European Heart Journal (1999) **20,** 858–866
Article No. euhj.1998.1484, available online at http://www.idealibrary.com on IDEAL®

Review Article

The sleep apnoea syndromes

K. G. van Houwelingen*, R. van Uffelen and A. C. M. van Vliet

Departments of Pulmonology and Internal Medicine, Drech-steden Ziekenhuis, Dordrecht, The Netherlands

Introduction

In recent decades, awareness of sleep apnoea syndromes has increased both in the public mind and among medical professionals. As a result, the number of patients referred for evaluation to a sleep clinic has increased dramatically[1]. The term sleep 'disordered breathing' comprises the whole continuum, from chronic snoring to obstructive sleep apnoea and the so-called 'Pickwick syndrome'[2].

Obstructive sleep apnoea syndrome is the most common type, occurring in 5–20% of adult men, although only about 20% of these individuals has symptoms[3]. It is characterized by recurring episodes of upper airway obstruction during sleep. This condition is usually associated with loud snoring and arousals, resulting in marked sleep fragmentation[4]. Increased daytime sleepiness is an important symptom[5]. The recurrent hypoxaemia and hypercapnia may lead to both pulmonary and systemic hypertension, cardiac arrhythmias and decreased survival[6–8].

The diagnosis of sleep apnoea syndrome is made by performing polysomnographia. However, the devices used vary in precision and reliability and there is also considerable variation in criteria for diagnosis[1,9,10].

At present, sleep apnoea syndromes are easily treatable. The objective of this review is to draw attention to the relationship of sleep apnoea syndromes with symptoms and signs of cardiovascular dysfunction[3,6,7].

A description is given of history, definitions, clinical features, epidemiology, pathophysiology and treatment of the sleep apnoea syndromes.

History

The sleep apnoea syndrome was described independently by two European research groups in 1965. Gastaut *et al.*[11] in France and Jung and Kuhlo[12] in Germany both reported their findings of the Pickwickian syndrome of sleep apnoea. Burwell *et al.*[13] in 1956 coined the term Pickwickian syndrome after the somnolent boy Joe from the *Pickwick Papers*. However, they evaluated their somnolent obese patients only while awake. Of course it was Charles Dickens, the narrator of the *Pickwick Papers*, who in 1835 was the first to describe the Pickwickian syndrome but his interest was purely literary.

In 1970, Tassinari and Lugaresi performed clinical sleep investigations in a large series of patients. They described sleep apnoea syndrome in obese and non-obese patients, showed a correlation with cardiovascular diseases and identified snoring and hypersomnolence as diagnostic indicators[14].

The definition of apnoea (duration and type) and the apnoea index (number of apnoeas per hour of sleep) were introduced by Guilleminault *et al.* in 1973[15]. Much later Gould *et al.* documented the relationship between daytime somnolence and nocturnal sleep disruptions caused by obstructive sleep apnoea/hypopnoea[16].

In relation to cardiovascular complications of the sleep apnoea syndrome, MacGregor *et al.* in 1970 described sudden death as a complication of the Pickwickian syndrome[17]. In 1972, Coccogna *et al.* demonstrated a relationship between pulmonary as well as systemic hypertension and sleep disordered breathing[18]. In 1977 Burack *et al.* described the hypersomnia–sleep apnoea syndrome as a major reversible hazard for cardiovascular complications[19]. In 1983 Guilleminault *et al.* described cardiac arrhythmias and conduction disturbances in relation to obstructive sleep apnoea syndrome[20]. This was followed by many reports looking at cardiac arrhythmia, hypertension, myocardial ischaemia and infarction, cerebrovascular accidents, and sudden death as sequelae of obstructive sleep apnoea syndrome[7,20–29].

Definitions

The terminology with regard to the sleep apnoea syndromes is inconsistent and confusing and includes:

Key Words: Sleep apnoea syndrome, cardiovascular symptoms, therapy.

Revision submitted 14 December 1998, and accepted 16 December 1998.

Correspondence: K. G. van Houwelingen, Department of Cardiology, Heart-Lung Institute, University Hospital Utrecht, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands.

0195-668X/99/120858+09 $18.00/0

Table 1 Definitions of sleep disordered breathing

Obstructive sleep apnoea	
(1)	Cessation of airflow during sleep or more than 10 s, despite ventilatory efforts
(2)	Five or more apnoea episodes per hour of sleep
(3)	Oxygen desaturation of at least 4%
Obstructive sleep hypopnoea	
(1)	A decrease in airflow of 30–50% during sleep, lasting at least 10 s
(2)	Fifteen or more hypopnoea episodes per hour of sleep
(3)	Oxygen desaturation of at least 4%
Upper airway resistance syndrome	
(1)	Absence of significant decreases in airflow during sleep
(2)	Fifteen or more arousals/awakenings per hour of sleep
(3)	No significant oxygen desaturations

'upper airway closure syndromes', 'sleep disordered breathing', 'sleep apnoea syndromes' and 'sleep hypopnoea syndromes'[9]. The definitions given in Table 1 are most frequently used.

With regard to upper airway closure during sleep, three syndromes are recognized: sleep apnoea, sleep hypopnoea and the upper airway resistance syndrome[30]. These syndromes share the following common features: snoring, excessive daytime sleepiness and disruption of sleep architecture due to arousals and awakenings.

The *obstructive sleep apnoea syndrome* is usually defined as:

(1) cessation of airflow during sleep of more than 10 s, despite ventilatory efforts[9,30].
(2) five or more apnoea episodes per hour of sleep (apnoea–index).
(3) oxygen desaturation of at least 4%.

