

Sleep and sleeping disorders

In the first article of three on sleep and sleeping disorders, **Susan Allen** looks at the function of sleep and the effects of sleep deprivation. Sleeping disorders discussed here include sleep apnoea, narcolepsy and restless legs syndrome



J. C. Reay/SPL

Sleep disorders can be investigated at a sleep centre

Although we have come a long way since Edgar Allen Poe described sleep as “little slices of death”, there are still many gaps in our understanding of it and its functions. Sleep is a vital component of a healthy life. The average adult — sleeping eight hours a night — spends 121 days of each year in slumber. The quantity and quality of this sleep can be a frequent preoccupation but usually each of us arrives at our own optimum number of hours sleep per night that we need to function effectively.

What is sleep?

We are at the tip of the iceberg for understanding the true nature of sleep. Until relatively recently, sleep was viewed as a passive, dormant side effect of living. However, we now know that our brains continue to be active and co-ordinated during sleep. Indeed, some areas of the brain are more active than when awake.

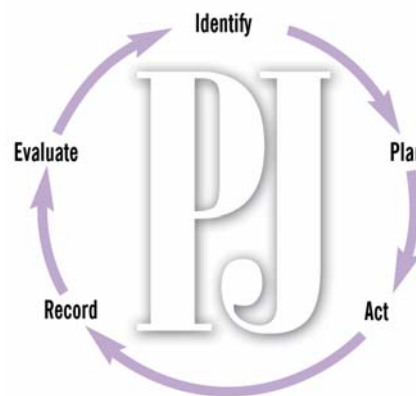
Panel 1: Circadian rhythm

Circadian rhythm can be defined as the regular variation in physiological parameters (eg, blood hormone levels) that occur daily (over 24 hours), ie, a repeating biological cycle. This is governed by a “biological clock” that, in humans, is located in the anterior hypothalamus. However, research indicates that circadian rhythm can persist in other tissues grown *in vitro*.

Biological clocks appear to have a genetic basis — genes responsible for rhythm have been identified in fruit flies, mice and humans.

It has been claimed that disturbances in normal circadian rhythm can result in poor health. For example, it can precipitate mania in people with bipolar disorder. And some conditions are more common at particular times of day (eg, heart attacks commonly occur in the morning).

Healthy, uninterrupted sleep is based on circadian rhythm and can be divided into five stages



Identify knowledge gaps

1. How would you advise someone suffering from sleep deprivation due to shift work or jet lag?
2. What are the symptoms of restless legs syndrome?
3. How is sleep apnoea managed?

Before reading on, think about how this article may help you to do your job better. The Royal Pharmaceutical Society’s areas of competence for pharmacists are listed in “Plan and record”, (available at: www.rpsgb.org/education). This article relates to “appropriate management of common symptoms” (see appendix 4 of “Plan and record”).

There are many hypotheses for why we sleep. These include to allow for body restoration and recovery, development and growth (50 per cent of the total amount of growth hormone secreted in 24 hours is released in the early part of sleep) and energy conservation. However, these nocturnal physiological happenings may be a function of circadian rhythm (see Panel 1) rather than sleep itself. And it is now thought more likely that the release of growth hormone is to protect against the fasting state of sleep by conserving protein and mobilising lipids. We also now know that sleep tends to follow a defined pattern, as shown in Figure 1 (p188).

Stages of the sleep cycle Healthy, uninterrupted sleep is based on circadian rhythm and can be divided into five stages. There are two main types of sleep: non-rapid eye movement (non-REM) sleep, which can be split into four stages (1–4), and rapid eye movement (REM) sleep (sometimes called stage 5). Adults normally cycle through the four stages of non-REM sleep, followed by a brief interval of REM sleep, five or six times a night. As the person reaches stage 4, it becomes increasingly difficult to wake him or her. As the night progresses, less time is spent in stages 3 and 4,

