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DIFFERENT VOICE

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At 12:30 AM on June 10, 2002, Israel Lane Joubert and his family of seven set out for a long drive home following a family reunion in Beaumont, Texas. Joubert, who had hoped to reach home in faraway Fort Worth in time to get to work by 8 AM, fell asleep at the wheel, plowing the family’s Chevy Suburban into the rear of a parked 18-wheeler. He survived, but his wife and five of his six children were killed.

The Joubert tragedy underscores a problem of epidemic proportions among workers who get too little sleep. In the past five years, driver fatigue has accounted for more than 1.35 million automobile accidents in the United States alone, according to the National Highway Traffic Safety Administration. The general effect of sleep deprivation on cognitive performance is well-known: Stay awake longer than 18 consecutive hours, and your reaction speed, short-term and long-term memory, ability to focus, decision-making capacity, math processing, cognitive speed, and spatial orientation all start to suffer. Cut sleep back to five or six hours a night for several days in a row, and the accumulated sleep deficit magnifies these negative effects. (Sleep deprivation is implicated in all kinds of physical maladies, too, from high blood pressure to obesity.)

Nevertheless, frenzied corporate cultures still confuse sleeplessness with vitality and high performance. An ambitious manager logs 80-hour work weeks, surviving on five or six hours of sleep a night and eight cups of coffee (the world’s second-most widely sold commodity, after oil) a day. A Wall Street trader goes to bed at 11 or midnight and wakes to his BlackBerry buzz at 2:30 AM to track opening activity on the DAX. A road warrior lives out of a suitcase while traveling to Tokyo, St. Louis, Miami, and Zurich, conducting business in a cloud of caffeinated jet lag. A negotiator takes a red-eye flight, hops into a rental car, and zooms through an unfamiliar city to make a delicate M&A meeting at 8 in the morning.

People like this put themselves, their teams, their companies, and the general public in serious jeopardy, says Dr. Charles A. Czeisler, the Baldino Professor of Sleep Medicine at Harvard Medical School. To him, encouraging a culture of sleepless machismo is worse than nonsensi-
cal; it is downright dangerous, and the antithesis of intelligent management. He notes that while corporations have all kinds of policies designed to prevent employee endangerment—rules against workplace smoking, drinking, drugs, sexual harassment, and so on—they sometimes push employees to the brink of self-destruction. Being “on” pretty much around the clock induces a level of impairment every bit as risky as intoxication.

As one of the world’s leading authorities on human sleep cycles and the biology of sleep and wakefulness, Dr. Czeisler understands the physiological bases of the sleep imperative better than almost anyone. His message to corporate leaders is simple: If you want to raise performance—both your own and your organization’s—you need to pay attention to this fundamental biological issue. In this edited interview with senior editor Bronwyn Fryer, Czeisler observes that top executives now have a critical responsibility to take sleeplessness seriously.

What does the most recent research tell us about the physiology of sleep and cognitive performance?

Four major sleep-related factors affect our cognitive performance. The kinds of work and travel schedules required of business executives today pose a severe challenge to their ability to function well, given each of these factors.

The first has to do with the homeostatic drive for sleep at night, determined largely by the number of consecutive hours that we’ve been awake. Throughout the waking day, human beings build up a stronger and stronger drive for sleep. Most of us think we’re in control of sleep—that we choose when to go to sleep and when to wake up. The fact is that when we are drowsy, the brain can seize control involuntarily. When the homeostatic pressure to sleep becomes high enough, a couple thousand neurons in the brain’s “sleep switch” ignite, as discovered by Dr. Clif Saper at Harvard Medical School. Once that happens, sleep seizes the brain like a pilot grabbing the controls. If you’re behind the wheel of a car at the time, it takes just three or four seconds to be off the road.

The second major factor that determines our ability to sustain attention and maintain peak cognitive performance has to do with the total amount of sleep you manage to get over several days. If you get at least eight hours of sleep a night, your level of alertness should remain stable throughout the day, but if you have a sleep disorder or get less than that for several days, you start building a sleep deficit that makes it more difficult for the brain to function. Executives I’ve observed tend to burn the candle at both ends, with 7 AM breakfast meetings and dinners that run late, for days and days. Most people can’t get to sleep without some wind-down time, even if they are very tired, so these executives may not doze off until 2 in the morning. If they average four hours of sleep a night for four or five days, they develop the same level of cognitive impairment as if they’d been awake for 24 hours—equivalent to legal drunkenness. Within ten days, the level of impairment is the same as you’d have going 48 hours without sleep. This greatly lengthens reaction time, impedes judgment, and interferes with problem solving. In such a state of sleep deprivation, a single beer can have the same impact on our ability to sustain performance as a whole six-pack can have on someone who’s well rested.

The third factor has to do with circadian phase—the time of day in the human body that says “it’s midnight” or “it’s dawn.” A neurological timing device called the “circadian pacemaker” works alongside but, paradoxically, in opposition to the homeostatic drive for sleep. This circadian pacemaker sends out its strongest drive for sleep just before we habitually wake up, and its strongest drive for waking one to three hours before we usually go to bed, just when the homeostatic drive for sleep is peaking. We don’t know why it’s set up this way, but we can speculate that it has to do with the fact that, unlike other animals, we don’t take frequent catnaps throughout the day. The circadian pacemaker may help us to focus on that big project by enabling us to stay awake throughout the day in one long interval and by allowing us to consolidate sleep into one long interval at night.

In the midafternoon, when we’ve already built up substantial homeostatic sleep drive, the circadian system has not yet come to the rescue. That’s typically the time when people are tempted to take a nap or head for the closest Starbucks or soda machine. The caffeine in the coffee temporarily blocks receptors in the brain that regulate sleep drive. Thereafter, the circadian pacemaker sends out a stronger and stronger drive for waking as the day progresses.
Putting yourself or others at risk while driving or working at an impaired level is bad enough; expecting your employees to do the same is just irresponsible.

Provided you're keeping a regular schedule, the rise in the sleep-facilitating hormone melatonin will then quiet the circadian pacemaker one to two hours before your habitual bedtime, enabling the homeostatic sleep drive to take over and allow you to get to sleep. As the homeostatic drive dissipates midway through the sleep episode, the circadian drive for sleep increases toward morning, maintaining our ability to obtain a full night of sleep. After our usual wake time, the levels of melatonin begin to decline. Normally, the two mutually opposing processes work well together, sustaining alertness throughout the day and promoting a solid night of sleep.

The fourth factor affecting performance has to do with what's called “sleep inertia,” the grogginess most people experience when they first wake up. Just like a car engine, the brain needs time to “warming up” when you awaken. The part of your brain responsible for memory consolidation doesn't function well for five to 20 minutes after you wake up and doesn't reach its peak efficiency for a couple of hours. But if you sleep on the airplane and the flight attendant wakes you up suddenly upon landing, you may find yourself at the customs station before you realize you’ve left your laptop and your passport behind. There is a transitional period between the time you wake up and the time your brain becomes fully functional. This is why you never want to make an important decision as soon as you are suddenly awakened—ask any nurse who’s had to awaken a physician at night about a patient.

Most top executives are over 40. Isn’t it true that sleeping also becomes more difficult with age?

Yes, that’s true. When we’re past the age of 40, sleep is much more fragmented than when we’re younger. We are more easily awakened by disturbances such as noise from the external environment and from our own increasing aches and pains. Another thing that increases with age is the risk of sleep disorders such as restless legs syndrome, insomnia, and sleep apnea—the cessation of breathing during sleep, which can occur when the airway collapses many times per hour and shuts off the flow of oxygen to the heart and brain, leading to many brief awakenings.

Many people gain weight as they age, too. Interestingly, chronic sleep restriction increases levels of appetite and stress hormones; it also reduces one’s ability to metabolize glucose and increases the production of the hormone ghrelin, which makes people crave carbohydrates and sugars, so they get heavier, which in turn raises the risk of sleep apnea, creating a vicious cycle. Some researchers speculate that the epidemic of obesity in the U.S. and elsewhere may be related to chronic sleep loss. Moreover, sleep-disordered breathing increases the risk of high blood pressure and heart disease due to the strain of starving the heart of oxygen many times per hour throughout the night.

As we age, the circadian window during which we maintain consolidated sleep also narrows. That’s why airline travel across time zones can be so brutal as we get older. Attempting to sleep at an adverse circadian phase—that is, during our biological daytime—becomes much more difficult. Thus, if you take a 7 PM flight from New York to London, you typically land about midnight in your home time zone, when the homeostatic drive for sleep is very strong, but the local time is 5 AM. Exposure to daylight—the principal circadian synchronizer—at this time shifts you toward Hawaiian time rather than toward London time. In this circumstance, the worst possible thing you can do is rent a car and drive to a meeting where you have to impress people with your mental acuity at the equivalent of 3 or 4 in the morning. You might not even make the meeting, because you very easily could wrap your car around a tree. Fourteen or 15 hours later, if you’re trying to go to bed at 11 PM in the local time zone, you’ll have a more difficult time maintaining a consolidated night’s sleep.

So sleep deprivation, in your opinion, is a far more serious issue than most executives think it is.

Yes, indeed. Putting yourself or others at risk while driving or working at an impaired level is bad enough; expecting your employees to do the same is just irresponsible. It amazes me that contemporary work and social culture glorifies sleeplessness in the way we once glorified people who could hold their liquor. We now know that 24 hours without sleep or a week of sleeping four or five hours a night induces an impairment equivalent to a blood alcohol level of .1%. We would never say, “This person is a great worker! He’s drunk all the time!” yet we continue to celebrate people who sacrifice sleep.
The analogy to drunkenness is real because, like a drunk, a person who is sleep deprived has no idea how functionally impaired he or she truly is. Moreover, their efficiency at work will suffer substantially, contributing to the phenomenon of “presenteeism,” which, as HBR has noted, exacts a large economic toll on business. [See Paul Hemp’s article “Presenteeism: At Work—But Out of It,” HBR October 2004.]

Sleep deprivation is not just an individual health hazard; it’s a public one. Consider the risk of occupational injury and driver fatigue. In a study our research team conducted of hospital interns who had been scheduled to work for at least 24 consecutive hours, we found that their odds of stabbing themselves with a needle or scalpel increased 61%, their risk of crashing a motor vehicle increased 168%, and their risk of a near miss increased 460%. In the U.S., drowsy drivers are responsible for a fifth of all motor vehicle accidents and some 8,000 deaths annually. It is estimated that 80,000 drivers fall asleep at the wheel every day, 10% of them run off the road, and every two minutes, one of them crashes. Countless innocent people are hurt. There’s now a vehicular homicide law in New Jersey (and some pending in other states) that includes driving without sleep for more than 24 hours in its definition of recklessness. There’s a man in Florida who’s serving a 15-year prison term for vehicular homicide—he’d been awake for 30-some hours when he crashed his company’s truck into a group of cars waiting for a light to change, killing three people. I would not want to be the CEO of the company bearing responsibility for those preventable deaths.

Sleep deprivation among employees poses other kinds of risks to companies as well. With too little sleep, people do things that no CEO in his or her right mind would allow. All over the world, people are running heavy and dangerous machinery or guarding secure sites and buildings while they’re exhausted. Otherwise intelligent, well-mannered managers do all kinds of things they’d never do if they were rested—they may get angry at employees, make unsound decisions that affect the future of their companies, and give muddled presentations before their colleagues, customers, the press, or shareholders.

What should companies be doing to address the sleep problem?
People in executive positions should set behavioral expectations and develop corporate sleep policies, just as they already have concerning behaviors like smoking or sexual harassment. It’s important to have a policy limiting scheduled work—ideally to no more than 12 hours a day, and exceptionally to no more than 16 consecutive hours. At least 11 consecutive hours of rest should be provided every 24 hours. Furthermore, employees should not be scheduled to work more than 60 hours a week and not be permitted to work more than 80 hours a week. When working at night or on extended shifts, employees should not be scheduled to work more than four or five consecutive days, and certainly no more than six consecutive days. People need at least one day off a week, and ideally two in a row, in order to avoid building up a sleep deficit.

Now, managers will often rationalize over-scheduling employees. I hear them say that if their employees aren’t working, they will be out partying and not sleeping anyway. That may be true for some irresponsible individuals, but it doesn’t justify scheduling employees to work a hundred hours a week so that they can’t possibly get an adequate amount of sleep. Of course, some circumstances may arise in which you need someone to remain at work for more than 16 consecutive hours. The night security guard, for example, can’t just walk off the job if his replacement isn’t there, so you will need to have a provision for exceptional circumstances, such as offering transportation home for a sleep-deprived worker.

Companies also need executive policies. For example, I would advise executives to avoid taking red-eye flights, which severely disrupt sleep. If someone must travel overnight internationally, the policy should allow the executive to take at least a day to adapt to the sleep deprivation associated with the flight and the new time zone before driving or conducting business. Such a policy requires some good schedule planning, but the time spent making the adjustments will be worth it, for the traveler will be more functional before going into that important meeting. And the sleep policy should not permit anyone, under any circumstances, to take an overnight flight and then drive to a business meeting somewhere—period. He or she should at least be provided a taxi, car service, or shuttle.

Companies can do other things to promote healthy sleep practices among employees.
What’s New in Sleep?

Sleep science is advancing on a number of frontiers that, over time, may cause us to rethink everything from our personal habits to public policy. Here’s a short sampling of these new developments.

Sleep is power. Your mother was right—to perform at your best, you need sleep. Discoveries about sleep cycles have given researchers new insight into the specific roles sleep plays in overall health and performance. For example, there is growing evidence that sleep aids in immune function, memory consolidation, learning, and organ function. “Some researchers now think sleep may be the missing link when it comes to overall health, safety, and productivity,” says Darrel Drobnich, the senior director of government and transportation affairs for the National Sleep Foundation. One new field of study is looking at a specific correlation between sleep and productivity, and the benefits of what sleep researchers call a “power nap”—a 20-minute period of sleep in the afternoon that heads off problems associated with cumulative sleep deficit.

Move over, Ambien. Ambien, the sleep aid from drugmaker Sanofi-Aventis, is now de rigueur for the sleepless, ringing up $1.4 billion annually in U.S. sales alone. While Ambien has fewer side effects than most over-the-counter sleep aids, it’s still a blunt instrument, neurophysiologically speaking. “All of the current products on the market, including Ambien, take a sledgehammer to specific receptors in the brain,” says Dr. Robert McCarley, the head of psychiatry at Boston VA Medical Center and a professor of psychiatry at Harvard Medical School. “They have several negative side effects, ranging from disassociated states of consciousness to potential addiction. They also tend to lose their effectiveness over time.” Researchers hope a new family of sleep-inducing drugs will function closer to the body’s natural sleep mechanisms and so avoid problems associated with sedatives like Ambien. One such new drug—Rozerem, from Japanese drug giant Takeda—targets melatonin receptors in the brain. As researchers learn more about the body’s internal sleep mechanisms, McCarley believes, sleep aids will inevitably improve.

