Porto Biomed. J. 2016;1(4):127–128

PORTO BIOMEDICAL JOURNAL
WHERE SCIENCE MEETS KNOWLEDGE

Porto Biomedical Journal

http://www.portobiomedicaljournal.com/

EDITORIAL

Exercise, Asthma and the Olympics: A 2000-year-old tale

Stefano Del Giacco*

Department of Medical Sciences and Public Health, University of Cagliari, Italy

Rio 2016 Olympics – the increasingly familiar scenes of asthmatic athletes decorating their necks with gold, silver and bronze medals can be seen again. Asthmatic athletes (many of whom former "children who could not play sports due to their asthma") have made of this a tradition that goes back to the first century A.D.. Back then, the renowned Greek physician Araeteus the Cappadocian first described exercise-induced respiratory symptoms: "if from running, gymnastics, or any other work, breathing becomes difficult, it is called *Asthma*".[1] Fast forward 20 centuries, in 1962 RS Jones *et al.* described for the first time the effects of exercise on ventilatory function in children, and introduced systematic exercise tests.[2]

Whilst we await data from this year's Olympic games, figures from the previous summer and winter Olympic Games show that, believe it or not, asthmatics have won more medals than their non-asthmatic peers, demonstrating beyond doubt that asthmatics have no limitations in sports practice if they receive adequate medical treatment.[3]

The general public and health care professionals are gaining interest in the potential health implications of asthma and allergy in top athletes. When present, the latter may affect their performance and achievements. However, the impact of asthma on sport and exercise goes nowadays beyond top athletes and it is increasingly expanding to the general population practicing exercise and sports at all levels.

Exercise, in general, is a concern for asthmatics. It has been claimed that up to 75-80% of asthma patients without an inhaled anti-inflammatory therapy may face asthmatic symptoms provoked by exercise. However, subjects without a previous asthma diagnosis may also experience the same problems. This is called "Exercise-Induced Asthma" (EIA). The terms "Exercise-Induced Asthma" and "Exercise-Induced Bronchoconstriction" (EIB) are often used interchangeably as synonyms. A consensus between the major American Societies of Allergy, Asthma and Immunology used the term "EIB with Asthma" to indicate EIB with clinical symptoms of Asthma and "EIB without asthma" to indicate airflow obstruction without clinical asthma symptoms. The European Academy of Allergy and Clinical Immunology (EAACI), together with the European Respiratory Society (ERS) agreed to use EIA to indicate symptoms of asthma after heavy exercise and EIB for a reduction in lung function occurring after heavy exercise as seen in a standardized exercise test, but without clinical symptoms of asthma. A glance in PubMed shows that EIA and EIB are areas of great interest to scientists, with more than 3,500 studies trying to complete the jigsaw of elements that make up this condition.

Fifty years ago, McNeill and collaborators attempted to explain the central mechanisms involved in EIA/EIB suggesting a role of the "parasympathetic nervous system" and of "chemical substances which occur in the body, and which can affect smooth muscles so that the possibility exists the exercise effect is either reflex or humoral in origin", concluding that "the mechanism by which exercise produces its effect is worthy of study because it may contain an important clue to naturally occurring bronchoconstrictor substance".[4] These initial definitions have evolved into the current classical theories behind EIA, the so-called "osmolar" or "vascular" (or "thermal") hypotheses, both based on the marked increase in ventilation during physical activity, leading to increased water and heat loss through respiration. In the osmolar theory, the increased osmolality of the extracellular fluid lining the bronchial mucosa leads to a release of inflammatory mediators from mast cells, eosinophils, neutrophils and other inflammatory cells. In the vascular theory, the respiratory heat loss that occurs as consequence of the oral breathing pattern of athletes and of the increased ventilation, stimulates the reflex parasympathetic nerve, which leads to bronchoconstriction.[5,6]

Both mechanisms may work together under conditions of significant heat loss and, as the reader can see, confirm the brilliant intuitions of 50 years ago.

However, in the most recent years, the changing view on the whole asthma issue, with the importance of phenotypes, endotypes and relevant biomarkers for a "personalized" medicine, has been reflected also in the current research trends in EIA/EIB. Albeit helpful in some ways, this new approach also restricts the current definition of the disease and open some questions, particularly with regards to the mechanisms mediating EIA/EIB.

