

# How to Treat

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# Sleep apnoea

## Introduction

SLEEP disorders can be broadly classified as 'respiratory sleep disorders' and 'non-respiratory sleep disorders'. The most common respiratory sleep disorder is obstructive sleep apnoea. However, there are other sleep and breathing disorders that medical practitioners need to be aware of, including central sleep apnoea, nocturnal hypoventilation, and upper airway resistance syndrome.

This article will discuss adult respiratory sleep disorders in more detail, including sections on central sleep

apnoea and nocturnal hypoventilation.

Obstructive sleep apnoea and upper airway resistance syndrome are associated with reduced or absent breathing during sleep due to narrowing and relaxation of the upper airway in sleep. Alternatively, central sleep apnoea and nocturnal hypoventilation are associated with patent upper airways, but there is reduced breathing in sleep through other mechanisms (for example, reduced impulses from the central nervous system to the respiratory

muscles, such as in neuromuscular and chest wall disorders).

Not only do respiratory sleep disorders impair sleep quality and lead to excessive daytime sleepiness, they can negatively affect other organ systems. Obstructive sleep apnoea, in particular, is closely linked to hypertension, cardiac failure, ischaemic heart disease, stroke, the metabolic syndrome, and contributes to mortality.

Non-respiratory sleep disorders will not be discussed in this article, due to space limitations. For more information on these conditions,

readers may wish to view a previous 'How to Treat' article (Desai AV, Kwan B. 'Excessive sleepiness of non-sleep apnoea origin'. *Australian Doctor* 2009, May 15).

Important non-respiratory sleep disorders include insomnia, narcolepsy, REM behaviour disorder, sleepwalking, restless legs syndrome and periodic limb movement disorder. All of these conditions can disrupt sleep and lead to important daytime consequences, including fatigue and sleepiness.

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## Obstructive breathing disorders

### Upper airway resistance syndrome

UPPER airway resistance syndrome can be thought of as a mild form of obstructed breathing in sleep, which leads to important and identifiable clinical consequences, namely daytime sleepiness. Patients with this syndrome do not have obstructive sleep apnoea on polysomnography. However, their sleep is fragmented by frequent EEG arousals from more subtle obstructive breathing events in sleep (table 1).

The definitive diagnosis requires oesophageal pressure monitoring during polysomnography, which is not routinely performed as it is a relatively invasive procedure. Most sleep physicians will consider this diagnosis without oesophageal pressure monitoring if the patient's sleep study shows frequent arousals from sleep due to snoring events or airflow limitation on inspiration.

In addition to these arousals from sleep on polysomnography, patients with upper airway resistance syndrome have excessive daytime sleepiness, for which no other cause is apparent. CPAP or oral appliances are often recommended for treatment.

### Obstructive sleep apnoea

Obstructive sleep apnoea (OSA) is characterised by recurrent episodes of partial or complete obstruction of the upper airway resulting in substantially reduced or complete cessation of airflow despite ongoing breathing efforts. This leads to intermittent disturbances in gas exchange (for example, hypercapnia and hypoxaemia) and fragmented sleep. Abnormal breathing events during sleep are defined as hypopnoeas and apnoeas and the frequency with which they occur during sleep are described by the Apnoea Hypopnoea Index (table 1).

### Definitions of respiratory events and indices

Apnoea can be described as a decrease in airflow or chest wall movements to an amplitude smaller than approximately 25%, while hypopnoea is defined as an amplitude smaller than 70%. These events must last at least 10 seconds and are associated with either oxygen desaturation of more than 3% or an arousal.

The Apnoea-hypopnoea index (AHI) measures the total number of apnoeas and hypopnoeas, divided by the hours of sleep. Respiratory effort-related arousal (RERA) measures the sequence of breaths, characterised by increasing respiratory effort leading to arousals from sleep, but not meeting the criteria for apnoea or hypopnoea. These events must fulfil the following criteria:

1. Pattern of progressively more negative oesophageal pressure, terminated by a sudden change in pressure to a less negative level and an arousal.
2. The event lasts 10 seconds or more.

The respiratory disturbance index (RDI) measures the total



**Tonsillar hypertrophy.**  
Source: Michaelbladon <http://bit.ly/1K0I01F>



	Sleepiness	Sleep-related obstructive breathing events/hour
Mild	Unwanted sleepiness or involuntary sleep episodes during activity requiring little attention (eg, watching TV, reading)	5-15
Moderate	Unwanted sleepiness or involuntary sleep episodes during activity requiring some attention (eg, meetings, concerts)	15-30
Severe	Unwanted sleepiness or involuntary sleep episodes during activity requiring active attention (eg, eating during conversation, operating a motor vehicle)	> 30

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number of apnoeas, hypopnoeas, and RERAs, divided by the hours of sleep.

### Grading severity of OSA

The severity of OSA is based on the number of obstructive breathing events during sleep.

A person with normal breathing during sleep has fewer than five obstructive breathing events per night, while sleep apnoea can be described as mild, moderate or severe (see table 1). In addition, daytime sleepiness can also be used to gauge severity of disease,

**Studies indicate that 60% of men and 40% of women between the ages of 41 and 65 habitually snore.**

however this can be quite subjective.

### Prevalence

OSA is a highly prevalent, chronic illness in adults, affecting an estimated 9% of middle-aged women and 24% of middle-aged men, with 4% and 9%, respectively, having moderate-to-severe disease.<sup>2</sup> The prevalence of OSA in Australia is probably increasing due to the obesity 'epidemic'.