On the other side of the equation, the pharmaceutical company Cephalon is now marketing modafinil, a drug that helps people function well on very little sleep without suffering the ill effects of common stimulants. Sold under the commercial trade name Provigil in the U.S., modafinil was originally prescribed to treat narcolepsy; it’s now used to promote wakefulness among those who can’t afford to go to sleep (such as field soldiers in war zones). Studies have shown that subjects taking modafinil are able to stay alert with only eight hours of sleep during an 88-hour period. While modafinil sounds like a dream drug, no one yet knows what effects may result from more than occasional use.

Car drowse alarms. By the end of the decade, automakers will offer cars outfitted with devices designed to keep drowsy drivers from falling asleep at the wheel. Some may use cameras to scan drivers’ eyes for droopiness, or to sense when people are loosening their grip on the steering wheel, and then sound an alarm. In 2005, Ford and Volvo announced that they were working on a system called Driver Alert, consisting of a camera that measures the distance between the vehicle and the markings on the surface of the road. If the driver starts to swerve, an alarm goes off and a text warning appears on the dashboard. Another approach under consideration by the U.S. National Highway Traffic Safety Administration is the development of “intelligent” highways equipped with specialized sensors that continuously track vehicle trajectory and speed.

Tomorrow’s workforce needs sleep now. Businesses need an educated workforce; ironically, school is interfering. The current high school schedule in the U.S., which typically begins around 7:20 AM, threatens the neurological development and health of adolescents, whose homeostatic drive operates differently from adults’. Most teens experience a delayed sleep phase, in which melatonin is released around 11 PM—an hour later than in most adults. Students who finally go to sleep by midnight and wake at 6 experience a chronic sleep deficit, which disrupts their ability to learn and puts them and you at risk on the roads. In the U.S., researchers and sleep advocates are now working closely with school districts, communities, and educators to change school start times so that students can get more sleep.

—Bronwyn Fryer
Educational programs about sleep, health, and safety should be mandatory. Employees should learn to set aside an adequate amount of time for sleep each night and to keep their bedrooms dark and quiet and free of all electronic devices—televisions, BlackBerries, and so on. They should learn about the ways alcohol and caffeine interfere with sleep. When someone is sleep deprived, drinking alcohol only makes things worse, further eroding performance and increasing the propensity to fall asleep while also interfering with the ability to stay asleep. Additionally, companies should provide annual screening for sleep disorders in order to identify those who might be at risk. For example, this past year our team launched a Web-based screening survey that any law enforcement officer in the U.S. can take to help identify whether he or she is suffering from sleep apnea, restless legs syndrome, narcolepsy, or other sleep disorders. Those whose answers place them at high risk are referred for evaluation and treatment by a specialist accredited by the American Academy of Sleep Medicine. [Accredited sleep centers may be found at www.sleepcenters.org.]

Finally, I would recommend that supervisors undergo training in sleep and fatigue management and that they promote good sleep behavior. People should learn to treat sleep as a serious matter. Both the company and the employees bear a shared responsibility to ensure that everyone comes to work well rested.

This corporate sleep policy of yours sounds a little draconian, if not impossible, given people's crazy schedules.

I don't think it's draconian at all. Business travelers expect that their pilots won't drink before flying an airplane, and all of us expect that no driver on the highway will have a blood alcohol level above the legal limit. Many executives already realize that the immediate effect of sleep loss on individuals and on overall corporate performance is just as important. A good sleep policy is smart business strategy. People think they're saving time and being more productive by not sleeping, but in fact they are cutting their productivity drastically. Someone who has adequate sleep doesn't nod off in an important meeting with a customer. She can pay attention to her task for longer periods of time and bring her whole intelligence and creativity to bear on the project at hand.

What do you think about the use of drugs that help people fall asleep or that shut off the urge to sleep?

These agents should be used only after a thorough evaluation of the causes of insomnia or excessive daytime sleepiness. Patients too often think there's a silver bullet for a problem like insomnia, and doctors too easily prescribe pills as part of a knee-jerk reaction to patient requests during the final minutes of an office visit. The causes of insomnia are subtle and need to be carefully investigated. These can be from too much caffeine, an irregular schedule, anxiety or depression, physical problems such as arthritis, use of other medications, and so on—and only a careful evaluation by a doctor experienced in sleep medicine can uncover the causes. I once saw a professor who complained of difficulty sleeping at night, and only after taking a careful history did we find that he was drinking 20 cups of coffee a day. He didn't even realize he was drinking that much and didn't think about the fact that so much caffeine, which has a six- to nine-hour half-life, would interfere with his ability to sleep. Prescribing a sleeping pill for his insomnia without identifying the underlying cause would have been a mistake.

There are non-pharmacological treatments for insomnia that seem very promising, by the way. Cognitive behavioral therapy, or CBT, helps people recognize and change thoughts and behaviors that might be keeping them awake at night. A researcher named Dr. Gregg Jacobs at Harvard Medical School has reported that CBT works better over both the short and the long term than sleeping pills do.

Sometimes executives simply have to function without much sleep. What are some strategies they can use to get by until they can go to bed?

Though there is no known substitute for sleep, there are a few strategies you can use to help sustain performance temporarily until you can get a good night's sleep. Obviously, executives can drink caffeine, which is the most widely used wake-promoting therapeutic in the world. Naps can be very effective at restoring performance, and if they are brief—less than a half hour—they will induce less gogginess upon awakening. Being in a novel or engaging circumstance will also help you stay alert. Exercise, standing in an upright po-
sition, and exposure to bright light are all very helpful. Human beings are amazingly sensitive to light. In fact, the color of light may also be important. Exposure to shorter wavelength blue light is particularly effective in suppressing melatonin production, thereby allowing us to stay awake during our biological night. Photon for photon, looking up at the blue sky, for example, is more effective in both resetting our biological clock and enhancing our alertness than looking down at the green grass.

While all these things can help an executive function in an emergency, I must reiterate that he or she should still not drive when sleep deprived, even if a cup of coffee or a walk on a sunny day seems to help for a little while.

**Do you get enough sleep?**
Like everyone else, I try to, but I don’t always achieve it.

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1. Dr. Czeisler is the incumbent of an endowed professorship donated to Harvard by Cephalon and consults for a number of companies, including Actelion, Cephalon, Coca-Cola, Hypnion, Pfizer, Respironics, Sanofi-Aventis, Takeda, and Vanda.

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WORK HOURS, SLEEP AND PATIENT SAFETY IN RESIDENCY TRAINING

CHARLES A. CZEISLER, PH.D., M.D.

BOSTON, MASSACHUSETTS

Case Presentation

In February, 2005, I was asked by the Department of Anesthesia at the Brigham and Women’s Hospital in Boston to attend their Morbidity and Mortality Weekly Report rounds to discuss a fall-asleep motor vehicle crash that had occurred on February 20, 2005 in one of their trainees. The trainee was a 39-year-old white male who was in his fifth postgraduate year of training as an anesthesia fellow (Case A.F.). At about 3 pm on February 20, 2005, A.F. fell asleep at the wheel and collided with a stopped vehicle while he was en route home from a 7-hour work shift at the Brigham and Women’s Hospital. There was no injury to the fellow, to the other driver or to her 5-year-old child—and hence there is no litigation involved—which is why I am able to present Case A.F. to you today. A.F. reported a similar incident four years earlier in which he had fallen asleep at the wheel while driving his car at high speed on an expressway during a commute home from a >30-hour extended duration work shift in his first postgraduate year of training. In that incident, A.F. was awoken by a rumble strip on the expressway and thereby avoided a potentially catastrophic motor vehicle crash. He said that he understood that the >30-hour shift had made him vulnerable to the fall-asleep incident while driving on the highway during his PGY1 year. However, he wondered why he experienced a fall-asleep crash during his PGY5 year, after working a much shorter, seven-

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Dr. Czeisler serves or has served as a paid consultant for Actilion, Avera Pharmaceuticals, Inc., Axon Sleep Research Laboratories, Cephalon, Hypnion, Lifetrac, Neurocrine, Sanofi-Aventis, Pfizer, Respironics, Takeda, Unilever and Vanda Pharmaceuticals; owns equity interest in Hypnion, Lifetrac and Vanda and has received clinical trial research contracts and investigator-initiated research grants from Cephalon and Pfizer. Dr. Czeisler’s laboratory has received unrestricted research and education funds from Cephalon and he serves as the incumbent of an endowed professorship provided to Harvard University by Cephalon.
hour shift. To address this question, I initiated a series of steps comparable to those which might be undertaken by investigators (such as local or state police departments or the National Transportation Safety Board) evaluating if sleepiness or sleep deprivation were a probable contributing factor to a transportation accident.

**Work-hour and Sleep-wake History**

As a PGY-5 anesthesia fellow, A.F.’s work schedule required that he be “on call” from home for the intensive care unit for two out of every three weeks. He reported that his sleep habits were as follows: (1) during non-call/non-work nights (which occurred 6 times per month) his nightly sleep episode was from 10 pm to 6:30 am; (2) during non-call/work nights (which occurred 7–14 times per month) his nightly sleep episode was from 10 pm to 4:30 am; (3) during on-call/work nights (which occurred 7–21 times per month) his nightly sleep episode was from 10 pm to 4:30 am and he was awoken by 3–4 pages from the intensive care unit per night. Finally, A.F. noted that he and his wife were typically awoken once per night by one of their three young children for about 20 minutes per night.

**Pharmacologic History**

A.F. denied alcohol or hypnotic drug use prior to the crash. He admitted using caffeine, which he reportedly administered in the form of “three shots of espresso” each morning and which he said he “titrated to effects” during the remainder of the day (typically two more small cups of coffee). He reported that he avoided caffeine most afternoons, including the day of the crash, in order to avoid disturbing his subsequent night of sleep.

**Hospital Paging Records**

The times at which A.F. was paged were downloaded from the Brigham and Women’s Hospital paging system records and are illustrated together with his reported sleep-wake times, as recollected by history, during the prior four nights, in Figure 1. On the night before the crash, A.F. was paged twice at the beginning of his sleep episode, then awoken by a page from the ICU again at about 1:30 am, then awoken by a page just before 2 am and then awoken by a page again at approximately 3 am before his final page during that sleep episode, which was at about 3:30 am. He arose at 4:30 am, showered, dressed and ate breakfast (including three shots of espresso) prior to commencing a 50-mile commute into the hospital at 5:45 am.
Sleep Disorders Evaluation

A.F. was referred to Dr. David White, who then directed the Brigham and Women’s Hospital Sleep Disorders Service, for an evaluation. He reported a history of loud snoring, particularly when sleep deprived and when sleeping on his back. He denied weight change, restless legs, history of sleep attacks or limb weakness with extreme emotion (cataplexy) or a history of difficulty falling asleep or staying asleep. His physical examination was unremarkable (Height: 6’3”; Weight: 180 lbs; BMI: 22.5). Dr. White ordered a polysomnographic recording, which revealed an hourly apnea/hypopnea index (AHI) of 20.5, with an AHI of 47 per hour when supine and 2 per hour when sleeping on his side. Oxygen desaturations to 86 percent were recorded during the apneic events. Dr. White diagnosed A.F. with positional sleep-related breathing disorder and behaviorally induced insufficient sleep syndrome.

In order to put the results of this evaluation into context, it is important to understand the physiology of sleep and wakefulness.

Background on Determinants of Alertness and Performance

Multiple factors influence the ability to sustain effective waking neurocognitive performance in young healthy individuals not taking
medications. These include consecutive waking hours; nightly sleep duration; biological time of day (i.e., circadian phase); and the recency of the last sleep episode (i.e., sleep inertia). While the effects of these circadian and homeostatic sleep regulatory processes can be modified by environmental conditions, physical activity and pharmacological agents (i.e., stimulant and hypnotic agents), there is no countermeasure known that can consistently overcome the impact of adverse circadian phase and/or sleep deprivation on performance. The interaction of these regulatory processes can create an imposing biological force which can overpower an individual’s ability to sustain alert wakefulness and remain attentive. This leads to impaired neurocognitive performance, including reduced memory consolidation, and deterioration of waking performance marked by increased rates of attentional failures (1). These consequences of misalignment of circadian phase and the wake-sleep schedule, cumulative sleep deprivation and lengthy prior wakefulness are particularly evident while attempting to sustain attention for a continuous duration of time (e.g., for 10–20 minutes or more) while performing a routine, highly over-learned task such as driving a motor vehicle.

The Sleep Homeostat

Without sleep, alertness and neurocognitive performance exhibit a steady deterioration attributable to sleep loss, onto which a rhythmic circadian variation is superimposed (2–18). Among individuals who win the struggle to remain awake, 24 hours of sleep deprivation has been shown to impair neurobehavioral performance to an extent that is comparable to a level of 0.10 percent blood alcohol content (19). In fact, the duration of time it takes to react to a visual stimulus (simple reaction time) averages three times longer after 24 hours of wakefulness than before an individual has stayed up all night (20) (Figure 2). Moreover, this is when the risk of attentional failures—in which the eyes begin rolling around in their sockets at the transition from wakefulness to sleep—is greatest. Within several days, chronic sleep restriction has been demonstrated to yield impairment in neurobehavioral performance and a risk of attentional failures that increased to a level comparable to that seen with acute total sleep deprivation (21,22). In fact, six hours of time in bed per night for a week or two brings the average young adult to the same level of impairment as 24 hours of wakefulness, whereas 4 hours of time in bed per night gets there in four to six days and induces a level of impairment comparable with 48 hours of wakefulness (i.e., two consecutive days and nights without sleep) after 10 days of restriction. As with alcohol intoxication, chron-
ically sleep-deprived individuals tend to underestimate the extent to which their performance is impaired, despite increasing impairment evident in objective recordings of the rate of lapses of attention (23). Objective measures of performance, including reaction time and memory, worsen. The effects of recurrent nights of sleep restriction are not overcome with a single night of sleep. Increasing sleep deprivation leads to an increased probability of experiencing lapses of attention,
episodes of automatic behavior and/or falling asleep while attempting to remain awake. In a condition of chronic sleep deprivation, even when wakefulness is scheduled during an appropriate circadian phase, the probability of a sleep-related attentional failure or neurocognitive performance failure while waking is markedly increased (23,24). Moreover, repeated interruptions of sleep, such as is experienced by physicians when they are on call, degrade the restorative quality of sleep compared to an equal amount of consolidated sleep. This is thought to be a primary basis for the excessive daytime sleepiness associated with sleep disorder breathing, which induces many brief arousals during the night. Interestingly, just being on call disturbs sleep, even when the individual is not called (25,26). Dr. Marshall Wolf and I learned this firsthand when recording the sleep of interns in a study that we did with Dr. Gary Richardson and that Dr. Wolf presented to this group fifteen years ago (27). As shown in Figure 3, the sleep of this young intern was acutely disturbed while he was on call, with little deep slow wave sleep and many awakenings that were not accounted for by the two pages that were received. This intern remained awake for almost an hour after being awakened by a page the second time.

