Cover: *"Nude,"* pastels, by David Maroni, a Rhode Island artist who works primarily in pastels.

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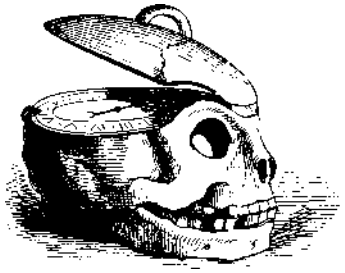
COMMENTARIES

"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 dramatically, 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 faciliated 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 abhorent 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 distateful 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.

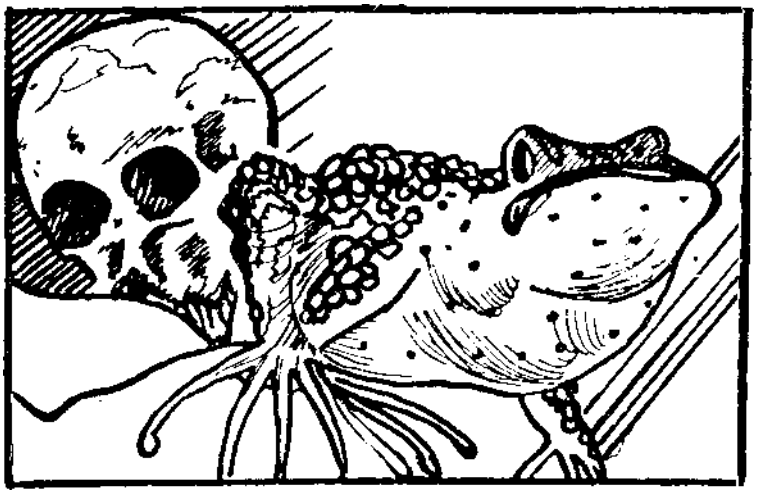
Shakespeare did not write his memorable plays in splendid isolation. His dramas reflected the fears, superstitions, and prejudices of the early 17th Century populace; and, accordingly, each of the ingredients in this witch's brew was known for its alleged magical powers. Some even represented standard 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 concotion 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 malevolvent 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, alll 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, delerium 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 concotions. But for something as monumental as a Scotttish 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 accidents[4] and cardiovascular complications. Associations have been made between obstructive sleep apnea and cerebrovascular disease,[5] angina, myocardial infarction[6] 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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Richard P. Millman, MD, is Director, Sleep Disorders Center of Lifespan Hospitals, and Professor of Medicine, Brown Medical School.

Correspondence:
Richard P. Millman, MD
Division of Pulmonary, Sleep and Critical Care Medicine
Rhode Island Hospital
593 Eddy Street
Providence, Rhode Island 02903
phone: (401) 444-2670
fax: (401) 444-3353
E-mail: Rmillman@Lifespan.org

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 residents[6] - 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. Finally, 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 occupational 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 study[14] 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 fufill 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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Judith A. Owens, MD, MPH, is Director, Pediatric Sleep Disorders Clinic, Hasbro Children's Hospital, and Associate Professor of Pediatrics, Brown Medical School.

Jennifer Blum is an undergraduate at Brown University.

CORRESPONDANCE:
Judith Owens, MD
Ambulatory Pediatrics
Rhode Island Hospital
593 Eddy St.
Providence, RI 02903
phone: (401) 444-8280
fax: (401) 444-6218 fax
e-mail: Owensleep@aol.com

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 Sleepiness[1]

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 by[2]
   * duration of wakefulness and quantity of prior sleep or "sleep debt"
   * quality of sleep
2. Time of the day - Circadian rhythm factor[2]
3. Sleep inertia - the period of reduced alertness following awakening[3]

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 Debt[4]

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.

Narcolepsy[6] 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 disorders[9] 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 disorder[10] 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

Polysomnography[11]

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 Sleepiness[12]

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

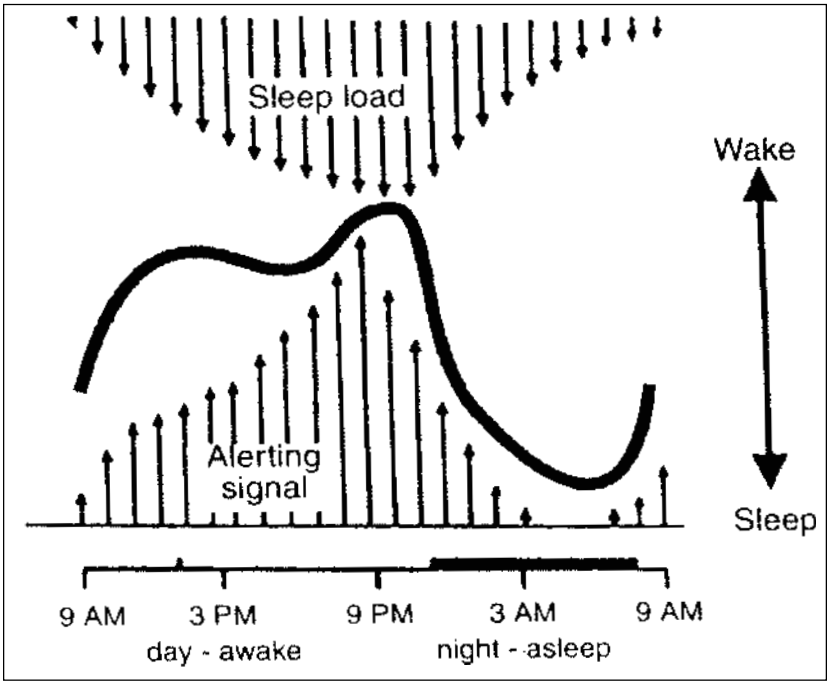

Figure 1. Regulation of sleep. The opponent process model proposes that the suprachiasmatic nuclei have an alerting function, opposing the sleep load that accumulates across the waking period. (Reprinted with permission from Kilduff[2] (p143).

to stay awake and monitored for 40 minutes each time. Mean sleep latency from 4-5 naps measures patientís 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 common 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 Sleepiness[13]

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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Rakesh M. Gupta, MD, is Director, Sleep Disorders Center, Division of Pulmonary, Critical Care and Sleep Medicine, Roger Williams Medical Center, and Assistant Professor of Medicine, Boston University School of Medicine.

Correspondence:
Rakesh M. Gupta, MD
Division of Pulmonary, Critical Care and Sleep Medicine
Roger Williams Medical Center
825 Chalkstone Avenue
Providence, RI 02908
phone: (401) 456-2302
fax: (401) 456-2016
e-mail: rgupta@pol.net

Behavioral Treatment for Chronic Insomnia

J. Todd Arnedt, PhD, Jennifer L. Martin, PhD, Donn A. Posner, PhD

Insomnia is a subjective complaint of insufficient or non-restorative nighttime sleep.[1] In a recent Gallup survey, 49% of US adults reported having occasional insomnia, while 12% reported having chronic insomnia.[2] In primary care settings, the overall prevalence of insomnia complaints may be as high as 69%.[3] Women are more likely than men to report problems sleeping,[2] and psychiatric and medical disorders are associated with an increased risk of insomnia complaints.

Insomnia is associated with adverse consequences, including daytime fatigue and sleepiness, decreased quality of life and deficits in daytime functioning.[4] Individuals with insomnia utilize more healthcare resources, miss more days of work, and report less rewarding interpersonal relationships.[5] Although sleep problems are common, many patients with insomnia do not discuss their complaints with their physicians.[2] People erroneously believe that sleep problems are normal as we get older, or are unaware that effective treatments for chronic insomnia exist that do not involve medication. It is the physician's responsibility to ask patients about sleep quality in the course of providing routine care.

The Evolution of Chronic Insomnia

Insomnia develops from the confluence of predisposing, precipitating, and perpetuating factors.[4] Predisposing factors can include age, gender, excessive worry, or depression. All can lower the threshold for developing insomnia. Precipitating factors are commonly defined as stressful life events (e.g., loss of employment, newly-diagnosed medical illness) that herald the onset of acute insomnia. In the face of such stressors, an individual may have transient difficulties with sleep initiation, frequent or extended nocturnal awakenings, or early morning awakenings with an inability to return to sleep. It is generally assumed that such individuals slept well before the onset of the stressor, and that the sleep problem is likely to remit once the stressor resolves. The patient is often best served by simple reassurance that the sleep problem will resolve with time. If the stressor is more severe and has a predictable course, the short-term use of hypnotic medication would be considered the treatment of choice.[6]

Perpetuating factors can be ongoing conditions or behaviors that are initiated to relieve the transient sleep problem, but instead exacerbate the difficulties. Chronic insomnia results when difficulties initiating and/or maintaining sleep occur three or more nights weekly for at least six months.[1] The primary focus of behavior therapy is to change these perpetuating factors.

Individuals with insomnia tend to spend excessive time in bed to compensate for sleep loss.

Medications and Chronic Insomnia

In the case of chronic insomnia, hypnotic medication is not recommended for long-term management.[7] There is little information about the long-term efficacy of hypnotic medications for chronic insomnia or the maintenance of benefits once medications are discontinued.[8] Other problems include drug tolerance, daytime hangover, dependence, and rebound insomnia. Finally, insomnia is a symptom of a variety of conditions including psychological (e.g., anxiety, depression), neurological (e.g., Parkinson's disease), medical (e.g., thyroid disorder, chronic pain) or other sleep disorders (e.g., sleep apnea, restless leg syndrome). Under these circumstances sedative-hypnotic medications cannot be considered more than a short-term band-aid.

Primary Insomnia

Chronic insomnia often results from inappropriate sleep-related behaviors (e.g. irregular sleep schedule, frequent napping), poor sleep habits (e.g. caffeine overuse, lack of exercise), and/or maladaptive thinking (e.g. excessive anxiety, worry, and rumination about sleep). Such a "Primary Insomnia" can exist as a co-morbid condition that persists after other causes have been treated. For example, the patient who becomes anxious about not sleeping after insomnia originally developed during an episode of depression may have improved mood with anti-depressant medications, yet continue to exhibit sleep problems. Rather than adding hypnotic medication, in these cases non-pharmacological, behavioral interventions are indicated.

The aim of the remainder of this paper is to highlight important assessment issues, and to outline some of the most effective behavioral techniques. These techniques are time-intensive and are likely best delivered by a behavioral sleep medicine specialist.

Assessment of Insomnia

A thorough evaluation of the predisposing, precipitating, and perpetuating factors of insomnia is critical. The assessment should clarify the nature and severity of the insomnia, and also reveal clues as to the insomnia's etiology. At a minimum this should consist of a clinical interview with the patient, and daily sleep diary monitoring. Patients often overestimate the frequency of insomnia. When patients prepare daily logs of their sleep, they often find that this is not the case. Typically, polysomnography is not included in the assessment of insomnia unless there is an indication that medical factors or a physiological sleep disorder (e.g., sleep apnea) are the primary etiological factors. If a patient with insomnia does undergo polysomnograpy, it is not unusual to

find that the patient overestimates how long it takes to fall asleep and underestimate how long s/he slept. Typically, sleep architecture will demonstrate an increase in light Stage 1 sleep and perhaps a deficiency in deep Stages 3-4 sleep.

The clinical interview

The clinical interview is a detailed analysis of the nature, severity, and historical course of the presenting sleep complaint. A good interview should rule out or identify medical, neurological, and psychological etiologies. A complete account of medications, as well as alcohol and other psychoactive substances (e.g., caffeine, nicotine) is essential for clarifying the interaction between medications and nighttime sleep patterns and daytime alertness or sedation. A thorough history of patients' sleep habits including exercise, naps, bed and wake times, meal times, and nighttime activities should be obtained. Finally, information should be collected regarding patients' thoughts and worries when they cannot sleep with special emphasis on ruminations about sleeplessness and/or daytime consequences of sleep deprivation.

