

hazard of long-term exposure to toners probably is not eliminated simply by removing nitropyrene. More animal tests are needed, he says, to determine the human risk associated with long-term exposure to airborne particles of carbon black. □

Mathematics teachers urge course reform

Responding to what it terms a "crisis" in school mathematics, the National Council of Teachers of Mathematics has set forth this week at its annual meeting in Seattle, Wash., a series of policy recommendations for mathematics education in the 1980s. Shirley Hill, Council president, challenged parents, policymakers and the general public to address three major problems that contribute to the crisis:

- School mathematics is not keeping pace with the changing needs dictated by developing technologies.
- Most students are not taking as much mathematics in high school as they will need for their future careers.
- The present shortage of qualified mathematics teachers is increasing dramatically, largely due to greater professional and financial rewards in other technological careers.

"Policymakers are not confronting the deepest problems," says Hill, "because the public and its representatives have been diverted by a fixation on test scores."

The Council recommends that mathematics programs at all levels concentrate on problem-solving, not just on acquiring techniques, and that the scope of basic knowledge of mathematics be expanded to include skills essential for the future, not merely those required for present needs. "Skills are tools, and their importance rests in the needs of the times."

In such a future-directed curriculum many skills formerly considered basic become obsolete. The Council cites as one example the continuing stress in elementary classrooms on multiplication and division of large numbers, even though all current work is done on calculators and computers. Indeed, the Council urges that mathematics programs take full advantage of calculators and computers at all grade levels, and that computer literacy become part of the education of every student.

The Council also urges that three years of mathematics in grades 9 through 12 should be required of all high school graduates, and cites evidence from a survey of parents supporting this recommendation. (In many states now only one year is required.) To help bring about this change, they urge colleges to stop awarding college credit for courses covering mathematics ordinarily taught in high school. This practice, the teachers believe, encourages students to take only the minimum requirements in high school. □

APRIL 19, 1980

Tracking the chemistry of depression

There are times when emotional depression is normal and expected: following the loss of a loved one, divorce, separation or certain other stressful life events. What concerns researchers, however, are the "pathological" depressions that — while they may be triggered by loss or misfortune — often persist regardless of outside events. Many scientists believe most such disorders involve chemical shifts in the brain. And the success (albeit variable) of various antidepressant drugs during the past two decades tends to support this biochemical view of depression, according to some experts.

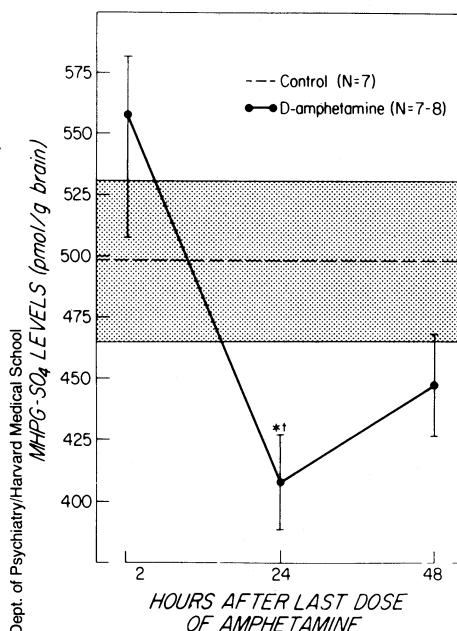
Pinning down the exact chemical mechanisms of such serious depressions is another matter. But researchers have been making steady progress toward this end, and recent studies in both animals and humans are consistently pointing toward specific neurochemical abnormalities in certain types of depressions.

Some of the latest work involving the study of behavior and brain tissue of experimental rats offers convincing support for what has been suggested in preliminary studies of humans: that manic-depressive illness, drug-induced depression and perhaps certain other forms of the disorder are accompanied by abnormally low levels of a brain chemical substance called MHPG. The results strongly indicate that the inability of a depressed individual to find pleasure in a normally rewarding experience — a job promotion, pay raise or whatever — may be related to these biochemical abnormalities in the brain.

