Sleep Medicine

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Contents

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Abstract

Sleep has important impacts on upper airway function, and thus the nature of sleep, the physiological changes that accompany it, and the disorders associated with it are of concern to oral medicine specialists. These concerns relate to both their role in helping manage upper airway problems during sleep – snoring and obstructive sleep apnea – and to the fact that these problems often exist in patients presenting with other functional or cosmetic abnormalities involving the upper airway. Additionally, oral medicine specialists help manage insomnia related to chronic orofacial pain and sleep bruxism. The purpose of this chapter is to provide a general overview of sleep and its disorders, hence a context within which to consider specific sleep-relevant issues. It is particularly important that specialists focused on the upper airway have a good understanding of the impacts of sleep, as problems with airway patency may only manifest in this state. Furthermore, such problems, in turn, disrupt sleep itself, causing sleep loss and other physiological disturbances which have their own impacts on symptoms and on well-being.

Keywords

Sleep disorders · Upper airway · Pharyngeal muscles · Inadequate sleep · Sleep disorders · Sleep apnea · Snoring · Sleep hypoventilation · Periodic breathing · Insomnia · Restless legs · Narcolepsy · Parasomnia · Bruxism

Introduction

Sleep occupies approximately one-third of adult life. Good sleep is an essential preparation for wakeful work, social and family activities that occupy the balance. For many sleep is inadequate, with more than one-third of the community complaining of this on a daily or near-daily basis. This may be because sleep is curtailed due to other demands or priorities, or because sleep quality is compromised by the existence of a sleep disorder. Whatever its source, the effects of sleep loss are pervasive, compromising psychological and physical well-being. Lack of sleep leads to cognitive, psychomotor, and emotional dysfunction which compromise daily activities, including safety and productivity. It also predisposes to health disturbances including vascular disease, diabetes, obesity, depression, and premature mortality. Furthermore, sleep itself is a vulnerable state with the physiological changes of sleep, such as decreased muscle activation and ventilatory drive, predisposing to sleep-related breathing disorders in predisposed individuals such as those with abnormal upper airway anatomy or obesity. The most common of these are snoring and obstructive sleep apnea (OSA), a widely prevalent problem with substantial comorbidities.

The issues of disturbed sleep, its causes, its consequences, and the ways of addressing these are highly relevant to oral medicine specialists given their interest and expertise in upper airway anatomy and physiology, orofacial pain, and bruxism (Sofi et al. 2014). There is a sleep component

to many of the cases presenting to them, either because of the predisposing nature of anatomical disturbances or because sleep is disturbed in other ways such as through orofacial pain or a more sleep-specific matter, such as sleep bruxism.

To assist in engaging with these problems, this chapter provides an overview of the nature of sleep, why and how it can be inadequate, the prevalence and consequences of such problems, and the special challenges posed by specific sleep disorders. Its purpose is to alert oral medicine specialists to the fact that disturbed sleep is commonly present in their patients and how this is best dealt with when it is.

The Nature of Sleep

Sleep is a natural state of decreased awareness and responsiveness which is readily reversed. The need for it progressively increases with time spent awake. The resulting drive for sleep as hours spent awake accumulates is known as "homeostatic drive." However, sleep is also episodic with a natural day-night wake-sleep circadian pattern governed by the internal body clock and largely dictated by light and dark. In general, the circadian drive for sleep is greatest between midnight and dawn. The homeostatic and circadian drives interact to determine sleep propensity at any given time (Borbely and Achermann 1999). Regular hours of overnight sleep takes best advantage of these drives.

During sleep, the skeletal muscles relax, and breathing efforts are less than during wakefulness. Breathing can be compromised by hypoventilation (under-breathing) if the muscles are weak (as with a variety of neuromuscular diseases) or overloaded (as with a variety of respiratory diseases or obesity). If the throat is narrow, relaxation of throat muscles during sleep may cause it to vibrate during breathing efforts causing snoring, or partially or completely obstruct, which is the basis of OSA (White 2005). Sleep is not uniform, having different stages with varying characteristics (Fig. 1). The most basic distinction is between rapid eye movement (REM) sleep and non-REM sleep. Dreams are more prevalent and better organized during REM than non-REM sleep; hence they are sometimes labeled

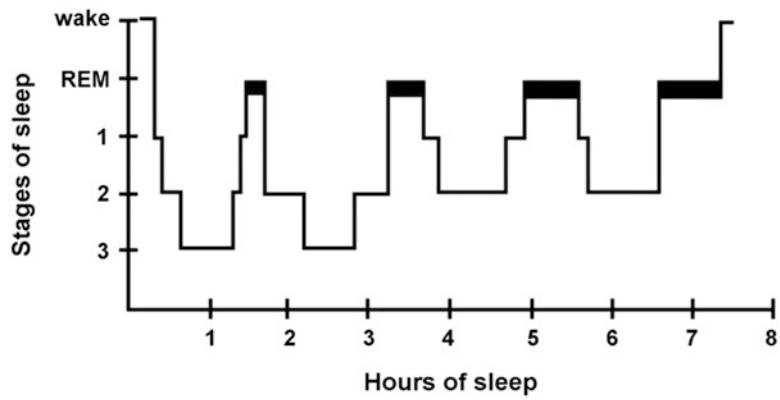

Fig. 1 Sleep hypnogram. This demonstrates the stages of sleep as a function of sleep time in a typical young adult. Each stage has its own electroencephalographic/ electro-oculographic/ electromyographic characteristics. Stage 1 sleep normally occupies less than 10% of total sleep time and is a transition stage between wakefulness and established sleep. Stage 2 sleep normally occupies 45–50% of sleep. Stage 3 sleep, also known as slow wave or deep sleep, occupies about 20% of sleep time and is usually concentrated in the first half of sleep. Collectively stages 1, 2 and 3 sleep are known as non-rapid eye movement (non-REM or NREM) sleep. Interposed with non-REM sleep are cycles of rapid eye movement (REM) sleep that occur at 60–90 min intervals, the first around 60 min after sleep onset. The length of these REM periods gets greater as the night progresses and REM sleep occupies about 25% of sleep time

"dreaming" and "non-dreaming" sleep, respectively. Muscle activation and drive to breathe are at their lowest during REM sleep, such that any tendency to under-breathe or to develop obstruction of the pharyngeal airway is most apparent during this sleep stage (White 2005).

The Need for Sleep

As most people understand from their own experience, sleep is necessary for rest and recuperation. Prolonged wakefulness causes exhaustion of heavily used neural circuits, as energy supplies become depleted, signal-to-noise ratios decrease, and learning is saturated (Tononi and Cirelli 2014). Adenosine, liberated from breakdown of intracellular adenosine triphosphate, exerts an inhibitory effect on many of the body's processes associated with wakefulness through its effects on adenosine receptors. Of note, adenosine receptors are blocked by caffeine, which competes for the same receptors, accounting for its stimulant effects. Sleep is associated with a decrease in utilization of these heavily utilized neural circuits, allowing restoration of synaptic strength and cellular homeostasis (Tononi and Cirelli 2014; Chikahisa and Sei 2011).

Despite recuperation of overworked circuits as part of its recovery function, parts of the brain are quite active during sleep. Important among these sleep activities are information processing and memory consolidation. Associations are built between new information and old with clearing of non-useful information, although traumatic memories tend to remain (Stickgold 2005). Memory is consolidated and "slept on" problems are sometimes solved. The brain is also active in monitoring vital functions and, to a limited extent, the local environment. During normal sleep, there are regular spontaneous arousals occurring several minutes apart, with frequency dependent, in part, on age (Jaimchariyatam et al. 2014). These arousals are characterized by several seconds of wakeful electroencephalographic activity: not enough to disturb sleep seriously, but presumably sufficient for surveillance purposes. Sleep is an inherently vulnerable state, and so, while one can only speculate about the reasons why spontaneous arousals occur, it makes sense that there might be a mechanism that allows sleep to lighten periodically, increasing the chance that unfavorable environmental disturbances are detected and acted upon.

Sleep requirement varies between individuals. Most adults know from their life experience what duration they require to feel good and function optimally the next day. The normal range of duration of sleep for adults is between 6 and 10 h, with most clustered in the "recommended" 7–9 h range, with an average duration of 8 h. Sleep times are longer for children and adolescents. Sleep need appears to stabilize around the age of 25 years and remains stable for most of adult life, decreasing a little beyond the age of 65 years (Fig. 2) (Hirshkowitz et al. 2015, b).

The Causes of Inadequate Sleep

Sleep can be adversely affected by a variety of social, psychological, and pathological factors. There are three broad categories of sleep disturbance: insufficient sleep duration, inappropriate timing of sleep, and impaired sleep quality.

