



Facets of chronic obstructive airways diseases

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The current issue starts out with a brilliant contribution authored by *Peter Lange (Herlev and Gentofte and Copenhagen University Hospitals, University of Copenhagen, Copenhagen) and Jørgen Vestbo (University of Manchester and Manchester Academic Health Science Centre, Manchester)*, past president of the *European Respiratory Society (ERS)*, two of the most productive investigators of the *Copenhagen City Heart Study (CCHS)*, a cornerstone and landmark research programme in chronic obstructive pulmonary disease (COPD). This review highlights several of the **key contributions to COPD achieved by the findings of the CCHS**. This long-term research programme started in the early 1980s focusing on cardiovascular problems using a solid methodology, including sequential measurements of spirometry and a thorough respiratory questionnaire. This facilitated the collection of a huge amount of data which has enriched our current knowledge of many facets of the natural history of COPD, a disorder known by its complexity and heterogeneity. During the last four decades the CCHS' investigators have disentangled difficult and complex areas related to COPD. In their non-exhaustive list of

achievements, these investigators have addressed some of the risk factors involved in the development of COPD, such as cigarette smoking and body mass index, the influential role of physical activity, the relevance of chronic mucus hypersecretion, the progressive decline of lung function, and, more specifically, the novel acknowledgment of the different trajectories of lung function leading to COPD, and its interplay with asthma-COPD overlap (ACO), without forgetting the predictive role of several biomarkers and that of blood eosinophils. Indeed, the CCHS represents one of the most enthralling pages of research in respiratory medicine.

The second paper focuses on the very timely and germane topic of **asthma-COPD overlap (ACO) and its Spanish features**, written by two investigators, *Borja G Cosío (Hospital Universitario Son Espases, Palma de Mallorca)*, and *Luis Pérez de Llano (Hospital Lucus Augusti, Lugo)*, who have been dazzlingly working on this

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concept over the last few years. They recall that there are several controversies related to the clinical and prognostic relevance of ACO, let alone mention that many respiratory experts question its own existence, including the criteria used to define its concept. According to several studies, this condition can lead to more frequent and serious exacerbations and to worse health-related quality of life, although others postulate the opposite. Be that as it may, the authors have made an excellent attempt to clarify the impact that ACO may have and how it can be identified using a simple approach, while addressing its potential management.

The next review, presented by *Irene Braithwaite, Ruth Semprini, and Richard Beasley* (all from the prestigious *Medical Research Institute of New Zealand, Wellington*), points to **the clinical relevance of periostin in asthma**, a matricellular protein which is generated by airway epithelial cells, partly regulated by interleukin (IL)-13 and IL-4, detectable in serum. One key take-home message of this paper is that periostin does not distinguish patients with asthma from those without it, nor does it allow assessment of disease severity. Periostin levels may be helpful in categorising the type-2 status of patients with severe asthma and may also predict treatment responses to monoclonal antibody treatment directed against IL-13 and immunoglobulin (Ig)E in patients with severe persistent allergic asthma. The authors, led by the scientific reputation of their senior author, *R Beasley*, critically conclude that serum periostin should be interpreted with caution when incorporating into decision-making about treatment for asthma patients, making analysis of levels challenging.

The next contribution, the use of **exercise physiology to assess therapeutic interventions in several chronic respiratory diseases**, is presented by *Luis Puente-Maestu* (*Hospital Universitario Gregorio Marañón and Universidad Complutense de Madrid*) and *William W Stringer*, under the leadership of *Richard Casaburi* (the latter two from *Los Angeles BioMedical Research Institute at Harbor-UCLA Medical Center, Torrance and Geffen School of Medicine at UCLA, Los Angeles, CA*). The authors, known by their vast experience in exercise physiology in chronic respiratory diseases, review the available evidence of the underlying mechanisms associated with the achieved improvements on exercise responses to various pharmacological and non-pharmacological therapeutic interventions. With the preamble that a gold standard test has not been identified as yet, we are alerted that the choice of testing modality is both disease- and intervention-specific, the mechanism of improvement induced by the intervention being different depending on the underlying disease process. Thus, in the presence of moderate-to-severe airflow limitation, as in COPD, the primary mechanisms are reduced ventilatory requirement and/or enhanced ventilatory capacity through reduction of dynamic hyperinflation, while in pulmonary arterial hypertension the effect of treatment is characteristically associated to haemodynamic improvement, in interstitial lung disorders the amelioration of arterial oxygenation seems to be the predominant physiological factor.

The fifth contribution addresses the novelties imposed by the current irruption of the **double and triple therapies in COPD** presented by *Mario Cazzola, Paola Rogliani* (*Department of Experimental Medicine and Surgery, University*

of Rome “Tor Vergata”, Roma), and Maria G Matera, (Department of Experimental Medicine, University of Campania “Luigi Vanvitelli”, Naples). Under the guidance of the first author, a world-wide renowned clinical pharmacologist, the authors unravel with precision pros and cons of the widespread spectrum of double and triple combinations to be potentially recommended in COPD. Of note that, although the available information has greatly increased in recent years, there is still no complete evidence to conclude whether and when addition of inhaled corticosteroids (ICS) to the established use of long-acting bronchodilators provides additional clinical value, so that a strong general recommendation cannot be generated as yet. Two other comments of interest are quoted: first, the intensification of the treatment in patients with clinically unstable COPD by adding ICS to the regular bronchodilator therapy can be helpful to control the disease but may not be necessary when patients are stable; second, it can be desirable to avoid a step-up (escalation) therapeutic approach when not needed rather than being forced later into a step-down (de-escalation) option in which the outcome is always unpredictable.

The last piece of work, built upon the **use of regular inhalers in chronic obstructive airways diseases**, is written by Matteo Bonini and Omar S Usmani, two international specialists with a solid reputation in the field, from Imperial College London & Royal Brompton Hospital National Heart and Lung Institute (NHLI). This is indeed a very important topic, unfortunately too often overlooked in clinical practice. The regular use of inhaler devices in the most

common chronic obstructive airways diseases is always challenging in respiratory medicine. The frequent significant misuse of inhalers in handling along with non-adherence towards recommended treatment regimens are key issues in the daily therapeutic efficacy and health economics of inhaled pharmacological interventions. The features contributing to adherence to inhaled agents are complex, but a crucial component is patients having the correct inhaler technique to ensure adequate drug delivery. Many of these difficulties are comprehensively addressed in this review. Importantly, the current massive launching of new devices and use of multiple different inhaler classes can be highly confusing for patients (and physicians as well!) and should be avoided, and recent data show multiple inhaler devices adversely affect disease outcomes. In wrapping up, I want to endorse the following words by the authors: ‘...In order to demystify inhaler therapy, there is a real need to educate healthcare professionals, particularly doctors, about the importance of each of the inhaler device classes used to deliver medication to patients with respiratory disease. There needs to be an appreciation by prescribers, and also patients, that the inhaler device is an integral part of the “drug prescription”, and not a bystander...’.

I am quite confident the reader will enjoy these six fascinating topics brilliantly authored by talented experts!

