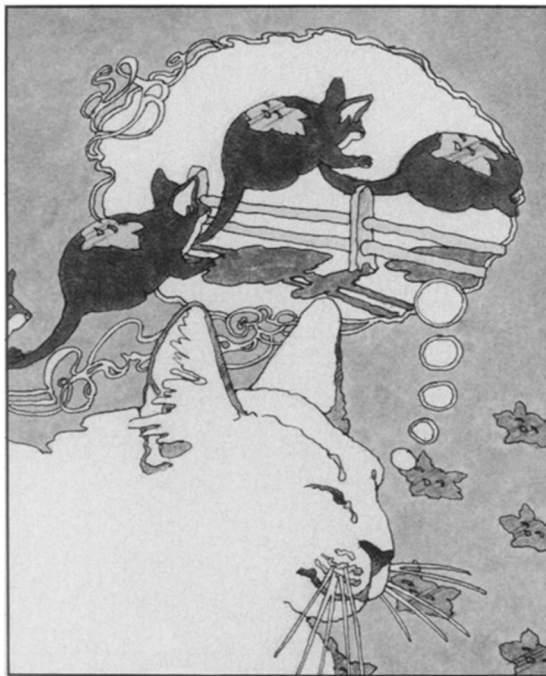


THE SCIENCE OF SLEEP

Researchers are probing the causes of sleep, the impact of sleep on mind, body and personality and the causes of, and treatments for, insomnia, sleep apnea, narcolepsy and other sleep disorders



BY JOAN AREHART-TREICHEL

At Harvard Medical School, a sleek cat snoozes in a relaxed position. His whiskers start to twitch as he dreams, perhaps of a juicy mouse canapé. Meanwhile, neurophysiologists record the electrical activity of his brainstem to see which neurons trigger his dreaming sleep. The activity sounds like pop! crack! tick, tick, tick. . . .

At Montefiore Hospital and Medical Center, human subjects invert their sleep-wake cycle as do people who work night shifts. They have trouble sleeping during the afternoon. Also their REM (rapid eye movement), or dream stage of sleep, occurs earlier than usual, and this change persists up to three weeks after they return to sleeping at night. . . .

Also at Montefiore, Norman S., who sleeps poorly at night because frequent cessations of breathing awaken him, agrees to a tracheotomy. A tiny hole is drilled in his throat so that air can bypass his upper airway tissues and thus allow him to breathe and sleep normally at night. . . .

These are but three examples of a relatively young field of research that is awakening increasing interest in the biomedical community—the study of sleep and sleep disorders. Noteworthy discoveries on the subject are emerging, as revealed at a recent conference in New York City sponsored by Montefiore Hospital and Medical Center, Bronx, N.Y., and the Upjohn Co., Kalamazoo, Mich.

A basic question sleep researchers have been tackling is what initiates sleep in

humans and other mammals. Studies during the 1960s revealed that the brainstem is involved. J. Allan Hobson of Harvard Medical School and a world authority on the neurophysiology of sleep, along with Robert McCarley and other colleagues, hypothesized that there were specific neurons in the brainstem that trigger sleep. To find these neurons, they hooked tiny electrodes to the brainstem of sleeping cats. This way they were able to detect the electrical activity of individual neurons at various stages of the cats' sleep. They found that certain neurons, known as giant cells, increase their firing intensity before and during REM sleep. In contrast, neurons known as locus coeruleus cells stop their electrical activity before and during REM sleep. So it looks as if giant cells switch on REM, and locus coeruleus cells switch it off (SN: 7/19/75, p. 36).

Thus, the short-term sleep clock in cats, and in humans, is controlled by specific neurons in the brainstem, Hobson believes. He is convinced that the expression of the brainstem clock is determined by some other oscillator, say the hypothalamus of the brain, which some investigators believe controls daily biological rhythms. "I recently examined a patient with severe destruction of the hypothalamus," says Hobson. "She had 90-minute-period attacks of epilepsy. Since REM and other sleep stages average 90 to 100 minutes each, these attacks might have been a readout of her brainstem sleep clock that had escaped daily control by

the hypothalamus."

Sleep investigators are also exploring the impact of sleep on the mind. Sleep appears to regulate people's daytime moods and mental alertness, according to recent research by Milton Kramer, a psychiatrist at the Veterans Administration Hospital in Cincinnati. The psychological qualities (dream content) of sleep, he has found, greatly affects unhappy, friendly and aggressive feelings during the daytime, whereas the physiological qualities of sleep greatly influence clear-thinking, sleepy or dizzy feelings the next day.

The effects of sleep on the human body are likewise being probed. For example, REM sleep and waking are characterized by low voltage; rapid electroencephalograph (brain) waves, and deep sleep stages are accompanied by high voltage, yet slow waves, reports Elliot D. Weitzman, director of the Sleep-Wake Disorders Unit at Montefiore Hospital and Medical Center. During sleep, muscle activity of the chin is near zero, he and his co-workers have found. However, the face twitches during dreams. And the range of human body temperature between sleep and waking is greater than they had predicted.