Sleep Diaries

The final step is a baseline assessment of typical sleep patterns by means of a nightly sleep diary maintained by patients. (Figure 1) We suggest a minimum of a two-week baseline period in order to provide a representative sample of usual sleep patterns. Once this information is compiled, a behavioral protocol can be implemented using one or more of the following techniques: Sleep Restriction, Stimulus Control, Sleep Hygiene education, Relaxation, and Cognitive techniques.

Components of Behavioral Therapy for Insomnia

Sleep Restriction

Sleep restriction curtails the time spent in bed each night to the estimated average total sleep time.[9] Individuals with insomnia tend to spend excessive time in bed to compensate for sleep loss. Contrary to expectation, this practice exacerbates and perpetuates the sleep problem by promoting fragmented, rather than consolidated, sleep. The initial goal of sleep restriction is to consolidate sleep over a prescribed "sleep window" no longer than the current average total sleep time based on data from the patient's sleep diary. The goal is to raise sleep efficiency (total sleep time/total time in bed) to greater than 85%. Once this goal is achieved, time in bed is progressively extended by moving the bedtime earlier until an "ideal sleep duration" is achieved. Morin[4] recommends increasing time in bed by 15 minutes every four days when sleep efficiency is greater than 85%, reducing it by 15 minutes when sleep efficiency is less than 80%, and keeping it constant when sleep efficiency falls between 80-85%. The determination of "ideal sleep duration" is based on a host of considerations, including sleep log data (e.g. the point just prior to a decline in

SLEEP DIARY
Rhode Island Hospital Insomnia Treatment Program

Name: _____ Week Ending: ___/___/___ Next Appointment: ___/___/___@___am/pm

Fatigue Rating Scale	0 extremely fatigued	25 moderately fatigued	50 mildly fatigued	75 somewhat energetic	100 very energetic

COMPLETE AT NIGHT in reference to today — COMPLETE IN MORNING in reference to previous night

Date	Unusual daytime stressors	Fatigue rating	Naps: Time & sleep length	Time you went to bed	Time it took you to fall asleep initially	Number of awakenings	Amount of time awake in the middle of the night	Time you got up for good	Total sleep time	Medication(s) used to sleep

Figure 1: Example of a daily sleep diary.

Table 1. Stimulus Control Instructions Bootzin & Nicassio[10]

1. Lie down intending to go to sleep only when sleepy.
2. Do not use your bed for anything except sleep; that is, do not read, watch television, eat, or worry in bed. Sexual activity is the only exception to this rule. On such occasions, the instructions are to be followed afterward when you intend to go to sleep.
3. If you find yourself unable to fall asleep, get up and go into another room. Stay up as long as you wish and then return to the bedroom to sleep. Although we do not want you to watch the clock, we want you to get out of bed if you do not fall asleep immediately. Remember that the goal is to associate your bed with falling asleep quickly! If you are in bed more than about 10 min without falling asleep and have not gotten up, you are not following this instruction.
4. If you still cannot fall asleep, repeat rule 3. Do this as often as is necessary throughout the night.
5. Set your alarm and get up at the same time every morning regardless of how much sleep you got during the night. This will help your body acquire a consistent sleep rhythm.
6. Do not nap during the day.

sleep efficiency), and patient report (e.g. significant improvement in daytime functioning).

While straightforward in theory, sleep restriction is often difficult to implement. Fearing "sleep loss," patients may initially be skeptical of the rationale and resist going to bed later than usual. They may need to be reassured frequently and reminded about the rationale. Sleep restriction can be integrated with other techniques such as stimulus control and sleep hygiene education.

Stimulus Control

Insomnia may also develop as a result of classical conditioning factors, where environmental sleep cues (bed/bedroom) become associated with wakefulness and sleep-incompatible behaviors (e.g. worrying, watching television). The primary goal of stimulus control therapy is to re-establish the connection between stimuli associated with sleep (e.g. the bed) and sleep itself.[10] This is typically achieved by discouraging sleep-incompatible behaviors in the bedroom, by reinforcing a regular sleep-wake schedule, and instructing patients to be in bed only when sleepy. (Table 1)

Encouraging adherence to stimulus control instructions can be a difficult task for the clinician. Patients may resist getting out of bed when awake during the night, or rising on time in the morning. The clinician should reiterate the rationale for the approach and help patients overcome barriers to successful treatment.

Sleep Hygiene Education

Sleep hygiene education focuses on general health behaviors and environmental factors that interfere with or facilitate sleep.[4] Although rarely the primary cause of chronic insomnia, poor sleep hygiene can limit the degree to which sleep duration can be increased during the extension phase of sleep restriction, and may increase the likelihood of insomnia relapse. Changing only one habit (e.g. stopping caffeine intake), particularly while maintaining several other poor habits, will rarely improve sleep. Thus, patients should adhere to as many good habits at once as possible. Likewise, changing habits for only a few days may not insure results. Good sleep hygiene should be considered a lifestyle change and should be implemented for 3-4 weeks before results can be expected. (Table 2)

Relaxation Therapy

Relaxation techniques can help in the treatment of insomnia as well. Clearly not all insomnia patients have anxiety disorders, but many are anxious specifically about their inability to sleep. Patients may also simply be physically tense. Studies of biofeedback training suggest that, when insomnia patients learn the techniques, their sleep quality improves.[11] Controlled studies examining progressive muscle relaxation have also shown that treatment improved subjective sleep quality.[12] Although relaxation therapies are more effective than placebos, they are generally less effective than other behavioral therapies.[13] Relaxation therapies are often part of multi-component treatments, and can be beneficial in combination with other strategies.

Cognitive-Behavioral Therapy

Cognitive-behavioral therapy (**CBT**) for insomnia refers to a group of treatments that target inappropriate

Table 2. Rules For Better Sleep Hygiene

1. Sleep only as much as you need to feel refreshed and awake during the day.
2. Wake up and go to bed at approximately the same time every day of the week.
3. Do not lie in bed if you cannot sleep.
4. Do not nap during the day.
5. Spend time outside in the light each day.
6. Exercise regularly but not within 3 hours of bedtime.
7. Make sure that your bedroom is comfortable, dark, and quiet.
8. Eat regular meals and eat a light snack before bed. Carbohydrates (e.g. crackers, bread, cereal) are best for a good nights sleep.
9. Do not consume caffeinated products (e.g. coffee, tea, many sodas, chocolate) in the evening.
10. Do not use alcohol to help you sleep and do not consume alcohol too close to bedtime.
11. Smoking disrupts your sleep.
12. Make the last hour before bed a "wind-down" time.

sleep-related behaviors and maladaptive sleep-related cognitions.[4] The behavioral component of CBT is typically some combination of the treatments outlined above. The cognitive component targets inaccurate beliefs and attitudes about sleep. Insomnia patients sometimes believe that "If I try hard enough, I'll fall asleep." Patients also "catastrophize" their sleep difficulties believing, for example, "If I don't catch up on sleep, I'll die." These beliefs perpetuate anxiety and insomnia, leading to more catastrophic thinking. Cognitive strategies challenge these thoughts directly, or through "evidence" collected by Socratic interviewing of the patient. For example, patients can be asked to count the number of catastrophic events that have occurred to them since the insomnia began. Although disruptive, insomnia rarely has catastrophic consequences in the short run. Such questioning forces the patient to re-evaluate his/her fears.

Efficacy Of Behavioral Interventions For Chronic Insomnia

Both single- and multiple-component treatment outcome studies have included samples ranging from general insomnia patients to specific sub-groups with insomnia such as older adults, and patients with psychiatric or medical disorders.[12] Two meta-analyses of more than 50 treatment studies found that behavioral interventions were effective in 70-80% of patients with primary insomnia with improvements in sleep latency and time awake after sleep onset to near-normal values.[13,14] Clinical studies commonly use multicomponent treatments that include sleep restriction, stimulus control, and sleep hygiene education.[15] These demonstrate efficacy for patients who complete treatment, and some data suggest that improvements are maintained or improved for at least several months after treatment ends. Patients also seem to prefer behavioral rather than pharmacological techniques to manage their insomnia.[16]

Behavioral and Pharmacological Interventions

Combined treatments

One drawback to behavioral treatment for insomnia is that it typically takes 4-6 weeks before the patient notes marked improvement. In some instances, the patient will fail to comply with the treatment protocol, or discontine treatment. In contrast, sedative-hypnotic medications ameliorate insomnia almost immediately. This would seem to suggest that a combination of the two approaches may enhance the efficacy of either alone. Unfortunately, the few studies to examine combined treatments have yielded equivocal results.

Recently, in a placebo-controlled trial using CBT and medication (temazepam), Morin et al.[17] found that individuals who received CBT + temazepam showed the greatest improvement at the conclusion of treatment, but improvement was more consistently maintained in the individuals who received CBT alone. These findings suggest that behavioral treatments alone are most effective for the long-term treatment of insomnia, and that the initial benefits of combination treatments may not be sustained over time. It is also possible that medication withdrawal after the study led to an overall decrease in sleep quality or, perhaps, patients attributed their initial gains primarily to the medication rather than to behavior changes. Continuation of the behavioral intervention after discontinuation of the medication may have improved the maintenance of treatment gains. Thus, the question remains open whether a combination of behavioral and pharmacological approaches may be better than either treatment alone for chronic insomnia.

Medication reduction and medication withdrawal

Behavioral treatment of insomnia may be beneficial for reducing or discontinuing the use of medications for sleep. Studies have shown that patients who participate in behavioral treatment of insomnia often reduce their use of sleep medications whether or not medication withdrawal is a specific goal of treatment.[18] Often individuals treated with hypnotic medications for extended periods experience psychological and physiological withdrawal as well as rebound insomnia when they

stop the medication. Some research suggests that targeting the maladaptive thinking and providing insomnia patients with behavioral tools to assist in coping with the short-term nature of medication withdrawal insomnia can be clinically beneficial.[19]

Summary and Conclusions

Insomnia is a common medical symptom with multiple causes and consequences. Identification of the predisposing, precipitating and perpetuating factors contributing to chronic insomnia is important to a complete assessment, which can help to determine etiology and points of intervention. Sedative-hypnotic medications can be useful in the treatment of short-term insomnia. For more chronic insomnias, it is best to identify primary medical, psychological, neurological or environmental etiologies and aggressively treat these. For patients who develop perpetuating behavioral strategies or anxiety-provoking cognitive ruminations that contribute to the chronic condition, behavioral interventions may be superior to pharmacotherapy.

Although many of the described techniques are effective, however, they are difficult for patients to carry out and require careful explanation, continued support throughout the process, and follow-up care. This can be time-consuming in the context of a primary care practice. As such, there are times when a referral to a sleep specialist to carry out the treatment may be warranted.

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J. Todd Arnedt, PhD, is an Instructor in the Department of Psychiatry and Human Behavior, Brown Medical School.

Jennifer L. Martin, PhD, is a Clinical Psychology Intern in the Brown University Clinical Psychology Training Consortium.

Donn A. Posner, PhD, is a Clinical Assistant Professor, in the Department of Psychiatry, Brown Medical School.