In contrast to the obstructive sleep apnoea syndrome, the central sleep apnoea syndrome involves no ventilatory effort (Fig. 1). The central sleep apnoea syndrome is common in Cheyne–Stokes respiration[31,32]. Although mixed obstructive sleep apnoea syndrome/central sleep apnoea syndrome can occur, aetiological features generally differ[31].

In the *obstructive sleep hypopnoea syndrome* there is, by definition, no cessation of airflow[9,16,30], but there is:

(1) a decrease in airflow during sleep of 30–50% lasting at least 10 s
(2) fifteen or more hypopnoea episodes per hour of sleep (hypopnoea index)
(3) oxygen desaturation of at least 4%[9,30].

The *upper airway resistance syndrome* is characterized by arousals and awakenings due to increased upper airway resistance and intrathoracic pressure swings. These patients are usually heavy snorers.

The following criteria should be met[30,33]:

(1) absence of a significant decrease in airflow during sleep (<30%), or if present, of less than 10 s duration.
(2) fifteen or more arousals/awakenings per hour of sleep.
(3) no significant oxygen desaturations.

In most publications, only the term obstructive sleep apnoea syndrome is used, in which apnoeas and hypopnoeas are combined, because distinguishing apnoea from hypopnoea has little or no effect on the approach to treatment. The term used to characterize 'obstructive sleep apnoea syndrome' in these situations is the apnoea–hypopnoea index: (the number of apnoeas plus the number of hypopnoeas per hour of sleep) also called the respiratory disturbance index. The apnoea–hypopnoea index which defines obstructive sleep apnoea syndrome in most publications varies from 5–15[1,30].

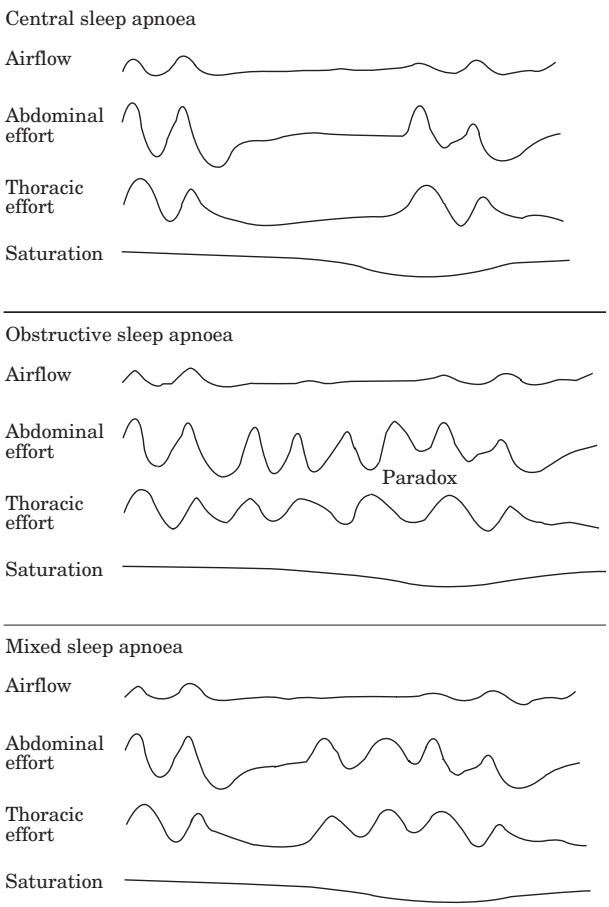

Figure 1 **Schematic representation of sleep apnoea syndromes: the central, obstructive and mixed type.**

Table 2 Clinical features

History
Snoring
Apnoea during sleep
Arousals
Awakenings
Choking spells
Nocturnal diaphoresis
Abnormal motor activity during sleep
Enuresis
Gastroesophageal reflux
Excessive day-time sleepiness
Headaches
Loss of memory and concentration
Personality changes
Depression
Chest pain
Diminished libido
Impotence
Physical examination
Hypertension
Overweight
Oral cavity abnormalities
Enlarged tonsils
Thickened uvula
Long and redundant soft palate
Cardiovascular symptoms
Systemic hypertension
Pulmonary hypertension
Cor pulmonale
Congestive heart failure
Angina pectoris
Myocardial infarction
Cardiac arrhythmia
Conduction disturbances
Sudden death
Cerebral ischaemia (transient ischaemic attack)

It should be emphasized that the clinical features that occur are most important in diagnosing and treating sleep apnoea syndromes.

Clinical features

Obstructive sleep apnoea syndrome has a broad spectrum of clinical features (Table 2). Snoring is one of the cardinal. Some snorers are not aware of their problem or its severity. An interview with the partner or other relatives is essential to obtain an accurate description. A pattern of intermittent loud snoring, with periods of silence lasting more than 10 s, is suggestive of the occurrence of sleep apnoea[1,5,34]. Another prominent symptom is excessive daytime sleepiness. Because this is a subjective complaint it is difficult to quantify[1,5]. It is important to consider other (e.g. metabolic) causes of daytime sleepiness when interviewing a patient.

Other possible symptoms include nocturnal arousals with or without choking spells, nocturnal diaphoresis, abnormal motor activity during sleep, enuresis, gastroesophageal reflux, headaches, chest pain, diminished libido, impotence, loss of memory and concentration, personality changes and depression[1].

On physical examination some features are suggestive of obstructive sleep apnoea. Obstructive sleep apnoea syndrome patients are frequently overweight and hypertensive. Examination of the oral cavity may reveal abnormalities such as enlarged tonsils, thickened uvula or a long and redundant soft palate. In patients with severe obstructive sleep apnoea cardiovascular symptoms are common[1,7,22,34].