![Image](image_url)

**Fig. 3.** Polysomnographic recording of sleep in an intern on call. The figure depicts the hypnogram and the effects of two pages during the night in an intern from the group not covered by a night float. “Pager” indicates an electronically recorded page was issued to the intern’s beeper at the time indicated on the X-axis. “Begin/End sleep period” indicate the times recorded by the intern for these events in the diary. This record demonstrates the variable impact of pages during sleep. The first page, from one of the nursing stations, occurred at approximately 4.08 am. The page occurred while the intern was in stage 4 and produced only a brief movement without unambiguous awakening. Approximately 28 minutes later, the same nursing station paged again, this time awakening the intern from REM sleep. The intern subsequently remained awake for almost an hour despite no additional pager activity. Reprinted with permission from Richardson et al (26). Copyright 1996 Associated Professional Sleep Societies, LLC.
The impact on the brain of resulting insufficient sleep is only beginning to be appreciated. Positron Emission Tomography (PET) imaging has revealed that sleep deprivation is associated with decreased metabolism in the thalamus, the pre-frontal cortex and the parietal cortex (28). Metabolic studies have demonstrated that such sleep curtailment also has adverse effects on the metabolic and immune systems.

**Sleep Attacks and Sleep Drunkenness**

Individuals struggling to stay awake in the face of elevated sleep pressure—whether due to acute total sleep deprivation, chronic sleep restriction or repeated interruption of sleep (due to external interruptions or the presence of a sleep disorder)—are not always able to do so by the sheer force of will. Sleep deprivation greatly increases the risk that an individual will succumb to the increased sleep pressure when their brain initiates an involuntary transition from wakefulness to sleep. This transition is initiated by the ventrolateral preoptic (VLPO) area of the hypothalamus, which Saper et al. have identified as the brain’s “sleep switch” (29). Another region of the hypothalamus, the suprachiasmatic nucleus (SCN), which serves as the central neural pacemaker of the circadian timing system, interacts with the VLPO such that there are two times of day at which such an involuntary transition from wakefulness to sleep is most probable: in the latter half of the night near the habitual wake time and in the mid-afternoon. Of course, once an individual has lost the struggle to stay awake and makes the transition from wakefulness to sleep, driving performance is much worse than that of a drunk driver, as the individual is unresponsive to the environment. Moreover, sometimes drowsy drivers linger in an intermediate state between sleep and wakefulness. The operator of a motor vehicle in this sleep-like condition—which probably represents a transitional state in which part of the brain is asleep while part of the brain remains awake—may maintain full pressure on the accelerator pedal and proceed for a considerable distance, even negotiating gradual turns, but fail to heed stop signals or respond appropriately to traffic conditions in a timely manner. This intermediate state, which has been termed “automatic behavior syndrome” or “sleep drunkenness” is characterized by retention of the ability to turn the steering wheel and to carry out rudimentary tasks and to provide semi-automatic responses to stimuli without appropriate cortical integration, often resulting in a complete loss of situational awareness and judgment (30). Some of you may have experienced this state when you suddenly realize that you have no idea how you went from point A to point B on the expressway—as if there were a missing segment in the
video of life. One drowsy driver who steered his car toward an oncoming car and then tracked it as the other driver swerved to avoid him reported “waking up” from this state just in time to observe vividly through his windshield a terrified look on the face of the other driver only a moment before he killed her in a head-on collision (31). A similarly impaired NASA ground controller working in the Mission Control Room of the Johnson Space Center during the middle of the night shift sent a Space Shuttle careening into a spin while crew members were asleep when he repeatedly overrode automatically generated coordinates designed to keep the shuttle on track.

Circadian Rhythmicity

Circadian rhythms, i.e., biological rhythms oscillating with an approximate period of twenty-four hours (from the Latin words: circa—about and dies—a day), are present at all levels of biological complexity from unicellular organisms to humans. Circadian rhythms are endogenous (i.e., internally generated), self-sustaining oscillations; therefore, rhythmicity persists in the absence of periodic external time cues. In humans, many physiological processes, including the body temperature cycle, endocrine patterns, renal and cardiac function, subjective alertness, sleep-wake behavior and performance vary according to the time of day (4,20,32–37). The circadian contribution to variations in alertness and performance is generated by a light-sensitive circadian pacemaker that also drives the circadian rhythms of core body temperature, plasma cortisol and plasma melatonin (5,38–50). The endogenous circadian clock is a major determinant of the timing and internal architecture of sleep in humans (5,6). Spontaneous sleep duration, sleepiness, REM sleep propensity, and both the ability and the tendency to sleep vary markedly with circadian phase or biological time of day and interact with a homeostatic process to regulate sleep propensity and daytime alertness and neurocognitive performance (7–10,51–53). As noted above, deep within the brain, two bilaterally paired clusters of hypothalamic neurons comprising the SCN of the hypothalamus act as the central neural pacemaker for the generation and/or synchronization of circadian rhythms (54–60). This endogenous circadian pacemaker is a major determinant of daily variations in subjective alertness and cognitive performance (4,9,11,12,20,24,38). These and other studies have shown that there is a prominent circadian variation in objective and subjective measures of alertness, performance (psychomotor, vigilance, memory) and attention or ability to concentrate, with a nadir in the latter half of the usual sleep time, just before our usual wake time (Figure 2). Similarly, the peak drive for
waking emanating from the hypothalamic circadian pacemaker occurs a couple of hours before our habitual bedtime. This paradoxical relationship between the output of the circadian pacemaker and the timing of the sleep-wake cycle is thought to help consolidate sleep and wakefulness in humans (8). Thus, under ordinary circumstances as the homeostatic drive for sleep increases throughout the 16-hour waking day, the circadian pacemaker sends out a stronger and stronger drive for waking during the latter half of the habitual waking day. Then, near the peak of the circadian drive for waking, about 1–2 hours before the habitual bedtime, the hormone melatonin is released. Activation of melatonin receptors on the surface of human SCN neurons suppresses the firing of those neurons. Since the SCN continues to oscillate with a near-24-hour period in the absence of SCN neuronal firing, this action of melatonin is thought to quiet the wake-promoting signal emanating from the SCN, thereby allowing us to fall asleep at our habitual hour. Similarly, the SCN sends out a strong drive promoting sleep in the latter half of the night, which helps to consolidate sleep once the pressure for deep slow-wave sleep is satiated in the first half of the night. The latter half of the night is richest in REM sleep, which has a very prominent circadian rhythm in its propensity. When one stays awake all night, in the latter half of the night near the habitual wake time, elevated homeostatic drive for sleep interacts with the circadian peak of sleep propensity to create a critical zone of vulnerability.

In the absence of periodic time cues, the period of the human circadian pacemaker is slightly longer than 24 hours (61,62). In order for the biological clock to coordinate its function with the timing of events in the external world that operates on a 24-hour schedule, daily information from the environment must therefore reach the circadian pacemaker. The circadian pacemaker is essentially reset by a small amount each day by this external stimulus in order to maintain synchrony with the 24-hour day (5,40,61).

Light is the principal environmental synchronizer of the mammalian SCN. The SCN is connected to specialized intrinsically photosensitive retinal ganglion cells containing the newly discovered photopigment melanopsin via a monosynaptic pathway called the retinohypothalamic tract (RHT), the presumed conduit by which information from the external light-dark cycle reaches the circadian clock. Properly timed exposure to light and darkness can rapidly shift the phase of the endogenous circadian pacemaker in humans (34,38–50,63,64). Both the magnitude and direction of the phase shifts induced by light are dependent on the timing, duration, intensity and wavelength of the light exposure (39,40,46–49,64–70). On average, light exposure occur-
ring during the first half of the biological night resets the circadian clock to a later hour; light received in the latter half of the biological night resets the circadian clock to an earlier hour. Thus, the circadian pacemaker of an individual living on a conventional schedule of day work and night sleep is synchronized by the naturally occurring light-dark cycle to oscillate at the same period as the Earth's solar day, i.e., 24 hours.

Sleep Inertia

Fifty years ago, following a crash inquiry, scientists in the U. S. Air Force Laboratory discovered that performance is markedly degraded during the transition from wakefulness to sleep (71–83). The extent to which this phenomenon, now called sleep inertia, interferes with neurobehavioral performance is related to the depth of the prior sleep episode (78). Thus, agents that interfere with sleep, such as caffeine, can mute the effect of sleep inertia (84). Remarkably, as we recently reported, the adverse impact of sleep inertia on performance can far exceed the impact of total sleep deprivation (83) (Figure 4). Once residents are able to get to sleep, these house officers—who are often subjected to acute total sleep deprivation after days, weeks or months of chronic sleep restriction—often experience very deep sleep. When this occurs while residents are on call in the hospital, they may be required to make critical care decisions or perform life-saving medical

![Figure 4: Impact of sleep inertia on cognitive performance upon awakening compared with 24 hours without sleep. Reprinted with permission from Wertz et al. (83). Copyright 2006 American Medical Association.](image-url)
procedures in an impaired state due to profound sleep inertia (15,83). Moreover, at times of night when they have the greatest patient care responsibilities due to the lack of on-site faculty supervision, resident physicians—who sleep on average just 2.6 hours while working 30-hour extended duration “on-call” shifts (85)—are likely to descend rapidly into deep stages 3 and 4 sleep during those two-hour naps, and then attempt to care for patients in an impaired confusional state—characterized by grogginess, disorientation in time or space, slowed mentation and slowed speech—immediately upon awakening.

There are a number of other factors that can have an impact on alertness and performance. These include the length of time on task, the level of environmental stimulation, the level of physical activity, posture, the level of task stimulation/novelty, and the use of pharmacologic agents with stimulant or hypnotic properties. Caffeine is the most widely used drug in the world. In fact, coffee beans are the second most widely traded commodity in the world, second only to oil. Caffeine administration can reduce the adverse impact of misalignment of circadian phase as well as increased homeostatic pressure on neurobehavioral performance (86). However, the dose and timing of administration is not always optimal. Specialty brand coffee, such as that available from retail outlets such as Starbucks and Dunkin’ Donuts, contain 3–4 times as much caffeine per ounce as does home brewed coffee. Super-size (e.g., 24 ounce) servings can thus contain more than a gram of caffeine, as much caffeine as an entire 10-cup pot of home-brewed coffee. When taken in the morning, these large doses of caffeine are being administered when sleep pressure is lowest, with levels declining throughout the day. When taken in the evening, caffeine—which has a 6- to 9-hour half life—may interfere with recovery sleep. When used as a wake-promoting therapeutic, the minimum effective dose of caffeine should be taken at the optimal time to help sustain performance when adequate sleep cannot be obtained. However, neither caffeine nor other wake-promoting therapeutics are a substitute for sleep. In fact, in a study of fatal-to-the-driver truck crashes, the National Transportation Safety Board (NTSB) found that plasma caffeine levels were highest in drivers involved in fatigue-related crashes (87). The NTSB interpreted high plasma caffeine data from those drivers as indicating that the drivers were taking caffeine to try to combat their fatigue. Unfortunately, even high levels of caffeine were insufficient to save those drivers from the effects of fatigue, which the NTSB found to be the leading cause of fatal crashes in those trucker drivers, equal to the fraction of crashes caused by both drugs and alcohol combined (87).
Underlying Medical Condition and Age

A number of medical conditions and/or the medications used to treat those conditions are associated with increased sleep tendency, increased risk of lapses of attention and increased risk of sleep-related accidents (88). These include primary sleep disorders, such as narcolepsy and sleep apnea, as well as sleep disturbance secondary to a medical condition or its treatment. Obstructive sleep apnea patients, for example, with an apnea/hypopnea index greater than 10, have a 6-fold increase in risk of traffic accidents (89). Age decreases the risk of sleep-related lapses of attention at night; in fact, young people are at the greatest risk of the hazards of sleep loss (90). Thus, at first blush, one might hypothesize that senior staff rather than new trainees should be assigned to work marathon overnight shifts. However, before you hastily assign all extended duration night work to your chiefs of service, I would caution you to recognize that as we get older, it becomes more and more difficult to obtain the recovery sleep that is needed following sleep deprivation. In fact, even when sleep deprived, older people have a great deal of difficulty sleeping at an adverse circadian phase (10,16,91).

Graduate Medical Education and Sleep

Extended duration work shifts, like many other features of graduate medical education in the United States, were the product of the postgraduate medical education curriculum developed by William Steward Halsted, M.D. Professor Halsted, who was Surgeon-in-Chief at the Johns Hopkins Hospital, was internationally renowned for his innovations in medical education. He founded the surgical training program at the Johns Hopkins Hospital in the 1890s, which served as a model for postgraduate medical education. He required physicians-in-training to live in the hospital (they were quite literally residents) and discouraged them from marrying so that they could devote themselves to medicine (92). He required residents to be on a “q1” call schedule, i.e. they were on call 362 of 365 days per year. He taught devotion to the profession by example, working heroic hours with his trainees. Only recently was it revealed how he maintained this grueling sleep-deprived schedule. Professor Halsted was in fact addicted to cocaine, an addiction that was an unfortunate by-product of his pioneering work developing cocaine as a surgical anesthetic (93). He spent more than a year in a rehabilitation program at a Rhode Island hospital trying to shed his cocaine addiction prior to his appointment as the first Professor of Surgery at Johns Hopkins Medical School. However he only
gained an addiction to morphine there, which had been used to treat his cocaine addiction (93).

