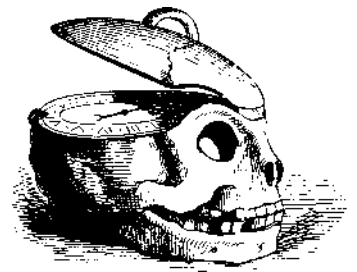


“No autopsy – he’s suffered enough.”



I was recently surprised to learn that a patient I had followed for several years had been autopsied. The family had requested that the patient’s brain go to a research foundation dedicated to the study of the degenerative disorder that so afflicted this poor woman. This was unusual for several reasons. The issues surrounding the obtaining of autopsies have been around for a long time. On the one hand hospitals need to perform a certain number of autopsies to remain accredited. On the other hand there is no reimbursement for these autopsies, which can be expensive if special stains are required so that pathology departments aren’t always clamoring for more. When patients die out of the hospital, funeral directors often dissuade families from autopsies, citing extra cost, time, effort and inconvenience. An out-of-hospital autopsy may cost \$300-400, to pay the funeral director; the bill goes to the family if the doctor requesting the autopsy does not pick up the expense. And the paperwork, which must be completed at the time, usually Sunday evening, while small, is not always easy to arrange. Lots of phone calls to doctors not always quick to answer pages, nursing supervisors, dieners, grieving spouse are required, even when the autopsy has been agreed to in advance.

Autopsies always inform. In this particular case I had erred in my diagnosis. Initially I had written the correct diagnosis in the chart, but as the illness progressed and took a peculiar turn, an alternative diagnosis seemed quite obvious. So I learned from this case. But more importantly, her brain joined a brain bank where her illness could be studied, and, although the illness still has no known etiology or treatment, our understanding of it over the last five years has progressed dra-

matically, largely due to newer staining techniques and advances in molecular genetics.

James Parkinson, known of course for his famous monograph on the disease that bears his name, was remarkably prescient in his unheralded forward to that monograph. He noted that his disease description was intended to put order into one area of medicine, as the term “shaking palsy” was then being used in an unrestricted manner. In the forward, however, he noted that until the pathology of this disorder was known, his description of a unitary disease was only conjecture. It took 100-150 years until the pathology became relatively well understood and even now surprises abound in the study of this one disease. Large lacunes in our knowledge base are obvious, and have become even more so now than 10 years ago.

It is primarily through the study of the actual diseased organ that medicine makes its earliest and most basic advances. Some pathological processes can be studied *in vivo*, but most brain degenerations cannot. Yet we doctors are remiss at obtaining these much needed brains. A prestigious group of clinical researchers devoted to the study of Parkinson’s disease, which has been in existence for 15 years, has enrolled a few thousand subjects in drug studies, and has obtained only three brains for research studies. Three brains! How could this be? Since I am partly to blame and have thought about this problem, I can speculate from my own perspective. For reasons I don’t understand, talking about death with a chronically ill patient is awkward. Our efforts are always in the opposite direction. Exercise more! Socialize more! Think more! Invest in your future! Yet we all share the same future and death is even more reliable than taxes. To talk

about death to someone who cannot be cured often suggests that the inevitable is just around the corner. I always have found it easier to ask for brain autopsies in patients who are quite healthy and not in imminent danger of demise. And when I do ask, the patients are often agreeable, but families are less so. An interesting aspect of American law is that the patient, on dying, loses all rights to determine what happens to his own corpse. This seems surprising since the patient’s will is a legally binding document. Thus a person can will his house but not his body. One of the common comments family members make is, “He suffered enough.” I am always stupefied by this since I think that virtually everyone believes that suffering stops with death. And given a choice of being completely decomposed by bacteria, worms, bugs and vermin, or having some organs cut into pieces and the rest decomposed by bacteria, worms, bugs and vermin and contributing to some future victim’s benefit, I don’t see much of a choice. But most people recoil from the idea of deforming a corpse. It is an act of anger and disparagement to mutilate corpses in wars. And it is thus considered important to protect and collect one’s fallen comrades in battle. Perhaps this idea extends into our civil life as well.

My autopsy rate is low. I do not routinely ask my patients to donate their brains to one of the Parkinson’s disease brain banks, although I should. When I do ask for the brain, I always say that I don’t expect it soon and that I don’t want it until the patient is “finished using it.” Like my colleagues I mostly get autopsies on the patients whose diseases I cannot diagnose, as this helps me learn, and often relieves the family’s anxieties about not having a label for their relative’s illness. This

leads to improved expertise for me, and perhaps case reports that enhance my curriculum vita, but, in truth, as important as these exceptional cases are, the real need is for the “routine” brains: normals to be controls, and the common disorders, PD, Alzheimer’s, etc. Every autopsy is a learning experience that improves our skills. In two large series of autopsies of presumed Parkinson’s disease patients diagnosed by experts, the error rate was about 20%! And when strict criteria were developed, based on the missed cases, then many cases with actual PD would not be diagnosed. In other words, PD overlaps so much with a handful of other disorders that there is no way to reliably distinguish them on clinical grounds alone.

Some families and doctors think that the MRI makes brain autopsies obsolete. If nothing else, MRI brain

imaging has demonstrated how little we understand about histological changes. Most neurodegenerative disorders have normal brain MRIs. “Small vessel ischemic disease” is a common MRI finding that has nothing to do with the reason for the test. “Small T2 enhancing patches that could represent vascular disease or demyelination.” “Small region of white matter change of uncertain significance.” The more brain autopsies we obtain, the sooner we will understand what these images mean and why patients with MS have such remarkably poor correlation between their MRIs and their clinical deficits.

