Punching the biological timeclock

It was 4 a.m. when the accident at Three Mile Island power plant occurred, and the employees on duty had that day "rotated" shifts, switching from the day shift to the night shift. Poor human performance has since been implicated as a major cause of the accident (SN: 2/23/80, p. 122). Abnormally high accident rates in other industries — trucking and navy, for example — have also been linked to human error. And increasingly, researchers have been looking to unnatural shift rotation as a possible cause of occupational mishap.

Scientists have now applied some basic principles of circadian rhythm — the natural sleep-wake cycle — to the design of an actual industrial work schedule, and they report that a more natural rotation pattern improves worker satisfaction and health and also causes an improvement in job performance.

According to Charles A. Czeisler of Harvard University and the Boston-based Center for Design of Industrial Schedules, one in four American workers works something other than the standard dayshift; and many of those who rotate shifts do so in a way that violates the natural timing of sleep and wakefulness. The workers at Great Salt Lake Minerals and Chemicals Corp. in Utah, the site of the experiment, had for 10 years rotated every week to the preceding shift — from days to nights to evenings to days, etc. With the cooperation of the company, Czeisler and his colleagues — Martin C. Moore-Ede of Harvard Medical School and Richard M. Coleman of Stanford Medical School — changed the schedules of 85 workers: 33 began rotating to a later shift every week, and 52 rotated to a later shift every three weeks. The researchers compared the subjects to 68 non-rotating shift workers on measures of job satisfaction, health, personnel turnover and productivity.

The results, reported in the July 30 SCIENCE, indicate that 70 percent of the workers preferred forward rotation; those who rotated weekly showed a 49 percent improvement in satisfaction, while those who rotated only every three weeks showed an 87 percent improvement. The latter group also showed an improvement in health, though they still fell short of the controls. In addition, personnel turnover decreased, and productivity increased 22 percent — a gain that was maintained nine months following the study. The company has since adopted the new rotation schedule for the entire plant.

The circadian principles underlying the schedule design are fairly simple, Czeisler says. Because the natural sleep-wake cycle, controlled by oscillations in deep body temperature, tends to run about 25 hours (SN: 7/3/82, p. 7), the natural tendency is to go to sleep later and later. But most people have the capacity to adapt to a change of one or two hours a day — delay or advance — without becoming "desynchronized"; in fact, people are constantly advancing their sleep by an hour a day to conform to the earth's 24-hour schedule. But when people rotate shifts, Czeisler says, the change in sleep cycle is too dramatic; the system becomes desynchronized and begins to "free run" — to drift forward on its natural 25-hour cycle until it is back in phase.

As long as the system is out of phase, the trough of the alertness cycle occurs during waking hours, explaining shift workers' complaints about exhaustion; the same desynchronization is the cause of jet lag. Because the internal 25-hour clock tends naturally to delay sleep, it is much easier to adapt to a shift rotation that requires sleep delay — a forward rotation. Backward rotation (like eastward jet travel) requires that sleep be advanced, which in turn forces the internal sleep-wake cycle to drift all the way around the clock to get back in phase — a process that, at an hour a day, may take a week or more. Some workers, Czeisler says, complain of never adjusting to a new shift; even a forward rotation requires a few days to become resynchronized, explaining why the 21-day schedule was more satisfactory and productive than the 7-day schedule.

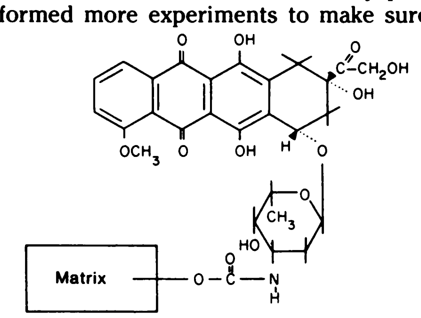
According to Czeisler, there is no single ideal schedule for all of industry, but it is essential that these basic physiological principles be considered in the design of any schedule that could interfere with sleep. The newly formed Center for Design of Industrial Schedules, he says, will be examining regulations that involve work scheduling where safety is an issue — Federal Aviation Administration and Nuclear Regulatory Commission regulations, for example.

According to Charles Ehret, a biologist at Argonne National Laboratory in Illinois, FAA and NRC regulations currently pay no attention to circadian principles. Based on his own survey of the American power industry, he says, at least half the power plants are rotating their workers the wrong way, causing sleep deprivation and dangerous desynchronization. "We cannot pinpoint the circadian contribution to the accident at TMI or to any single maritime or aircraft accident," he says, "but there's no doubt that cognitive function, visual acuity, and psychometric performance are way, way down under these circumstances." —*W. Herbert*

Cancer drugs: A surface attack

Cancer drugs have long been thought to kill cancer cells by acting on their DNA. Now one of the most important cancer drugs, adriamycin, appears also to act on their plasma (outer) membranes, Thomas R. Tritton and Gene Yee of Yale University School of Medicine in New Haven, Conn., report.

During the past several years scientists have begun to suspect that adriamycin might kill cancer cells more than one way. What's more, they have learned that various activities of the plasma membranes of healthy cells can be regulated by adriamycin. Tritton and Yee wanted to determine whether adriamycin might be able to destroy cancer cells simply by acting on their plasma membranes. To test this hypothesis, they chemically attached adriamycin to insoluble agarose beads (synthetic polymeric material) that were too large to get into cells. They exposed cancer cells to the adriamycin-bonded beads. The cancer cells died. They performed more experiments to make sure that adriamycin attached to the beads was not able to leak into cancer cells and to act on their DNA, and that agarose beads without adriamycin attached were not able to kill cancer cells. Thus adriamycin appears capable of destroying cancer cells solely by interacting with their plasma membranes, Tritton and Yee conclude. J.A.R. Mead, deputy associate director of the National Cancer Institute's Developmental Therapeutics Program, says he agrees with the conclusion after reading the report in the July 16 SCIENCE.



Tritton/Science

Adriamycin linked to polymeric matrix.

There are also practical implications to it, Tritton explains. Adriamycin exerts serious toxic effects on the hearts of cancer patients, probably by interacting with heart cell DNA. If adriamycin could be manipulated to act only on the plasma membranes of cells in a cancer patient's body, it might well destroy the patient's cancer cells yet spare the heart cells of any undesirable effects. However, because agarose beads are a material foreign to the human body, they would probably be rejected by a cancer patient's immune system, making it necessary to attach some other material than the beads to adriamycin to get it to act on a patient's plasma membranes. "Plasma membrane proteins are one possibility," Mead suggests.

Tritton, in fact, sees "the cell surface as a promising target in the design of a new generation of anticancer agents." Mead concurs: "I could see a surface attack on a tumor cell as a possible development of the future." —*J.A. Treichel*