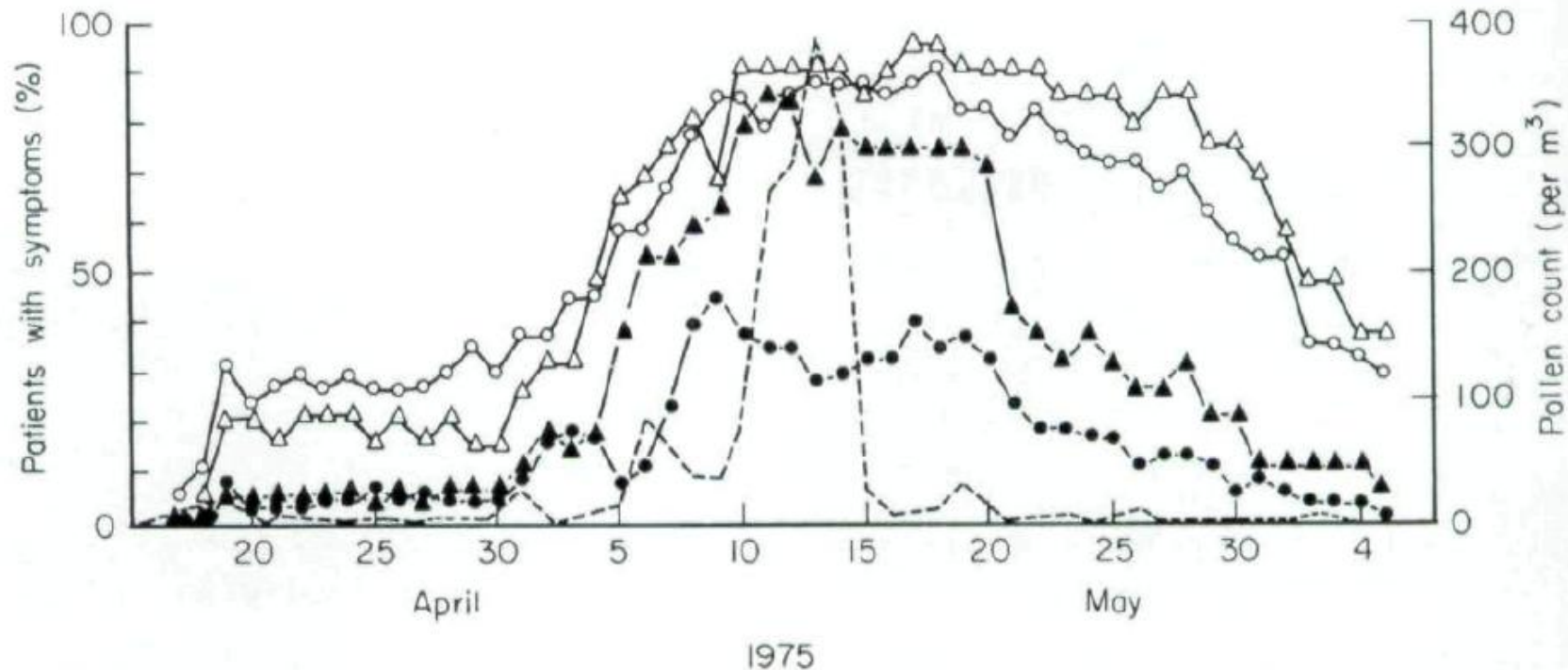
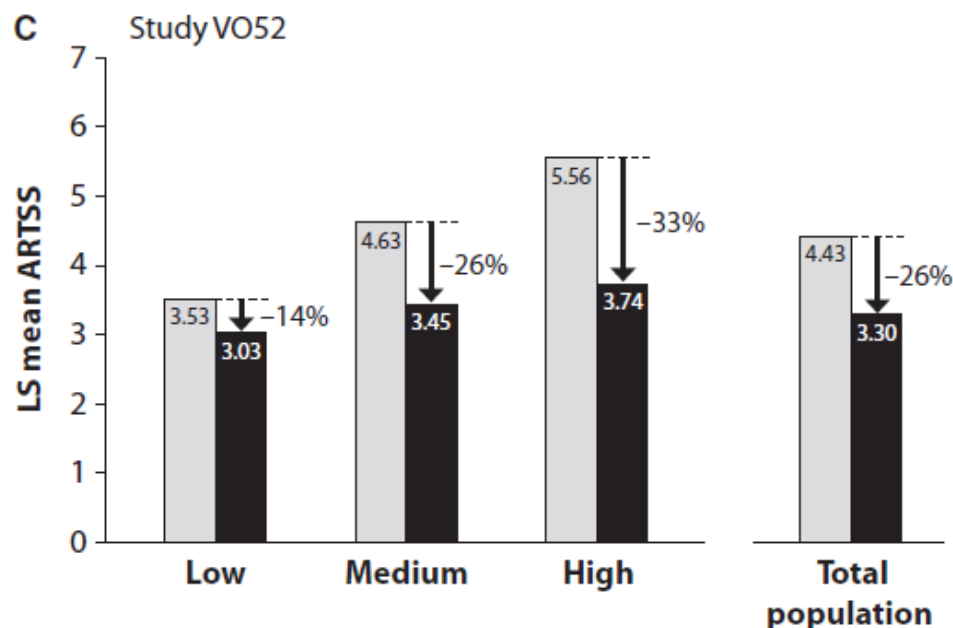