Today, the use of powerful stimulants to allow personnel to remain awake during extended duration work shifts is restricted to certain branches of the military, such as the United States Air Force, which still distributes methamphetamine routinely to pilots required to fly lengthy missions and to other critical military personnel. Of course, neither medical school faculty nor their hospital trainees are allowed to use cocaine or methamphetamine to stay awake for long hours, nor should they be allowed to do so. Yet, based on a 19th century tradition dated to the time of Halsted, academic medical centers continue to single out physicians-in-training as the only group of hospital employees who are required to work for 30 consecutive hours and to work more than double the standard work week. Using a validated survey instrument, we found that in 2002–2003, half of the interns we studied worked more than 80 hours per week, with 11% working more than 100 hours per week (Figure 5). Some were required to work more than 120 hours per week (85), which is remarkable given that there are only 168 hours in a week. During that year, we estimate that physicians-in-training worked 20,000 shifts in the United States that exceeded 40 consecutive hours, with about 2,000 shifts exceeding 64 consecutive

![Figure 5](https://example.com/fig5.png)

**FIG. 5.** A total of 17,003 person-months of data were collected from a nationwide sample during 2002–2003. The distribution of the percentages of reported weeks with a given range of work hours is shown in this chart. Reprinted with permission from Barger et al (85). Copyright 2005 Massachusetts Medical Society.
hours (85) (Figure 6). Theoretically, the work-hour reforms instituted by the Accreditation Council of Graduate Medical Education (ACGME) in 2003 should have reduced the duration of the longest of these shifts to 30 consecutive hours, although there has been no independent

Fig. 6. The longest shifts reported by participants are shown in the chart at the top. The chart at the bottom shows the number of surveys in which participants reported shifts that exceeded 40 hours. Reprinted with permission from Barger et al (85). Copyright 2005 Massachusetts Medical Society.
verification that these voluntary guidelines are being consistently enforced. Moreover, the new ACGME guidelines largely sanctioned what was already the status quo in most hospitals, since interns averaged 70.7 ± 26.0 work hours per week (85) before the ACGME instituted an 80- to 88-hour limit (averaged over four weeks) and the average duration of the extended duration “on-call” shifts was 32.0 ± 3.7 hours before the ACGME instituted their limit of 30 consecutive work hours per shift. On many of these marathon ~30-hour shifts, we found that trainees obtained little or no sleep (85) (Figure 7). Even among interns who spent the greatest amount of time in the hospital per week, less than 5% of that time was spent sleeping (85) (Figure 8). In fact, we found that interns averaged only 2.6 ± 1.7h of sleep on extended duration (>24-hour) work shifts, and that those who were covered by night floats only obtained an additional half hour of sleep (85).

The recent discovery that memory consolidation and learning depends on the sleep obtained after training on a task has called into question the wisdom of keeping residents awake all night as part of their education (94–98). In order to address the impact of such schedules on patient care, the Harvard Work Hours, Health and Safety Group (HWHHSG) conducted a clinical trial for the Medical Intensive Care (MICU) and the Coronary Care (CCU) Units at the Brigham and Women’s Hospital in Boston (1, 99). Interns were randomly assigned to work a three week rotation in the CCU or the MICU either on the traditional “q3” schedule, in which they worked an extended duration (~30 hour) work shift every other shift, or an intervention schedule in which the 30-hour extended duration work shift was split in half such that no scheduled work shift exceeded 16 consecutive hours. Dr. Steven Lockley, Dr. Daniel Aeschbach and our colleagues in the HWHHSG examined the relationship between work hours, sleep and the ability to sustain attention in these trainees. We found that on the traditional schedule, 85% of all work hours occurred on extended duration (>24h) work shifts, whereas none of their work time was spent on extended duration shifts on the intervention schedule (1) (Figure 9). Moreover, on the traditional schedule, interns were twice as likely to have slept less than 2 hours in the 24 hours prior to each hour worked, whereas on the intervention schedule, they were twice as likely to have obtained at least 8 hours of sleep in the prior 24 hours (1). We found that the interns worked fewer hours and slept more hours per week on the interventional schedule, and that there was a negative correlation between hours worked and hours slept (1) (Figure 10). We found that interns working extended duration shifts were twice as likely to expe-
Fig. 7. The greatest number of hours without sleep as a percentage of monthly reports is shown in the chart at the top. The chart at the bottom shows the number of surveys in which participants reported more than 40 continuous hours without sleep. Reprinted with permission from Barger et al (85). Copyright 2005 Massachusetts Medical Society.
experience attentional failures while working at night than were interns scheduled to work no more than 16 consecutive hours (1) (Figure 11).

But what about patient care? Prior research at the Brigham and Women’s Hospital had found that discontinuity in patient care (patient handoffs) increased the risk of preventable adverse events (100), although this increase could be eliminated by use of a computerized sign out system (101). Reduction in the duration of extended work shifts by half would necessarily double the number of required handoffs of care. Thus, we wondered which was safer for the patient, a tired intern who remained with the patient throughout the night after admission, or a better-rested intern to whom care of the patient was transferred. In order to answer that question, we teamed up with the Patient Safety Center for Excellence led by Dr. David Bates at the Brigham and Women’s Hospital and obtained research support for a study from the Agency for Healthcare Research and Quality and the National Insti-
Institute for Occupational Safety and Health. Dr. Christopher Landrigan, Dr. Jeffrey Rothschild and our colleagues in the HWHHSG then hired a team of physicians to monitor these interns around the clock while they worked in the MICU and CCU. In addition, we hired research nurses to review the medical records of their patients and search for medical errors. Finally, we presented all events noted by these observers to a panel of reviewers who were blind to condition and rated each event. Only serious medical errors were analyzed.

Interns working extended duration “on call” shifts made 35.9% more serious medical errors, including more than 5 times as many serious diagnostic mistakes, as interns scheduled to work no more than 16 hours each day. Fig. 9 shows the proportion of total work hours plotted against the duration of the shift during the Traditional Schedule (top chart) and the Intervention Schedule (bottom chart). Reprinted with permission from Lockley et al (1). Copyright 2004 Massachusetts Medical Society.
We found that interns working extended duration shifts made more serious mistakes that reached the patients than those who worked shorter shifts, notwithstanding the fact that there were twice as many handoffs of patient care with the intervention schedule (99). We found that most of the serious medical errors were due to slips and lapses, i.e., failures to carry out intended plans of action, rather than knowledge-based mistakes (105).

In a companion nationwide survey study supported by the National Institute of Occupational Safety and Health, Dr. Laura Barger, Dr. Najib Ayas and our colleagues in the Harvard Work Hours, Sleep and Safety Group evaluated the impact of extended duration work shifts on

![Graphs showing subjective mean hours of work per week, duration of sleep, and the relationship between the duration of work and the duration of sleep for 20 interns during the Traditional schedule and the Intervention schedule.](image-url)
the risk of motor vehicle crashes among interns. We gathered 1,417 person-years of monthly survey data from 2,737 interns nationwide in 2002–2003. During that time, interns reported 320 motor vehicle crashes. Eighty-two percent of those crashes were documented by a police report, insurance claim, automobile repair record, medical record, photograph of the damaged vehicle or a written description of the motor vehicle crash. More than forty percent of the motor vehicle crashes were judged to be consequential, i.e., leading to treatment in an emergency department, more than one thousand dollars property damage or filing of a police report. No additional motor vehicle crashes were identified by a search of the Social Security Death Index or through participant’s emergency contacts.

In a prospective analysis of scheduled shifts (across individuals), we found that for each extended duration work shift scheduled per month, interns had an 8.8 percent (CI: 3.2%–14.4%) increased monthly risk of any reported motor vehicle crash, and a 16% (95% CI: 7.6% to 24.4%) increased monthly risk of a reported motor vehicle crash on the commute from work. Trainees who work 10 extended duration shifts per month on a “q3” schedule would thus have a 160% increased monthly risk of a reported motor vehicle crash on the commute from work. In a separate case-controlled analysis of the same data set, we found that the odds ratio for reporting a motor vehicle crash during the commute

-0.69 (traditional) vs. 0.33 (intervention) attentional failures per hour, p=0.02

-Non-significant trend toward decreased day / evening attentional failures as well

FIG. 11. Mean (+SE) number of attentional failures among the 20 interns as a group and individually while working overnight (11 pm to 7 am) during the Traditional schedule (filled bar) and the Intervention schedule (open bar). Reprinted with permission from Lockley et al (1). Copyright 2004 Massachusetts Medical Society.
from the hospital was 2.3 times (95% CI: 1.6 to 3.3) greater after an extended duration (>24h) work shift than after a non-extended work shift (85). The odds ratio for reporting a near miss crash was 5.9 (95% CI: 5.4 to 6.3) during the commute from work after an extended duration work shift as compared to the commute from a non-extended duration work shift (85).

Overall, based on this work, we found that the traditional practice of scheduling interns very long work weeks and extended duration work shifts was hazardous both to the intern themselves as well as to their patients (106). For this reason, the Sleep Research Society (SRS) which represents more than a thousand sleep scientists in the United States, together with the National Sleep Foundation (NSF) in Washington have endorsed legislation in Massachusetts that would limit resident work hours. This legislation is sponsored by Massachusetts State Senator Richard Moore, who requested guidance from the SRS regarding establishment of safer work hours for medical and surgical trainees. Table 1 illustrates the features of the pending legislation. Of note, the SRS and NSF recommend that all physicians be required to notify their patients and receive permission from the patients before caring for them if the physician has slept less than 2 hours in the prior 24 hours. In fact, a nationwide NSF poll found that 86 percent of people would feel anxious about their safety if they learned that their sur-

<table>
<thead>
<tr>
<th>Schedule Feature</th>
<th>Proposed Directive</th>
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<tr>
<td>Weekly Work Hours</td>
<td>Optimal maximum: 60 hours per week</td>
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<td></td>
<td>Fixed limit: 80 hours in any week</td>
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<tr>
<td>Consecutive Work Hours</td>
<td>Optimal maximum of 10 consecutive hours</td>
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<td></td>
<td>Fixed maximum of 18 consecutive hours</td>
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<tr>
<td>Maximal frequency of 18-hour night shifts</td>
<td>No more than one 18-hour overnight shift every 3 days</td>
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<td>Minimum Hours Off per Day</td>
<td>Minimum Hours Off</td>
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<td>- after 10-hour shift</td>
<td>- Optimum ≥12 consecutive hours off/day;</td>
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<td></td>
<td>minimum of 10 hours off per day</td>
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<tr>
<td>- after ≥18-hour shift</td>
<td>- Minimum of 16 consecutive hours off/day</td>
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<tr>
<td>High-intensity settings</td>
<td>Optimal limits required</td>
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<tr>
<td>Patient notification</td>
<td>Caring physician awake 22 of prior 24 hours</td>
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<tr>
<td>Consecutive Hours Off Duty per Week</td>
<td>Optimum ≥48 consecutive hours off/week</td>
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<td>Minimum 36 consecutive hours off/week, including two consecutive nights weekly.</td>
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<td>Minimum of 60 consecutive hours off duty each month.</td>
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geons had been on duty more than 24 hours, and 70% would likely ask for a different doctor (102). Given the findings that I have reported to you today, the SRS and NSF have concluded that a patient has the right to know if his/her physician were sleep deprived, so that the patient can decide whether or not be treated by that physician.

Probable Cause of Sleep-related Crash in Case A.F.

As shown in the initial case I presented today, there are many pathways that can lead physicians to become sleep deprived. The practice of scheduling physicians to be on call for weeks at a time covering busy services from home may seem innocuous compared to the practice of requiring physicians-in-training to work 30 consecutive hours. However, both sleep curtailment and frequent interruptions of sleep, alone or in combination as in this case, can lead to chronic cumulative sleep deprivation that can severely degrade performance and increase the risk of harm or injury. Case A.F. fell asleep at the wheel and crashed into a car with a 5-year old passenger after having been awake for only 10 hours, but he had been averaging only 5.8 hours per night of interrupted on-call sleep, and had worked seven consecutive days without a day off. The crash occurred in the mid-afternoon nap zone, which made him more vulnerable to the impact of sleep deprivation. In addition to behaviorally induced insufficient sleep syndrome, the trainee suffered from positional sleep-related breathing disorder. Taken together, this crash was certainly not an accident. A comprehensive fatigue management program that includes education regarding the principles of sleep and circadian physiology, implementation of safer policies regarding work hours (such as the limits endorsed by the SRS and NSF), and a comprehensive program to screen for sleep disorders would greatly reduce the risk of sleep-related errors and accidents like this one. Like alcohol-related crashes, sleep-related motor vehicle crashes are a preventable cause of injury. The National Highway Transportation Safety Administration estimates that there are more than 250,000 drowsy driver crashes annually; the Institute of Medicine estimates that drowsy driver crashes account for 20 percent of all injuries in motor vehicle crashes (107). With approximately 100,000 residents in training nationwide, steps should be taken to eliminate this preventable cause of injury.

Legal, Moral and Ethical Considerations

Given that drivers in the United States (Colorado, Massachusetts, Michigan and Florida) and Britain have been convicted of driving when impaired by sleepiness, and that the State of New Jersey has recently
amended its vehicular homicide statute to add driving after 24 hours without sleep to the definition of “reckless,” the legal and ethical question is raised as to who should be held responsible for the next motor vehicle crash in which a sleep-deprived resident kills or maims another motorist or pedestrian. No one falls asleep at the wheel without having struggled to stay awake beforehand, so the driver certainly bears legal and moral responsibility just as a drunk driver would. However, institutions that have put their trainees in harm’s way by requiring them to work for so many consecutive hours that they are virtually incapacitated by sleep deprivation cannot reasonably walk away from their responsibility to care for those who have been injured by sleep-deprived trainees. Take for example the case of Dr. Sook Im Hong. Dr. Hong was in the second week of her internship at Rush-Presbyterian-St. Luke’s Medical Center in Chicago when she fell asleep at the wheel after a 36-hour hospital shift and rear-ended another car, causing massive brain injuries to Heather Brewster (103). It is shocking to me that Rush Medical Center Attorney George F. Galland, Jr. succeeded in arguing that under Illinois law, the institution that required Dr. Hong to work for 36 consecutive hours does not bear any responsibility for the lifelong care of Ms. Brewster, a former college volleyball star who was a graduate student in physical therapy at the time of the crash. By arguing, on one hand, that the intern alone bears responsibility for sleep-related errors and accidents, and by requiring, on the other hand, that interns work 30-hour shifts as a condition of their employment, interns are being put in a “Catch 22” bind while they are at work. Moreover, given that appeals courts in two states (Oregon and West Virginia) have ruled that an employer’s responsibility for fatigue-related crashes can continue even after they have left work—similar in concept to the dramshop tort liability incurred by establishments serving alcohol to drivers subsequently involved in alcohol-related motor vehicle crashes—it is likely that courts will eventually hold hospitals that require trainees to work extended duration work shifts, notwithstanding evidence of the hazards of this practice, similarly liable. What about the trainees’ physicians? In California, physicians have an obligation to report to the Department of Motor Vehicles patients with conditions characterized by lapses of consciousness. Given that the interns working traditional 30-hour shifts in our study averaged more than five lapses of attention per night (99), do California physicians therefore have an obligation to report all house staff with behaviorally induced insufficient sleep syndrome under their care to the California Department of Motor Vehicles? All these questions will be left for the courts to decide.