### Risk factors

The most common risk factors for adult OSA are age, sex, obesity, race and craniofacial abnormalities. Middle-aged men are most frequently affected by OSA, although after menopause, the prevalence of OSA in women increases sharply. Exogenous testosterone has been shown to increase upper airway collapsibility and induce sleep apnoea, which may explain some of the sex differences in the prevalence of OSA.

In both males and females, the

strongest risk factor for OSA is obesity. The prevalence of OSA progressively increases as the BMI and associated markers (including, neck circumference, waist-to-hip ratio) increase. A 10% increase in weight has been shown to predict a 32% increase in the AHI and a six-fold increase in the chance of developing moderate to severe OSA.

Craniofacial and upper airway soft tissue abnormalities each increase the likelihood of having or developing OSA. These factors are well recognised in Asian patients. Examples of such abnormalities include an abnormal maxillary or short mandibular size, a wide craniofacial base, tonsillar hypertrophy and adenoid hypertrophy.

### Clinical presentation

The diagnosis of OSA is based on the combination of clinical features together with objective sleep study findings. When interviewing a patient with suspected OSA, it is highly desirable to also interview their partner, who can usually provide important additional information based on direct observation of the patient while asleep.

### Nocturnal symptoms

#### Snoring

Snoring is the hallmark symptom of sleep apnoea because it reflects the basic pathophysiology underlying the disorder, namely a critical narrowing of the upper airway. Studies indicate that 60% of men and 40% of women between the ages of 41 and 65 habitually snore.

Snoring is the most frequent symptom of OSA, occurring in up to 95% of patients, but it has poor predictive value because of the high prevalence in the general population.

#### Witnessed apnoeas

These events are a good diagnostic predictor of OSA, but do not predict severity of the disorder. Concern by the bed partner about witnessed breathing pauses during sleep is a common reason for referral to a sleep specialist.

#### Nocturnal choking or gasping

Many patients with OSA report waking at night with a choking sensation and this is a very useful individual finding for identifying patients with OSA.

Other nocturnal symptoms include restless sleep, periods of silence terminated by loud snoring, nocturnal angina, nocturia, and impotence.

### Daytime symptoms

#### Excessive daytime sleepiness

This symptom is not very specific for OSA as it can be seen in 30-50% of the general population and in many other sleep disorders. The severity of excessive daytime sleepiness can be assessed subjectively by various questionnaires; the most widely used is the Epworth Sleepiness Scale.

Other daytime symptoms include fatigue, memory impairment, poor concentration and work performance, irritability, and morning headaches.

## Diagnosis

### Physical characteristics

COMMON findings on physical examination include obesity (especially central obesity), a crowded oropharyngeal airway, large neck circumference (more than 48cm) and hypertension.

### Investigations

Polysomnography performed in a sleep laboratory is the gold standard for diagnosing OSA, providing detailed information about sleep stage, respiratory and gas exchange abnormalities, in addition to a range of other variables including heart rate and rhythm, body position, and limb movements. Full polysomnographic studies generally involve a minimum of 12 channels of recordings including EEG, ECG, electromyogram, oronasal airflow, chest wall effort, body position, and oxygen saturation.

The duration of the diagnostic study should be at least six hours to allow adequate assessment of variables during sleep. This is best performed in a sleep laboratory, where technicians are on hand throughout to troubleshoot during the study.

The number of home-based sleep studies has risen in response to the



Patient with OSA prepared for sleep evaluation, wearing a CPAP mask covering his nose only. Source: Halicki <http://bit.ly/1ELBcCV>

increasing number of patients presenting for assessment of possible OSA. In Australia, mainly multichannel home sleep studies are offered and these attract a Medicare rebate. Despite the obvious advantages of home-based studies,

the lack of technical support may result in suboptimal data. More complex sleep conditions, such as upper airway resistance syndrome, central sleep apnoea and nocturnal hypoventilation (discussed below) are also more likely to be missed.

From a clinical perspective, it is important to understand that home-based sleep studies are most useful at diagnosing OSA in patients with a high clinical suspicion for the condition, rather than excluding it in low risk patients.

Polysomnography performed in a sleep laboratory is the gold standard for diagnosing OSA.

## Complications of untreated OSA

### Neurocognitive

IN addition to excessive daytime sleepiness, OSA can impair cognitive functions such as memory, attention, concentration and learning. The prevalence of depression in OSA varies from 24% to 45%, while anxiety, depression and irritability are also common associations.

