

Guest Editors



W.T. McNicholas

W.T. McNicholas is Newman Clinical Research Professor at University College Dublin (UCD; Ireland) and Past President of the European Respiratory Society (ERS). He is also Director of the Pulmonary and Sleep Disorders Unit at St. Vincent's University Hospital, Dublin, Ireland. He graduated in medicine from UCD in 1974 and was awarded the postgraduate MD degree by thesis in 1982 on "Pathophysiological mechanisms in sleep apnoea". Following specialist training and research at the University of Toronto (1977–1982), he established the Sleep Research Laboratory at St. Vincent's University Hospital in 1983 and was appointed Consultant Respiratory Physician in 1984. His research interests include: the cell and molecular mechanisms and consequences of intermittent hypoxia; the pathophysiology, treatment and outcomes of sleep apnoea syndrome; the cardiovascular consequences of the disorder; and sleep disturbances in chronic obstructive pulmonary disease and other chronic respiratory disorders. He was Chair of the EU COST Action B26 on cardiovascular risk in obstructive sleep apnoea syndrome (2006–2010) and also chaired the ERS Task Force on Public health and medico-legal implications of sleep apnoea, which provided the first data on driver licensing regulations in Europe relating to sleep disorders. He has been an Associate Editor for the *European Respiratory Journal* and Past President of the Irish Thoracic Society and the British Sleep Society. He was recently elected President of the European Board for Accreditation in Pneumology. He has published over 150 papers in PubMed listed journals in addition to 25 book chapters, and has edited two other textbooks on breathing disorders during sleep.



M.R. Bonsignore

M.R. Bonsignore is Associate Professor of Respiratory Medicine at the Biomedical Department of Internal and Specialist Medicine, Section of Pneumology, University of Palermo, Italy, and is undertaking research on respiratory pathophysiology during sleep and exercise at the Institute of Biomedicine and Molecular Immunology, National Council of Research, University of Palermo. M.R. Bonsignore is currently the Italian representative in the COST Domain Committee for Biomedicine and Molecular Biosciences. From 2005 to 2006 she was the Chair of the EU COST Action B26 on cardiovascular risk in obstructive sleep apnoea syndrome. In 2008 she was an assembly delegate in the ERS Council, and from 2005 to 2009 she was the Director of the Residency Programme in Respiratory Medicine at the University of Palermo. M.R. Bonsignore graduated in medicine from the University of Palermo in 1979 and carried out her postdoctoral training at institutions in America, Norway and Italy. She has been awarded several honours including the Parker B. Francis Foundation Fellowship in 1983, the American Heart Association of California Fellowship in 1985, the Young Investigator Award Societa' Italiana di Fisiopatologia Respiratoria in 1990 and the ERS Young Investigator Award in 1991. M.R. Bonsignore is an active member of several scientific societies including the American Physiological Society, ERS, Societa Italiana di Cardiologia and the American Thoracic Society. She is currently a member of the Editorial Board for *Chest* and serves as a reviewer for the *European Respiratory Journal*, *Journal of Physiology*, *Hypertension*, *Medicine*, *Science in Sports and Exercise*, *British Journal of Sports Medicine*, *Japanese Journal of Physiology* and *Thorax*. She is author of over 60 publications on sleep apnoea and exercise physiology.

Preface



In Greek mythology Hypnos, the personification of sleep, was the twin brother of Thanatos, the personification of death, and images of Hypnos were often found close to images of death. Although a good sleep is a prerequisite for good health it is not too far fetched to associate sleep with death. It has been observed for a long time that sleep is related to a number of pathological conditions. This has become even more obvious in the last decades, during which time sleep-related disorders have attracted great interest, both from a scientific and a clinical perspective. In 1998 a *European Respiratory Monograph* focusing on sleep-related disorders was published. In that issue, sleep apnoea was a focus but nocturnal asthma and sleep and breathing in COPD also had their own chapters. The current *ERM* is entirely dedicated to sleep apnoea and it is obvious that there has been a tremendous development within this field during the last 12 yrs. Thus, in this issue a number of new fields of interest have been covered. For example, sleep apnoea in children, diabetes and the metabolic aspects of obstructive sleep apnoea syndrome, public health and legal implications (in which transportation safety is discussed), relation to systemic hypertension, drug treatment and weight-loss treatment are now presented in separate chapters. The Guest Editors Walter McNicholas and Marisa Bonsignore are to be congratulated for a very comprehensive and important book aimed at a field which possesses a great interest in a large area of the medical profession.

