BusinessWeek's Cover Story: Effects of Troubled Sleep

Latest Cover Story Reveals Harmful Effects of Troubled Sleep

82 Million Americans Labeled Troubled Sleepers

BusinessWeek's latest cover story (January 26, 2004), "I Can't Sleep," is an extraordinary, eye-opening descent into the world of troubled sleep. The extensive article reports that 82 million Americans—nearly 40% of the teen and adult population—routinely have trouble falling asleep. And only 32% of Americans get the recommended eight hours of sleep on weeknights, according to the National Sleep Foundation. The results of this epidemic are catastrophic:

- 70,000 highway accidents with injuries per year
- 1,550 highway deaths per year
- a reliance on drugs to assist sleep, and
- an estimated $45 billion in costs to our economy.

"All Nikken Wellness Consultants should hear the world's cry for help and respond by sharing the benefits of our sleep technology," says Bob Richards, Nikken director of sales. "I implore you to read this article and continue your mission to implement Wellness Homes around the world."

The effects of this epidemic are felt not just in the home. The article points out that nearly half of all office workers sleep poorly at least a few times per week and more than 65% say they have trouble concentrating after a sleepless night, according to the National Sleep Foundation.

How Can Nikken Help?

Nikken sleep technology is designed to give exactly what the article points out is missing: a quality night's sleep. With ergonomic design, correct support and Far-Infrared and Magnetic Technologies, Nikken sleep systems provide the comfort that people around the world are lacking. *BusinessWeek* labels these people as

being “…part of a giant and growing class: worn-out, dragged-out denizens of a sleep-robbed netherworld.” Nikken can help.

To read the *BusinessWeek* article please click here. (See below) (http://www.businessweek.com/magazine/content/04_04/b3867001_mz001.htm)

COVER STORY JANUARY 26, 2004

"I Can't Sleep"

Insomnia and other sleep disorders are wreaking havoc on our health and taxing the economy. Drug companies see an opportunity

Insomnia has left Ron Hansen a desperate man. In the 16 years since he suffered his first bout of sleeplessness, he has tried seven different types of mattresses. He has gulped down gallons of warm milk and herbal tea. He once bought a dog, hoping the pooch's presence would calm him. Instead, he wound up watching his pet sleep. Much to the annoyance of his wife and four children, the 45-year-old Hansen is still up in the middle of the night, doing paperwork or shuffling around the house for hours, until he finally collapses back into bed. The days can get ugly, too.

To avoid nodding off at the wheel, Hansen talks to himself as he drives from his home in Manalapan, N.J., to New York City, where he works selling credit-card processing services to hotels and restaurants. He often worries that crushing bouts of fatigue after a bad night make his sales pitches less than compelling. And that worry further fuels his insomnia. "There is nothing worse than knowing you have a 10 a.m. meeting with an important client, wanting to get a good night's sleep, and just not being able to," he says.

Last year, Hansen's quest for rest drove him to participate in a trial for Estorra, an experimental sleep drug from Sepracor Inc. (SEPR) in Marlborough, Mass., that's expected to hit the market by midyear.

Hansen is part of a giant and growing class: worn-out, dragged-out denizens of a sleep-robbed netherworld. More than 82 million Americans -- nearly 40% of the teen and adult population -- suffer from some form of insomnia, meaning they routinely have trouble falling asleep and staying asleep. Even for those who grapple with transient insomnia a few times a year, the bouts of sleepless nights are an ordeal, like a bad, recurring flu. On the other side of the empty bed are countless people who cheat on sleep so they can squeeze more hours out of the day.

Only 32% get the recommended eight hours of shut-eye on weeknights, according to a 2002 poll by the National Sleep Foundation. They won't outgrow the problem, either. Studies show that as we age, the quality of our sleep deteriorates (table). And our wired, 24/7 society makes it worse, bombarding us with news of mad cow disease and other coming calamities while beckoning us late at night to finish our work online.

While we've been busy burning the midnight oil, scientists have been amassing evidence that sleep deprivation is a hazardous state. Insomnia has been fingered as a major risk factor for depression, alcoholism, and obesity. Other ruinous effects may be on display right in your office. Surveys indicate that nearly half of all office workers sleep poorly at least a few times a week, and more than 65% confess that they have trouble concentrating after a sleepless night, according to the National Sleep Foundation.