But, coming back to the Olympics, the question arises: why Olympic athletes have such a prevalence of asthma? It is accepted that two clearly separated phenotypes of EIA/EIB exist: the "classical" one, i.e. the asthmatic patient, often allergic, experiencing symptoms while exercising, and the "sports asthma" phenotype, i.e. the late-onset asthma developed by competitive, top-level athletes, linked to epithelial damage, reduced repair and subsequent inflammation. In fact, a recent study has identified two

* Tel.: +39-070-6754150; fax: +39-070-6754086.
E-mail address: stedg@medicina.unica.it

http://dx.doi.org/10.1016/j.pbj.2016.10.001

distinct asthma phenotypes in elite athletes through latent-class analysis. LCA retrieved two clusters: “atopic asthma”, defined by allergic sensitization, rhinitis and allergic co-morbidities and increased exhaled nitric oxide levels; and “sports asthma” defined by exercise-induced respiratory symptoms and airway hyperresponsiveness without allergic features. Evidence also suggests that that winter and water sports athletes are particularly at high risk of developing the “Sports Asthma” phenotype.[7] This might explain the high prevalence of asthma amongst Olympic Athletes, for whom is not uncommon to show a “Sports Asthma” phenotype, therefore raising the prevalence of asthma in this special category. However, reassuringly, the mechanism leading to this phenotype has been demonstrated to be partially reversible at the end of the athlete’s career.[6]

Switching to the daily life, one dilemma for the doctors caring for the asthmatic children and adolescents is what kind of recommendation should be given to those suffering from asthma, i.e.: which sports can be recommended for asthmatic youngsters? it is nowadays clear that endurance and winter sports are at high-risk of EIA, team sports bear a medium risk and sports in which the effort is of a short duration (less than 5-8 minutes) are at low risk. But a question remains: is swimming beneficial or detrimental for asthma? Swimming has been considered as a safe and healthy sport for children with asthma, due to the warm and humid air inhaled in the swimming pools. However, recent data in children show an association between an increased swimming pool attendance in children and the risk of asthma: the “pool chlorine hypothesis”. This suggests that a link exists between chlorine-based irritants exposure and risk of asthma in children, probably on a cumulative basis.[8–10] This hypothesis was further supported by studies comparing non-chlorinated and chlorinated swimming pool exposures and by studies in mouse models on hypochlorite-induced airway hyperreactivity.[11] The central role of chlorine exposure is in part contradicted by a large birth cohort study showing that British children did not increase their asthma risk with swimming pool attendance.[12] On the other side, competitive swimmers show an increased asthma prevalence, with a mixed eosinophilic-neutrophilic airway inflammation, also when measured by FeNO.[13,14] In conclusion, if the question is not completely clear for development of asthma throughout childhood, there is no doubt that competitive swimming exposes to a higher risk of asthma in comparison to other sports.

Another central topic in the field of EIA, the so-called “doping issue” has been for many years under the spotlight. Initially, the common belief was that the asthma drugs might improve performance, and the World-Anti-doping Agency (WADA) issued strict regulations for their use. However, several studies demonstrated that inhaled corticosteroids, and most of the inhaled beta-2 agonists, do not improve performance at therapeutic doses. Currently, no restrictions exist for inhaled corticosteroids and for salmeterol, formoterol and salbutamol. The same applies to leukotriene antagonists, ipratropium bromide and omalizumab. The “prohibited list” is usually updated yearly and can be found on the WADA website (www.wada-ama.org).

Finally, in the recent years it has been demonstrated, both from murine models and preliminary studies on humans, that low-to-moderate intensity aerobic exercise can decrease airway inflammation, remodeling,[15] bronchial hyperresponsiveness,[16] total and allergen specific IgE[17] and Th-2 cytokines,[18] showing that aerobic exercise programs can be beneficial for asthmatics and should be included in asthma action plans.[6]

In summary, the lesson we can all learn from the “Exercise, Asthma and the Olympics” tale is that asthmatics athletes –as long as they work hard with self-mastery and discipline – can compete on par with the others, and only the sky can be the limit.