Insufficient Sleep Duration

Some individuals have naturally short sleep requirements and do well with less sleep than is considered normal. However, many others suffer from insufficient duration of sleep. In some, this can be the result of insomnia, a sleep problem characterized by difficulty in achieving or maintaining sleep which is discussed later in this chapter. In others, and increasingly commonly, inadequate sleep duration occurs because of other priorities and demands posed by work, family life, and social activities including social media, the Internet, and other technologies (Adams et al. 2017). Some of these demands are unavoidable and temporary. A sleep debt is accumulated which is subsequently repaid by "catch up" sleep, although compromised function is present for the time the sleep debt is present. In other cases, sleep is avoidably but repeatedly

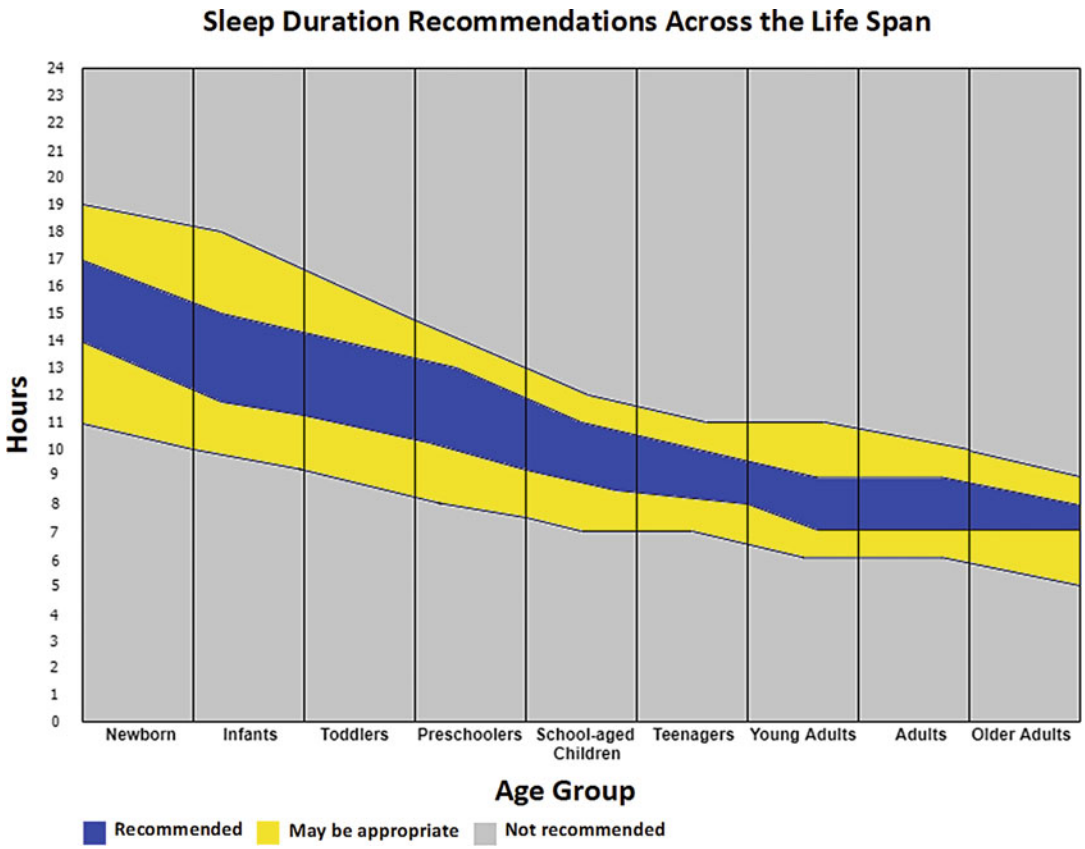

Fig. 2 National sleep foundation sleep duration recommendations. Reduction in sleep requirements during childhood is demonstrated, with sleep requirements stabilizing in early adulthood (Reproduced from Hirshkowitz et al. 2015a, b)

compromised in an attempt to allow more time for other pursuits with the individual enduring the effects of sleep restriction and persevering despite them (Owens 2014). If the boundaries of sleep restriction are pushed too far, then the need for sleep becomes overwhelming and involuntary micro-sleeps supervene (Poudel et al. 2014).

Environmental disturbance from noise, light, and hot or cold conditions is another cause of insufficient sleep duration (Freedman et al. 1999). Sleep is facilitated by dark, quiet, thermoneutral (20–22°C, if covered) sleeping conditions.

While average adult sleep requirement is approximately 8 h, 50% of the population need more than this, with up to 10 h considered within the normal range (Hirshkowitz et al. 2015a). Beyond this there are people who are natural long sleepers: they are otherwise healthy but need to sleep longer than 10 h/night regularly to function adequately the next day. These people are to be distinguished from those with excessive daytime sleepiness because of a sleep disorder that impairs sleep quality, referred to below.

Inappropriate Timing of Sleep

A significant proportion of the Western workforce are shift workers (Australian Bureau of Statistics 2008). This situation can disrupt their sleep as those on evening and night shift, and those starting early have the challenge of sleeping when their internal body clock is programmed to be awake and working when it is programmed to be asleep. While some are more disturbed by this than others, overall it presents a major impediment to safety and

productivity. The work-related accident rate of shift workers is double that of non-shift workers (Australian Bureau of Statistics 2008).

Jetlag is a commonly experienced manifestation of the power of these circadian influences, with retiming of the internal body clock to match local clock time taking up to 1 day per time zone crossed, disadvantaging working and sporting team travelers as well as tourists. The effect of these time zone shifts on performance at destination is the subject of intense ongoing interest (Waterhouse et al. 2007). While circadian misalignment and accompanying sleep disturbance and sleep loss are likely to be major influences, the general disruption and changes in routine associated with travel have additional impacts.

Impaired Sleep Quality

In cases where its duration appears adequate and it is taken at normal times yet sleep is unrefreshing and excessive daytime sleepiness is present, a compromise in sleep quality is likely to be present. This is the domain of sleep medicine as sleep disorders are prime causes of this problem.

Sleep can be disturbed by a variety of medical, psychological, and psychiatric conditions. Symptoms such as breathlessness, pain, anxiety, and depression resulting from these conditions may disturb sleep. In turn, disturbed sleep may aggravate these symptoms. For example, sleep is disturbed by pain, but disturbed sleep can also aggravate pain through changes in pain perception (Edwards et al. 2015). Equally depression disrupts sleep, and disturbed sleep aggravates depression. Indeed many symptoms of sleep loss are shared by depression, such as difficulty achieving sleep, recurrent awakenings, unrefreshing sleep, cognitive dysfunction, and mood disturbance (Edwards et al. 2015). Asthma and ailments such as gastroesophageal reflux are often worse during sleep (and recumbence) than wakefulness.

Beyond these nonspecific disturbances of sleep due to other disorders lie specific sleep disorders. They are common and widely prevalent. For example, OSA is estimated to affect 9% of adults, 13% of men, and 6% of women, to a clinically significant degree (Peppard et al. 2013). Insomnia is common, with primary insomnia, that is, insomnia not attributable to some other cause such as pain or psychological disturbance, affecting approximately 3% of the population on a long-term basis (Roth and Roehrs 2003). Willis-Ekbom disease ("restless legs syndrome") affects 2.7% of adults, with its prevalence increasing with age (Allen et al. 2005). Apart from these common disorders, there are more than 70 other sleep disorders described in the International Classification of Sleep Disorders which describe conditions associated with difficulty initiating or maintaining sleep, abnormal sleep behaviors, disturbed physiological function, and/or excessive daytime sleepiness (Table 1) (American Academy of Sleep Medicine 2005). Some of the more common sleep disorders are dealt with in greater detail in section "Consequences of Inadequate Sleep" below.

Table 1 Spectrum of sleep disorders

Dyssomnias: *difficulty initiating, maintaining sleep or excessive sleepiness*	
Intrinsic sleep disorders	e.g., primary insomnia, narcolepsy, periodic limb movement disorder, obstructive sleep apnea, central sleep apnea
Extrinsic sleep disorders	e.g., inadequate sleep hygiene, drug/alcohol/toxin-dependent disorders, nocturnal eating
Circadian sleep disorders	e.g., jetlag, shift work, delayed/advanced sleep phase
Parasomnias: *disorders of arousal, partial arousal, and sleep stage*	
Arousal	e.g., confusional arousals, sleep walking, sleep terrors
Sleep-wake transition	e.g., sleep talking, sleep starts
REM sleep associated	e.g., nightmares, sleep paralysis, REM sleep behavior disorder
Other	e.g., bruxism, enuresis
Medical/Psychiatric: *sleep disorders associated with medical or psychiatric disease*	
Psychiatric	e.g., associated with psychoses, mood disorders, anxiety
Neurological	e.g., dementia, parkinsonism, epilepsy
Other	e.g., gastroesophageal reflux, asthma
Other:	
Proposed	e.g., short/long sleepers, sleep-related laryngospasm

Prevalence of Sleep Impairment

While sleep disorders affect approximately 10% of the adult population, twice as many complain of inadequate sleep on a daily or near-daily basis. This fact has been demonstrated in sleep surveys conducted in the USA and Australia which suggest that over 20% of adults complain of poor-quality sleep and/or excessive daytime sleepiness with such regularity (National Sleep Foundation 2005; Hillman and Lack 2013). These complaints are observed across a wide span of ages, with greatest prevalence in people of working age. Women appear more affected than men, except in the case of snoring and related difficulties. Although there are potential limitations with telephone surveys (e.g., because of low response rates to landline phone calls), these findings are in broad agreement with those of two large community-based studies, one in the USA and the other in Germany, and with the 2008 US Center for Disease Control and Prevention study which reported that 28% of US adults had insufficient sleep or rest (<7 h/night) on a majority of nights over a 30-day survey period (Center for Disease Control and Prevention 2011; Stein et al. 2008; Unruh et al. 2008).

Consequences of Inadequate Sleep

Sleep is essential for cognitive and psychomotor function, emotional modulation, memory consolidation, and learning (Siegel 2005; Walker and Stickgold 2006). Loss of sleep causes lapses in attention and ability to stay focused, reduced motivation, compromised problem-solving, confusion, irritability, memory disturbance, impaired communication, slowed or faulty information processing and judgment, diminished reaction times, and indifference and loss of empathy (Joint Commission 2011). Motor vehicle and work-related accident risks are significantly increased where sleep is inadequate (Smolensky et al. 2011).

Apart from its negative impacts on cerebral function, sleep loss also appears to be pro-inflammatory in effect and to increase insulin resistance, predisposing to metabolic disorders such as diabetes (Leproult et al. 2014). Inadequate sleep is associated with obesity (Nielsen et al. 2011). It also appears to predispose to vascular disease (strokes and heart attack) (Sofi et al. 2014; Cappuccio et al. 2011). It is suggested that it may increase cancer risk, with hormonally dependent cancers a particular risk, perhaps related to circadian effects on hormonal levels across the day (Lie et al. 2011). All-cause mortality rates are higher in habitually short sleepers (< 6 h/night) than those whose sleep is within the normal range (Cappuccio et al. 2011).