Now think about the people responsible for your safety. A huge proportion of pilots -- not to mention policemen and doctors -- admit to making errors in sleep-deprived states, according to Alertness Solutions, a consulting company in Cupertino, Calif. "It's not as if people are off their game by 1%," says Mark K. Rosekind, president of the company. "They're way off." What's more, all this tossing and turning is putting a damper on the economy. Sleep deprivation costs $45 billion a year in lost productivity, health-care bills, and expenses related to traffic accidents -- rivaling the impact of depression, say, or stroke. As Stanley Coren, a sleep researcher and psychology professor at the University of British Columbia, often preaches: "Lack of sleep makes people clumsy, unhappy, stupid, and dead."

To the world's growth-starved pharmaceutical companies, sleep deprivation spells opportunity. While drug company execs are aware that some insomniacs can be helped by exercise, diet, and keeping regular hours, they note that millions aren't cured by such regimens, or can't stick to them. The drug industry has barely dipped into this pool. Market researcher Decision Resources Inc. estimates that no more than 40% of insomniacs are diagnosed, and only half of those are treated with prescription drugs. The total market for prescription sleep aids is a skimpy $2 billion a year, mostly spent on a single blockbuster, Ambien, from Paris-based Sanofi-Synthelabo (SNY).

In pharmaceutical circles, Ambien is a symbol of what one sleep drug can achieve. When it was launched in 1993, it was hailed as a breakthrough because it promoted sleep with only a minor risk of hangovers and other side effects. As sales took off, at least a half-dozen companies began developing novel sleep aids, which could start hitting the market in 2004. Some exploit entirely new discoveries about how and why we sleep. And all of them claim to improve on Ambien's powers. Dr. Kris H. Jenner, portfolio manager of the T. Rowe Price Health Sciences Fund (PRHSX), estimates that the market for sleep drugs will more than double, to $5 billion, by 2010. "This market is set to explode," he says.

Drug companies will make sure that the sleep-deprived hear their message. But they have a mammoth task ahead convincing people first that insomnia is a serious condition, and second that it can be treated safely with drugs. Historically, sleep aids have been linked with addiction, depression, and suicide. Even though newer drugs are designed to avoid such troubles, many physicians and insomniacs are frightened that there will be unforeseen complications. Insomnia, in short, is an enticing pharmaceutical frontier -- but one with more than its share of treacherous passes.

Many Mysteries

To forge better remedies for sleep disorders, scientists have had to struggle with some

fundamental mysteries. We spend a third of our lives in bed, yet no one has been able to explain the necessity, and bona fide scientific studies are barely a few decades old. We have learned, for example, that the need for sleep varies greatly by species and is related to physical size: Opossums snooze for 18 hours a day, while elephants need just three hours. Even where sleep is inconvenient or dangerous, evolution provides work-arounds. Dolphins, for example, shutter only half of their brains at a time, remaining half-awake when they sleep.

By dragging humans into sleep labs and hooking them up to monitors, scientists have made a handful of discoveries about what the body does when it's asleep. During the deepest phases of slumber, growth hormone is released, facilitating cell repair and energy restoration. And much has been observed about REM (rapid eye movement) sleep, when our eyes dart frantically beneath our eyelids and we dream vividly of talking petunias and killer clams. Many scientists believe REM and non-REM sleep work together to consolidate memories and experiences and burn them permanently into our brain's hard drive. That could explain why some people wake up and suddenly have a solution to a problem that seemed insurmountable the day before. But the connection to sleep is still unclear.

The consequences of sleeplessness are much better understood. Deprivation messes up the body's metabolism, putting insomniacs at risk for a host of diseases. In a 1999 study at the University of Chicago, healthy men who slept just four hours a night for six nights suffered a 30% shortfall in their ability to secrete and respond to insulin -- the hormone that regulates blood sugar. That large a drop can be an early warning of diabetes.

Blithering Idiots

More recent studies at the University of Chicago demonstrate a possible link between sleeplessness and obesity. Preliminary results show that study participants who were allowed just four hours of sleep a night for two nights suffered a 20% drop in leptin, a hormone that controls body weight. At the same time, their stomachs produced 20% more ghrelin, a hormone that makes people feel hungry. Sleep-deprived subjects craved high-fat, very sweet foods, and "their appetites increased beyond the extra calories they needed to stay awake," says Eve Van Cauter, a professor at the University of Chica- go's medical school and the director of many sleep studies.

Taken to extremes, sleep loss can reduce us, at least temporarily, to blithering idiots. In two studies at the University of Pennsylvania, 48 healthy adults were split into several groups that slept four, six, or eight hours a night for two weeks. All the participants performed tasks that tested their motor skills and memory. By day 14, the four-hour group made an average of 14 times as many errors as they did when they took the tests fully rested. The eight-hour sleepers performed the tasks consistently well -- and actually got better at them each day. And the six-hour sleepers, corresponding to the corporate everyman, may as well have been thoroughly sleep-starved. They scored 11 times as many errors as they normally would make -- about as bad as a test group that stayed awake for two straight days.