Not every patient can enter a research study while alive. Not every patient wants to. Yet, with the exception of the occasional patient with religious objections, and the common reluctance to pay the extra \$300 to the

funeral director, every patient with a disease that needs to be studied further should be asked to donate his brain to a research brain bank. Only through studies of actual diseased human brains will our neurological afflictions be solved. As an eminent neuropathologist noted, “the practical answers will come from those PhDs who can’t distinguish the ganglion cells of an earthworm and Einstein’s brain.” But unless we get Einstein’s brain there won’t be anything to study. And without the clinician, there will be no correlation with the disease process. The pace of breakthroughs will reliably increase and the patient and family can feel, as my patient’s family did, that in death they can try to help others to avoid her crippled fate.

– Joseph H. Friedman, MD

A Witch’s Brew, Scottish Style

Requiring children to memorize speeches from the Shakespearean repertory is a sure way of dissuading them from ever enjoying the Bard when they reach adulthood. These segments, remembered by rote, are rarely recalled in later life except, perhaps, as disconnected fragments. A phrase such as “double, double toil and trouble” may come to mind at odd moments; but only with intense concentration may it then bring up the further image of three witches casting poisoned entrails into their caldron. It is a curious scene, with three witches talking in mystical terms of terrible things yet to happen [Macbeth, Act IV, scene 1]. Access to these visions of things to be is then facilitated by a distasteful assemblage of gory objects to be incorporated into their seething caldron. The often memorized words are as follows:

All Witches: “Double, double toil and trouble; Fire burn and caldron bubble.”

Second Witch: Fillet of a feeny snake,
In the caldron boil and bake;
Eye of newt, and toe of frog,
Wool of bat, and tongue of dog,
Adder’s fork, and blind-worm’s sting,
Lizard’s leg, and owlet’s wing, -
For a charm of powerful trouble;
Fire burn, and caldron bubble.”

There then follows a recipe of further ingredients for this sinister brew, including scale of dragon, tooth of wolf,

root of hemlock [dug in the dark] and sundry body parts of blaspheming infidels. The final, black concoction pleases Hecate, who declares that it is now suitable for its evil purposes in hastening Macbeth’s path to perdition.

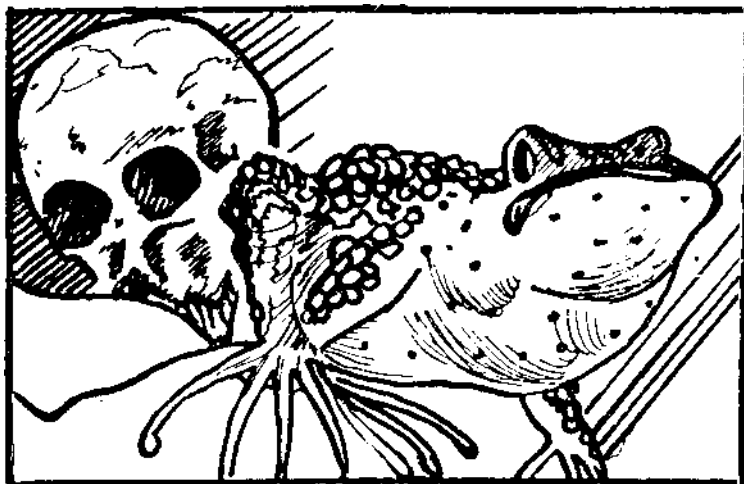


Why did Shakespeare select these particularly abhorrent objects for this witch's brew? Were they randomly selected names to achieve, perhaps, some felicitous rhyming? Were the ingredients arbitrarily chosen merely for their distasteful nature so as to evoke maximal squeamishness in his audience? After all, each of these ingredients, by itself, represented something quite foreign to the daily experience of the average playgoer. But collectively, they served to create an atmosphere of evil mystery, especially if accompanied by appropriate incantations.

Shakespeare did not write his memorable plays in splendid isolation. His dramas reflected the fears, superstitions, and prejudices of the early 17th Century populace; and, accordingly, each of the ingredients in this witch's brew was known for its alleged magical powers. Some even represented standard preparations found on the shelves of any Elizabethan apothecary.

Take, for example, the eye of the newt. To the credulous west European alchemist, the living newt [or salamander] could withstand the effects of flames and hence became a symbol of fire, or at least incombustibility, and incorruptibility. Mention of the newt's eye, however, made this contribution to the witch's brew specifically emblematic of divine insight and enduring knowledge. A third eye, set in Shiva's forehead, bespoke of the Hindu god's capacity to perceive the future. Indeed, those deprived of an eye [and hence left with but one eye such as Wotan of Nordic legendry] were said to become all-powerful and blessed with uncommon vision. Even the back of the American dollar bill has a disembodied eye sitting at the apex of a pyramid. No self-respecting mystical concoction was therefore considered complete without the eye of a newt or lizard.

The addition of bits of tongue, either from an adder or hound, provided the concoction with the elements of boundless power. The sheer potency of the tongue is expressed scripturally: "Death and life are in the power of the tongue" [Proverbs 18:21]. When the tongue is viewed metaphorically, as an instrument of wickedness [the evil tongue] it again suggests that even an isolated fragment of tongue may be endowed with a potent life of its own.



The snake, or its more auspicious relative the serpent, is a necessary ingredient in any sorceress's brew. The serpent, a creature of darkness, typifies all the malevolent qualities feared by the trusting human: coldness, guile, slitheriness, absence of soul and utter ruthlessness. In so many stories of creation, the serpent is the first creature embodying evil. In a few cultures, the Toltec, for example, all of humanity is derived from the blood of a serpent injured by the talons of a giant bird. In Malaysia, the Batak peoples believe that a cosmic serpent occupies the Underworld of the dead and that pieces of this creature will give its possessor power to foretell the future. There is a curious myth that the infant Cassandra and her twin brother were once left unattended in the temple of Apollo. When the parents returned they found snakes licking their children. They screamed and the snakes slithered away. But both Cassandra and her brother demonstrated a gift of prophesy when they matured. If one survives an intimacy with snakes, it seems, one is then granted the capacity to foretell the future.

