



# Featuring Characteristics of Chronic Obstructive Pulmonary Disease, Procalcitonin and Lower Tract Infections and Inert Gas Studies

R Rodriguez-Roisin MD, PhD

The last issue of BRN Reviews for the current year sets out two first-class observational studies devoted to the complexities of the natural history of chronic obstructive pulmonary disease (COPD). The first refers to **SubPopulations and Intermediate Outcome Measures in COPD Study (SPIROMICS)**, a multicentre, cohort study of nearly 3000 never-smokers and ever-smokers with and without COPD. This outstanding work is reviewed by *Wassim W Labaki*, from *University of Michigan (Ann Arbor, MI)* together with two distinguished members of the *Global Initiative for Obstructive Lung Disease (GOLD) Science Committee*, *FJ Martinez*, from *Weill Cornell Medical College (New York, NY)*, and *MeiLan K Han*, from the same university as the first author, who leads the publication, a talented worldwide COPD researcher. This huge observational study focuses on the natural history of COPD, funded by the United States (US) *National Institutes of Health (NIH)*, and represents a milestone in the effort to further phenotype the challenging complexity and heterogeneity of COPD. Indeed, SPIROMICS has generated significant knowledge on the clinical phenotypes of COPD through the identification of distinct subgroups and the investigation of various chest

and imaging biomarkers. Through the description of the major findings achieved by SPIROMICS, the reader is invited to pay special attention to table 2 that includes a very thorough summary of the strengths and shortcomings of the study. I will give just one example, that one of on exposures. It is observed that second-hand smoke exposure and ever-use of e-cigarettes are associated with a higher burden of respiratory symptoms in subjects with COPD; however, a lot of work on long-term effects of e-cigarette use on respiratory health, lung function and clinical effects in individuals with COPD remains to be investigated.

The second review in this field is centred on **new insights for primary care application from the Canadian Cohort Obstructive Lung Disease (CanCOLD)**, presented by *Jean Bourbeau*, a lifelong active member of the GOLD governance, *Wan Tan*, and *Helene Perrault*, from *McGill University (Montreal, Quebec)*, *University of British Columbia (Vancouver, British*

Received in original form: 08-09-2019

Accepted in final form: 09-09-2019

DOI: 10.23866/BRNRev:2019-M0064

Columbia), and University of Ottawa (Ottawa, Ontario), respectively, nicely reflecting its underlying Canadian multi-centred origin. *Jean Bourbeau*, a very active researcher on COPD heads this review on this fascinating population-based study. Qualified as a world-widely unique study, CanCOLD is based on random sampling of the population as opposed to more traditional cohorts built on convenience samples of patients seen in a clinical setting. As underlined by the authors, this distinctive characteristic makes CanCOLD the first population-derived COPD cohort for characterising the progression of the COPD from normality, or at-risk because of smoking exposure, on to spirometrically-defined COPD, including mild and/or early through moderate disease. This review highlights clinically relevant insights on aspects of COPD natural history, such as disease prevalence, presence in never smokers, functional diagnosis, misdiagnosis, among many others, to eventually facilitate a personalised COPD therapy.

The latter two papers are complemented by a third outstanding review on **current controversies on acute exacerbations of COPD (AECOPD)**, by *Shawn D Aaron*, from University of Ottawa (Ottawa, Ontario, Canada), a brilliant researcher in numerous facets of chronic airway disorders. While sticking largely to the script, the author accurately addresses five key areas of controversies. First, the long-life controversy on AECOPD definition, still unsettled after more than 20 years; second, the complexities of its underlying pathobiology; third, the difficulties of the prediction of AECOP and early intervention at an individual level; fourth, the interactive role of patient self-management and action plans for therapy; and, lastly, the contentious debate on the

use of antibiotics in the outpatient setting. In wrapping up, it is concluded that the current diagnostic criteria for AECOPD are unspecific with a desperately need to be refined hoping that in an early future the chances to phenotype AECOPD can be advanced, including the identification of an appropriate biomarker. This hopeful objective would facilitate the aetiology and subsequent early management of COPD exacerbations to be optimised and also personalised.

The fourth paper, written by *Meropi Karakiouli* and *Daiana Stolz*, from Aristotle University of Thessaloniki (Thessaloniki, Greece) and University Hospital (Basel, Switzerland) respectively, is focussed on the **role of procalcitonin (PCT) in lower respiratory tract infections (LTRIs)**. Dr *Daiana Stolz*, an established European research scholar on several topics, such as respiratory infections and COPD biology and therapy, and actively involved in the European Respiratory Society (ERS) leadership, has developed a solid experience on the role of PCT in LTRIs over the last years. Here, the relevance of PCT, a precursor of the hormone calcitonin, a molecule responsible for the metabolic regulation of calcium and phosphate throughout the body, is extensively addressed. Although numerous clinical studies have demonstrated that PCT serum levels tend to be higher in bacterial than viral infections, several approaches on the use of serum PCT for the prescription of antibiotics also have toned down its recommendations. As a biomarker, PCT unveils a wide range of sensitivity and specificity, likely related to the lack of isolation of distinct bacterial microorganisms in patients with LTRIs. In this context, the take-home message of further studies in patients with comprehensive pathogen testing

to eventually warrant a better understanding of the role of PCT to better optimise its diagnostic accuracy across infections and patient populations, is more than welcome.

The final review features *Peter D Wagner* from *University of California, San Diego (UCSD) (San Diego, CA)*, who comprehensively reviews the **basic principles and some of the clinical applications in chronic respiratory disorders of the multiple inert gas elimination technique**, also known by its popular nickname (i.e., **MIGET**). Qualified as one of the giants in chest medicine and considered to be one of the 10 top respiratory physiologists, Dr *Wagner's* distinctive clarity and critical consideration led him to design, to develop and to apply MIGET since the mid-1970s. The development of this very robust research gas exchange tool has facilitated extraordinary contributions to respiratory physiology and pathophysiology, largely complemented by the substantial success of its author in mentoring and scientific worldwide leadership at all levels<sup>1</sup>. I fully support the latter projection as I personally benefited from a postdoctoral fellow during 1980-82 at UCSD and then closely collaborated with him in an intense

joint research programme for more than 25 years. Although the international breakthrough of MIGET in pulmonary gas exchange studies has already been previously addressed in this journal<sup>2</sup>, here the basics of MIGET are brilliantly exposed by its principal designer and mentor along with some of the most characteristic clinical applications in chronic respiratory diseases, namely COPD, bronchial asthma and idiopathic lung fibrosis, since the inception of MIGET 46 years ago.

I hope that these new five reviews written by talented scholars may be food for thoughts after the summer break. Please, enjoy them.

## REFERENCES

1. Simonson TS. Giants in Chest Medicine: Emeritus Professor Peter D. Wagner, MD. *Chest*. 2019; 155: 9-11.
2. Hedenstierna G. Anaesthesia: lung imaging and gas exchange abnormalities. *BRN Rev*. 2019; 5: 135-49.