But what about the superhumans we all seem to know -- the co-worker who intentionally gets five hours of sleep a night yet outperforms everyone else? Sleep experts say basic biology eventually catches up with these deliberate sleep cheaters. "We have no evidence that CEOs, astronauts, or doctors are exempt from the dangers," says David F. Dinges, chief of the division of sleep and chronobiology at Penn's school of medicine.

Whether people are cheating on sleep or succumbing to insomnia, the perils are the same. Studies show that someone who has been awake for 24 hours has the same mental acuity as a person with a blood-alcohol level of 0.1, which is above the legal limit for driving in most states. That means an executive who is up all night worrying about the quarterly earnings report -- or worse, a hospital resident who takes over in a late-night emergency -- is about as sharp as a light drinker who suddenly downs four margaritas. No wonder drowsy drivers cause 70,000 injury crashes per year, of which 1,550 are fatal.

Narcoleptic Dogs

In the quest to understand and combat sleep disorders, researchers have made some riveting conceptual advances. They have noted that bad sleepers have higher metabolic rates, heart rates, and body temperatures than normal sleepers. They also consume more oxygen and secrete more of the stress hormone cortisol. Even when they're sleeping, they're just more wound-up than normal people. Sleep experts call it "hyperarousal," and most believe some segment of the population is simply born that way -- predisposed to a dreadful life of tossing and turning. "These people are not neurotic," says Dr. Tom Roth, director of the sleep disorders center at the Henry Ford Hospital in Detroit. "There's a physical element to this. Once we fully understand it, we'll get to the day when we can better treat this as a disorder."

There are many foot soldiers in the campaign to understand insomnia. One of them is Pepper, a six-year-old Doberman pinscher born with narcolepsy, the puzzling disorder that causes its victims to fall asleep suddenly. When she plays in the yard of her home at the Greater Los Angeles Health Care Center in North Hills, Calif., her hind legs periodically buckle, her eyes droop, and she stops in her tracks. Scientists are studying Pepper to figure out what makes narcoleptics drop off against their will. Three years ago, simultaneously with a team at Stanford University, they had a breakthrough. They found that a wakefulness-promoting neurotransmitter called hypocretin played an important role in the disorder. Then, exploring the brains of deceased people who had suffered from the disease, North Hills sleep scientist Jerome M. Siegel found that human narcoleptics lack most of the neurons that produce hypocretin. "Here's this chemical that was around for hundreds of millions of years, yet we had no idea it was there," says Siegel, a psychology professor at the University of California at Los Angeles and chief of neurobiology research at the North Hills facility. "It's possible that hypocretin might also be quite important in sleep."

New insights into sleep pathology are certainly needed. Virtually every drug on the market today targets a single neurotransmitter called GABA (gamma-amino-butyric acid), which promotes sleep by preventing brain cells from firing. Ambien, for example, binds to receptors in the brain that make GABA more effective. Older drugs on the

market, including valium, also enhance GABA activity. But by targeting specific subtypes of GABA receptors, Ambien avoids some of the side effects that plagued older sleep aids, such as next-day hangovers, memory loss, and clumsiness.

Halcion Days

The drawback of Ambien is that it wears off too quickly in some patients. Neurocrine Biosciences Inc. (NBIX) sees that failing as an opportunity. The San Diego company has created a time-release version of its experimental GABA drug, called Indiplon. It also plans to market a short-acting version so that people who wake up in the middle of the night can pop the pill and get a few extra hours of shut-eye without waking up groggy. Ambien is not approved for those patients.

Neurocrine will file for Food & Drug Administration approval of Indiplon in early 2004. And it hopes to score another coup: a label that says Indiplon can be used nightly for months on end -- unlike all current sleep drugs, which are approved only for short-term use. Such a label would go a long way toward easing some of the fears about the safety of insomnia drugs. Many physicians and patients were spooked by a debacle in the early 1990s involving a drug called Halcion. A small group of patients who took it became violent and delusional, and the drug fell out of favor.

Even before Halcion, the FDA was jittery about sleep aids. The agency has always classified this whole category of drugs as addictive, even though many doctors argue that the newer drugs are not. Either way, health-related concerns are holding back the market. "Fear is a complication that encumbers the practice of sleep medicine," says Dr. Andrew Krystal, associate professor of psychiatry and director of the sleep research lab at Duke University Medical Center.