Specific Sleep Disorders

To this point general issues relating to causes of sleep loss and their shared consequences have been discussed. This section deals with some important specific sleep disorders, describing their pathophysiological basis, symptoms, consequences, and methods for effective diagnosis and treatment.

Sleep-Disordered Breathing

Sleep is a vulnerable time for breathing because of sleep-related reductions in ventilatory drive, activation of upper airway and respiratory muscles, and decrease in arousal responses (White 2005). Sleep-disordered breathing can take several different forms, although these frequently coexist. It may involve upper airway dysfunction (snoring and OSA), inadequate ventilation from non-obstructive causes (sleep hypoventilation), or breathing instability (periodic breathing).

Snoring and Obstructive Sleep Apnea

Snoring and OSA are very common problems. Regular loud snoring affects up to 30% of middle-aged men and 18% of middle-aged women on a regular basis (Bloom et al. 1988). OSA is present to at least a moderate degree in 13% of men and 6% of women (Peppard et al. 2013). The gap in OSA prevalence between the genders starts to close after menopause.

Pathophysiology: Snoring and OSA generally occur because of the combined influences of a

relatively narrow throat and the permissive effect of sleep-related pharyngeal muscle relaxation (White 2005). The predisposing narrow throat may be an inherited characteristic (family histories of snoring and OSA are common) or result from narrow skeletal confines (e.g., retrognathia or maxillary hypoplasia), increased pressure around the airway from obesity, pharyngeal muscle weakness, and/or obstructing lesions within the pharynx, such as adenotonsillar hypertrophy (Watanabe et al. 2002). Low lung volumes may also contribute through a reduction in longitudinal tension on the upper airway (Stanchina et al. 2003). The tonic and phasic pharyngeal muscle activity that acts to stabilize the upper airway during wakefulness decreases during sleep, to a profound degree during REM sleep. The airway wall then becomes unstable, tending to vibrate (snore) and to obstruct partially or completely during inspiration producing hypopneas and apneas, respectively. An obstructive apnea is a $\geq$ 10 s cessation in flow with ongoing respiratory effort. A hypopnea is a $\geq$ 10 s reduction in flow of $\geq$30% relative to pre-event baseline associated with $\geq$3% oxygen desaturation from pre-event baseline. These breathing events are usually terminated by brief (<15 s) arousals or, relatively infrequently, by longer awakenings. The number of hypopneas plus apneas divided by the hours of sleep provides a measure of OSA severity – the apnea-hypopnea index or AHI. In addition to apneas and hypopneas, the term "respiratory effort-related arousal" (RERA) is used to describe flow-limited breathing that does not result in a significant drop in oxygen saturation levels but is sufficient to cause an arousal. The respiratory disturbance index (RDI) includes these events as well as apneas and hypopneas in its calculation of events per hour of sleep.

AHI is the most commonly used metric of OSA severity. Among other things it reflects the amount of sleep disruption caused by the condition and is readily measured using simple portable monitoring tools. Other indices of sleep disruption, such as arousal index (the number of arousals per hour of sleep), require more sophisticated electroencephalographic measures. There are other OSA metrics that usefully reflect aspects of the disorder, including length of obstructive events and measures of oxygenation. Long events suggest the person's threshold for arousal is high: there are inherent differences in individual arousal thresholds, and these thresholds are also subject to increase with alcohol or sedative drug use. Measures of oxygenation include minimum arterial oxygen saturation (SaO_2) overnight (nadir SaO_2) or the percentage of sleep time spent below a specified SaO_2 threshold. While it is important to detect significant hypoxemia where it exists, these measures do not adequately reflect OSA severity in many people: for example, lean individuals may have quite severe OSA in terms of number of events and/or their length but have relatively little hypoxemia.

In adults, an AHI of <5 events/hr is considered normal, 5–15 obstructive events/hr mild OSA, 15–30 events/hr moderate OSA, and >30 events/hr severe OSA. Supine sleep has an influence, with 50% of people having at least twice as many events supine as lateral, referred to as supine-dependent or positional OSA (Oksenberg and Silverberg 1998). In some people, OSA is restricted to supine sleep. OSA also tends to be more severe in REM sleep where the muscles are most relaxed and protective reflexes are depressed. Events can last from 10 s (below which, by convention, they are not counted) to well over a minute in some cases. This variability in duration may reflect individual variability in arousal thresholds for these events.

In children (<18 years), severity of OSA is categorized differently with most centers regarding an AHI $\leq$1 event/hr as normal, >1–5 obstructive events/hr as mild OSA, 5–10 events/hr as moderate OSA, and >10 events/hr as severe OSA.

Clinical presentation: Given these phenomena, the cardinal symptoms of OSA are loud, socially disturbing, habitual snoring, witnessed events, and excessive daytime sleepiness from the arousal-/awakening-associated sleep fragmentation. However, while these symptoms are common, they are not invariably present, even in severe cases. Some patients suffer from recurrent awakenings overnight, sometimes with gasping or momentary choking, while others are unaware of the disrupted nature of their sleep, only recognizing the effect

of recurrent brief (<15 s) arousals on sleep quality from its unrefreshing nature.

Comorbidities: Apart from their impact on sleep quality, the recurrent arousals are associated with hypoxemia and sympathetic activation. These factors have a negative impact on vascular and metabolic function, and, together with the sleep disruption, metabolic disturbance and pro-inflammatory effects appear responsible for the occurrence of comorbidities such as hypertension, vascular disease, diabetes, and depression. Workplace and vehicle accident risk increase several fold as a result of the destructive effect of sleep loss on cognitive and psychomotor function. Productivity suffers for the same reasons.

The presence of moderate or severe OSA appears to treble the risk of developing new hypertension, and a high proportion of patients with drug-resistant hypertension have unrecognized OSA (Logan et al. 2001; Peppard et al. 2000). OSA appears to more than double the risk of both incident stroke and cardiovascular death, with greater likelihood of these outcomes apparent with increasing OSA severity as judged by AHI (Loke et al. 2012). It is recognized that OSA is highly prevalent in individuals with type 2 diabetes and, conversely, that metabolic conditions such as insulin resistance, glucose intolerance, and type 2 diabetes are commonly present in OSA. These associations appear to be independent of shared risk factors such as age and obesity (Moon et al. 2015). OSA also appears highly prevalent among individuals with major depressive disorders (Stubbs et al. 2016). Indeed, depression and disrupted sleep appear to have a bidirectional relationship with depression disturbing sleep and disturbed sleep aggravating depression. Furthermore, depressive symptoms are common in patients with untreated OSA, creating the potential for diagnostic confusion: recognition of OSA is important in such patients as the depressive symptoms often resolve with its treatment (Edwards et al. 2015). Accident risk increases with untreated OSA: the odds of a work-related accident double in workers with OSA as does the risk of motor vehicle accidents in individuals with OSA (Garbarino et al. 2016; Tregear et al. 2009).

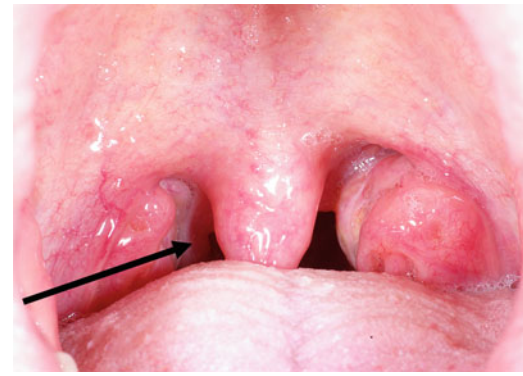

Fig. 3 Photograph of oropharyngeal crowding. Note narrow oropharyngeal isthmus (*arrow*) (Image courtesy of Clinical Associate Professor Ramesh Balasubramaniam, Perth Oral Medicine & Dental Sleep Centre, Perth WA, Australia)

Diagnosis: Clinical suspicion is raised by the presence of symptoms and the signs associated with predisposing features such as obesity, increased neck circumference, and craniofacial abnormalities such as retrognathia and a crowded oropharyngeal appearance (Fig. 3) (Schellenberg et al. 2000). The presence of comorbidities offers further clues. Questionnaires seeking some of these features are useful screening tools. One of the most widely used of these is the eponymous STOP-BANG questionnaire (Chung et al. 2016, 2008). It has eight questions relating to presence of loud ***S***noring, daytime ***T***iredness, ***O***bserved obstructive events during sleep, high blood ***P***ressure, ***B***ody mass index of greater than 35 kg/m^2, ***A***ge over 50 years, ***N***eck circumference greater than 40 cm, and male ***G***ender. One point is scored for each positive answer, and a score of ≥3 is 84% sensitive and 56% specific for the presence of OSA (AHI >5 events/h) (Chung et al. 2008). Its high sensitivity and simplicity make it an attractive screening tool, as a score 0–2 allows OSA to be reasonably confidently excluded. However, it is relatively nonspecific, reflecting the nonspecific nature of many of these features, so that the false-positive rates are high, as they also are with similar instruments, such as the Berlin questionnaire (Chung et al. 2016).