Many of these features, however, are nonspecific and a definitive diagnosis cannot be made by interview and physical examination alone. The gold standard for diagnosing obstructive sleep apnoea syndrome is still polysomnography in the sleep laboratory[1,10]. Complete polysomnography consists of undertaking an electroencephalogram, an electrooculogram, an electromyogram, an electrocardiogram, airflow measurement, and recording of thoracic and abdominal ventilatory effort registration and snoring. Nowadays multi-channel ambulatory systems are often used to screen patients suspected of obstructive sleep apnoea syndrome. Most of these systems are sufficiently reliable to give a diagnosis of obstructive sleep apnoea syndrome.

Epidemiology

The first large studies on habitual snoring (irrespective of the diagnosis of obstructive sleep apnoea syndrome) indicated a prevalence of 25% in men and 15% in women (overall data). The prevalence increases significantly with age[35].

In the early 1980s, estimates of the prevalence of obstructive sleep apnoea syndrome were made on clinical signs and symptoms of severe obstructive sleep apnoea syndrome. In a cross-sectional study, Lavie *et al.* estimated the prevalence of obstructive sleep apnoea syndrome among male industrial workers to be at least 1%[36]. Two Scandinavian studies reported prevalences between 0·4 and 1·9%[37,38].

When considering an apnoea–hypopnoea index greater than 10 pathological, a prevalence of 2·7% was found. In the age group over 40 years, the prevalence reached 3·4–5·0%[39].

A more recent study in the United States examined 602 employed men and women aged 30–60 years. The subjects were evaluated by a questionnaire and overnight polysomnography. Two percent of women and 4% of men were estimated to have the obstructive sleep apnoea syndrome, as defined by the combination of an apnoea index greater than 5 and the occurrence of daytime sleepiness. In subjects aged 50–60 years, 4% of women and 9·1% of men were diagnosed as having obstructive sleep apnoea syndrome[40].

Methodological differences in the study protocol may explain some of the differences, but other factors may exist. The prevalence of obstructive sleep apnoea syndrome in patients with 'essential' hypertension is very high. In several studies of patients with hypertension, prevalences of 26–49% are reported, whereas in the

control groups the prevalence varied from 0–12%[36,41–43]. Since these figures are so high, patients with hypertension should always be asked about snoring, daytime sleepiness and possible apnoea during sleep.

More than 25% of individuals over 65 years of age have more than five episodes of apnoea per hour of sleep[44]. This does not mean that these people have obstructive sleep apnoea syndrome. It has still to be established whether the high prevalence of apnoea during sleep in the elderly has clinical relevance. In another study, a cohort of 198 elderly individuals (mean age at entry 66 years) were followed for 12 years. Obstructive sleep apnoea syndrome, as defined by an apnoea–hypopnoea index of over 10, increased the mortality ratio[45], suggesting that 'natural' death during sleep in the elderly may be associated with obstructive sleep apnoea syndrome. There is also a strong relationship between sleep disordered breathing and congestive heart failure. In patients with left ventricular dysfunction and patients on a heart transplant waiting list, a prevalence of sleep-disordered breathing of 40–45% has been reported[46]. In these studies, apnoeas were mostly of the central type and occurred in the pattern of Cheyne–Stokes respiration. It has been demonstrated that respiratory-system instability can produce obstructive as well as central apnoea[46,47].

Other factors related to a higher prevalence of obstructive sleep apnoea are early childhood (related to changes in craniofacial characteristics or the size of pharyngeal and tonsillar tissue), gender (in general population samples, the male:female ratio is approximately 2–3:1), obesity (body mass index over 28 $kg \cdot m^{-2}$) and race (higher prevalence in blacks)[34]. Based on these epidemiological data, several risk factors for sleep-disordered breathing can be identified.

Strong factors are obesity, age, gender and family history of obstructive sleep apnoea syndrome. Additional conditions that may predispose patients to obstructive sleep apnoea syndrome are race, alcohol and tobacco consumption, low vital capacity, snoring, sleepiness and medications[4,34,48]. At the moment most cases of obstructive sleep apnoea syndrome still go unrecognized. The explanation is, in part, the lack of knowledge about this 'new' syndrome, its complications and treatment. The other part of the explanation is that sleep-disordered breathing is a chronic disease for which it is difficult to obtain reliable epidemiological information. There is thus a discrepancy between the prevalence of obstructive sleep apnoea syndrome and the medical appreciation of its impact or presence in patient populations[34]. To diagnose and treat all potential patients with obstructive sleep apnoea syndrome will have a great impact on the capacity of sleep clinics and on the budget for public health care[76].

Mortality

For mortality due to the sleep apnoea syndromes we still have to refer to studies performed prospectively on retrospective cohorts of sleep apnoeic patients.

MacGregor *et al.*[17] investigated 22 patients (10 men, mean age 50 years and 12 women, mean age 58 years) diagnosed with the Pickwickian syndrome between 1959 and 1969. These patients had severe respiratory failure, pulmonary emboli and morbid obesity. Seven of the 22 subjects died suddenly shortly after being diagnosed (five patients died within 16 days).

Between 1978 and 1986 He *et al.*[26] evaluated 706 men with obstructive sleep apnoea syndrome. End-points were mortality and current symptoms, as checked by follow-up questionnaires. Unfortunately, the response rate was only 54·5% (n=385). Of these subjects, 246 were not treated by nasal continuous positive airway pressure, tracheostomy or uvulopalatopharyngoplasty. Irrespective of the cause of death, obstructive sleep apnoea syndrome patients with an apnoea index over 20 had a cumulative mortality of 37% vs a cumulative mortality of 4% in the controls. None of the patients treated with tracheostomy or nasal continuous positive airway pressure died.