Neurocrine and other companies hope eventually to change the federal regulators' stance. And while that won't happen right away, the companies are chipping away at some of the FDA's objections. In October, Sepracor released data showing that patients who took its experimental drug, Estorra, for six months straight did not build up a tolerance to it, nor did they suffer significant side effects. Estorra is under FDA review. The company is pushing for a label that says it can be used for longer than a week. Some doctors believe Estorra could usher in a new era for such medicines. "This is the first long-term study of a sleep drug, and that will help educate the market," says Dr. William C. Dement, professor of psychiatry at Stanford and director of its sleep clinic.

Changing regulators' attitudes toward sleep aids won't be the only hurdle for the makers of these new products. They'll also have to convince insomniacs that there's nothing wrong with taking sleeping pills. To that end, Sepracor and Neurocrine -- along with its Big Pharma partner, Pfizer Inc. (PFE) -- are gearing up for major direct-to-consumer advertising blitzes. The strategy worked for Sanofi. When it pumped $55 million into U.S. print and TV ads for Ambien in 2002, annual sales of the drug jumped to $1.5 billion, nearly twice the level in 2000. Says Neurocrine CEO Gary A. Lyons: "The market is ripe for an approach where we reach out and tell people there's something they can do to sleep better."

The total sleep market could continue to expand as drugs that reach beyond the GABA system come out of the pipeline. Takeda Pharmaceuticals North America has developed a drug called Ramelteon that takes its cue from a popular sleep supplement, the hormone melatonin. Both substances trick the body's internal clock, triggering the brain to switch into sleep mode. But Ramelteon is designed as a more potent trigger and could possibly help individuals who don't respond to melatonin.

Several companies, including Sanofi and Aventis (AVE), are developing drugs patients can take to avoid waking up in the middle of the night. They prevent the brain chemical seratonin from disrupting slumber. Perhaps more radical, some researchers aim to alter the very architecture of sleep. Pfizer has a compound that slows down overactive synapses in the brain, thus prolonging the deepest, most restorative phases of sleep.

These new drugs will address only one slice of our sleep-deprived society. There are legions of people who, because of the demands of their jobs, can't find time to rest. That's a hot-button issue in many industries. For example, in hospitals residents often work more than 100 hours a week. Many are forced to stay awake for more than 24 hours straight. "After 24 hours, we might be performing surgery on someone," says Dr. Lauren Oshman, president of the American Medical Student Assn. (AMSA), who will begin her residency in July. "That's a problem." AMSA is lobbying Congress to pass laws limiting workweeks for med students and residents to 80 hours.

Disturbing Questions

Regulations may help, but high-pressure environments will always take a toll on sleep. Now, research on sleep disorders is yielding medications for those who must stay awake at all costs. Cephalon Inc. of Westchester, Pa., markets a drug, Provigil, that tricks the body into believing it has slept when it has not. It works by zeroing in on a cluster of nerve cells in the brain that trigger the awakening process. Provigil produces less of a buzz than amphetamines and is less likely to become addictive. It's currently approved for people with narcolepsy, but the company expects to broaden the label to include others who are weary during the day. Analysts believe the market for Provigil and other upcoming wakefulness drugs will eventually top $1 billion a year. And it's likely, they say, that some users will take the drugs for purposes not sanctioned by the FDA. One can envision, years down the road, an underground market of healthy adults who think sleep is a waste of time.

The scenario of whole societies popping insomnia and wake-up pills as if they were aspirin raises disturbing questions. Are drugmakers so intent on seeding an insomnia market that they have grown insensitive to the hype their marketing campaigns may fuel? And what about the long-term impact of messing with the brain's natural sleep processes? Unknown. Until drugmakers can point to long-term safety data, physicians, patients, and regulators can be forgiven for harboring reservations. "Hormone replacement therapy stopped hot flashes, but look what happened," says UCLA's Siegel, referring to reports that surfaced last year showing the popular menopause treatment increases women's risk of breast cancer. "We have to prove it's healthy to take sleeping pills."

For millions of sleepless sufferers, effective remedies can't come soon enough. Insomniac Richard Evans, who runs a business in Raleigh, N.C., that creates indexes of technical books, has endured stretches when he sleeps no more than an hour a night. He picks fights with his wife, and once lost a longtime client after a petty argument he's sure would never have happened if he had rested. One evening, after five sleepless nights in a row, he stared at the .44 revolver in his nightstand drawer and contemplated suicide. "I looked forward and saw a black abyss," he says. Evans, 57, has found some relief in testosterone injections -- a relatively new form of therapy. It's not a lifelong solution, but for the first time in a decade, he says, "I'm now sleeping." Those insomniacs still left behind may someday also discover that a good night's rest is much more than a dream.

By Arlene Weintraub