Correspondence:
J. Todd Arnedt, PhD
Department of Psychiatry and Human Behavior
Box G-BH, Brown University
Providence, RI 02912
phone: (401) 444-1943
fax: (401) 444-1948
e-mail: J_Todd_Arnedt@Brown.edu

A Review of the Adult Primary Sleep Parasomnias

Brian Kimble, MD, Alice E. Bonitati, MD, Richard P. Millman, MD

The parasomnias are a group of disorders characterized by motor, verbal, experiential, or physiologic phenomena occurring during sleep. The phenomena are unintended and may cause distress either to the individual or significant others. The primary parasomnias describe disorders involving the process of sleep itself; the secondary parasomnias are disorders of various organ systems which manifest themselves during sleep. Examples of the latter include nocturnal seizures, cardiac arrhythmias, nocturnal angina pectoris, nocturnal asthma, and gastroesophageal reflux. This review will focus on the primary parasomnias, offering brief descriptions with treatment options. A final section will address some of the medico-legal issues surrounding the parasomnias, specifically the forensic implications of crimes committed while asleep. Multiple comprehensive reviews of this topic published elsewhere proved invaluable in the preparation of this manuscript.[1-4]

While it was once thought that the awake state was an active process compared to the passive state of sleeping (defined as the absence of wakefulness), we now know that this is not the case. Sleep is actually an active process and is composed of two entirely different states: **non-rapid eye movement (NREM)** sleep and **rapid eye movement (REM)** sleep. Each of the three states that characterize the human mind (wake, NREM, REM) is unique and involves different degrees of excitation and inhibition of various regions of the central and peripheral nervous systems. The wake state is characterized by low-voltage, fast (beta and alpha) waves on the EEG (representing cortical activation), an awareness by the individual of his surroundings, resting muscle tone, and voluntary control of motor function. NREM sleep is characterized by high-voltage, slower (theta and delta) waves on the EEG (representing cortical deactivation), lack of awareness by the individual of his surroundings, decreased muscle tone compared to the wake state, and loss of voluntary control of motor function. REM sleep is characterized by an EEG similar to that seen in the wake state (cortical activation), lack of awareness by the individual of his surroundings, absence of muscle tone (while there is activation of the motor cortex during REM, there is inhibition of the spinal motoneurons with resultant atonia[5]), and loss of voluntary control of motor function. NREM sleep usually predominates in the first 1/3 of the night while REM sleep is usually concentrated in the final 1/3 of the night.

The mechanisms governing the maintenance of these three states as well as the change from one state to another are complex. The parasomnias manifest when these mechanisms fail to function properly. This results in a rapid fluctuation between states, a fusion of features of different states, or the absence of a feature usually associated with a state. Because the manifestations are state-dependent, the primary parasomnias are commonly grouped according to the state in which they occur, namely NREM or REM.

Normal NREM Phenomena

Before discussing the abnormal NREM parasomnias, brief mention should be made of two common phenomena that may present to a physician's attention. The first, hypnagogic imagery, is the experience of dream-like sequences occurring at sleep onset. While conventional wisdom holds that dreaming is associated solely with REM sleep, this is in fact not the case. Dreaming can occur in NREM sleep as well as during relaxed wakefulness.[1] This is important to note since the presence of dream imagery at sleep onset should not necessarily be seen to imply sleep-onset REM periods, a feature common to narcolepsy (reviewed elsewhere in this issue).

The second normal phenomenon is the sleep start or hypnic jerk. Most commonly these involve sudden brief episodes of motor activity occurring at sleep onset. They can also involve sensory phenomena of a visual, auditory, or somesthetic nature. While normal, the pathophysiology is not understood.

NREM Parasomnias (Disorders of Arousal)

Perhaps the most common parasomnias, the disorders of arousal encompass behaviors that have features of both wake and NREM sleep. The three major classifications are : (1) confusional arousals, (2) sleep terrors, and (3) sleepwalking. Common to all three is a genetic predisposition and childhood presentation (though persistence into adulthood can occur and rarely they can manifest for the first time in adults). They occur predominantly early in the night and are associated with stage 3/4 sleep (slow-wave or delta sleep). During an episode patients are only vaguely aware of their environment. While still capable of performing complex actions (such as driving a car) they almost always appear confused to observers. These behaviors are often associated with vague dream imagery at the time of the event. Additionally, patients are almost universally amnestic concerning the event when questioned afterwards.

Confusional arousals (also termed sleep drunkenness) are defined as relatively brief (0.5-10 min) confusional states that occur when a patient transitions from stage 3/4 sleep directly to wakefulness. The patient stays in bed and may mumble or perform some stereotyped action such as pick up an object as if to answer a phone call. The episodes are usually not associated with fear and are usually not aggressive unless attempts to complete the stereotyped action are blocked.

Sleep terrors are characterized by a sudden partial arousal from slow-wave sleep accompanied by a loud piercing cry and autonomic/behavioral features suggesting intense fear. Peak

prevalence occurs between 5 and 7 years of age, with the prevalence in adults being < 1%. Duration of the episodes is generally less than 10 minutes and during this time the patient is completely inconsolable. While usually staying in bed, patients may exhibit a flight response causing them to jump out of bed and run around the room potentially injuring themselves or others. Like the other disorders of arousal, patients when awakened have only vague dream recall ("bugs in the bed" or "someone in the room").

In sleepwalking (somnambulism), patients engage in complex behavioral automatisms following a partial arousal from stage 3/4 slow-wave sleep. As in the other NREM parasomnias, patients are only incompletely aware of their surroundings and usually do not respond appropriately to environmental cues. These automatic behaviors take varied forms, from simply walking around the room or house to dressing to preparing meals to driving a car. In general the behaviors are not aggressive although published cases exist of crimes committed while sleepwalking (see section on Medico-Legal Issues below). In common with the other NREM parasomnias (and in distinction to the REM parasomnias) there is usually only vague dream imagery accompanying the episodes and the patients are usually amnestic for the events when awakened.

Mahowald et al. described a patient with a dramatic disorder of arousal.[6] This 67-year-old man presented with a 40-year history of symptoms consistent with a combination of night terrors and sleepwalking. He would jump out of bed screaming in terror and run into objects and walls. On four occasions he had jumped out of his second-story bedroom window, once landing on his head and sustaining a C3 fracture. In the year prior to presentation he had tyed himself to the bed with a restraint jacket to prevent injury.

Two other disorders which may be related to the NREM parasomnias deserve mention. The first, nocturnal eating, while sharing many of the features of the disorders of arousal is currently classified as an extrinsic sleep disorder. Nocturnal eating is characterized by unintentional eating at night in a patient who does not have a daytime eating disorder.[7-9] Patients are usually mildly confused and have varying degrees of awareness of their environment. Unlike the NREM parasomnias, patients often remember the episodes the following day. These nocturnal binges can account for substantial caloric intake, averaging 1200 kcal per night in one study. Significant obesity can result with all of the attendant morbidities associated with that condition. One of us (RM) reported on an obese male with **obstructive sleep apnea (OSA)** and nocturnal eating disorder who lost a significant amount of weight when incarcerated due to the lack of available food at night.[10] As a result his OSA resolved as documented by **polysomnography (PSG)**. On release his nocturnal eating disorder became active again, resulting in weight gain and reappearance of PSG-documented OSA.

Another reported entity which may be a form of sleepwalking has been termed sleepsex.[11] In a case report a woman related that her partner would awaken her in the first portion of the night to engage in sexual activity. She reported that he was a completely different person during these nocturnal sessions than during the daytime, being much more aggressive, biting, and "talking dirty" to her. The following morning he would deny any recollection of the previous night's events. The woman became suspicious one night when her partner began loudly snoring while performing the sexual act, prompting them both to seek medical attention.

Treatment for the NREM parasomnias is twofold. First, the patients should avoid if possible the environmental factors which can contribute to excessive amounts of slow-wave sleep or fragment sleep; e.g., drugs (sedatives, hypnotics, stimulants), alcohol, sleep deprivation (rebound phenomenon), stress, environmental stimuli, pain, pregnancy, and migraine headaches. Pharmacologic therapy can include trials of benzodiazepines such as triazolam, clonazepam, or diazepam which may decrease the number of episodes, possibly by decreasing the amount of slow-wave sleep. Tricyclic drugs such as imipramine, desipramine, and clomipramine may also prove effective.

Table 1. Comparison of Common Features of Various Parasomnias

	Confusional Arousals	Sleep Terrors	Sleepwalking	Nightmares	RBD	Complex PS
Time of night	Early	Early	Early to mid	Late	Late	Any
Sleep stage at start	SWS	SWS	SWS	REM	Dissociated REM	Any
EEG discharges	No	No	No	No	No	Usual
Screams	No	Yes	No	Rare	Rare	Rare
CNS activation	Minimal	Extreme	Minimal	Mild	Mild	Mild
Myoclonus	No	No	No	Rare	Common	Rare
Walking	No	No	Yes	No	Rare	Common
Returns to bed	Stays	Stays	Usual	Stays	Unusual	Unusual
Awakens	Uncommon	Uncommon	Uncommon	Common	Common	Common
Duration	0.5-10 min	1-10 min	2-30 min	3-20 min	1-10 min	5-15 min
Confusion (after)	Usual	Usual	Usual	Very rare	Rare	Usual
Reduced in lab	Yes	Yes	Yes	No	No	No
Episodes in wake	No	No	No	No	No	Usual
Usual Age	Child	Child	Child	Any	Adult	Adult
Genetic transmission	Yes	Yes	Yes	No	No	Rare
Organic CNS lesions	No	No	No	No	Common	Common
Potential for violence	Yes	Yes	Yes	No	Yes	Yes

Modified from ref. [2]. CNS, central nervous system; dissociated REM, sleep consisting of REM sleep without atonia; PS, partial epileptic seizures; RBD, REM sleep behavior disorder; SWS, slow-wave sleep (i.e. stages 3 and 4).

REM Parasomnias

Dream anxiety attacks, commonly referred to as nightmares, can occur in both children and adults. While they may be frightening and associated with autonomic symptoms, they can be differentiated from night terrors (see above) by the fact that there are usually no behavioral manifestations, there is usually excellent recall of associated vivid dream imagery, and if an arousal occurs the patient is usually immediately aware of his environment. Several drugs have been reported to increase the incidence of nightmares including thiothixene, beta-blockers, fluoxetine, triazolam, verapamil, among others. Treatment involves psychotherapy or various cognitive-behavioral interventions.

REM **sleep behavior disorder (RBD)** is the major REM parasomnia. The disorder is characterized by a loss of atonia during REM sleep resulting in the acting out of dream content (termed oneiric behaviors). Oneiric behaviors were first described by Jouvet in 1965 in a feline model.[12] In these studies, REM sleep without atonia was noted following bilateral lesions of pontine regions surrounding the locus ceruleus. Not until 1986 was RBD first described in humans.[13] Like the NREM parasomnias, patients with RBD have impaired perception of their surroundings. However, unlike the patients with delta sleep parasomnias, patients with RBD report vivid dream imagery, are generally alert at the termination of an episode, and do not experience amnesia for the event on the following morning.

Acute forms of RBD result from drug withdrawal (alcohol, meprobamate, pentazosine, nitrazepam) or intoxication (biperiden, tricyclic antidepressants, MAO inhibitors, caffeine). While the chronic form may also occur secondary to medications (tricyclic antidepressants, fluoxetine, venlafaxine, selegiline treatment of Parkinson's disease, anticholinergic treatment of Alzheimer's disease), it is most commonly either idiopathic or associated with neurologic disorders. Affected individuals note that at the time of onset of the disorder their dream content changes to include more episodes of violence than usual. This violence or aggression is translated into behaviors manifested during REM sleep, frequently resulting in injury to the patient or their spouse/bedpartner. In the original description of RBD, Schenck et al. reported some tape-recorded dream recollections from one of their patients.[13]:

Patients initially diagnosed with idiopathic RBD are at risk of manifesting a neurodegenerative disorder such as Parkinson's disease, progressive supranuclear palsy, or multisystem atrophy at some point in their future.

"I was on a motorcycle going down the highway when another motorcyclist comes up alongside me and tries to ram me with his motorcycle. Well, I decided I'm going to kick his motorcycle away and at that point my wife woke me up and said, 'What in heavens are you doing to me?,' because I was kicking the hell out of her."