Diagnosis can only be confirmed and severity quantified by an overnight sleep study. The gold standard is polysomnography, which involves

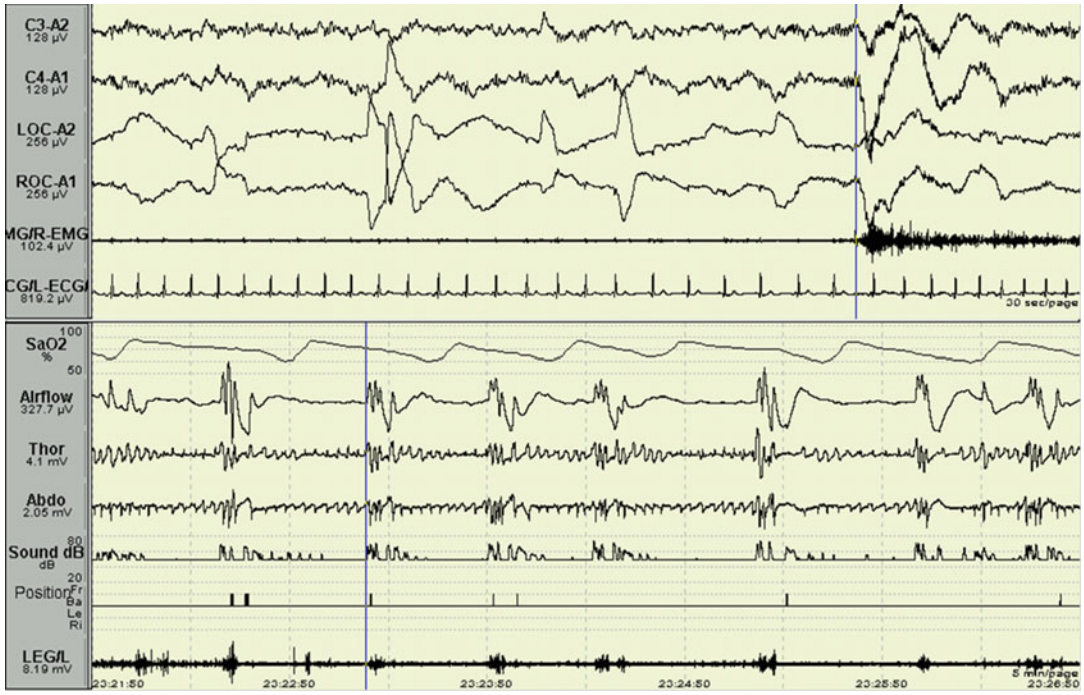

Fig. 4 Patient with obstructive sleep apnea (OSA) and obesity hypoventilation, before treatment Observed during rapid eye movement (REM) sleep. Note the repetitive apneas, each lasting approx. 20–40 s and each characterised by a period of no airflow despite thoracic and abdominal efforts, oxygen desaturations and EEG arousals (including return of submental EMG, leg EMG and loud snoring). Same patient on the same night also displayed in Figs. 2 and 3). *Top panel* shows a 30 s epoch of two electroencephalograms (C3-A2, C4-A1), two electrooculograms (LOC-A2, ROC-A1), submental electromyogram (R-EMG), and electrocardiogram (ECG). *Bottom panel* shows a 5-min epoch of oxygen saturation (SaO_2), transduced nasal pressure (Airflow), thoracic and abdominal movement (Thor, Abdo), sound (dB), body position (front, back, left, right) and leg electromyogram (LEG/L). Vertical *blue line* represents iso-time for the *top* and *bottom panels*

monitoring of both respiratory variables and sleep state allowing a comprehensive picture of the breathing disturbance and its impacts on sleep to emerge (Fig. 4). Polysomnography may be performed in a sleep laboratory or, usually with a more limited number of parameters recorded, at home. More simply than these comprehensive polysomnographic studies, limited portable sleep studies are available that involve monitoring of respiratory variables alone (typically oximetry, oronasal airflow, and chest wall motion). Their relative simplicity makes them well suited for use in unattended settings outside the sleep laboratory environment, such as home. The results of these are quite specific, complementing the sensitivity of questionnaires such that positive findings in a patient with a questionnaire response indicating a high pretest probability confirm diagnosis. However, they are not sufficiently sensitive to exclude diagnosis if their findings are negative (Collop et al. 2007). Because many home tests do not quantify sleep, uncertainty about its presence and depth during the assessment adds to their imprecision. Polysomnography is the final arbiter in such cases.

Treatment: There are a number of treatment options for OSA. These range from lifestyle changes (such as weight reduction and reduction in alcohol intake), surgery where an obvious predisposing factor such as tonsillar and adenoidal hypertrophy is present, through to a range of devices aimed at stabilizing the upper airway during sleep.

Of these devices, ***continuous positive airway pressure (CPAP) therapy*** remains the gold

standard for more severe forms of OSA (Fig. 5) (Antic et al. 2011). It involves the administration of air under low positive pressure to the upper airway via a mask applied to the nose or nostrils and, in the case of nasal obstruction, mouth. This pneumatically splints the airway, assuring its patency during sleep (Fig. 6). It is highly efficacious in doing this, but its intrusive nature makes

Fig. 5 CPAP therapy for obstructive sleep apnea. Photograph shows bedside appliance, tubing and nasal mask

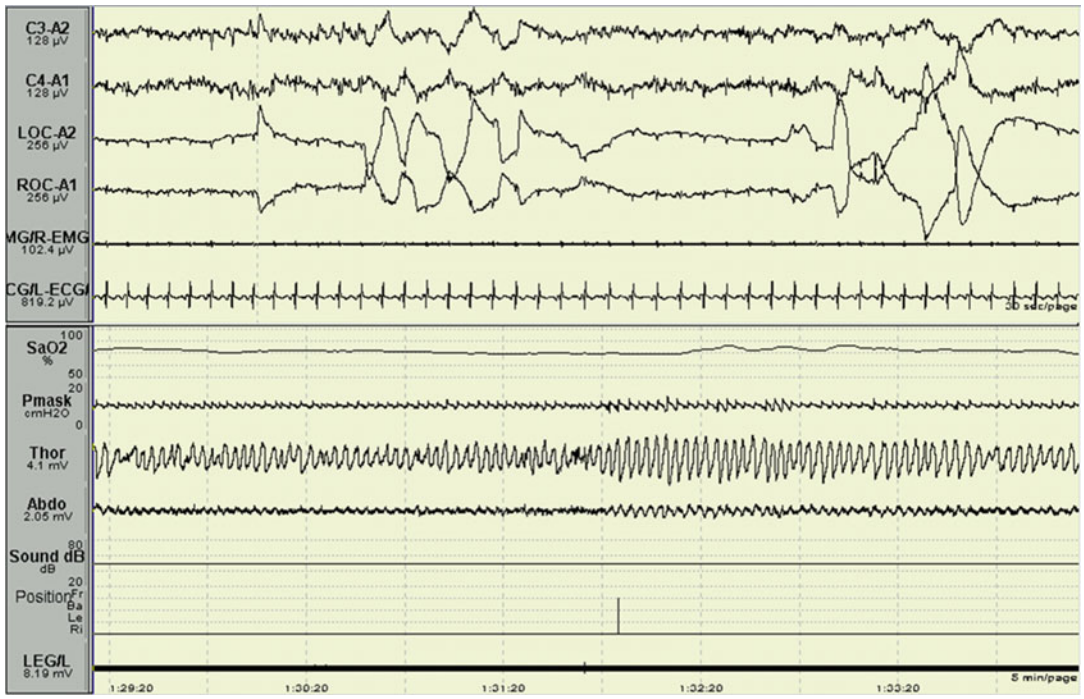

Fig. 6 Patient with obstructive sleep apnea (OSA) and obesity hypoventilation, now on CPAP treatment. Patient displayed in Fig. 4 is now (later on same night) on CPAP treatment. Again, observed during rapid eye movement sleep. Note the abolition of obstructive apneas but presence of persistent severe hypoxemia despite CPAP set to deliver a nasal mask pressure (Pmask) of approximately 12 cmH_2O. *Top panel* shows a 30 s epoch of two electroencephalograms (C3-A2, C4-A1), two electrooculograms (LOC-A2, ROC-A1), submental electromyogram (R-EMG), and electrocardiogram (ECG). *Bottom panel* shows a 5-min epoch of oxygen saturation (SaO_2), mask pressure (Pmask), thoracic and abdominal movement (Thor, Abdo), sound (dB), body position (front, back, left, right) and leg electromyogram (LEG/L)

it unacceptable to some patients – particularly those with milder disease and less symptomatic burden.

The therapy is available in two basic modes: fixed pressure and auto-titrating (sometimes known as automatic positive airway pressure or APAP). In fixed pressure mode, the pressure is adjusted sufficiently high to control most of the events (as determined during sleep laboratory titration or during an initial phase of APAP therapy), and this pressure is continuously applied throughout sleep. Pressures used are generally in the range of 6–16 cm H_2O, although occasional patients require more. Provided pressure is not excessively high, most patients tolerate fixed pressure satisfactorily. APAP auto-titrates pressure within a range set by the prescriber (often 6–16 cm H_2O) to abolish flow limitation, which the device detects from breath-by-breath analysis where it is evident from flattening of the inspiratory flow profile. APAP has the advantage of keeping the pressures low (e.g., during overnight awakenings) only increasing in response to flow limitation. Some patients find this therapy more comfortable than fixed pressure, particularly those who require relatively high pressures during sleep.

While CPAP is highly efficacious, making it first-line therapy for the moderate-to-severe OSA, many patients find it intrusive and some find it claustrophobic. Other complaints relate to noise, inconvenience, mask leaks or discomfort, nasal congestion, mouth dryness, and aerophagia. While these problems are usually amenable to adjustments in the treatment, including mask changes, addition of humidifiers or chin straps, and activation of various comfort settings on the device, many patients desist with therapy. Even in good hands, long-term compliance is approximately 70% – higher in those with more severe OSA but lower in those with milder disease (Kohler et al. 2010). Therapeutic alternatives to CPAP are needed for such cases.