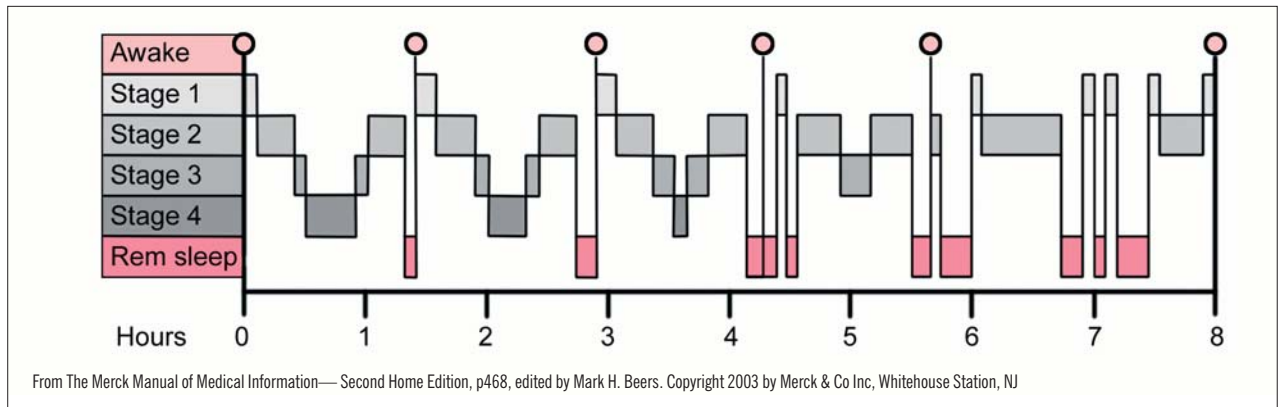


Figure 1: Stages of the sleep cycle

the deep stages of sleep, and more time is spent in REM sleep.

REM sleep is interrupted by brief returns to stage 1, the lightest sleep. The sleeper is easily roused from REM sleep. REM sleep is regulated by the hypothalamus and the circadian clock and is considered “active sleep”. During REM sleep the eyes may move under closed lids and body processes, such as breathing, heart rate and blood pressure, speed up, while muscle tone reduces drastically, almost to a state of paralysis. Elaborate dreams can occur. However, REM sleep appears to be dispensable since people can be deprived of it for months with no apparent ill effect as when taking tricyclic antidepressants. Infants spend most of their sleep time in REM sleep and this has led to the proposal that REM sleep is involved in brain development. Adults, by contrast, spend around 50 per cent of their total sleep time in stage 2 and only around 20 per cent in REM sleep.

How much sleep do we need?

From birth to old age our sleep patterns and sleep requirements vary. A newborn infant's sleep requirements are high, at around 17 hours per day, and sleeping hours occur around the clock. When infants reach 16 weeks old, sleep falls into a clear diurnal pattern and they tend to sleep for between 14 and 15 hours out of 24. Sleep requirements gradually decrease further as infants grow, to 11 hours by the age of three to five years and to 10 hours or less by the age of 10 years. As adulthood approaches, night-time sleep requirements continue to fall, though adoles-

cents have an increased tendency to fall asleep during the daytime. The seven to eight hours' sleep that most adults achieve is simply the mid-point of a normal, bell-shaped distribution — many people need less sleep whereas others need more.

There is some disagreement about whether or not older people need less sleep. It appears that nocturnal sleep diminishes to six or seven hours a night with age but an increase in daytime napping can mean that the total sleep of young and old adults, within 24 hours, is similar. However, the time spent in deep sleep diminishes with increasing age and often becomes non-existent by the age of 75 years. Consistent with this finding, older people tend to be easily woken by noise and environmental factors and to have a more fragmented night's sleep.

