

Allergy, Asthma and the Athlete

Sergio Bonini

*Professor of Medicine
Second University of Naples
Institute of Translational Pharmacology
Italian National Research, Rome
se.bonini@gmail.com*

Cancun December 7, 2011

The GA2LEN Olympic Study Study Protocol

- **History**
 - **Questionnaires (AQUA, SF36, QUAQUA)**
- **Physical examination**
- **Skin tests**
- **Pulmonary function tests**
 - **Spirometry, Broncho-dilator and –constrictor (methacholine, exercise, EVH, mannitol) tests**
- **eNO and exhaled breath condensate**
- **Serum**
- **Urines**

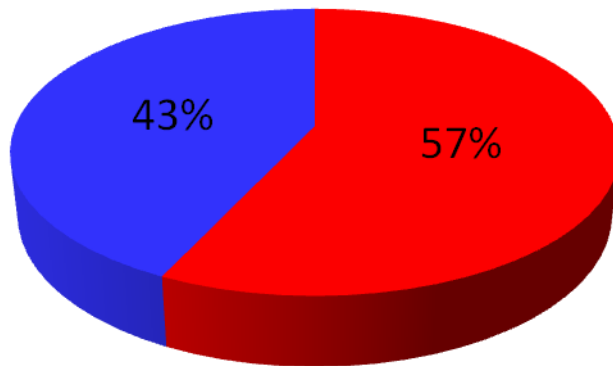
The GA2LEN Olympic Study

Study population by Country

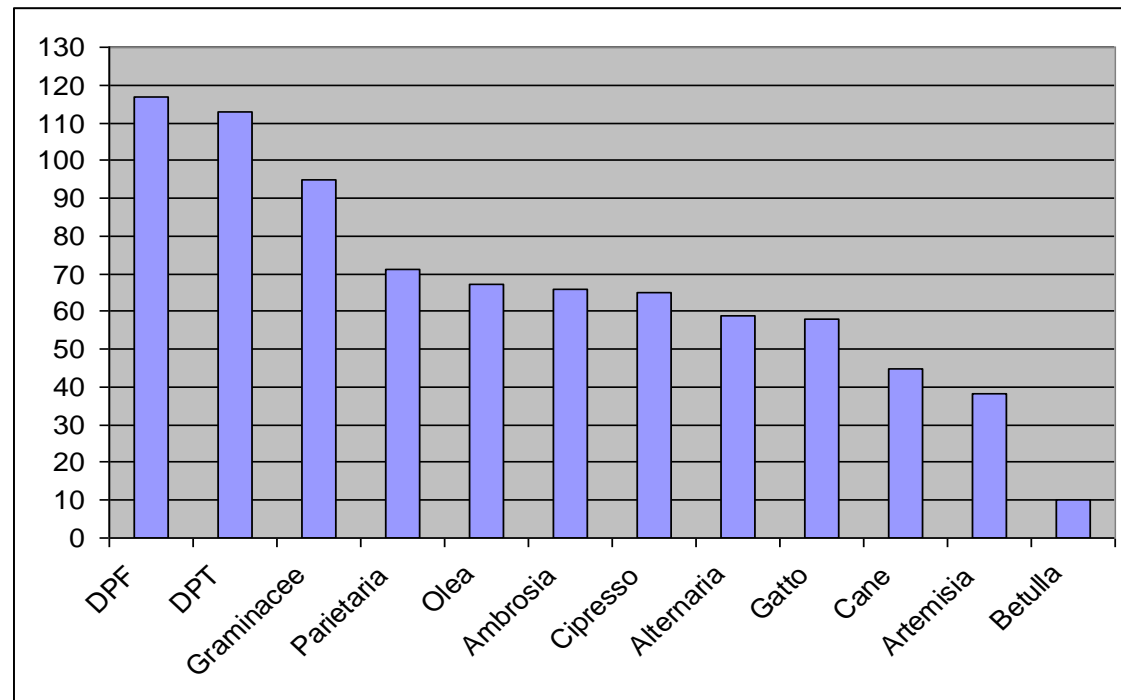
Country	Athletes participating in the Olympics	Athletes not qualifying for the Olympics	Total
Denmark	59	17	76
Finland	25	3	28
Greece	56	47	103
Germany	337	0	337
Norway	59	22	81
Poland	222	0	222
Portugal	61	0	61
Spain	176	0	176
Italy	208	227	435
Total	1203	316	1519

