In June 1979, an international symposium was held at the Firestone Respiratory and Allergy Clinic at St. Joseph’s Hospital and McMaster University in Hamilton, ON, Canada. The symposium was chaired by Dr Freddy Hargreave from McMaster University and was titled “Airway Reactivity: Mechanisms and Clinical Relevance.” The meeting focused on airway hyperresponsiveness (AHR) in asthma and was attended by >40 speakers from Canada, the United States, Australia, The Netherlands, France, Sweden, and the United Kingdom. Although methods for measuring AHR had been described, their reproducibility evaluated, and their clinical relevance examined in the previous 3 to 4 years, this was very much an emerging area of research in asthma at this time. A book reporting the presentations and discussions at this meeting was published the following year.³

In one of the presentations at the meeting, Dr Anne Woolcock from the University of Sydney, who was a pioneer in the area of research, stated, “It is clear that an increase in nonspecific airway responsiveness is an important feature of asthma. Its measurement should be as essential to the diagnosis and management of asthma as the glucose tolerance test is to diabetes.” Now, 30 years later, these comments have been validated by well-conducted clinical trials, and the role of measuring airway responsiveness in establishing a diagnosis of asthma is firmly established.

In July 2009, another symposium was held at the Firestone Institute for Respiratory Health at St. Joseph’s Hospital, Hamilton, to commemorate the 30th anniversary of that important meeting. The symposium was titled “Airway Hyperresponsiveness in Asthma: Its Measurement and Clinical Significance,” and it again brought together experts from Canada, the United States, and Australia to discuss the progress in the understanding of these measurements. On this occasion, there was an additional focus on the indirect measurement of airway inflammation and its interaction with AHR, as well as the role of measuring airway inflammation in the management of asthma.

This supplement publishes the main presentations of this meeting. The opening lecture discussed the relationship between AHR and airway inflammation and was presented by Dr Bill Busse from the University...
of Wisconsin at Madison. The lecture focused on the interaction between acute and chronic airway inflammation, the development of structural changes in the airway (airway remodeling), and the development of AHR in asthma. This was followed by a presentation by Dr John Brannan from the Royal Prince Alfred Hospital in Sydney on the value of measuring AHR in the assessment of asthma control. This presentation discussed the concepts of asthma control and how airway responsiveness measurements can aid in establishing the optimal treatment requirements in patients with asthma. The next two presentations, by Dr Don Cockcroft from the University of Saskatchewan and Dr Sandra Anderson from the University of Sydney, described the various methods available to measure airway responsiveness using both direct inhalational challenges with mediators that directly contract airway smooth muscle, such as methacholine, or indirect inhalational challenges with substances that cause airway mediator release, such as mannitol. Both methacholine and mannitol challenges are approved by the US Food and Drug Administration in the United States as investigations for the diagnosis of asthma and are used worldwide for that purpose.

Exercise-induced bronchoconstriction is an important consequence of AHR in asthma, and the mechanisms and management of this clinical issue in elite athletes was presented by Dr Louis-Philippe Boulet from Laval University in Quebec. The final series of presentations focused on indirect methods for measuring airway inflammation and their role in asthma management, and were presented by Dr Freddy Hargreave and Dr Param Nair, both from the Firestone Institute. These methods include measurements of inflammatory cells (particularly eosinophils) in induced sputum and measurements of the fraction of exhaled nitric oxide.

In the closing remarks of the meeting in 1979, Dr Roland Ingram from Harvard University commented “neither I, nor I suspect anyone else here, truly understands the genesis, modulating mechanisms, and importance of increased airway reactivity.” Interestingly, the complexity of the mechanisms of AHR in asthma remains unresolved today. Much of the focus in 1979 was on abnormalities of specific airway receptors and neurogenic control, as well as the differences in airway responses to a variety of constrictor agonists. There were no insights, at that time, into the importance of airway inflammation in changing airway responsiveness, as the first studies identifying these relationships, in animal models, were published in 1983. Shortly afterward, airway inflammation was associated with persisting AHR in asthma and then with induced changes in AHR caused by inhalation of environmental allergens or occupational sensitizers. Now, the management of asthma is predicated on eliminating airway inflammation.

Research during the past 30 years has resulted in a much greater understanding of pathobiology of asthma, in particular the immunologic responses in the airways that lead to airway inflammation. There is much greater precision in making the diagnosis, particularly because airway challenge tests have become established and have been validated, and there are very effective and safe medications available to treat asthma. There remains, however, a need to better understand the mechanisms of the persisting AHR that characterizes asthma. Perhaps another symposium, 30 years hence, will regard this as a problem that has been solved.

Acknowledgments

Financial/nonfinancial disclosures: The author has reported to CHEST the following conflicts of interest: Dr O’Byrne has been on advisory boards for Abbott Laboratories, AstraZeneca, Asmacure, GlaxoSmithKline, Merck, Topigen, and Wyeth and has received lecture fees from these and other pharmaceutical companies, including Chiesi Pharmaceuticals, Inc. In addition, he has received grants-in-aid for research studies from AstraZeneca, Boehringer Ingelheim, Genentech, GlaxoSmithKline, Medimmune, Merck, Pfizer, and Wyeth.

Other contributions: We at the Firestone Institute for Respiratory Health express our deep appreciation to those colleagues from across Canada, the United States, and beyond North America for their engagement in this symposium and also to Pharmaxis Inc, who provided an “arm’s length” grant that enabled the symposium to be held.

References


Airway Hyperresponsiveness in Asthma