EDITORIAL: INFLAMMATORY AIRWAY DISEASES AND CLINICAL ALLERGY ASSEMBLY

Inflammatory airway diseases and clinical allergy

Inflammatory Airways Diseases and Clinical Allergy Assembly contribution to the celebration of 20 years of the ERS

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Assembly 5 of the European Respiratory Society (ERS) is the Inflammatory Airway Diseases and Clinical Allergy Assembly and consists of three Scientific Groups: 1) Airway Pharmacology and Treatment; 2) Monitoring Airway Diseases; and 3) Allergy and Immunology. The original focus of the Assembly was mostly on asthma, but in recent years, it has increasingly begun to encompass chronic obstructive pulmonary disease (COPD). A substantial number of pharmacologists and basic scientists have joined clinicians to work together to unravel mechanisms of and improve diagnosis and treatment of these common chronic airway diseases.

The Airway Pharmacology and Treatment Group focuses its activities on the pharmacology of the drugs used in asthma and COPD, and the development of scientific rationales for new drugs. The Monitoring Airway Disease Group evolved from the Airway Regulation and Provocation Group. Initially, focus was on the evaluation of bronchial responsiveness but in the past 20 years, important new technologies have developed, such as sputum induction, and measurement of exhaled nitric oxide (eNO) and exhaled breath condensate for noninvasive evaluation of airways inflammation. The Allergy and Immunology Group focuses mainly on airway and lung immunology, a rapidly advancing field that is crucial to our understanding of cellular and molecular backgrounds of allergy and inflammatory airways diseases.

IMPROVED ASTHMA MANAGEMENT

The majority of adult asthma patients can now be treated by a combination of inhaled corticosteroids and long-acting inhaled β_2 -agonists. Combination inhalers are highly effective, relatively inexpensive and safe. The scientific rationale is based on knowledge derived from both basic science and landmark clinical trials, in which prominent members of our Assembly have taken the lead [1–3]. More recently, the scientific rationale for using a combination inhaler containing formoterol and budesonide as a rescue inhaler in addition to maintenance therapy has been elucidated [4].

Concepts of asthma severity and control are important in the evaluation of patients and their responses to treatment. Originally, asthma guidelines focused on the classification of asthma patients according to severity; now, however, the focus

is on asthma control. An American Thoracic Society (ATS)/ERS Task Force has developed these concepts [5]. The overall severity of asthma is assessed primarily on the patient's clinical characteristics prior to commencing treatment. Asthma control refers to the extent that manifestations of asthma have been removed or reduced by treatment. The ATS/ERS Task Force recommendations have provided a basis for a multicomponent assessment of asthma by clinicians, researchers and other relevant groups in the design, conduct and evaluation of clinical trials, and in clinical practice [6].

SEVERE ASTHMA

There is as yet no cure for asthma, but it is controllable in the majority of patients. The asthma of ~5–10% of patients is not controlled, despite use of effective inhaled therapy. These patients account for a disproportionate amount of healthcare spending as they are admitted to hospital, use a lot of medication and miss time at work or school [7]. More than 10 years ago, an ERS Task Force was set up to address major issues relevant to difficult/therapy-resistant asthma. It produced the first document to establish diagnostic criteria, define clinical phenotypes and present pathways for clinical evaluation of these patients [8]. It was followed by a European Union-sponsored cross-sectional European multicentre study of the clinical phenotype of chronic severe asthma called ENFUMOSA (European Network for Understanding Mechanisms Of Severe Asthma) [9].

BRONCHIAL CHALLENGE

Bronchial challenges are used for the diagnosis and monitoring of asthma. Indirect challenges act by causing the release of endogenous mediators that cause the airway smooth muscle to contract [10]. This is in contrast to direct challenges, where agonists such as methacholine or histamine cause airflow limitation predominantly *via* a direct effect on airway smooth muscle. Direct airway challenges have been used widely and are well standardised. They are highly sensitive but not specific to asthma, and can be used to exclude current asthma in a clinic population. Indirect bronchial stimuli, particularly exercise, hyperventilation, hypertonic aerosols, and adenosine, might more directly reflect the ongoing airway inflammation and are therefore more specific to the identification of active asthma [11]. An ERS Task Force has addressed the issue of direct and indirect bronchial challenges in detail [12].