But let us move beyond the legal questions. What moral or ethical responsibility should be borne by the program director who required a
trainee to work an extended duration shift that resulted in such an accident? What about the department chair or hospital president who requires or allows the program director to do so, knowing that such schedules increase the risk of motor vehicle crashes by more than 160%? Does the ACGME bear responsibility for continuing to sanction extended duration work shifts in the face of evidence that has revealed the hazards of such shifts? In my view, too many trainees on the thresholds of a medical career have already been killed or seriously injured in sleep-related crashes—or have killed or seriously injured others in sleep-related crashes—while attempting to commute home after working extended duration shifts. Even Professor Halsted never envisioned one of his charges getting behind the wheel of a car and attempting to drive at a speed of 60 miles per hour after working for 30 consecutive hours. These marathon work shifts are a vestige of a bygone era in which the pace of the hospital was much slower at night. There were no intensive care units in 19th century hospitals. There were no all night hospital laboratories. Resident physicians were not routinely expected to stay up all night admitting patients who had been kept in a holding area of the Emergency Department until the late evening. Hospitals today are round-the-clock operations focused on reducing patient length of stay by admitting patients only during the most acute phase of their illnesses. The work schedules to which our trainees are scheduled must now be changed to recognize that trainees can no longer sleep in the hospital. Moreover, resident physicians are now allowed to leave the hospital, live in the community and raise families. Our institutional training practices must therefore allow our trainees to take on these additional responsibilities during their training without endangering themselves, their families or others. Given the dictum “Physician, do no harm,” I would urge you as the leaders of American medicine to implement policies that eliminate the practice of scheduling trainees to work extended duration shifts. In the meantime, until this practice has been eliminated, our data indicate that institutions have an obligation—at the very least—to provide round trip transportation to trainees who are required to work extended duration shifts, as it is unsafe to expect or even allow them to drive with inadequate sleep. For this reason, the SRS, NSF and American Academy of Sleep Medicine have recently endorsed model drowsy driver legislation in Massachusetts. Of course, provision of transportation for trainees after extended duration work shifts begs the question as to whether it is appropriate for physicians who are too tired to drive home from work to be caring for patients (104).
Summary

The work schedules of physicians in training require them to work extraordinarily long work shifts and long work weeks. These schedules, which are based on a tradition that dates back to the 19th century, result in acute and chronic sleep deprivation. Sleep deprivation, misalignment of circadian phase and sleep inertia adversely impact cognitive performance and increase the risk of error and accident. Interns working extended duration shifts make significantly more serious medical errors while caring for patients in intensive care units, and make five times as many serious diagnostic mistakes. In addition to the deleterious effects of extended duration work shifts on patient safety, we also found that the risk of motor vehicle crashes is more than doubled driving home from work after such shifts. We conclude that the practice of working extended duration work shifts, which continues to be allowed by new ACGME regulations, are hazardous to both interns and their patients. Academic medical centers are urged to eliminate this now-dangerous tradition.

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REFERENCES


53. Dijk DJ, Shanahan TL, Duffy JF, Ronda JM, Czeisler CA. Variation of electroencephalographic activity during non-rapid eye movement and rapid eye movement sleep with phase of circadian melatonin rhythm in humans. J Physiol (Lond) 1997; 505.3:851–858.


Medical and Genetic Differences in the Adverse Impact of Sleep Loss on Performance: Ethical Considerations for the Medical Profession

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Abstract

The Institute of Medicine recently concluded that—on average—medical residents make more serious medical errors and have more motor vehicle crashes when they are deprived of sleep. In the interest of public safety, society has required limitations on work hours in many other safety sensitive occupations, including transportation and nuclear power generation. Those who argue in favor of traditional extended duration resident work hours often suggest that there are inter-individual differences in response to acute sleep loss or chronic sleep deprivation, implying that physicians may be more resistant than the average person to the detrimental effects of sleep deprivation on performance, although there is no evidence that physicians are particularly resistant to such effects. Indeed, recent investigations have identified genetic polymorphisms that may convey a relative resistance to the effects of prolonged wakefulness on a subset of the healthy population, although there is no evidence that physicians are over-represented in this cohort.

Conversely, there are also genetic polymorphisms, sleep disorders and other inter-individual differences that appear to convey an increased vulnerability to the performance-impairing effects of 24 hours of wakefulness. Given the magnitude of inter-individual differences in the effect of sleep loss on cognitive performance, and the sizeable proportion of the population affected by sleep disorders, hospitals face a number of ethical dilemmas. How should the work hours of physicians be limited to protect patient safety optimally? For example, some have argued that, in contrast to other professions, work schedules that repeatedly induce acute and chronic sleep loss are uniquely essential to the training of physicians. If evidence were to prove this premise to be correct, how should such training be ethically accomplished in the quartile of physicians and surgeons who are most vulnerable to the effects of sleep loss on performance without unacceptably compromising patient safety? Moreover, once it is possible to identify reliably those most vulnerable to the adverse effects of sleep loss on performance, will academic medical centers have an obligation to
evaluate the proficiency of both residents and staff physicians under conditions of acute and chronic sleep deprivation? Should work-hour policy limits be modified to ensure that they are not hazardous for the patients of the most vulnerable quartile of physicians, or should the limits be personalized to enable the most resistant quartile to work longer hours? Given that the prevalence of sleep disorders has increased in our society overall, and increases markedly with age, how should fitness for extended duration work hours be monitored over a physician’s career? In the spirit of the dictum to do no harm, advances in understanding the medical and genetic basis of inter-individual differences in the performance vulnerability to sleep loss should be incorporated into the development of work-hour policy limits for both physicians and surgeons.
Introduction

After a comprehensive review of the medical and scientific literature as part of a year-long study initiated at the behest of the United States Congress and supported by the Agency for Healthcare Research and Quality, the Institute of Medicine (IOM) Committee on Optimizing Graduate Medical Trainee (Resident) Hours and Work Schedules to Improve Patient Safety concluded this past year that working for more than 16 consecutive hours without sleep is unsafe for both physicians in training (residents) and their patients (1). This latest IOM report builds on earlier work by the IOM Committee on Sleep Medicine and Research, which conducted an independent review of the adverse effects of sleep loss on neurobehavioral performance, learning, cognition, health and safety (2). The IOM recommendations are consistent with the recommendations promulgated by the Association for American Medical Colleges (AAMC) in 2001 that resident physician work shifts be limited to no more than 12 consecutive hours in all high intensity clinical settings, such as intensive care units (ICUs) and emergency departments (3). Nearly forty years ago, it was recognized that—on average—interns made twice as many mistakes detecting cardiac arrhythmias when they were sleep deprived as compared to when they were more well rested (4). More recently, laparoscopic surgical simulator studies have revealed that, on average, error rates doubled in residents when they performed simulated surgery after a night on call as compared to when they were more well rested (5) (Fig. 1). In a meta-analysis cited by the IOM, which was conducted by Accreditation Council on Graduate Medical Education (ACGME) Senior Vice President of Field Activities, Dr. Ingrid Philibert, she concluded that after 24-30 hours of sleep deprivation, individual cognitive performance of the average person drops from the 50th to the 15th percentile of their performance when rested (6), and that clinical performance of physicians drops from the 50th to the 7th percentile of their performance when rested (6). There is also growing evidence that sleep plays an essential role in learning and memory consolidation, and that chronic sleep deprivation has many deleterious
health consequences, including an increased risk of obesity, diabetes, depression and cardiovascular disease (2;7-15).

The conclusion that acute sleep loss impairs both cognitive and psychomotor performance and increases the risk of error among healthy young adults in both laboratory evaluations (16;17) and in clinical settings (18) is consistent with previously published laboratory research on participant volunteers (2;19;20) and with the field data (21-26). As shown in Fig. 2, sleep deprivation combined with misalignment of circadian phase creates a critical zone of vulnerability in the latter half of the night (17). Paradoxically, instead of slowing down to preserve accuracy as reaction time increases, sleep deprivation often leads people to make hasty decisions based on inadequate information (27). This results in increased rates of errors on selective attention tasks that require a search for targets in the visual field (27). 40% of interns working extended duration ‘on call’ shifts slept less than 2 hours in a 30-hour interval, and more than 15% obtained less than 1 hour of sleep during that interval (24) (Fig. 3). Residents randomized to work extended duration (>24 hour) shifts experienced twice as many attentional failures (22) and—on average—made 36% more serious errors caring for patients in intensive care units, including 460% more serious diagnostic mistakes, as compared to the same physicians when they were scheduled to work no more than 16 consecutive hours in intensive care units (23). Nationwide, interns have a 168% increased risk of a motor vehicle crash driving home from extended duration (>24-hour) shifts (24) and were 73% more likely to suffer from a percutaneous injury when performing a procedure after their 20th hour of work than during shifts that averaged less than 12 hours in duration (26).

On average, after being awake for 24 hours, impairment on a simple reaction time test in individuals who remain awake during testing is comparable with the impairment observed at a blood alcohol concentration of 0.10 g/dL (17;28). In a survey of 2,737 resident physicians, our group found that one out of five first-year residents reported making a fatigue-related mistake that
injured a patient, and one out of twenty first-year residents reported making a fatigue-related mistake that resulted in the death of a patient (25). In months when interns worked more than 5 extended duration (>24-hour) work shifts, the risks of such fatigue-related injuries and deaths increased by 700 and 300%, respectively.

Many within and outside the profession of medicine have hailed the IOM report as a long-overdue acknowledgement by the medical profession of the dangers of an obviously hazardous tradition (29). Yet, many conscientious physicians and surgeons argue vehemently that working for 24 consecutive hours is safe and that working such long hours is essential for the training of physicians and inherent in the practice of medicine (30;31). What might be fueling such a passionate difference of opinion?

Wherever I have presented data on the average impact of sleep loss on performance, the most common question that I have been asked is about inter-individual differences. “Aren’t some people more resistant to the effects of sleep loss than others?” The follow-up comments by such questioners usually reveals an underlying premise that individuals in certain professions (e.g., police officers, fire fighters, physicians, surgeons, aviators, special forces, astronauts) may be more resistant than the average person to the effects of acute sleep loss or chronic sleep restriction on performance. In fact, even among healthy young adults, there are profound inter-individual differences in the impact of sleep loss on performance (2;32-38). In addition, healthy sleepers are likely to be much more resistant to the effects of sleep loss than the 50 to 70 million Americans who suffer from chronic disorders of sleep and wakefulness (2). In this paper, I will review the evidence for such differences and address the ethical implications of such diversity both for residents and for practicing physicians.
Inter-individual differences in tolerance to sleep loss in healthy young adults

Differences in vulnerability to sleep loss due to prior sleep-wake history. The ability to sustain attention, maintain cognitive performance and prevent attentional failures deteriorates when sleep is chronically restricted to 7 or fewer hours per night for a week or longer (2;39-41) (Fig. 4). Many habitually short sleepers may be harboring substantial sleep debt, as reflected by higher sleep tendency, suggesting that their habitually short sleep durations may not reflect a reduced underlying sleep need (42;43). Long work weeks together with commuting time often require others, who are not habitually short sleepers, to restrict the time available for sleep. This occurs to physicians during residency training, when weekly sleep durations are curtailed as weekly work hours increase (22;24;44). Yet, our data also reveal up to a two-hour difference in average nightly sleep durations among interns working the same number of hours per week in an ICU (22).

There are many factors that may lead to the inter-individual differences in the average amount of sleep obtained by residents working the same number of hours in the hospital, including differences in their responsibilities outside the hospital. The very concept of residency has changed since it was first introduced in the U.S. at the Johns Hopkins University School of Medicine by Professor William Stewart Halsted in the 1890s. At the time, residents were required to live at the hospital and were discouraged from marrying (45). In contrast, today residents live outside the hospital and many of these young physicians have families and become new parents during residency. The sleep of new mothers and fathers is often interrupted and curtailed by newborns, resulting in increased daytime fatigue (46;47). Multiple births exacerbate post-partum sleep deprivation and daytime fatigue, particularly for fathers (48). Children with sleep or health problems may also lead to sleep fragmentation, sleep deprivation and increased daytime fatigue in parents (49;50). Behaviorally induced insufficient sleep syndrome affects 7% of patients with excessive daytime sleepiness (EDS) in Japan and is associated with a high motor vehicle crash risk.
Both acute and chronic sleep loss, whether cause by work schedules, family responsibilities, social activities or health problems, will degrade tolerance and increase performance vulnerability to the sleep deprivation imposed by extended duration (>24-hour) work shifts.

Moreover, preliminary evidence suggests that even after 8 to 12 hours of recovery sleep, individuals with a history of recent exposure to chronic sleep loss may be more vulnerable to the effects of re-exposure to sleep restriction, exhibiting nearly double the deterioration in performance on a vigilance task upon acute sleep restriction to 4 hours of time in bed as compared with their response to the same challenge when their recovery sleep was not preceded by exposure to chronic sleep debt (52). Thus, resident work schedules that cause chronic sleep restriction and provide for only one night of recovery sleep per week may generate a deterioration of performance that becomes progressively greater with additional weeks of sleep curtailment. Despite intermittent opportunities for recovery sleep, individuals exposed to such schedules may become increasingly vulnerable to the adverse effects of sleep loss on performance. Four weeks of scheduled sleep extension (14 hours per night) can reduced fatigue and increased energy levels, but only after an average of more than 30 hours of accumulated sleep debt has been repaid (53). Irregularity in the timing of sleep and wakefulness can impede circadian adaptation to altered work-rest schedules (54); loss of circadian entrainment, in turn, impairs cognitive performance (55). Thus, available evidence indicates that prior sleep-wake history, including exposure to both acute and chronic sleep restriction, to sleep extension, and to irregular sleep-wake schedules, may greatly affect an individual’s resiliency in the face of sleep loss (2).

Age-related differences in the vulnerability to sleep loss. Thirty consecutive hours of sleep loss induces marked deterioration in neurobehavioral functions in health young participants (17). So long as participants remain awake, average reaction time after 24 hours without sleep is three times longer than when the same individuals are rested (17) (Fig. 2). The risk of lapses of attention is
Inter-individual Differences in Sleep-Deprived Performance Vulnerability  Czeisler

much higher during the latter half of the night, with the slowest 10% of reaction times lengthening to nearly six seconds after 24 hours without sleep (17). Remarkably, the impact of a single night of acute sleep deprivation on such measures is much less pronounced in older participants over the age of 55 years (56-58) (Fig. 5). This may be due to age-related loss of neurons in the ventro-lateral pre-optic (VLPO) area of the hypothalamus, which enables mammals to make the transition from wakefulness to sleep; age-related loss of VLPO neurons may also explain why the prevalence of insomnia rises with age. Because older people have greater difficulty obtaining recovery sleep at an adverse circadian phase (59), they are more vulnerable to the effects of a sequence of night shifts (60). Nonetheless, the data reveal that young adults are most severely affected by acute sleep deprivation; in fact, 55% of sleep-related motor vehicle crashes occur in drivers age 25 years or younger (61) (Fig. 6). Thus, it is both ironic and alarming that young resident physicians in this most vulnerable age group are subjected to acute sleep deprivation during 30-hour shifts twice per week while caring for patients and these young physicians then attempt to commute home from work.

