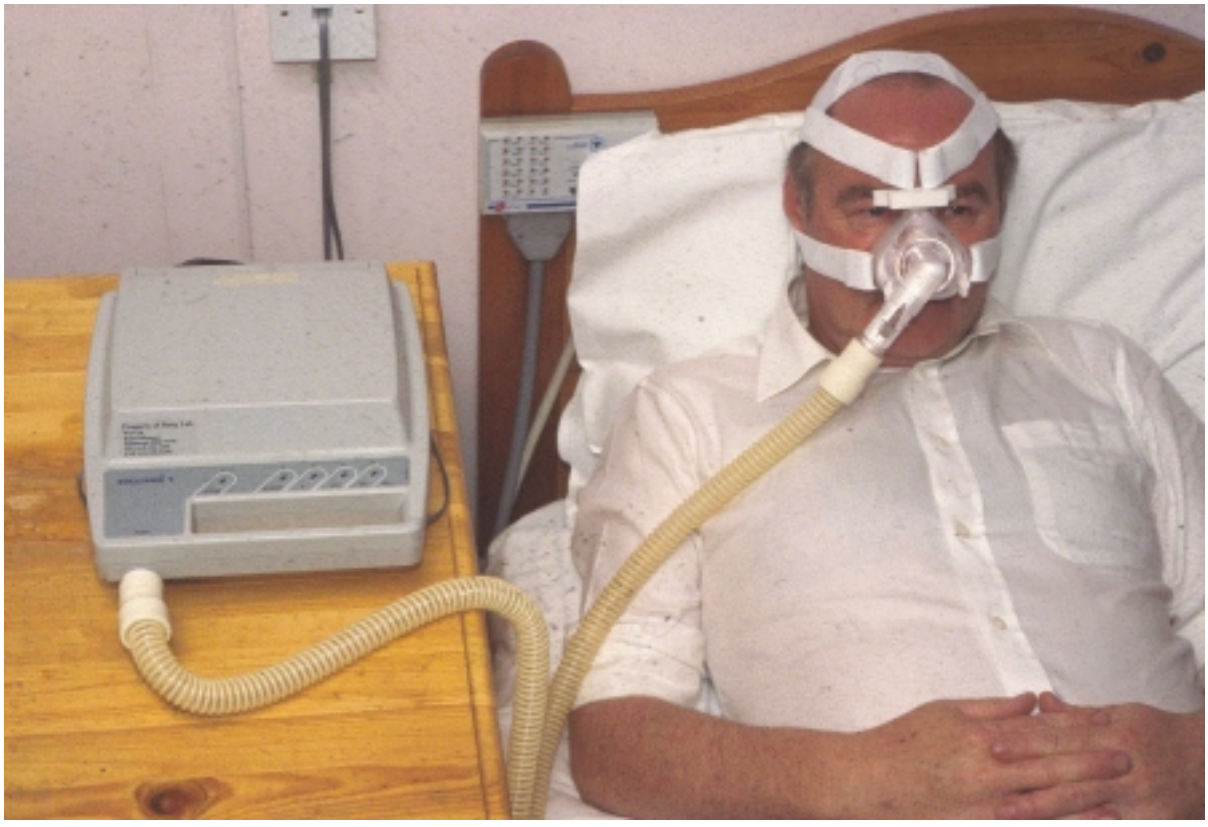
The obstructive sleep apnoea



A patient with the obstructive sleep apnoea/hypopnoea syndrome wearing a Continuous Positive Airways Pressure (CPAP) machine.

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e a/hypopnoea syndrome

INTRODUCTION

In the last decade there has been a rapid increase in the number of patients diagnosed with the obstructive sleep apnoea/hypopnoea syndrome (OSAHS). Indeed, in many respiratory clinics OSAHS is now the most common diagnosis. Neurologists need to be familiar with the OSAHS because it may present rather like some primarily neurological conditions, and because patients with neurological and neuromuscular disorders can develop the OSAHS. Indeed, in the February 2002 issue of *Practical Neurology*, Sam Berkovic and Philip King urged neurologists to wake up to sleep medicine (Berkovic & King 2002).

