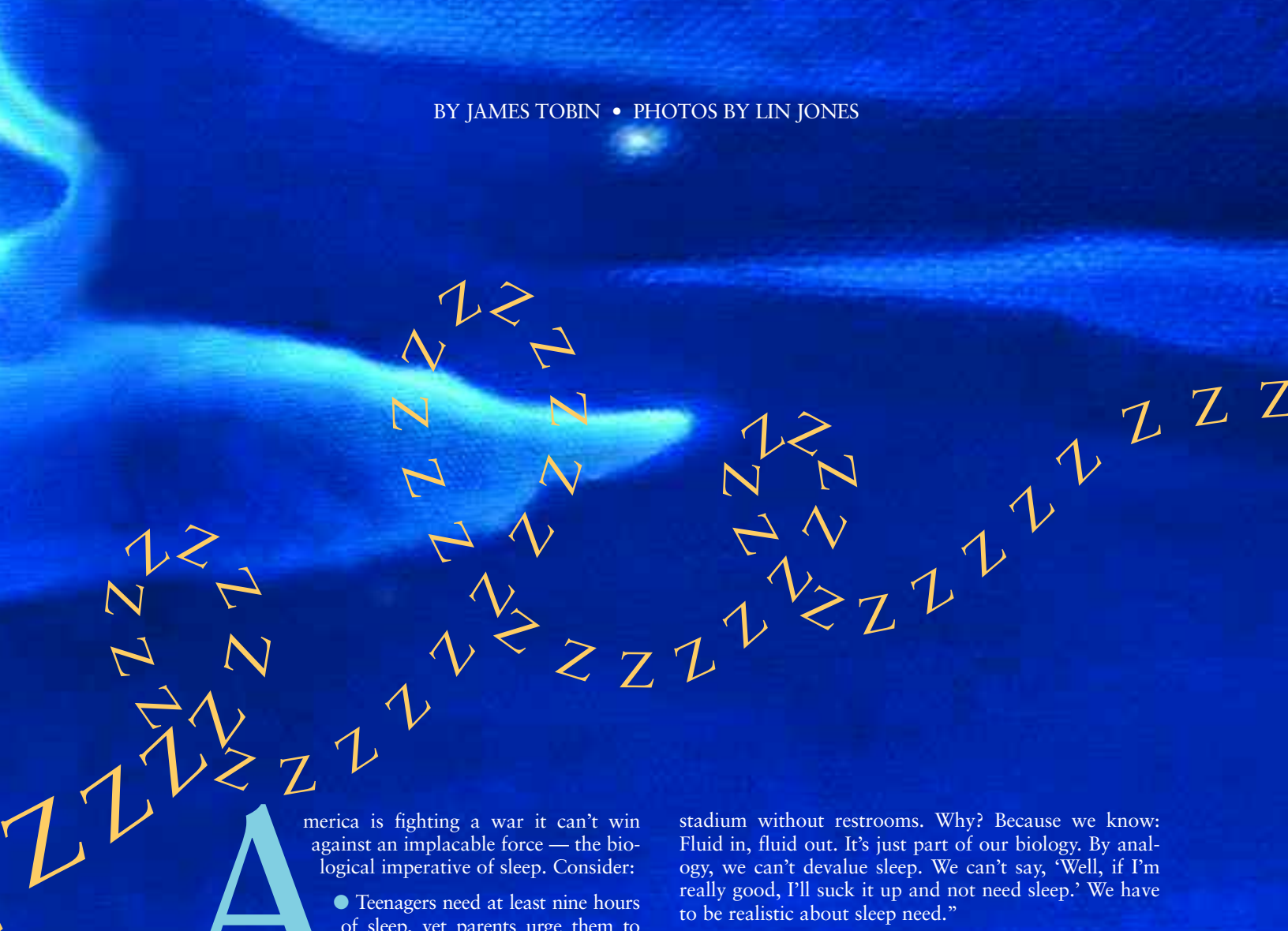
COUNTING SHEEP AND THE STUDY OF SLEEP, FROM A TO ZZZZ

BY JAMES TOBIN • PHOTOS BY LIN JONES



America is fighting a war it can't win against an implacable force — the biological imperative of sleep. Consider:

- Teenagers need at least nine hours of sleep, yet parents urge them to pack their nights with activities and homework — and school starts as early as 7:15 a.m.
- Many college students party Thursday night through Saturday night, and "all-nighters" before exams remain routine
- TV and the Internet offer dusk-to-dawn diversion to the sleepless
- Many workers are laboring later and longer as employers schedule more jobs in late-night shifts
- Business travelers traverse the time zones multiple times each month
- From "energy drinks" to aggressively advertised sleeping pills, chemical aids foster the belief that we can manipulate the body's need for sleep.