Trait differences in vulnerability to sleep loss. There are also inter-individual differences in the vulnerability of well-rested, healthy young adults to sleep loss. In my laboratory, among healthy participants who have maintained a schedule of 8 hours of sleep at the same time each night for three weeks, we have found that approximately one-quarter of the participants account for roughly two-thirds of the attentional failures recorded during ~30 hours of wakefulness. Interestingly, inter-individual differences in the vulnerability to sleep loss in healthy young adults appear to be task dependent, such that reaction time in a sustained attention task is most affected by sleep loss in some individuals as compared to others, whereas sleep loss most adversely affects working memory in other individuals (32;34). Van Dongen and his colleagues have found that when subjects are brought back to the laboratory for repeat visits, the same ones remain particularly vulnerable while
others remain resistant to the adverse effects of sleep loss on cognitive performance. While all the subjects studied had more lapses of attention when performing the psychomotor vigilance task (PVT, a measure of simple reaction time) after a night without sleep, some individuals averaged only 10 lapses per 20-minute PVT test (about one lapse of attention every 2 minutes), whereas other individuals experienced nearly 100 lapses of attention per 20-minute PVT test (nearly five lapses of attention every minute) (32) (Fig. 7). In a relatively homogeneous sample of healthy young adults, they reported that stable individual trait differences accounted for 67% to 92% of the variance in the cognitive performance decrement induced by sleep loss (Fig. 7). These inter-individual differences appear to be trait differences, since they persist even when participants are either comparably sleep satiated (12 hours in bed per night for a week) or comparably sleep restricted (6 hours in bed per night for a week) before they stay awake all night (32).

While the performance of most people deteriorates significantly when wakefulness extends beyond 16-18 hours, there are considerable inter-individual differences in the magnitude of this effect. There are likely also inter-individual differences in the effects of exposure to chronic partial sleep deprivation for several weeks.

*Potential genetic vulnerability to sleep loss.* Genetic polymorphisms may account for differences in the tolerability to acute sleep loss. A variable length tandem repeat polymorphism in the *PER3* gene (*PER3*<sup>5/5</sup>) has been reported to confer a particular vulnerability to the performance-impairing effects of 24 hours of wakefulness in those with 5 rather than 4 copies of the sequence on both chromosomes (62;63). This polymorphism is present in about 10-15% of the population. When individuals with the *PER3*<sup>5/5</sup> polymorphism are deprived of sleep at an adverse circadian phase, their cognitive performance at night is significantly worse than individuals with the *PER3*<sup>4/4</sup> genotype (63) (Fig. 8). Individuals with the *PER3*<sup>5/5</sup> polymorphism reportedly experience significantly more attentional failures, as measured by slow rolling eye movements, than individuals
with the \textit{PER3}^{4/4} polymerism. Executive functioning of the brain’s pre-frontal cortex is said to be particularly compromised by the \textit{PER3}^{5/5} polymorphism (Fig. 8). On the other hand, a haplotype of the adenosine A2A receptor gene (ADOR\textit{A2A}), may be associated with resistance to the effects of sleep loss on performance (64). These preliminary data suggest that it may soon be possible to identify from a simple cheek swab a subset of individuals who will exhibit minimal performance degradation when deprived of sleep and another subset whose performance will deteriorate markedly when they are sleep deprived.

\textbf{Food, drugs and pharmaceutical agents}

\textit{Soporific agents}. Sleepiness is one of the most frequent side effects of prescription medications, including some anti-depressants, statins, anti-hypertensive agents, hypnotics, anti-anxiety medications, pain management medications, anti-epileptic agents, muscle relaxants and medications to block stomach-acid secretion. Many common over-the-counter drugs have effects on sleep propensity. For example, diphenhydramine is sold under various trade names, including Benadryl\textsuperscript{®} for relief of allergies. Few who take diphenhydramine for allergies realize that, because of its action as an anti-histamine, the very same drug—diphenhydramine—is also the active ingredient in many of the most popular over-the-counter sleeping pills in the U.S. It is marketed as an over-the-counter sleep aid under the trade names Unisom\textsuperscript{®,} Nytol\textsuperscript{®,} Sominex\textsuperscript{®,} Tylenol Simply Sleep\textsuperscript{®} and, with acetaminophen, in Tylenol PM\textsuperscript{®}. Thus, many people attempting to control their allergies during the daytime may be unwittingly taking a sleeping pill on their way to work, and thereby greatly reducing their tolerance to sleep loss. Diphenhydramine affects the areas of the brain that control the transition from wakefulness to sleep and thereby impairs performance. Even some newer ‘non-sedating’ anti-histamines cause drowsiness in a substantial fraction of patients. Some decongestants, in turn, disrupt nocturnal sleep, which can increase sleep pressure the following day.
**Stimulants and drugs of abuse.** Stimulants and drugs of abuse can have a profound effect on the ability to sustain alertness and performance in the face of sleep loss. Caffeine is the most widely used psycho-active agent in the world. In fact, it is the most widely used drug in the world, fueling our 24/7 society. Because caffeine antagonizes the actions of adenosine (65), a neuromodulator that mediates the sleep-inducing effects of prolonged wakefulness (66), at the adenosine A2A receptor, it can mask some of the effects of sleep deprivation on sleep propensity. Caffeine is marketed in coffee, colas and so-called energy drinks, and mixed with alcoholic beverages to increase the amount of alcohol that consumers can drink before becoming overcome with alcohol-induced fatigue. Caffeine is also available in tablet form, gum and in energy bars. Caffeine enhances performance during the daytime, although we have found that chronic caffeine administration in subjects on a demanding schedule may increase sleepiness, perhaps due to interference with recovery sleep (67).

The National Transportation Safety Board (NTSB) found that plasma caffeine levels were highest in drivers involved in fatigue-related fatal crashes (68). The NTSB concluded that the high levels of caffeine were insufficient to save those drivers from the effects of fatigue, which the NTSB found to be the leading cause of heavy truck crashes, equal to the fraction of crashes caused by both drugs and alcohol combined (68). Moreover, while 80 to 90% of adults report regular consumption of caffeine-containing beverages and foods, some people who avoid or limit caffeine consumption report experiencing adverse effects of caffeine—such as anxiety, tachycardia, nervousness or tremors—even at low to moderate doses (69). Twin studies have yielded heritability estimates of up to 77% for caffeine use and for tolerance to the side effects of caffeine, leading to the recent discovery that a genetic polymorphism in the adenosine A2 receptor gene is associated with both reduced caffeine consumption (69) and with greater subjectively and objectively measured sensitivity to the adverse effects of caffeine on sleep (70). Thus, while most physicians
use caffeine extensively to cope with sleep deprivation induced by extended duration work shifts and long work weeks, hundreds of thousands of physicians may be less able to avail themselves of the wake-promoting effects of caffeine due to a genetic variation in the adenosine 2A receptor that increases their sensitivity to the side effects of caffeine.

With 7.74% of children ages 4-17 diagnosed with ADHD and 4.33% (6.2% of boys and 2.4% of girls) receiving ADHD medications, amphetamines and other stimulants used to treat ADHD are now readily available (71). An unintended consequence of this popularity is that one-third of college students illegally use the mixed amphetamine salts in Adderall to “stay awake to study” when academic workload is high (72). It is unknown whether the illegal use of such stimulant medications, which can induce insomnia, will persist when this cohort of students enters medical school and then residency training. If so, this trend would hark back to the man who established and directed the first surgical residency program at Johns Hopkins in the 1890s, as it was cocaine use (73) that enabled Professor William Stewart Halsted, who laid the foundation for present-day graduate medical education work-hour policies, to maintain his reputation as an indefatigable surgeon (74). Sedation, sleep deprivation and insomnia are common side effects of opiates, to which Dr. Halsted was also addicted (75-77). In healthy subjects, morphine and methadone decrease deep slow wave sleep (78). It is also likely that opiates increase the risk of attentional failures and degrade performance under conditions of sleep deprivation.

Alcohol, another major drug of abuse, is a central nervous system depressant that increases sleep propensity during wakefulness but disrupts sleep consolidation after sleep onset. One third of U.S. medical students regularly drink alcohol excessively (79). An estimated 4.9% of emergency medicine residents meet diagnostic criteria for alcoholism (80). An estimated 10-12% of practicing physicians in the United States develop a substance use disorder (81), with 50% of physicians in rehab centers treated for abuse of alcohol, 36% for opiates and 8% for stimulants (81).
These various agents, used commonly by a substantial fraction of practicing physicians and residents, have a profound effect on sleep-wake homeostasis and vulnerability to the effects of acute and chronic sleep loss on alertness and performance. Even low doses of alcohol synergistically interact with sleep loss to greatly increase sleep propensity, degrade driving performance and increase crash risk in a driving simulator (82-84). Healthy professional drivers who were awake for 18 to 21 hours \textit{and} were exposed to legal low-dose alcohol (blood alcohol concentration of 0.03 g/dL) had significantly more attentional failures and greater variation in both lane position and speed in a driving simulator than they did when their blood alcohol concentration exceeded 0.05 g/dL—a level associated with significantly increased risk of a motor vehicle crash (85). Few programs have adopted the random drug testing procedures recently introduced for anesthesia residents, but not for practicing physicians, at the Massachusetts General Hospital in Boston (86). Therefore, physicians whose performance has been compromised by the use of such agents—even on non-work days—are not being identified and are being scheduled to work lengthy shifts of the same duration (e.g., 30 consecutive hours) and at the same frequency (e.g., twice per week) as those who have not used such agents. The practice of scheduling physicians to work for 30 consecutive hours without sleep does not take into account the widespread use among physicians of psychoactive agents that affect tolerance to sleep loss.

\textbf{Impact of medical condition on vulnerability to sleep loss}

A number of medical conditions and/or the medications used to treat those conditions are associated with increased sleep tendency, increased risk of attentional failures and increased risk of sleep-related errors and accidents (87). These common conditions make it more difficult to sustain wakefulness during the day and increase performance vulnerability to sleep loss. For example, pregnancy is a non-pathologic condition that often interferes with sleep, particularly in the last
trimester, induces fatigue and can greatly affects stamina and the ability to cope with sleep loss. Yet many residents are scheduled to work 30-hour shifts throughout pregnancy. Many infectious diseases also increase sleep tendency, including the common cold, mononucleosis and hepatitis. Other conditions, such as chronic pain and nocturnal asthma, cause chronic sleep loss that reduces tolerance to further sleep deprivation. Primary sleep disorders, such as narcolepsy and sleep apnea, as well as disturbances of sleep or wakefulness secondary to a medical condition or its treatment can affect tolerance to sleep loss. While there are 90 recognized sleep disorders (2), I have selected five to illustrate the issues raised by these common conditions, which collectively affect at least one out of five residents and practicing physicians in the U.S.

Sleep-related breathing disorders. Obstructive sleep apnea/hypopnea (OSAHS) syndrome results in sleep fragmentation and consequent daytime sleepiness. EDS is reported in about 80% of patients with OSAHS, 80 to 90% of whom remain undiagnosed and untreated; it often takes several years from the time a patient presents to a physician with symptoms until the correct diagnosis is made (2). Performance related to executive functions such as verbal fluency, planning and sequential thinking—the purview of the frontal cortex, an area of the brain that imaging studies has revealed to be exquisitely sensitive to sleep loss—is very adversely affected by OSAHS (88). Vigilance and the ability to sustain attention are also degraded in patients with OSAHS. Reaction times on a sustained attention task in patients with mild to moderate OSAHS have been reported to be comparable to or worse than those of a young adult with a blood alcohol concentration of 0.080 g/dL (89). Untreated patients with OSAHS perform much more poorly in a driving simulator (in terms of lane deviations, tracking errors, off-road events and collisions with obstacles) and are 6 to 10 times (i.e., about 500% to 1,000%) more likely to have an actual motor vehicle crash than people without OSAHS (90-103).
It is not known how many physicians in training or practicing physicians suffer from OSAHS. Snoring and the occurrence of attentional failures when driving a motor vehicle are cardinal symptoms of OSAHS (2). Obesity is the most prominent risk factor for OSAHS (2), though OSAHS can occur without obesity. Obesity confers such a high risk of OSAHS that Medical Advisory Board of the Federal Motor Carriers Safety Administration (FMCSA) has recommended mandatory objective OSAHS screening of all commercial motor vehicle drivers with a body mass index (BMI) greater than 30 kg/m², as measured at the bi-annual commercial driver license (CDL) physical exam. Data from available cohorts suggest that at least 50,000 practicing physicians and up to 10,000 residents would be affected if similar criteria were applied to those seeking to obtain or renew a license to practice medicine, as an estimated 6% to 18% of practicing physicians (104-107) and 10% of residents (108) are obese (BMI > 30 kg/m²). Since long work hours leave little time for exercise, and sleep restriction increases ghrelin levels, decreases leptin levels and increases carbohydrate craving, appetite and weight (2), physicians in training gain weight during residency (109;110), exacerbating the condition.

Thus, it is likely that a significant fraction of both residents and practicing physicians are at risk for OSAHS. Nearly two decades ago, the prevalence of OSAHS in the U.S. was estimated to be 4% of adult men and 2% of adult women (111). With the increased prevalence of obesity in the U.S. (112), the prevalence of OSAHS among both residents and practicing physicians is now at least 3 to 4 times higher. We have recently found that over one-third of a younger cohort of 4,471 North American employed law enforcement officers (mean age: 38.5 ± 8.3 years; mean BMI: 28.7 ± 4.6 kg/m²) screened with a sensitive and specific survey instrument were at high risk for OSAHS (113).

Fortunately, for the 10 to 20% of OSAHS patients who are correctly diagnosed and treated, there are a number of therapies available that can improve the subjective sleepiness associated with this condition. Splinting the airway open with continuous positive airway pressure (CPAP)
treatment has been the standard treatment for this condition for more than two decades. While the symptoms of OSAHS, including the increased risk of motor vehicle crashes, are usually significantly improved with CPAP treatment (101;114-116), less than half of patients diagnosed with OSAHS actually use CPAP for at least 4 hours on 70% of observed nights (117). Moreover, while the impact of CPAP treatment on the most widely used objective measure of daytime sleepiness, the Multiple Sleep Latency Test (MSLT), is statistically significant, it is rather modest in size, with the improvement in sleep latency averaging less than one minute (118).

Thus, a substantial fraction of patients who are compliant with CPAP therapy remain pathologically sleepy. Daily use of modafinil (200 mg.) has been demonstrated to be effective as an adjunct therapy in the treatment of residual subjective sleepiness in this population of OSAHS patients treated with CPAP (119). However, subjective sleepiness was only normalized (Epworth Sleepiness Scale < 10) in half of the modafinil-treated patients and objective sleep tendency, as measured by the MSLT, was not significantly improved by modafinil treatment (119). In summary, OSAHS is likely to have a substantial prevalence among physicians and most physicians with this condition will remain impaired by EDS for the following reasons: lack of diagnosis and treatment in 80-90% of those affected, failure to comply with nasal CPAP treatment in half of those diagnosed, and residual impairment notwithstanding compliance with CPAP treatment and adjunctive pharmacotherapy in others (2). Increased sleepiness and neurobehavioral deficits due to chronic sleep loss and sleep fragmentation will likely render physicians afflicted with OSAHS much more susceptible to the adverse effects of acute and chronic sleep deprivation induced by extended duration work schedules typically required of both residents and practicing physicians.