The best definition of the OSAHS is at least five, some would say 15, breathing pauses (apnoeas) or hypopnoeas (near apnoeas), each lasting 10 s or more, per hour of sleep in association with sleepiness or at least two other major symptoms, including difficulty concentrating, unrefreshing nocturnal sleep or nocturia (Table 1). Numerous studies have shown that the prevalence of OSAHS in adults is between 0.3 and 4%.

Patients report:
Sleepiness
Difficulty concentrating
Daytime fatigue
Unrefreshing sleep
Nocturnal choking
Nocturia
Depression
Decreased libido
Partner's report:
Snoring
Apnoeas
Restless sleep
Irritability

Table 1 Symptoms of the obstructive sleep apnoea/hypopnoea syndrome

The obstructive breathing events occur in people with narrow throats, usually due to retrognathia or obesity (Fig. 1). Their throats narrow even further during sleep when the upper airway dilating muscles become hypotonic. Each breathing pause terminates with an arousal from sleep and it is this sleep disruption which produces many of the features of the syn-

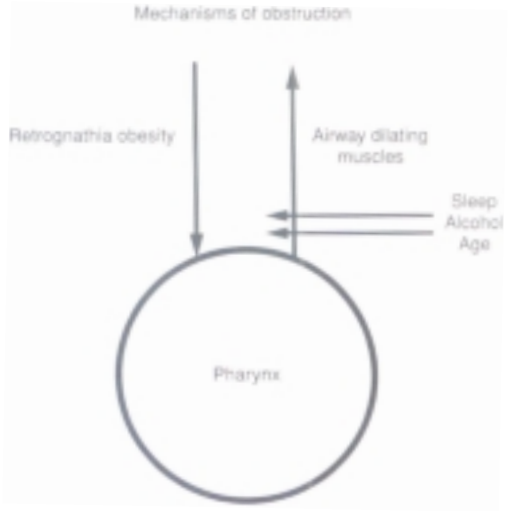

Figure 1 Factors predisposing to upper airway occlusion in the obstructive sleep apnoea/hypopnoea syndrome.

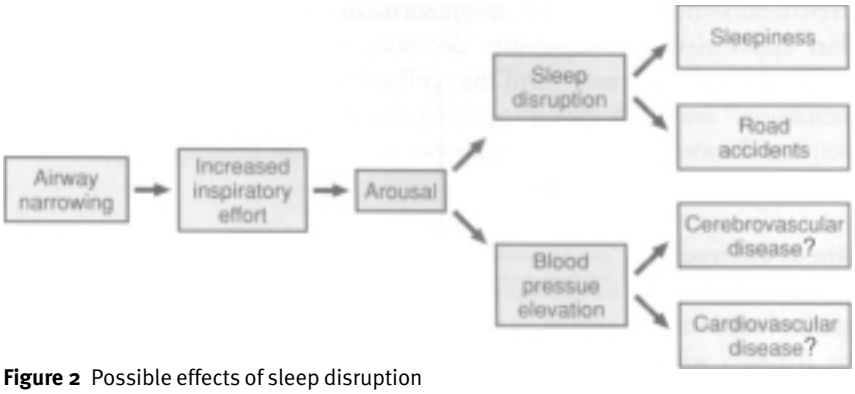

Figure 2 Possible effects of sleep disruption on patients with the obstructive sleep apnoea/hypopnoea syndrome.

Table 2 The Epworth Sleepiness Scale.

How often are you likely to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently try to work out how they would have affected you. Use the following scale to chose the *most appropriate number* for each situation:

0 = would *never* doze
1 = *slight* chance of dozing
2 = *moderate* chance of dozing
3 = *high* chance of dozing

Situation	Chance of dozing
Sitting and reading	.....
Watching TV	.....
Sitting, inactive in a public place (e.g. a theatre or a meeting)	.....
As a passenger in a car for an hour without a break	.....
Lying down to rest in the afternoon when circumstances permit	.....
Sitting and talking to someone	.....
Sitting quietly after lunch without alcohol	.....
In a car, while stopped for a few minutes in traffic	.....
TOTAL out of 24	_____

drome, with some additional effects from the associated hypoxaemia (Fig. 2).