In general this is a disorder of older (> 50 year old) men (80-90%). Patients initially diagnosed with idiopathic RBD are at risk of manifesting a neurodegenerative disorder such as Parkinson's disease, progressive supranuclear palsy, or multisystem atrophy at some point in their future. In one series, 38% of patients initially thought to have idiopathic RBD subsequently developed Parkinsonism a mean 3.7 years after the diagnosis of RBD, and a mean of 12.7 years after the initial onset of RBD symptoms.[14] For this reason it is crucial that patients with idiopathic RBD receive careful neurologic follow up.

Effective therapy exists for RBD, underscoring the importance of establishing the diagnosis in affected individuals. Clonazepam is initiated at 0.5 mg at bedtime (usual effective range 0.25 to 4 mg) and is usually immediately effective. Chronic clonazepam has been shown to be safe and effective without the emergence of tolerance over time. It should be noted that relapse is common whenever doses are missed. In patients intolerant of clonazepam there are anecdotal reports of success with melatonin, gabapentin, or pramipexole.

Table 1 shows a comparison of some of the common features of various parasomnias, although dagnosis is not always as clear-cut as the table may suggest. Patients may in fact have features of more than one disorder. Schenck et al. reported on 33 patients exhibiting what they termed an overlap disorder with features of sleepwalking, sleep terrors, and RBD.[15]

Disorders Which Resemble Parasomnias

Multiple entities may produce behaviors similar to those observed with the primary parasomnias. These are usually divided into organic disorders and psychogenic disorders. The organic disorders include transient global amnesia (a vascular disorder), mass lesions (either producing increased intracranial pressure or residing in deep structures), toxic/metabolic syndromes, limbic encephalitis, and seizures. Psychogenic causes include the dissociative states (fugues, multiple personality disorder, psychogenic amnesia) and post-traumatic stress disorder. While the history may be highly suggestive of the underlying pathological process, it is difficult to distinguish these entities on clinical grounds alone. For this reason, obtaining an overnight PSG with video recording and full EEG montage can be an important step when evaluating patients manifesting behaviors suggestive of a parasomnia.

Medico-Legal Issues

Many of the primary parasomnias can manifest as behavior that is injurious to the patient or those around him

or her. In extreme cases the behaviors can be violent to a degree resulting in criminal proceedings.

Perhaps the best known example is the case of Kenneth Parks, a 23-year-old who beat and stabbed-to-death his mother-in-law and non-fatally strangled his father-in-law, all while apparently asleep.[16] Mr. Parks had been experiencing a great deal of stress in his life related to a gambling addiction and the subsequent strain it placed on his marriage. At the time of the incident he was also sleep-deprived secondary to insomnia. Alcohol or drugs were not believed to be involved. On repeated inquiry Mr. Parks denied recall of the events in question, including the 23 km drive to his in-laws' house. The legal defense was one of homicide during noninsane automatism as part of a presumed episode of somnambulism. In support of this argument was the lack of any motive, the known affection which he held for his in-laws, the evident sincerity of his grief, the lack of other medical causes for his behavior, the known personal and family history of sleepwalking, and the presence of factors known to precipitate sleepwalking (e.g. sleep deprivation and stress). Mr. Parks was acquitted.

An automatism can be defined from a medical point of view as the presence of complex behavior in the absence of conscious awareness or volitional intent.[14] From a legal point of view these behaviors are divided into "sane" and "insane." Sane automatisms result from external factors and are thus not likely to recur. If successful, defendants are released without follow up. Insane automatisms result from internal or endogenous factors and are felt to be more likely to recur. For this reason, hospitalization in a mental health facility is mandatory following a successful insane automatism plea. Schenck and Mahowald have argued that in the case of parasomnias a third category should exist that requires medical follow up but not mandatory hospitalization.[17]

Conclusion

The primary parasomnias result in a blurring of the normally sharp lines separating the states of wakefulness, NREM sleep, and REM sleep. In their milder forms they may cause anxiety or annoyance in family members or friends. More severe manifestations may place the patient or those around him in danger of suffering physical violence. Full PSG with video recording can be an important adjunct to the history in establishing a diagnosis. Treatment consists of avoiding factors that may precipitate the parasomnia and may include medications to keep the condition under control. The latter is especially important in RBD which has a very high success rate when treated with clonazepam. With regard to the medico-legal issues involved in this group of disorders, at the time of this writing persons are not legally accountable for actions committed while manifesting a parasomnia.

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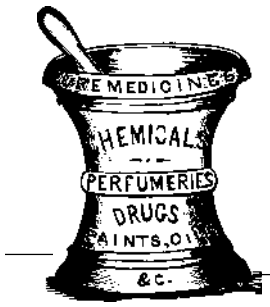
Brian Kimble, MD, is a Sleep Medicine Fellow, Division of Pulmonary, Sleep, and Critical Care Medicine, Rhode Island Hospital, and Clinical Instructor in Medicine, Brown Medical School.

Alice E. Bonitati, MD, is a Diplomat, American Sleep Disorders Association, and Clinical Assistant Professor of Medicine, Brown Medical School.

Richard P. Millman, MD, is a Diplomat, American Sleep Disorders Association, and Professor of Medicine, Brown Medical School.

Correspondence:
Richard P. Millman, MD
Division of Pulmonary, Sleep, and Critical Care Medicine
Rhode Island Hospital
593 Eddy Street (APC-4)
Providence, RI 02903
phone: (401) 444-2670
fax: (401) 444-3353
e-mail: rmillman@lifespan.org



Advances in Pharmacology

Therapy of Insomnia

Richard P. Millman, MD

Fearing that patients may become "addicted," many physicians hesitate to use medications to treat insomnia.[1] As a result, patients with acute insomnia may not receive aggressive enough therapy to prevent the development of chronic insomnia. Studies have shown it only takes three to four weeks of nightly insomnia to become a chronic insomniac. More aggressive use of hypnotic-sedative agents during an acute insomnia episode is appropriate to break the cycle to prevent the development of chronic insomnia. If one agent does not work, the primary care physician needs to either increase the dose or choose an alternative therapy.

Patients with coexistent conditions such as chronic pain, chronic headaches, fibromyalgia, or depression often need to use a sedative-hypnotic chronically as well along with other medications dictated at the underlying condition.. Fibromyalgia and chronic pain are exacerbated by lack of sleep. In addition, the pain and stiffness that the patient experiences may exacerbate the sleep problem causing a vicious cycle.

Restless leg syndrome is being increasingly recognized as a cause of sleep disruption and insomnia. Symptoms include dysesthesias and discomfort in the legs, and occasionally the arms. Some patients describe it as aching, and others describe it as "creeping-crawling" sensation. Patients with insomnia and restless legs typically need medications to calm the legs down. Sedative-hypnotic agents are generally not effective. Many patients respond to Parkinson-type drugs that increase dopamine levels in the brain; a current popular agent is pramipexole. Other patients respond to increasing opiate levels using drugs such as hydrocodone.

The remaining part of this paper will deal with various pharmacological agents that have been used for sleep in an attempt to give appropriate guidelines for their use to physicians.

Antihistamines

Various over-the-counter medications have been used to treat insomnia. Diphenhydramine or doxylamine are the most common agents used. The biggest problem with these agents is that they have significant side effects. Sedation may last long into the daytime, and they also have significant anticholinergic properties. Growing evidence demonstrates an association with falling in elderly nursing home patients and these medications. In some patients, the drugs can actually be stimulating and disrupt sleep more. These agents should not be recommended as first-line therapy for insomnia.

Sedating Anti-depressant Agents

Certain anti-depressant agents tend to have significant sedative side effects. Since these agents do not have the stigma associated with a pure sedative-hypnotic drug, they have become extremely popular among primary care physicians. A classical example of this is trazadone given at a dose of 50 to 150 mg. This is a very long-acting agent and daytime side effects can be minimized by giving the drug an hour and a half to two hours before bedtime. Typically one starts at a low dose of 50 mg and slowly increases the dose by 25 mg at weekly intervals. The main side effect in men is priapism; clinicians need to be on the lookout for this rare side effect.

Older tricyclic anti-depressants such as amitriptyline and nortriptyline may also be used for insomnia. One starts at 10 mg and increases the dose at 10 mg intervals. Again, these agents tend to be very sedating the next day and may be given an hour and a half to two hours before bedtime. These agents are typically used in patients with chronic pain, chronic headaches or fibromyalgia-type symptoms. These agents may cause significant anti-cholinergic side effects.

Psychiatrists frequently will use mistazepine at a dose of 15 to 30 mg to promote sleep. This drug seems to have a significant sedative component at low doses. This drug has side effects and is best used if other drugs fail.

Benzodiazepine Agents

Over the last few decades, benzodiazepines have replaced barbiturates

as the drug of choice for sedation because of a relatively low toxicity and clinical efficacy. They induce sleep by facilitating GABAa receptor transmission in the presence of GABA leading to the opening of chloride channels.[2]

Not all benzodiazepines are equivalent. Flurazepam, diazepam, and quazepam often last for several days because their metabolites are active sedative agents. This prolonged sedation may become a problem in many patients and has been shown to lead to an increased incidence of hip fractures in elderly patients.[3]

Intermediate-acting benzodiazepines such as temazepam and triazolam are associated with less daytime sedation and performance impairment. The shortest acting agent, triazolam actually can cause rebound insomnia when its effect wears off in the middle of the night and has been associated with a significant degree of tolerance and anterograde amnesia.

Tolerance may be related to changes in receptor binding at the GABA receptor. Nightly use of benzodiazepines is generally not recommended for longer than four weeks because more chronic administration may lead to physiological and possible psychological dependence.[2] Patients also may be associated with temporary impairment of information acquisition and subsequent recall.

Selective Benzodiazepine-receptor Agonists

Two new agents, an imiazopyridine (zolpidem) and a pyrazolopyrimidine (zalepon) were recently introduced into this country. They act at the BZ1 receptor subtype rather than the BZ2 or BZ3 receptor subtypes at the GABA receptor. Since they selectively bind to the BZ1 receptor, they tend to cause sedation without the other effects typically seen with benzodiazepines including anxiolytic properties, muscle relaxation or anti-seizure effects. Zolpidem is typically given at a 10 mg dose. It has been recommended that the dose be decreased to 5 mg in the elderly or in the presence of hepatic failure. The agent is an excellent agent for patients who have trouble initiating and maintaining sleep. It is also a reasonable agent for third-shift workers who try to go to sleep at 8:00 in the morning and would otherwise be unable to sleep during the daytime.

Zaleplon seems to be somewhat shorter-acting and seems to be best in patients either who have a pure initiation problem or pure maintenance problem. Typically, the dose of zaleplon is 10 mg in the elderly.[4] Young and middle-aged adults may potentially tolerate 15 or 20 mg. It is recommended that the dose be decreased in hepatic failure to 5 mg as with zolpidem. There appears to be no impact on cognitive function with this drug even if given in the middle of the night.[5,6] It is therefore ideal for somebody who intermittently wakes up in the middle of the night and cannot fall back to sleep. Zolpidem given in the middle of the night does cause problems with daytime cognitive function.[6]

These newer agents have no impact on sleep architecture, specifically deep slow wave sleep as opposed to benzodiazepines, antihistamines, and sedating anti-depressants.[2] There appears to be no tolerance with these agents even after being used for long periods of time.[2]

Melatonin

Recently, melatonin has received a lot of attention in the lay press as a treatment for insomnia. Studies on the hypnotic effects of melatonin have been conflicting and controversial; it is generally recommended in the sleep field that melatonin not be used for insomnia.[7]

Conclusion

A wide range of sedating agents may be used for sleep. In an acute setting, aggressive use of sedative-hypnotics may prevent the development of chronic insomnia. Long-term use of agents is appropriate in situations where there is a co-existent condition such as chronic pain, fibromyalgia, chronic headaches, depression, or restless leg syndrome. It is not inappropriate to give shift workers sedative-hypnotics during the work week so that they can sleep during the daytime. There are agents such as zolpidem and zaleplon that have less chance of tolerance. Zaleplon seems to have the least effect on daytime cognitive function, and is the only agent available for use in the middle of the night. In patients with chronic insomnia who do not want to be on medications or in whom medications have failed in the past, a strict course of behavior modification using a combination of sleep restriction, stimulant control, and relaxation therapy would be more appropriate.