Shift Work Disorder. Excessive sleepiness and/or insomnia that occur in association with work that is scheduled during hours usually reserved for sleep are symptomatic of a condition known as Circadian Rhythm Sleep Disorder (CRSD), Shift Work Type (Shift Work Disorder, SWD) (120).
About 5 to 10% of such workers suffer chronically from moderate to severe SWD (121). Most employees nod off or fall asleep regularly while working at night or while commuting to or from night work (122). One-third of nurses who work at night report that they fall asleep in the hospital every week of night work (123), with half admitting that they fall asleep at the wheel while driving to or from the hospital; twice as many night-working nurses reported making medication errors or having motor vehicle crashes as compared to those who worked the day and evening shifts, but did not work at night (123).

Extended duration work shifts that routinely exceed 24 consecutive hours combined with very long work weeks that do not allow sufficient time for sleep can elicit attentional failures during work in most if not all employees (22), effectively inducing SWD in all workers in the same way that depriving people of food will eventually induce malnutrition in all people who are starved. Exposure to less extreme work schedules reveals considerable variability in the ability of individuals to cope with the demands of work schedules that require employees to work during times that they would otherwise be asleep. Continuous polysomnographic monitoring of 80 licensed commercial drivers without OSAHS during 7,500 hours of long-haul trucking operations revealed that more than half of the long-haul truck drivers experienced episodes of drowsy driving, mostly during night driving (124). Predictably, these episodes of drowsy driving were not distributed evenly across the 80 drivers. In fact, more than half of the drowsy driving episodes occurred in just 8 (10%) of the 80 drivers (124), revealing the differential vulnerability of this subset of drivers to the sleep deprivation and circadian misalignment associated with night driving. This is consistent with the differential vulnerability to nocturnal sleep loss observed in laboratory studies (32;35-37;125;126). A number of countermeasures and treatments can be effective in treating the symptoms of SWD, including improvements in work scheduling, use of properly timed exposure to light, administration of nutritional supplements such as caffeine and melatonin, and use of
pharmacologic agents such as the wake-promoting therapeutic modafinil (22-24;67;122;127-130), although none eliminate them.

Insomnia. Insomnia is the most common sleep disorder, with symptoms of disturbed sleep affecting most adults at some time in their lives (2). The clinical definition of insomnia is a chronic (> 6 months) complaint of latency to sleep onset or awakenings from sleep of at least a half hour occurring at least three times per week. The prevalence of insomnia associated with a daytime complaint of increased sleepiness or fatigue is 8% to 18% (131). Broadly, insomnia may be psychophysiologic or secondary to the sleep environment, an irregular sleep schedule, a sleep-related movement disorder, a psychiatric condition, a medical condition, a medication or substance, or a CRSD such as SWD (2). Insomnia in non-depressed adults is a risk factor for depression (132). Insomnia syndrome, which includes increased daytime sleepiness, it is associated with an increased rate of work absenteeism, reduced productivity and increased risk of accidents (2;133).

Narcolepsy. Narcolepsy is a neurological sleep disorder characterized by “EDS that typically is associated with cataplexy and other REM sleep phenomena such as sleep paralysis and hypnogogic hallucinations (120).” Cataplexy, a sudden muscular weakness often brought on by strong emotion, together with disturbed nocturnal sleep, are hallmarks of this condition, which affects about 5 out of every 10,000 adults in the U.S. Thus, an estimated 50 resident physicians and 400 practicing physicians in the United States have narcolepsy, assuming that the affected individuals have not self-selected out of the profession. Since narcolepsy often presents late in the second decade or in the third decade of life, affected individuals may already be in medical school or in a residency program before clinical symptoms are manifested. Despite the severity of sleep-wake impairment associated with this primary sleep disorder, it often takes more than five years from the time of symptom presentation to a physician until the correct diagnosis is made. Patients with narcolepsy often have difficulty sustaining attention during the day, and must rely on wake-promoting
therapeutics to reduce EDS and minimize the occurrence of sleep attacks. This may be due to a deficiency of the hypothalamic neurotransmitter orexin (hypocretin), which is often associated with narcolepsy. Patients with narcolepsy perform more poorly on a driving simulator and have a significantly higher rate of motor vehicle crashes than do control subjects (99).

**Psychiatric Disorders.** Sleep disturbance is often secondary to a number of psychiatric disorders and other conditions that may render affected individuals more susceptible to the effects of sleep deprivation. These include several medical and psychiatric disorders such as depression, which is common among practicing physicians and residents. A recent large-scale multi-site study revealed that 12% of medical students and residents had probable major depression and 9.2% had probable mild/moderate depression (134). Burnout has been reported by half of medical students in two studies (135;136); 11.2% of the medical students reported suicidal ideation. 20% of pediatric residents meet screening criteria for depression, and 74% meet the criteria for burnout (137).

Sleep disturbance is one of the most common symptoms of burnout, anxiety disorders and mood disorders, including depressive disorders and bipolar disorder. Burnout is also associated with persistent insomnia (138), with increased arousals and sleep fragmentation (139). Abrupt awakenings often occur in anxiety disorders, such as post-traumatic stress disorder, in which sleep is frequently disturbed by nightmares. Burnout, which is precipitated by occupational stress, induces EDS and mental fatigue throughout the day, which may be a consequence of the sleep disturbance (139). While insomnia is one of the most common features of mood disorders, hypersomnia can occur as well, especially during depressive episodes. Changes in sleep architecture, including reductions in deep slow wave sleep and earlier onset of REM sleep, occur in depression. Acute sleep deprivation can have an immediate anti-depressant effect, although its therapeutic effect is reversed as soon as recovery sleep is obtained. Sleep disturbance is one of the most common residual symptoms after effective treatment of depression, estimated to continue in up to 44% of
patients in remission (131). For these reasons, the cognitive performance of physicians with mood disorders is likely to be more vulnerable to the effects of sleep loss and misalignment of circadian phase. Many of the medications used to treat these patients have side effects that affect sleep tendency. The adverse effects of depression and its treatment on sleep and consequent daytime functioning probably contribute the increased risk of medical errors in depressed pediatric residents, who make 6.2 times as many medication errors per resident month as residents who are not depressed (137).

**Ethical Considerations**

The evidence upon which the ACGME and the IOM have relied in developing resident work-hour policy limits has been largely derived from laboratory studies of healthy subjects who have passed physical examinations and volunteered to participate in relatively brief sleep restriction or sleep deprivation studies. In continuing to sanction every other work shift to be 30-consecutive hours in duration (Fig. 9) throughout years of residency training, the ACGME has implicitly assumed that the population of residents is entirely healthy, highly resistant to the effects of sleep deprivation, and free of concurrent family responsibilities, premises that are not accurate. Working such long hours that the risk of unnecessary patient injury rises sharply violates the ethical principle of *nonmaleficence* (140). The principle of *beneficence* requires implementation of safer work schedules that reduce risk by not scheduling physicians to care for patients after 16 hours without sleep. Exhausted physicians who have worked >16 consecutive hours without sleep should not endanger themselves and others by driving automobiles (141;142). Since 24-hours of wakefulness degrades performance comparably to alcohol intoxication (28;143-147), the principle of *autonomy* requires that physicians respect the right of the patient to be informed of the impairment and to withhold consent to the risk of receiving care from sleep-deprived providers (140). The principle of
justice requires that those most vulnerable to sleep loss not shoulder a disproportionately large burden [i.e., a higher rate of fatigue-related errors, accidents and adverse health effects (2)] than those who are resistant to sleep loss (140), particularly for the convenience or financial benefit of teaching faculty or academic medical centers.

Systematic falsification of resident work-hour records (Fig.10)(1;148-150), which the IOM found to be widespread (1) and the ACGME recently admitted after years of official denial (151), violates the principle of truthfulness and honesty (140). It sets a regrettable precedent for trainees, especially when it occurs out of fear of reprisal from (152) or with the tacit approval, awareness or expectation of residency program directors or institutional leaders (151). Falsification of work-hour records by those who have caused harm have led to felony convictions, hefty fines and imprisonment, not only for those who falsified reports but for chief executives and supervisors complicit in the falsifications of work-hour records (153-163). At its core, resident work hour reform is an issue of human dignity for patient and physician (140). Burdening a physician with a workload that s/he cannot carry creates an ethical dilemma in which—on the one hand—the more hours that the physician works, the greater is the risk to both the patient and to the physician, whereas—on the other hand—the physician cannot ethically stop working and abandon a patient in need of medical care. Sleep deprivation should not be presented as a proxy for dedication.

Education about the impact of sleep deprivation and sleep disorders on performance, health and safety should be provided so that physicians and trainees understand that working when sleep deprived constitutes working in an impaired state, comparable to being under the influence of alcohol (1;2;17;28;82-84;143-147). 30-hour work shifts are not necessary for training physicians, since GME programs in many other countries (1)(Table) and in the U.S. have eliminated them years ago, including the surgical residency training program at the Brigham and Women’s Hospital in Boston. As in other safety-sensitive industries in the U.S. and in residency training in other
countries (1;164), work-hour limits for residents should be based on work hours that are safer for most people, not a select few (Table). Prior to the threat of federal legislation (151), many medical and surgical training programs in the U.S. required residents to work 120 to 140 hours per week (21;24), as they currently do in El Salvador (165)(Table). 25 years ago, the tragic death of Libby Zion thrust the issue of resident work hours onto the national stage (166). As the IOM has recently concluded, now is the time for meaningful resident physician work-hour limits (1), which the federal government has the authority to implement (167) and for which the boards of directors of the Sleep Research Society and the National Sleep Foundation have endorsed enforcement by law or regulation (21;168;169).

**Conflict Of Interest Disclosure**

Dr. Czeisler is/was a consultant for: Actelion, Ltd.; Cephalon, Inc.; Delta Air Lines, Inc.; Eli Lilly and Co.; Garda Siochana Inspectorate; Global Ground Support; Johnson & Johnson; Koninklijke Philips Electronics, N.V.; Portland Trail Blazers; Respiricons, Inc; Sanofi-Aventis Groupe; Sepracor, Inc.; Sleep Multimedia, Inc.; Somnus Therapeutics, Inc.; University of Wisconsin; Vanda Pharmaceuticals, Inc.; and Zeo, Inc.; and received royalties from McGraw Hill and Penguin Press. Dr. Czeisler owns an equity interest in Lifetrac, Inc.; Somnus Therapeutics, Inc.; Vanda Pharmaceuticals, Inc.; and Zeo, Inc. Dr. Czeisler has also received research support from Cephalon, Inc.; Tempur Pedic International, Inc; and Resmed, Inc. The Sleep and Health Education Program of the Harvard Medical School Division of Sleep Medicine has received support from Cephalon, Inc.; Takeda Pharmaceuticals North America, Inc.; Sanofi-Aventis Groupe; and Sepracor, Inc. Dr. Czeisler has received awards with monetary stipends from the American Clinical and Climatological Association; American Academy of Sleep Medicine; Association for Patient-Oriented Research; National Institute for Occupational Safety and Health and National Sleep
Inter-individual Differences in Sleep-Deprived Performance Vulnerability  Czeisler

Foundation; and the Sleep Research Society. Dr. Czeisler is the incumbent of an endowed professorship provided to Harvard University by Cephalon, Inc. and holds a number of process patents in the field of sleep/circadian rhythms (e.g., photic resetting of the human circadian pacemaker). Since 1985, Dr. Czeisler has also served as an expert witness on various legal cases related to sleep and/or circadian rhythms.

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**Figure Legends**

Figure 1: Effect of Partial Sleep Loss during Hospital Call on Errors Committed by Surgeons during Simulated Surgery. Simulated laparoscopic surgery performance of surgical residents (median age 34) measured by a laparoscopic surgery simulator (task 6 of the MIST-VR, Mentice Medical Simulation, Gothenburg, Sweden) before and after a night on call (17.5 hours from 3:30 pm to 9 am; median reported sleep time 1.5 h; range 0-3 h). Horizontal bands indicate median number of errors on this task, boxes show 25th and 75th centiles, and whisker lines show the highest and lowest error values. Figure and legend reprinted with permission from: Grantcharov TP, Bardram L, Funch-Jensen P, Rosenberg J. BMJ 2001;323:1222-1223 (5).

Figure 2: Impact of Acute Total Sleep Deprivation on Reaction Time Performance. Time course of psychomotor vigilance task (PVT) performance [mean, median, 10% slowest and fastest reaction times in milliseconds (logarithmic scale)] during more than 28 hours of continuously monitored wakefulness under constant environmental and behavioral conditions are shown averaged across 10 subjects ± standard error of the mean. All data are binned from 10-minute PVT tests administered at 2-hour intervals and expressed with respect to elapsed time since wake time (designated as a Relative Clock Hour of 8), which was scheduled at its habitual hour. Figure and legend reprinted

Figure 3: Sleep Duration in the Hospital. Average hours that interns reportedly slept in the hospital during extended duration (greater than 24 hour) on-call shifts as a percentage of 17,003 monthly survey reports collected from 2,737 resident physicians. Average hours of sleep obtained during extended duration shifts reported by interns for each week were averaged over the four weeks of each month to derive the value for each monthly survey report. Figure and legend reprinted with permission from: Barger LK, Cade BE, Ayas N, Cronin JW, Rosner B, Speizer FE, Czeisler CA, N Engl J Med 2005;352:125-134 (24).

Figure 4: Repeated Nights of Sleep Loss Result in Cumulative Cognitive Impairment. Higher number of attentional performance failures on the PVT indicates poorer performance and more unstable alertness. Upper panel shows the average number of lapses of attention recorded during 10-minute PVT tests administered eight times daily (every two hours) during 14 consecutive days when the amount of time in bed was limited to 4 hours, 6 hours or 8 hours per night. Lower panel shows the average number of lapses of attention recorded during 10-minute PVT tests administered four times daily during 7 consecutive days when the amount of time in bed was limited to 3 hours, 5 hours, 7 hours or 9 hours per night. B signifies data from the baseline day. Figure and legend reprinted with permission from the 2006 IOM Report entitled: Sleep Deprivation and Sleep Disorders: An Unmet Public Health Problem (2).