In 1988, the Stanford Sleep Disorders Clinic reported a prospective follow-up study based on two retrospectively selected cohorts of patients with obstructive sleep apnoea syndrome[49]. The study consisted of 198 subjects: 71 were treated by tracheostomy and 127 conservatively (weight loss by dietary measures). The tracheostomy cohort had a significant higher body weight, had more apnoeas and was younger than the conservative treatment cohort. Nevertheless the 5-year mortality in the conservative treatment group was 11% compared to 0% in the tracheostomy group. This study clearly indicated that mortality, especially cardiovascular mortality, is increased in conservatively treated patients with the obstructive sleep apnoea syndrome.

Unrecognized obstructive sleep apnoea syndrome is reported to be a cause of mortality from highway crashes and industrial accidents[34,50]. Obstructive sleep apnoea syndrome is strongly suspected of producing serious adverse effects, including peri-operative mortality from anaesthesia and during recovery from surgery[34].

Pathogenesis and pathophysiological considerations

Snoring is a consequence of changes in the configuration and properties of the upper airway that occur during sleep[51]. Narrowing or closure may occur at one or more sites in an unstable upper airway. Upper airway dysfunction and the specific sites of narrowing or closure are influenced by the underlying neuromuscular tone, upper airway muscle synchrony, and the stage of sleep. These events are generally most prominent during rapid-eye-movement sleep because of the hypotonia of the upper airway muscles characteristic of this stage of sleep[4,8,30].

Anatomical features, genetic and environmental factors also influence the size of the upper airway[4,8,52–55].

The sound of snoring is produced by the vibration of the soft tissues of the pharynx, soft palate, and perhaps the uvula. Snoring occurs during inspiration and expiration and can be heard during exclusively nasal breathing. Flow rate through the airway, its geometry, and resistance will determine whether the instability of airway walls will remain oscillatory or become permanent, as in apnoea[51].

Retrospective studies indicate that there is an association of sleep apnoea with morbidity and mortality due to cardiovascular and cerebrovascular causes, independent of other risk factors such as obesity, age and sex[4,7,30,56]. Despite the results of these retrospective studies, the link between obstructive sleep apnoea and cardiovascular and cerebrovascular disease remains highly controversial[77]. A major difficulty in investigating the independent health effects of sleep apnoea is in adjusting out the effect of confounding factors: many patients with obstructive sleep apnoea syndrome are obese or have other cardiac risk factors. The American Sleep Heart Health Study (in progress) will probably help to resolve these problems.

The cardiovascular effects of obstructive sleep apnoea syndrome have a multifactorial pathogenesis. The risk of cardiovascular complications appears to be mediated by the complex interaction between the mechanical and chemical effects (hypoxia, hypercapnia) or repetitive upper airway closure and its effect on the autonomic nervous system.

The acute changes in obstructive sleep apnoea syndrome may resemble reflexes occurring in voluntary apnoea or diving, but those effects are modified by the mechanical effects of intrathoracic pressure changes secondary to airway obstruction[6].

The responses to peripheral and central chemoreceptor activation by hypoxia and hypercapnia are influenced by the sleep state, as well by circulatory control mechanisms. Although parasympathetic tone is high during sleep, the sympathetic nervous system is activated during apnoeas and arousals/awakenings and is likely to be involved in obstructive sleep apnoea syndrome-induced circulatory changes, such as (pulmonary) hypertension and cardiac arrhythmias[4,6–8,20,21,23,56]. Chronic sleep deprivation and sleep fragmentation caused by frequent arousals and awakenings contribute to excessive daytime sleepiness (EDS), chronic fatigue, irritability, loss of concentration, decrease of intellectual functions and personality changes[30,56].

The long-term circulatory changes in obstructive sleep apnoea syndrome are determined by its multifactorial pathogenesis.

During normal sleep, there is a significant reduction in systemic blood pressure in both normotensive and hypertensive subjects[7]. However, in patients with moderate-to-severe obstructive sleep apnoea there is an increase of about 25% in systolic and diastolic blood pressure. Due to hypoxemia and frequent arousals (apnoea termination) there is strong sympathetic activation, with peripheral vasoconstriction and high plasma catecholamine levels. Locally in the vessel wall hypoxaemia and hypercapnia lead to acidosis which is followed by the release of many vasoactive agents, such as prostacyclin, thromboxane, endothelin and arginine-vasopressin[7,8,30,56].

The above factors lead to increased afterload of the left ventricle and eventually left ventricular hypertrophy[22]. Following an apnoeic episode, there is a period of hyperventilation with increased negative pressures in the thorax. This leads to an increased venous return to the heart with stretching of the right atrium, followed by an increase in atrial natriuretic peptide levels and consequent nocturnal diuresis[7].

In addition to nocturnal pressure elevations, most studies have reported a high prevalence of hypertension in patients with obstructive sleep apnoea syndrome during wakefulness. The remarkably high prevalence of hypertension in obstructive sleep apnoea syndrome (up to 50%), combined with numerous reports of reductions in systemic blood pressure following effective treatment of obstructive sleep apnoea syndrome, has led to the conclusion that obstructive sleep apnoea syndrome contributes to the development of diurnal hypertension[57–60].