The Olympic Study

Sensitizations



- Skin test + athletes
- Skin test - athletes



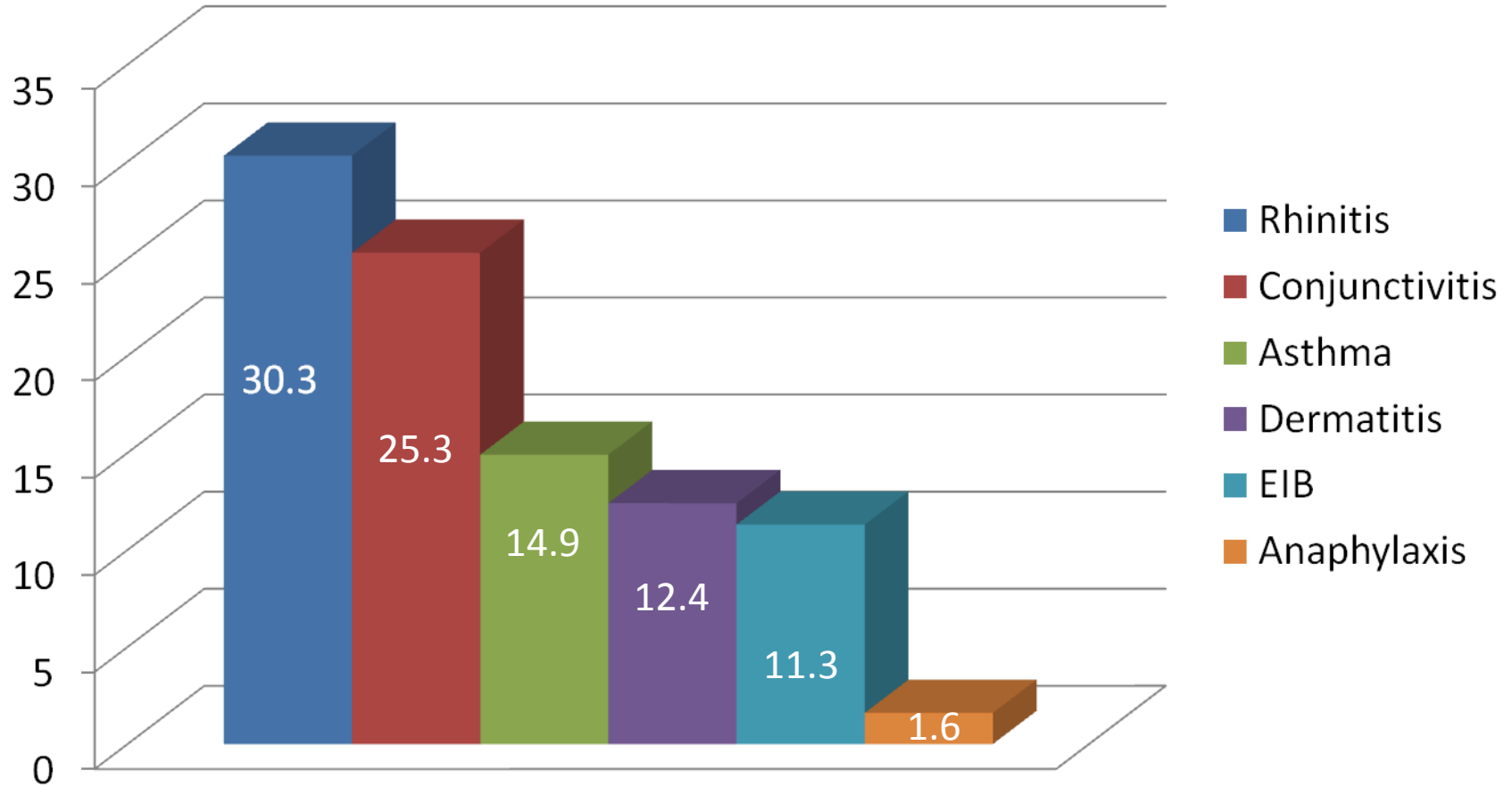


- Sensitization 32.6%



- Sensitization 56.5%
in 84.4% to multiple
allergens

The Olympic Study



One in three had respiratory complaints

Cross sectional; n=1662 athletes qualified for the 2008 Olympics

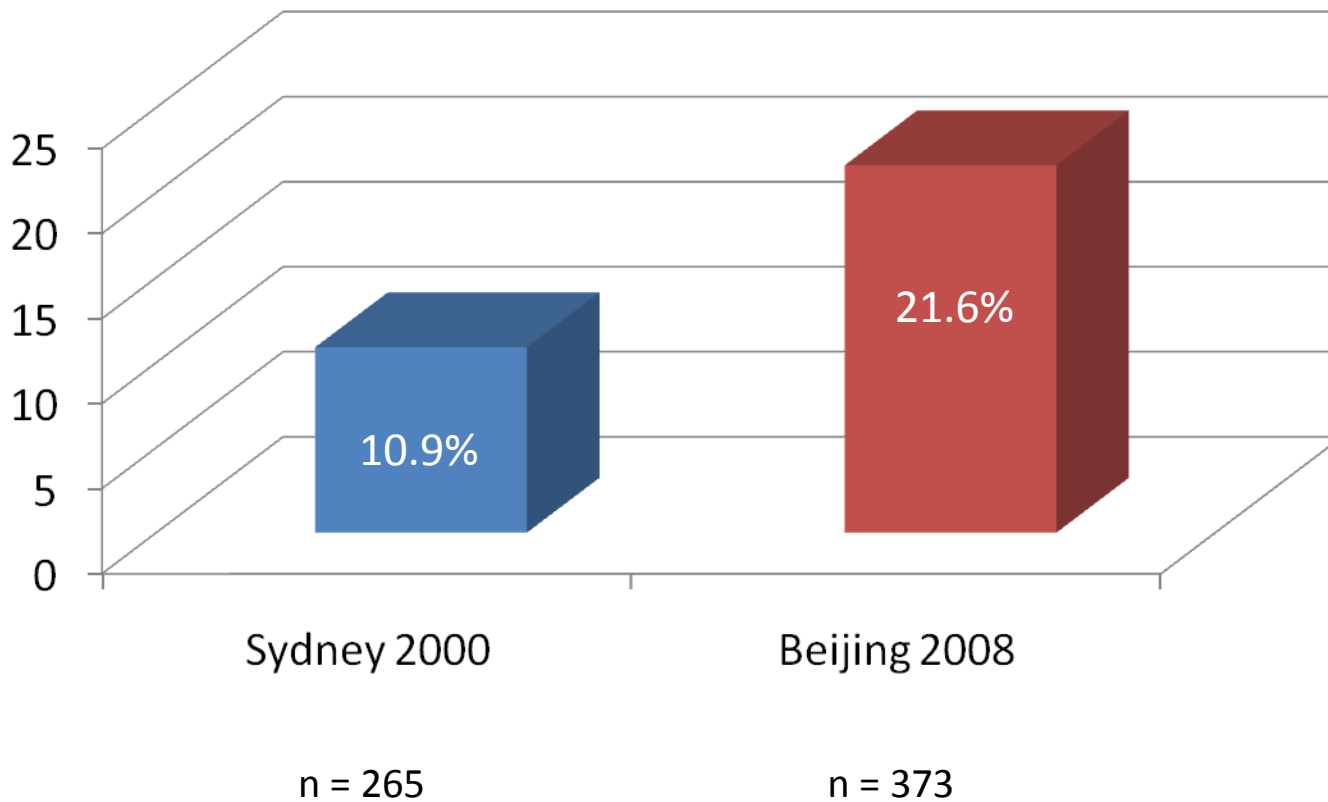
<i>Country</i>	<i>Chest tightness</i>	<i>Shortness of breath</i>	<i>Allergic rhinitis</i>	<i>Allergic conjunctivitis</i>	<i>Atopic eczema</i>	<i>Anaphylaxis</i>
Norway	23 (30.6%)	35 (44.9%)	17 (21.5%)	5 (6.4%)	23 (29.5%)	6 (7.8%)
Denmark	41 (56.2%)	41 (56.2%)	20 (27.4%)	9 (12.3%)	21 (28.8%)	11 (15.7%)
Finland	10 (40.0%)	12 (48.0%)	12(48%)	10 (40%)	10 (40%)	1 (4%)
Poland	37 (16.7%)	11 (23.4%)	60 (27%)	27 (12.2%)	59 (26.7%)	38 (17.2%)
Germany	74 (22.5%)	105 (31.9%)	68 (20.7%)	41 (12.5%)	154 (46.8%)	42 (12.8%)
Greece	36 (29.3%)	48 (38.7%)	26 (21.0%)	15 (12.1%)	45 (36.3%)	4 (3.2%)
Italy	37 (12.1%)	46 (15.1%)	46 (15.0%)	38 (12.5%)	61 (20%)	9 (2.9%)
Spain	57 (30.7%)	60 (34.1%)	46 (26.1%)	36 (20.5%)	51 (29%)	3 (1.7%)
Portugal	9 (20%)	14 (31.1%)	9 (20%)	2 (4.4%)	11 (24.4%)	2 (4.4%)
Total	324 (23.6%)	372 (30.9%)	304 (22.0%)	183 (13.3%)	435 (31.6%)	116 (8.5%)



The Olympic study



Asthma and exercise induced bronchospasm (EIB)



Prevalence of asthma among summer sports athletes

Athlete group (n)	Method	Prevalence %	Reference
Australian 1976 Olympic team (185)	Physical examination	9.7	Fitch KD, 1984 ¹⁷
Australian 1980 Olympic team (106)	Physical examination	8.5	Fitch KD, 1984 ¹⁷
US 1984 Olympic team (597)	Questionnaire, treadmill exercise test in selected athletes	4.3	<u>Voy RO</u> , 1984 ¹⁸
1986 Football players from University of Iowa (156)	Questionnaire, methacholine challenge	11.5	<u>Weiler et al.</u> , 1986 ¹⁹
Swiss athletes from various sport events (2060)	Questionnaire	3.7	<u>Helbling and Muller</u> , 1991 ³
Spanish 1982 Olympic team (495)	Questionnaire	4.4	<u>Drobic F</u> , 1994 ²⁰
Runners from Finnish national team (103)	Questionnaire	15.5	<u>Tikkanen and Helenius</u> , 1994 ²¹
Swimmers from United States (738)	Questionnaire	13.4	<u>Potts J</u> , 1996 ⁵
US Track and Field Championship games (73)	Exercise test (competition)	15.1	<u>Schoene RB et al.</u> , 1997 ²²
Track and Field athletes, swimmers (162)	Questionnaire, spirometry, histamine challenge	22.8	<u>Helenius et al.</u> , 1998 ²³
US 1996 Olympic team (699)	Questionnaire	15.3	<u>Weiler et al.</u> , 1998 ⁶
Australian 2000 Olympic team (214)	Questionnaire, skin test	21.9	<u>Katellaris et al.</u> , 2000 ⁷
Italian 2000 Pre-Olympic team (265)	Questionnaire, skin test, spirometry	10.9	<u>Lapucci et al.</u> , 2003 ¹⁰