Fig. 3. Percentage of hyposensitized and control patients with symptoms in relation to the daily pollen counts in 1975. (○) and (△) All hyposensitized and control patients with symptoms; (●) and (▲) hyposensitized and control patients with severe symptoms (i.e. symptom score 3 or more); (---) daily birch pollen count.

Analysis of allergen immunotherapy studies shows increased clinical efficacy in highly symptomatic patients

P. Howarth¹, H.-J. Malling², M. Molimard³ & P. Devillier⁴

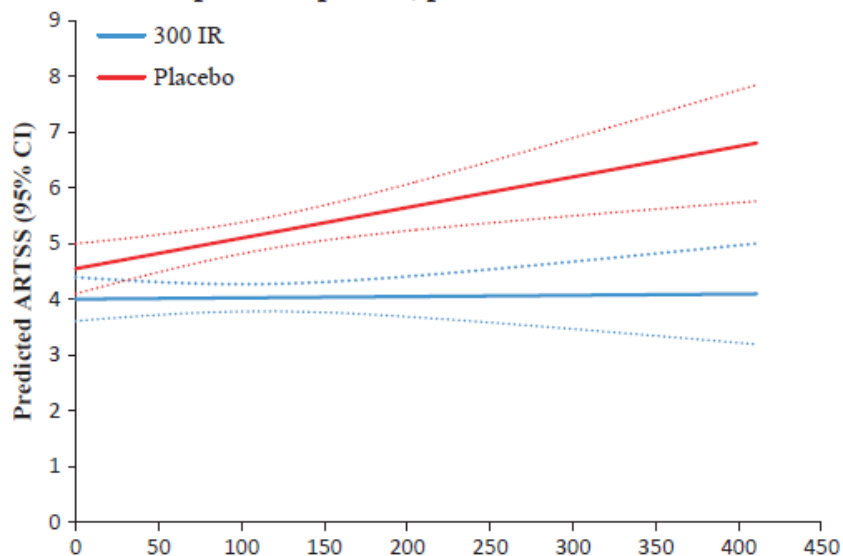
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Figure 1 Treatment effect increases with greater disease severity – Average Rhinoconjunctivitis Total Symptom Score by tertiles in three clinical studies. ARTSS, Average Rhinoconjunctivitis Total Symptom Score; IR, index of reactivity.