A six-year Californian study of the sleeping habits of more than a million people with similar characteristics concluded that those who slept for six to seven hours a night tended to live longest. The death rate was higher in those who regularly slept for four hours or less and in those who regularly slept eight hours or more. Those regularly sleeping for eight hours a night were 12 per cent more likely to die within the six-year study period than those sleeping for seven hours a night. Even those with as little as five hours a night tended to outlive the eight-hour sleepers.¹

Sleep deprivation Laboratory animals that are totally deprived of sleep die after about 14 days. No such official research exists for humans, although victims of torture have been subjected to long periods without sleep. The effects of depriving individuals of one to three nights' sleep has been studied frequently. Up to three nights' sleep deprivation has a negative effect on mood, motivation, attention, alertness, short-term memory and ability to complete routine tasks, but does not appear to induce physical or psychological illness. The temporary changes to the immune system that result when individuals are deprived of sleep are poorly understood. However, recovery from lack of sleep is quick — only around a third of the lost sleep needs to be regained for return to full alertness and normal behaviour.

The prefrontal cortex appears to be most affected by sleep deprivation. Being responsi-

Panel 2: Tips for shift workers

- Try to develop a regular eating schedule
- Have your main meal in the middle of your awake period and a couple of hours before starting night duty (to allow digestion to fit in with the gastric circadian rhythm which is at its lowest function at night)
- Eat lightly but nutritionally during the night
- Avoid caffeine
- Control sugar intake to avoid sugary peaks during the night

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ble for directing and sustaining attention and concentration and for some aspects of memory and flexible thinking, it is not surprising that driving when tired is a major cause of road traffic accidents. Indeed, some of the world's major disasters have occurred as a result of misjudgements by night-workers in the early morning (eg, the disasters at Chernobyl and Three Mile Island nuclear power plants).

Shift work Night-shift workers have a unique set of sleep problems. Night shifts clearly disrupt the circadian sleep rhythm and a worker's total 24 hour sleep-time tends to be between one and a half and two hours less than normal nocturnal sleep. In the long term, this results in an accumulating sleep debt that catches up with the worker after a number of days. It can take more than a week to adjust to a new waking-sleeping pattern.

Long-term shiftworkers are more susceptible to gastric disturbances, for example, irregular bowel movements, constipation, dyspepsia and heartburn. Epidemiological studies show an increased prevalence of gastrointestinal disorders, such as chronic gastritis, gastroduodenitis, peptic ulcer and colitis. One explanation for the increased digestive problems experienced by shiftworkers is the desynchronisation of meal times and gastrointestinal phases.

Further health problems more commonly seen in night shift workers are anxiety, depression and cardiovascular disease (40 per cent increase). Careful shift planning (eg, fixed shifts including only two to four short consecutive night shifts) is thought to cause less disruption to circadian rhythms.

As workers reach their 40s, the negative health effects of prolonged night work becomes more pronounced. Tips for night shift workers are given in Panel 2 (p188).

Sleep-related problems

Sleep-related problems include insomnia, jet lag, sleep apnoea, narcolepsy and restless legs syndrome. Insomnia and its management is discussed in the next CPD article (*PJ*, 26 February).

Jet lag Jet lag and its symptoms (disturbed sleep, loss of concentration, irritability, fatigue and difficulty in initiating and maintaining sleep at night) can be a consequence of long-haul air travel. The pineal gland in the brain secretes melatonin and its action controls circadian rhythm. Secretion is influenced by the external pattern of light and darkness. Melatonin is normally released at night.

It takes several days for external factors to shift the body clock to a new time zone. Melatonin, taken orally at bedtime, can be effective in reducing or even preventing jet lag, but it is only available on prescription on a named-patient basis in the UK. In the US, melatonin is available over the counter, where it is sold as a food supplement and antioxidant, and elderly insomniacs use melatonin freely.



Mark Clarke/SPL

Adolescents have an increased tendency to fall asleep during the day

Sleep-related problems include insomnia, sleep apnoea, narcolepsy and restless legs syndrome

The non-drug management of jet lag involves using light to help adjust circadian rhythm to the destination's time zone. It is worth trying to alter your sleeping pattern in the direction of that of your destination a little before departure. After a westward flight, try to stay awake while it is daylight and sleep when it gets dark. After an eastward flight, stay awake but avoid bright light in the morning and stay outdoors as much as possible in the afternoon. This helps to turn on the body's melatonin secretion at the right time.