### Quality of life

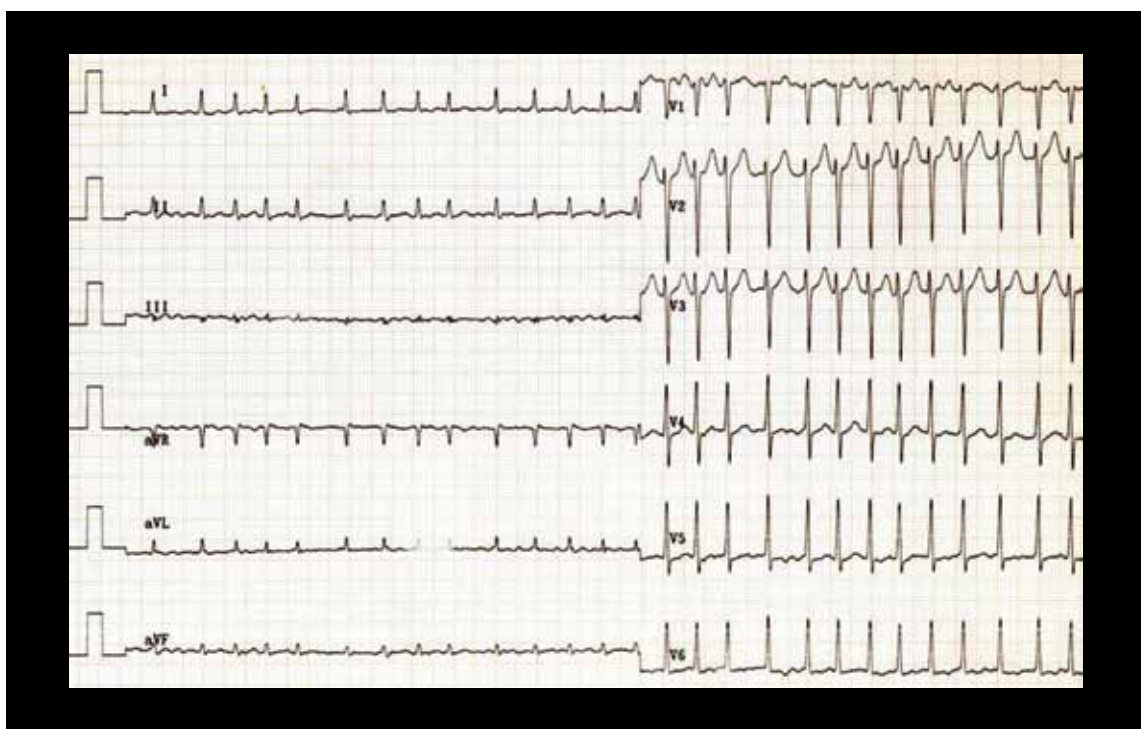
Factors affecting quality of life in OSA include disturbed sleep, excessive daytime sleepiness, snoring, low libido and obesity-related problems. Snoring in OSA can negatively affect the sleep of a bed partner and hence their quality of life as well.

### Motor vehicle and occupational accidents

Motor vehicle accidents are 2-3 times more common among patients with OSA than without OSA, and may have a greater impact on morbidity and mortality than the cardiovascular sequelae of OSA. All patients should be warned about an increased risk of accidents associated with untreated OSA and the potential consequences of driving or operating other dangerous equipment while sleepy. Successful treatment with CPAP reduces the risk of motor vehicle and occupational accidents.

### COPD and OSA overlap syndrome

In patients with COPD, the coexistence of OSA is associated with an increased risk of developing pulmonary hypertension, hospitalisation because of COPD exacerbation and death from any cause. Effective treatment with CPAP is associated with improved survival and decreased hospitalisations.<sup>4</sup>



Atrial fibrillation.

Source: Meddoc13 <http://bit.ly/1HZBPIP>



### Cardiovascular disease Hypertension

Epidemiological evidence implicates OSA as one of the modifiable and highly prevalent factors in the devel-

opment of hypertension. Hypoxaemia, arousals, and increased sympathetic activity occurring during respiratory events have been hypothesised to increase daytime

blood pressure in patients with OSA. Results of meta-analyses consistently report a 2mmHg antihypertensive effect of treatment with CPAP.<sup>5</sup>

### Coronary artery disease and cardiac failure

OSA is associated with an increased risk of incident cardiac failure in middle-aged and older men, and men with an AHI greater than 30 were 58% more likely to develop cardiac failure than those with an AHI below five. There is also an increase in coronary artery disease in this group.<sup>6</sup>

### Cardiac arrhythmias

Bradycardia and asystole are the most prominent rhythm dis-

turbances associated with OSA. Patients with OSA have a higher prevalence of nocturnal atrial fibrillation, non-sustained ventricular tachycardia, and complex ventricular ectopy. OSA may be associated with recurrent atrial fibrillation, with one study showing the recurrence of AF at 12 months after cardioversion was halved following treatment of OSA.

### Stroke

The Sleep Heart Health Study found that modest to severe OSA in men is associated with a threefold increased risk of ischaemic stroke, making it a risk factor comparable to that of a 10-year increase in age or AF.<sup>7</sup>

### Metabolic

OSA has been shown to be an independent risk factor for hypertension and insulin resistance. The prevalence of OSA in the metabolic syndrome, a cluster of cardiovascular risk factors, is as high as 85%. Three months of CPAP therapy in a group of patients with moderate-to-severe OSA was associated with a decrease in both systolic and diastolic blood pressure, lipid levels, glycated haemoglobin levels, BMI, and abdominal fat content.<sup>8</sup>

### Mortality

Patients with untreated severe OSA (an AHI equal to or more than 30 events an hour) have a two- to threefold increased risk of all-cause mortality compared with individuals without OSA, independent of other risk factors such as obesity and cardiovascular disease. The association is more pronounced in men than in women and in younger patients compared with older patients.<sup>9</sup>

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## Treatment

ONCE the diagnosis of OSA is confirmed and its severity determined, review the results of all testing with the patient. Educate the patient about the risk factors, natural history, and consequences of OSA. Importantly, warn all patients about the increased risk of motor vehicle accidents associated with untreated OSA, and the potential consequences of driving or operating other dangerous equipment while sleepy.