Oral appliances (mandibular advancement appliances (MAAs) (Fig. 7) and various tongue-retaining devices) offer a useful alternative in many of those who fail CPAP therapy and as a first-line therapy in snoring with or without mild-to-moderate OSA (Sutherland et al. 2014). While

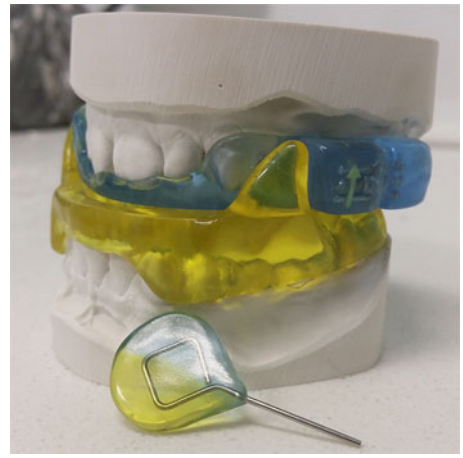

Fig. 7 Mandibular advancement appliance shown on dental models. Note this is a Dorsal appliance with screw adjustment at the sides which allows for adjustment of the degree of mandibular protrusion (Image courtesy of Mr Brett Chalklin, Digident Laboratory, Jandakot WA, Australia)

less consistently efficacious, they are less intrusive and more acceptable to patients. Recent data indicate that health outcomes with optimal MAA or CPAP treatment can be similar in patients with moderate-to-severe OSA, as the greater efficacy of CPAP is offset by inferior compliance with it relative to MAAs, resulting in similar effectiveness (Phillips et al. 2013). The use of oral appliances is covered in detail in this book in the chapter on ▶ "Oral Appliance Therapy for Sleep-Disordered Breathing".

Oral pressure therapy (OPT) is a relatively new therapy based on the understanding that most patients with OSA develop narrowing and collapse in the region behind the soft palate. The OPT device has been designed to "suck" the uvula and soft palate anteriorly, increase the size of the retro-palatal airway, and stabilize the tongue (Colrain et al. 2013). The system has three main components: an oral interface, a pump, and tubing (Fig. 8) (Colrain et al. 2013). When inserted in the mouth and activated, the pump applies a continuous negative pressure via the oral interface that moves the soft palate anteriorly into contact with the tongue. Breathing is via the nose while a continuous negative pressure, applied by the pump, maintains a continuous seal between the

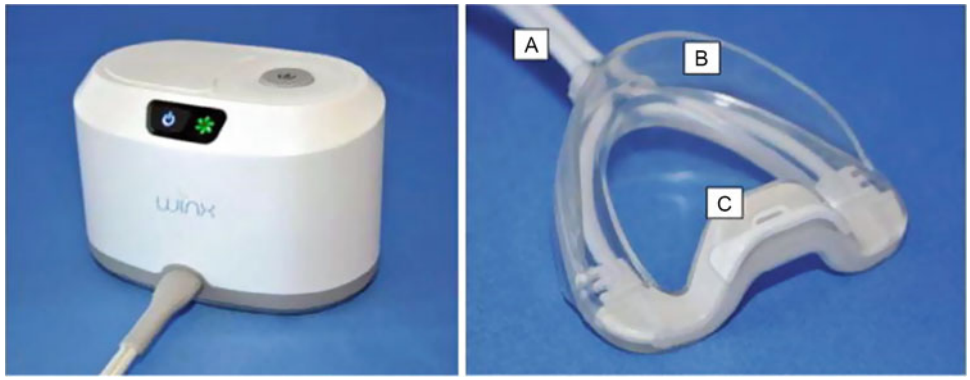

Fig. 8 Oral pressure therapy (Winx™). Photographs shows the vacuum pump and mouthpiece (*A*: vacuum pressure and sensor tubing, *B*: lip seal, *C*: vacuum aspiration port) (From Colrain et al. 2013)

interface, the soft palate, and the tongue. The OPT device appears to increase the size of the retro-palatal airway in both the lateral and anterior-posterior dimensions, more so in those who respond to the therapy than those who do not (Schwab et al. 2014).

A clinical trial using the device showed it to be safe and well tolerated and resulted in clinically significant improvements in sleep quality, AHI, degree of overnight desaturation, and daytime sleepiness but only in approximately 40% of the patients studied (Colrain et al. 2013). A recent systematic review on the effectiveness of OPT in patients with OSA reported that the success rate of OPT varied between 25% and 37% (when defining success as at least a 50% reduction from baseline AHI and the post-OPT treatment residual AHI less than or equal to 10) (Nigam et al. 2016). A meta-analysis of these data (on a total of 140 patients) concluded that OPT provided a 43% reduction in AHI but that severity of OSA could not be used to identify those who would most benefit from the therapy (Camacho et al. 2016).

The OPT device remains a promising therapy for OSA, particularly in those individuals who do not tolerate CPAP. Data on its effectiveness is scarce although it appears that the therapy should be targeted at patients who have retro-palatal obstruction and a lower minimum and higher maximum anterior-posterior airway in the retro-palatal and retro-glossal regions (Colrain et al. 2013).

Nasal expiratory positive airway pressure (nEPAP) valves have been developed as a potential alternative therapy for patients with OSA who cannot tolerate CPAP. Two small, disposable, one-way valves are placed over each nostril with adhesive tape (Fig. 9). The valves offer resistance to expiration but minimal resistance to inspiration and thereby use the patient's own breathing to generate a small positive end-expiratory pressure (Colrain et al. 2008; Rosenthal et al. 2009). Mechanisms thought to underlie any beneficial effects of nEPAP valves on OSA include (i) the development of positive pharyngeal pressure during expiration persisting for the start of inspiration and splinting the airway during the initiation of inspiratory effort; (ii) the development of positive pharyngeal pressure during expiration increasing end-expiratory lung

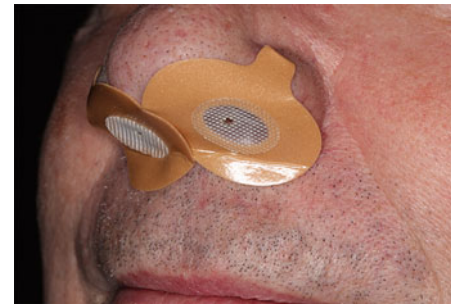

Fig. 9 Nasal expiratory positive airway pressure therapy. Photograph shows two small, disposable, one-way valves are placed over each nostril with adhesive tape (Image courtesy of Dr Amanda Phoon, UWA Dental School, University of Western Australia, Perth WA, Australia)

volume and increasing the caudal forces placed on the pharyngeal walls, stiffening the walls and thereby decreasing pharyngeal collapsibility; and (iii) breathing against an expiratory resistance resulting in hypoventilation and producing hypercapnia, with resultant increases in neural drive to the pharyngeal muscles responsible for maintaining airway patency.

To date only two randomized, placebo-controlled trials have been published on the effectiveness of nEPAP. One studied patients with mild-to-moderate, untreated OSA and reported a reduction in AHI in a group using nEPAP but not in the placebo group (Berry et al. 2011). In contrast, another study found no differences between a nEPAP and placebo group for severity of overnight oxygen desaturation, AHI, or daytime sleepiness. The reasons for the different results are not clear but might relate to the differences in OSA severity between the studies. A recent systematic review and meta-analysis showed that nEPAP reduced overall AHI by 53% and oxygen desaturation index by 42% and improved lowest oxygen saturation by 3% and reduced daytime sleepiness (Riaz et al. 2015). The study also noted that there were no clear characteristics (demographic factors, medical history, and/or physical exam finding) that could predict a favorable response to nEPAP (Riaz et al. 2015).

The main challenge to the therapeutic efficacy of nEPAP appears to be the ability of the patient to generate and maintain elevated end-expiratory pressures, as mouth leak and arousal occur in approximately 50% of patients (Patel et al. 2011). Given the requirement to breathe via the nose, the treatment appears particularly challenging for patients with nasal obstruction (Friedman et al. 2016).

Hypoglossal nerve stimulation (HGNS) (Fig. 10) is a method of reversing the sleep-related loss of pharyngeal muscle tone that is a key factor underlying upper airway narrowing and collapse in individuals with OSA. The hypoglossal (XII cranial) nerves (HGN) bilaterally innervate the genioglossus muscle, the largest and most commonly studied of the pharyngeal dilator muscles. Activation of the genioglossus muscle via the HGN causes protrusion of the tongue which increases the size of the posterior airway space and decreases the collapsibility of the pharyngeal airway. Early studies (Eisele et al. 1997; Schwartz et al. 2001) provided a "proof of concept" for a potential therapeutic role for long-term unilateral stimulation of the HGN. More recently several

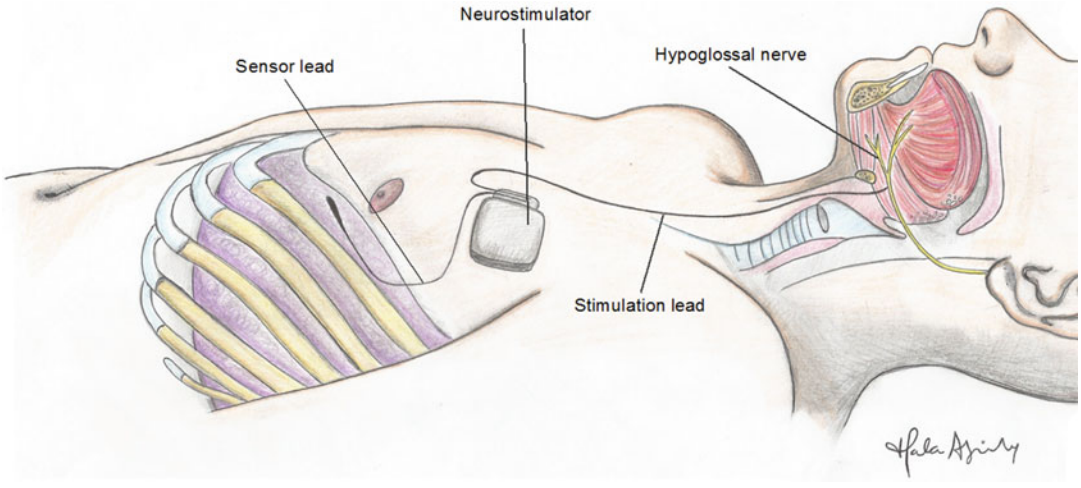

Fig. 10 Hypoglossal nerve stimulation. Figure shows diagrammatic representation of hypoglossal nerve stimulation system with implanted neurostimulator, sensing leads to detect respiratory effort (to coordinate hypoglossal stimulation with inspiration) and a stimulating lead to an electrode placed unilaterally on the distal hypoglossal nerve (Original drawing by Dr Hala Al Janaby, Perth WA, Australia)

new HGN stimulation devices to treat OSA have been developed:

- The Apnex device (Apnex Medical Inc., St. Paul, MN, USA) uses a cuff electrode positioned around one HGN (i.e., unilateral stimulation) to deliver stimulation during inspiration. Initial studies showed it to be safe and well tolerated and at 6 months post-implantation reduced OSA severity (AHI by greater than 50%), improved overnight oxygen saturation, improved quality of life, and reduced the degree of daytime sleepiness (Eastwood et al. 2011). These changes persisted at 12 months following implantation (Kezirian et al. 2014). A pivotal trial using this device (ClinicalTrials.gov number, NCT01446601) failed to show a between-group difference in the reduction of sleep apnea, owing to unanticipated improvements in the control group (Malhotra 2014). The study was terminated and commercialization of the device not pursued.
- The Inspire device (Inspire Medical Systems, Maple Grove, MN, USA) also delivers inspiratory-synchronous stimulation. A pilot study showed it to be safe and well tolerated and at 6 months post-implantation resulted in a $>$ 50% reduction in AHI, improvements in overnight oxygen saturation and quality of life, and reduced daytime sleepiness (Van de Heyning et al. 2012). A seminal pivotal trial (the *S*timulation *T*herapy for *A*pnea *R*eduction (STAR) Trial) in the Inspire device reported similar improvements in objective and subjective measurements of the severity of OSA (Strollo et al. 2014). Follow-up studies undertaken at 6, 18, 24, 36, and 48 months have shown that these improvements are maintained and that adverse events are uncommon (Woodson et al. 2016; Strollo et al. 2015; Gillespie et al. 2017; Soose et al. 2016; Heiser et al. 2017a). The Inspire device received approval from the US Food and Drug Administration (FDA) in April 2014.
- The ImThera device (ImThera Medical Inc., San Diego, CA, USA) using unilateral constant (tonic) HGNS has also been developed (Mwenge et al. 2013). At 12 months post-implant, a pilot study in the ImThera device showed it to be safe and well tolerated and accompanied by a 53% decrease in AHI, improved overnight oxygen saturation, and reduced daytime sleepiness. A recent feasibility study of the same device also reported it to be safe and at 6 months post-implant to be accompanied by a 27% decrease in AHI, improved overnight oxygen saturation, and reduced daytime sleepiness.
- The Nyxoah device (Nyxoah Inc., Mont-Saint-Guibert, Belgium) is implanted in the chin area, under the genioglossus muscle, and provides stimulation to both sides of the genioglossus muscle (i.e., bilateral stimulation). The electrodes are activated by an adhesive, disposable patch/chip system which is attached to the skin under the patient's chin. Initial clinical trials of this device are underway.

Patients included in these trials have all been adults with a diagnosis of moderate-to-severe OSA who would not accept or adhere to treatment with CPAP. Generally the trials avoided including individuals who were obese and had severe OSA; a preponderance of central, mixed, or obstructive apneas; large tonsils; and/or complete concentric collapse of the velopharynx (Eastwood et al. 2011; Van de Heyning et al. 2012; Strollo et al. 2014; Mwenge et al. 2013; Vanderveken et al. 2013). Despite the use of such criteria which were aimed at targeting those individuals who might best respond to the therapy, a finding common to all of these clinical trials was that approximately one-third of patients using HGNS had residual OSA and failed to demonstrate an adequate response.

Responders to HGNS appear to be characterized by those in whom stimulation results in tongue protrusion of 1 cm (Hofauer et al. 2017) a greater increase in retro-palatal than retro-lingual area, (Safiruddin et al. 2015) and bilateral protrusion of the tongue and tongue base (Heiser et al. 2017b). Such findings highlight the extremely complex relationships that exist between the specific HGN segment over which to apply the

electrical current and the movement patterns of the genioglossus muscle (Delaey et al. 2016) and the degree to which anterior movement of the tongue is "coupled" to anterior movement of the velopharyngeal wall, presumably via the palatoglossus muscle (Heiser et al. 2017b).

While results to date are very positive, it remains unknown whether still greater beneficial effects of HGNS can be achieved with further innovations, such as combining tonic and phasic stimulation, performing bilateral stimulation, or further refining patient selection, pharyngeal evaluation, and surgical technique.

Surgery can be used for the treatment of OSA. Its place continues to be debated both within and without the surgical community (Kotecha and Hall 2014). A wide range of surgical options exist that, if effectively targeted, are useful adjuncts to other treatments (such as nasal surgery to facilitate application of CPAP in those with nasal obstruction) or treatments in their own right (Kotecha and Hall 2014). For example, tonsillectomy and adenoidectomy is well-established and widely applied treatment for pediatric OSA, as tonsillar and adenoidal hypertrophy is a common and well-recognized cause of the problem (Marcus et al. 2013). Similarly, maxillamandibular advancement has a recognized role in treating OSA in the case of failure to accept CPAP, although it is a highly invasive procedure. Surgery for abnormalities of the facial skeleton where there is an associated esthetic issue is another area where the place of surgery is well defined and the surgery is aimed at improving both appearance and upper airway function. Other surgical options are also available for OSA and may be deployed in the absence of such overt predisposing issues. These include palatal surgery (Fig. 11) (radiofrequency or laser-assisted uvulopalatoplasty or uvulopalatopharyngoplasty), with or without tongue reduction surgery or hyoid suspension. These operations are devised to reduce pharyngeal collapsibility and/or increase pharyngeal dimensions. They are variably successful in alleviating OSA as they are designed to address a collapsible segment in the upper airway and may fail because the wrong level in the upper airway has been targeted or because the collapsible segments extend beyond the level directly addressed by the surgery, a factor driving a multilevel approach to the problem. The importance to OSA treatment of bariatric surgery to help secure substantial weight loss should not be forgotten in considering the role of surgery in OSA treatment, given the substantial predisposing role of obesity in OSA pathogenesis (Young et al. 2002).

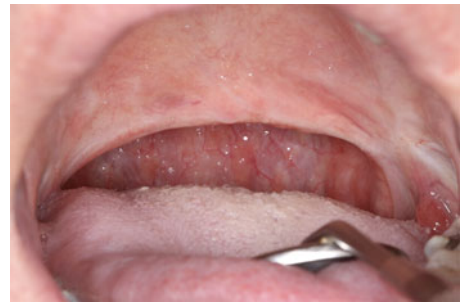

Fig. 11 Photograph shows uvulopalatopharyngoplasty in a patient with mild obstructive sleep apnea (Image courtesy of Dr Hala Al Janaby, Perth Oral Medicine & Dental Sleep Centre, Perth WA, Australia)

Sleep Hypoventilation

Sleep hypoventilation involves inadequate ventilation during sleep from non-obstructive causes. OSA frequently coexists with it because of shared predisposing factors such as morbid obesity and neuromuscular disease.

Pathophysiology: Sleep hypoventilation occurs in circumstances where there is an unfavorable imbalance between the load on respiratory muscles and their capacity to cope (Hillman et al. 2014). This can happen where the loads are excessive, such as with morbid obesity or respiratory diseases associated with increased lower airway resistance, such as chronic obstructive pulmonary disease, or decreased lung or chest wall compliance that occurs with interstitial lung disease or kyphoscoliosis. It can also happen where the respiratory muscles are weakened with a neuromuscular disease or inefficient as seen in those with the low flat diaphragm associated with some forms of chronic obstructive pulmonary disease, thus compounding the problems caused by excessive loading from increased airways resistance. While such load-capacity imbalances can culminate in daytime respiratory failure, in their

milder forms, sleep hypoventilation may be present without hypoventilation during wakefulness. This finding can be explained by the fact that sleep is a particularly vulnerable time for them as it is associated with a state-related reduction in ventilatory drive, such that breathing efforts are reduced. This occurs especially during REM sleep where ventilation is largely diaphragm dependent and sleep hypoventilation is usually most obvious. Compounding the effect of decreased ventilatory drive, the recumbency of sleep adds to load as the weight of abdominal contents compresses the diaphragm. Upper airway obstruction during sleep, which is frequently coexistent, also increases the load on the respiratory muscles. In its more severe forms, lengthy periods of sleep hypoxemia and hypercapnia are present culminating in established respiratory and right heart failure and, in some cases, polycythaemia (Hillman et al. 2014).

Clinical presentation and comorbidities: In its early stages, sleep hypoventilation may be relatively asymptomatic and only suspected because the patient has an obvious predisposition such as morbid obesity or respiratory muscle weakness. In such instances, the hypoventilation may only be evident during REM sleep. However, as the underlying conditions progress, compounded by aging, and the sleep hypoventilation worsens, evidence of sleep disruption emerges with increased daytime lethargy. If untreated, symptoms and signs of respiratory and right heart failure appear with further progression (Hillman et al. 2014).

Diagnosis: In its early stages, diagnosis of hypoventilation depends on clinical suspicion, based on knowledge of the underlying predispositions referred to above, confirmed by sleep study. Because, when subtle, it can be state dependent, polysomnography with capnometry is preferred to simpler monitoring of respiratory variables alone. The additional knowledge provided by extra channels, including presence and stage of sleep, allows far more precise evaluation of the presence and severity of the hypoventilation problem.

Treatment: Treatment of underlying conditions is important, where available, but may take months to achieve. Obesity management is such an example. While some associated neuromuscular and respiratory diseases improve with time and treatment, many are progressive – some slow and some relatively rapid. Where present to a significant degree, as indicated by sleep-related hypoxemia and hypercapnia, the treatment of choice is noninvasive ventilatory (NIV) assistance, using a simple ventilator to deliver bi-level ventilatory support via a nasal or face mask (Ozsancak et al. 2008). NIV differs from CPAP in that, in addition to providing a background pressure to ensure upper airway patency and to recruit areas of lung atelectasis, the therapy provides positive pressure support with each inspiratory effort, effectively augmenting ventilation (Fig. 12). In its more sophisticated forms, the ventilator will detect and compensate for periods where little or no effort is made, such as during REM sleep in advanced neuromuscular disease.

