For years, many physicians and patients had their eyes closed to the prevalence of sleep disorders. Although there are few things better than feeling well rested in the morning, some people have come to accept either being sleepy during the day or awake at night as a fact of life instead of talking to their physician about it. This was especially true for many patients who felt they had a more severe condition that warranted more attention from a physician, who may not have felt sleep disorders were worth discussing during a check-up.

Recently, though, there has been more emphasis placed on the therapeutic value of sleep. Not only can being well rested significantly improve quality of life, it can go a long way towards keeping medical, and especially neurological, conditions under control. Problems that either keep patients up at night or put them asleep during the day are now recognized as significant issues in treatment, whether they are a comorbid disorder, a symptom of a neurological condition, or an adverse effect of medication.

Practitioners and researchers from all specialties have come to realize how sleep medicine is intertwined with neuroscience, as evidenced by everything from the growing number of sleep labs to the expanding proportion of seminars offered sleep-related topics offered at conferences. Making sure patients sleep well is quickly becoming a vital component of the standard of care, and failure to diagnose sleep-related problems can aggravate an existing condition.

In this article, we'll look at the existing evidence about the relationships between neurological conditions and sleep disorders.
Whether a symptom of a disease, an adverse effect of medication, or a comorbid problem in its own right, sleep disorders severely impair a patient’s life. Here’s how to help.

A Function of the Brain
Michael H. Silber, MBChB, Professor of Neurology at the Mayo Clinic College of Medicine in Rochester, MN and president-elect of the American Academy of Sleep Medicine, says the field of sleep medicine is getting more recognition. While most sleep practitioners have backgrounds in internal medicine, psychiatry and pediatrics, Dr. Silber says there is a growing need for experts with a neurological background, particularly when one thinks of sleep as a function of the brain. “Twenty to 25 percent of sleep specialists are neurologists, and as a neurologist myself I’d like to see that number rise,” he says, adding that a neurological condition can often worsen an existing sleep disorder.

Antonio Culebras, MD, Professor of Neurology at the Upstate Medical University of the State University of New York and a consultant for The Sleep Center of Community General Hospital in Syracuse, is happy with the increased attention practitioners and scientists are paying to this field. “Sleep is a function of the brain and neurologists should be heavily involved in sleep medicine at the clinical and research levels,” he says. “Neurologists should at least be cognizant of sleep disorders.”

Dr. Culebras says that while some sleep problems are directly related to the patient’s neurological disorder as either symptoms or adverse effects of treatment, other co-morbid conditions can exist in these populations at the same frequency as they appear in the general population. A co-existing sleep problem can complicate treatment if it is not recognized. “Virtually every condition can be aggravated by a lack of sleep,” Dr. Culebras stresses.

He notes that neurologists will rarely see cases of primary insomnia, one of the most common causes of lost sleep. This condition is usually treated by a general practitioner and referred to a psychologist or psychiatrist for further treatment should the case prove intractable. Neurologists do, however, commonly see insomnia as a consequence of neurological disease or therapy, most notably dopamine agonist therapy for Parkinson's disease. Many other conditions, such as apnea and somnolence, could present in the patient in neurology practice. Managing these conditions without undermining an effective treatment strategy for the patient’s other neurological condition often entails a difficult balancing act.

Neurodegeneration Nightmares
Both Drs. Silber and Culebras say the conditions that cause the greatest amount of sleep problems are those that fall into the categories of neurodegenerative and neuromotor conditions. Like other functions of the brain, sleep begins to suffer and get progressively worse during the course of the disease.

Dr. Culebras says the conditions that lead to dementia, particularly Alzheimer's and Parkinson's, are usually the ones that prompt patients to present with sleep problems. The conditions themselves can indirectly lead to fragmentation of sleep, difficulties maintaining sleep, confusion, pathological sleepiness and disorientation. Some patients also develop sleep apnea while these diseases run their course.

Alzheimer's disease, in particular, is known to disrupt circadian rhythms. The sleep/wake cycle is affected, causing patients to be rarely awake or asleep for a full hour during a 24-hour period. The depression and other cognitive defects associated with the condition can also lead to sleep problems, and medication may not be a complete solution.

PD has been linked to several sleep disorders, including excessive daytime sleepiness, restless leg syndrome, sleep apnea, sleepwalking and talking, nightmares, terrors, and panic attacks. Dr. Culebras says this population has a high incidence of rapid eye movement disorders that cause them to physically act out their dreams, possibly harming themselves or their spouses in the process.

Since both the physical symptoms and the underlying psychological factors could be at work, and an ideal treatment plan would address both areas by combining behavioral interventions with therapeutic methods. Dr. Culebras warns, though, that some psychiatric treatments could aggravate parkinsonian presentations, so it is important for the practitioner to know what the patient is on and how it can affect their condition. For instance, he says that sedatives can worsen an existing case of sleep apnea and anti-depressants, such as tricyclics, can aggravate leg jerking. In these cases, he advises using other medications when possible.