Finally, determine whether specific treatment, in addition to behaviour modification, is indicated and, if so, which therapy is most appropriate.

### Behaviour modification

#### Weight loss

Recommend weight loss to all patients who are overweight or obese. This is based on evidence that weight loss improves overall health, decreases the apnoea hypopnoea index, improves quality of life, and decreases daytime sleepiness. Surprisingly, exercise has shown to modestly improve OSA, even in the absence of significant weight loss, and should be encouraged as part of approach to weight loss.

#### Avoiding alcohol and certain medications

Tell patients to avoid alcohol and some medications (for example, benzodiazepines) that can depress the central nervous system, exacerbate OSA, worsen sleepiness, and promote weight gain.

#### Sleep position

In some patients, OSA may develop or worsen during sleep in the supine position. Avoiding supine sleep — if possible and practical — may improve OSA in such patients. However, long-term compliance is generally poor.

#### Positive airway pressure

Positive airway pressure therapy is considered first-line treatment for OSA, particularly in moder-



Mandibular advancement device.

Source: Grey Geezer <http://bit.ly/1i6QJnv>

ate to severe cases. Positive airway pressure therapy splints the upper airway open and, as a result, respiratory events due to upper airway collapse are prevented.

It can be delivered by continuous positive airway pressure (CPAP), bi-level positive airway pressure (BPAP), and autotitrating positive airway pressure (APAP).

CPAP delivers positive airway pressure at a level that remains constant throughout the respiratory cycle, while APAP increases or decreases the level of positive airway pressure in response to a change in airflow, circuit pressure or a snore.

Nocturnal CPAP significantly reduces the frequency of respiratory events during sleep, decreases daytime sleepiness, improves systemic blood pressure, and improves quality of life across a range of disease severities. Despite suggestions from observational studies that CPAP use

leads to decreased mortality, there is yet to be a randomised trial to demonstrate a mortality benefit from CPAP in OSA.

Adherence to CPAP treatment is the largest factor impacting on the effectiveness of treatment. Often adherence issues are related to adverse effects, including dry nose or mouth, nasal congestion, mask leaks, claustrophobia and nocturnal awakenings. Many of these adverse effects can be mitigated with humidification, and a review of mask fit and selection.

It is currently recommended that CPAP titration be performed during a laboratory-attended full sleep study to determine required pressures and troubleshoot mask-related issues in order to maximise comfort and effectiveness of therapy.<sup>1</sup>

Home titration is possible with APAP, but reduced technical oversight may lead to poorer tolerance

and incorrect pressures in some cases. Home titration in patients with congestive heart failure, COPD, or central sleep apnoea is not currently recommended.

Both CPAP and APAP can be used to manage OSA at home after the titration is complete. Studies have concluded that there is no difference in the hours of use between CPAP and APAP, despite a small decrease in the overnight pressure delivered with APAP. Some patients prefer APAP, possibly because of the lower mean pressures delivered, and this is a potential advantage particularly for those patients that require high pressures.

However, APAP machines are considerably more expensive than fixed pressure devices, and as mentioned above, are not suitable for some patient groups, such as those with congestive heart failure, COPD, or central sleep apnoea.

### Alternative therapies

#### Mandibular advancement devices

Mandibular advancement devices act by protruding the mandible forward (mandibular advancement splints) or holding the tongue in a more anterior position (tongue-retaining devices), thereby splinting the soft tissues of the oropharynx away from the posterior pharyngeal wall and maintaining upper airway patency.

These devices are indicated for patients with primary snoring (snoring disturbing others where OSA is excluded) or as an alternative for patients with mild to moderate OSA who decline or fail to adhere to positive airway pressure therapy and who have a preference for such treatment.

In these groups, mandibular advancement devices reduce sleep apnoea and subjective daytime sleepiness and improve quality of life compared with control treatments. There is also emerging evidence of beneficial cardiovascular effects.<sup>10</sup>

There are a large number of

mandibular advancement devices commercially available, some with more evidence to support them than others. It is important that patients have devices individually fitted and then have a repeat sleep study with the device in-situ to verify splint efficacy. Oral device therapy should be avoided in patients in whom rapid initiation of treatment is desirable (due to severe symptoms or hypoxaemia) or in co-existing temporomandibular joint or periodontal disease. Side effects of these devices include temporomandibular joint (TMJ) pain, tooth pain, myofascial pain, dry mouth, gum irritation, and morning-after occlusal changes.

In the long term, tooth movement and bite changes are possible and regular dental follow-up is recommended. Ongoing sleep specialist follow-up is also recommended to assess for worsening OSA over time.

#### Upper airway surgery

Surgical treatment appears to be most effective in patients who have OSA due to a severe, surgically correctable, obstructing lesion of the upper airway, for example, severe tonsillar hypertrophy or severe anatomical nasal obstruction. Nasal surgery alone can be effective in opening up the nasal airway as an adjunct to device therapy (CPAP or mandibular advancement devices) to make device therapy easier. Nasal surgery, soft palate surgery and tongue base procedures (for example, coblation) can reduce snoring and mild OSA, but will not treat more significant OSA. Extensive surgical approaches (namely, maxillomandibular advancement), should only be considered in selected patients when positive airway pressure or a mandibular device has been declined or ineffective.<sup>10</sup>

#### Others

Drugs, nasal dilators and apnoea-triggered muscle stimulation are not recommended as effective treatments of OSA.<sup>10</sup>

## Central sleep apnoea

CENTRAL sleep apnoea (CSA) is characterised by recurrent episodes of apnoea during sleep, resulting in repetitive periods of insufficient ventilation and compromised oxygen supply. It is important to differentiate CSA from OSA as it has a different aetiology and management.