Sleep researchers are also providing some valuable insights into the effects of sleep on hormones in the body. Levels of growth hormone and thyroid-stimulating hormone rise when subjects go to sleep. Luteinizing hormone and follicle-stimulating hormone do not change during the sleep-wake cycle of men, but LH decreases before sleep when women ovulate or menstruate. Adolescents secrete ample LH and FSH before going to sleep, and this rise can be lessened if they go to bed in the early morning hours rather than at night.

Regarding this latter finding, Weitzman speculates that if adolescents do not sleep at regular hours, it might delay the onset of puberty. In fact, John Money of Johns Hopkins University has found that puberty is delayed in adolescents whose parents abuse them, and he believes that the delay may be the result of the parents not allowing the children to sleep normal hours.

Still other discoveries about what happens when sleep is disrupted are coming to the fore. Inverting people's wake-sleep cycles upsets their REM stages of sleep for three weeks after they return to a normal cycle. Weitzman and his colleagues also report that when they put human subjects on a three-hour sleep-wake cycle for 10 days, the subjects had trouble maintaining it because there were certain hours of the day when they slept poorly.

"There is some kind of a normal clock that says you can sleep now," says Weitzman. "This finding has large implications for people who have to work night shifts and odd hours or travel by jet. People coming to us from work shifts show even more disturbed sleep than do subjects shifted in the lab."

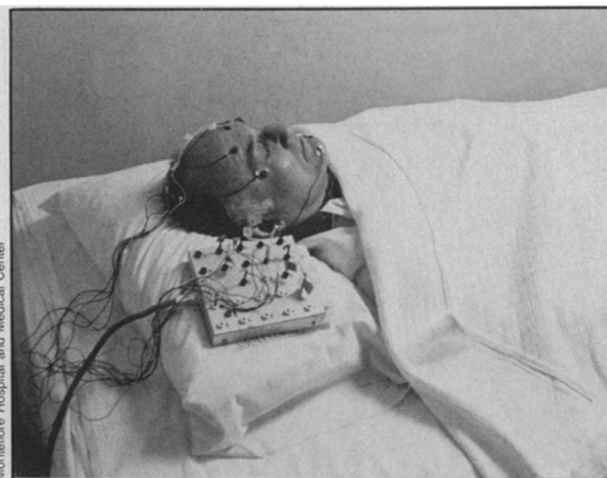
Does disrupting sleep disturb people's

personalities? After ample experiments during the late 1950s and 1960s, William C. Dement, director of the Sleep Disorders Clinic and Laboratory of Stanford University Medical School, concluded that it does not. Gerald Vogel, director of the Sleep Laboratory at the Georgia Mental Health Institute in Atlanta has since confirmed these results. In fact, REM deprivation can actually counter depression in patients with endogenous depression, he has found. Endogenous depression is usually severe. It occurs during the middle of the night or in the early morning hours on awakening and usually strikes people over age 40, versus depression that is triggered by a specific life event and that usually hits people under 40. Concludes Dement: "Since the brainstem seems to be responsible for the inhibition of REM sleep, it may be a cause of endogenous depression."

Depression, on the other hand, is often responsible for a sleep disorder that debilitates some 35 million Americans. This is insomnia (difficulty falling asleep, frequent awakenings during the night, early morning arousal). A large number of insomniacs suffer from depression or psychological upsets, Kramer says. However, insomnia can also result from poor bedtime habits, heavy coffee or alcohol consumption, disease, restless legs while sleeping (a cause of some 20 percent of all insomnia), disturbed biological rhythms or a condition called sleep apnea. The latter, the problem of the earlier mentioned Norman S., is far more common than sleep researchers used to think. It afflicts some 100,000 persons in the United States—mostly men. It also frequently goes undiagnosed and untreated, yet can be life threatening. The most blatant symptoms are loud snoring during sleep with pauses in respiration.

Sleep apnea is also a cause of another sleep disorder—daytime sleepiness—where a victim gets so little restful sleep at night that he often falls asleep during the day, even while standing or driving. A more frequent initiator of daytime drowsiness is narcolepsy. Its symptoms include recurring periods of daytime sleep and cataplexy, a rapid loss of voluntary muscle control leading to partial muscle weakness or complete body collapse for several seconds to several minutes. There are some 250,000 narcoleptics in the United States; it strikes men and women equally. (Animals can be afflicted with cataplexy, too. At the New York sleep conference, a film was shown of a dog leaping for a dog biscuit, then keeling over to the floor during a cataplectic attack.)

