Sleep has long been considered a tonic capable of soothing an array of ailments, but patients suffering from dementia often experience just the opposite: an increase in symptoms, and the associated anxiety, at nightfall. Nocturnal exacerbation of delirium has been recognized since the time of Hippocrates; however, in the modern era, Cameron appears to have been the first to explore what has come to be known as “sundowning” in demented patients. He reported that demented patients brought into a dark room during the daytime soon became agitated and confused.

Despite its prolonged history, sundowning remains a poorly defined entity. A typical definition describes sundowning as the appearance or worsening of behavioral problems in the afternoon or evening hours. In actuality, however, peak temporal patterns of behavior likely vary by the type of behavior and the environment, with considerable heterogeneity. The phenomenon is all too common in dementia, which worsens quality of life for the patient and family. Fortunately, lifestyle modifications and adjustments to the medication regimen may be able to ameliorate the sundowning effect. This article will review the phenomenon’s origins, interrelationship with the sleep cycle, and potential management strategies.

Clinical Manifestations
Caregivers of demented patients often complain that patients become agitated, confused and disoriented, and wander at specific times of day, particularly during the night or in the early evening hours (sunset). This behavior represents an increased burden for the families and can be a primary factor leading to the decision to institutionalize the patient. Actigraphic studies of caregivers of demented patients have shown that bedtime and arising times of demented patients coincide with peaks of caregiver activity. Behavioral disturbance in dementia may relate to actigraphic measures of the rest/activity rhythm most strongly in the early stages of dementia. Families may be able to manage the incontinence, disorientation, and other abnormal behaviors during daytime hours, but the family’s inability to obtain overnight respite from these stressors may precipitate or hasten institutionalization.

Typical patient behaviors reported by family members include wandering (often outside), turning on kitchen appliances, and watching television or listening to the radio at high volumes. A recent 24-hour actigraphic study of institutionalized dementia patients stud-
ied over seven days proposed four types of abnormal rhythms in such patients, including an aperiodic type, a free-running (phase delayed) type, an ultradian rhythm type with a cycle of about three to four hours, and a flattened amplitude type, in which patients were largely bedridden. The phase delay of activity rhythms in Alzheimer’s disease patients, and their higher levels of overall nocturnal activity, were confirmed by Harper and colleagues, who also noted that patients with neuropathologically confirmed frontotemporal degeneration were more likely to show a phase-advance of their rest and activity cycles. The phase-delayed patients were also more likely to be described by staff as “sundowning.”

Several studies using time-lapse video monitoring or systematic in-person caregiver observations have confirmed that inefficient “travel” behavior and repetitive, maladaptive physical behaviors peak in the late afternoon or early evening. Real-time observations of disruptive vocalizations in nursing home patients indicate a linear increase in the frequency of such behaviors from 8:00am to 8:00pm. Not all studies of dementia patients agree with this temporal window for peak activity, however. Martin and colleagues, for example, reported that agitation was most pronounced at about 2:30pm. Observational data of sleep in institutionalized patients indicate that severity of dementia is correlated with extent of sleep disruption at night. In some demented patients, particularly those with mixed depressive syndromes, nocturnal awakenings may also be frequent but may not be associated with agitation.

Less well appreciated than the nocturnal disturbances are the daytime correlates of such disruptive behavior. Demented patients who become delirious at sundown are often docile during the daytime hours; they may sleep excessively and are usually not management problems. Sleep during the daytime appears to be inversely related to nocturnal sleep and positively related to wakefulness at night. This vicious cycle may perpetuate nighttime behavioral disruption. Excessive daytime napping may be more subject to environmental effects than has heretofore been recognized. Schnelle and colleagues have shown that huge differences across nursing homes exist, with residents sleeping two to three times as much in some facilities relative to others. These findings could not be attributed simply to more or less time spent in bed.

As night falls, many dementia patients experience a worsening of their symptoms. Here’s a look at what causes the “sundowning” phenomenon and your options for minimizing its effects.