To induce such an insensitivity to reward in rats, a Harvard University Medical School team suddenly withdrew the animals from amphetamine after administering the drug in increasing doses for several days. Amphetamine withdrawal has been shown to produce depressive symptoms in humans. But the experiment may also be valuable in "shedding some light on the pathophysiology of some naturally occurring depressions [such as] bipolar manic-depressive depressions," says Harvard psychologist Geraldine Cassens. She presented the research in Hartford, Conn., last week at the annual meeting of the Eastern Psychological Association.

During the experiment, the rats learned that by pressing a lever they could receive a pleasurable pulse of electricity through electrodes implanted in the hypothalamus area of the brain. Through a complex procedure that entailed electric current stimulation only on certain lever presses, the researchers were able to measure the animals' "reinforcement behavior" — an indication of their sensitivity to, or "enjoyment" of, the rewarding stimuli.

After their last, and highest, amphetamine dose, the rats exhibited extreme sensitivity to the electric pulses. But



Rat brain MHPG levels drop drastically following withdrawal from amphetamine.

during the next 24 to 48 hours, each of the rats showed a "marked decrease in sensitivity" to the electric current, compared with no essential change in control rats that had been injected with salt water. The experimental rats continued to show varying levels of "depressed" behavior until most returned to normal from 96 to 144 hours after withdrawal. However, for two of the rats, it took 9 to 11 days to return to baseline levels of sensitivity to electrical stimuli. In addition, the rats during withdrawal also exhibited other symptoms such as extreme passivity and little spontaneous motor activity.

Such symptoms are similar to those observed in humans who are "crashing" following prolonged amphetamine use — as well as those with naturally occurring depressions, particularly of the manic-depressive type — according to Cassens and Joseph J. Schildkraut, professor of psychiatry at Harvard and director of the neuropsychopharmacology laboratory at the Massachusetts Mental Health Center in Boston. But Schildkraut has also found that correlating almost exactly with the intensity of depressive symptoms in certain patients is a significant drop in levels of MHPG, which is a metabolite of the brain transmitter norepinephrine. The implication of low norepinephrine (as measured through MHPG) as a cause of certain depression has still been open to some question, though, because such chemical levels cannot be measured directly in the brains of living persons; they must be measured peripherally in the person's urine or blood.

However, in the second stage of their studies with rats, Cassens, Schildkraut,

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... Depression

Paul J. Orsulak and their colleagues have examined the animals’ brains at various time intervals following their withdrawal from amphetamine and subsequent depressed behavior.

The researchers report surprisingly close parallels between MHPG levels in the rats’ brains and those in the urine of certain depressed human patients—sharp drops in MHPG closely matched the animals’ decreased sensitivity to the electrical pulses. “I was amazed to find it was so remarkably parallel,” Cassens says.

Both Schildkraut and Cassens caution that the low MHPG findings appear to apply only to manic depression and amphetamine-withdrawal depression and perhaps certain other related forms. And, Schildkraut notes, other studies in his lab indicate other forms of depression may involve unusually high MHPG levels. In addition, Schildkraut points out that because of the “species difference” between rat and man, the results are “by no means definitive” in terms of humans.

Nevertheless, he says, the finding that the direct measurement in the animal brain matches that found in human urine is “intriguing.” Knowledge about MHPG could help psychiatrists distinguish which type of depression a person might have, and consequently aid in the selection of appropriate drug treatment, Schildkraut suggests.

The study results also help open the door to future investigations of how and why antidepressant drugs work. While lithium, for example, is believed to somehow affect the brain’s catecholamine system (which includes norepinephrine and MHPG), relatively little is known about how it specifically seems to help alleviate manic-depressive mood swings. Cassens says she is planning to further examine the mechanisms of lithium and tricyclic antidepressant drugs in the brain. □

Interferon factory

Human interferon can be produced by recombinant DNA technology (SN: 1/26/80, p. 52), but the process is still experimental. Aroused interest in interferon’s potential as an antiviral agent possible cancer fighter, however, has encouraged the Weizmann Institute in Rehovot, Israel, to announce plans for producing interferon by a more conventional method. The foreskins of circumcised males will provide the tissues, which then will be grown in the laboratory. Mass production of interferon, most of which will be reserved for research, is scheduled to begin this June in the institute’s \$1 million pilot plant. Other laboratories have recently announced stepped-up production of interferon from white blood cells (SN: 11/10/79, p. 328) and from fibroblasts—cells of human connective tissue grown in the laboratory (SN: 3/15/80, p. 166). □