Not unexpectedly, sleeping pills are the major form of treatment for insomnia of psychological origin. The typical physician spends three minutes on insomnia complaints and then prescribes sleeping pills without investigating the causes. Eighteen percent of all psychiatric visits



Sleeping subject wears electrodes that connect to polysomnograph machine which records brain waves, chin muscle tone, breathing and heart rate. Below is measurement of oxygen in blood, breathing and awakening (eye opening) in patient with sleep apnea. Oxygen saturation and respiration coincide when patient breathes, which is frequent. Awakening precedes each breath.



are for sleeping pills, Kramer says, and sleeping pills are a \$175 million annual business in the United States. Yet many sleeping pills are not very effective, especially those that are nonprescription, Ernest L. Hartman, director of the Sleep and Dream Laboratory of Boston State University, points out. What's more, these pills lose their effectiveness if used continually for two weeks. In fact, if they are used for months on end, which is common among chronic insomniacs, they are physically addictive and can actually cause severe sleep disturbances rather than counter them. Says Dement: "We withdrew one patient over a two-year period from six kinds of sleeping medications that she had been using for 30 years. This withdrawal led to a substantial improvement in her sleeping time." Barbiturates, a major category of sleeping pills, are also a frequent cause of overdose and both accidental and intentional deaths.

Obviously, the best way for insomniacs with psychological problems to cope with insomnia is to try to overcome their psychological difficulties before they become hooked on sleeping medications. Biofeedback, various relaxation therapies and meditation have been used successfully in treating some cases. Also, a sleeping medication is looming on the horizon that promises to be more effective and safer than those currently available. It is the amino acid tryptophan. It puts human subjects to sleep much faster than a placebo does, Hartman has found. Also, tryptophan is already on the market in Britain as an antidepressive agent and appears to be safe even if used in large amounts. Meanwhile, there is a good natural source of tryptophan for insom-

niacs—a glass of milk.

If poor sleeping habits or heavy coffee or alcohol consumption are the cause of insomnia, then changing these behaviors is the most rational therapy. If disease is the source, the best countermeasure is disease treatment or pain medication. Insomnia triggered by jerking or restless legs (nocturnal myoclonus and the restless leg syndrome) can be most effectively treated by correcting the physical causes. However, the antispasmodic and anticonvulsant drugs used to treat these conditions are only partially successful. So sleep scientists are trying to better understand the causes of these abnormalities. Nocturnal myoclonus is accompanied by an aroused EEG pattern. Some researchers theorize that the condition may be caused by improper regulation of the REM sleep mechanism that suppresses skeletal muscle tone. According to this view, the jerks may be an overreaction to this irregularity. The restless leg syndrome, in turn, appears to be a result of nocturnal myoclonus.

"To better understand patients with these conditions," Dement says, "more and more sleep clinics will be monitoring such patients by closed-circuit television."

As for insomnia due to disturbed biological rhythms, Dement and his colleagues have seen some patients whose body temperature curve is out of phase with normal sleeping time. Their body temperature, for instance, is highest at 11 p.m. so that they cannot go to sleep. But if they attempt to sleep at a time appropriate for their body temperature cycle, they manage to do so. Thus, Dement and

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... Sleep

his co-workers theorized that if they moved these patients' sleeping time slowly around the clock by having them sleep a little later every 24 hours, they could bring the patients' body temperature clocks back into synchrony with the environment. They have tried the treatment on one patient so far, and it has worked. They call it "chronotherapy."

Although certain drugs can help sleep apnea patients, they are far from ideal. Dement and his colleagues, as well as sleep scientists at several other centers, have sought another solution to the problem, and it seems to be working. It is an ordinary tracheotomy, where a tiny hole is drilled in the windpipe carrying air from upper airway tissues to the lungs. That way air is able to bypass an obstruction in the upper airway tissues that appears to be triggered by a defect in the central nervous system. The patient wears a plug over the hole during the day, then unplugs the hole before he goes to sleep. The technique not only is providing desperately needed sleep to select sleep apnea patients in the United States and abroad but is actually saving them from heart failure and death due to cessation of breathing during the night. The method is also sparing their bedpartners from gargantuan snores—relaxation of muscles in the upper airway to counter the airway's resistance to breathing.

Finally, how about treatment for narcolepsy? In the sleep lab, the most common feature of narcolepsy is the presence of REM sleep at the onset of a nighttime period. In healthy persons, sleep begins with a non-REM period, and REM appears only after some 90 minutes. Narcolepsy has been explained in terms of an intrusion of REM sleep into the waking state. Consequently, drugs that suppress REM sleep in healthy persons are used to prevent narcoleptics' cataplectic attacks. Narcoleptics also receive stimulant drugs to help them stay awake during the day.

In spite of all the advances being made in understanding sleep and sleep disorders and in treating the latter, an enormous amount still remains to be learned. "It is mind-boggling, the strange things you encounter in people's sleeping habits," Dement says, "everything from night terror attacks and head-shaking to tooth-grinding and sleep paralysis." Yet sleep researchers are enthusiastic about the challenges facing them. They are confident that many more discoveries about sleep and sleep disorders will be made during the next few years, and that these findings will be integrated into neurobiology, one of the most active fields of biomedicine today.

"Sleep science combines the drama of hunting with the patience of trout fishing," Hobson avows. "Since sleep and dreams are ubiquitous experiences, sleep research provides a scientific entry into the mind of Everyman." □

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