Origins and Pathology

The cause of sundowning in dementia is unknown. Disturbance of the circadian rhythm of body temperature may be a factor, as agitation near the time of sunset may reflect a “wake maintenance zone” described in chronobiological studies. Because some agitated behavior clearly arises from sleep, other speculation has focused on the role of disinhibition of motor systems usually inactivated in REM sleep (REM sleep behavior disorder). At least one such case with neuropathologically verified Lewy body disease has been described, and 38 percent of older men initially diagnosed with idiopathic REM sleep behavior disorder were reported to later develop Parkinson’s disease.

When equated for gross level of cognitive impairment, patients with Lewy body dementia and parkinsonism had significantly more sleep disturbance than patients with Alzheimer’s disease. Similarly, patients with Lewy body dementia had greater locomotor circadian rhythm disturbances than patients with Alzheimer’s disease, although both dementias displayed abnormalities compared to nondemented age-matched controls.

The neural mechanisms underlying delirium in dementia are complex and may involve activation of dopaminergic, serotonergic, glutamatergic and GABAergic systems, as well as activation or inhibition of the cholinergic system. At least one study has noted a greater likelihood of sleep disturbance in Alzheimer’s disease patients with the apolipoprotein E 3/4 genotype relative to the apolipoprotein E 4/4 or 3/3 subtypes. Because sundowning appears to have a temporally specific occurrence in patients prone to this type of behavior disruption, some efforts to understand the phenomenon have linked such agitation to dysfunction of the circadian time-keeping system.

In mammals, control of circadian rhythms is maintained by the suprachiasmatic nucleus of the anterior hypothalamus. Animal studies have indicated that lesions in this area result in a relative asynchrony of circadian rhythms of body temperature, sleep and wakefulness, food and water intake, and various hormones. Early neuropathological studies of this region suggest that the predominantly vasopressinergic neurons show selective degeneration in patients with Alzheimer’s disease, although neurofibrillary plaques and tangles characteristic of Alzheimer’s disease were not present in these samples.

With few exceptions, most studies examining circadian
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rhythms (the putative output of this neural circuitry) of Alzheimer's patients have not shown marked perturbations in the body temperature cycle compared to age-matched controls. Satlin and colleagues initially showed that both the rest/activity and body temperature cycle are phase delayed in Alzheimer's patients. Uchida and colleagues found that a higher proportion of Alzheimer's disease patients showed absence of diurnal variation in melatonin rhythm relative to elderly controls, and Liu and colleagues reported that post-mortem CSF of Alzheimer's disease patients was characterized by melatonin levels about 20 percent of controls, with this effect being most pronounced in the APO-E 4/4 genotype.

Some evidence suggests that individuals with subcortical vascular dementia may incur relatively greater circadian sleep disruption than individuals with Alzheimer's disease. Mishima and colleagues have shown that patients with multi-infarct dementia have a lower amplitude of body temperature rhythm relative to Alzheimer's disease patients. Volier and colleagues reported that Alzheimer's disease patients who were described by staff as sundowning showed temperature rhythms that were less robust and had a poorer curve fit relative to nonsundowning Alzheimer's disease patients. Also, a decrease in phase difference between sleep-wake cycle and skin temperature has been described in ambulatory Alzheimer's disease patients as compared to nondemented age-matched controls.

Can We Prevent Sundowning?

Clues to prevention are suggested by a study that showed more sundowning in incontinent patients, in individuals with a greater number of medical diagnoses, and in persons who had recent room transfers. Little and colleagues reported that sedative-hypnotic medication use is associated with nurses' observations of sundowning, though cause-and-effect relationships remained unclear. Numerous medications including narcotics, sedative-hypnotics, histamine-2 receptor blockers, antiparkinsonian medications, and anticholinergics may be associated with delirium. To what extent such symptoms were uniquely nocturnal in these studies was unclear.

Many other factors may also be relevant for nocturnal agitation. As described previously, alterations in the circadian sleep-wake cycle have been noted in dementia patients. A recent study of demented elderly patients in nursing homes suggested that the best predictors of circadian sleep-wake cycle maintenance were daytime physical and psychosocial activity. Sundowning tends to be worse in the winter relative to the autumn, perhaps because illumination levels are lower in the winter.