Modified from Helenius and Hahtela, 2000⁸

Prevalence of asthma among winter sports athletes

<u>Athlete group (n)</u>	<u>Method</u>	<u>Prevalence %</u>	<u>Reference</u>
Cross-country skiers (42)	Questionnaire, <u>spirometry</u> , <u>methacholine challenge</u>	54.8	<u>Larsson et al., 1993</u> ²⁵
Cross-country skiers (171)	Questionnaire, <u>spirometry</u> , <u>methacholine challenge</u>	12 (Norway) 42 (Sweden)	<u>Sue-Chu et al., 1996</u> ²⁶
Figure <u>skaters</u>	Exercise test	35 (exercise-induced <u>bronchospasm</u>)	<u>Mannix et al., 1996</u> ²⁷
Ice hockey players	Questionnaire, <u>spirometry</u> , <u>methacholine challenge</u> , exercise test	19.2 11.5 (exercise-induced <u>bronchospasm</u>)	<u>Leuppi et al., 1998</u> ²⁸
US 1998 winter Olympic team (196)	Questionnaire	21.9 60.7 (cross-country, etc.) 24 (alpine, etc.) 2.8 (<u>bobsled</u> , etc.)	<u>Weiler et al., 2000</u> ⁷
US 1998 winter Olympic team	Exercise challenge, <u>spirometry</u>	23 (all, exercise-induced <u>bronchospams</u>) 50 (cross-country)	<u>Wilber et al., 2000</u> ²⁹
Ice hockey players	Questionnaire, <u>spirometry</u> , histamine challenge	22 (total <u>asthma</u>) 13 (<u>current asthma</u>)	<u>Lumme et al., 2003</u> ³⁰

Prevalence of allergic rhinitis in athletes

16.8%

Helbling et al. 1991

29.0%

Katelaris et al. 2000

25.3%

Bonini et al. 2003

30.3%

Bonini et al. 2008

Allergic skin diseases

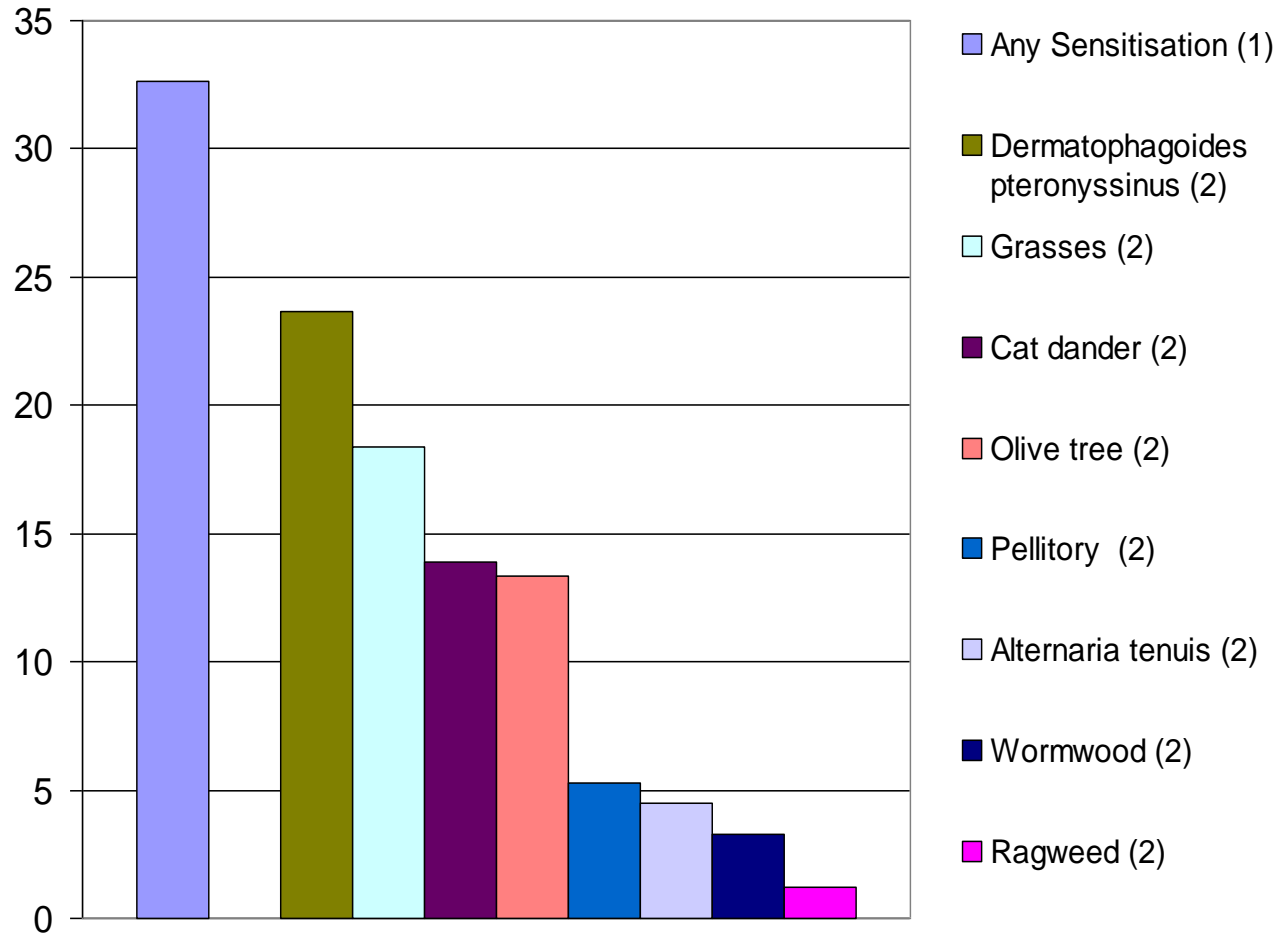
- **Exercise-induced urticaria**
(cold, aquagenic, solar, pressure)
- **Contact dermatitis**
(from rubber masks, dresses, instruments)