Periodic Breathing

A further form of sleep-disordered breathing is periodic breathing, so named because breathing efforts wax and wane cyclically (Fig. 13). The usual settings in which it is observed are heart failure and cerebrovascular disease (Eckert et al. 2007). It is also seen in association with chronic opioid use where the pattern may be less regular but periodic nonetheless. It may also be seen to a limited degree during REM sleep, where breathing effort is variable. The underlying cause is disturbed neurological control of breathing with overly sensitive ventilatory drive combined with under-damped or delayed responses in the feedback control loops modulating it. While it may be evident during wakefulness, it is invariably more prominent during sleep because of removal of the dampening effect wakeful stimulation has on fluctuations in ventilatory drive. During sleep, it can be associated with marked hypoxemia and with sleep disruption with arousals typically occurring during the peaks of inspiratory effort. Treatment starts with addressing underlying factors such as heart failure or opioid use. Where severe and intractable, it can be effectively treated with another form of positive airway pressure therapy – adaptive/auto-servo ventilation (ASV). This technology provides increased positive airway

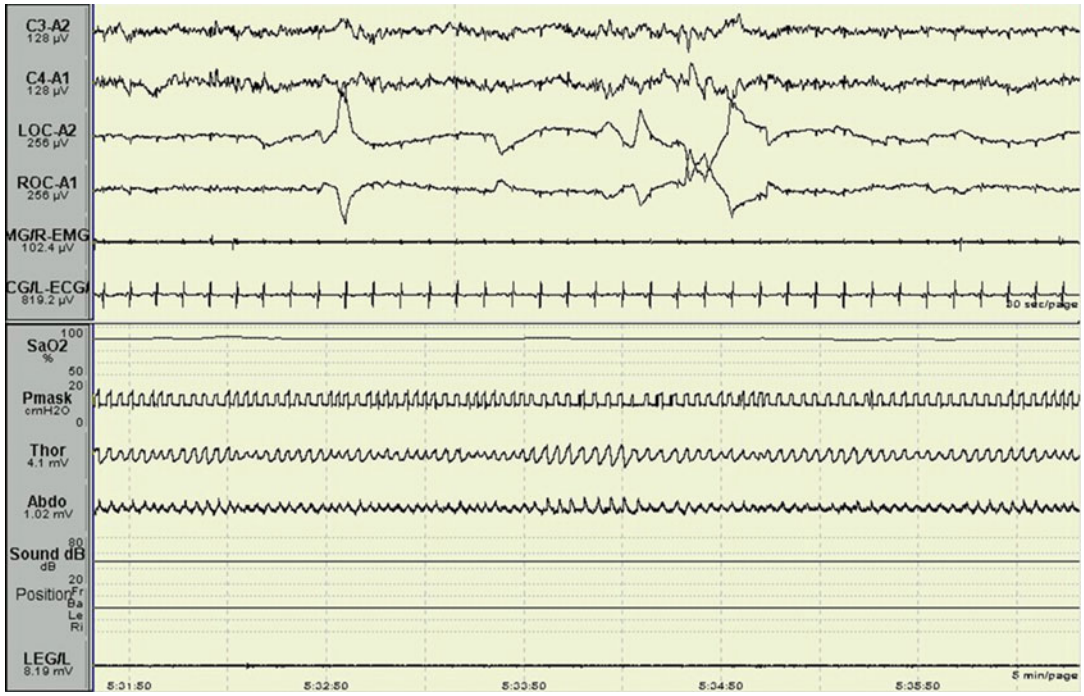

Fig. 12 Patient with obstructive sleep apnea (OSA) and obesity hypoventilation, now on NIV treatment. Same patient as shown in Figs. 4 and 6 has now (in the last part of the night) been commenced on non-invasive ventilation set to deliver an expiratory nasal mask pressure (Pmask) of approximately 12 cmH_2O and inspiratory mask pressure of approximately 19 cmH_2O. Again, shown during rapid eye movement sleep. Note the abolition of both obstructive apneas and hypoxemia on this treatment. *Top panel* shows a 30 s epoch of two electroencephalograms (C3-A2, C4-A1), two electrooculograms (LOC-A2, ROC-A1), submental electromyogram (R-EMG), and electrocardiogram (ECG). *Bottom panel* shows a 5-min epoch of oxygen saturation (SaO_2), mask pressure (Pmask), thoracic and abdominal movement (Thor, Abdo), sound (dB), body position (front, back, left, right) and leg electromyogram (LEG/L)

pressure support to breathing during the cyclical reductions in effort, reducing this support as spontaneous ventilatory effort increases during the cyclical increases in effort. ASV has the effect of decreasing the waxing and waning in ventilation, in turn reducing the accompanying intermittent hypoxemia and sleep disruption from hyperpnea-related arousals. However, the role of this form of positive airway pressure has been questioned where the periodic breathing is associated with severe heart failure and impaired ventricular systolic function (Ayas et al. 2015).

Other Sleep Disorders

While sleep-disordered breathing – especially snoring and OSA – is of particular interest to oral medicine specialists, many other sleep disorders exist with more than 70 individual conditions referred to in the International Classification of Sleep Disorders (Table 1) (American Academy of Sleep Medicine 2005). These include unusual and arcane problems, and the more common issues are specifically referred to in this section.

Insomnia

Insomnia is a collection of disorders characterized by difficulty in achieving sleep, either initially or following overnight awakening. It is very common regularly affecting around 10% of adults (Ancoli-Israel and Roth 1999). It often occurs secondary to other medical and psychological issues, such as conditions associated with pain, breathlessness, nocturia, or anxiety/depression. It may also occur with problems with sleep/wake timing, as can arise

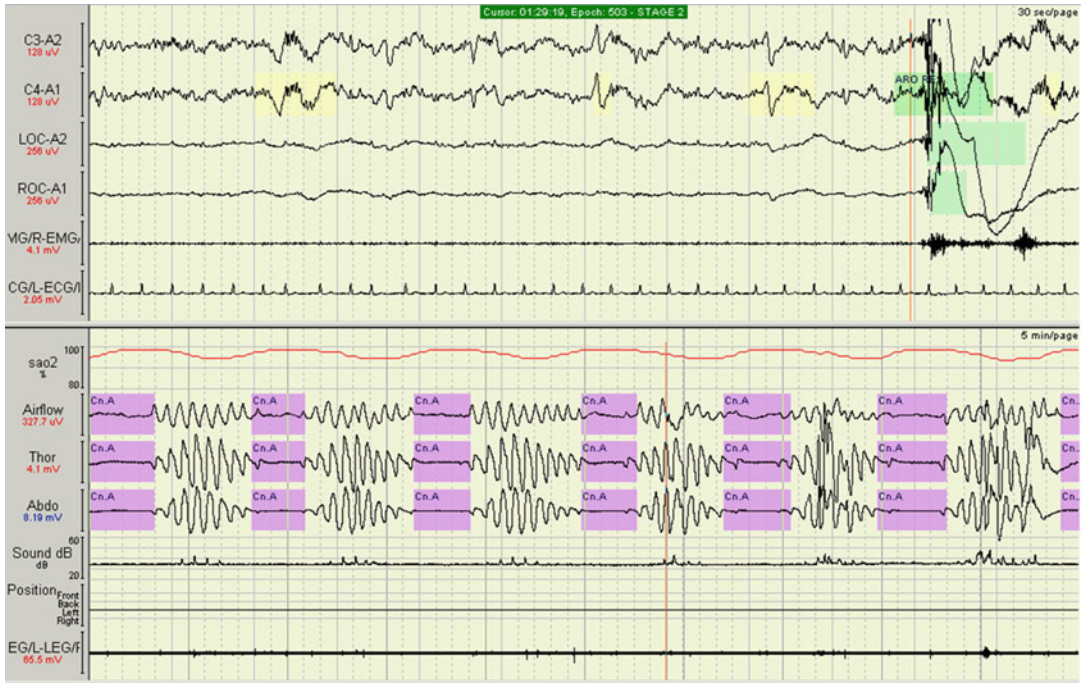

Fig. 13 Periodic breathing This figure demonstrates the typical waxing-waning (crescendo-decrescendo) breathing pattern of a patient with periodic breathing. Note the cyclical waxing and waning in respiratory effort on the thoracic and abdominal movement channels with concordant waxing and waning of the airflow pattern. A delay time in the recording of hypoxemia means that the dips in saturation that correspond to periods of hypoventilation follow these events. *Top panel* shows a 30 s epoch of two electroencephalograms (C3-A2, C4-A1), two electrooculograms (LOC-A2, ROC-A1), submental electromyogram (R-EMG), and electrocardiogram (ECG). *Bottom panel* shows a 5-min epoch of oxygen saturation (SaO_2), nasal pressure (Airflow), thoracic and abdominal movement (Thor, Abdo), sound (dB), body position (front, back, left, right) and leg electromyogram (LEG/L). Vertical *red line* represents iso-time for the *top* and *bottom panels*

with shift work disorders and other changes in sleep phase. Other sleep disorders, such as OSA and periodic limb movement disorder, may present with insomnia. Poor sleep habits with irregular hours of sleep and inadequate sleep environments due to light, noise, or other discomforts can also contribute. Some drugs may also have a role, either directly (e.g., stimulants, including caffeine) or as the result of withdrawal (e.g., after prolonged use of sedatives). Some insomnia is "primary" in that it has no such predispositions, although in many such cases a precipitating event can be identified that may be long resolved but leave persisting poor sleep as an aftermath (Morin 2004). A careful history is essential to determine the pattern of the insomnia, the nature of the sleep habits, and the presence of factors that may be contributing to or perpetuating the problem. Where an underlying condition exists, attention is directed there. Where this is not the case, then the problem often responds well to psychological measures that include attention to sleep habits, instruction in relaxation techniques, and, importantly, provision of cognitive behavioral therapy that, through counseling, addresses the beliefs and maladaptive behaviors that perpetuate the problem (Morin et al. 1999). If used at all, sedative/hypnotic medications have a small, temporary role.