Hemlock is derived from the roots of a widely distributed plant variously known as water hemlock, poison parsnip, or wild carrot. The cut root exudes a pungent fluid smelling vaguely like parsnip. In significant dosage, hemlock is a lethal poison causing somnolence, confusion, delirium and agonal seizures. The Athenians used draughts of hemlock as one of their means of capital punishment. [In 399 B.C.E., Socrates was put to death by hemlock ingestion for the crime of corrupting, through his teachings, the young of Athens.] In smaller doses, hemlock was used for some nervous disorders of humans. By the 18th Century it was dispensed occasionally as a sedative. John Keats [registered surgeon and sometime poet] wrote an ode to a nightingale which included the line: "My heart aches, and a drowsy numbness pains my senses, as though of hemlock I had drunk." Keats, as a licensed physician, was of course familiar with the pharmacologic effects of hemlock. Shakespeare's warning that the hemlock be dug in the dark reflects the common fear that those who dare to dig up botanicals such as hemlock or mandrake expose themselves to punishment unless they remove these roots under cover of darkness or have animals uproot them.

Vulnerable 17th Century plain folk, struggling with imponderables and uncertainties, desperately sought ways of foretelling what tomorrow might bring. The friendly neighborhood apothecary, just recently graduated from primitive alchemy, provided all manner of visionary herbs and brews. For simple clairvoyance such as next week's weather or the success of a marriage, there were simple concoctions. But for something as monumental as a Scottish thane's future, one needed a boiling caldron supervised by three ordained witches.

– Stanley M. Aronson, MD, MPH

Sleep Disorders: Common But Often Unrecognized Medical Problems

Richard P. Millman, MD

Sleep disorders can be approached by assessing specific symptoms. These include excessive sleepiness, insomnia, and abnormal movements during sleep (parasomnias).

Approximately 50% of the population complains of excessive sleepiness.¹ The major causes of excessive sleepiness include insufficient sleep, shift work, and organic sleep disorders (with sleep apnea being the most common of the latter). Insufficient sleep and shift work plague the medical profession, and as a result, medical students, residents, and practicing physicians often complain about being excessively sleepy. This could potentially lead to a skewed perspective towards patient sleep complaints. A patient may tell his physician that he or she is excessively sleepy. Since the physician may also be excessively sleepy, the patient's complaint may not trigger a sympathetic response. Dr. Judith Owens and Jennifer Blum discuss the lack of sleep during medical education in this issue. Dr. Rakesh Gupta presents a logical approach to help physicians determine the cause and diagnostic strategies for patients with excessive sleepiness. Obstructive sleep apnea is not reviewed in detail in this edition of *Medicine & Health/Rhode Island*, because Dr. Naomi Kramer discussed the topic in the February 2002 issue.

Insomnia is a subjective complaint defined as an inability to fall asleep initially or maintain an inability to sleep or a perception that sleep is nonrestorative. Patients suffering from insomnia typically have problems with daytime fatigue, memory, attention concentration and performance. Patients on the surface may appear depressed. One of the mistakes that physicians typically make is to label a patient with insomnia as having primary depression rather than

primary insomnia. Insomnia has been reported to occur in 49% of adults in this country at one time or another. Twelve percent of the adult population has chronic insomnia.² Drs. Arnedt, Martin and Posner discuss behavioral therapy for chronic insomnia. Pharmacological approaches to insomnia are discussed in *Advances in Pharmacology*.

The other major sleep complaint dealt with in this issue is abnormal movements during the night; for example, sleep talking, sleep walking, sleep eating or night terrors arising from deep or delta sleep (Stages III-IV). Over the last several years, it has been recognized that predominantly male patients may actually act out their dreams during **rapid eye movement (REM)** sleep. This is known as the REM sleep behavior disorder. There is a loss of the typical hypotonia seen in REM sleep allowing patients to act out their dreams. The ability to act out dreams may result in significant injuries to the patient or their spouse. Drs. Brian Kimble, Alice Bonitati, and Richard Millman discuss this topic in detail.

Even though sleep disorders are common, little time is spent in medical school education to train medical students and postgraduate trainees in sleep disorders. Though obstructive sleep apnea is as common as asthma in adults in this country,³ minimal curricular time is spent on sleep medicine in the first two years of medical school compared to asthma. Even though one could argue that asthma is more dangerous to a patient, obstructive sleep apnea has been associated with increased motor vehicle accidents⁴ and cardiovascular complications. Associations have been made between obstructive sleep apnea and cerebrovascular disease,⁵ angina, myocardial infarction⁶ and hypertension.⁷ There is increasing evidence that sleep

apnea not only raises blood pressure at night but can also cause daytime hypertension.⁸ A recent survey of medical schools, however, revealed an average of only 2.1 hours of sleep medicine education in the curriculum.⁹ When primary care physicians send patients for all-night polysomnography, the physicians consistently choose patients with sleep apnea. In fact, 96% of 68 patients referred to our center by primary care physicians from the former HCHP-NE had sleep apnea by polysomnography testing.¹⁰ These 68 patients represented, however, only 0.13% of the total primary care patient profile. Thus, many patients with less obvious sleep apnea are being missed.

So what is a practicing physician to do about sleep disorders? Most physicians do not ask the appropriate questions about sleep.¹¹ Primary care physicians, including pediatricians, internists and family physicians, need to ask questions about sleep in their review of systems. Pediatricians are tuned into sleep disorders in younger children, but not necessarily in adolescents and teenagers. For this group and adults, physicians could ask patients three basic questions. Obviously a positive answer to any one should lead to more detailed questioning.

Typical questions could be the following:

- * Are you rested during the daytime, or do you find that you are excessively sleepy and doze easily?
- * Do you snore or has anybody told you that you snore loudly?
- * Do you have any problems sleeping at night?