Exercise-induced anaphylaxis

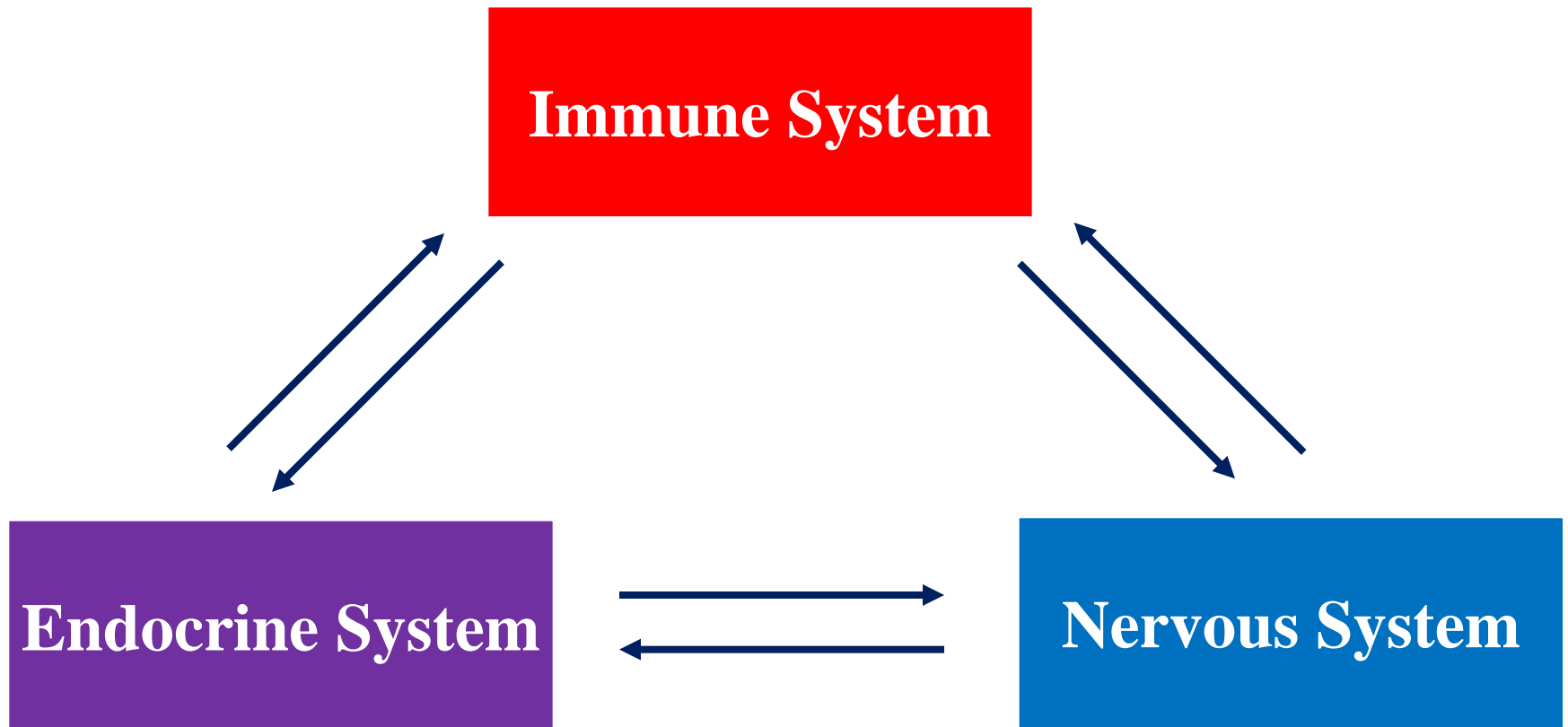
- **Often associated with food allergy**
- **Consider allergens contaminating food**
- **Consider in polysensitized subjects cross-reacting or pan-allergens (PR-10 proteins, profilins, tropomyosins,etc) or molecular allergens potentially responsible for severe allergic reactions (Ara h 1,2,3; Pru p 3; Cor a 8)**

Why Allergy and Asthma
are so frequent in athletes ?

Allergens responsible for sensitisation

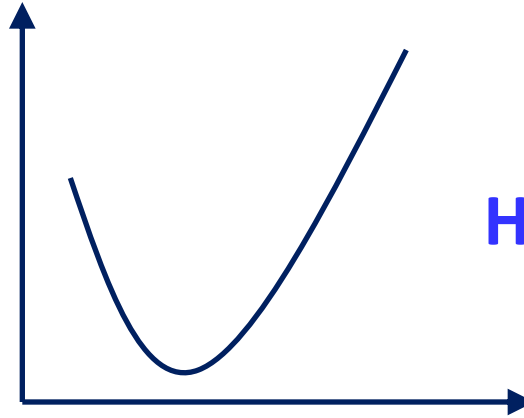


Physical exercise induces a neuro-endocrine-immune adaptative response aimed at maintaining homeostasy