Figure 5: Subjective Sleepiness, Reaction Time, Lapses of Attention, and Attentional Failures Across 26 Hours of Wakefulness in Young and Older Participants. Group average data (± standard error of the mean) are plotted with respect to time since scheduled awakening for 11 healthy older (mean age 68.1 ± 3.6 years; range 65 to 76 years; filled symbols) and 26 healthy young (mean age 21.9 ± 3.3 years; range 18 to 29 years; open symbols) adults. Dashed box indicates time of usual
Inter-individual Differences in Sleep-Deprived Performance Vulnerability  Czeisler

sleep episode. Subjective sleepiness ratings from the Karolinska Sleepiness Scale (KSS; scale range from 1 = very alert to 9 = very sleepy) are presented in Panel A. Mean reaction time (RT, in milliseconds) from each 10-minute PVT is presented in Panel B. As indicated in the first 16 hours of data, the RT on the PVT in well-rested individuals averages ~250 milliseconds during the daytime, with minimal variability. The total number of lapses of attention (RT >500 milliseconds) from each 10-minute PVT are presented in Panel C. Well-rested individuals typically have very few (<5 per test administration) lapses of attention under these conditions. Attentional failures, defined as intrusions of slow eye movements (SEM) from continuous electro-oculographic recordings during EEG-verified wakefulness, were summed hourly and are presented in Panel D. Well-rested individuals typically have very few SEM under these conditions. Figure and legend reprinted with permission from: Duffy JD, Willson HJ, Wang W, Czeisler CA. J Am Geriatr Soc 2009; In Press. (56).

Figure 6: Age Distribution of Crashes in Which Driver Was Not Intoxicated But Judged to Have Been Asleep. Data from 4,333 fall asleep crashes in North Carolina, where standard crash report forms, as mandated by state law, include ‘fatigued’ and ‘asleep’ in driver condition. Data for years 1990-1992, inclusive. In 55% of fall-asleep crashes, driver was age 25 or younger. Peak age of crashes was at age 20 years. Figure and legend reprinted with permission from: Pack AI, Pack AM, Rodgman E, Cucchiara A, Dinges DF, Schwab CW. Accid Anal Prev 27: 769, 1995 (61).

Figure 7: Neurobehavioral responses to total sleep deprivation after two different prior sleep extension conditions. Each episode of sleep deprivation followed a week during which time the participants spent 12 hours in bed each night. The average number of lapses on 20-minute PVT tests administered every two hours over the last 24 hours of total sleep deprivation is shown. The abscissa shows the 19 individual participants, who were arbitrarily assigned the labels A through U. The participants are ordered by the magnitude of their impairment (averaged over the 2 sleep
deprivations), with the most resistant participants on the left and the most vulnerable participants on the right. Responses in the first exposure to sleep deprivation following 7 days of prior sleep extension (mean ± standard deviation of the average nightly sleep duration of 8.5 ± 1.0 hours) are marked by boxes; responses in the second exposure to sleep deprivation following 7 days of prior sleep extension (mean ± standard deviation of the average nightly sleep duration of 8.8 ± 1.3 hours) are marked by diamonds. The panel reveals that subjects differed substantially in their responses to acute sleep deprivation, while the responses were relatively stable within subjects between the two exposures to acute sleep deprivation. Figure and legend reprinted with permission from: Van Dongen HPA, Baynard MD, Maislin G, Dinges DF. Sleep 2004; 27: 423-433 (32).

Figure 8: Polymorphism in Period Gene and Vulnerability to Sleep Loss. Left Hand Side: Deterioration of waking performance and increase of theta EEG activity and slow eye movements during sleep deprivation is greater in \(PER3^{5/5}\) than in \(PER3^{4/4}\) participants. Time course of central EEG theta (5–8 Hz) activity during wakefulness (Panel A), incidence of slow eye movement (SEMs) (percentage of 30 s epochs containing at least one SEM) (Panel B), and waking performance (composite performance score) (Panel C) are plotted relative to the timing of the plasma melatonin rhythm (Panel D) in ten \(PER3^{5/5}\) (open symbols) and 14 \(PER3^{4/4}\) (filled symbols) homozygotes. EEG theta activity, SEMs, and waking performance data were averaged per 2-hour intervals, relative to the midpoint of the melatonin rhythm. (* indicates a significant difference between genotypes, p < 0.05; upper abscissa indicates approximate wake duration.) Right Hand Side: Overnight performance on the paced visual serial addition task in \(PER3^{5/5}\) and \(PER3^{4/4}\) participants. Mean numbers of correct responses are plotted relative to the midpoint of the melatonin rhythm (Panel E). Overnight performance on the serial reaction time task in \(PER3^{5/5}\) and \(PER3^{4/4}\) participants. Mean switch costs, i.e., increase in time to respond to random rather than learned sequences of stimuli, are plotted relative to the melatonin midpoint. Higher values indicate
poorer performance (Panel F). Overnight performance on spatial N-Back performance in relation to memory load in \( \text{PER3}^{5/5} \) and \( \text{PER3}^{4/4} \) participants. Mean numbers of correct responses, are plotted separately for the 1-, 2-, and 3-back, relative to the melatonin midpoint (Panel G). Overnight performance on verbal N-Back performance in relation to memory load in \( \text{PER3}^{5/5} \) and \( \text{PER3}^{4/4} \) participants. Mean numbers of correct responses are plotted separately for the 1-, 2-, and 3-back, relative to the melatonin midpoint (Panel H). * \( P < 0.05 \), Bonferroni corrected. Error bars represent the standard error of the mean. Figures and legends reprinted with permission from: Viola et al., Curr Biol, 2007 (62) (left hand side); and Groeger JA, Viola AU, Lo JC, von Schantz M, Archer SN, Dijk DJ. Sleep 2008;31:1159 (63) (right hand side).

Figure 9: Illustration of Eight Consecutive Days of a Typical Resident Physician Work Schedule Sanctioned by Current 2009 ACGME Guidelines. Every other shift is 30 hours in duration on this schedule. Because each 30-hour shift includes two calendar days, this schedule results in the resident physician spending every third night in the hospital. Black bar indicates scheduled 30-hour shifts. Hatched bar indicates an 8- to 10-hour swing shift, when resident physicians are not scheduled to work overnight. Box on right indicates how many hours residents are not scheduled to work for each 24-hour interval, beginning at 6 am each day.

Figure 10: Reported Non-Compliance with ACGME Work-Hour Limits as Reported by Residents Non-Confidentially to the ACGME vs. Confidentially to the Harvard Work-Hours Health and Safety (HWHS) Group. After the ACGME implemented the 2003 limits on resident physicians work hours, 83.6% of interns reported to the HWHS Group work hours that were in violation of the ACGME standards during 1 or more months. Working shifts greater than 30 consecutive hours was reported by 67.4% of interns (open bar, middle pair). Averaged over 4 weeks, 43.0% of interns reported working more than 80 hours weekly (open bar, right pair), and 43.7% reported not having 1 day in 7 off work duties (data not shown). Violations were reported during 61.5% of months.
during which interns worked exclusively in inpatient settings. Violations were reported to the HWHS Group from 85.4% of the 707 represented residency programs (open bar, left pair). During the same reporting period, the ACGME reported near-universal compliance with the ACGME standards (filled bars), claiming that only 5.0% of residency training programs were not compliant with the standards and that only 3.3% of surveyed residents reported violations of the 80-hour rule. Differences between the ACGME and HWHS Group data were statistically significant on each of these measures (p < 0.001). Data and legend from: Landrigan CP, Barger LK, Cade BE, Ayas NT, Czeisler CA. JAMA 2006;296:1063 (148) Figure courtesy of Christopher P. Landrigan, M.D., M.P.H.
Table. Summary of work-hour regulations for various occupations in selected countries.

## Current Work-Hour Regulations

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Limits</th>
</tr>
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<tbody>
<tr>
<td>U.S. Airplane Pilots (1-2 pilot airplanes): 1950s</td>
<td>&lt;8 daily flight hours</td>
</tr>
<tr>
<td>U.S. Nuclear Power Plant Operators: 1982; 2009</td>
<td>&lt;16 consecutive work hours</td>
</tr>
<tr>
<td>U.S. Railroad Operators: 1907, modified 1969 &amp; 1976</td>
<td>&lt;12 work hours per day</td>
</tr>
<tr>
<td>U.S. Interstate Truck and Bus Drivers</td>
<td>&lt;11 driving hours within a 14-hour interval</td>
</tr>
<tr>
<td>E.U. All Occupations (including resident physicians and practicing physicians): 2004; 2009</td>
<td>&lt;13 consecutive work hours</td>
</tr>
<tr>
<td>New Zealand Resident Physicians: 1985</td>
<td>&lt;16 consecutive work hours (labor agreement)</td>
</tr>
<tr>
<td>U.S. Resident Physicians</td>
<td>UNLIMITED: no federal laws of regulations</td>
</tr>
<tr>
<td>El Salvador Resident Physicians</td>
<td>UNLIMITED</td>
</tr>
</tbody>
</table>
References


(3) AAMC. Assuring Quality Patient care and Quality Education. Association of American Medical Colleges 2001;1-10.


(29) USA Today Editorial Board. Our view on doctors in training: Sleep deprivation studies fail to wake up teaching hospitals. Why are residents still working marathon shifts, endangering patients? USA Today 2006 Dec 19.

(31) Leach DC. Opposing view: More hours, better doctors. Good patient care is complex; residents are students, not workers. USA Today 2006 Dec 19.


(37) Van Dongen HPA. Shift work and inter-individual differences in sleep and sleepiness. Chronobiol Int 2006; 23(6):1139-1147.


(39) Van Dongen HPA, Maislin G, Mullington JM, Dingess DF. The cumulative cost of additional wakefulness: Dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. Sleep 2003; 26(2):117-126.


(52) Banks S, Van Dongen H, Dingess D. Response to sleep restriction depends upon pre-existing sleep debt. Sleep Abstract Supplement[30], A119. 2007.


(65) Dunwiddie TV, Masino SA. The role and regulation of adenosine in the central nervous system. Annu Rev Neurosci 2001; 24:31-55.


(68) National Transportation Safety Board. Safety Study: Fatigue, Alcohol, Other Drugs, and Medical Factors in Fatal-to-the-Driver Heavy Truck Crashes (Volume 1). NTSB/SS-90/01, 1-181. 1990. Washington, DC, National Transportation Safety Board.


(82) Horne JA, Reyner LA, Barrett PR. Driving impairment due to sleepiness is exacerbated by low alcohol intake. Occup Environ Med 2003; 60(9):689-692.


(90) George CF, Nickerson PW, Hanly PJ, Millar TW, Kryger MH. Sleep apnoea patients have more automobile accidents. Lancet 1987; 2:447.


(108) Mihalopoulos NL, Berenson GS. Cardiovascular risk factors among internal medicine residents. Prev Cardiol 2008; 11(2):76-81.


(130) Wyatt JK, Dijk DJ, Ritz-De Cecco A, Ronda JM, Czeisler CA. Sleep facilitating effect of exogenous melatonin in healthy young men and women is circadian-phase dependent. Sleep 2006; 29:609-618.


(140) University of Washington School of Medicine. Ethics in Medicine. 


(143) Falleti MG, Maruff P, Collie A, Darby DG, McStephen M. Qualitative similarities in cognitive impairment associated with 24 h of sustained wakefulness and a blood alcohol concentration of 0.05%. J Sleep Res 2003; 12(4):265-274.


(148) Landrigan CP, Barger LK, Cade BE, Ayas NT, Czeisler CA. Interns' compliance with accreditation council for graduate medical education work-hour limits. JAMA 2006; 296(9):1063-1070.


(151) Nasca TJ. Open letter to the GME community. 2-16-2009.


(153) California trucking company safety director and four drivers sentenced for their role in a false driver's log book scheme. 7-21-2008. U.S. District Court, Fresno, California.

(154) Two sentenced in case involving falsification of truck drivers' logs. 3-11-1998. U.S. District Court, Abington, VA.


(156) Trucking firm and president sentenced in hours-of-service violations. 7-24-2002. U.S. District Court, Bangor, ME.

Inter-individual Differences in Sleep-Deprived Performance Vulnerability Czeisler

(158) South Dakota trucking firm and president ordered to pay over $325,000 in driver logbook falsification case. 9-22-2005. U.S. District Court, Sioux Falls, SD.

(159) Former executive, dispatcher, and two drivers of Virginia trucking company sentenced for their roles in falsifying drivers' logbooks. 1-18-2006. U.S. District Court, Lynchburg, VA.

(160) Former owner and dispatcher for Pennsylvania trucking company sentenced in logbook falsification case. 3-14-2006. U.S. District Court, Williamsport, PA.

(161) Virginia truck driver gets jail time for falsifying logbooks. 8-11-2006. U.S. District Court, Brunswick, GA.

(162) Four truck drivers sentenced in logbook falsification case. 2009. U.S. District Court, Fresno, CA.

(163) Pennsylvania truck driver sentenced to 2 years in prison for vehicular homicide relating to hours-of-service violations. 3-7-2007. State Court, Easton, PA.


(168) Moore RT. An act relative to safe work hours for physicians in training and protection of patients. Senate Docket No. 1178. 12-30-2008.

Figure 1

Before Overnight Call
After Overnight Call

Number or Surgical Errors

0 2 4 6 8 10 12 14

Figure 1
Psychomotor Vigilance Performance

- • 10% slowest reaction time
- ○ mean reaction time
- ■ median reaction time
- □ 10% fastest reaction time

Figure 2
Figure 3

Reported hours of sleep obtained during extended duration work shifts

Percentage of monthly reports

N = 2,737

Mean = 2.6 h sleep/night

>40%

↑ Acuity +
↓ LOS →
↓ Sleep

0 5 10 15 20 25 30

0 1 2 3 4 5 6 7 8
Figure 4

A) Mean number of performance lapses over days for different time in bed:
- Circles: 4 hours
- Diamonds: 6 hours
- Squares: 8 hours

B) Mean number of performance lapses over days for different time in bed:
- Circles: 3 hours
- Triangles: 5 hours
- Squares: 7 hours
- Black squares: 9 hours

Day
Figure 5

Habitual Sleep Episode

A
Subjective Sleepiness

B
Mean RT (msec)

C
Lapses of Attention

D
Slow Eye Movements

Time Awake (h)
Figure 6

The graph shows the number of crashes against the age of drivers. The x-axis represents the age of the driver in years, ranging from 16 to 82, while the y-axis represents the number of crashes. The data indicates a peak in the number of crashes for drivers aged 16 to 22, with a gradual decline as the age increases.
Figure 7

PVT performance lapses
(greater impairment →)

subjects

UOQNF CAGBJ HMTKS IRL E

Figure 7
Figure 8

A. EEG Theta Activity (μV/Hz)

B. Slow Eye Movements (% of time)

C. Waking Performance composite score

D. Melatonin (pg/ml)

E. Paced Serial Addition

F. Serial Reaction Time

G. Spatial 3-Back

H. Verbal 3-Back

Figure 8
Figure 9

Time of Day

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• 83.6% of residents non-compliant with ACGME limits
• Residents non-compliant in 61.5% of inpatient months