Abnormalities in the ventilatory control system are a possible mechanism for CSA. CSA causes hypoxaemia and frequent arousals, which may result in insomnia and subsequent daytime sleepiness.

CSA is often classified as hypercapnic and non-hypercapnic central sleep apnoea. Hypercapnic CSA is largely due to nocturnal ventilatory failure in patients who have marginal daytime ventilatory status or worsening of chronic ventilatory failure.

Patients groups that tend to be affected include those with muscular dystrophy, kyphoscoliosis and post-polio syndrome. There is an overlap in the classification of hypercapnic



Facial features of acromegaly.

Source: Philippe Chanson and Sylvie Salenave <http://bit.ly/1JL8FLc>

central sleep apnoea with nocturnal hypoventilation, which is discussed in more detail below.

Non-hypercapnic central apnoea is the most common form of CSA. This form of sleep apnoea has many causes (see box: 'Causes of central sleep apnoea'). It can be found in

healthy individuals at the onset of sleep or at high altitudes, can be secondary to drugs (especially opioids), and can be associated with medical conditions such as cardiac failure and stroke.

CSA commonly takes the form of Cheyne-Stokes respiration or 'peri-

### Causes of central sleep apnoea

Central apnoea of sleep onset
Periodic breathing at high altitude
Congestive cardiac failure
Stroke
Drugs
Acromegaly
Hypothyroidism
Chronic renal failure
Idiopathic CSA

odic breathing', which is characterised by periods of hyperventilation with varying tidal volumes alternating with periods of central apnoea.

This pattern of breathing is defined by a cyclical crescendo and decrescendo change in breathing amplitude, which can be formally diagnosed on polysomnography and occasionally observed at the

bedside in unwell patients.

### Central sleep apnoea associated with heart failure and stroke

About 40% of patients with heart failure have CSA and Cheyne-Stokes respiration.<sup>11</sup> In one study, risk factors for CSA/ Cheyne-Stokes respiration included male gender, atrial fibrillation, aged more than 60, and hypocapnia during wakefulness.<sup>12</sup>

This study provides useful parameters that allow doctors to identify heart failure patients at high risk for the presence of CSA/ Cheyne-Stokes respiration and to determine who needs further testing with polysomnography.

The common sleep-related symptoms of patients with these conditions are insomnia and difficulty falling asleep. Some patients report paroxysmal nocturnal dyspnoea. Although sleep structure is disrupted due to frequent awakenings,

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patients less commonly report snoring and excessive daytime sleepiness, which is seen in OSA.

Both obstructive and central sleep apnoea can coexist in some patients with heart failure.

The clinical relevance of CSA/Cheyne–Stokes respiration in patients with heart failure is its association with poor prognosis. It has been reported that after controlling for potentially confounding risk factors, CSA remains the strongest predictor of heart failure readmissions, and an independent risk factor for death or cardiac transplantation.<sup>13</sup>

While OSA may be a risk factor for having a stroke, CSA is the predominant sleep-related breathing disorder following a stroke and an independent prognostic determinant of mortality.<sup>14</sup> Available data support the need to diagnose sleep apnoea and initiate treatment in the post-stroke period, then re-evaluate the severity of disease with neurological recovery.<sup>15</sup>

## Treatment of non-hypercapnic central sleep apnoea

The heterogeneity of non-hypercapnic CSA dictates an individualised approach to therapy and several considerations must be taken into account. For CSA associated with sleep onset, it is critical to determine pathology versus physiology.

Central apnoea may occur at sleep onset and resolve with consolidation of sleep. This may not require treatment in an asymptomatic individual



AP portable chest X-ray of a patient in acute pulmonary oedema. Source: Frank Gaillard, Jeremy Jones <http://bit.ly/1LhaCmy>

who is free of significant comorbidity.

The first-line therapy for CSA associated with heart failure is optimisation of medical therapy for cardiac failure (for example, with diuretics, beta-blockers and cardiac resynchronisation therapy). Supplemental oxygen and CPAP therapy are the next line of therapy.

Supplemental oxygen may exert its effect in CSA/Cheyne–Stokes respiration by ameliorating hypoxaemia and minimising subsequent ventilatory overshoot and/or by decreasing sympathetic activity. In small studies, supplemental oxygen

has been shown to increase ejection fraction by a modest 5% and should be titrated during polysomnography to monitor its effect on central events. CPAP therapy should be trialled initially when OSA and CSA/Cheyne–Stokes respiration are found to coexist, particularly if the obstructive events are more frequent than central events.

Another positive airway pressure device used to treat CSA is adaptive pressure support servoventilation (ASV), which was designed to provide variable amounts of ventilatory support during different phases of periodic breathing. The support is minimal during the hyperpneic

phase of periodic breathing, and maximal during periods of diminished breathing and central apnoea. Until recently this treatment was thought to be particularly helpful in heart failure patients unresponsive to other therapies.