Hopefully, the addition of these questions to a standard review of systems will lead to early and better rec-

ognition of sleep problems and their consequences.

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Sleep, Fatigue, and Medical Training: An Overview

Judith A. Owens, MD, MPH, and Jennifer Blum

Numerous studies have documented the devastating consequences that both short and long-term total sleep loss (sleep deprivation), and acute and chronic partial sleep deprivation (sleep restriction) have on mood, cognition, and performance. Many studies have documented significant performance impairments when sleep is restricted to four hours or less under experimental conditions; one recent study documented that restricting sleep to 5 hours of sleep per night over a one week period results in a level of cognitive impairment equivalent to 2 nights of total sleep deprivation.¹ Memory, vigilance, mental processing of complex information, and decision making skills represent only a few of the cognitive domains integral to performance of daily tasks that are negatively affected by sleep loss. In addition, substantial evidence suggests that the detrimental effects on performance resulting from even modest amounts of sleep loss over time, or "sleep debt", may be cumulative. Finally, human circadian physiology dictates that wakefulness and alertness are at optimal levels during daylight hours and that sleep propensity is maximized at

night. Failure to adhere to this need for both appropriately-timed and adequate amounts of sleep can increase sleepiness and fatigue levels and reduce waking function.

Yet modern society measures performance and productivity on a 24-hour basis. Round-the-clock operations, in manufacturing, transportation, and healthcare, often takes precedence over the basic physiologic principles governing sleep and wakefulness, at times with devastating results. As a result of such fatigue-related accidents as the Exxon Valdez oil spill and of the increased recognition of the repercussions of prolonged work hours and shift work, both the level of scientific inquiry and the magnitude of public concern regarding sleep loss and fatigue in the work place have increased.

In contrast, the issue of work-related sleep loss and fatigue in the medical profession, particularly during residency training, has until recently received less attention. On the research front, relatively few studies have examined the impact of sleep loss and fatigue in the medical setting, and many of those are methodologically flawed.

From the standpoint of policy, in the fifteen years since the Libby Zion case and the Bell Commission galvanized changes in work hours and residents' schedules in New York state, there have been few additional attempts to implement similar or other interventions. Not only have other states failed to adopt similar work hour legislation, but the New York State regulations have not been rigorously heeded.

The consequences of sleep loss and shift work for physicians in training can occur in a number of domains; i.e., personal and family consequences (mood disturbances, increased stress, adverse health consequences, negative effects on personal relationships, increased potential for alcohol and substance abuse, and increased risk of motor vehicle crashes) and negative effects on cognitive and neurobehavioral functioning (attention, reaction time, vigilance, memory, as well as motivation). In addition, there is an impact on the performance of professional duties (e.g., IV insertion, EKG interpretation, and taking patient histories), as well as implications for the quality of medical education (decreased retention of

information, impaired information processing, and decreased motivation to learn). Finally, sleep loss and fatigue in residency training can lower the quality of patient care and increase errors in the hospital.

The lack of a coordinated and comprehensive body of research has hampered a consensus on the effects of sleep loss and fatigue in medical training. Although substantial empirical evidence has documented the impact of sleep loss on human performance in the laboratory setting and in other occupational settings, the evidence linking fatigue with performance deficits during medical training is less consistent. A number of the several dozen studies on this topic have documented substantial impairment in physicians following sleep loss in a variety of domains, but several comprehensive reviews of the literature have suggested that, overall, these studies are inconclusive. Furthermore, many of these studies have significant methodological shortcomings. For example, most of these studies have not considered the confounding variable of chronic partial sleep deprivation in the research design. Therefore, the validity of any comparisons of performance under conditions of acute sleep restriction ("post-call") versus a "rested baseline" is likely to be compromised by the fact that most resident physicians are routinely functioning under a considerable chronic sleep debt. Moreover, most of these studies have relied upon self-report assessments of sleep amounts rather than more objective sleep-wake measures, such as actigraphy. The different outcome measures used to assess the effects of sleep loss and fatigue in these studies, which have ranged from performance on psychometric tests of vigilance and reaction time, to the ability to correctly answer national board-type questions, to performance on work-related tasks, has not only contributed to variability in results, but also raises concerns about the potential relevance of some of these measures to actual work performance ("ecological validity"). Alternatively, outcome measures of many potentially significant domains of impact, such as

the quality of physician-patient communication and complex problem-solving skills, have not been adequately assessed.

Given these limitations, what conclusions may be drawn from the current literature regarding the effects of sleep loss and fatigue on physicians-in-training?

The lack of a coordinated and comprehensive body of research has hampered a consensus on the effects of sleep loss and fatigue in medical training.



IMPACT ON QUALITY OF LIFE AND HEALTH OF MEDICAL TRAINEES

One of the most consistent effects of sleep loss in general is a detrimental impact on mood: individuals have an increased incidence of anxiety, hostility, tension, and confusion after a lack of sleep. Much of the research on the negative effects on mood as a result of long work hours and lack of sleep in medical trainees is based on subjective reports by residents. Almost all describe themselves as less happy and less clear thinking during and after long shifts, especially night shifts.² Many residents also report a marked decrease in motivation. In one study, total and subscale (Tension-Anxiety, Confusion, Fatigue, and Vigor) scores on the **Profile of Mood States (POMS)**, a self-report measure of affective state deteriorated significantly following a 32 hour shift in a group of house officers.³ At least one study has also suggested that these negative mood effects persist for several days post-call.