CLINICAL FEATURES

Sleepiness

Over 90% of patients report sleepiness. This is not invariable, perhaps because some patients have lost their frame of reference for 'normal' sleepiness. Alternatively some may present because they have become aware that their ability to concentrate is impaired before they are excessively sleepy. Also, those working on their feet may have no opportunity to be sleepy at work, but they usually report sleepiness after work.

There is no gold standard definition of pathological subjective sleepiness. However, in practice it is important to note whether the patient falls asleep frequently against their will, particularly in dangerous situations such as driving. Various scales have been developed to quantify sleepiness but they are often poorly related to either the severity of objective sleepiness, or to the frequency of apnoeas and hypopnoeas. The most widely used, the Epworth Sleepiness Scale (ESS) named after the Melbourne district of its origin, asks the patient to rate his or her likelihood of falling asleep in eight different situations (Table 2). The original report suggested that an ESS score of more than 10 out of 24 was abnormal. A larger study using a British population of normal middle-aged people suggested that the 95th centile for the ESS was 11. Thus I regard an ESS of 12 or more out of 24 as abnormally sleepy.

The lack of a good correlation between the ESS score and apnoea/hypopnoea frequency is equally true whether the patient's or their partner's estimation of the ESS is used. Partly this may be because the patient's perception of sleepiness is sharper after the OSAHS has been treated; those on treatment consistently score themselves as having been more sleepy prior to treatment than they originally reported at presentation.

In practice, the Epworth score can be a clinically useful pointer to whether the patients perceive themselves to have a problem with sleepiness. A high score should alert the clinician to the need to find a cause. An ESS of < 12, if corroborated by the partner, and also if direct questioning reveals no problems falling asleep driving or against their will, suggests that sleepiness is not a clinical problem. However, one must be aware that patients whose livelihoods depend on continuing to drive, fly or operate dangerous machinery may stand to gain from under reporting their sleepiness, and often their partner shares these concerns and colludes with them.

Thus my own threshold for further investigation is unexplained sleepiness, defining sleepiness as:

- an Epworth sleepiness score > 11 according to either the patient or their partner; or
- recurrent sleepiness when driving, or which interferes with work.

Impaired concentration

Some patients absolutely deny any problems with sleepiness but may be seriously inconvenienced by difficulty concentrating and impaired work performance. They are usually aware that they are more mentally tired than before but do not see themselves at risk of falling asleep. Of course, impaired concentration is a very difficult symptom to assess. Depression, anxiety and dementia often enter the differential diagnosis. Nevertheless, poor concentration is often a dominant feature in sleep apnoea and whenever it is associated with other pointers to the syndrome the patient should be investigated for the OSAHS. The situation is further confused because depression is a common *consequence* of the OSAHS.

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Unrefreshing sleep

Most OSAHS patients say their sleep is unrefreshing. After a normal duration of nocturnal sleep they still wake up feeling sleepy. The majority believe they sleep fairly soundly and are unaware of the recurrent arousals from sleep which are too brief to be recalled.

Nocturnal choking

Around a third of patients can recall intermit-

tent waking up and choking, and some vividly describe episodes where they waken but are unable to breath for many seconds. Some patients have even run from the house into their garden in understandable panic before being able to breathe. Such episodes seem to be more common in patients with only a few apnoeas and hypopnoeas per night, giving the impression that the cortical arousal response is blunted in severe OSAHS. Nocturnal choking attacks need to be differentiated from left heart failure and nocturnal asthma, usually easy on the basis of the attacks lasting seconds with total resolution instantly thereafter, their occurrence around sleep onset as a rule, and their association with loud snoring.

Depression

Many OSAHS patients report feeling depressed and this improves with effective therapy. As depression itself may cause sleepiness, it can be difficult to distinguish the cart from horse on history alone.