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Richard P. Millman, MD, is Director, Sleep Disorders Center of Lifespan Hospitals, and Professor of Medicine, Brown Medical School.

Correspondence:
Richard P. Millman, MD
Division of Pulmonary, Sleep and Critical Care Medicine
Rhode Island Hospital
593 Eddy Street
Providence, Rhode Island 02903
phone: (401) 444-2670
fax: (401) 444-3353
e-mail: Rmillman@Lifespan.org

Rhode Island Quality Partners, Inc.

The Controversy Over Screening Mammography

Deidre Spelliscy Gifford, MD, MPH

Why the controversy?

In late 2001, screening mammography became the subject of debate in the lay and medical press. The source of the controversy is a "systematic review" published in the October 2001 issue of *The Lancet*, which questions the effectiveness of screening mammography.[1] Many groups have stepped forward to challenge the assertions in the *Lancet* publication. The following is an explanation of the issues surrounding that publication.

The study was performed by members of the Cochrane Collaboration, an international group of scientists who collect and analyze clinical trial data. This group has refined and standardized many techniques in meta-analysis and is in general highly respected for their thoroughness and objectivity. Ole Olsen and Peter C. Gøtzsche are members of the Nordic Cochrane Center, and are the authors of the controversial Lancet publication on screening mammography. A study similar but not identical to the *Lancet* article was published in the *Cochrane Library*.[2]

Systematic Reviews and Meta-analysis

A systematic review pulls together in one place the results from all relevant studies meeting a minimum quality standard. It may also include a "meta-analysis," a technique for combining the quantitative results of multiple clinical trials in order to obtain results which could not be derived from any one individual trial. The method usually includes an assessment of the quality of the studies to be included. Some authors suggest a "weighting system" by which results from higher quality studies are given more weight than results from less rigorous studies. As an alternative, authors may exclude studies from the review altogether if their quality is judged to be unacceptable. This process is at the heart of the current controversy.

Meta-analysis of screening mammography studies

There have been eight large, randomized trials of screening mammography from North America and Europe. A previous meta-analysis of these trials supported an approximately 25% reduction in breast cancer mortality in screened vs. unscreened women aged 50-74.[3] However, not every individual randomized trial shows such a benefit; accordingly, which individual studies are included and not included in the meta-analysis will have an impact on the overall result. In the most recent analysis by Olsen and Gøtzsche, the authors closely examined the quality of each randomized trial, and classified them as "high-quality," "medium-quality," "poor-quality,"or "flawed." They based these classifications on the randomization process, baseline comparability of study groups, exclusions after randomization and the consistency (across various publications) of reported numbers of women randomized. These factors were chosen because they are known to be associated with bias in study results. As there is no universally accepted measure of study quality, the authors' classification was subjective, based on a classification system of their own design. Only the two authors of the study classified quality. There was no outside review to confirm or verify the authors' classification.

After the quality of each study had been classified, the authors performed a "sensitivity analysis." (Table 1) In this process, various groups of studies are combined and the results of different combinations compared. Sensitivity analysis is recommended in cases such as this one, where the studies being combined are of varying quality. The au-

Table 1
Sensitivity Analysis

	Medium Quality Studies	Poor Quality Studies
Overall mortality	No benefit	No benefit
Breast Cancer mortality	No benefit	32% reduction

Table 2
Relative Risk of death due to breast cancer in screened vs. unscreened women aged 50-74.

Study	RR (95% CI)	Years of follow-up	Quality Assessment
Edinburgh	0.85 (0.63-1.14)	10	Flawed
Malmo (Sweden)	0.86 (0.64-1.16)	12	Medium
Kopparberg (Sweden)	0.67 (0.50-0.90)	12	Poor
Ostergotland (Sweden)	0.75 (0.57-0.99)	12	Poor
Canadian	0.97 (0.62-1.52)	7	Medium
HIP (New York)	0.68 (0.49-0.96)	10	Flawed
Stockholm	0.65 (0.40-1.08)	8	Poor
Gothenburg	0.91 (0.53-1.55)	7	Poor

thors separately combined the "medium" quality studies, and the "poor" quality studies (no studies were classified as "high-quality"), and analyzed both overall mortality and mortality due to breast cancer after 13 years of follow-up. They did not include the "flawed" studies in any analyses.

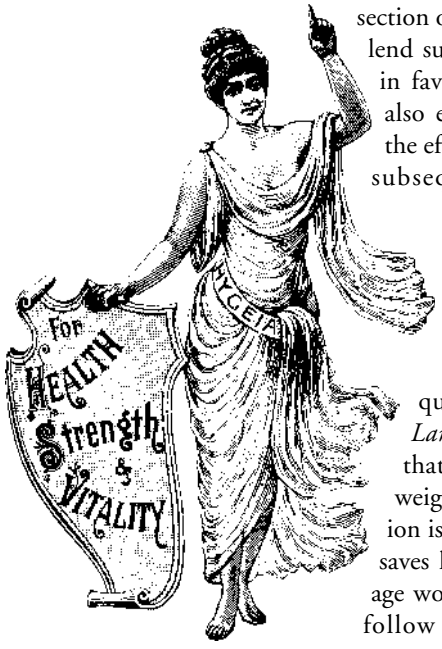
Neither the medium quality studies nor the poor quality studies showed any benefit in overall mortality in screened vs. unscreened women. However, the authors note that even when combined, these studies had insufficient power to detect a benefit of mammography in overall mortality.

For breast cancer mortality, "medium" quality studies showed no benefit to screening. In the "poor" quality studies, there was a relative risk of 0.68 (95% CI 0.58-0.78), suggesting a 32% reduction in breast cancer mortality. Based on these analyses, Olsen and Gøtzsche conclude that "the currently available reliable evidence has not shown a survival benefit of mass screening for breast cancer."

Table 2 illustrates how this result can be obtained. The table lists the eight trials of screening mammography, and the original Relative Risks (and 95% confidence intervals) of death due to breast cancer for women aged 50-74 in screened vs. unscreened women. (A confidence interval which includes 1.0 suggests no benefit to screening). The final column describes the quality of the study as judged by Olsen and Gøtzsche. Note that the Edinburgh and HIP studies were both rated as "flawed," and both showed a benefit of screening mammography. Therefore, these results were not included in the Olsen and Gøtzsche analyses.

Response to the *Lancet* analysis

The authors' sensitivity analysis and their conclusions have caused controversy. The version of the review published in the Cochrane library is different from that published in the *Lancet*. The Cochrane library version includes statements in the main result section of the abstract which lend support to arguments in favor of screening. It also excludes data about the effects of screening on subsequent treatment, which the authors had wished to include to support their conclusions. The American Cancer Society quickly disputed the *Lancet* report, stating that the overwhelming weight of scientific opinion is that early detection saves lives. They encourage women to continue to follow current screening guidelines (annual mammography for women aged 50 and over, and annual or biennial mammography for women aged 40-49).[4] To date, no professional organizations have modified their screening mammography recommendations based on the *Lancet* article.



How to counsel patients

Because the *Lancet* article received much attention in the media, your patients may come to you questioning the value of screening mammography. It may be beneficial for patients to understand that this report was not based on new information, but rather is a re-interpretation of data which have been available for many years. These same data can and have been interpreted by other scientists as strongly supporting screening mammography. Olsen and Gøtzsche have pointed out many flaws in the evidence. The question is to what extent these flaws have biased our understanding of the effectiveness of screening mammography. At this time, that question does not appear to have a definitive answer. Mammography has its limitations. False positive tests can lead to unnecessary anxiety and interventions, and false negative tests can miss cancers that are present. However, mammography is currently the best available method for early detection of breast cancer. Further research is needed to develop better methods for detecting and preventing breast cancer in the future.

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Correspondence:
Deidre Spelliscy Gifford, MD, MPH
phone: (401) 528-3255
fax: (401) 528-3210
e-mail:ripro.dgifford1@sdps.org
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The author assumes full responsibility for the accuracy and completeness of the ideas presented. This article is a direct result of the Health Care Quality Improvement Program initiated by the Health Care Financing Administration, which has encouraged identification of quality improvement projects derived from analysis of patterns of care, and therefore required no special funding on the part of this Contractor. Ideas and contributions to the author concerning experience in engaging with issues presented are welcomed.

Edited by John Pezzullo, MD

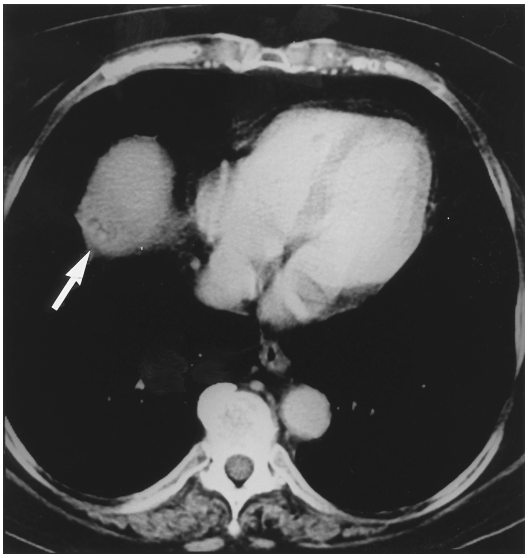

Figure 1.

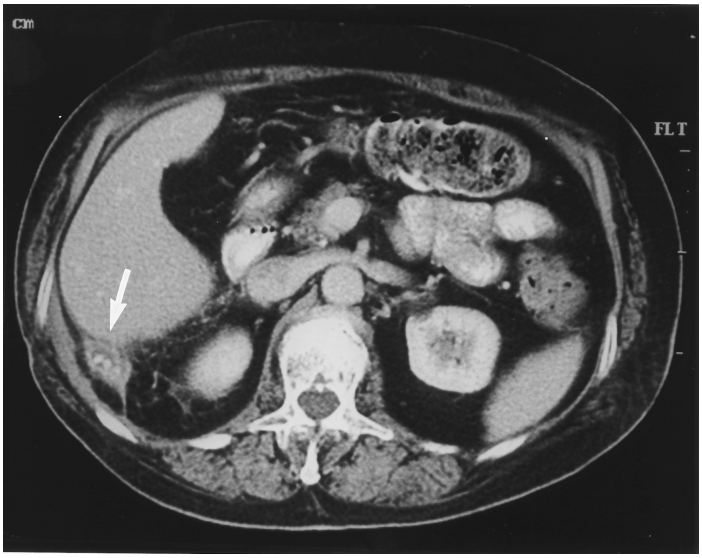

Figure 2.

"Dropped" Gallstones

A 77 year-old female presented with a 5-month history of intermittent right upper quadrant pain radiating to the right shoulder. Past surgical history was significant for laparoscopic cholecystectomy 8 months prior, during which the gallbladder was ruptured resulting in spillage of gallstones into the abdominal cavity. A CT examination of the abdomen performed at admission demonstrates two calcifications adjacent to the hepatic dome (Figure 1), and an infrahepatic collection containing multiple similar calcifications (Figure 2). CT guided percutaneous aspiration of this collection confirmed the presence of an abscess.