Physical exercise

Risk of infections



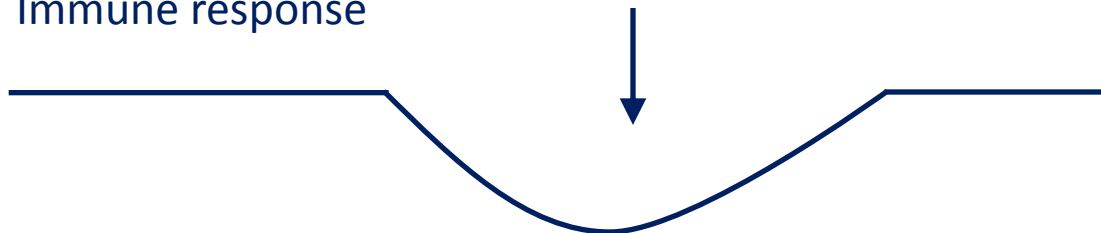
Hook Hypothesis

Physical exercise

Overtraining

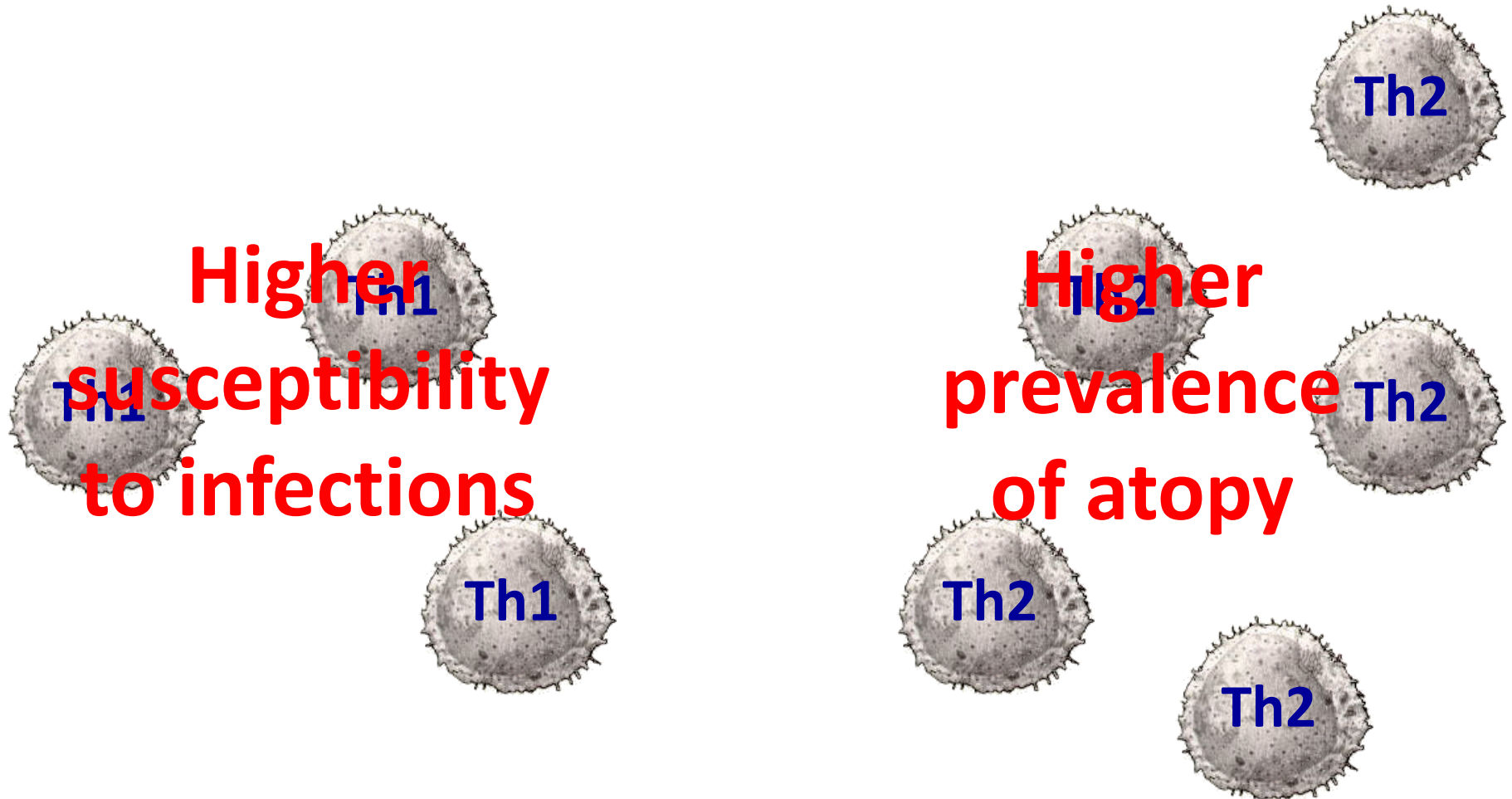
Open Window Hypothesis

Immune response



Transient immunodeficiency

Effect on T helper sub-populations balance



Infectious diseases

AIDA study: Allergy and Infectious Diseases in Athletes

- 265 pre-Olympic athletes
- 3 or more than 3 URTI episodes in the last 12 months in 15.9%
- More than 1 Herpes labialis episode in the last 12 months in 12.1%
- Decreased number of CD3+ lymphocytes in 17.0% of athletes with a preferential reduction of CD4+ subpopulation (40,7+/-8,2), well related to clinical picture

Cytokine	A vsCTRL	AA vs NAA
IL-1ra	↓ < 0,0001	↑ NS (0,9280)
IL-4	↓ < 0,05	↑ NS (0,0784)
IL-6	↓ < 0,0001	↑ NS (0,1882)
IL-7	↓ < 0,0001	↑ NS (0,3663)
IL-8	↓ < 0,0001	↑ NS (0,9875)
IL-12	↓ < 0,0001	↑ NS (0,9093)
IL-10	↓ < 0,0001	↑ NS (0,1366)
IL-13	NS (0,1659)	NS (0,9436)
IL-17	↓ < 0,0001	↑ NS (0,3984)
Eotaxin	↓ < 0,0001	↑ NS (0,9749)
IFN-gamma	↓ < 0,0001	↑ NS (0,8752)
IP-10	↓ < 0,0001	↑ NS (0,5584)
MCP-1	↓ < 0,0001	↑ NS (0,5427)
MIP-1alfa	NS (0,0852)	NS (0,9187)
MIP-1beta	↓ < 0,0001	↑ NS (0,2979)
RANTES	↓ < 0,05	↑ NS (0,8690)

Cytokine serum profile in allergic and non-allergic top athletes

- AA = 41; NAA = 51; CTRL = 49
- Luminex assay
- For all cytokines measured, apart from IL-13 and MIP-1a, serum levels in athletes were significantly lower than in controls
- No differences were observed between allergic and non-allergic athletes
- The median value of the IFN γ /IL-4 ratio was lower in athletes than in controls (33.0 vs. 37.9), particularly in the allergic ones (27.8)



Bonini M. et al.

Abs. presented to the 2011 AAAAI Congress

Physical exercise as a trigger on target organs

- Increased ventilation
- Nasal filter by-pass
- Climate condition (cold-dry air)
- Exposure to indoor and outdoor allergens
- Exposure to pollutants (O_3 , $PM_{2.5-10}$, NO_2 , SO_2)
- Exposure to irritants (chlorine)

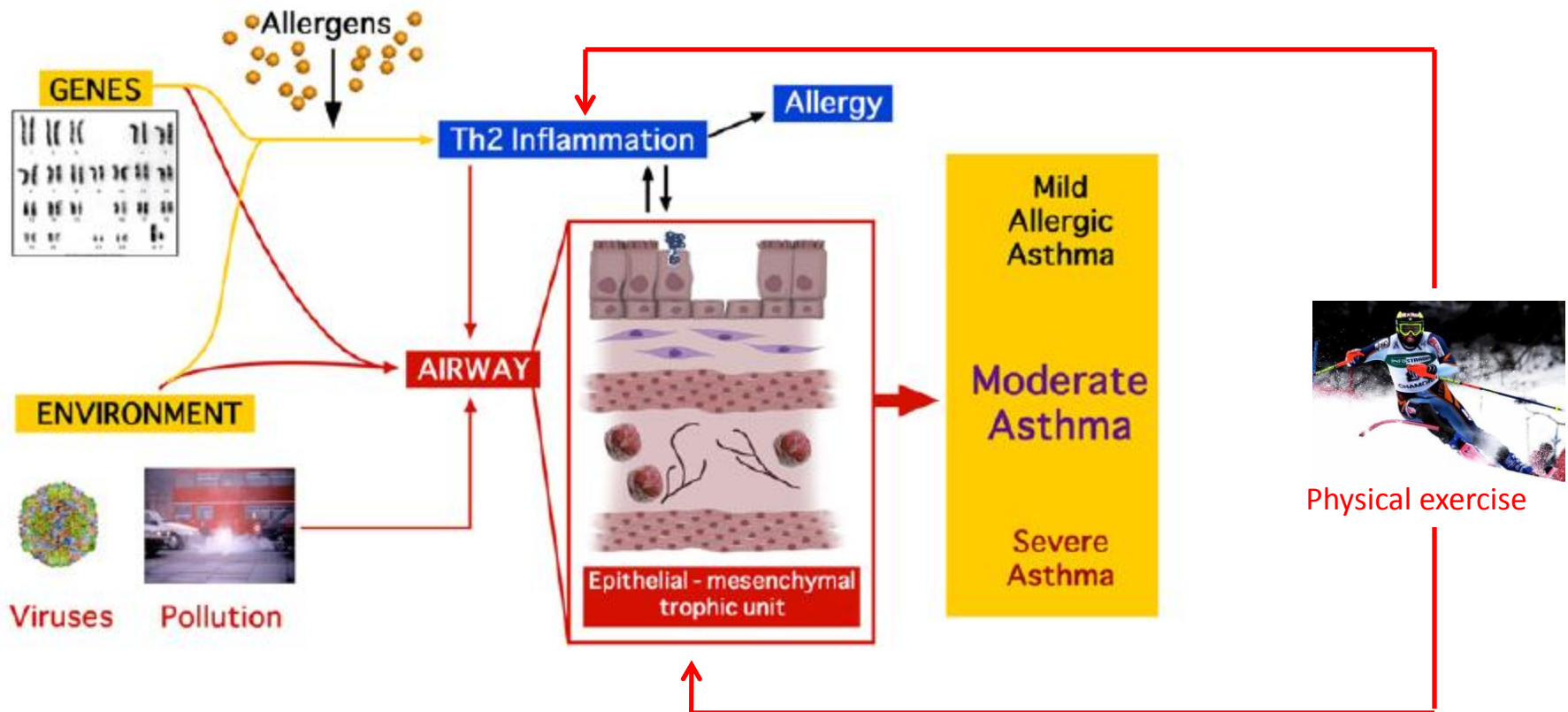
Current reviews of allergy and clinical immunology