In addition to psychological complaints, individuals who have been deprived of sleep experience physical problems. Studies have shown a positive correlation in a group of house officers between the number of hours slept per shift and the number of somatic symptoms reported during the

previous year. Research has also examined the effects of work hours and stress on pregnancy in female residents, although these are mostly retrospective self-report studies which examine the impact of work load, rather than sleep loss, *per se*. Some studies did not find any adverse effects of work on the fetus, but others found significant relationships between occupational fatigue and premature birth, especially in residents working more than 100 hours per week. Other problems included pregnancy-induced hypertension, abruptio placenta and pre-term labor, low birth weight and intrauterine growth retardation.⁴

Another risk to physical health is that of motor vehicle accidents experienced by sleep-deprived residents, particularly post-call and following night shifts. Lack of sleep can lead to lapses in attention from very brief "microsleeps," when the individual has not even recognized the microsleep. Again, most of this work has been based on retrospective self-report studies. For instance, in one study residents reported receiving more traffic citations and experiencing more **motor vehicle collisions (MVCs)** on post call days than on other days; 44% of residents surveyed also admitted to falling asleep while stopped at red lights.⁵ Another study, after showing that MVCs were positively related to the number of night shifts worked per month, concluded that driving home after night shifts presented a serious occupational risk for residents⁶ - both for the residents themselves and for others on the road.

IMPACT ON RESIDENTS' PERFORMANCE

A number of studies have probed the effects of sleep deprivation on performance, using neurobehavioral tests, including neuropsychological and psychomotor assessments, as well as on simulated tasks involving common medical procedures. Reaction time, manual dexterity, and memory recall are among the parameters typically affected by sleep loss in these studies. One common theme is that the speed or efficiency of task completion is more

likely to be affected by restricted sleep than the quality or accuracy of performance. In terms of subjective self-report, however, many residents felt unable to perform at their optimal level when they had not received sufficient sleep.

Another common finding is that tests involving longer periods of sustained vigilance are more sensitive to sleep deprivation, as are newly-learned tasks, although increased mental effort can mitigate these effects in the short-term. One study found that partial sleep deprivation produces a higher decrement in performance than either long-term or short-term sleep deprivation. In addition, an individual's performance after being awakened from sleep or even when anticipating being awakened from sleep suffers in comparison to that during normal waking.

Several studies have simulated medical procedures to measure the effects of sleep deprivation. The same decrements found in neuropsychological tests are found in these simulated tasks; i.e., more significant declines in speed of completion compared to accuracy. This trend has been found in tests that involve procedural skills. For instance, in one study residents with sleep deprivation took more time to perform a simulated intubation task than did non-fatigued residents.⁷ At least one study found that sleep-deprived residents made more mistakes interpreting ECGs than those who were rested. Documentation of medical histories has also been shown to be affected by sleep loss. A number of studies, however, failed to find a significant effect of sleep deprivation on performance of some clinical tasks or failed to find performance decrements with specific groups, such as surgical residents.⁸

IMPACT ON MEDICAL EDUCATION

Surveys of medical students as well as residents report a correlation between the amount of sleep loss and their perceived ability to learn and retain information. With sleep loss, many people experience a decrease in motivation-to-learn. There have been mixed results as to the impact of sleep-deprivation on standardized test scores. Fi-

nally, in one study of surgical residents which utilized sleep logs and monthly surveys of operative participation, every other night call was associated not only with increased levels of fatigue and stress and decreased overall satisfaction, but also with participation in fewer operative cases per month compared to every third and every fourth night call schedules.⁹ This finding suggests that, contrary to common wisdom, increased time in the hospital is not necessarily associated with increased opportunity for learning.

IMPACT ON MEDICAL ERRORS

The fact that sleep deprivation has been shown to alter performance has led to speculation that these decrements in performance increase the incidence of medical errors. Attempts to correlate sleep loss and fatigue in medical trainees with adverse clinical outcomes have included both surveys of provider-identified risk factors for medical errors, and antecedent studies of actual reported errors. For example, 61% of anesthesiologists in the US and 86% in Australia report having made fatigue-related errors.¹⁰ Surveys of trainees' perceptions of risk factors for medical errors have linked prolonged work hours, fatigue, and lack of sleep and self-reported decreased efficiency in performance of work-related tasks commission of medical errors while on call, and overall compromised quality of patient care.¹¹ In one investigation almost half of residents cited fatigue as the cause of their most significant medical mistake.

Few studies have examined the contribution of sleep deprivation to actual medical errors; and most of these studies can only implicate, rather than prove, sleep deprivation as an important causal factor. In one study of anesthetic incidents in New Zealand, fatigue-related events constituted 2.7% of the 5600 reported errors occurring over a 10 year period.¹² In an Australian study, fatigue was considered a contributing factor in 10% of medication errors.¹³ A study of serious anesthesia incidents found that one half were related to factors potentially correlated with fatigue, such as decreased vigilance. Some of the medical occu-

pational tasks that have been shown to be impaired in sleep-deprived medical students or physicians include ordering medications, monitoring anesthesia, documenting patient histories, and performing surgical operations. Other studies, however, have found no significant correlation between lack of sleep and increased medical mishaps. One study¹⁴ that looked at surgical complications in relation to call status of the operating surgical resident failed to find any significant differences in post-operative complication rates.

CONCLUSION

The literature on the precise effects of sleep and fatigue on medical trainees is not conclusive. Research findings overall point to a potentially negative impact on the quality of life of medical residents, on their ability to fulfill their clinical responsibilities, and on the opportunity for them to benefit optimally from the training regimen. We know little about the relative efficacy in the medical setting of various proposed remedial strategies, including regulation of work hours and implementation of alertness management and "countermeasure" (napping, strategic caffeine use, etc), used successfully the transportation and aeronautics industries. For example, one study used a "night float" coverage system, but found that the "covered" residents slept less than the residents who were not relieved by the night float: the "covered" residents did not sleep, but caught up on work.¹⁵ Ultimately, effective interventions for sleep loss and fatigue in medical training will involve a combination of approaches that includes education about sleep and sleep hygiene, sophisticated monitoring systems for medical errors, work hour regulations, and a shift in the "culture of medicine" to one which emphasizes the well-being both of physicians and patients.