Nursing home patients seldom receive over 100 lux in illumination, and even Alzheimer's patients residing at home seldom receive the duration and intensity of sunlight that unimpaired individuals do. More severely demented nursing home patients spend less time in bright light than moderately demented patients. Exposure to bright light may help to optimize the sleep-wake cycle in dementia, and light treatment may be useful for some agitated Alzheimer's patients, although optimal timing of such light exposure (i.e., morning, afternoon or evening) is uncertain.

Until recently, preventing daytime napping has been assumed to promote better nocturnal sleep. It has been shown experimentally to increase the duration of nocturnal sleep in the nondemented geriatric population and may be as effective in the demented population since the homeostatic regulation of sleep and wakefulness appears preserved even in the late stages of dementing illness. However, Sloane and colleagues presented data suggesting that nursing facilities that routinely put patients in bed during the afternoon for naps had lower rates of agitation relative to facilities that did not employ this routine.

As agitation is often temporally related to awakenings by staff, the wisdom of frequent nocturnal awakenings (though required by the Omnibus Budget Reconciliation Act guidelines to prevent skin breakdown) in nursing homes is suspect. Geriatricians whose primary focus is incontinence have recently begun to recognize the disruptive effects of such procedures and to gain a greater appreciation that such patients are typically capable of a considerable amount of spontaneous movement during sleep, which would preclude the necessity for such repeated disruptions for repositioning and avoidance of bedsores. Common aspects of the nursing home environment, such as failure to maintain a quiet environment and failure to minimize hall lighting, may also contribute to interruption of sleep, although interventions to abate excess noise and light at night may be difficult to implement at levels that impact on sleep disturbance.

A well-done prospective study examining the development of delirium over nine days in a geriatric population, although not explicitly examining nocturnal delirium, offered several variables shown to be associated with incident (new-onset) delirium. In this study, malnutrition (serum albumin less than 30g/l), use of physical restraints, insertion of a bladder catheter, addition of four or more medications, and any iatrogenic events (infection, pulmonary embolism, falls, fecal impaction) predicted development of delirium.

Work-up and Differential Diagnosis

Evaluation for nocturnal delirium should involve a complete medication review with special consideration of drug interactions, even when taken in therapeutic dosages. Anticholinergic and antiparkinsonian drugs should be scrutinized particularly carefully. Routine blood chemistries and a complete blood count should be obtained with special concern for the possible presence of uremia, diabetes and other endocrinopathies, liver dysfunction, vitamin B-12 and folate deficiency, heavy metal intoxica-
tion, systemic infection, and anemia. Alcohol or benzodiazepine withdrawal and the effects of recent surgery are other potential contributors.

Nocturnal delirious states can occur in a wide variety of infectious, toxic, metabolic, and drug-induced conditions. The simultaneous presence of any such condition in a demented patient may result in agitated behavior that presents as sundowning. If such disruptive behavior occurs in the absence of these conditions, assume that the agitation is related to the neurodegenerative disease process itself.

Prognosis and Complications
Some component of sundowning probably affects most demented patients at some point in their illness, although estimates of incidence and prevalence vary widely in the literature. Alzheimer’s patients who sundown have a faster rate of decline in mental function in the years prior to the nocturnal behavior disruption.59 Clinically significant sleep disturbance in Alzheimer’s patients typically occurs sometime after the loss of ability to dress oneself, but before the loss of ability to self-feed, ambulate or maintain eye contact.60 The one-year mortality rate for delirious geriatric patients has been reported as 38 to 46 percent.60 A one-month mortality rate of 17 to 25 percent has also been reported,62 and a mortality rate of 65 percent was found in a group of delirious, primarily geriatric, patients admitted to an acute medical unit.63 Body temperature minimum in the late afternoon (a time when body temperature customarily peaks), although not specifically related to sundowning, was strongly associated with reduced survivorship in nursing home patients.64