In oral medicine, insomnia is often observed in relationship to orofacial pain, as it is in relationship to other painful conditions. Pain and disturbed sleep have a bidirectional relationship: pain disturbs sleep, and disturbed sleep aggravates pain by amplifying pain perception (Finan et al. 2013). Hence, besides relief of pain, normalization of sleep is a relevant therapeutic endpoint in

addressing such issues. Some cases of insomnia, having being triggered by a painful interlude, may persist despite relief of pain. In such cases, the help of a clinical psychologist skilled in insomnia management should be sought to help resolve this difficulty, generally using a cognitive behavioral approach.

Periodic Limb Movement Disorder

This is another common sleep disorder, estimated to affect up to 3% of the adults to a clinically significant degree, but becomes more common with increasing age (Rye and Trotti 2012). It involves cycles of leg and (often) arm movements periodically overnight. It tends to be worst during the evening through to the early hours of the morning. It is often, but not always, accompanied by wakeful "restless legs" at these times. This leg restlessness may be very aggravating to the sufferer who, in the absence of treatment, may only obtain relief by getting up and moving around. Indeed, it may be of sufficient degree to interfere with sleep onset and can be associated with insomnia, with sleep only consistently achieved in the early hours of the morning as the intensity of leg restlessness, which is often greatest during the evening, starts to wane. The leg movements during sleep may be asymptomatic but can be the source of important sleep disruption and, thereby, daytime sleepiness. Patients without wakeful restless legs or a bed partner that notes their frequent leg movements during sleep may be unaware that they have the condition and therefore unaware of the source of their disrupted, unrefreshing sleep. A polysomnographic sleep study can readily demonstrate the problem (Fig. 14). Iron deficiency is a predisposing factor, as is use of antidepressant drugs. Where symptomatic despite normal serum iron levels, it usually responds well to dopamine agonist drugs in relatively low dose (Rye and Trotti 2012). Other drug treatments include benzodiazepines and gabapentin.

Narcolepsy

Narcolepsy is the most common of a number of neurological conditions that cause hypersomnia or excessive sleepiness (Scammell 2015). It involves an impairment in the brain's ability to regulate the switching between wake and sleep, particularly REM sleep, resulting in unplanned intrusions of sleep behaviors (sleep itself, dreaming/hallucinations, and muscle relaxation in the form of cataplexy) on wakefulness and wakefulness on sleep (waking from sleep momentarily unable to move – sleep paralysis). It relates to a deficiency in hypocretin (orexin) projecting neurones in the lateral hypothalamus of the brain, which are important components in sleep regulation. While the cause of hypocretin cell loss is not yet clear, an autoimmune basis is suspected. Although not specific to narcolepsy, most narcolepsy patients carry the human leukocyte antigen DQB1*0602. Diagnosis is made on the basis of history, supplemented by sleep study and a (daytime) multiple sleep latency test that demonstrate short latent periods between going to bed and sleep onset (sleep latency) and between sleep onset and the first cycle of REM sleep (REM sleep latency). Untreated, the condition can be a major impediment to normal daytime function as well as, paradoxically, disrupting sleep. Treatment generally involves stimulant therapy during wakeful hours, commonly with an amphetamine analog, and sometimes with additional therapy to suppress cataplexy where it is problematic.

Parasomnias

The parasomnias are a collection of sleep conditions characterized by unusual and unwanted behaviors during sleep including abnormal movements, perceptions, and dreams (Giglio et al. 2005). They involve conditions such as sleep walking, nightmares, night terrors, confusional arousals, bruxism, REM sleep behavior disorder, and isolated sleep paralysis. These represent partial arousal states in the transition between wakefulness and sleep and can occur in both non-REM sleep, in the case of sleep walking, night terrors and confusional arousals, and REM sleep in the case of REM sleep behavior disorder and sleep paralysis. While some are temporary, such as sleep walking in childhood, others are not and can be the source of considerable distress. Underlying conditions may be involved, such as narcolepsy in the case of some sleep paralysis, or other sources of sleep disruption predisposing to states

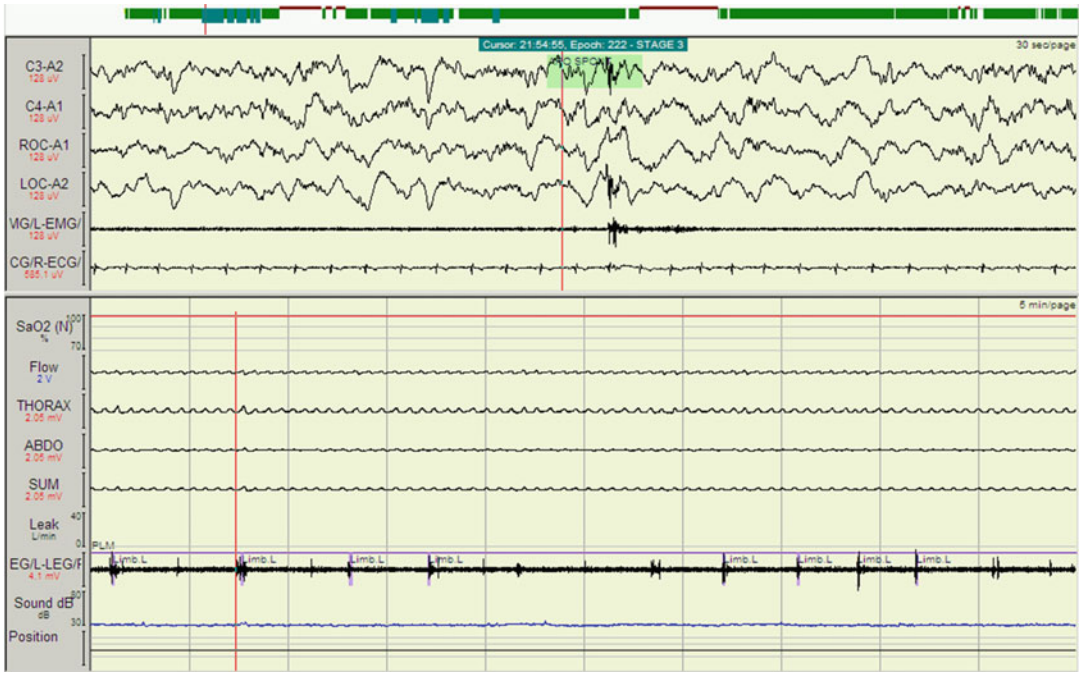

Fig. 14 Periodic leg movement disorder Note the repetitive leg activity evident on the leg electromyogram (bursts of activity in LEG/L-LEG/R) in this figure. Normally this signal is isoelectric. Some of these leg movements disrupt sleep, causing brief arousals and, occasionally, awakenings. Such sleep disruption is responsible for the tiredness and lethargy this condition can cause some of its sufferers. *Top panel* shows a 30 s epoch of two electroencephalograms (C3-A2, C4-A1), two electrooculograms (ROC-A2, LOC-A1), submental electromyogram (EMG/L-EMG-R), and electrocardiogram (ECG). Bottom panel shows a 5-min epoch of oxygen saturation (SaO2), nasal pressure (Flow), thoracic and abdominal movement and their sum (Thorax, Abdo, SUM), leg electromyogram (LEG/L-LEG/R). sound (dB) and body position. Vertical *red line* represents iso-time for the *top* and *bottom panels*. Note the arousal (*top panel*) that follows the leg movement (*bottom panel*)

of partial arousal, as occurs with sleep walking. However, in many cases, there is no obvious predisposing factor, and the treatment is based on symptom relief, often with sedatives to raise arousal thresholds to counteract the partial arousal states that these conditions involve, thereby facilitating sleep.

Bruxism

Bruxism, excessive jaw clenching or tooth grinding, is a parasomnia that deserves special mention given its direct relationship to oral health. While bruxism may occur during wakefulness, it is more commonly present during sleep (Bader and Lavigne 2000). It can vary in severity, causing significant dental damage and discomfort in its more severe forms. Why it occurs is not well understood: it appears to be multifactorial in origin. The subject is dealt with in detail in the chapter on ► "Sleep Bruxism".

The Oral Medicine Specialist's Role in Diagnosis and Treatment

Oral medicine specialists are destined to have a growing role in the diagnosis and treatment of upper airway problems affecting or affected by sleep. Their understanding of upper airway structure and function puts them in an ideal position to identify patients at risk of OSA, a widely prevalent but underdiagnosed problem with substantial comorbidities. They are also in prime position to treat snoring and OSA, particularly in its milder forms, through oral appliances and, in selected cases, refer patients for orthognathic surgery.

This work requires a multidisciplinary approach, with dental, medical, and (in some cases) psychological expertise combining to facilitate access by patients to a range of diagnostic and treatment modalities tailored to their individual circumstances. In addition, oral medicine specialists are involved in treating chronic orofacial pain, a significant cause of sleep disturbance in its own right.

Conclusions and Future Directions

Given sleep's potent effects on upper airway function, it is essential that oral medicine specialists understand the nature of sleep, the physiological changes that accompany it, and the various disorders with which it is associated. Oral medicine skills are important in aspects of treatment of OSA, one of the most prevalent sleep disorders. Furthermore, many of the patients with whom oral medicine specialists deal have OSA because the craniofacial issues with which they present predispose to the problem. While their sleep disorders may be clear or have been previously diagnosed, they are often covert and unrecognized. Insight and vigilance are protections against failure to recognize them and the potential harms with which they are associated.

Cross-References

- Diagnostic Imaging Principles and Applications in Head and Neck Pathology
- Headache
- Normal Variation in the Anatomy, Biology, and Histology of the Maxillofacial Region
- Oral Appliance Therapy for Sleep-Disordered Breathing
- Orofacial Pain and Sleep
- Sleep Bruxism

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