Editorial

Gender and Sleep
"Morning Came, As It Always Does"

My patients complain of many things, both great and small. But one of the most ubiquitous, pervasive miseries for men and women alike is insomnia. I've observed some striking and completely unexpected patterns: for example, my menopausal patients invariably tell me that their witching hour—eerily and strikingly the same for all—is 2 AM. These ladies call themselves members of the "sweat and fret" club. With or without the drenching sweats departing estrogen leaves in its wake, they find themselves staring into the dark, beset with anxieties they manage to tamp down during the day but which make them frantic, they all agree, at precisely the same time.

My own case of insomnia is world class. I've learned firsthand the virtues of the soothing combination of hot milk and yesterday's editorial page at 2 AM, when simply turning over and rearranging the covers doesn't work. The problems I appear to deal with so effectively during the day crowd into my wide-awake brain and somehow seem larger than life, and on the worst nights, even insurmountable. Last year, I asked one of my favorite patients for a reassuring quotation in needlepoint from the exquisite fable, *Amos and Boris*, by William Steig.[1] This marvelous tale, as engrossing for adults as it is for children, recounts the travails and triumphs of an adventurous mouse, Amos, who sets out to explore the world on a beautifully outfitted boat of his own design. Like all of us, though, Amos runs into significant challenges: for one, his boat sinks in a storm and he almost drowns. Boris, a whale traveling through the ocean waters on his way to a convention, spies the hapless mouse and eventually carries him to safety. As the two negotiate the voyage together, Amos, not surprisingly, finds sleeping on the whale's back problematic and suffers all the classic anxieties of the insomniac. Steig describes Amos' frame of mind after a painfully anxious night and tells us that as the sun rose, the mouse's usual optimistic view of the world was restored. Commenting on Amos' renewed confidence, Steig wrote: "Morning came, as it always does." Like Amos' exaggerated nighttime fears, our own recede as the sun comes up and the world somehow, magically, becomes manageable once more.

What is the purpose of sleep? Darwin must have wondered what evolutionary advantage ensued from being unaware of the world around us for at least a third of every day. The science of sleep and our understanding of its neurologic underpinnings are relatively new. Before the 1950s, the mechanics of how we fall, and stay, asleep and then wake in an orderly sequence were not clearly understood. Sleep was viewed as a type of passive "time out" from waking life, and why humans needed to spend 7 to 9 hours in this state of altered consciousness was simply not known. We now understand that, far from a period of suspended animation, the brain is very active during sleep, performing specific tasks that not only have an impact on our ability to form memories, but maintain our physical and mental capacities as well.

One of the important roles sleep plays in our bodily economy, then, is to repair the neurons we use while we're awake. Equally important, other neuronal connections that might deteriorate from nonuse may be exercised only during sleep. The youngest of us profit from a surge in growth hormone during sleep. Moreover, activity in those areas of the brain that control emotions, help us make decisions, and govern social interactions is all lessened during sleep, presumably giving the brain a chance to rest and repair these vital centers. Shakespeare was right on target when he observed that sleep "knits up the ravelled sleeve of care."[2]

The cycles of sleep are divided into 5 different phases. Within 70 to 90 minutes, these sequences of plateaus of increasingly deep sleep lead to rapid eye movement (REM) sleep, a unique period during which we experience a paradoxical combination of enhanced sympathetic activity (our breathing becomes

faster, irregular, and more shallow, and our eyes jerk rapidly in various directions; men develop erections during REM sleep) and paralyzed limb muscles. The latter fascinating phenomenon is the result of impulses from the pons that shut down the activity of the spinal cord neurons. If this process is interrupted or doesn't happen at all, spinal neurons continue to fire. The bizarre phenomena we call dreams occur during REM sleep. Freud's belief that dreams were a release for unconscious desires seems to be contradicted by the observation that infants have REM sleep. According to the experts, dreams may be our attempt to harvest the random signals that the cerebral cortex receives during REM sleep and make "stories" of them. Sleepers will "act out" the dreams that occur during REM sleep, and may actually rise from their bed and carry out a complex motor activity such as throwing a ball. Apparently, REM sleep is also essential to the solidification of memory. If subjects are deprived of non-REM sleep, their memory of a recently learned skill is not affected, but if REM sleep is eliminated, the subjects cannot remember what they have learned.