After 4 yrs as Editor in Chief it is now time for me to move on. I would, therefore, like to take this opportunity to thank the European Respiratory Society (ERS) for appointing me to this position and entrusting me with such an excellent publication, it has been both an interesting and pleasurable task for me to undertake. I have had the great privilege of working with an excellent editorial board, consisting of John Gibson, Fan Chung, Phillippe Camus and Kai-Håkon Carlsen, who all expertly contributed to each publication by providing invaluable opinions regarding content and author structure. I also wish to thank the ERS Publications Office in Sheffield, UK, for a marvellous job throughout these 4 yrs. The *ERM* is produced by real professionals and it has been a pleasure to work with you all.

It is now clear that the *ERM* is highly appreciated among the ERS members and that it is used as a valuable source of information within the whole area of respiratory medicine. I want to congratulate Tobias Welte on taking over the responsibility as Editor in Chief, knowing that he has a very interesting work assignment for the years to come. I am convinced that the *ERM* will go from strength to strength and become even more popular under his management.

Editor in Chief
K. Larsson

Introduction

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Sleep-related breathing disorders, particularly obstructive sleep apnoea (OSA) syndrome (OSAS), are highly prevalent and represent an increasing part of clinical respiratory practice. OSAS is now recognised to be one of the most common chronic respiratory disorders, with only asthma and possibly chronic obstructive pulmonary disease having a higher prevalence. Thus sleep apnoea represents an important topic for the *European Respiratory Monograph*, and the present volume provides a comprehensive overview, with chapters ranging from basic mechanisms to clinical practice. This issue provides an update of a previous Monograph on *Respiratory Disorders during Sleep* published in 1998 [1].

Humans spend up to a third of life asleep, and yet surprisingly little is known about the biological role of sleep. There is general agreement that sleep is beneficial. William Shakespeare's Macbeth described sleep as the "chief nourisher in life's feast", and the age-old remedy for the sick person is to get "plenty of sleep". Some classical writers, however, have viewed sleep with deep suspicion. Sir Thomas Browne wrote "Sleep, in fine, is so like death, I dare not trust it with my prayers", and Alfred, Lord Tennyson described sleep as "death's twin brother".

There have been many references to presumed sleep apnoea in the classical literature and throughout history, including several kings of ancient Greece, and a detailed review of the historical aspects of OSAS is provided in the previous Monograph on *Respiratory Disorders during Sleep* [2]. Furthermore, the giant in the tale of Jack and the beanstalk very probably suffered from OSAS, and Charles Dickens's description of Joe, "a wonderfully fat boy", in *The Posthumous Papers of the Pickwick Club*, clearly demonstrates features of OSAS. Dickens noted that Joe snored heavily, "as if the roaring of cannon were his ordinary lullaby". He was plethoric, "red-faced", had dropsy (peripheral oedema), cognitive dysfunction ("the fat boy's perception being slow") and "divided his time into small alternate allotments of eating and sleeping". These descriptions strongly indicate that Joe suffered from the sequelae of untreated OSAS, with excessive daytime sleepiness, intellectual impairment and cor pulmonale. The term Pickwickian was first used by William Osler, in 1905, to describe similar patients with hypersomnolence and obesity, and was used to describe many early cases of sleep apnoea reported in the medical literature [2]. However, this term is rarely used today, as there may be different causes of obesity and hypersomnolence.

Although sleep apnoea was first described as a specific clinical entity in the late 1950s, there are several descriptions in earlier clinical journals that clearly refer to the disorder. The sleeping characteristics of obstructive apnoea were clearly described by BROADBENT [3] in the late nineteenth century: "there will be perfect silence through two, three, or four respiratory periods, in which there are ineffectual chest movements; finally air enters with a loud snort, after which there are several compensatory deep inspirations".

The practice of modern sleep medicine and the investigation and diagnosis of sleep-related breathing disorders owes much to the development of appropriate diagnostic tools and techniques. The pivotal discovery of electroencephalography by BERGER [4], in 1930, demonstrated clear differences between wakefulness and sleep. The use of the electro-oculogram by

ASERINSKY and KLEITMAN [5], in the early 1950s, revealed the presence of slow and rapid eye movement (REM) during sleep, and they observed that REM is associated with a lightening of sleep, dreaming and a number of cardiovascular and respiratory phenomena. The association of REM sleep with muscle relaxation was later made by JOUVET *et al.* [6].