The drugs used to treat PD can also lead to problems. Dr. Silber says that, in theory, all dopaminergic medications could cause sleep disorders through insomnia (for more, see page 25 of this issue). Paradoxically, he notes that some dopamine agonists and levodopa can cause daytime sleepiness including “sleep attacks” while the patient is driving, and a recent study reported that patients taking pramipexole, pergolide or ropinirole were almost three times as likely to have episodes of uncontrollable somnolence compared with all other PD medication users (Arch Neurol. 2005;62:1189).

Dr. Silber says it is important to take this into account when prescribing a regimen, and to counter the sleepiness he suggests...
instructing patients to take their medication before bed. However, he adds that these treatments can sometimes cause insomnia if they’re taken just before the patient tries to sleep. Nevertheless, they can be invaluable in helping patients sleep, as treatment will allow patients to shift and turn over during the night and wake up feeling refreshed. If insomnia does present, he suggests using controlled or late release levodopa to let the patient get sleep.

Above all, it is important to get the patient to talk about their disorders and take a good history. According to Clin Cornerstone 2004;6 Suppl 1A:s7-15, the PD patient will need a thorough assessment including complete medical and psychiatric histories, sleep history and a one to two-week sleep diary or Epworth Sleepiness Scale evaluation. Dr. Silber says it’s also important to get a collateral history from the partner or caregiver to determine if the patient is acting out dreams while unconscious. “Practitioners should become comfortable and proficient with taking a sleep history,” he says.

Sleeping Without Seizures or Pain

While treating neurodegenerative diseases often means improving the quality of life the best a physician can, some of the more treatable conditions in neurology can also be complicated by sleep disorders. As Dr. Silber says, “There’s a relationship between epilepsy and sleep, and headache and sleep.”

Dr. Culebras says that sleep is known as a powerful modulator of epilepsy, so being deprived of it can aggravate seizures, increasing their frequency. Dr. Silber adds that sleep apnea can also increase the frequency of episodes, making it important for the epileptologist to ask if the patient is snoring or tossing and turning while breathless at night. Treating this condition may lead to improved seizure control.

It’s also important for neurologists to monitor the treatment regimen, as Dr. Silber says some AEDs can cause insomnia while others cause somnolence. Here the neurologist need only follow the standard rule of epilepsy treatment, acknowledging sleep problems as another adverse effect that should be included when one assess AED efficacy.

Sleep complaints in epilepsy should be evaluated by a multifactorial approach, according to Susan T. Herman, MD, Assistant Professor of Neurology at the University of Pennsylvania. A standard history can elicit some complaints, but some may not volunteer the information without being specifically asked about sleep. She says that since rating scales give little information about the possible etiologies of a sleep disorder, it may be necessary to have the patient fill out an extensive sleep questionnaire to uncover a disorder’s source and relationship to epilepsy.

Headaches can also disrupt sleep, says Dr. Silber, particularly those that rarely interfere with the patient’s waking life. “There are some headaches that occur specifically at night, such as cluster headache and hypnic headache,” he says, noting that REM sleep disorders are common in this population.

Dr. Silber says a co-morbid case of sleep apnea can play a role here by either triggering a headache or worsening an existing one. In these situations, treating the apnea can reduce the intensity and frequency of the attacks. “It’s worth asking headache patients about their breathing at night and if they snore,” he says.

Sleeping on AEDs

The effects of AEDs on sleep are difficult to separate from the effects of epilepsy on sleep, as the changes may be direct effects of treatment or secondary to an improvement in seizure frequency. Determining which would be the best choice for patients from the standpoint of seizure is an individual decision.

The agents themselves can either increase or decrease sleepiness, and depending on the patient’s presentation this can be to their benefit or detriment. Phenobarbital can decrease sleep

- Keep the patient on as regular a schedule as possible. Get him or her out of bed at the same time each morning and put the patient to bed at the same time each night. Try to discourage multiple naps during the day, although one hour-long nap in the afternoon would be acceptable.
- Expose the patient to bright light during the day. Ideally, the patient should get several hours of exposure and taken outside when feasible.
- Keep the environment dark at night. A nightlight is acceptable for patients who are prone to wander, but bright light can disrupt circadian rhythms.
- Try to keep the patient from ingesting coffee, tea, chocolate or soda.
- Have the patient exercise whenever possible, with whatever motions he or she is capable of performing.
**Sleep Disorders**

**Dopaminergics Before Bedtime**

A lack of dopamine can keep Parkinson's patients awake at night, especially if a long interval passes between their last dose of medication and the time they go to bed. Scheduling a dose closer to bedtime can solve this problem. In *The Parkinson's Disease Treatment Book*, J. Eric Ahlskog, MD suggests these tips to optimize dosing:

- If the patient is only taking a dopamine agonist with each meal and the daytime parkinsonism is well controlled, there are two options: the patient can take the third agonist dose a little before bedtime instead of suprapertime, or the patient can add a fourth dose just before bedtime.
- If a dopamine agonist is the only medication and it is not controlling daytime parkinsonism, the physician may need to add carbidopa/levodopa, including a bedtime dose.
- If the patient is taking carbidopa/levodopa one hour before each meal, he or she may benefit from a fourth dose of the same amount just before going to bed. The patient could also move his/her third dose to bedtime instead of before supper, but this may cause an evening off-time state since the noontime dose if there is a short-duration levodopa response.
- If the patient has had Parkinson’s for a number of years and has a short-duration carbidopa/levodopa response, another dose an hour before bedtime can help.