Although laparoscopic cholecystectomy has many benefits relative to an open procedure, there is a higher rate of gallbladder perforation (15-30%), and late infection caused by dropped gallstones (0.3%). Irrigation during the procedure and stone migration/fistulization afterwards results in multifocal abscesses remote from the gallbladder fossa, including in the abdominal wall, right pleural space, trocar sites, incisional hernias, or scrotum. The infection that arises is often indolent. The time from dropped stones to onset of symptoms averages two years. The correct diagnosis is further delayed, as the radiologist is invariably unaware of the prior laparoscopic complication. Only 40% of late infections caused by dropped gallstones on CT or US are diagnosed prospectively. Surgical removal of the abscess and stones is curative.

MARK GEIST, MD

Mark Geist, MD, is a fellow in cross-sectional imaging at the Rhode Island Hospital.

REFERENCE

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CORRESPONDENCE:

Mark Geist, MD
Department of Diagnostic Imaging
Rhode Island Hospital
phone: (401) 444-5184
e-mail: MGeist@lifespan.org

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Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Jay S. Buechner, PhD

Achieving Universal Health Care Coverage in Rhode Island: Where are the Challenges?

Colleen Ryan, MPH, Jana E. Hesser, PhD, Jay S. Buechner, PhD

For the year 2010, Rhode Island has adopted state health objectives addressing each of the ten **Leading Health Indicators (LHIs)** that were selected as part of the national Healthy People 2010 process.[1,2] One objective adopted at both the state and national levels addresses the LHI for Access to Care, specifically the barrier to access posed by the lack of health insurance. This objective is:

- Increase the proportion of people with health insurance.
- Target: 100% of people under age 65 years.

Achieving this objective would result in universal health care coverage for the people of Rhode Island.

Healthy People 2010 also adopted an over-arching goal of eliminating health disparities among population groups defined by gender, race/ethnicity, education or income, disability, geographic location, and sexual orientation.[2] Here we present current data on disparities in health insurance coverage in the Rhode Island working age population (ages 18-64) that help to identify which groups face the greatest obstacles to achieving universal coverage.

Methods

The **Rhode Island Department of Health (HEALTH)** surveys a sample of Rhode Island adults by telephone annually concerning key health risk behaviors, participation in health screening and access to health care. This survey is performed as part of the national **Behavioral Risk Factor Surveillance System (BRFSS)**, funded in all 50 states, DC, and three territories by the Centers for Disease Control and Prevention (CDC) in order to monitor state and national trends for these health risk factors.[3]

In Rhode Island, the BRFSS has been conducted continuously since 1984, and by a professional survey contractor since 1990. During the years 1991 through 1997, about 1,800 Rhode Island adults were interviewed each year, or approximately 150 per month. For 1998 through 2000 the annual sample size was increased to approximately 3,600, with 300 interviews per month.

The BRFSS has included basic questions on health insurance coverage since 1991, including an initial screening question for health coverage of any kind, a probing question for those with coverage that identifies their particular type of health plan or program, and a verification question for those without coverage to assure they considered all major sources of coverage in determining their answer. Any respondent stating he or she had

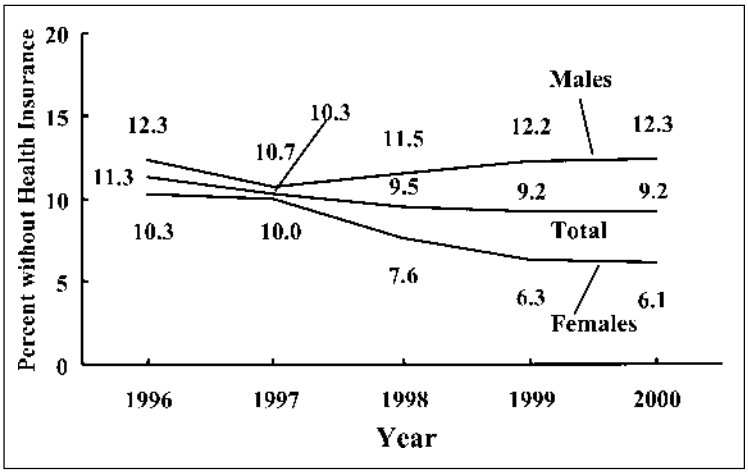

Figure 1. Percentage without Health Insurance Coverage, Ages 18-64 Years, by Gender, Rhode Island, 1996-2000

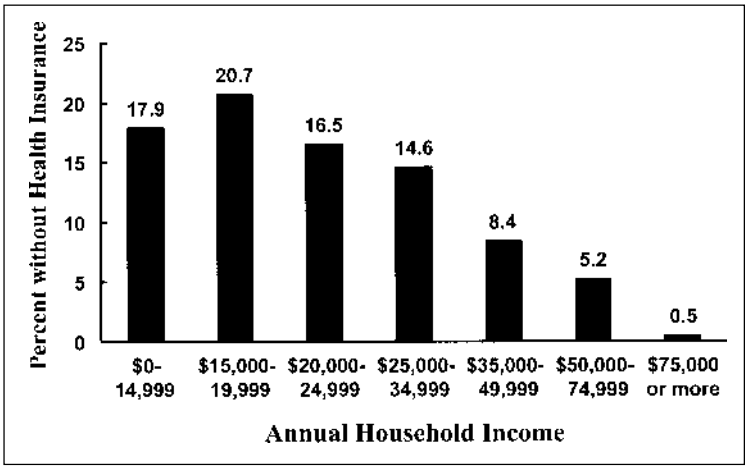

Figure 2. Percentage without Health Insurance Coverage, Ages 18-64 Years, by Income, Rhode Island, 2000

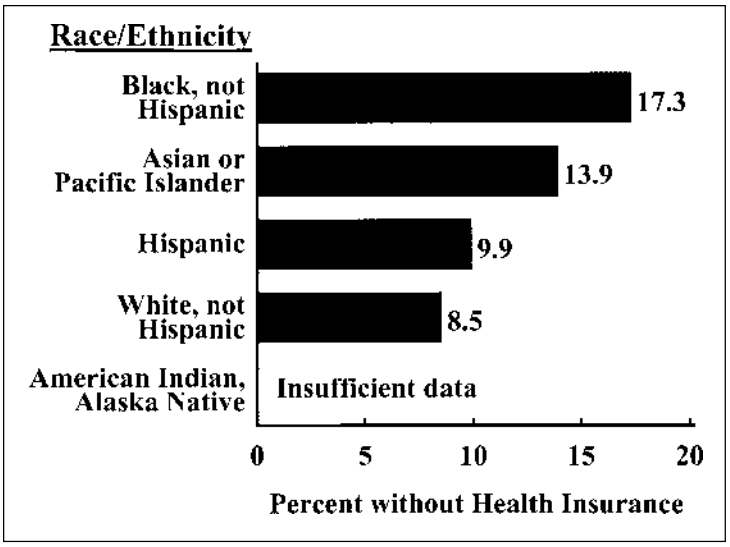

Figure 3. Percentage without Health Insurance Coverage, Ages 18-64 Years, by Race and Ethnicity Rhode Island, 1998-2000

coverage in response to the screening or verification questions is considered to be insured, unless the initial positive response was reversed during the probing question.

(Note: In previous publications of BRFSS data on health coverage,[4] only positive responders to the screening question were considered to be insured, in accordance with national analyses. Data in those publications may differ from data presented here, especially data on Hispanic residents. The change in methodology results in fewer Hispanic respondents being assigned to the uninsured group. We are continuing to investigate the possible reasons for this finding.)

Results

The uninsured rate in Rhode Island is decreasing among women and increasing among men. (Figure 1) The decrease in the overall rate of uninsured in Rhode Island from 1997 to 2000 is due to the substantial decline in the rate among females. Over the same period, rates among men in Rhode Island remained higher than for women and actually increased slightly, so the disparity in coverage has increased.

The poor and near-poor are more likely to be uninsured than middle-income and upper-income residents. (Figure 2) Lack of health insurance coverage is highest among people with annual household incomes under $20,000. The proportion without coverage among people with annual household incomes of $15,000-19,999 is four times higher than among people with incomes of $50,000 or higher.

Certain racial/ethnic groups in Rhode Island have high proportions with no health care coverage. (Figure 3) Black non-Hispanic adults and Asian adults are substantially more likely to be uninsured during 1998-2000 than white, non-Hispanic adults. Hispanic residents have only slightly more uninsured than non-Hispanic whites. (See important note concerning Hispanic data at end of Methods section.)

Disparities in health care coverage also exist among groups in Rhode Island defined by employment status and age. In 2000, unemployed persons were more than three times as likely to be uninsured (27.7%) as employed persons (8.4%). By age, young adults ages 18-24 years were most likely to lack health insurance, with rates (18.2%) nearly three times the rate for older working age adults (6.3% among those ages 35-64 years) and 30 times the rate for the elderly (0.6%).

Discussion

A recent national study has shown Rhode Island to have the lowest proportion among all states of persons who had been continuously without health coverage for one year (6.2%).[5] Given this strong base, achieving universal coverage in the state's population will involve identifying those groups most likely to be without coverage and developing sources of coverage for them.

Some of those groups in Rhode Island have been identified in the results presented here. Over the last four years, the proportion of uninsured men has increased, while the proportion of uninsured women has fallen, creating a substantial disparity between genders. The poor and near-poor, as well as those who are unemployed, are also at higher risk of not having health insurance coverage. Young adults show very high rates of being uninsured, and all working age adults have much higher rates of non-coverage than the elderly.

Perhaps most significantly, all minority populations defined by race and ethnicity have higher proportions of uninsured persons than do non-Hispanic whites. This is of special concern because growth in minority populations accounts for all of the recent population growth in the state. Between the 1990 Census and the 2000 Census, the non-white and Hispanic populations taken together grew 77% and now comprise 18% of the Rhode Island population.[6] If the disparities in insurance coverage persist for these groups as they continue to grow in number, then achieving the goal of universal coverage in Rhode Island will prove increasingly difficult.

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Colleen Ryan, MPH, is Public Health Epidemiologist, Office of Health Statistics.

Jana E. Hesser, PhD, is Program Manager for Health Surveys, Office of Health Statistics, and Coordinator for Rhode Island's BRFSS.

Jay Buechner, PhD, is Chief, Office of Health Statistics, and Clinical Assistant Professor of Community Health, Brown Medical School.

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Transplantation in Rhode Island

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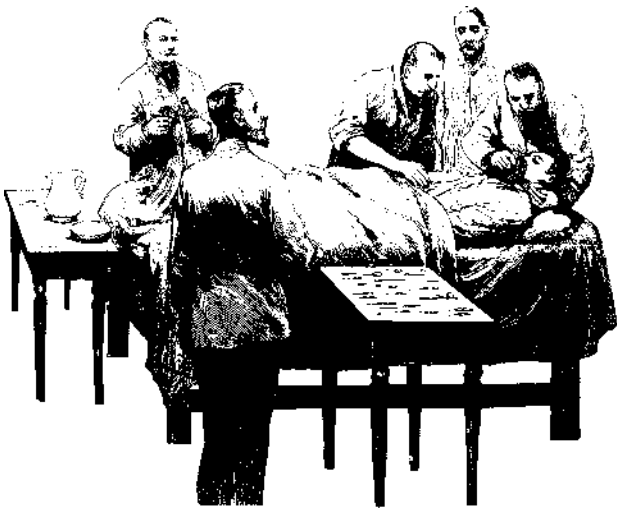

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PUBLIC HEALTH BRIEFING

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by John P. Fulton, PhD

Smallpox: Clinical and Epidemiologic Features

D. A. Henderson, MD

Smallpox is a viral disease unique to humans. To sustain itself, the virus must pass from person to person in a continuing chain of infection and is spread by inhalation of air droplets or aerosols. Twelve to 14 days after infection, the patient typically becomes febrile and has severe aching pains and prostration. Some 2 to 3 days later, a papular rash develops over the face and spreads to the extremities. The rash soon becomes vesicular and later, pustular. The patient remains febrile throughout the evolution of the rash and customarily experiences considerable pain as the pustules grow and expand. Gradually, scabs form, which eventually separate, leaving pitted scars. Death usually occurs during the second week.