Management Strategies
Renal and hepatic disease, systemic infection, hypovolemia, acid-base and electrolyte imbalances, and hypovitaminosis should be corrected if possible. Special attention should be focused on the patient’s behavior and level of alertness during the daytime hours. Reports of docility may reflect daytime sleep rather than cooperativeness. Caregivers and nursing staff should be instructed to prevent daytime dozing even to the point of manual stimulation. Incorporation of physical activity into the patient’s routine and the exposure to outdoor sunlight may be useful adjuncts. Increased physical and social activity were reported to increase stages 3/4 sleep in somewhat higher functioning elderly residents in a retirement home, yet had no effect on circadian measurements of body temperature.65 Recent data have shown that aggres-
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Savage attempts at behavioral strategies emphasizing good sleep hygiene can be helpful in treating nighttime behavioral disturbances.66,67

Light is a powerful zeitgeber for the sleep-wake cycle in both demented and nondemented geriatric patients, although whether the effect is mediated by the circadian timing system or by a direct alerting effect of illumination (thereby keeping patients awake to improve sleep at night) is unknown. There is also disagreement as to whether such light is best used in the morning, afternoon or evening. One large study68 found that morning bright light delayed the acrophase of the activity rhythm, which might improve the ability to care for these individuals by making their activity patterns more in line with typical social norms. Studies of light therapy use 2000 lux to 2500 lux (equivalent to outdoor exposure on at least a partially sunny day) for at least several hours. Merely exposing patients to a window while indoors is probably insufficient. Furthermore, many geriatric patients have visual impairments due to retinal or optic nerve disease, which may reduce transduction of altered illumination levels via the retinohypothalamic tract even with optimal outdoor light exposure.

Disturbances of the diurnal rhythm of melatonin may contribute to sleep disruption in dementia patients. Haimov and colleagues reported beneficial effects of low-dose (2mg) melatonin in elderly nondemented patients.69 Hughes and colleagues recently published a double-blind, placebo controlled, crossover study of melatonin in nondemented geriatric patients that showed melatonin to have sleep-promoting and body-temperature-lowering effects but minimal effects on sleep maintenance and sleep continuity.70 However, another double-blind crossover study failed to demonstrate improvement in total sleep time, awakenings, or sleep efficiency in demented patients.71 Moreover, a large multicenter trial of several different doses of melatonin failed to demonstrate improvement in total sleep time, awakenings, or sleep efficiency in demented patients.72 These have been open-label and uncontrolled. Two large placebo-controlled double-blind studies have been performed, however, which demonstrate significant improvement in psychotic and aggressive behavior in demented patients treated with low-dose (approximately 1mg/day) risperidone.76,77

The popularity of the atypical antipsychotics has been boosted by their reportedly better safety profile, including a lower incidence of extrapyramidal symptoms. However, evidence has suggested an increased risk of cerebrovascular disease in older patients taking risperidone,78 as well as a heightened risk of diabetes in individuals taking the agent.79 A large multi-center study currently is in progress to compare the atypical antipsychotics risperidone, olanzapine, and quetiapine, as well as the selective serotonin reuptake inhibitor citalopram to placebo in treating psychosis and agitation in outpatients with Alzheimer’s disease.80

There are anecdotal reports of success with propranolol, trazodone or clonidine, although their mechanisms of action on sun-downing and their unequivocal success have yet to be established.

In the institutional environment, some nursing homes have activities or an occupational therapist who works in early morning hours (e.g., 2:00am to 4:00am) to provide a supervised structured activity for patients who may otherwise be a disruptive influence to other patients and staff. Since the 1987 Omnibus Budget Reconciliation Act guidelines, use of all psychoactive medication has decreased in many nursing homes.81

The Sun Also Rises

For dementia patients and their families, the daytime hours are filled with myriad anxieties and symptomatic manifestations, and many rightfully despair at the prospect of nighttime exacerbations. With greater identification of the sun-downing phenomenon and diligent efforts to overcome it, dementia patients (like many others) can enjoy the restorative qualities of a sound, uneventful night’s sleep and greet the sunrise with the enthusiasm and energy needed to maintain productive, rewarding lives. PN

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Steven E. Gentry, MD is Assistant Professor of Medicine at Eastern Virginia Medical School in Norfolk, VA. He is also Director of the Intensive Care Unit and Director of the Sleep Lab at the Veterans Affairs Medical Center in Hampton, VA.