References

1. Adams F. The extant works of Aretaeus, the Cappadocian. London: Sydenham Society; 1856.
2. Jones RS, Buston MH, Wharton MJ. The effect of exercise on ventilatory function in the child with asthma. British journal of diseases of the chest. 1962;56:78–86.
3. Fitch KD. An overview of asthma and airway hyper-responsiveness in Olympic athletes. British journal of sports medicine. 2012;46:413–6.
4. McNeill RS, Nairn JR, Millar JS, Ingram CG. Exercise-induced asthma. Q J Med. 1966;35:55–67.
5. Del Giacco SR, Carlsen KH, Du Toit G. Allergy and sports in children. Pediatric allergy and immunology: official publication of the European Society of Pediatric Allergy and Immunology. 2012;23:11–20.
6. Del Giacco SR, Firinu D, Bjermer L, Carlsen KH. Exercise and asthma: an overview. Eur Clin Respir J. 2015;2:27984.
7. Couto M, Stang J, Horta L, Stensrud T, Severo M, Mowinckel P, et al. Two distinct phenotypes of asthma in elite athletes identified by latent class analysis. The Journal of asthma: official journal of the Association for the Care of Asthma. 2015;52:897–904.
8. Bernard A, Nickmilder M, Voisin C, Sardella A. Impact of chlorinated swimming pool attendance on the respiratory health of adolescents. Pediatrics. 2009;124:1110–8.
9. Nickmilder M, Bernard A. Ecological association between childhood asthma and availability of indoor chlorinated swimming pools in Europe. Occupational and environmental medicine. 2007;64:37–46.
10. Bernard A, Nickmilder M, Dumont X. Chlorinated pool attendance, airway epithelium defects and the risks of allergic diseases in adolescents: Interrelationships revealed by circulating biomarkers. Environ Res. 2015;140:119–26.
11. Hox V, Vanoirbeek JA, Callebaut I, Bobic S, De Vooght V, Ceuppens J, et al. Airway exposure to hypochlorite prior to ovalbumin induces airway hyperreactivity without evidence for allergic sensitization. Toxicology letters. 2011;204(2–3):101–7.
12. Font-Ribera L, Villanueva CM, Nieuwenhuijsen MJ, Zock JP, Kogevinas M, Henderson J. Swimming pool attendance, asthma, allergies, and lung function in the Avon Longitudinal Study of Parents and Children cohort. American journal of respiratory and critical care medicine. 2011;183:582–8.
13. Moreira A, Delgado L, Palmares C, Lopes C, Jacinto T, Rytila P, et al. Competitive swimmers with allergic asthma show a mixed type of airway inflammation. The European respiratory journal: official journal of the European Society for Clinical Respiratory Physiology. 2008;31:1139–41.
14. Couto M, Andrade P, Pereira M, Araujo J, Moreira P, Delgado L, et al. Effect of competitive swimming on airway inflammation: a 3-yr longitudinal study. Pediatric allergy and immunology: official publication of the European Society of Pediatric Allergy and Immunology. 2014;25:193–5.
15. Vieira RP, Toledo AC, Ferreira SC, Santos AB, Medeiros MC, Hage M, et al. Airway epithelium mediates the anti-inflammatory effects of exercise on asthma. Respiratory physiology & neurobiology. 2011;175:383–9.
16. Franca-Pinto A, Mendes FA, de Carvalho-Pinto RM, Agondi RC, Cukier A, Stelmach R, et al. Aerobic training decreases bronchial hyperresponsiveness and systemic inflammation in patients with moderate or severe asthma: a randomised controlled trial. Thorax. 2015;70:732–9.
17. Moreira A, Delgado L, Haahtela T, Fonseca J, Moreira P, Lopes C, et al. Physical training does not increase allergic inflammation in asthmatic children. The European respiratory journal: official journal of the European Society for Clinical Respiratory Physiology. 2008;32:1570–5.
18. Del Giacco SR, Scorcu M, Argiolas F, Firinu D, Del Giacco GS. Exercise Training, Lymphocyte Subsets and Their Cytokines Production: Experience of an Italian Professional Football Team and Their Impact on Allergy. BioMed Research International. 2014;2014:6.