The disease most commonly confused with smallpox is chickenpox, and during the first 2 to 3 days of rash, it may be all but impossible to distinguish between the two. However, all smallpox lesions develop at the same pace and, on any part of the body, appear identical. Chickenpox lesions are much more superficial and develop in crops. With chickenpox, scabs, vesicles, and pustules may be seen simultaneously on adjacent areas of skin. Moreover, the rash in chickenpox is more dense over the trunk (the reverse of smallpox), and chickenpox lesions are almost never found on the palms or soles.

In 5% to 10% of smallpox patients, more rapidly progressive, malignant disease develops, which is almost always fatal within 5 to 7 days. In such patients, the lesions are so densely confluent that the skin looks like crepe rubber; some patients exhibit bleeding into the skin and intestinal tract. Such cases are difficult to diagnose, but they are exceedingly infectious.

Smallpox spreads most readily during the cool, dry winter months but can be transmitted in any climate and in any part of the world. The only weapons against the disease are vaccination and patient isolation. Vaccination before exposure or within 2 to 3 days after exposure affords almost complete protection against disease. Vaccination as late as 4 to 5 days after exposure may protect against death. Because smallpox can only be transmitted from the time of the earliest appearance of rash, early detection of cases and prompt vaccination of all contacts is critical.

Smallpox vaccination is associated with some risk for adverse reactions; the two most serious are postvaccinal encephalitis and progressive vaccinia. Postvaccinal encephalitis occurs at a rate of 3 per million primary vaccinees; 40% of the cases are fatal, and some patients are left with permanent neurologic damage. Progressive vaccinia occurs among those who are immunosuppressed because of a congenital defect, malignancy, radiation therapy, or AIDS. The vaccinia virus simply continues to grow, and unless these patients are treated with vaccinia immune globulin, they may not recover. Pustular material from the vaccination site may also be transferred to other parts of the body, sometimes with serious results.

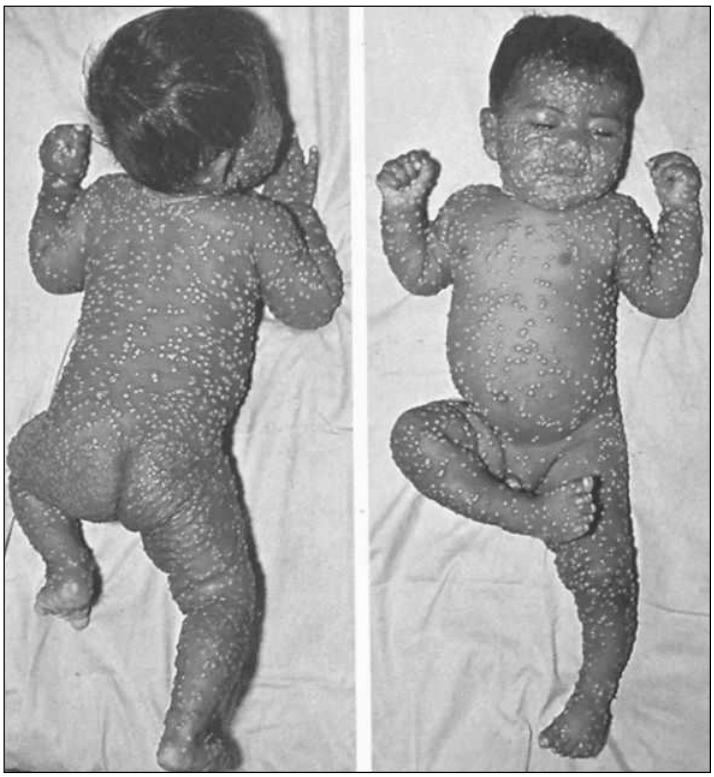

Figure 1.
http://www.cdc.gov/ncidod/eid/vol5no4/hender sonG .htm#f ig1
Most cases of smallpox are clinically typical and readily able to be diagnosed. Lesions on eac h ar ea of the body are at the same sta ge of development, ar e deeply embedded in the skin, and ar e mor e densely concentrated on the face and extremities.

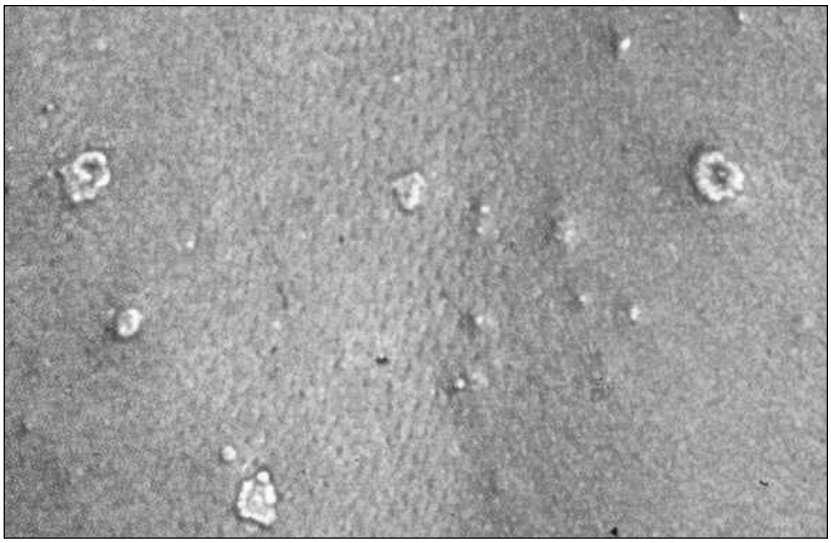

Figure 2.
http://www.cdc.gov/ncidod/eid/vol5no4/hender sonG .htm#f ig2
The lesions of chickenpox develop as a ser ies of "cr ops" over several days and ar e very superf icial. Papules, vesicles, pustules, and sca bs can be seen adjacent to eac h other . The tr unk is usuall y more affected than the f ace or extremities.

Routine vaccination is only recommended for laboratory staff who may be exposed to one of the orthopoxviruses. There are two reasons for this. First is the risk for complications. Second, U.S. national vaccine stocks are sufficient to immunize only 6 to 7 million persons. This amount is only marginally sufficient for emergency needs. Plans are now being made to expand this reserve. However, at least 36 months are required before large quantities can be produced.

The potential of smallpox as a biological weapon is most dramatically illustrated by two European smallpox outbreaks in the 1970s. The first occurred in Meschede, Germany, in 1970.[1] This outbreak illustrates that smallpox virus in an aerosol suspension can spread widely and infect at very low doses.

Another outbreak occurred in Yugoslavia in February 1972.[1] Despite routine vaccination in Yugoslavia, the first case in the 1972 outbreak resulted in 11 others; those 11, on average, each infected 13 more. Other outbreaks in Europe from 1958 on showed that such explosive spread was not unusual during the seasonal period of high transmission, i.e., December through April. One can only speculate on the probable rapidity of spread of the smallpox virus in a population where no one younger than 25 years of age has ever been vaccinated and older persons have little remaining residual immunity.

Where might the virus come from? At one time, it was believed that the smallpox virus was restricted to only two high-security laboratories, one at the Centers for Disease Control and Prevention in Atlanta, Georgia, and one at the Russian State Centre for Research on Virology and Biotechnology, Koltsovo, Novosibirsk Region. By resolution of the 1996 **World Health Assembly (WHA)**, those stocks were slated to be destroyed at the end of June 1999. The desirability of such an action was reaffirmed by a World Health Organization Expert Committee in January 1999. On May 22, 1999, WHA, however, passed a resolution postponing destruction until 2002, by which time any promise of the variola virus stocks for public health research could be determined. Destruction of the virus would be at least one step to limit the risk for the reemergence of smallpox. However, despite widespread acceptance of the 1972 Bioweapons Convention Treaty, which called for all countries to destroy their stocks of bioweapons and to cease all research on offensive weapons, other laboratories in Russia and perhaps in other countries maintain the virus. Iraq and the Soviet Union were signatories to the convention, as was the United States. However, as reported by the former deputy director of the Russian Bioweapons Program, officials of the former Soviet Union took notice of the world's decision in 1980 to cease smallpox vaccination, and in the atmosphere of the cold war, they embarked on an ambitious plan to produce smallpox virus in large quantities and use it as a weapon. At least two other laboratories in the former Soviet Union are now reported to maintain smallpox virus, and one may have the capacity to produce the virus in tons at least monthly. Moreover, Russian biologists, like physicists and chemists, may have left Russia to sell their services to rogue governments.

Smallpox is rated among the most dangerous of all potential biological weapons, with far-reaching ramifications.

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D.A. Henderson, MD, is a distinguished service professor at the Johns Hopkins University, holding an appointment in the Department of Epidemiology. He directed the World Health Organization's global smallpox eradication campaign (1966-1977) and helped initiate WHO's global program of immunization in 1974. He also served as deputy assistant secretary and senior science advisor in the Department of Health and Human Services.

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Correspondence:
D. A. Henderson, MD
Johns Hopkins Center for Civilian Biodefense Studies
111 Market Place, Ste. 850
Baltimore, MD 21202
fax: 410-223-1665
e-mail: dahzero@aol.com.

Judicial Diagnosis

Sleep Disorders and a Physician's Responsibility

John Bello, JD

When persons affected by sleep disorders, like sleep apnea or narcolepsy, get behind the wheel of a car, they may be endangering not just themselves, but their passengers, other drivers, and pedestrians. Because of this danger, many state legislatures mandate that physicians report patients who have ailments that cause them to lose consciousness to the state division of motor vehicles. The State of Rhode Island does not have such a statute on the books. But even without a statutory mandate to report patients with sleep disorders to the division of motor vehicles, doctors in Rhode Island may still face potential tort liability when treating patients with sleep disorders.

When a physician treats a patient, the physician is normally responsible only to the patient. In fact, rules for confidentiality preclude any sharing of medical information, or personal information disclosed during a visit. A third party, however, may enter the picture. That third party can be a specific person, or a generalized "public." In certain situations a special relationship exists between the third-party plaintiff and the physician; for example, when the clinician has reason to know that a patient is likely to harm an identified person, a person not identified, or a generalized "public," the clinician may be expected to breach confidentiality. In short, the clinician has a responsibility to that third party.

In order to protect the public, courts across the United States have struggled with the issue of clinicians' responsibility to people other than their patients. Obviously a patient can sue his/her doctor. The question is: can a non-patient - a third party - sue that physician? Some courts have said yes; others no. Because there is no clear consensus on how these third party plaintiff actions should be ruled and because the issue has not been litigated in a Rhode Island court, it is unclear how a similar case would be resolved in the Ocean State.

In some cases, when third party plaintiffs have sued physicians, arguing that the physicians had a "special relationship" with the third party, the courts have found that there was not a special relationship and that there was also not a sufficient link between the two parties to give rise to a cause of action.[1] For example, in New York a patient susceptible to blackouts killed another while driving. The patient had been living in a health care institution under the medical direction of a physician, who discharged the patient. The court found no "special relationship," because the doctor, although the director of the instituion, was not the patient's primary treating physician. Thus he had no duty to warn the patient of the dangers of driving. The doctor was not held liable. Courts have also found that if the disorder is obvious and the patient has suffered from it for some time, the physician is not responsible for warning the patient of obvious dangers. In Kansas a patient who had been suffering from a sleep disorder knew of the potential dangers of driving, yet that patient drove, and seriously injured two bicylcists. The bicylcists sued the physician. A Kansas court determined that the doctor did not have a duty to warn this patient because it would be a redundancy and accomplish nothing.[2]

Other cases, though, have held physicians liable to third party plaintiffs. Those courts have determined that there is a duty from the physician to the driving public when the physician knows or reasonably should know that a patient's ability to drive is affected.[3] In *Gooden v. Tips*, 651 S.W.2d 364 (1983), the court found that a physician who prescribed specific drugs either knew - or should have known - their potential impact on the driver's ability to drive: "the doctor was under a duty to take whatever steps were reasonable under the circumstances to reduce the likelihood of injury to other motorists." "Thus the harm resulting to the plaintiffs " ...was in the general field of danger which should reasonably have been foreseen by the doctor when he administered the drug."