Chronic (over-) stimulation of the sympathetic nervous system leads to down-regulation of the baroreceptor reflex and to autonomic dysfunction[4,7,56]. Together with activation of the renin-angiotensin-aldosterone system and decreased sensitivity of the kidney to atrial natriuretic peptide this may lead to fixed hypertension, left ventricular hypertrophy, pulmonary hypertension, congestive heart failure[22,47,61,62] and an increased risk of stroke, myocardial infarction and sudden death[4,6,7,22,24,26,28–30,34,56].

Therapy

Who should be treated for sleep apnoea?

Although the generally accepted criteria for diagnosis of obstructive sleep apnoea syndrome are an apnoea index of over 5 per hour or an apnoea–hypopnoea index of over 15 per hour, it is not clear when patients should be considered for specific therapy[1,3]. When regarding the risk of mortality, treatment should be considered in obstructive sleep apnoea syndrome, and the higher the apnoea index or apnoea–hypopnoea index, the more aggressive one should be in terms of the mode of therapy recommended[1].

The severity of the clinical complaint (i.e. excessive daytime sleepiness) is also an indication for treatment, even when the apnoea index or apnoea–hypopnoea index are 'low': for example, in the case of upper airway resistance syndrome with frequent arousals[1,3]. Thus, treatment decisions should not be based solely on the results of sleep studies (Table 3).

General measures

All patients with obstructive sleep apnoea syndrome should be counselled about the potential benefits of

Table 3 Treatment of the sleep apnoea syndrome

General measures
Counselling
Discourage intake of alcohol and sedatives
Weight reduction
Medication
Protriptyline
Fluoxetine
Theophylline
Progesterone
Acetozolamide
Nocturnal oxygen supply
Surgical treatment
Correction of anatomic obstruction of the upper airway
Tracheostomy
Maxillofacial surgery
Uvulopalatopharyngoplasty (UPPP)
Positive airway pressure
Nasal continuous positive airway pressure (nCPAP)
Bilevel continuous positive airway pressure (bi-PAP)
Oral appliances to reduce snoring

therapy as opposed to the risks of conservative treatment. Some general measures should be taken[30].

The use of alcohol should be discouraged. Alcohol selectively reduces upper airway muscle tone and increases the frequency of disordered breathing during sleep; alcohol also prolongs apnoea by delaying arousal. In the same way, sedatives and hypnotic agents should be avoided because they are known to aggravate sleep apnoea. In obese patients, weight loss can significantly decrease the severity of apnoea and also reduces the frequency of apnoea episodes during sleep[1,30]. Patients should also be advised about their diminished ability to drive vehicles[1,50].

Medication

Although a number of medications have been tried, the results have been disappointing. Only protriptyline, fluoxetine, theophylline and progesterone have been used with varying degrees of success in mild cases of obstructive sleep apnoea syndrome[1,30,63].

In the case of central apnoeas in congestive heart failure, theophylline and acetozolamide improved the breathing pattern and reduced daytime sleepiness[31,64]. Nocturnal oxygen therapy should be prescribed with caution, especially in patients with hypercapnia[1,30].

Surgical treatment

In all patients, correctable anatomical obstruction of the upper airway should be sought for during physical examination. Removal of enlarged tonsils and adenoids is beneficial if they contribute to a narrowing of the oropharynx. Other patients may benefit from nasal surgery to correct septal deviation or to remove nasal polyps[1].

Tracheostomy

Permanent tracheostomy was the first efficacious surgical procedure performed for the treatment of obstructive sleep apnoea syndrome[65]. It has a success rate of almost 100% in reversing signs and symptoms of obstructive sleep apnoea syndrome. Although tracheostomy can be life-saving, additional medical and psychological morbidity may be associated with this treatment. In most patients, it remains a treatment of last resort when other therapies have failed[1,30,65].

Maxillofacial surgery

Patients with obstructive sleep apnoea syndrome who have major craniofacial abnormalities may benefit from maxillofacial surgery, with or without uvulopalatopharyngoplasty. These operations are not uniformly successful, although individual patients have had excellent results[1,30,65].

Uvulopalatopharyngoplasty

Uvulopalatopharyngoplasty was first described for the treatment of habitual snoring in 1964. It is based on the observation that more than 90% of snorers have a narrowing of the oropharynx caused by an elongated soft palate and uvula, and redundant lateral pharyngeal mucosa. With minor modifications, the first uvulopalatopharyngoplasty for the treatment of obstructive sleep apnoea syndrome was performed in 1981. Uvulopalatopharyngoplasty frequently results in symptomatic improvement and eliminates habitual snoring in more than 90%. However, several reports have shown that significant objective improvement in the apnoea index and oxygen saturation levels with postoperative polysomnography is only 40–60%[1,30,65]. Complications of uvulopalatopharyngoplasty include nasal regurgitation, infection, pain, wound dehiscence, bleeding and partial pharyngeal stenosis. Post surgical deaths have resulted from the combination of pharyngeal edema and narcotic use[1,65].

Positive airway pressure

Nasal continuous positive airway pressure therapy for obstructive sleep apnoea syndrome was introduced in 1981[63]. The objective of nasal continuous positive airway pressure is to provide sufficient pressure in the collapsible segment of the upper airway to counteract the inspiratory suction pressure. Nasal continuous

positive airway pressure is produced by a high-flow blower that delivers a continuous stream of room air into a sealed nasal mask that the patient wears while sleeping. The positive pressure created in the circuit pneumatically splints the pharyngeal airway open by preventing the soft palate and tongue from occluding it. The result is rapid restoration of normal sleep, reduction of daytime sleepiness and improvement in neuropsychiatric function[1,30,63].

Cardiac arrhythmia, (pulmonary) hypertension, and congestive heart failure have also been effectively treated, probably by correcting nocturnal desaturation and lowering nocturnal catecholamine release[1,30,32,66–69].