Other symptoms

Nocturia and decreased libido often occur. Morning headache was initially thought to be a feature of OSAHS, but whether this is a true association is debatable. There is no doubt that patients with respiratory failure who hypoventilate during sleep may have morning headaches due to CO_2 retention but the evidence for this in uncomplicated OSAHS is not compelling.

Partner's report

The obstructive sleep apnoea/hypopnoea syndrome impacts on both the sufferer and their families, particularly on their partner. Thus, if possible, a history should always be obtained from the patient's partner. Many partners complain that the patient thrashes around in bed at night and almost all report loud snoring. The few patients without a history of snoring may have never had a partner or witness, or their partner may be deaf or a very deep sleeper. Snoring usually occurs every night and in severe OSAHS it happens in all body postures,

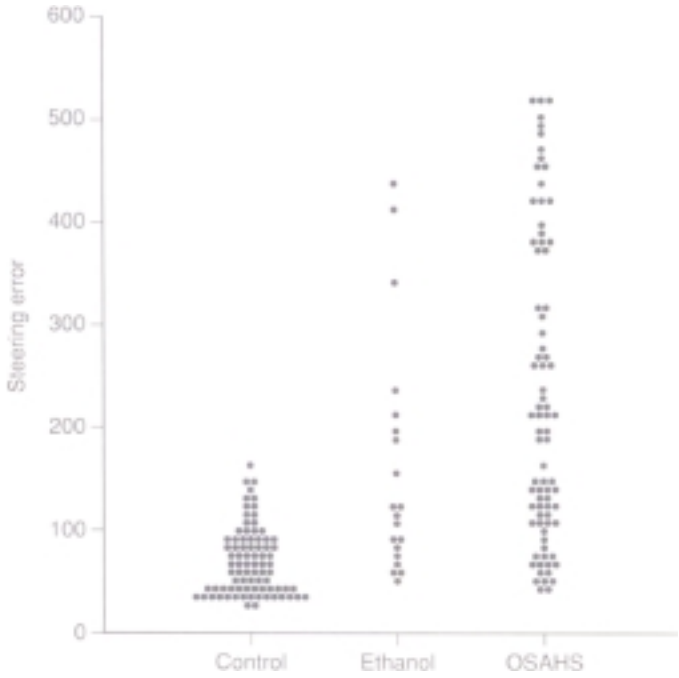

Figure 3 Steering error (cms) on a driving simulator in obstructive sleep apnoea/hypopnoea syndrome (OSAHS) patients and controls matched for age, gender and driving experience. The controls were restudied following alcohol ingestion (mean blood alcohol 95 mg%). The sober OSAHS patients drove worse than the drunk (or sober) controls. Adapted from George et al. (1996).

not just lying on the back. Loud but intermittent snoring is one of the best pointers to the OSAHS. Most partners have noticed breathing pauses and for many these are the prime concern. Finally, most partners of OSAHS patients report the patient is much more irritable than before.

POSSIBLE CONSEQUENCES OF THE OBSTRUCTIVE SLEEP APNOEA/ HYPONOEA SYNDROME

Accidents

Many patients admit to falling asleep at the wheel and over a third admit to having had an accident or near accident because of falling asleep when driving. Not surprisingly, underreporting of sleep-related driving problems by OSAHS patients is common. As well as self-reported driving difficulties, there is clear objective evidence of a 1.3–12 fold increase in accident rates among those with sleep apnoea. There is also convincing evidence from vigilance tasks and driving simulators that performance is impaired in patients with the OSAHS. Indeed drunk normal subjects perform better than sober OSAHS patients (George *et al*. 1996; Fig. 3). Interestingly the impairment is not just limited to periods when patients actually fall asleep; their response is also impaired when they are awake, due to impaired vigilance and delayed reaction times. Little attention has been paid to accidents at work, but there is evidence that OSAHS patients have a 50% increased risk of work place accidents.