Sleep apnoea People with sleep apnoea suffer repetitive periods during sleep when they stop breathing for at least 10 seconds. There are three types of sleep apnoea: obstructive, central and mixed. Obstructive sleep apnoea is the most common, affecting between 1 and 4 per cent of people.

When we breathe in, the pressure in our throat and chest drops below the outside atmospheric pressure, drawing air into our lungs. The higher pressure in the atmosphere tries to squeeze our throat closed as we breathe in, but the throat muscles resist this. When we fall asleep these muscles relax and the throat narrows. If the throat narrows a lot, the throat structures vibrate as air squeezes through, producing snoring. In obstructive sleep apnoea the throat is sucked closed during sleep, and breathing temporarily stops, depriving the brain of oxygen. This partially awakens the sleeper who fights for breath and takes a loud gasp of air before falling back into sleep. This happens many times a night and the sufferer, though often unable to remember, has a poor night's sleep and experiences daytime fatigue and sleepiness.

Sleep apnoea requires medical attention. Patients usually seek advice because of snoring complaints or their partner's concern over their prolonged apnoeas. Patients should be referred to their GP and then on for diagnosis by polysomnography, a study that measures a range of functions during sleep (eg, electrical activity in the brain, leg muscle activity, chin muscle tone, eye muscle movement, heart function, breathing patterns, and blood oxygen saturation). Investigations are usually carried out in a sleep laboratory or sleep clinic. Most sleep centres require referral from a GP, but some accept self-referrals if the patient is self-funding.

Treatment Treatment usually involves blowing a gentle stream of air through the nose at night by means of a continuous positive airway pressure (CPAP) machine. This keeps the pressure in the throat higher than atmospheric pressure, so keeping it open. CPAP machines are available on the NHS through sleep clinics. They can also be purchased by patients but this should be on the advice of their doctor or consultant.

An alternative treatment is a mandibular advancement splint, a light plastic device that fits onto the teeth like a gum shield and pushes the jaw slightly forward, so increasing the space at the back of the tongue.

If untreated, obstructive sleep apnoea is associated with a poorer long-term outcome and an increased risk of cardiovascular, pulmonary and other diseases.

Sleep apnoea has been associated with obesity, smoking and drinking alcohol, so these areas might be worthwhile self-help targets.

Restless legs syndrome Restless legs syndrome (or Ekbom syndrome) is a common neurological disorder affecting between 5 and 15 per cent of the UK population. Restless legs syndrome is characterised by:

- “Uncomfortable sensations” in the legs (these have been described as “fidgety”, “jittery”, “throbbing” and “crawling” but some patients have difficulty describing the sensations)
- An urge to move the legs to relieve aching
- The onset or worsening of symptoms when at rest
- Symptoms that are worse or only occur in the evening or at night

Many patients with restless legs syndrome also have periodic limb movements during sleep and relaxed wakefulness. Restless legs syndrome is more common in middle-aged or pregnant women and in people with kidney disease, rheumatoid arthritis, neuropathy, chronic venous insufficiency or iron deficiency anaemia. There is often a family history of the disorder. Restless legs syndrome can itself be a cause of insomnia.

Treatment There is no cure for restless legs syndrome and currently no licensed medicines to treat it in the UK. General healthy lifestyle measures can help, including stopping smoking. Some benefit has been shown with nutritional supplements of vitamin E, B₁₂ and folic acid and, when there is anaemia, iron. Some people find massaging and stretching their legs or taking a hot bath in the evening helpful.

Where drug treatment is indicated, dopaminergic agents (eg, levodopa) and dopamine agonists, such as pergolide, pramipexole, cabergoline or ropinirole, are regarded as the treatment of choice. A common problem with long-term use of dopaminergics is augmentation of symptoms, which occur progressively earlier in the day. Increases in dose give short-term relief but, ultimately, symptoms appear even earlier along with a decrease in the duration of action and effectiveness of the drug.