A producer of ASV machines, ResMed, released an urgent recall in May for patients using their ASV machines to treat CSA with symptomatic chronic heart failure and an ejection fraction less than 45% following preliminary data showing a 33% increase in cardiovascular death in this group. Information about the future role of ASV in CSA should become clearer after further

analysis of this data.

Pharmacological therapy for CSA has achieved only limited and modest success. There are two medications that have demonstrated promise in small clinical studies: acetazolamide and theophylline. Neither drug has been studied in large-scale clinical trials. Acetazolamide is a carbonic anhydrase inhibitor and a weak diuretic that causes mild metabolic acidosis. Acetazolamide ameliorates CSA when administered as a single dose of 250mg before bedtime. However, long-term effects in patients who have CSA are unknown. There is evidence that theophylline ameliorates Cheyne–Stokes respiration in patients with congestive heart failure. However, the available literature is based on small case series rather than robust clinical trials and theophylline's narrow therapeutic window precludes widespread use.

The development of effective, physiologically based pharmacological therapy is greatly needed.

For idiopathic CSA, there is evidence that many patients respond to a trial of positive airway pressure, either CPAP, bi-level positive pressure or ASV. The optimal pressure settings should again be titrated during polysomnography and the addition of oxygen therapy considered if significant desaturation is noted following apnoeic events.

Finally, acetazolamide has been used successfully in selected patients who have idiopathic CSA and have failed or been unsuitable for other therapies.

## Nocturnal hypoventilation

THERE are many conditions that can cause a patient to 'under-breathe' to the point that oxygen levels fall and carbon dioxide levels rise, causing respiratory failure. Respiratory failure from hypoventilation may be more prominent or occur first in sleep due to altered respiratory physiology in sleep, including reduced tidal volumes and altered chemo-responsiveness for respiration.

Examples of disorders that may be associated with nocturnal hypoventilation include patients with neuromuscular disorders, chest wall deformities, lung disease (ie, cystic fibrosis and COPD), congenital breathing abnormalities and obesity. A full discussion of this complicated topic is beyond the scope of this article however, obesity hypoventilation syndrome will be discussed in some detail as an example and to aid recognition of this important condition in general practice.

### Obesity hypoventilation syndrome

The obesity hypoventilation syndrome (OHS) was originally described in 1955 in subjects with obesity, chronic daytime hypercap-



Clubbing of the fingers is a classic feature of cystic fibrosis, although not present in many patients. Source: Jerry Nick, M.D. <http://bit.ly/1iNizM>

nia and hypoxaemia, polycythaemia, hypersomnolence, and right ventricular failure.

In 1956, the term 'Pickwickian syndrome' was coined for these patients because they resemble the messenger boy Joe in Charles Dickens' *The Pickwick Papers*.

Clinically, OHS can be thought of as a very severe form of OSA in morbidly obese patients. Many patients with OHS will have underlying OSA (often severe), but

in addition to blocking their upper airway, they also 'under-breathe' or hypoventilate, leading to more marked hypoxaemia and hypercapnia during sleep.

This in turn leads to daytime respiratory failure, with hypoxaemia and hypercapnia.

Fat deposition in and around the abdomen and rib cage causes reduced thoracic compliance and functional residual capacity of the lungs, requiring greater work

of breathing in morbidly obese patients.

Additionally, the body's response to hypoxaemia and hypercapnia is reduced, contributing to hypoventilation.

Patients usually present with typical symptoms of OSA, including snoring, witnessed apnoeas and daytime hypersomnolence.

On more detailed assessment, patients may have morning headaches, evidence of daytime hypoxaemia or hypercapnia, polycythaemia, pulmonary hypertension or right heart failure.

The condition should be suspected in all morbidly obese patients and needs to be considered carefully in addition to OSA, as the treatment differs from OSA alone.

Pulmonary, neuromuscular, chest wall, and metabolic diseases need to be excluded prior to making a diagnosis of OHS. A laboratory-based diagnostic sleep study, with transcutaneous CO<sub>2</sub> monitoring and arterial blood gas testing are sufficient to make the diagnosis, and plan treatment.

Importantly, the recent trend towards limited home sleep studies could lead to a significant number of patients with OHS going

undiagnosed and inappropriately treated if a full clinical evaluation is not concurrently performed.

There is increasing evidence that timely and appropriate treatment of OHS patients is crucial in reducing the significant morbidity and mortality associated with this disorder.

Weight loss clearly remains the critical long-term goal. Bariatric surgery should be considered for those who cannot manage to lose weight by other approaches.

Both CPAP and BPAP have been used clinically to manage patients with obesity hypoventilation syndrome. A recent Australian study has suggested that milder forms of this condition (with less severe nocturnal hypoxaemia/hypercapnia) can be successfully managed with CPAP alone.<sup>16</sup>

For those with more severe OHS, BPAP is usually required and supplemental nocturnal oxygen may be necessary.

Patients with OHS are best managed by sleep physicians and sleep units with experience in this area as long-term follow-up is required, including surveillance sleep studies and regular arterial blood gas testing.

## Future directions

THERE is a need for GPs to become increasingly aware of sleep disorders in general, to appreciate sleep disorders besides OSA, and to understand how to alter their investigations and

management if alternate sleep disorders are suspected.

More research is needed to characterise how our current treatments — including CPAP and oral appliances

— impact on patient outcomes and mortality, particularly with respect to metabolic and cardiovascular disease in OSA.

