

Preface

Exercise-Induced bronchoconstriction



Sandra D. Anderson, PhD, DSc, MD(Hon)
Editor

The invitation by the editor, Rafeul Alam, to guest edit this issue on exercise-induced bronchoconstriction (EIB) allowed me to bring together investigators from physiology to cellular biology of EIB. The preface contains information on how some of the contributors came together and identifies some conferences that helped broaden the scientific research in EIB in asthmatic children to include healthy elite athletes. The contributors come from Australia, Canada, Denmark, England, France, Israel, Sweden, Netherlands, and the United States and trained in pediatric, respiratory, and sports medicine and science. Most have either obtained a doctoral degree in EIB or supervised one.

My first encounter with EIB was at Royal Prince Alfred Hospital, in Sydney, in 1968. In January 1970 I started research in EIB with Simon Godfrey in the Department of Paediatrics at the Brompton Hospital in London. Over the next 3 years, under Simon's enthusiastic guidance, a group of us carried out many studies on various aspects of EIB.

In 1968 Ken Fitch from Perth, Australia observed severe EIB when supervising an exercise test on an 18-year-old asthmatic Olympic swimmer, who 3 months later won an Olympic Gold Medal in Mexico. This induced Ken to do his MD in EIB. Both Simon and Ken's laboratories were coincidentally investigating the effect of different forms of exercise to provoke EIB. In 1971, both laboratories reported running as the most provocative exercise. Being ahead of their time, Ken and Simon wrote an article in 1976 on the topic of Asthma and Athletic Performance. They now celebrate the 50 years of research since the modern description of EIB in children by R.S. Jones of Liverpool, United Kingdom, in 1962. In 1973 Simon moved to the Hammersmith Hospital and later, in 1977, to Israel, where he continued his studies, among many others, on refractoriness and EIB. The article by Larsson and coworkers discusses these early studies and presents a new hypothesis to explain refractoriness following EIB.

On my return to Sydney we studied the effects of β_2 -agonists and in 1975-1976 reported that tablets failed to inhibit EIB, relative to an inhaled aerosol, when both gave an equivalent bronchodilator effect. The mast cell, situated superficially in the airway, was proposed as a second site of action for the inhaled β_2 -agonist to prevent EIB. Down-regulation of mast cell β_2 -receptors is now recognized as a contributing factor to the tolerance that develops to β_2 -agonists. Vibeke Backer writes about the benefits and limitations of β_2 -agonists and other drugs in the treatment of EIB.

In May 1982 a symposium was held in Oslo, Norway (The Asthmatic Child in Sport and Play. Oseid S, Edwards A, editors. Bath, UK: Pitman Press: 1983:1-396). Most topics related to EIB and included standardization of testing, the effect of climatic conditions, the role of mast cell mediators, refractoriness, and the effect of both short and prolonged periods of exercise. This meeting reflected the growing interest in EIB research by 1982.

In 1984 a conference was held in Palm Springs on Special Problems and Management of Allergic Athletes (J Allergy Clin Immunol 1984;73(5 Part 2):629-748). In addition to the assessment and treatment of EIB, the topics included doping, air pollution, and the management of allergic Olympic athletes. The osmotic hypothesis, as an alternative to the cooling hypothesis, of EIB was presented for the first time. In part, this hypothesis was based on the finding, by the Perth and Sydney groups, that severe EIB occurred when hot dry air was inhaled during exercise. Later, in 1984, at the American Thoracic Society (ATS) in Miami, Moira Aitkin from Seattle reporting similar findings with hot dry air.

The osmotic hypothesis was the first of a series of articles on calculating water loss from the airway surface by E. Daviskas. The concepts of water loss from the airway surface ultimately led to the proposal that airway injury from water loss may be important in the pathogenesis of EIB, particularly in athletes. The topic is covered by Pascale Kippelen and me in the second article. One of the aspects of water loss and airway injury is the shedding of the airway epithelium, a subject studied by Teal Hallstrand. Since his presentation at ATS in 1996, Teal has taken the subject of EIB from the physiologic aspects to molecular biology. His article on cells and mediators in EIB demonstrates how sophisticated EIB research is today.

