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SERIES EDITORIAL—PROLOGUE:
RESPIRATORY SLEEP DISORDERS

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Update in respiratory sleep disorders: Prologue to a modern review series

Key words: sleep apnoea, sleep disorders.

Abbreviations: CANPAP, Canadian Continuous Positive Airway Pressure for Patients with Central Sleep Apnea and Heart Failure; COPD, chronic obstructive pulmonary disease; OSA, obstructive sleep apnoea; P4, personalized, predictive, preventative and participatory; PAP, positive airway pressure; PREDICT, Continuous Positive Airway Pressure in Older People with Obstructive Sleep Apnoea Syndrome; REM, rapid eye movement; SASM, Society of Anesthesia and Sleep Medicine; SAVE, Sleep Apnea Cardiovascular Endpoint; SERVE-HF, Treatment of Sleep-Disordered Breathing with Predominant Central Sleep Apnea by Adaptive Servo Ventilation in Patients with Heart Failure; STAR, Stimulation Therapy for Apnea Reduction.

Sleep is a period of great vulnerability for ventilation. Pharyngeal muscle tone decreases, particularly during rapid eye movement (REM) sleep, resulting in upper airway narrowing and collapse in predisposed individuals. Pharyngeal reflexes are also dampened, compromising the capacity of the upper airway muscles to activate in response to airway narrowing and collapse. A sleep-related loss in chest wall muscle activation results in reduced end-expiratory lung volume which, in turn, reduces longitudinal traction on the upper airway, which also acts to increase its collapsibility. Furthermore, low end-expiratory lung volumes are associated with atelectasis in the dependent parts of the lung, compromising gas exchange. Notably, these effects are aggravated by obesity, which is associated with exaggerated sleep-related decreases in lung volume. In addition to sleep-related effects on upper airway stability and gas exchange, the decreased muscle activation of sleep can lead to hypoventilation and the loss of the behavioural effects of wakefulness can result in periodic breathing in those prone to it, even if this problem is not manifest when awake. While these various sleep-related problems can occur in isolation, they may be seen in combination, for example coexistent obstructive sleep apnoea (OSA) and sleep hypoventilation in morbid obesity.

Sleep and breathing are governed by complex interrelated physiological mechanisms. The key protective mechanism in response to sleep-related breathing events is arousal from sleep, with transient restoration of wakefulness homeostasis. Absence of protective arousal responses, as is seen during general anaesthesia, creates a vulnerability to asphyxia, with maintenance of airway patency and adequate ventilation often dependent on the use of mechanical aids, utilized by the attending anaesthetist. The post-operative period presents additional challenges, as opioids and sedatives may cause depression of protective respiratory responses, a hazard in unmonitored environments. Sleep compounds these drug effects. The parallels between sleep and anaesthesia, including concerns regarding the vulnerability of patients with sleep-related breathing disorders to perioperative respiratory complications, have led to the formation of a new professional body, the US-based Society of Anesthesia and Sleep Medicine (SASM), whose mission is to advance standards of care for clinical problems shared by anaesthesiology and sleep medicine.

Sleep is a whole-body state and so problems with it can affect many organ systems (e.g. cardiovascular, metabolic and endocrine) and aggravate the effects of other diseases (e.g. asthma, heart failure, COPD and dementia). The daytime consequences of sleep-related breathing disorders are now well appreciated (e.g. feelings of sleepiness and fatigue, impaired cognition, mood and psychomotor function, impaired productivity, increased accident risk, hypertension, vascular disease, metabolic disturbance and depression). While the prevalence of these disorders appears to be increasing in some parts of the world, at least in part due to increasing obesity and an ageing population, so is our understanding of their pathogenesis. For example, OSA was for many years attributed to poor pharyngeal anatomy. Today, it is widely accepted that the pathogenesis of OSA is multifactorial in nature, with the effects of unfavourable anatomy augmented by other variable influences including lung volume, pharyngeal muscle responsiveness, arousal thresholds and stability of ventilatory control.[1]

Improved understanding of the mechanisms underlying sleep-related breathing disorders, and appreciation of their complex multifactorial nature has driven the development of a variety of treatment options. While positive airway pressure (PAP) therapies are a mainstay, they are not suitable for all patients and compliance with them is problematic for many. Alternative treatments include oral appliances, body positioning devices, hypoglossal nerve stimulation, a diversity of surgical procedures and lifestyle modification including weight loss. Better understanding of neurophysiology may, in time, lead to useful pharmacological approaches, although there is little to offer for these disorders clinically at present.

The multiple potential contributors to the pathogenesis of sleep-related breathing disorders and their co-morbidities and their variable influence between individuals are reflected in the mixed results of several high profile multicentre therapeutic trials. Studies such

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as the Canadian Continuous Positive Airway Pressure for Patients with Central Sleep Apnea and Heart Failure (CANPAP) trial,[2] the Treatment of Sleep-Disordered Breathing with Predominant Central Sleep Apnea by Adaptive Servo Ventilation in Patients with Heart Failure (SERVE-HF) trial,[3] the Sleep Apnea Cardiovascular Endpoints (SAVE) trial,[4] the Continuous Positive Airway Pressure in Older People with Obstructive Sleep Apnoea Syndrome (PREDICT) trial[5] and the Stimulation Therapy for Apnea Reduction (STAR) trial[6] all show improvement in disease severity in some, but not all, patients. This variability in outcome is despite the use, in each study, of methods to ensure participants were diagnostically homogenous and considered likely to benefit from the therapy being tested. These inconsistent results make it clear that we need to understand better individual predisposing characteristics to these problems and tailor treatments to address them[7]: we are entering an era of personalized treatment for sleep-related breathing disorders.

The purpose of this *Review Series* is to summarize our current understanding of the mechanisms, consequences and treatment of sleep-related breathing disorders. It includes commentary on their prevalence, genetic basis, pathophysiology, diagnosis and treatment. Perioperative management is considered as well as their effects on cognition, ageing and cardiometabolic risk and their interactions with asthma, heart failure and COPD. In all of this series, there is an emphasis on personalized, predictive, preventative and participatory (P4) medicine.

We would like to thank the many individuals we approached who readily agreed to contribute to this *Review Series*. They are all internationally recognized experts in their fields and we hope that their papers will be of interest to those involved in studying, caring for or living with sleep-disordered breathing.

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