(Supported by an unrestricted educational grant from Genentech, Inc. and Novartis Pharmaceuticals Corporation)

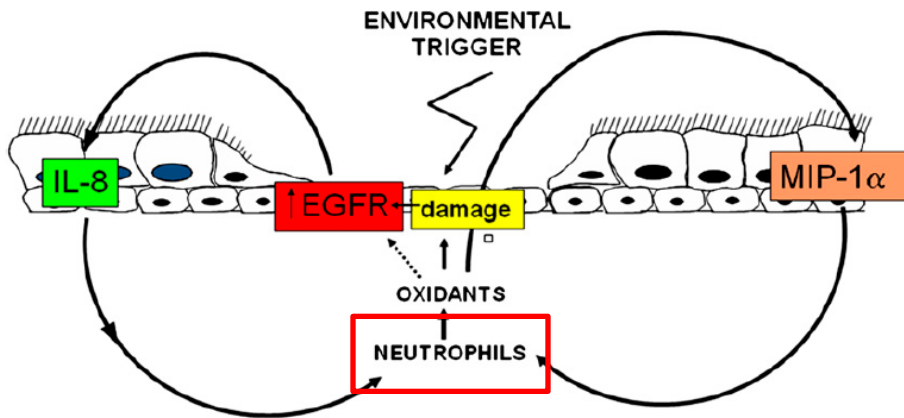
Series editors: Donald Y. M. Leung, MD, PhD, and Dennis K. Ledford, MD

Epithelium dysfunction in asthma

Stephen T. Holgate, MD, DSc *Southampton, United Kingdom*



Potential role of epithelium damage in EIB



The Role of the Airway Epithelium and its Interaction with Environmental Factors in Asthma Pathogenesis

Stephen T. Holgate¹, Graham Roberts¹, Hasan S. Arshad¹, Peter H. Howarth¹, and Donna E. Davies¹

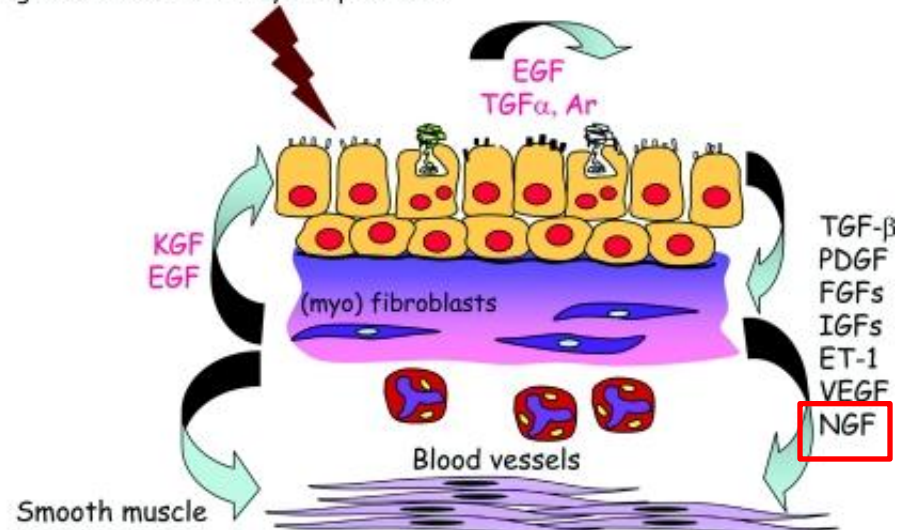
Proc Am Thorac Soc Vol 6, pp 655–659, 2009
 DOI: 10.1513/pats.200907-072DP
 Internet address: www.atsjournals.org

A new look at the pathogenesis of asthma

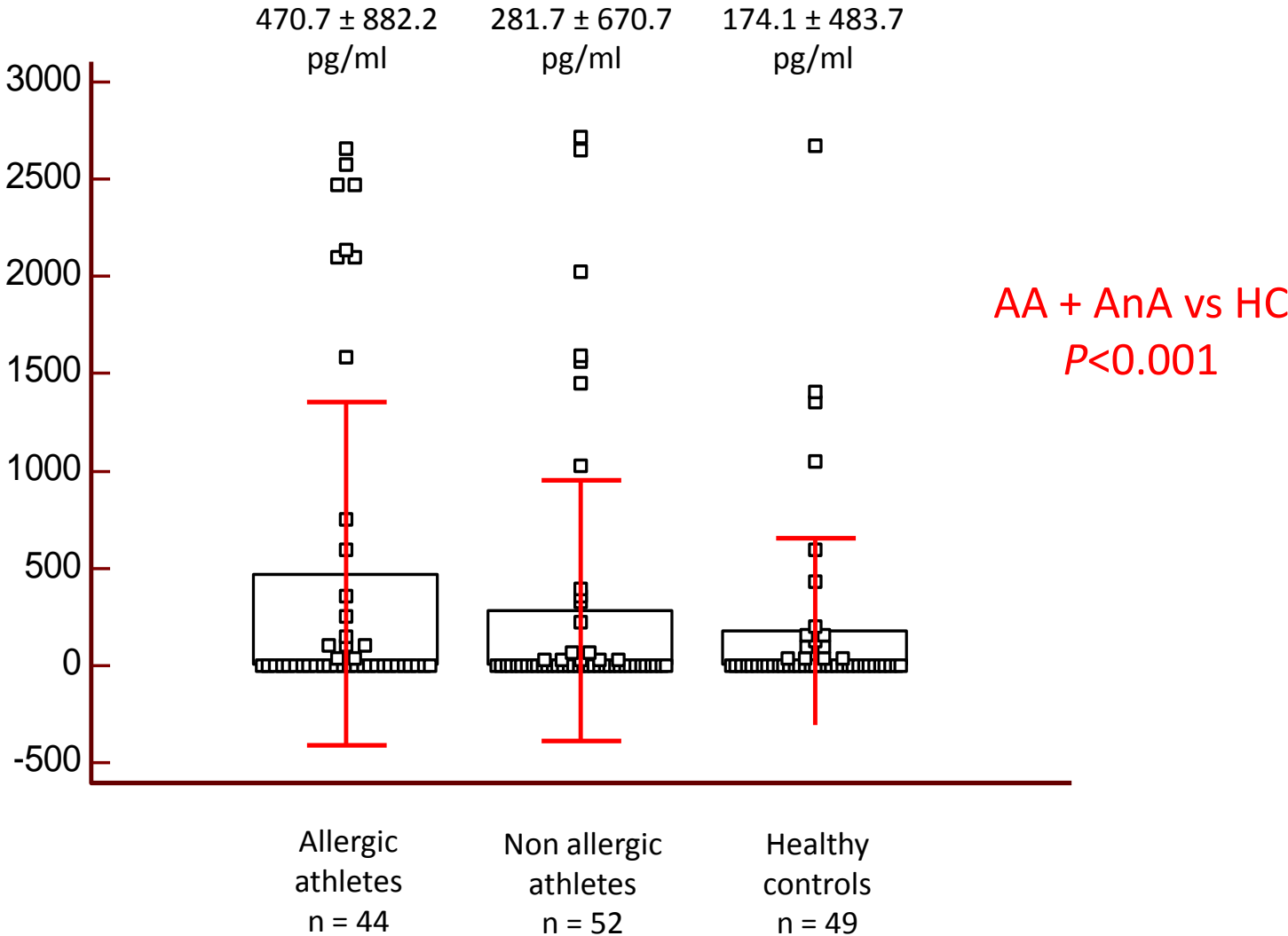
Stephen T. Holgate,^{*} Hasan S. Arshad,^{*} Graham C. Roberts,^{*} Peter H. Howarth,^{*} Philipp Thurner,[†] and Donna E. Davies^{*}