In sheer defiance of nature, we are stretching our 16-hour bodies into 24-hour lives.

"Our culture has this idea that we can work at this unrelenting pace, and the more we do it, the better," says Ralph Lydic, Ph.D., the Bert La Du Professor of Anesthesiology, professor of physiology, and a leader of U-M sleep research. "We would never build a football stadium without restrooms. Why? Because we know: Fluid in, fluid out. It's just part of our biology. By analogy, we can't devalue sleep. We can't say, 'Well, if I'm really good, I'll suck it up and not need sleep.' We have to be realistic about sleep need."

Lydic directs basic research on sleep at the U-M. Ronald Chervin, M.D., the Michael S. Aldrich Collegiate Professor of Sleep Medicine and professor of neurology, directs the clinical work of the Sleep Disorders Center. They and their colleagues — some 30 clinicians and scientists working in 15 departments — are part of a broad effort to turn back the tide of the 24-hour culture and treat the sleep problems it spawns.

With new impetus from the Institute of Medicine, which in April 2006 declared that sleep disorders and deprivation constitute a large and unmet need in public health, they are building an integrated Center for Sleep Science that will coordinate and accelerate Michigan's exploration of the uncharted regions of sleep and its disorders.

A TIRED ISSUE

The scope of the problem is enormous. The Institute of Medicine concluded that some 50 to 70 million Americans suffer from sleep problems, with attendant risks to daytime functioning and long-term health. Yet 80-90 percent go undiagnosed. Some of the most widespread problems are insomnia, obstructive sleep apnea and restless legs syndrome, trailed by less frequent, but still common, disorders such as narcolepsy and rapid eye ➤

movement (REM) sleep behavior disorder. Chronic sleep deprivation — simply not getting enough sleep — likely is a bigger problem still, but it's only recently become a research focus.

In a society that increasingly depends on complex systems and machines, sleepy people are dangerous. Fatigue has been implicated in nuclear accidents and chemical spills, disastrous train and truck accidents, even the ill-fated decision to launch the doomed Challenger space shuttle in 1986. Sleepiness is second only to intoxication among causes of car crashes. According to the National Highway Traffic Safety Administration, driver fatigue is the direct cause of some 100,000 auto accidents and more than 1,500 traffic deaths in the United States annually — a statistic that has led many prosecutors and the state of New Jersey to declare that a sleep-deprived driver who causes a death in an accident can be tried for vehicular homicide.

Before a recent series of reforms, American hospitals long relied on residents working extended shifts without sleep, a practice tied to the epidemic of medical errors documented by numerous studies. Indeed, research led by Michigan's J. Todd Arnedt, Ph.D., a clinical assistant professor of psychiatry and neurology, found that medical residents were just as impaired after a month of "heavy call" rotations as they were after drinking enough alcohol to be moderately intoxicated.

The sleep-deprived endanger their own health, too. Shortage of sleep can hurt the cardiovascular and immune systems. It can trigger overeating, obesity and diabetes. And sleep is woven through the delicate fabric of mental health.

"How important is sleep? Stay awake two nights and you'll be hallucinating," Lydic says. "A person who is not mentally ill, if they miss sleep for long enough, will exhibit all the signs of mental illness."

Other consequences of sleep loss are less severe, yet they make daily life miserable. "Being sleepy is unpleasant," Chervin says. "Our patients don't feel well. We have patients who can't drive safely. Or they fall asleep during one-on-one meetings with their boss. We've had reports of people falling asleep during sex. They don't see the end of the movie. They can't read because they can't stay awake."

ROUSING A SLEEPY SUBJECT

Long after scientists penetrated the mysteries of other human systems, sleep remained a locked box. For purely practical reasons, it was hard for scientists to study sleep. For one thing, there are few animal models for sleep disorders — none at all for insomnia — so test subjects were hard to identify. And there was the inconvenient fact that sleep is best studied at night, the most difficult time to staff a research lab.

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A basic conceptual problem also stifled research — the misconception that sleep represented the absence of activity in the body and brain. That notion began to give way with the discovery of REM sleep in the 1950s, leading to the understanding that sleep is not the simple absence of wakefulness — a "nothing state," as some put it. Rather, it is a different state than wakefulness, with all sorts of active and important things going on in the brain and body.