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Approach To the Sleepy Patient

Rakesh M Gupta, MD

Excessive daytime sleepiness (EDS) and insomnia are two major symptoms of sleep disorders. Although insomnia is more prevalent, sleepiness has been the predominant reason for patients' referral to sleep disorders clinics. Patients with insomnia may have daytime sleepiness due to the lack of sleep or from a separate cause. The National Sleep Foundation's 2001 "Sleep in America" poll found that one in five adults (22%) is so sleepy during the day it interferes with daily activities a few days a week or more. When they feel sleepy during the day, two-thirds of those surveyed (65%) say they are very likely to accept their sleepiness and keep going, apparently disregarding its effects. This article will primarily focus on the basic physiology relevant to genesis of sleepiness, differential diagnosis and methods of evaluating EDS. References are provided for excellent reviews on individual sleep disorders.

THE PHYSIOLOGIC BASIS OF SLEEPINESS¹

Although we have made great strides in our understanding of sleep, we cannot yet answer basic questions such as "why do we sleep?"

Sleepiness/alertness is a continuum of behavioral states rather than all or none phenomenon. Conceptually, sleepiness can be considered a composite of three factors: physiologic sleepiness, manifest sleepiness and introspective sleepiness.

Physiologic sleepiness is the result of biological drive to sleep. At a given moment, the following factors (Figure 1) influence that drive:

1. Homeostatic sleep drive (sleep pressure) influenced by²
 - * duration of wakefulness and quantity of prior sleep or "sleep debt"
 - * quality of sleep
2. Time of the day - Circadian rhythm factor²
3. Sleep inertia - the period of reduced alertness following awakening³

As the sleep debt increases, sleepiness increases. This feeling is modulated by the circadian rhythm, which provides the alerting signal (mediated by suprachiasmatic nucleus - the master clock). Sleep inertia is usually brief (a few minutes) in normal individuals but can be considerably prolonged in subjects with increased sleep debt (due to sleep deprivation or sleep disorders). More drowsy feeling is noted if waking out of slow wave sleep compared to other stages.

Manifest sleepiness is the behavioral effect of physiologic drive modulated by individual motivation and environmental factors (soporific v/s active situations) - ranging from droopy eyelids, reduced performance to actual episodes of involuntary sleep in spite of volitional efforts to stay awake.

Introspective sleepiness is the ability of an individual to judge the internal state. Most individuals can clearly feel the sleepiness after acute sleep loss; but when sleep loss is chronic or onset of sleep disorder is insidious, the person becomes habituated to the symptoms, and underestimates the sleepiness. This failure to recognize sleepiness can not only prevent a person from seeking medical evaluation but can also precipitate accidents (automobile and/or industrial) and loss of productivity.

SLEEP REQUIREMENTS AND SLEEP DEBT⁴

The sleep need is defined as the amount of sleep needed to feel alert and rested during wake period. Sleep Debt accumulates if the average amount of sleep is less than an individual's need. Most individuals need 7-8 hours of sleep/24 hours. Individual variations from 4-10 hours are known to exist, but are uncommon. These variations are determined to a large extent by genetic makeup e.g. the CLOCK gene

Table 1. Common Causes of Excessive Sleepiness

Behavioral or Lifestyle issues

- Insufficient sleep syndrome
- Inadequate sleep hygiene

Primary disorders of sleepiness

- Narcolepsy
- Idiopathic CNS hypersomnia
- Post-Traumatic hypersomnia

Disorders causing fragmented sleep

- Obstructive sleep apnea/hypopnea syndrome
- Upper airway resistance syndrome
- Other sleep related breathing disorders - central sleep apnea, nocturnal hypoxemia in severe lung diseases (obstructive or restrictive including neuromuscular or kyphoscoliosis related restriction), obesity hypoventilation syndrome
- Restless Legs Syndrome
- Periodic Limb Movement Disorder
- Other Medical conditions - chronic pain of any cause, pulmonary (e.g. poorly controlled asthma or COPD), GI (e.g. acid reflux, IBS), nocturia, other disorders that may disrupt sleep.

Circadian Rhythm Disorders

- Shift work sleep disorder
- Delayed sleep phase syndrome
- Advanced sleep phase syndrome

Medications and Sleepiness

- Hypnotics, antihistamines, antidepressants, narcotic analgesics, anticonvulsants, neuroleptics
- Drug or alcohol abuse

Psychiatric disorders

- Depression
- "Psychogenic hypersomnia"

Other CNS disorders (many causes - only few examples are listed)

- Strokes
- Tumors
- Multiple Sclerosis

regulating the length of circadian cycle. Our natural sleep requirements have not changed, but artificial light and modern lifestyle have reduced our sleep time by 25% over the last century. Thus, as a society, we are living under a higher sleep pressure. This can magnify the impact of sleep disorders. It is not an uncommon clinical experience to see patients with obstructive sleep apnea who habitually sleep 6 hours and complain of EDS as well as patients who have increased their TST (total sleep time) to compensate. These patients may deny feeling sleepy.

THE OFFICE EVALUATION OF A SLEEPY PATIENT Identifying Sleepiness

EDS may be difficult to recognize because the patient uses a multitude of nonspecific terms to describe the feeling. Also, the patient may discount the sleepiness, believing, erroneously, that "it is normal to feel sleepy in a boring or monotonous situation." Because the onset of symptoms is often insidious, it is not uncommon for patients to deny sleepiness only to be countered by collateral observations of the spouse. Compensatory strategies may mask sleepiness too; e.g. extending total sleep time to prevent sleepiness when awake, or accepting reduced pace or efficiency to avoid errors at work.