Clin Sci (Lond). 2009 December 23; 118(Pt 7): 439–450.

Increased susceptibility of epithelium to damage by environmental agents and inflammatory cell products

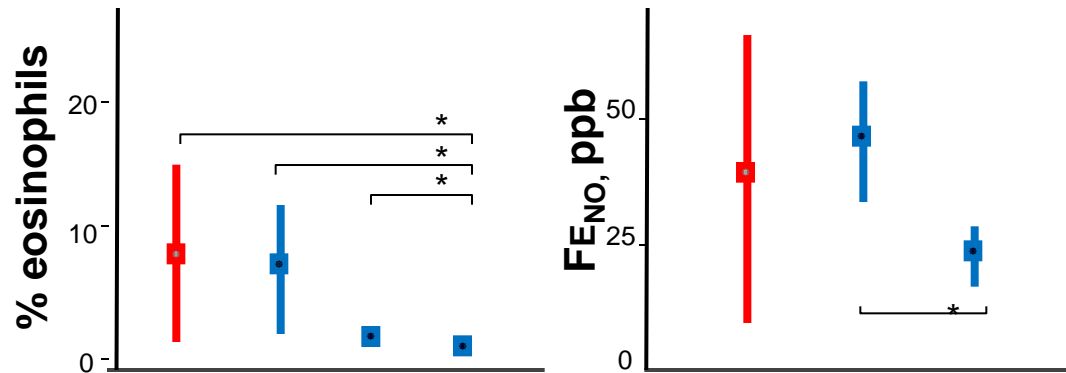


NGF serum levels in elite athletes

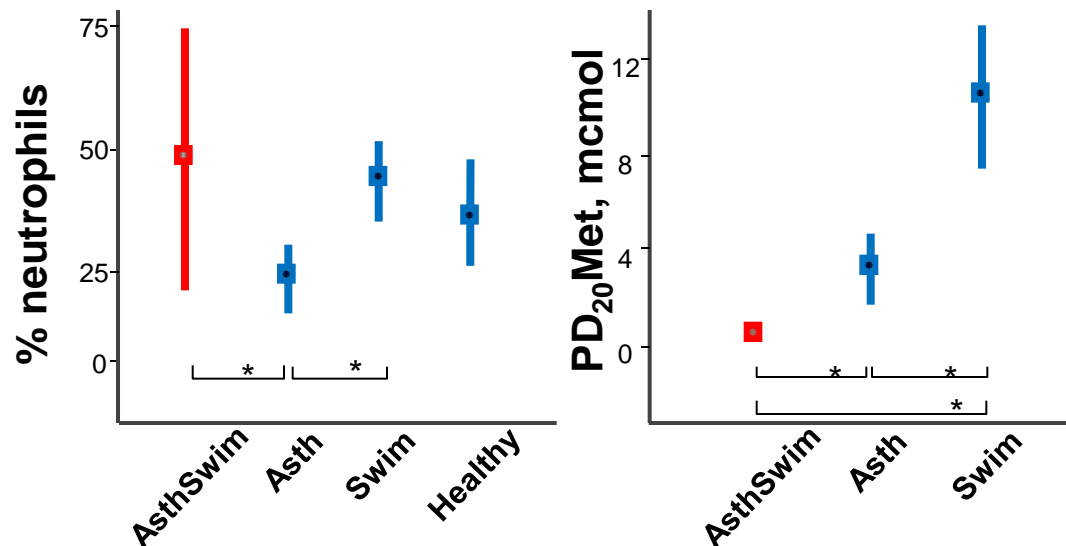


Airway inflammation in asthmatic competitive swimmers may result of mixed type effects

Sputum eosinophilia and increased FE_{NO} of the allergic inflammation



Sputum neutrophils and airway responsiveness of training/environment exposure





Allergic rhinitis in 16/40 (40.0%)

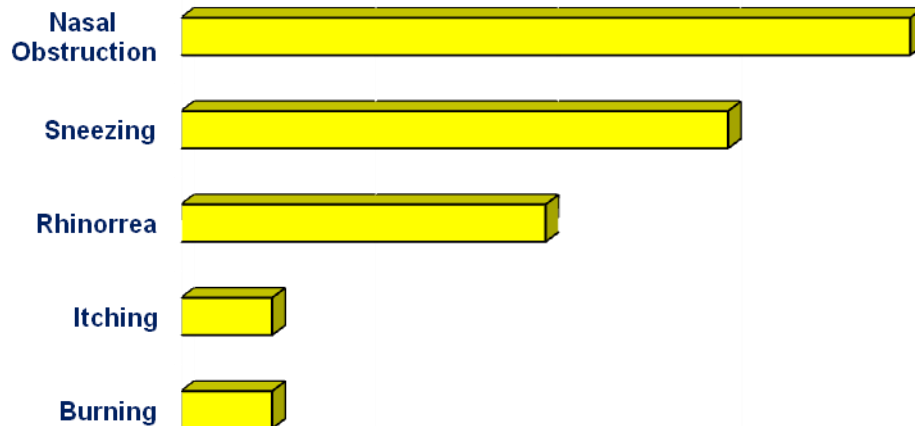
NARES in 2/40 (5.0%)

Infective rhinitis 2/40 (5.0%)

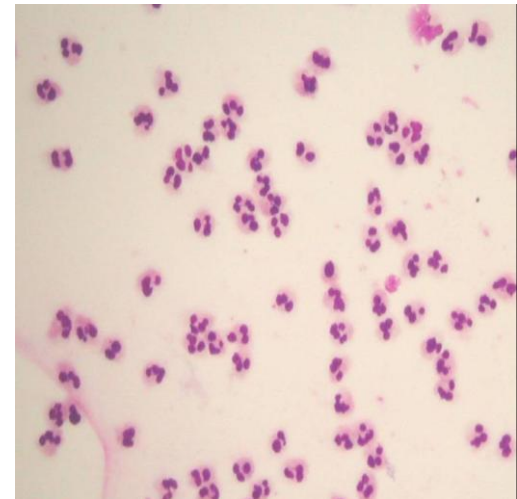
“Swimmer’s nose” in 20/40 (50.0%)