A better understanding of the

range of sleep apnoea phenotypes and predictors of treatment response is required to allow doctors to tailor their choice of treatment to the individual patient.

## References

Available on request from [howtotreat@cirrusmedia.com.au](mailto:howtotreat@cirrusmedia.com.au)

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## Case studies

### Case study 1: Undiagnosed OSA in a commercial driver<sup>17</sup>

FRANK's semi-trailer collides with the back of a car that is stopped at traffic lights, killing two people. Frank has no recollection of the period before this accident.

Frank gives a long history of talking in his sleep and occasional sleepwalking. In the two years immediately before the accident, Frank's spouse had become aware of worsened snoring and apnoeas during his sleep. During this time, Frank describes a problem with daytime sleepiness, including frequently taking pseudoephedrine while driving.

After the accident, a sleep study shows moderate OSA. Frank's daytime sleepiness is objectively confirmed with sleep testing. His urine tests positive for amphetamines at the time of the accident.

#### Comment

Frank had a serious accident killing other people after falling asleep at the wheel. His untreated OSA contributed to his falling asleep at the wheel. Frank was taking amphetamines to keep himself awake while driving and was therefore knowingly driving while sleepy. After the accident, he pleaded guilty to a culpable driving offence and was jailed.

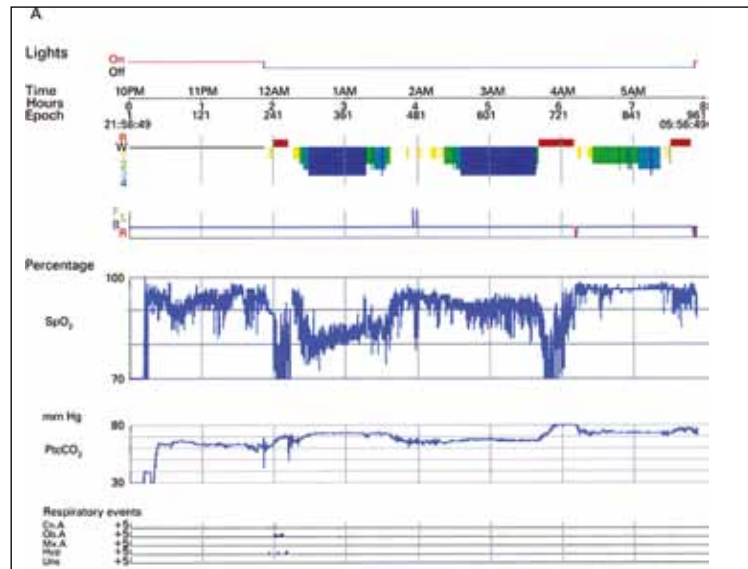
pable driving offence and was jailed.

### Case study 2: Obesity hypoventilation syndrome

Carol, 61, presents with a history of intermittent snoring in association with weight gain of 20kg. There are no reports of witnessed nocturnal apnoeas or gasping. Her average sleep time is around seven hours a night, usually waking up fresh in the morning. She describes mild daytime sleepiness, for instance, frequently falling asleep in the evening while watching television. She does not drive. Carol had a history of hypertension, diabetes mellitus, hypercholesterolaemia and a thyroid resection in 2003.

On examination, her BMI is 38 and her posterior oropharynx is markedly crowded. She is centrally obese. Her oxygen saturation on room air is 93%. Carol appears euthyroid, her chest is clear and cardiac examination is unremarkable, with no evidence of right heart failure.

Laboratory sleep study testing reveals very severe sleep disordered breathing. Her total AHI is 71/hour, with a minimum oxygen saturation of 61%. There is marked hypoxaemia throughout sleep, with her baseline oxygen saturation falling to the



**Figure 1: Eight-hour polysomnogram of obesity hypoventilation syndrome (OHS) in 22-year-old man (weight 228 kg, height 158 cm, PaCO<sub>2</sub> 67 mm Hg). Note spiralling oxygen saturation (SpO<sub>2</sub>) with inadequate correction above 90%, marked and progressive hypercapnia across the night and fragmented sleep.**

mid-80s on average when asleep.

Finally, there are more sustained oxygen drops in REM sleep, suggesting REM hypoventilation (See figure 1).

Arterial blood gas in daytime resting (room air) PaO<sub>2</sub> is 61mmHg and PaCO<sub>2</sub> is 66mmHg. Her Alveolar-arterial oxygen gradient is 7, which is normal, suggesting that her daytime hypoxaemia

and hypercapnia are all due to daytime hypoventilation (which in turn is secondary to her nocturnal hypoventilation).

Carol has severe OSA, obesity hypoventilation, and type 2 respiratory failure. Importantly, CPAP is unlikely to be able to control this condition. Other management includes weight loss, BPAP and nocturnal oxygen.

#### Take-home messages

- Obstructive sleep apnoea accounts for 85% of all respiratory sleep disorders. However, GPs should be familiar with other disorders, especially central sleep apnoea and obesity hypoventilation syndrome.
- Obstructive sleep apnoea is a significant and independent risk factor for hypertension, coronary artery disease, cardiac failure, stroke, metabolic syndrome and all-cause mortality.
- Untreated OSA in drivers puts them at higher risk of motor vehicle and occupational accidents, and has implications for various occupations.
- Central sleep apnoea is common in patients with heart failure and stroke, and needs to be differentiated from obstructive sleep apnoea as treatment differs.
- Obesity hypoventilation syndrome should be suspected in the morbidly obese patient and a referral made to a sleep clinic for early diagnosis and treatment.
- GPs should be aware of the limitations of home sleep studies, and the need for careful clinical assessment and medical supervision of sleep disorders therapy.