There is a 25-hour cycle for our periods of sleep and wakefulness. The clock that regulates this periodicity, termed *circadian rhythm*, is in the hypothalamus' suprachiasmatic nucleus, which contains ~20,000 neurons whose activity is regulated by the daily cycle of light and darkness. The suprachiasmatic nucleus receives daylight signals that travel along the optic nerve to the pineal gland, which then ceases production of melatonin, the "sleep hormone." The level of melatonin gradually increases as the day progresses, causing drowsiness as darkness falls. Disturbances in circadian rhythm are essentially due to changes in the timing and duration of dark and light cycles (this is what creates jet lag). Administration of the hormone melatonin or exposure to bright lights, or both, can reset our own circadian rhythm. People who are blind almost predictably have frequent insomnia and sleep disturbances, because they are immune to the ordinary signals that control the suprachiasmatic nucleus' production of melatonin.

Despite the similarity of the symptoms in both sexes, sleep apnea is underdiagnosed in women. This sleep disorder is caused by the collapse of the upper airway during sleep, and the ensuing struggle to inhale awakens the patient. Sleep apnea is more common in older or obese individuals. It is a risk factor for heart disease, high blood pressure, stroke, and arrhythmias. In studies of young men and women, Trinder et al[3] found an increase in upper-airway resistance during non-REM sleep that intensified as sleep progressed in both sexes. This increase in upper-airway resistance, however, was more profound in men and may constitute a gender-related susceptibility to sleep apnea that is greater than that for women.

Other interesting gender-specific facts about sleep include the observation by Elsenbruch et al[4] that men have a greater decrease in vagal tone while awake and increased sympathetic tone during REM sleep than do women. Summoning up one of my frequent imaginary discussions with Darwin, I would ask him whether or not he believed this gender-specific change in autonomic nervous system activity rendered men more ready to defend their habitat against predators when awake or when danger roused them from sleep. Yet another striking difference between the sexes is the progressive increase in the lighter, stage 1 sleep as men age that is not observed in women. Generally, older women sleep better than older men. However, total time asleep declines with age: older subjects (aged 50–70 years) have been found to sleep 46 minutes less than younger subjects (aged 20–34 years).[5] This reduction is commonly due to increased waking periods during the hours of sleep. Again, Darwin might postulate an advantage for the more fragile, older sleepers to spend less time in the deep unconsciousness of phase 3 and 4 sleep so that they can monitor the environment for threats. Indeed, this unique pattern of sleep in older males might have rendered them particularly valuable as sentinels while the younger, stronger members of the social group rested and repaired the damage of the day to their more active brains and bodies.

Some of us are definitely responsible for our own insomnia. Heavy smokers have less REM sleep and sleep more lightly than nonsmokers. People who try to remedy their sleep difficulties by drinking alcohol rob themselves of both REM sleep and the deep restorative phases of rest that lead up to it; they can be, and frequently are, more easily awakened than those who resist the "nightcap" as a soporific.

As for insomnia in the postmenopausal patient, there is no question that estrogen therapy restores normal sleep patterns to the members of the "sweat and fret" club. It is interesting to consider whether some forms of insomnia in older men might be due to falling levels of testosterone. In men, testosterone is converted to estrogen, which promotes refreshing and uninterrupted sleep in both sexes.

We are just beginning to understand why sleep is a crucial part of our day and how the nervous system governs its onset and quality. The ubiquitous and frequent insomnia that besets our patients takes a significant toll on their physical and emotional health—they are right to complain about it and right to demand that we address this fundamental issue. All insomnia is not the same. It is important to learn why depressed patients awaken early, why anxiety crescendos in the early hours of the morning and awakens the troubled patient, and why some patients have critical problems with turning off the day's demands and quietly descending into sleep. The development of effective therapy depends on an accurate understanding of how our sex-specific brain chemistry, and the impact of our individual world on that chemistry, disrupts our capacity for rest and renewal.

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doi:10.1016/j.clinthera.2008.05.007