"People have often assumed that nothing happens differently in sleep than in wakefulness, or that sleep is simply a rest period when everything in the body shuts down," Chervin says. "In fact, nothing could be further from the truth. It's become only more apparent in recent years that virtually every system of the body functions differently in sleep than during wakefulness."

Still, the question of precisely why sleep is essential, and how it restores vigor to the body's systems, remains one of the burning mysteries of biology, Chervin says. But researchers, including many at the U-M, are advancing toward better understanding.

Sleep helps the body's immune system. Studies have shown that in sleep-deprived people, the killer-cells of the immune system are suppressed, making it harder for the body to fight disease. Initial data from research conducted by U-M faculty Flavia Consens, M.D., assistant professor of neurology, and Mark Opp, Ph.D., professor of anesthesiology and of molecular and integrative physiology, suggest the response of the immune system to a simple flu shot is impaired when the patient has a sleep disorder.

Sleep also facilitates the repair of muscles damaged by hard use. This has been demonstrated in marathon runners: monitors of runners sleeping after a race show tremendous activity in the muscles of the legs as cells are rebuilt and strengthened.

Also, by mechanisms that are only starting to be understood, sleep appears to have a kind of cleansing effect on the body's chemical system.

As Lydic explains, the body can be seen as a plant for the capture and conversion of energy. Supplied by food, we manufac-

Ronald Chervin

ture molecules called ATP, which supply the energy that every cell in the body uses to do its job — pumping blood, thinking, contracting muscles, and so on. But whenever energy is converted into action, there are by-products. In this case, the burning of ATP leaves a by-product called adenosine, which builds up as the cells slog through their long, hard day. And what happens when the adenosine build-up hits overload? It signals the brain that the cells need to replenish their energy stores — and with that signal, we get sleepy. Then, when we give in to the inevitable, the adenosine is processed out of the system, other restorative action occurs, and by morning the cells are ready for another day of work. This, by the way, is where caffeine comes in: it blocks adenosine receptors in the brain.

Pushing the body onward without allowing this restorative process, Lydic says, is like running a car without oil. All the metabolic machinery just begins to shut down. "Think about how we feel after we've had a really good night of sleep. You feel almost as if your body has been cleansed of a toxin," he says.

This only begins to explain what happens in the brain during sleep. Scientists also believe sleep is essential to learning — that is, to the consolidation and storage of memories.

"If you sleep-deprive people, they won't learn as well," says Helen Baghdoyan, Ph.D., professor of anesthesiology and pharmacology, who, with Lydic, her husband, teaches U-M's first course on sleep science. "We tell our students that pulling an all-nighter is the worst thing you can do before an exam. Do they listen to us? Of course not. But we tell them every year. You can do it in the short-term but you won't consolidate. If it's something you really want to know, in the long term, you won't."

Sleep appears to be even more important to children's brains, with some of the most important evidence emerging from Chervin's research.

In a survey of more than 800 hyperactive children and their parents, Chervin and his colleagues discovered that a surprisingly large number of the children in the sample had chronic snoring, a key symptom of obstructive sleep apnea, which interrupts sleep many times per night. In further research, they found that in those children who underwent adenotonsillectomy — often a remedy for sleep-disordered breathing in children — there was a marked reduction in hyperactivity. That improvement, Chervin believes, may be the result of better sleep.

"We think that's the underlying reason," he says. "I wouldn't say we've proven it, but our study provides some of the best evidence out there that sleep apnea is causing or contributing to inattention and hyperactivity during the day — possibly because children who are sleepy still have such a drive to stay awake ➤

Battling for breath and a good night's sleep

As Randy Darnall climbs into the soft bed with plain white sheets and pale comforter, he sports a ponytail of sorts, freshly sprouted from his short-cropped hair. And for the first time in many a night, he claims a double bed all to himself.

The ponytail is not hair, but a slew of bundled wires connected to 20-plus electrodes placed all over his body to measure statistics such as brain waves, breathing effort, blood oxygen saturation, heart rate and snoring. And the bed is empty because Darnall is not at his home in Highland, Michigan — he is spending the night at the U-M Sleep Disorders Laboratory in the KMS Building on South State Street.

Darnall suffers from sleep apnea, a condition which causes him to stop breathing in his sleep for 10 seconds or more, and can awaken him 50 times per hour. The 42-year-old father of four has come to the University of Michigan to take part in a study he hopes will identify solutions to help him sleep better at night.

His wife, Colleen, was the impetus for Darnall's trip to the lab. His condition has worsened such that he gets only four hours of sleep per night. Between that and his almost-constant snoring, Colleen urged her husband to see a specialist.

