



ERS | *monograph*

Obstructive Sleep Apnoea

Edited by
Ferran Barbé and
Jean-Louis Pépin

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Editor in Chief
Tobias Welte

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Preface

Tobias Welte, Editor in Chief

When the first prevalence studies on OSA were published 50 years ago, it was considered a rare disease. In 1981, a letter to the *Lancet* even questioned whether OSA existed in the UK [1]. With the improvement of diagnostics, however, it became clear that OSA is a common disorder with serious consequences for the morbidity and mortality of patients, and with a tremendous influence on quality of life. Today, the prevalence of moderate-to-severe OSA (defined by an AHI of ≥ 15 events·h⁻¹) is >10%. The prevalence increases with age and the disease is more common in women than in men. Both the costs of the disease itself (*i.e.* limited working capacity, rate of traffic accidents due to sleeping while driving) and the costs of the resulting comorbidities (particularly cardiovascular and metabolic diseases) are significant.



With the introduction of nocturnal CPAP therapy, the prognosis and quality of life of OSA patients significantly improved. Ventilators have now become more powerful, less noisy and better to use, thanks to rapid technological development. New ventilation modes have also been developed that allow a more individualised therapy, better adapted to the patient's needs. A number of other treatment options besides CPAP have also been introduced into the therapeutic portfolio of OSA.

In the beginning, the management of OSA patients was more art than science. Evidence increased rapidly and sleep medicine became an evidence-based specialty of pulmonary medicine. The requirements for training specialists, however, have been constantly growing over time. This issue of the *Monograph* summarises the current knowledge about sleep apnoea, from basic research to clinical practice; future developments are also presented. I want to congratulate Ferran Barbé and Jean-Louis Pépin for compiling such an extensive book. We hope this *Monograph* will be helpful to clinicians and scientists involved in the management of this disease, as well as public health bodies and industry connected with this condition.

Reference

1. Shapiro CM, Catterall JR, Oswald I, *et al.* Where are the British sleep apnoea patients? *Lancet* 1981; 2: 523.



Guest Editors

Ferran Barbé

Ferran Barbé received his degree in medicine in 1985 and his PhD in 1999 from the University of Barcelona (Barcelona, Spain). He followed a training programme in respiratory medicine at the Hospital de Bellvitge (Barcelona, Spain). In 1992, he received the Diplôme D'Université in Sleep Physiology from the University René Descartes (Paris, France). He was the Director of the Sleep Unit at the Son Dureta University Hospital (Palma de Mallorca, Spain) for 14 years. In 2005, he moved to Lleida (Spain) as Head of the Respiratory Department at the Arnau de Vilanova University Hospital and Professor of Respiratory Medicine at the University of Lleida. He achieved his European certification in sleep medicine in 2013. Since May 2014 he has been the Director of the Biomedical Research Networking Center Consortium for Respiratory Diseases (CIBERES, Madrid, Spain).



Ferran Barbé's work focusses on sleep apnoea and CVDs. His research aims to achieve a better understanding of the pathogenesis of the cardiovascular consequences for sleep apnoea patients, and to evaluate new diagnostic and therapeutic options in such patients.

Ferran Barbé has had 150 papers published in peer-reviewed journals; these papers have received over 3300 citations. His H-index is 31. He is a member of the Editorial Advisory Board for *Lancet Respiratory Medicine*.

Jean-Louis Pépin

Jean-Louis Pépin received his medical doctorate from Montpellier University (Montpellier, France) in 1987. He was a resident in respiratory medicine at Montpellier University and obtained his certificate as a specialist in sleep medicine during 1987–1989. In 1990, he obtained a Master's Degree in animal biophysiology (neuroscience) from Claude Bernard University of Lyon (Villeurbanne, France). He gained his PhD in biology (cardiovascular adaptations induced by chronic hypoxia) from Joseph Fourier University (Grenoble, France) and was a visiting professor at the Laboratory of Pulmonary Physiology of Harvard University in 1999 (Boston, MA, USA). He achieved his European certification in sleep medicine in 2013.



Jean-Louis Pépin's education, training and research has focussed on clinical and translational research into the cardiovascular consequences associated with chronic and IH, sleep apnoea, COPD, chronic respiratory failure and noninvasive ventilation.

Jean-Louis Pépin is currently: Professor of Clinical Physiology and Medical Director of the Regional Homecare System for Chronic Respiratory Failure at Joseph Fourier University; Head of the HP2 Laboratory Clinical Research Team (INSERM U1042, Grenoble, France) (hypoxia pathophysiology: cardiovascular consequences of IH); and a member of the Faculty of Medicine at the Joseph Fourier University, where he holds a 5-year INSERM Interface full-time research contract. He is Head of the Clinic of Physiology, Sleep and Exercise Department, Scientific Director of Clinical Research Administration and presides over the Research Division at Grenoble University Hospital (Grenoble, France). He runs the French registry of sleep apnoea (which includes more than 90 000 individuals) and is involved in the European Sleep Apnoea Database (ESADA). He is involved in several European Respiratory Society (ERS) and American Thoracic Society (ATS) Task Forces.