While some patients are alarmed when they fall asleep while driving, often they complain of tiredness, fatigue, poor motivation, poor attention/concentration, not feeling refreshed or lack of energy, which may all be consequences of sleepiness but are nonspecific. It is a challenge for most patients to describe their internal physiologic state. Because of the high prevalence of sleep disorders and the fact that most of them are treatable, a high index of suspicion should be maintained for sleep disorders.

History and Physical Exam

Once sleepiness is identified as the clinical issue, the patterns of sleep and rest and the variations in these routines, especially on weekends, can provide an estimate of average total sleep time per 24 hours. Sleep diaries and sleepiness scales are helpful tools. A longer sleep

period on weekends along with short, fairly consolidated nocturnal sleep period and improvement in symptoms following longer sleep periods (as on vacations) is typical of inadequate sleep time. Other symptoms that are specific to the sleep disorder causing sleepiness should also be looked for.

...artificial light and modern lifestyle have reduced our sleep time by 25% over the last century.



Obstructive sleep apnea syndrome (OSAS)⁵ is the most common cause of EDS identified in sleep disorders clinics. It is characterized by loud snoring, episodes of apnea usually observed by spouse or awakening with a gasping/choking sensation. Obesity, increased neck size (>17" in males, >16" in females), retrognathia, and hypertension also predict increased risk of OSAS. It is not clear how common sleep apnea is but it is at least as common as asthma in adults and is frequent in the elderly.

Narcolepsy⁶ results from intrusion of **rapid eye movement (REM)** sleep components (skeletal muscle paralysis, vivid dreams) into wakefulness or **non rapid eye movement (NREM)** sleep. It typically starts in teens or early adulthood and is characterized by unwanted episodes of sleep, sleep paralysis (transient feeling of paralysis on arousing from sleep), sleep onset hallucinations and cataplexy (sudden loss of muscle tone triggered by laughter or other strong emotion resulting in fall, buckling of knees or barely noticeable sagging of jaw; without impairment of consciousness). While cataplexy is more specific for narcolepsy, many patients present only with EDS.

With **restless legs syndrome (RLS)**⁷ patients may find it difficult to describe their symptoms but typically have disagreeable sensory feelings in the legs that create an irresistible urge to move legs. Movement (stretching, walking) provides temporary relief. These symptoms are most prominent at bedtime or when relaxing. The urge to

move, relief with movement and circadian pattern of symptoms are important to differentiate RLS from akathisia, anxiety, neuropathy or musculoskeletal complaints. Spouse may report involuntary leg jerks during sleep but periodic leg movement disorder is primarily a polysomnographic diagnosis.

Idiopathic **central nervous system (CNS) hypersomnia**⁸ represents EDS (documented by a **multiple sleep latency test (MSLT)**) of neurological origin when other causes have been excluded. Patients generally report a long nocturnal sleep period with few awakenings and still feel sleepy in daytime. They may feel unrefreshed even after long naps.

Circadian rhythm sleep disorders⁹ typically present with nocturnal insomnia and daytime sleepiness. The cause of symptoms is the desynchrony between circadian clock and expected behavior. With delayed sleep phase syndrome (clock period >24 hours), commonly seen in adolescents and young adults, the pattern is one of difficulty falling asleep at night and morning sleepiness. In contrast, advanced sleep phase (clock period <24 hours), commonly seen in elderly, results in evening sleepiness, tendency to go to bed early and early morning insomnia. In both conditions, in absence of social pressures, if the individuals could follow their preferred sleep schedule, their awake performance will be normal.

Shift work sleep disorder¹⁰ is most prominent in night shift workers. Most individuals return to diurnal pattern on days off work. Shift workers consistently report reduced total sleep time. Sleepiness, fatigue, gastrointestinal dysfunction and performance decrements are common symptoms. Increased cardiovascular morbidity is seen in shift workers. In addition to circadian rhythm disturbances, social aspects contribute significantly to overall impact of shift work.

Although sleep disturbance is commonly seen with stress and mood disorders, sleepiness out of proportion to mood disturbance usually indicates a coexisting sleep disorder.

Physical exam reveals various upper airway abnormalities in patients with OSAS. In most other primary sleep disorders, exam primarily serves the

Table 2: Epworth Sleepiness Scale

How likely are you 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 choose 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 theater 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 a lunch without alcohol	_____
In a car, while stopped for a few minutes in traffic	_____

purpose of identifying co-morbid conditions or secondary causes of sleepiness.

QUESTIONNAIRES OR SLEEPINESS SCALES:

Epworth Sleepiness Scale (ESS) (Table 2) which measures introspective sleepiness is designed to assess overall behavioral sleepiness and is useful for identifying sleepiness in situations commonly encountered in daily life. Because not all patients have experienced all 8 situations, patients are asked to imagine how they might feel in those situations. Patients must distinguish sleepiness from fatigue or depressed feelings. These factors limit the usefulness of the ESS to an adjunct to clinical evaluation. While a score of 10 or more should raise a red flag prompting further evaluation of sleepiness, a lower score does not exclude significant sleep disorder.

OBJECTIVE EVALUATION OF SLEEPINESS

Polysomnography¹¹

An overnight polysomnography is indicated in most patients with EDS. It is primarily used to identify sleep disorders such as OSAS or **periodic limb movement disorder (PLMD)** rather than measuring sleepiness. OSAS is defined by an apnea-hypopnea index > 5/hour. Some patients have loud snoring and increased arousals (which

can be identified as respiratory effort related arousals if esophageal pressure is monitored too) but have an **apnea hypopnea index (AHI)**<5. These patients are grouped under the diagnosis of upper airway resistance syndrome. PLMD is defined by a periodic leg movement index of > 5/hour. The prevalence of PLMD increases with age and is almost 30% by age 50. While 80% of patients with restless legs syndrome have PLMD, most patients with PLMD are asymptomatic.