Neuropsychological impairment

There have been relatively few good studies examining neuropsychological function in OSAHS patients in comparison with an adequate number of well-matched controls, but these have suggested that cognitive function is impaired. More convincingly, marked improvements following continuous positive airway pressure (CPAP) treatment indicate that cognition was impaired by untreated OSAHS. The deficits are broad ranging affecting attention, concentration, vigilance, manual dexterity, visuomotor skills, memory, verbal fluency and executive function.

Hypertension

Early epidemiological investigations suggested increased blood pressure among snorers and patients with the OSAHS but there were potential confounders such as obesity, age, alcohol and smoking. Nonetheless, recent epidemiological studies in normal populations, in which strenuous attempts have been made to exclude the effect of confounders, strongly suggest an association between apnoeas during sleep and daytime hypertension. Further and direct evidence that the OSAHS causes hypertension comes from studies showing that CPAP therapy reduces 24 h blood pressure (BP) but the overall decrease was small, averaging only 1.5 mmHg over 24 h (Faccenda *et al*. 2001). The decrease was greater in those with significant nocturnal hypoxaemia with more than twenty 4% desaturations per hour of sleep, in whom the mean 24 h diastolic blood pressure fall was 5 mmHg. The BP drop was also greater in those who used CPAP most.

Taken together, these studies convincingly indicate that OSAHS causes raised blood pressure, which is most marked during sleep. Averaged over the 24 h day, this increase may be relatively small but it must be seen in the context that randomised trials have shown that a 5 mmHg fall in 24 h diastolic pressure decreases cardiac risk by 20% and stroke risk by 40% over a 5–10-year period.

Surprisingly, despite the link between hypertension and OSAHS, there is no convincing direct evidence of an association between the OSAHS and cardiac disease or stroke. Irregular breathing during sleep is very common *after* stroke with increased obstructive apnoeas and hypopnoeas in most patients, especially in the first few weeks (Bassetti & Aldrich 1999). This may contribute to sleep disruption, daytime sleepiness and inattention, which might impair recovery from stroke and even predispose to further stroke by increasing arterial blood pressure. As yet it is uncertain whether screening all patients with stroke for OSAHS is either sensible or cost effective. At present my impression is that unless patients are aware that they are being hampered by sleepiness, further investigation or treatment is unlikely to be helpful.

Neuromuscular disease

Breathing problems during sleep are very common in patients with neuromuscular problems. Firstly, upper airway dilating muscle failure can occur in myotonic dystrophy and in other neuromuscular conditions. This predisposes to the development of the obstructive sleep apnoea/hypopnoea syndrome with all the classical symptoms, and CPAP therapy can be useful. Secondly, inspiratory pump failure during

sleep results from the marked dependence on the diaphragm during REM sleep when intercostal activity is depressed due to generalized hypotonia of postural muscles. Thus patients with bilateral diaphragmatic paralysis become severely hypoxaemic during REM sleep. This is not the obstructive sleep apnoea/hypopnoea syndrome, but rather REM sleep-related hypoventilation. Nevertheless, this contributes to the development of cardio-respiratory failure, especially in those with co-existing lung disease. Such diaphragmatic weakness is found in a wide range of neuro-muscular diseases including muscular dystrophies, myotonic dystrophy, motor neurone disease, myasthenia gravis, post polio syndrome and Charcot-Marie-Tooth disease. Patients with Duchenne muscular dystrophy often develop marked kyphoscoliosis, which may result in inefficient diaphragmatic angle of action and consequences similar to diaphragm palsy. Treatment of REM sleep-related hypoxaemia due to diaphragm malfunction is by nocturnal Intermittent Positive Pressure Ventilation (nIPPV) using a nasal or face mask. The usual indications for nIPPV are morning headache with documented associated carbon dioxide retention, ventilatory failure or marked daytime sleepiness.

Epilepsy

Some patients with both OSAHS and epilepsy have been reported to gain significantly better control of their epilepsy once their OSAHS is treated.

MAKING THE DIAGNOSIS

Be suspicious!