Patients should be observed in a sleep laboratory to determine the optimal continuous positive airway pressure level. Depending on several factors, this will vary from patient to patient and time to time[1,30,63,70]. The major concern with nasal continuous positive airway pressure is patient compliance[1,30,63,71]. Minor complications are common, including local skin irritation, drying of the nasal or oropharyngeal mucosa, nasal congestion and discharge, and eye irritations. Major complications, such as pneumocephalus, bacterial meningitis, massive epistaxis, and atrial arrhythmias have rarely been reported[1,30,63,70,72].

Discontinuation of nasal continuous positive airway pressure was followed by immediate return to pretreatment levels of sleepiness and psychomotor disturbances[1]. The compliance rate does not appear to be related to minor complications. Rather, the patients with significant improvement in daytime symptoms appear to be most motivated to continue with the therapy[1,70,73].

To increase patient compliance, attempts are being made to improve the device and its mask to increase its use. Examples of this would include a ramp feature, which starts at a lower pressure and increases gradually after the patient falls asleep, and a bilevel continuous positive airway pressure (biPAP), which has different expiratory and inspiratory pressures[63,70,74].

Oral appliances

Several studies have demonstrated that oral appliances can be an alternative to nasal continuous positive airway pressure or surgery in obstructive sleep apnoea syndrome. The rationale for its use is to modify the position of the mandible so as to enlarge the upper airway or reduce its collapsability. These appliances are worn only during sleep and are generally well tolerated. Late complications may include temporomandibular joint discomfort and occlusive malalignment[1,30,51,63,75].

Summary

The sleep apnoea syndrome is a complex of symptoms that can be very disabling for the patient who is suffering from it. Currently many cases of obstructive sleep apnoea syndrome are unrecognized which leads to unnecessary morbidity and even mortality.

It is important for general physicians to consider the diagnosis obstructive sleep apnoea syndrome in patients who have two or more clinical features of obstructive sleep apnoea syndrome that cannot be explained by any other known disease. Patients suspected of sleep-disordered breathing have to be referred to a sleep clinic for evaluation. Depending on the severity of the complaints and the results of polysomnographia, patients have to be treated to relieve their symptoms and to improve their prognosis.

There are three steps in treating a patient with obstructive sleep apnoea syndrome. The first step is counselling, the second is general measurements to reduce symptoms and the last is to start any specific treatment regimen. At the moment nasal continuous positive airway pressure is the treatment of choice in clinically important sleep apnoea. To diagnose and to treat all potential patients with obstructive sleep apnoea syndrome will have a great impact on the capacity of sleep clinics and on the budget for public health care.

The writers thank Professor Dr E. O. Robles de Medina for reviewing the manuscript.

References

[1] Man GCW. Obstructive sleep apnea. Diagnosis and treatment. Med Clin North Am 1996; 80: 803–20.
[2] Fleetham JA. A wake up call for sleep disordered breathing. Br Med J 1997; 314: 839–40.
[3] Bennett LS, Stradling JR. Who should receive treatment for sleep apnea?. Thorax 1997; 52: 103–4.
[4] Deegan PC, McNicholas WT. Pathophysiology of obstructive sleep apnoea. Eur Respir J 1995; 8: 1161–78.
[5] Johns MW. Daytime sleepiness, snoring, and obstructive sleep apnea. The Epworth Sleepiness Scale. Chest 1993; 103: 30–6.
[6] Bonsignore MR, Marrone O, Insalaco G, Bonsignore G. The cardiovascular effects of obstructive sleep apneas: analysis of pathogenic mechanisms. Eur Respir J 1994; 7: 786–805.
[7] Shepard Jr JW. Hypertension, cardiac arrhythmias, myocardial infarction, and stroke in relation to obstructive sleep apnea. Clinics in Chest Med 1992; 13: 437–58.
[8] White DP. Pathophysiology of obstructive sleep apnoea. Thorax 1995; 50: 797–804.
[9] Moser NJ, Phillips A, Berry DTR, Harbison L. What is hypopnea, anyway?Chest 1994; 105: 426–8.
[10] van Sweden B, Wauquier A, Arends JBAM, Declerck AC., Meten van slaap als hersen (dys) functie via polysomnografie. Acta Neuropsychiatrica 1991; 3: 48–54.
[11] Gastaut H, Tassarini C, Duron B. Etudes polygraphiques des manifestations episodiques (hypniques et respiratoires) du syndrome de Pickwick. Rev Neurol 1965; 112: 568–79.
[12] Jung R, Kuhlo W. Neurophysiological studies of abnormal night sleep and the Pickwickian syndrome. Prog Brain Res 1965; 18: 140–59.
[13] Burwell CS, Robin ED, Whaley RD, Bickelmann AG. Extreme obesity associated with alveolar hypoventilation. A Pickwickian syndrome. Am J Med 1956; 21: 811–18.
[14] Lugaresi E, Coccagna G, Mantovani M. Hypersomnia with periodic apneas. New York: Spectrum, 1978.
[15] Guilleminault C, Eldridge F, Dement WC. Insomnia with sleep apnea: a new syndrome. Science 1973; 181: 856–8.