MEASURING PHYSIOLOGIC SLEEPINESS¹²

Multiple Sleep Latency Test (MSLT)

MSLT documents EDS. Its main use is for the diagnosis of Narcolepsy and Idiopathic CNS hypersomnia. The time taken to fall asleep in a standardized sleep conducive environment, repeated 4 to 5

times at 2 hour intervals after morning awakening throughout the day (to account for circadian effects) when patient is not resisting sleep is measured as sleep latency. To avoid the effects of inadequate prior sleep, the patient keeps a sleep diary for 1-2 weeks before MSLT. CNS active medications, which may affect REM sleep or sleepiness, are discontinued for 1-2 weeks. Polysomnography is performed on the night preceding MSLT to ensure adequate sleep time and rule out other sleep disorders. The mean of sleep latencies (the time from lights out to first epoch of recorded sleep, inability to fall asleep in 20 minutes results in sleep latency of 20 minutes for that nap) is more than 10 minutes in normal individuals. Mean sleep latency of < 5 minutes indicates pathologic sleepiness, 5-8 minutes indicates milder EDS and 8-10 minutes is considered gray zone. In addition to EDS, presence of 2 or more sleep onset REM episodes (REM sleep occurring within 15 minutes of first recorded sleep) is required for the diagnosis of narcolepsy.

MEASURING MANIFEST SLEEPINESS Maintenance of Wakefulness Test (MWT)

The procedure followed for MWT is the same as MSLT except the patient is left in a sitting position in bed, asked

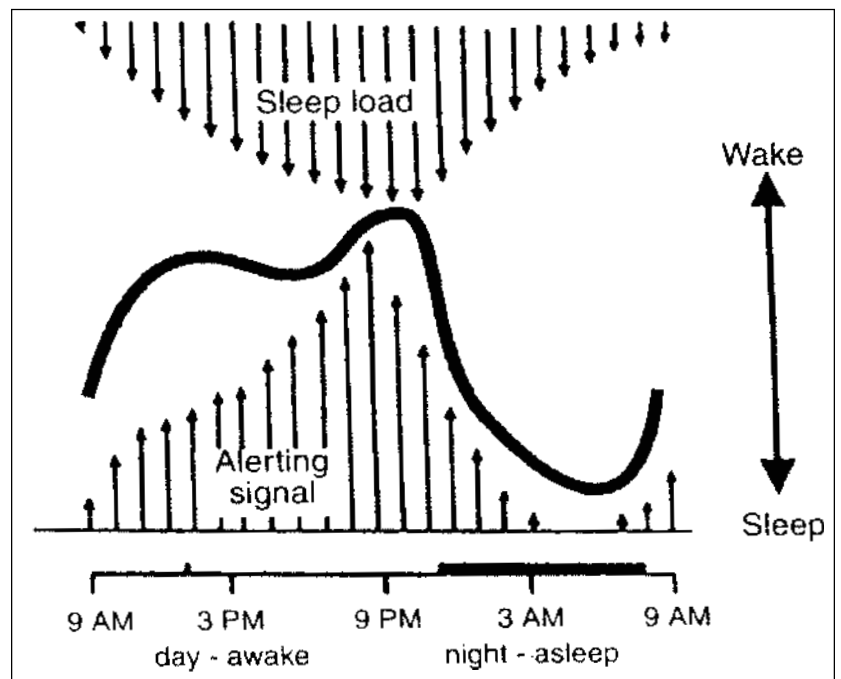


Figure 1. Regulation of sleep. The opponent process model proposes that the suprachiasmatic nuclei have an alerting function, opposing the sleep load that accumulates across the waking period. (Reprinted with permission from Kilduff² (p143).

to stay awake and monitored for 40 minutes each time. Mean sleep latency from 4-5 naps measures patient's ability to stay awake. Its primary use is to follow treatment effects, as ability to stay awake is more relevant clinically. Normative data are not as robust as for MSLT. While it is impossible to fake EDS on MSLT, patient cooperation is important for reliable MWT results.

Performance and vigilance tests (PVT)

These tests measure ability to sustain attention or identify cognitive slowing. They are primarily used in a research setting.

PUTTING IT ALL TOGETHER

Unless insufficient sleep or other explanation clearly accounts for the degree of sleepiness, polysomnography is indicated. An exception can be made for the patient with typical symptoms of RLS and no symptoms suggestive of coexisting sleep disorder. Treatment for RLS can be initiated on the basis of clinical diagnosis but polysomnography should be done if sleepiness is not corrected by treatment. If narcolepsy is suspected, no obvious cause is identified clinically or if there is doubt whether patient's symptoms represent true sleepiness, nocturnal polysomnography followed by MSLT the next day is helpful. EDS with > 2 SOREMs are typical of narcolepsy. EDS without SOREMs, in the absence of other identifiable sleep disorder by history or polysomnography suggests idiopathic hypersomnia. A patient may have two or more sleep disorders. A sequential approach is generally taken in such patients by treating the most prominent disorders first. For example, a patient with OSAS and mild RLS is often treated for OSAS first followed by RLS treatment if indicated. Some patients with OSAS report residual sleepiness after adequate treatment. A repeat polysomnography followed by MSLT is a reasonable approach in such patients and usual criteria for the diagnosis of narcolepsy or idiopathic hypersomnia are applied. As PLMD is com-

mon but not always clinically significant, whether it is an adequate explanation for sleepiness has to be decided in an individual patient based on history and subtleties of polysomnographic findings.

TREATMENT OF EXCESSIVE SLEEPINESS¹³

Treatment of the underlying cause is important. In disorders where sleepiness is of CNS origin such as narcolepsy or idiopathic hypersomnia, or in other disorders when symptomatic treatment is necessary, stimulant agents can be used. Availability of Modafinil[®], which is a centrally acting wake promoting agent without the addictive or cardiovascular side effects of amphetamines, has made treatment of sleepiness easier. Strategically scheduled brief naps can be a useful therapeutic adjunct.

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