During the late 1950s and early 1960s, several different clinical reports described the causative associations between obesity, chronic hypoventilation, pulmonary hypertension and cor pulmonale, but the excessive sleepiness was typically attributed to hypercarbia and depression of the respiratory centre. Cor pulmonale was associated with tonsillar and adenoidal hypertrophy and micrognathia in other reports, but the underlying aetiology was not clarified. In 1965, GASTAUT *et al.* [7] provided the first comprehensive account of OSAS, describing polysomnography in obese hypersomnolent patients with frequent nocturnal apnoeas. During the following decade, the clinical and pathophysiological features of OSAS were described, and it became clear that the pathophysiological basis of obstructive apnoea fundamentally relates to a narrowing of the upper airway, which is partly genetic in origin, but to which acquired factors, such as obesity, also contribute. This narrowing compromises the balance between collapsing forces affecting the upper airway during inspiration and the counteracting forces of upper airway dilating muscles. Although early research focused on clinical and pathophysiological aspects, recent research has increasingly focussed on genetic and molecular aspects, particularly in the development of comorbid conditions, such as cardiovascular and metabolic disease. OSAS is now recognised to be highly prevalent in disorders such as congestive heart failure, systemic hypertension and renal failure. Although much has been learnt, substantial knowledge deficits remain, and the basic mechanisms and consequences of OSAS represent an exciting area for future research.

The relatively recent clinical and pathophysiological descriptions of OSAS are surprising given that the disorder is now widely recognised and highly prevalent, affecting $\geq 4\%$ of adult males and $\geq 2\%$ of adult females in the developed world, and with this prevalence growing in parallel with the growing prevalence of obesity. However, most of these cases are clinically unsuspected, since the two most common symptoms of loud snoring and a tendency to fall asleep during the daytime are often considered normal variants, and patients frequently do not seek medical attention. Unfortunately, many patients who do seek medical attention are dismissed as having no significant illness, without formal assessment, and it is very common for patients who have been symptomatic for many years to present to sleep clinics.

The failure to recognise clinically significant OSAS is particularly unfortunate for many reasons. First, the condition carries significant morbidity and mortality, and is associated with an increased risk of heart attack and stroke [8], in addition to a significant risk of automobile accidents and injury in the workplace as a consequence of excessive sleepiness [9]. Secondly, the condition is very treatable, and severe forms of OSAS can respond dramatically well to the continued home use of nocturnal nasal continuous positive airway pressure (CPAP) therapy. Additional clinical challenges in the assessment and management of OSAS include the presentation of OSA without sleepiness and the clinical spectrum of OSA in the elderly and in females. Although OSAS has traditionally been regarded as a disease affecting males, there is increasing recognition that the disease is also prevalent in females, particularly after the menopause, and that the clinical manifestations may differ from those in males [10]. OSA is prevalent in the elderly population, but affected patients appear to be relatively less symptomatic, and the disorder may have less severe clinical consequences in this age group [11].

Treatment approaches to OSAS have evolved in parallel with the increased pathophysiological understanding. Most treatment modalities have been mechanistic, with nasopharyngeal airways and tracheostomy being used as a means of bypassing the site of obstruction in the upper airway in the 1970s [12]. However, these treatments were neither indicated nor acceptable to patients without very severe disease. Surgical approaches to enlargement and/or stiffening of the upper airway were also developed, the most widely used being uvulopalatopharyngoplasty, which was described by FUJITA *et al.* [13] in 1981. The development by SULLIVAN *et al.* [14], in 1981, of CPAP

therapy delivered *via* a nasal mask was a crucial development in the history of sleep-related breathing disorders, providing a highly effective but noninvasive modality of treatment for OSAS that revolutionised the whole field of sleep medicine. CPAP is now the mainstay of therapy, particularly in moderate and severe cases of OSAS.

The high prevalence of OSAS has focused attention on simplified approaches to diagnosis, and there is an increasing trend towards diagnosis and therapy in the ambulatory setting. Although polysomnography remains the gold standard for diagnosis, such studies are resource-intensive since they generally require the facilities of a full sleep laboratory and a trained technician. Thus polysomnography is impractical in many sleep centres for routine assessment in the majority of patients with typical clinical presentations of OSAS. An increasing number of limited diagnostic systems are available to meet the high clinical demand, and ongoing research is directed at identifying novel signals in order to simplify and improve the diagnosis of OSAS in the home setting.

Statement of Interest

None declared.

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