

NUMBER 49 / SEPTEMBER 2010

EUROPEAN RESPIRATORY *monograph*

CLINICAL HANDBOOKS FOR THE RESPIRATORY PROFESSIONAL

Exhaled Biomarkers

Edited by I. Horvath,
J.C. de Jongste.



ERS

EUROPEAN
RESPIRATORY
SOCIETY

every breath counts

Guest Editors



I. Horvath

I. Horvath works at the Dept of Pulmonology of the Semmelweis University in Budapest, Hungary. She trained as a physiologist and then as a specialist in pulmonology and worked in the National Institute of Health (Bethesda, MD, USA) and at the Imperial College (London, UK). She currently works as a pulmonologist within a busy practice and teaches at Semmelweis University. She is Head of the research programme on chronic inflammatory airway diseases, which includes biomarker discovery studies for disease diagnosis and monitoring and also translational research in asthma and COPD pathomechanism, in collaboration with other national and international centres. Her major focus is exhaled biomarkers including exhaled nitric oxide, exhaled breath condensate and electronic smell prints. I. Horvath is a reviewer for many international scientific journals including the *American Journal of Respiratory and Critical Care Medicine*, *European Respiratory Journal*, *Chest*, *Thorax* and the *Journal of Applied Physiology* among others. She is also on the Editorial Board of the *Journal of Breath Research*. From September 2010, I. Horvath takes up the position of Secretary of the European Respiratory Society (ERS) Inflammatory Airway Diseases and Clinical Allergy Assembly. She is also a member of the HERMES Examination Committee and one of the organisers of the popular ERS School course on monitoring airway diseases. I. Horvath has received national and international awards for her scientific achievements including, in 2006, the UNESCO-Loreal Hungary Scientific Award. She is a member of the consortium that received the EU Innovative Medicines Initiative grant on severe asthma in 2009.



J.C. de Jongste

J.C. de Jongste is Professor of Paediatrics and Head of the Dept of Paediatric Respiratory Medicine at Erasmus University Medical Center - Sophia Children's Hospital in Rotterdam, The Netherlands. He is currently actively involved as a clinician, teacher and clinical researcher. His PhD thesis was concerned with the pharmacophysiology of human airway smooth muscle, for which he was awarded the Steven Hoogendijk Prize of the Batavian Society for Experimental Philosophy and the Jaap Swieringa Prize of the Netherlands Society for Pulmonology and Tuberculosis. He was founder of the specialty clinic "KinderHaven" for paediatric atopic diseases in Rotterdam. His main research interests are paediatric asthma, exhaled biomarkers of inflammation and asthma epidemiology. He was Chair of the ERS Scientific Group on Paediatric Asthma and Allergy and was a member of the ERS Long Range Planning Committee and was once the ERS National Delegate of the Netherlands. He is currently a member of the ERS Standing Scientific Committee. He was European editor of *Paediatric Pulmonology* and was an Editorial Board member of the *American Journal of Respiratory and Critical Care Medicine* and *Mediators of Inflammation*. He is a reviewer for many respiratory journals and several general scientific journals including the *New England Journal of Medicine* and *The Lancet*. He has participated in many scientific advisory boards including those of the Dutch Asthma Fund and the Netherlands Cystic Fibrosis Association. He is a member of the Netherlands' Health Council, Chair of the Netherlands Paediatric Respiratory Group, and has chaired and participated in numerous ERS, American Thoracic Society and Netherlands' Health Council task forces.

Preface



Research within in the field of airway and lung inflammation has expanded tremendously during recent decades. Attempts are continuously being made to find novel methods to mirror and monitor inflammatory reactions related to airway disorders and dysfunction. The lungs are particularly well suited for this purpose as we have easy access to exhaled air and thereby a possibility to develop methods that measure compounds directly released from them. As this area of interest is rather new this is the first issue of the *European Respiratory Monograph* to focus on inflammatory markers. As this field is rapidly expanding it was decided, after some initial discussions, to limit this Monograph to markers in exhaled air and to produce a comprehensive update of the entire field. The Guest Editors have succeeded in attracting leading experts within the field to author the chapters. Five chapters have been devoted to different aspects of nitric oxide measurement. Carbon monoxide and volatile organic compounds in exhaled air have been thoroughly reviewed as has the assessment of exhaled breath condensates, which is probably the most expansive area within the field.

The Guest Editors are to be congratulated for this excellent Monograph, which fills the need for a comprehensive review of this very important field. I am convinced that both scientists and clinicians will repeatedly use this Monograph and find it useful in their daily practice.

Editor in Chief
K. Larsson

Introduction

I. Horvath* and J. de Jongste#

*Dept of Pulmonology Semmelweis University Budapest, Hungary. #Dept of Pediatrics/Respiratory Medicine Erasmus MC - Sophia Childrens' Hospital, Rotterdam, The Netherlands.

Correspondence: I. Horvath, Dept of Pulmonology, Semmelweis University, Dios arok 1/C, Budapest, 1125, Hungary, Email: hildiko@elet2.sote.hu

Breath testing has existed in medical practice for centuries; for example, the sense of smell of patients with advanced renal or hepatic diseases. Breath testing has come a long way from ancient knowledge and anecdotal reports to cutting-edge research and the current clinical applications within the field. At present, exhaled biomarker measurements range from the US Food and Drug Administration approved use of exhaled nitric oxide fraction (F_{eNO}) to the determination of volatile organic compounds (VOCs) and the profiling of exhaled breath condensate (EBC) constituents. Being completely noninvasive, sampling of the breath allows clinicians and researchers to assess different body functions in a convenient and flexible way. The vast majority of constituents suggested as biomarkers are present in trace amounts, making detection a challenging task. The application of highly sensitive cutting-edge technologies in sample analysis, including proteomics, metabolomics, mass spectrometry, gas chromatography–mass spectrometry and ion mobility spectrometries, has provided major advancements and offers great potential for the field of exhaled biomarker profiling. However, due to the increasing sensitivity of new detection techniques the purity of the samples is becoming a major hurdle.

Exhaled breath biomarkers have been assessed to understand pathological mechanisms and to aid clinical decision making of extensively different diseases, including asthma, chronic obstructive pulmonary disease, lung cancer and systemic diseases. Entirely different strategies have been implemented for both purposes, including the determination of individual biomarkers and the recognition of signal patterns created by undefined compounds. In order to establish exhaled biomarkers in clinical practice they have to be validated just like any other biomarker and, to date, only a few have been put through the necessary steps.

This issue of the *European Respiratory Monograph (ERM)* provides a state-of-the-art summary of this rapidly progressing field. Our aim was to introduce the topic beginning with the best known biomarker, F_{eNO} , then moving on to carbon monoxide, exhaled VOCs and the wide range of EBC biomarkers. We, as Guest Editors, are grateful to the authors for putting together chapters with detailed information of the different aspects of exhaled biomarker measurements covering everything from pathophysiological issues through methodological issues to clinical applications and implications. The authors not only cover current knowledge and provided an elegant selection of references but also express their opinions, and highlight the unknown aspects and the need for future research. We greatly enjoyed putting together the content for this *ERM* and the interaction we experienced with the authors. Our aim is to lead the reader through the different exhaled biomarkers by providing information relevant both at bench and bedside. We hope that you will find new and relevant information regardless of whether you are just starting to study this exciting field or already have vast experience in it.

We wish you an enjoyable journey when reading this issue of the *ERM* and hope that you will not only use the information provided but will also form questions and comments, and conduct some research that will facilitate further improvement in the field.