Biomedicine

The nightmare of sleepless nights

The insomniac's worst nightmare has been reported in the Oct. 16 NEW ENGLAND JOURNAL OF MEDICINE. Italian and U.S. researchers detail the case of a 53-year-old man who, in effect, died from insomnia. And though this case is an isolated one, it enabled the physicians to gain insight, through an autopsy, into some possible brain mechanisms involved in insomnia.

After a lifetime of relatively normal sleep (five to seven hours a night), the patient rather abruptly began to lose sleep at age 52; within a few months after the problem started, he was down to only one hour a night. During subsequent hospital admissions, the man's progressive deterioration became increasingly evident — he sank deeper and deeper into a vegetative stupor, his speech became unintelligible, his movements erratic and he was soon unable to perform simple tasks. He did not respond to sleep medications. In his exhausted, debilitated state, he developed a lung infection and, eventually, died.

An autopsy revealed that the man had lost 95 percent of the large neurons, or brain cells, within two nuclei of the thalamus, according to Elio Lugaresi and his colleagues of the University of Bologna (Italy) Medical School, who performed the study along with scientists from Case Western Reserve University in Cleveland. Moreover, the researchers found a similar thalamus deterioration in the brain of one of the man's sisters, who apparently had died in the same way. In a number of his relatives, in fact, researchers were not able to detect any brainwave sleep pattern in electroencephalograph tests.

The role of certain parts of the thalamus in sleep had been proposed previously but "was later ignored or rejected," according to Lugaresi and his colleagues. But, they write, these new findings do "indicate that the . . . thalamus has a role in integrating and expressing sleep, autonomic functions and neuroendocrine circadian rhythm."

How to snort a martini

Biochemist Daniel Malamud had just returned home from another hard day at his University of Pennsylvania lab and fixed himself his usual Gibson martini — the kind with onions, rather than olives. As is his custom, he ate the tiny onions off the wooden toothpick first. Not wanting to mess the furniture with a wet toothpick, he dropped it back into the glass. "My wife is a neatness freak," he explains. "After 25 years, I guess she's got me well trained."

He then proceeded to drink. During the last gulp, the toothpick "floated" out of the glass and into his mouth. "It was lodged *someplace*," he says. "I couldn't breathe; I ran into the bathroom and tried to make myself throw up." He succeeded — to a point. The toothpick vaulted into his nasal passage.

Waiting in the emergency room of Philadelphia's Lankenau Hospital, Malamud sat and stared at the blackboard, on which the nurse had written, simply, "Malamud. Toothpick up nose." "It was right there among all those people who had been shot, battered or beaten," he recalls with some pain.

Finally, after physician Mary Harlan Murphy had appeared and removed the toothpick, patient and doctor put their heads together and planned the next logical step — at least for people in the medical and academic communities: Publish. "You know, Dr. Murphy," Malamud said, "I think we may have a paper here."

Sure enough, a short account of the incident appears in the "correspondence" section of the Oct. 16 NEW ENGLAND JOURNAL OF MEDICINE. "The reverberations," Malamud told SCIENCE NEWS, "are already being felt throughout the medical community." One physician has written to Malamud saying he removed a martini toothpick from a lawyer's stomach in 1974. But that may not have been a Gibson, which was supposedly named for a U.S. ambassador to England who couldn't hold his liquor, and. . . . But that may be another paper.

Human monoclonals produced

Researchers from the National Institutes of Health (NIH) report they have coaxed monoclonal antibodies from a human cell line. The feat may remove a limitation of conventional monoclonal antibodies imposed on them by their heritage.

Monoclonal antibodies are widely used in medical diagnosis and are hot prospects as therapeutic agents. They are currently produced by fusing antibody-producing spleen cells from rodents and "immortal" rodent cancer cells.

But the antibodies, inasmuch as they come from rodent cells, are foreign to humans. Many researchers believe that people will build up an immune response after repeated injections of the antibodies, and various approaches to getting human cells to produce monoclonals have been tried.

Producing human monoclonals the same way rodent monoclonals are produced is out — few people would be willing to give up their spleens. White cells in the bloodstream also produce antibodies, but hybrids of human white blood cells and cancer cells tend to lose crucial chromosomes.

Another approach is to vaccinate a person with a protein, collect antibody-producing white blood cells, "immortalize" those cells with Epstein-Barr virus and select the cells producing the desired antibodies. While this technique has generated monoclonals, there is a limiting factor: The antibody in question has to be against a fairly benign substance so that a person could be vaccinated with it.

The NIH group figured out a way to circumvent the vaccination step, which they describe in the Oct. 24 SCIENCE. They started with a general population of white blood cells donated by healthy individuals, and exposed the cells to fluorescently tagged proteins. The proteins stuck to cells producing antibodies against them, and a cell sorter picked out the protein/white blood cell complexes. The white cells were then immortalized with Epstein-Barr virus.

Abner Louis Notkins of the National Institute of Dental Research, one of the investigators, says the advantage of the procedure is that the antibody-producing cells can be obtained without vaccinating the patient. Larry Steinman of Stanford University, who is working on a way to put human and mouse antibody genes into bacteria so that the bacteria produce a "hybrid" antibody, says the all-human approach could prove better than the hybrid approach if it works for other proteins besides the two tested. "If you can get human monoclonal antibody production totally *in vitro*," he says, "it's really a major advance."

Killing bacteria effectively and safely

Dormant bacteria can be difficult to get rid of with conventional antibiotics, which work on dividing bacteria but leave resting ones alone. Nondormant bacteria that are killed by antibiotics can also present a problem. Two studies presented by New York City researchers at the recent American Society for Microbiology meeting suggest solutions to an example of each problem.

Elaine Tuomanen, Alexander Tomasz and their colleagues at Rockefeller University tested a recently developed class of antibiotics called penems against dormant bacteria. The penems, they found in *in vitro* studies, can somehow kill dormant bacteria.

The group also tackled the question of why successful antibiotic therapy against nondormant bacteria that cause meningitis doesn't ensure survival. Hypothesizing that components of the killed bacteria cause potentially fatal inflammation of already-inflamed nerve tissue, they gave anti-inflammatory agents along with antibiotics to rabbits with induced meningitis. The agents limited inflammation and improved the rabbits' survival rate.