Jean-Louis Pépin is the co-author of over 250 published scientific papers (H-index 38). He is the former President of the French Sleep Research and Medicine Society, a member of the ERS and ATS, and an associate editor of *Thorax* for the sleep medicine field.



Introduction

Ferran Barbé^{1,2} and Jean-Louis Pépin^{3,4,5}

OSA is a syndrome caused by recurrent episodes of partial or complete pharyngeal collapse during sleep. It is a common and progressive chronic disease that is responsible for a high number of comorbidities and it is related to an increase in mortality, including a rise in the rate of sudden cardiac death. OSA affects millions of people worldwide; it is a heterogeneous condition with distinct phenotypes, varying from lean young adults with maxillofacial abnormalities and limited IH, to obese middle aged OSA patients with metabolic syndrome, obesity hypoventilation syndrome or overlap syndrome (*i.e.* a combination of OSA and COPD). Two-thirds of HF patients exhibit CSA or OSA. OSA is highly prevalent in specific populations, such as those with hypertension, stroke, coronary heart disease and patients exhibiting arrhythmias. Sleep fragmentation and chronic IH, the markers of OSA, induce intermediate mechanisms, such as oxidative stress, sympathetic nervous system activation and systemic inflammation, responsible for symptoms and cardio-metabolic consequences.

This issue of the *ERS Monograph* begins by addressing the pathogenesis of OSA, with new insights from animal models and integrated physiology. These chapters provide new clues to understanding OSA-related cardiovascular morbidity, as well as ways of phenotyping patients for better prediction of their response to different therapeutic modalities. Leg fluid volume shift from the legs to the neck during the night, a recently demonstrated mechanism that may precipitate UA collapse, is also put into clinical perspective. Another recent hot topic is the link between OSA and cancer; the excess mortality associated with OSA has not only been attributed to cardio-metabolic consequences but also to cancer. This was first suggested in animal studies that demonstrated an association between IH, carcinogenesis and the acceleration of tumour growth; this has recently been confirmed in clinical and epidemiological studies.

The individual populations in which OSA is highly prevalent are considered in subsequent chapters. Specific diagnostic strategies are necessary because OSA recognition modifies risk stratification and requires therapeutic intervention. The authors provide state-of-the art updates on various clinical scenarios, including OSA in children, during pregnancy, in overlap and obesity hypoventilation syndromes and in patients undergoing bariatric surgery.

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Comorbidities are of major importance in OSA because they have a significant impact on healthcare use and mortality. Effective OSA treatment may represent an important target for improving cardio-metabolic risk. However, CPAP, the first-line therapy for OSA, fails to alter metabolic or inflammatory markers in obese OSA patients. This emphasises the need to offer a combination of multiple treatment modalities, including weight loss through lifestyle intervention, bariatric surgery or physical activity, and new medications for the reduction of cardiovascular risk that are specifically dedicated to OSA patients. As OSA-related comorbidities lie in different medical specialties, patients may not receive a totally integrated treatment regime due to poor collaboration across different medical services. It is necessary to establish whether an integrated, remote monitoring approach actually improves patient medical outcomes in a cost-effective manner. Telemedicine could be used not only to monitor CPAP compliance, leaks and residual events but also to record physical activity and self-measurements of BP and oximetry at home. This would allow the implementation of individually tailored therapeutic strategies. A panorama of the different therapeutic modalities and strategies together with OSA e-health are presented in the final chapters of this *Monograph*.

As editors, we hope that you will find this issue of the *Monograph* a useful overview of OSA that aids understanding of the condition and may influence your management of the disease. The chapters are well referenced and should stimulate research initiatives and new management pathways. We are very grateful to all the authors who have contributed excellent chapters to this *Monograph*.

List of abbreviations

AHI	Apnoea–hypopnoea index
BMI	Body mass index
BP	Blood pressure
BPAP	Bilevel positive airway pressure
COPD	Chronic obstructive pulmonary disease
CPAP	Continuous positive airway pressure
CSA	Central sleep apnoea
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
EDS	Excessive daytime sleepiness
EPAP	Expiratory positive airway pressure
ESS	Epworth Sleepiness Scale
FEV1	Forced expiratory volume in 1 s
FRC	Functional residual capacity
FVC	Forced vital capacity
HF	Heart failure
IH	Intermittent hypoxia
IL	Interleukin
IPAP	Inspiratory positive airway pressure
MAD	Mandibular advancement device
ODI	Oxygen desaturation index
OSA	Obstructive sleep apnoea
PAP	Positive airway pressure
PSG	Polysomnography
RCT	Randomised controlled trial
RDI	Respiratory disturbance index
REM	Rapid eye movement
SBP	Systolic blood pressure
TNF	Tumour necrosis factor
UA	Upper airways