Augmentation is reported less often with dopamine agonists and these are increasingly used. Pilot studies suggest that cabergoline is effective and without the side effects of the dopaminergics. Anti-convulsants, opioids and benzodiazepines are sometimes used as second line agents.

Leg cramps are a common sleep-related problem. Although a few patients with restless legs syndrome may describe their symptoms as “cramps”, there is no knotting of muscle or severe local muscle pain. Nocturnal leg cramps are treated with quinine (taken before going

Modafinil at a dose of 200–400mg daily, is used first line to increase wakefulness and daytime alertness with narcolepsy

Action: practice points

Reading is only one way to undertake CPD and the Society will expect to see various approaches in a pharmacist's CPD portfolio.

1. Integrate advice about preventing or managing jet lag into interactions with customers about holiday medicines.
2. Visit www.rls.org and read about the latest treatment options for restless legs syndrome.
3. Do you have a patient with narcolepsy? Ask them to give you an insight into what it is like to suffer from this condition.

Evaluate

For your work to be presented as CPD, you need to evaluate your reading and any other activities. Answer the following questions:

- What have you learnt?
How has it added value to your practice? (Have you applied this learning or had any feedback?)
What will you do now and how will this be achieved?

to bed), and should not be confused with restless legs syndrome.

Narcolepsy Narcolepsy is a serious disorder that affects 0.03 to 0.06 per cent of the population. It is characterised by sudden, uncontrollable attacks of sleep lasting from 30 seconds to 30 minutes or more. An attack can happen at any time (eg, while eating or talking) and is caused by a malfunction of the system that regulates sleeping and waking. Another symptom is excessive daytime sleepiness. Narcolepsy can also be associated with cataplexy (sudden loss of muscle function, usually triggered by strong emotions), sleep paralysis and hallucinations.

Narcolepsy usually begins at adolescence, but can occur at any age. The first symptom is excessive daytime sleepiness, with other symptoms developing months or years later. The condition is life-long and the sufferer frequently finds their social, personal and professional life disrupted. In narcolepsy, the order and length of NREM and REM sleep periods are disturbed, with REM sleep occurring at sleep onset instead of after NREM sleep.

People with narcolepsy often find it hard to hold down a job. In addition, they are required to declare their condition to the Driver and Vehicle Licensing Agency. The DVLA will issue a temporary licence (three years maximum) to the person only if his or her GP convinces the DVLA that the narcolepsy is under control.

Treatment There is clinical evidence that frequent, short, day-time naps reduces excessive daytime sleepiness. Also, keeping to strict bedtimes, taking regular exercise and keeping stress levels to a minimum is important.

In the UK, modafinil (Provigil), at a dose of 200–400mg daily, is used first line to increase wakefulness and daytime alertness and is effective in around 75 per cent of cases. For the remaining patients, the centrally acting stimulant dexamphetamine is often used to control symptoms. As for all prescribed Controlled Drugs, when travelling abroad, the patient is advised to carry a letter from his or her GP or consultant stating that the dexamphetamine has been properly prescribed.

Associated cataplexy is managed separately, often using tricyclic antidepressants and selective serotonin reuptake inhibitors.

References

1. Spurgeon D. People who sleep for seven hours a night live longest. *BMJ* 2002;324:446.

Resources

- The Narcolepsy Association UK. At: www.narcolepsy.org.uk
- The Restless Legs Syndrome Foundation. At: www.rls.org
- British Snoring & Sleep Apnoea Association. At: www.britishtsnoring.co.uk
- Jet lag and melatonin. Available at: www.GPnotebook.co.uk (accessed 18 October 2004).
- Dopamine agonists for restless legs syndrome. Available at: www.druginfozone.org (accessed 12 January 2005).
- The Sleep Research Centre, Loughborough University at: www.lboro.ac.uk/departments/hu/groups/sleep