[16] Gould GA, Whyte KF, Rhind GB *et al*. The sleep hypopnea syndrome. Am Rev Respir Dis 1988; 137: 895–8.
[17] MacGregor MI, Block AJ, Ball WS. Serious complications and sudden death in the Pickwickian syndrome. Johns Hopkins Med J 1970; 126–127: 279–95.
[18] Coccogna G, Montovani M, Brignani F *et al*. Continuous recording of the pulmonary and systematic arterial pressure during sleep in syndromes and hypersomnia with periodic breathing. Bull Physiopathol Respir 1972; 8: 1159–72.
[19] Burack B, Pollack C, Borowiecki B *et al*. The hypersomnia-sleep apnea syndrome (HAS): A reversible major cardiovascular hazard. Circulation 1977; 56: 177.
[20] Guilleminault C, Connolly SJ, Winkle RA. Cardiac arrhythmia and conduction disturbances during sleep in 400 patients with sleep apnea syndrome. Am J Cardiol 1983; 52: 490–4.
[21] Bauer T, Ewig S, Schafer H *et al*. Heart rate variability in patients with sleep-related breathing disorders. Cardiology 1996; 87: 492–6.
[22] Bradley TD. Right and left ventricular functional impairment and sleep apnea. Clinics in Chest Med 1992; 13: 459–78.
[23] Ferini-Strambi L, Zucconi M, Oldani A, Smirne S. Heart rate variability during sleep in snorers with and without obstructive sleep apnea. Chest 1992; 102: 1023–7.
[24] Franklin KA, Nilsson JB, Sahlin C, Naslund U. Sleep apnea and nocturnal angina. Lancet 1995; 345: 1085–7.
[25] Hanly P, Zuberi-Khokhar N. Daytime sleepiness in patients with congestive heart failure and Cheyne-Stokes respiration. Chest 1995; 107: 952–8.
[26] He J, Kryger MH, Zorick FJ *et al*. Mortality and apnea index in obstructive sleep apnea. Experience in 385 male patients. Chest 1988; 94: 9–14.
[27] Loui WS, Blackshear JL, Frederickson PA, Kaplan J. Obstructive sleep apnea manifesting as suspected angina: report of three cases. Mayo Clin Proc 1994; 69: 244–8.
[28] Mooe T, Rabben T, Wiklund U *et al*. Sleep-disordered breathing in women: occurrence and association with coronary artery disease. Am J Med 1996; 101: 251–6.
[29] Schafer H, Koehler U, Ploch T, Peter JH. Sleep-related myocardial ischemia and sleep structure in patients with obstructive sleep apnea and coronary heart disease. Chest 1997; 111: 387–93.
[30] Strollo PJ, Rogers RM. Current concepts: obstructive sleep apnea. N Engl J Med 1996; 334: 99–104.
[31] DeBacker WA, Verbaecken J, Willemen M *et al*. Central apnea index decreases after prolonged treatment with acetazolamide. Am J Respir Crit Care Med 1995; 151: 87–91.
[32] Naughton MT, Benard DC, Rutherford R, Bradley TD. Effect of continuous positive airway pressure on central sleep apnea and nocturnal pCO2 in heart failure. Am J Respir Crit Care Med 1994; 150: 1598–604.
[33] Guilleminault C, Stoohs R. The upper airway resistance syndrome. Sleep Res 1991; 20: 250.
[34] Strohl KP, Redline S. State of the art: recognition of obstructive sleep apnea. Am J Respir Crit Care Med 1996; 154: 279–89.
[35] Lugaresi E, Cirignotta F, Coccagna G, Pina C. Some epidemiological data on snoring and cardiocirculatory disturbances. Sleep 1980; 3: 221–4.
[36] Lavie P, Ben-Yosef R, Rubin AE. Prevalence of sleep apnea among patients with essential hypertension. Am Heart J 1984; 108: 373–6.
[37] Gislason T. Sleep apnea: clinical symptoms, epidemiology and ventilatory aspects. Acta Univ Uppsala 1987; 78: 1–48.
[38] Telakivi T, Partinen M, Koskenvuo M *et al*. Periodic breathing and hypoxia in snorers and controls: validation of snoring history and association with blood pressure and obesity. Acta Neurol Scand 1987; 76: 69–75.
[39] Cirignotta F, D'Alessandro R, Partinen M *et al*. Prevalence of every night snoring and obstructive sleep apneas among 30–69 year old men in Bologna, Italy. Acta Psychiatr Scand 1989; 79: 366–72.
[40] Young T, Palta M, Dempsey J *et al*. Occurrence of sleep disordered breathing among middle-aged adults. N Engl J Med 1993; 328: 1230–5.
[41] Fletcher EC, Debehnke RD, Lavoi MS *et al*. Undiagnosed sleep apnea in patients with essential hypertension. Ann Intern Med 1985; 103: 190–4.
[42] Kales A, Bixler EO, Cadieux RJ *et al*. Sleep apnoea in a hypertensive population. Lancet 1984; 2: 1005–8.
[43] Williams AJ, Houston D, Finberg S *et al*. Sleep apnea syndrome and essential hypertension. Am J Cardiol 1985; 55: 1019–22.
[44] Kripke DF, Ancoli-Israel S. Epidemiology of sleep apnea among the aged: is sleep apnea a fatal disorder? In: Guilleminault C, Lugaresi E, eds. Sleep/Wake disorders: natural history, epidemiology and long term evaluation. New York: Raven Press, 1983: 137–42.
[45] Bliwise DL, Bliwise NG, Partinen M *et al*. Sleep apnea and mortality in an aged cohort. Am J Public Health 1988; 78: 544–7.
[46] Lofaso F, Verschueren P, Dubois Rande JL *et al*. Prevalence of sleep disordered breathing in patients on a heart transplant waiting list. Chest 1994; 106: 1689–94.
[47] Klink ME, Sethi GK, Copeland JG, Quan SF. Obstructive sleep apnea in heart transplant patients. Chest 1993; 104: 1090–2.
[48] Chaouat A, Weitzenblum E, Krieger J *et al*. Association of chronic obstructive pulmonary disease and sleep apnea syndrome. Am J Respir Crit Care Med 1995; 151: 82–6.
[49] Partinen M, Jamieson A, Guilleminault C. Long-term outcome for obstructive sleep apnea syndrome patients: Mortality. Chest 1988; 94: 1200–4.
[50] Strohl KP, Bonnie RJ, Findley L *et al*. Sleep apnea, sleepiness, and driving risk: official statement of the American Thoracic Society. Am J Respir Crit Care Med 1994; 150: 1463–73.
[51] Hoffstein V. Snoring. Chest 1996; 109: 201–22.
[52] Guilleminault C, Partinen M, Hollman K *et al*. Familial aggregates in obstructive sleep apnea syndrome. Chest 1995; 107: 1545–51.
[53] Mathur R, Douglas NJ. Family studies in patients with the sleep apnea-hypopnea syndrome. Ann Intern Med 1995; 122: 174–8.
[54] Pillar G, Lavie P. Assessment of the role of inheritance in sleep apnea syndrome. Am J Respir Crit Care Med 1995; 151: 688–91.
[55] Redline S, Tishler PV, Tosteson TD *et al*. The familial aggregation of obstructive sleep apnea. Am J Respir Crit Care Med 1995; 151: 682–7.
[56] Peter JH, Koehler U, Grote L, Podszus T. Manifestations and consequences of obstructive sleep apnoea. Eur Respir J 1995; 8: 1572–83.
[57] Fletcher EC. The relationship between systemic hypertension and obstructive sleep apnea: facts and theory. Am J Med 1995; 98: 118–28.
[58] Garpestad E, Ringler J, Parker A *et al*. Sleep stage influences the hemodynamic response to obstructive apneas. Am J Respir Crit Care Med 1995; 152: 199–203.
[59] Hla KM, Young TB, Bidwell T *et al*. Sleep apnea and hypertension. A population-based study. Ann Intern Med 1994; 120: 382–8.
[60] Hoffstein V. Blood pressure, snoring, obesity, and nocturnal hypoxaemia. Lancet 1994; 344: 643–5.
[61] Javaheri S, Parker TJ, Wexler L *et al*. Occult sleep-disordered breathing in stable congestive heart failure. Ann Intern Med 1995; 122: 487–92.
[62] Noda A, Okada T, Yasuma F *et al*. Cardiac hypertrophy in obstructive sleep apnea syndrome. Chest 1995; 107: 1538–44.
[63] Thornton WK, Roberts DH. Nonsurgical management of the obstructive sleep apnea patient. J Oral Maxillofac Surg 1996; 54: 1103–8.
[64] Javaheri S, Parker TJ, Wexler L *et al*. Effect of theophylline on sleep-disordered breathing in heart failure. N Engl J Med 1996; 335: 562–7.