A physician can control these effects by organizing the patient’s regimen. Agents that could cause somnolence should be started as monotherapy at the lowest effective doses, and those that cause insomnia should be timed to be taken well before the patient goes to sleep. Polytherapy can make this situation more complex, and in such situations it may be best to avoid AEDs that could aggravate a sleep disorder.

**Strokes From Stopped Breath**

Clinicians in the vascular care community have a particular reason to ask their patients about snoring. Dr. Culebras says sleep apnea raises the risk of stroke by elevating blood pressure and changing the mechanisms of the heart. These factors also lead to a higher instance of atrial fibrillation and blood pressure in apnea patients, which can aggravate other risk factors.

Apnea can also increase the risk of an incident by making patients sleep more during the day. The results from the Western Stroke Screening Study, which were presented at the American Stroke Association's 26th International Stroke Conference in 2001, found individuals who slept more than eight hours a day had nine percent more strokes than average and those who had daytime somnolence experienced 10 percent more. The data also showed the risk of stroke was independently and significantly affected by snoring.

Dr. Culebras says that it is more common for patients to develop apnea after their first stroke, estimating that this disorder exists in about 70 to 75 percent of this population. Again, taking a thorough sleep history can determine the presence of apnea and help the clinician gauge its severity, whether it is a benign or mild case that can be treated by continuous positive airway pressure or if the patient needs surgery to remove obstructive tissue.

**MS and Missed Zzz’s**

Multiple sclerosis is well known for its capricious nature, and its reputation for unpredictability carries over into the realm of sleep. Although the symptoms of this condition can cause a sleep disorder themselves, their presence can also make an existing condition even worse. Whether the physician will be helping the patient stay awake during the day or stay in bed at night depends on the individual.

Fatigue appears in an estimated 70 to 80 percent of MS patients, and Dr. Culebras says a few MS patients may show excessive daytime somnolence. “There are some well defined narcolepsy cases in this area as well,” he says.

Thomas Leist, MD, PhD, of the Department of Neurology at Thomas Jefferson University in Philadelphia, makes it a point to ask the MS patients he works with every day about how well they’re sleeping. While they often have fatigue, he says others complain of not being able to get to sleep at night, and the problem may be caused by another condition such as apnea. “In MS, often the patient either has a primary sleep disorder or there could be sleep disorders underlying their condition,” he says.

The symptoms commonly associated with MS, such as incontinence and paralysis, may directly keep a patient awake at night. Dr. Leist says it’s not uncommon to have a patient report they have to go the bathroom many times during the night. Some may also suffer spasms that jar them awake. Still others may be simply unable to sleep for no obvious physical reason.

Dr. Leist says the medications often used to treat MS symptoms may lead to sleep-related problems. For instance, seizure medication or stimulants can result in hypersomnolence.
Some drugs for psychiatric conditions, such as methylphenidate (Ritalin), may also interfere with rest patterns.

Although a lack of sleep will not trigger an MS relapse, it can worsen some of the symptoms, especially cognitive disorders and spasticity. Dr. Leist says he assesses the patient’s sleep by asking them the following questions:

• “Are you sleeping? If not, what is the problem?”
• “If you fall asleep, do you stay asleep or wake up often?”
• “Are you rested in the morning?”

He says he also asks the spouse or caregivers if the patient wakes up during the night and, if so, why.

The first step towards treating these conditions, Dr. Leist says, is to remove anything that could make it worse. This can mean anything from adjusting the patient’s behavioral medications to asking them to restrict their fluid intake before going to bed.

After these factors have been eliminated or taken into account, Dr. Leist says the physician should encourage patients to develop a ritual to calm themselves down before they turn out the lights. For a half-hour or an hour before bedtime every night, the patient should take some time to be quiet. This can mean reading a book, having a glass of warm milk, or just enjoying the silence. The patient’s family and caregivers can help by not bringing up any new issues or concerns during this time.

“The key is that the patient should not try to go to sleep with a busy mind,” Dr. Leist says. “Just before bed is not the time to balance your checkbook.”

**Better Days for Sleepers**

There has been a rapidly growing interest in sleep medicine in the past few years among the public and medical community, and it shows no signs of slowing down. This trend has made it necessary to take a patient’s sleep habits into account for any condition, with an eye on whether the problems stem from symptoms of the underlying disorder or if there is another factor that must be diagnosed.

Dr. Culebras says this is a good time for neurologists to become more associated with the field, and as more of the professional medical associations in neurology add a sleep section to their conferences practitioners will have more resources to learn practical applications of the latest discoveries. “We are beginning to see sleep as a condition of the brain, so naturally we as neurologists should be involved,” he says. **PN**