VO34.04-pollen exposure, placebo and 300 IR – ARTSS



Daily mean RTSS and grass pollen counts (2005)

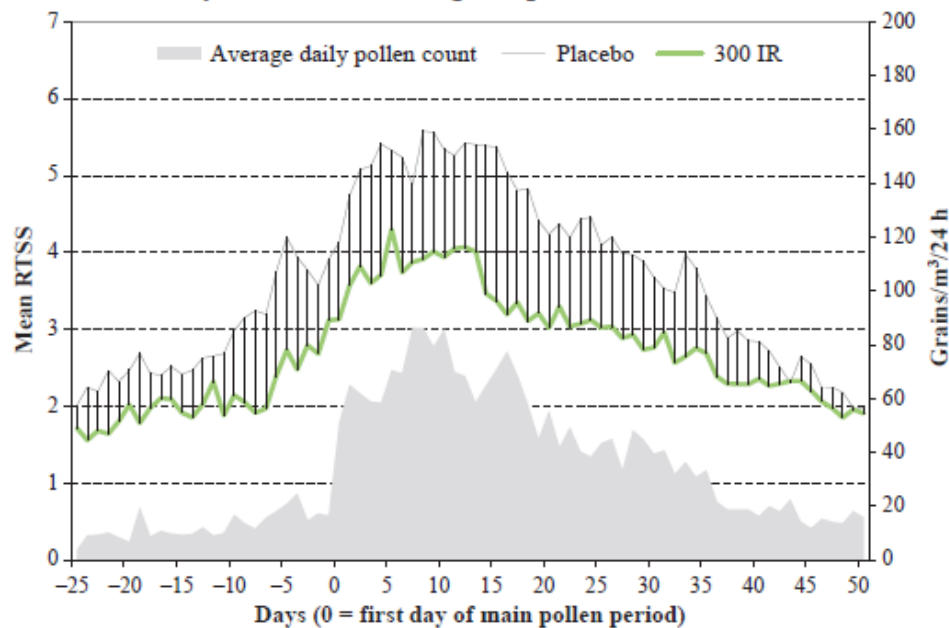


Figure 4 Daily mean symptom scores and grass pollen counts (data from study VO34). IR, index of reactivity; RTSS, Rhinoconjunctivitis Total Symptom Score.

“Aerobiology of pollinosis”

William R. Solomon. JACI 1984

.....*nonostante oltre un secolo di studi sempre piu' attivi, i dati pollinici continuano ad offrire:*

1. Indizi su potenziali agenti causali in popolazioni non ancora studiate
2. Evidenze sui trend di esposizione delle popolazioni già in possesso di dati
3. Dati su intense esposizioni per brevi periodi utili per correlazioni cliniche e per uso investigativo

Projections of the effects of climate change on allergic asthma: the contribution of aerobiology

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Abstract

Climate change is unequivocal and represents a possible threat for patients affected by allergic conditions. It has already had an impact on living organisms, including plants and fungi with current scenarios projecting further effects by the end of the century. Over the last three decades, studies have shown changes in production, dispersion and allergen content of pollen and spores, which may be region- and species-specific. In addition, these changes may have been influenced by urban air pollutants interacting directly with pollen. Data suggest an increasing effect of aero-allergens on allergic patients over this period, which may also imply a greater likelihood of the development of an allergic respiratory disease in sensitized subjects and exacerbation of symptomatic patients. There are a number of limitations that make predictions uncertain, and further and specifically designed studies are needed to clarify current effects and future scenarios. We recommend: More stress on pollen/spore exposure in the diagnosis and treatment guidelines of respiratory and allergic diseases; collection of aerobiological data in a structured way at the European level; creation, promotion and support of multidisciplinary research teams in this area; lobbying the European Union and other funders to finance this research.

Utilità dei dati aerobiologici nella prevenzione

- **Prescrizione terapia farmacologica nei tempi corretti**

- **Educazione del paziente all'uso dei dati pollinici e alla gestione della terapia**

- **Campagne di Informazione sui rischi di Autorità sanitarie locali , Medici di Medicina Generale, strutture d'emergenza**

SCELTA DEL VERDE PUBBLICO E MANUTENZIONE

“Verde pubblico e malattie allergiche”

**Gruppo di studio della Società Italiana di
Allergologia – A. Passaleva, G. Rolla**

It J Allergy Clin Immunol 2010;20:117-145

(monografia)



GRAZIE PER L'ATTENZIONE