[65] Tiner BD. Surgical management of obstructive sleep apnea. J Oral Maxillofac Surg 1996; 54: 1109–14.
[66] Becker H, Brandenburg U, Peter JH, von Wichert P. Reversal of sinus arrest and atrioventricular conduction block in patients with sleep apnea during nasal continuous positive airway pressure. Am J Respir Crit Care Med 1995; 151: 215–18.
[67] Krieger J, Grucker D, Sforza E *et al*. Left ventricular ejection fraction in obstructive sleep apnea; effects of long-term treatment with nasal continuous positive airway pressure. Chest 1991; 100: 917–21.
[68] Lenique F, Habis M, Lofaso F *et al*. Ventilatory and hemodynamic effects of continuous positive airway pressure in left heart failure. Am J Respir Crit Care Med 1997; 155: 500–5.
[69] Naughton MT, Liu PP, Benard DC *et al*. Treatment of congestive heart failure and Cheyne-Stokes respiration during sleep by continuous positive airway pressure. Am J Respir Crit Care Med 1995; 151: 92–7.
[70] Yamashiro Y, Krijger MH. CPAP titration for sleep apnea using a split-night protocol. Chest 1995; 107: 62–6.
[71] Hoffstein V, Viner S, Mateika S, Conway J. Treatment of obstructive sleep apnea with nasal continuous positive airway pressure. Patient compliance, perception of benefits, and side effects. Am Rev Respir Dis 1992; 145: 841–5.
[72] Pepin JL, Leger P, Veale D *et al*. Side effects of nasal continuous positive airway pressure in sleep apnea syndrome. Study of 193 patients in two French sleep centers. Chest 1995; 107: 375–81.
[73] Meurice JC, Dore P, Paquereau J *et al*. Predictive factors of long-term compliance with nasal continuous positive airway pressure treatment in sleep apnea syndrome. Chest 1994; 105: 429–33.
[74] Reeves-Hoche MK, Hudgel DW, Meck R *et al*. Continuous versus bilevel positive airway pressure for obstructive sleep apnea. Am J Respir Crit Care Med 1995; 151: 443–9.
[75] O'Sullivan RA, Hillman DR, Mateljan R *et al*. Mandibular advancement splint: An appliance to treat snoring and obstructive sleep apnea. Am J Respir Crit Care Med 1995; 151: 194–8.
[76] Phillipson EA. Sleep apnea — a major public health problem. N Engl J Med 1993; 328: 1271–3.
[77] Wright J, Johns R, Watt I *et al*. Health effects of obstructive sleep apnoea and the effectiveness of continuous positive airway pressure: a systematic review of the research evidence. Br Med J 1997; 314: 851–60.