One of the biggest problems in making the diagnosis of the OSAHS is that many doctors do not consider the possibility unless patients actually complain of sleepiness plus snoring. It is important to remember that patients with OSAHS may complain about non-specific symptoms such as difficulties with concentration, work problems and depression rather than sleepiness. Thus a high index of suspicion is needed to make the diagnosis in such patients. Sleep histories should always be part of routine history taking, whatever the presenting symptoms (Table 3).

The main diagnoses to be considered are listed in Table 4. Usually the most difficult differential is between the OSAHS, narcolepsy and idiopathic hypersomnolence (IHS) (Table 5).

Physical examination is not as vital as the history in making the diagnosis of the OSAHS, but it is critical for the exclusion of other causes for the patient's symptoms as well as for the detection of any causes and consequences of OSAHS and thus to the planning of treatment. The key features to note include retrognathia, obesity, possible acromegaly or hypothyroidism, and blood pressure.

INVESTIGATIONS

The basic requirement is the demonstration of breathing irregularity during sleep in a symptomatic patient. In the UK this is usually done without neurophysiological recording, although I very often use polysomnography in patients with equivocal 'limited monitoring' studies. There is no doubt that a positive limited study is sufficient to make the diagnosis, but a negative one in a symptomatic patient cannot exclude the OSAHS. Much fuller discussion of this issue can be found elsewhere (Douglas 2002).

TREATMENT

(See Table 6.) General measures such as weight loss where applicable and alcohol avoidance rarely suffice. Continuous positive airway pressure (CPAP) treatment is the therapy with the firmest evidence base. CPAP works by blowing the airway open at night, using a gentle air

Table 3 Key sleep questions

Do you fall asleep against your will?
Do you fall asleep at the wheel?
Do you snore?
How long do you sleep each night?
Is nocturnal sleep refreshing?
Do you work shifts?

Table 4 Other causes of sleepiness to be considered in possible obstructive sleep apnoea/hyponoea syndrome

Inadequate sleep
Shift work
Depression
Drugs (sedatives, hypnotics, etc.)
Narcolepsy
Idiopathic hypersomnolence
Restless leg syndrome/periodic limb movement disorder
Sleep phase disorders

Table 5 Clinical pointers in the sleepy patient

	OBSTUCTIVE SLEEP APNOEA/HYPOPNOEA SYNDROME	NARCOLEPSY	IDIOPATHIC HYPERSOMNOLENCE
Age of onset (year)	35–60	10–30	10–30
Prevalence	2%	0.04%	0.004%
Night sleep			
Duration	Normal	Normal	Long
Awakenings	Occasional	Frequent	Rare
Snoring	Yes	Occasional	Occasional
Morning drunkeness	Occasional	Occasional	Common
Daytime naps			
Frequency	Usually few	Many	Few
Time of day	Afternoon/evening	Afternoon/evening	Morning
Duration	‹ 1 h	‹ 1 h	› 1 h

Table 6 Treatment of the obstructive sleep apnoea/hypopnoea syndrome

Weight loss if appropriate
Alcohol avoidance
CPAP
If CPAP fails consider mandibular repositioning splint

stream applied via a nasal or face mask. Many randomised controlled trials have shown that CPAP improves symptoms, subjective and objective sleepiness, and quality of life. Unequivocal objective improvements are found in symptomatic patients with more than 15 apnoeas plus hypopnoeas per hour slept, or more than 10 4% oxygen desaturations per hour. Prospective studies have also found that CPAP improves patient performance on driving simulators and decreases the frequency and severity of road accidents.

Mandibular repositioning splints are the best second line treatment for patients who are intolerant of CPAP. There is generally no role for surgery or drugs. Some patients with retrognathia benefit from surgery to advance the mandible and maxilla, but the long-term success of these procedures is under review.

Patients should be advised not to drive if sleepy and to notify the driving authorities if they have episodes of sleepiness when driving.

CONCLUSIONS

The obstructive sleep apnoea/hypopnoa syndrome is common, easily diagnosed and easily treated. Appropriate treatment prevents accidents and may reduce vascular risk. All neurologists need to keep the OSAHS in mind when seeing patients especially those with sleepiness, difficulty concentrating or morning headache.

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