Furthermore, courts that have held physicians liable to third party plaintiffs have for the most part determined that the physician's duty to warn is satisfied by warning the patient. In *Pate v. Threlkel*, the court reasoned that the burden on a physician to warn others of a patient's condition would place too heavy a burden on the physician.[4] The standard of care applied in these cases is the same that has historically been applied to medical malpractice claims, where physicians are held liable if their actions do not satisfy the standard of care established by expert testimony. For instance, a patient with a history of seizures had a seizure, which led to a car accident. The court found the patient's doctor negligent and liable to an injured third party plaintiff because the clinician failed to employ recognized procedures to determine the cause of the patient's seizures.[5] If a physician satisfies this threshold level of care, s/he will probably not be held liable for his/her actions.

A third party need not necessarily be a stranger to the patient. For example, consider a minor child, injured while driving with a parent who suffers from a disorder that causes him/her to lose consciousness. That child might plausibly be considered a reasonably foreseeable plaintiff, one who should be afforded a special relationship status.

For Rhode Island courts, this area of tort law is an issue of "first impression" (not yet litigated). Even without Rhode Island case law, however, Rhode Island physicians who meet or exceed the standard of care established for the questioned treatment and warn patients with sleep disorders about the potential dangers of driving may be able to shelter themselves from liability.

This advice, though, is based on case law in other jurisdictions. Only when cases have been litigated in Rhode Island will there be solid precedent; and only then will the standard for physician responsibility to third parties be clear in Rhode Island.

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John Bello, JD, is an Associate at Hinckley Allen & Snyder, LLP.

Correspondence:
John Bello, JD
Hinckley Allen & Snyder, LLP
1500 Fleet Center
Providence, RI 02903
phone: (401) 274-2000
fax: (401) 277-9600
e-mail: JBello@haslaw.com

Vital Statistics

Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Roberta A. Chevoya

Rhode Island Monthly Vital Statistics Report

Provisional Occurrence Data from the Division of Vital Records

Underlying Cause of Death	Reporting Period			
	March 2001	12 Months Ending with March 2001		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	296	3,073	293.1	4,353.5 **
Malignant Neoplasms	190	2,372	226.3	6,624.0
Cerebrovascular Diseases	46	496	47.3	690.0
Injuries (Accident/Suicide/Homicide)	33	376	35.9	6,996.5
COPD	41	498	47.5	480.0

Vital Events	Reporting Period		
	September 2001	12 Months Ending with September 2001	
	Number	Number	Rates
Live Births	1234	13,302	12.7*
Deaths	780	10,191	9.7*
Infant Deaths	(12)	(99)	7.4#
Neonatal deaths	(12)	(85)	6.4#
Marriages	1,129	8,603	8.2*
Divorces	120	3,341	3.2*
Induced Terminations	411	5,466	410.9#
Spontaneous Fetal Deaths	105	993	74.7#
Under 20 weeks gestation	(94)	(914)	68.7#
20+ weeks gestation	(11)	(79)	5.9#

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 estimated population of 1,048,319

(c) Years of Potential Life Lost (YPLL)

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

* Rates per 1,000 estimated population # Rates per 1,000 live births
** Excludes two deaths of unknown age.

– A Physician's Lexicon –

Humor Me, Dear Galen

To most primitives, a person became ill only when some malevolent, supernatural force had descended upon him. It is to the credit of the ancient Greeks that they brought illnesses down to a secular level, ascribing them to some internal derangement or imbalance involving the body's fluid humors. [*Humor* is a Greek word meaning moisture; and, later, a Latin word, *umor*, meaning wetness, as in the word humidity.] Rational medicine, both Western and Arabic, was captive to this humoral theory of disease for over two millennia. Indeed, until the 19th Century, the theory was staunchly advocated to the exclusion of alternate systems of belief in virtually all European medical schools.

These four humors were yellow bile, blood, phlegm, and black bile; and, since each humor possessed certain singular attributes, an excess of each was readily identifiable. Thus, persons with too much blood were said to be sanguine [Latin, *sanguineus*, of blood], courageous, outspoken, often apoplectic. Those with too much yellow bile were choleric [Greek, *cholos*, meaning bile], passionate, prone to bursts of rage, perhaps jaundiced. Those with an excess of phlegm [Greek, *phlegmos*, meaning inflammatory swelling] were said to be cold, dull, slow to anger, phlegmatic. And finally, those burdened with an excess of black bile [in Greek, *melancholia*] were atrabilious, subject to spells of profound sadness, and also given to rare episodes of anger [but only when they were *splenetic*, the spleen being the alleged origin of black bile].

Therapy for disease consisted of any medical intervention which might rectify the excess of one or another humor. A sanguineous person, hence, was bled repeatedly. Other therapies might include cathartics [rhubarbs, mercurials, jalaps, salts], agents such as paragoric or laudanum to retard bowel evacuation; and emetic medications to promote vomiting.

Medicine increasingly doubted the validity of the humoral theory of disease; yet until the advent of the cellular theory of disease in the 19th Century, there was little to replace these old Galenic formulations; and so they were advocated but without enthusiasm. Playwrights in Britain and France used the rapidly discredited theory as a basis for their comic efforts; and gradually the word humor became a synonym for travesty and satire. When Shakespeare at the beginning of the 17th Century talked of "a humorous sadness," he was referring to melancholy. A century later, when Addison wrote: "In all thy humors whether grave or mellow, Thou'rt such a touchy, testy, pleasant fellow; Hast so much wit, and mirth and spleen about thee," he was using the word, humor, in both meanings. But by the 20th Century, the word was employed unambiguously to convey the sense of comedy. "Men will confess to treason, murder, arson, false teeth, or a wig," said Colby, "How many of them will own up to a lack of humour?"

– Stanley M. Aronson, MD, MPH

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Ninety Years Ago

[February, 1912]

Listing the names of the 218 members and friends who had contributed to the new Medical Library Building, the Journal called on the 100+ non-contributing members to join the campaign.

"In Superior Sanitary Quality of Rhode Island Oysters," Frederic P. Gorham, a Sanitary Expert on the Rhode Island Shellfish Commission, defended the state's oysters. The federal Board of Food and Drug Inspection had ruled that oysters "sown in sewage-polluted water, or...fattened by 'floating' or 'drinking' in sewage-polluted waters" could not leave a state, under Interstate Trade rules; and Dr. Wiley from the Board had found certain Rhode Island oysters "polluted with sewage." The author argued that the danger of sewage-polluted oysters lay in their potential for disease, specifically typhoid. Yet oysters taken directly from beds (even the polluted beds of Rhode Island) had led to no cases of typhoid. [He conceded that floating posed a danger, but Rhode Island fishermen did not "float" their oysters.] Also, the author cited the observation of Dr. Chapin: "Very few oysters are eaten by laboring people, but at present laboring people furnish fully their share of typhoid fever."

Ellen A. Stone, MD, a member of the Committee on Midwifery of the American Association for the Study and Prevention of Infant Mortality, personally interviewed all 40 midwives in Rhode Island. In "The Midwives of Rhode Island," she summarized the results. Half the midwives lived in Providence. Most were Italian (23), followed by Hebrew, Portuguese, American, and English (3 midwives each). They delivered "an immense number of infants": 3 delivered 150 babies each, five delivered over 100 babies. Providence midwives delivered 4788 babies, or 42% of the total births in the city in 1910. Dr. Stone found the midwives' education, training, equipment, and personal cleanliness "far from ideal": 22 could not read sufficiently to fill out the birth certificates; 19 could show no equipment. Although all 40 "professed to scrub their hands well before making vaginal examinations" and 29 used bichloride solution, only 2 understood its significance. Dr. Stone reported folk practices: dressing the umbilical cord with snuff; giving a mixture of molasses and a child's urine to an infant as a physic; and binding the umbilical cord so its cut end pointed upward "to insure no 'bed-wetting' as the child grew older." The Rhode Island legislature was considering whether to recognize midwives. Dr. Stone urged: "Cannot Rhode Island extend her obstetrical charities by out-patient services for the poor and proper semi-charity hospital accommodations for those in moderate circumstances, and then, having secured for all women at confinement the means of obtaining proper obstetrical skill, gradually abolish the midwives till they are no more?"

Frank E. Peckham, MD, in "Post-Operative Roentgenization in Cancer," explained that surgeons discounted this treatment: "...patients come for such treatment, not because they have been sent by the surgeon, but because they have heard of some else being benefited." He abstracted comments from a supportive editorial in *JAMA*; e.g., "The doubters of the curative powers of the x-ray are not found in the ranks of those who know the agent."

Fifty Years Ago

[February, 1952]

In "Acne Conglobata Treated with Aureomycin," Bencel L. Schiff, MD, and Arthur B. Kern, MD, described a 45 year-old male, who at age 18 had developed lesions on his face, followed by lesions on his neck, scrotum, gravis, thighs. He had had numerous hospitalizations. He worked until age 38, when the pain and stiffness in his hips forced him to stop. The profuse prurulent and bloody discharge had led to 2 divorces. After a regimen of aureomycin (500 mg 4 times/day for 9 months, then 1 gram daily for 4 months, then a mixture of Kutapressin and aureomycin), the patient had been "converted from a socially unacceptable semi-invalid to one who is able to carry on his usual duties."

An Editorial "Hat for Health" ridiculed the Congressional Record notation of a recent report from "Hat Life," the organ of the hat workers' association. A Congressman from Fairfield, Connecticut, "the hat center of the world," had submitted the report. Briefly, 100 ear, nose and throat specialists were asked the question: "In your opinion, does a hatless man particularly invite sinus trouble?" Of 22 respondents, 15 answered "yes." The editorial cautioned, "Wait until bureaucratic medicine is in the saddle." To promote health, the government might make hat-wearing compulsory.

Twenty Five Years Ago

[February, 1977]

In a Message from the Dean, Stanley M. Aronson, MD, reported on "Interships obtained by Brown University Medical Students, Class of 1977:" 11 students went to New York programs; 10 stayed in Rhode Island; 13 enrolled in Family Medicine, up from 4 for each of the two previous years.

In "Tuberculin Dual Testing: A New England Pilot Study," Ralph A. Redding, MD, FRCP, Francis Segarra, MD, FACCP, and Fredy Roland, MD, concluded that the "technique can be useful in reducing doubtful interpretation to less than 2% of cases." They had tested 1018 Memorial Hospital employees, on a voluntary basis.

Peter B. Reilly, MD, and Lauren B. Cohen, BA, from Harvard Medical School, had presented "Lithium as an Anti-Depressant: Discoveries through Clinical Observations" at the Annual Research Day Program, The Miriam Hospital. The Journal reprinted their talk.

James P. Cooney, Jr., PhD, CEO, RI Health Services Research, Inc. [SEARCH] contributed "Cost Containment and Qaulity of Care: Are They Both Possible?" Likening the two to Scylla and Charybis, he nevertheless concluded: "The old dictum of the greater good for the greatest number with the funds available is still valid."

An Editorial called for the repeal of the Delaney Amendment. "The recent banning of saccharin by the FDA because it caused bladder cancer in rats is ridiculous." Although saccharin had been available for 80 years, physicians had attributed no case of bladder cancer to it.