In 1997 at a conference in Oslo, Norway (Exercise-induced Asthma and Sports in Asthma. Carlsen KH, Ibsen TB, editors. Copenhagen: Munksgaard; 1999:1-114), Malcolm Sue Chu and colleagues reported pathologic and inflammatory changes in the airways of healthy elite cross-country skiers. A few years later in 1999, Ken Rundell, a sports physiologist, also studying cold weather athletes at the US Olympic Committee facility at Lake Placid, New York, attended an International Olympic Committee conference held in Sydney. In 2001 he reported that the respiratory symptoms, associated with exercise and asthma, were neither sensitive nor specific for predicting EIB. This study confirmed the need for objective tests for a correct diagnosis to be made. A later study reported eucapnic voluntary hyperpnea (EVH) to be a reliable test to identify EIB in elite cold-weather athletes. Ken and Malcolm write on air quality and EIB.

In 2003, Pascale Kippelen, also a sports physiologist, came from Montpellier in France to do a post-doctoral in Sydney. At the time our laboratory was active in assessing defense force recruits and intending scuba divers for asthma and EIB. It was the need to assess "healthy" subjects for EIB and the low yield for exercise to identify EIB that had led John Brannan and me to use surrogates such as EVH and mannitol to identify potential for EIB. Exercise and these surrogates for exercise are discussed in the article on assessment of EIB. At that time, we were working on the urinary excretion of mediators following inhalation of mannitol with Sven Erik and Barbro Dahlen from the Karolinska Institute in Stockholm, who had published on

mediators in EIB some years earlier. With Pascale, the studies were extended to include mediators following EVH. Johan Larsson joined the Dahlens for his PhD and remains involved with studies with Pascale, who is now in London.

In 2001 Ken Fitch involved me in a meeting at the IOC headquarters in Lausanne to discuss testing for asthma. The outcome was a policy requiring athletes, seeking to use a β_2 -agonist before an event, to submit the results of provocation tests before the Winter and Summer Olympics of 2002 and 2004. Over the years, Ken Fitch met Ken Rundell, Pascale Kippelen, Malcolm Sue Chu, Louis-Philippe Boulet, Vibeke Backer, and Valerie Bougault and most came together at a second meeting in Lausanne in 2008. Valerie and Louis-Philippe were studying the swimming pool environment and athletes. Their findings were timely, as swimmers represented a high proportion of the athletes taking β_2 -agonists. They write here on airway disorders and the swimming pool.

At the Winter Games in Vancouver (2006) and the Summer Games in Beijing (2008), Fitch noted that most (~62%) athletes reporting asthma for the first time were over the age of 23 years. Malcolm's study in young skiers, showing a high percentage with hyperresponsiveness to methacholine, supported both the earlier and the later findings of Louis-Philippe's group in cold weather athletes and swimmers. All these observations suggest that years of training, as well as the environment, may be important in the pathogenesis of hyperresponsive airways and EIB and emphasize the need to have strategies to prevent airway injury. Ken Fitch is to be commended for all his effort, through his long membership of the IOC Medical Commission, to encourage testing and measurement in athletes and to monitor use of β_2 -agonists. This approach has resulted in better recognition and treatment of asthma in athletes, an outcome in keeping with a focus on the health of athletes. In 2011 the responsibility for approval of drugs was taken over by the World Anti-Doping Authority and testing is now no longer required to use the commonly available aerosols of β_2 -agonists. In 2011 in Monaco at an IOC Conference, many writing here presented at a symposium entitled Intensive Exercise and Respiratory Health (Br J Sports Med 2012;46(6):379-421; Br J Sports Med 2012;46(7):471-476).

Boony Thio, a pediatrician from The Netherlands, came to Sydney for 3 months in December 2008 and we discussed tolerance to β_2 -agonists and EIB. A few years later, I met Boony's PhD students, Elin Kersten, Jean Driessen, and Janneke Van Leeuwen. They reported, in a pilot study, the benefit of withdrawing β_2 -agonists on EIB severity. They were using a new skating rink for testing for EIB. The children ran on a treadmill in environmental conditions similar to those outside. They demonstrated breakthrough EIB during exercise in a large proportion of asthmatic children. They also developed a new test for EIB in very young children using a jumping castle. They write on the assessment of EIB in adolescents and young children. EIB research seems to be returning to where it started...enthusiastic pediatricians like R.S. Jones and Simon Godfrey guiding students in the study of EIB in children. In the last article, this group and other members of the younger generation ask where to from here for EIB and what are the unanswered questions.

Finally, I would like to thank all the contributors for their enthusiasm in writing for this issue and for being on time with both their original and revised articles.

Sandra D. Anderson, PhD, DSc, MD(Hon)
Department of Respiratory and Sleep Medicine
Royal Prince Alfred Hospital
Camperdown, New South Wales 2050, Australia

E-mail address:
sandra.anderson@sydney.edu.au