Negative Skin Prick-test

Prevaling symptoms



Neutrophilia



Diagnosis of allergy in athletes

AQUA[®]: Allergy Questionnaire for Athletes: Development and Validation

MATTEO BONINI^{1,10}, FULVIO BRAIDO^{1,10}, ILARIA BAIARDINI^{1,10}, STEFANO DEL GIACCO², CLAUDIA GRAMICCIONI^{3,10}, MASSIMO MANARA⁴, GIULIA TAGLIAPIETRA⁵, ANNA SCARDIGNO⁶, VITTORIO SARGENTINI⁷, MARIO BROZZI⁸, GUIDO RASI^{3,10}, and SERGIO BONINI^{3,9,10}

¹Department of Internal Medicine, University of Genoa, ITALY; ²Department of Medical Sciences, University of Cagliari, ITALY; ³Italian National Research Council, Institute of Neurobiology and Molecular Medicine (CNR-INMM, ARTOV), ITALY; ⁴F.C. Parma Calcio, Parma, ITALY; ⁵Brescia Calcio, Brescia, ITALY; ⁶Centro Studi di Medicina dello Sport, Università Cattolica del Sacro Cuore, Rome, ITALY; ⁷ASL Roma A, Rome, ITALY; ⁸A.S. Roma (RomaLab), Rome, ITALY; ⁹Department of Internal Medicine, Second University of Naples, ITALY; and ¹⁰Member of GA²LEN Unit, ITALY

ABSTRACT

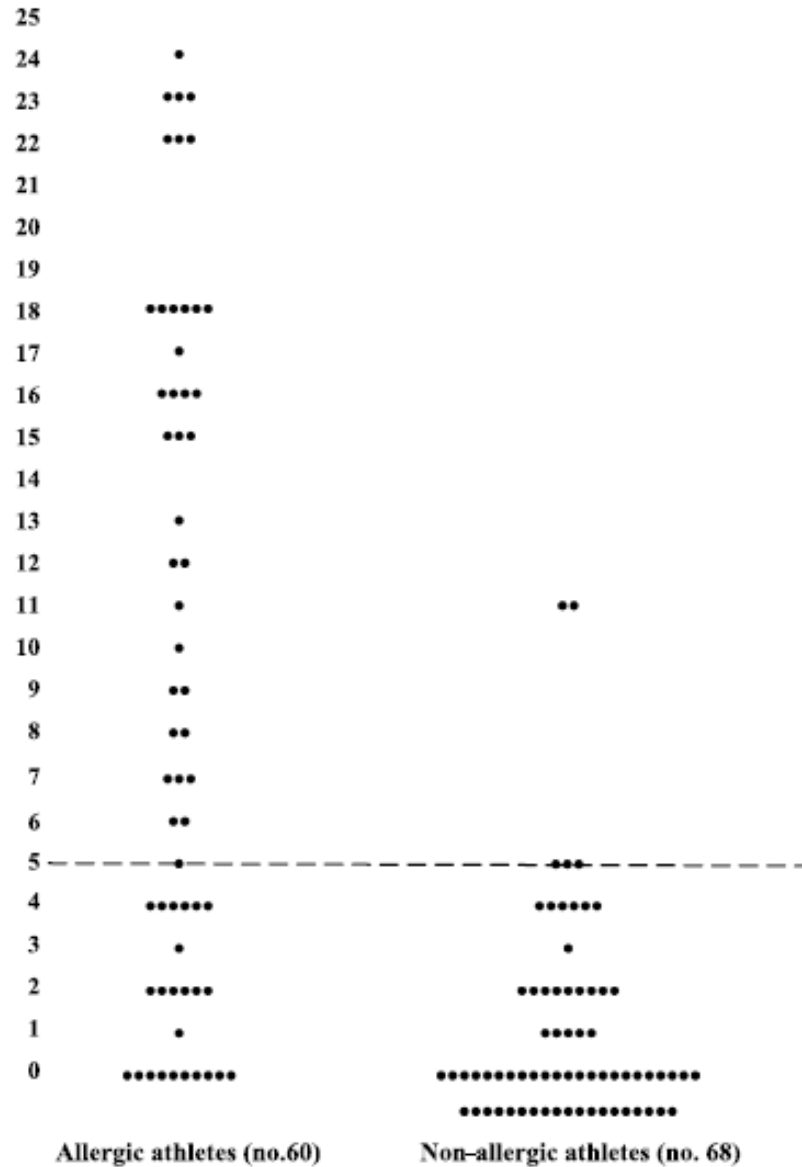
BONINI, M., F. BRAIDO, I. BAIARDINI, S. DEL GIACCO, C. GRAMICCIONI, M. MANARA, G. TAGLIAPIETRA, A. SCARDIGNO, V. SARGENTINI, M. BROZZI, G. RASI, and S. BONINI. AQUA[®]: Allergy Questionnaire for Athletes: Development and Validation. *Med. Sci. Sports Exerc.*, Vol. 41, No. 5, pp. 000–000, 2009. **Purpose:** Despite the high and increasing prevalence of allergic diseases in athletes, allergy diagnostics is not part of the routine medical examination in sports medicine. This study reports the development and validation of an easy and reliable questionnaire for screening allergy in athletes. **Methods:** AQUA[®] was derived from the European Community Respiratory Health Survey Questionnaire. On the basis of open interviews with team doctors, coaches, and athletes, questions were added about: the type, duration, and intensity of training; exercise-related allergic and infectious symptoms; social habits (smoking); drug and food supplements intake; antidoping regulations. The final version of the questionnaire, made of 25 selected questions, was validated in 128 professional soccer players who underwent accurate history taking, medical examination, skin prick testing, and/or specific IgE determination. On the basis of the correlation with objective allergy (positive skin tests to at least one allergen), questions were scored from 1 to 5 according to their positive likelihood ratio. **Results:** Skin tests (gold standard for validation) were positive in 46.8% of soccer players. Mean total AQUA[®] score was 9.4 ± 7.8 in allergic athletes versus 1.3 ± 2.3 in nonallergic athletes. A total AQUA[®] score of ≥ 5 was shown to have the best positive predictive value for allergy (0.94) with a specificity of 97.1% and a sensitivity of 58.3%. **Conclusions:** AQUA[®], produced in 10 European languages, is a validated, easy, and reliable tool for calling attention on the high prevalence of allergy in athletes. **Key Words:** SOCCER PLAYERS, SPORTS ALLERGY, EXERCISE-INDUCED ASTHMA, EXERCISE-INDUCED BRONCHOCONSTRICTION, UPPER RESPIRATORY TRACT INFECTIONS

AQUA

(Methodology)

- Derived from the ECRHS questionnaire
- On the basis of interviews with team doctors, coaches and athletes specific questions were added
- Preliminary administration to verify comprehensiveness and reproducibility
- Administration to 128 professional soccer players of 6 elite teams
- Validation against documented clinical allergy (Anamnesis, OE, Skin-prick-test and/or Phadiatop)
- Key-questions scored from 1 to 5 on the basis of their positive likelihood ratio

AQUA: total score



AQUA

(Results)

- A total score > 5 showed the best positive predictive value for allergy (0.93) with a specificity of 97.1% and a sensitivity of 58.3%.
- The questionnaire, translated in 10 languages was used in the framework of the GA2LEN Olympic Study
- The questionnaire, protected by copyright, is available on request (free for non commercial use)