"She has seen me stop breathing for a minute and a half," Darnall says. "She sits there wondering if I am going to breathe again." The apnea leaves him understandably fatigued during the day. "When I wake up, I feel like I did not sleep," he says. "I find myself sluggish all the time, but just figure, hey, I'm getting old."

Darnall assumes the episodes wake him, but he is not sure. This is common, according to Garnett Hegeman, a supervising technologist at the lab. He has worked in sleep medicine for more than 20 years and has seen thousands of patients with sleep apnea.

Photo: Kevin Bergquist

Garnett Hegeman attends to Randy Darnall in the sleep lab

"At night, while asleep, you really are not aware of what is happening to you," Hegeman says. "You may think you are sleeping fine, but then you wake up not feeling rested. Some patients say, 'I slept eight hours, why do I feel so bad?'" If it is sleep apnea, they may be unaware of hundreds of brief arousals they have had during the night, he says.

After hooking up Darnall to machines that monitor his movements and vital signs, Hegeman is confident the lab is tracking a classic case of sleep apnea. Hegeman should know, as he has had the same plight for several years.

"Have a good night," Hegeman says at 10:15 p.m. as he shuts off the light and closes the door to one of the lab's nine sleep rooms.

Darnall falls asleep at 10:40 p.m., and it is not long before episodes of apnea halt his breathing and, for the next seven hours, put him in and out of wakefulness, even though he may not realize it. His night is documented on a computer that constantly records 18 measurements. The output is equal to 800-plus pages of data, which are sent to a U-M physician for interpretation.

A few hours into the study, perspiration causes several of the electrodes to slip, so Martha Mock, a polysomnography technician who will watch Darnall throughout the night, slips into his room with a fan to cool him down.

Darnall climbs out of bed at 5:30 a.m. and drives back to Grand Rapids for training for his job. He will return to the clinic in two weeks to be tested on CPAP (continuous positive airway pressure), which increases air pressure in the throat, keeping tissues in his airway from collapsing when he breathes.

The technologists will re-create his ponytail of wires and electrodes, and he will climb back into bed at the lab to begin his treatment. "He is likely to see a big difference," Hegeman says. "It's like night and day."

Adds Darnall, "I hope so, because I just want it fixed."

—Kevin Bergquist

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that they'll jump up, fidget, or create their own stimulus in order to stay awake."

EXPLORING NEW TREATMENTS

U-M researchers hope their discoveries about sleep's intricate mechanisms will lead to the development of new drugs to treat sleep disorders more effectively and with fewer side effects than the current crop of popular pharmaceuticals, such as Ambien and Lunesta. Those drugs generally are safe, they say, but taking them may become a habit over time, and they often do nothing to reverse the underlying causes of sleep disorders.

On that front, Arnedt, who directs the U-M Behavioral Sleep Medicine Program, is using non-pharmacological techniques to help people with chronic insomnia — not just the occasional difficulty in falling asleep or waking up early, but a pattern of problems recurring three or more times a week over an extended period. Such people — perhaps as much as 20 percent of the population — appear to have a built-in disposition to insomnia; the nerve centers in their brains that regulate sleep tend to remain hyper-aroused. So when stress or pain shows up, they are particularly vulnerable to insomnia. Sleep aids can help them, Arnedt says, but he has greater long-term success with an extended program of behavioral therapy. This includes stricter regulation of caffeine and alcohol and careful planning of sleeping times and bedroom habits. He also helps them change the thoughts that prevent sleep — fears about not being able to function the next day without adequate sleep, for example.

This approach has been highly effective — a result that is mirrored throughout the U-M clinics that treat the sleepless.

"We have some of the happiest patients in the medical center," Chervin says. "They're not all curable, but, by and large, they're treatable. People come back and say, 'I feel 10 years younger; I didn't know I had this problem; now I have so much more energy.'"

For doctors, scientists and patients alike, the study and treatment of sleep leads to a profound respect for this mysterious state in which we spend a third of our lives — if we get enough of it as we should, that is.

"As sleep researchers, we try to put out the word that there's no better alternative than sleep," Arnedt says. "You can't cheat the sleep system. In the end, you'll pay the price."

Lydic hopes his research will foster advances in sleep pharmacology and anesthesia.

"The other value I hope will come from my work," he says, "is that it will contribute to this sea change in societal attitudes, so that we'll value sleep as a key part of our lives in the same way that people value food and being in athletic shape. It helps us do our jobs better and be better people."