## How to Treat Quiz

Sleep Apnoea — 16 October 2015

#### INSTRUCTIONS

Complete this quiz online and fill in the GP evaluation form to earn 2 CPD or PDP points. We no longer accept quizzes by post or fax.

The mark required to obtain points is 80%. Please note that some questions have more than one correct answer.

#### GO ONLINE TO COMPLETE THE QUIZ

[www.australiandoctor.com.au/education/how-to-treat](http://www.australiandoctor.com.au/education/how-to-treat)

#### 1. Which TWO statements regarding the background to sleep apnoea are correct?

- Obstructive sleep apnoea and upper airway resistance syndrome are associated with reduced or absent breathing during sleep due to narrowing and relaxation of the upper airway in sleep.
- Obstructive sleep apnoea in particular is closely linked to hypertension, cardiac failure, ischaemic heart disease, stroke and the metabolic syndrome.
- The second most common respiratory sleep disorder is obstructive sleep apnoea.
- Sleep disorders can be broadly classified as 'central sleep disorders' and 'peripheral sleep disorders'.

#### 2. Which THREE statements regarding upper airway resistance syndrome are correct?

- Upper airway resistance syndrome leads to daytime sleepiness.
- The sleep of patients with upper airway resistance syndrome

is fragmented by frequent electroencephalogram arousals from more subtle obstructive breathing events in sleep.

- Patients with upper airway resistance syndrome have obstructive sleep apnoea on polysomnography.
- CPAP or oral appliances are often recommended for treatment.

#### 3. Which TWO statements regarding obstructive sleep apnoea (OSA) are correct?

- OSA is characterised by recurrent episodes of partial obstruction of the upper airway resulting in substantially reduced or complete cessation of airflow despite ongoing breathing efforts.
- The severity of OSA is based on the number of obstructive breathing events during sleep.
- The Apnoea Hypopnoea Index describes the degree of hypoxia that occurs during sleep in OSA.
- OSA leads to intermittent disturbances in gas exchange and fragmented sleep.

#### 4. Which THREE statements regarding OSA are correct?

- OSA is more common in women than in men.
- In both males and females, the strongest risk factor for OSA is obesity.
- Snoring is the hallmark symptom of sleep apnoea because it reflects the critical narrowing of the upper airway.
- Snoring is an excellent predictor of OSA.

#### 5. Which TWO statements regarding the symptoms of OSA are correct?

- Nocturnal symptoms include choking, restless sleep, periods of silence terminated by loud snoring, nocturnal angina, nocturia, and impotence.
- Witnessed apnoeas are a good diagnostic predictor of the severity of OSA.
- Excessive daytime sleepiness is seen in about 40-60% of the general population.
- Daytime symptoms include fatigue, memory impairment,

poor concentration and work performance, irritability and morning headaches.

#### 6. Which THREE features are commonly found on examination in OSA?

- Diabetes
- Obesity
- A crowded oropharyngeal airway
- A large neck circumference

#### 7. Which TWO statements regarding polysomnography are correct?

- The duration of the diagnostic study should be at least two hours to allow adequate assessment of variables during sleep.
- Polysomnography performed in a sleep laboratory is the 'gold standard' for diagnosing OSA.
- Polysomnographic studies generally involve a minimum of 12 channels of recordings.
- The data yielded from home-based polysomnography is of a quality as high as that from laboratory-based studies.

#### 8. Which THREE are complications of untreated OSA?

- Impaired cognitive function
- Obesity
- Increased risk of motor vehicle accidents
- Cardiac failure

#### 9. Which TWO are treatments for OSA?

- Weight loss
- Soporifics (for example, benzodiazepines)
- Positive airway pressure
- Avoidance of prone sleep if possible and practical

#### 10. Which THREE statements regarding central sleep apnoea (CSA) are correct?

- It is important to differentiate CSA from OSA as it has a different aetiology and management.
- About 40% of patients with heart failure have CSA.
- Hypercapnic central apnoea is the most common form of CSA.
- Pharmacological therapy for CSA has achieved only limited and modest success.

#### CPD QUIZ UPDATE

The RACGP requires that a brief GP evaluation form be completed with every quiz to obtain category 2 CPD or PDP points for the 2014-16 triennium. You can complete this online along with the quiz at [www.australiandoctor.com.au](http://www.australiandoctor.com.au). Because this is a requirement, we are no longer able to accept the quiz by post or fax. However, we have included the quiz questions here for those who like to prepare the answers before completing the quiz online.



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Next week's How to Treat explores the toxicity of modern oncology therapies, discussing the role of the monoclonal antibodies and tyrosine kinase inhibitors. These new therapies offer proven effectiveness and better tolerability over the previous generation of chemotherapies. The authors are Dr Malmaruha Arasaratnam, medical oncology advanced trainee, Sydney Adventist Hospital, and Royal North Shore Hospital, NSW; and Dr Joseph Rutovitz, consultant oncologist for Northern Haematology and Oncology Group and Sydney Adventist Hospital, Sydney, NSW.