INFLAMMATORY MECHANISMS IN AIRWAY DISEASES

In the past 20 years, techniques enabling us to study inflammatory processes in the airways have revolutionised our understanding of asthma [13] and COPD [14, 15]. Most of

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the initial observations were made in studies using fibreoptic bronchoscopy in conjunction with bronchoalveolar lavage and bronchial biopsy. With the development of simple, safe and valid noninvasive techniques for the assessment of airway inflammation, routine measurement in clinical practice has become a reality. A number of techniques are available, ranging from measurement of inflammatory cells and mediators in induced sputum, to breath analysis. There have been important advances in the use of induced sputum to assess airway inflammation in asthma and COPD [16, 17]. Increased concentrations of NO in the breath were first reported in 1993 [18] and since then, there has been an explosion of studies on eNO in asthma and COPD. The ERS Task Force on exhaled and nasal NO provided the first guidelines on measuring eNO and offered a framework for future research [19]. More recently, eNO at different flows has been used to study central and peripheral origins of eNO in severe asthma and COPD [20, 21]. Collection of exhaled breath condensate is another noninvasive method for obtaining samples from the lungs; an ATS/ERS Task Force provided recommendations for standardising the collection of samples [22].

IMMUNOLOGICAL MECHANISMS

The field of immunology and inflammation is advancing rapidly, and this has greatly increased our understanding of the cellular and molecular mechanisms of asthma and COPD [23]. Dendritic cells (DCs) are generally held responsible for initiating and maintaining allergic T-helper cell (Th) type 2 responses to inhaled allergens in asthma [24]. Although the epithelium was initially considered to function solely as a physical barrier, it is now seen as playing a central role in the Th2 sensitisation process by influencing the function of DCs. Clinically relevant allergens, as well as known environmental and genetic risk factors for allergy and asthma, often interfere directly or indirectly with the innate immune functions of airway epithelial cells and DCs. As innate and adaptive immune responses are activated in COPD, DCs could also play a role in the pathogenesis of this disease. Indeed, cigarette smoke appears to modulate DC function *in vitro* and alters DC number and function in cigarette smoke-exposed mice. The number of pulmonary DCs differs between COPD patients, smokers and nonsmokers. Moreover, the number of Langerhans-type DCs increases with the severity of the disease [25].

Knowledge of the role of various immune and inflammatory cells in the pathogenesis of asthma has been moved forward to a large extent by the application of *in vitro* model systems and animal, particularly murine, models [26]; the merits and disadvantages of murine models have been discussed in an ERS Task Force [27]. A whole series of new treatments based on targeting a single mediator or receptor have been put forward. However, until now, these treatments have either proven to be unsuccessful (e.g. anti-tumour necrosis factor in asthma and COPD) or only active in a very select subgroup of patients (e.g. anti-immunoglobulin E or anti-interleukin-5 in subgroups of patients with severe asthma). The results of new initiatives, such as U-BIOPRED (Unbiased Biomarkers for the Prediction of Respiratory Disease Outcomes) which is sponsored by the Innovative Medicines Initiative (IMI), are welcome. The hypothesis of U-BIOPRED is that biomarker profiles from high dimensional molecular, physiological and clinical data integrated by an innovative systems biology

approach to distinct handprints will enable the prediction of therapeutic efficacy and the identification of novel targets in the treatment of severe asthma [28].

CONCLUSION

The last 20 years has seen astounding developments in our understanding and treatment of asthma and COPD. However, more research is needed to understand the underlying mechanisms and overlap of these common diseases, as there is a pressing need to develop new anti-inflammatory treatments for severe asthma and COPD.

STATEMENT OF INTEREST

Statements of interest for both authors of this article can be found at www.erj.ersjournals.com/misc/statements.dtl

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