NIDA Aims to Fight Drugs with Drugs

The agency is planning a massive search for medications to treat cocaine and other addictions: A "Manhattan Project for chemists"

WITH THE "JUST SAY NO!" approach to drug abuse treatment looking more and more helpless in the face of crack cocaine, the National Institute on Drug Abuse (NIDA) is sharply expanding its efforts to attack addiction from a different direction: not as a lack of moral fiber but as a disease of the brain. Starting with $27 million in seed money this year and expanding to twice that next year, NIDA plans to be spending upwards of $100 million per year by the early 1990s—all in search of medications that could break the addiction cycle for cocaine and other illicit substances.

"It's the Manhattan Project for chemists in the war on drugs," says Bristol-Myers Company senior researcher Duncan P. Taylor, who spoke at a special drug abuse symposium held recently by the American Chemical Society (ACS).* Indeed, if NIDA's "Medications Development Program" is funded at the level the agency anticipates—and congressional enthusiasm seems high—it would nearly double the agency's budget and would rival the government's expenditures on drug trials for AIDS.

"We're attempting to develop medications that can interfere with the drug-taking behavior and restore some degree of normality to [a drug addict's] brain function," says program director Marvin Snyder of NIDA, who appeared at that same ACS symposium in an explicit effort to get the word out to chemists and pharmaceutical companies alike.

Indeed, he says, "we need a variety of medications: to block the high, to block the craving, to block the withdrawal symptoms"—to give addicts at least a chance of reconstructing their lives. Drugs such as methadone have already been used with partial success against heroin, he says. But there is currently nothing for cocaine.

As Snyder is the first to admit, however, NIDA has a lot of catching up to do: although its research into drug abuse medications had gotten well under way by the late 1970s, the funding quickly vanished when the Reagan Administration started its first round of budget cutting. And in the prevailing "Just say No!" atmosphere of succeeding years, it proved very difficult to get that money back again—a fact that was particularly galling for NIDA officials last year when a conservative White House panel on drug abuse charged the agency with failing to work on solutions to the drug crisis (*Science*, 5 August 1988, p. 648).

Pharmacologist Louis Harris of Virginia Commonwealth University, who organized the ACS symposium, says he couldn't agree more: "There was a refusal on the part of the Administration to see addiction as a biomedical problem. It was a law enforcement problem, an interdiction problem, a moral problem—everything but a disease."

On another front, meanwhile, there has been a distinct lack of enthusiasm from the pharmaceutical houses. "A lot of companies don't view treatment of junkies as much of a market," says William T. Comer, vice president for research at Bristol-Myers. The brutal fact is that addicts as a group either cannot or will not pay for such treatment.

In just the past few years, however, researchers say that a confluence of factors has changed the attitudes toward drug abuse treatment radically. First, the wildfire spread of crack cocaine has made police and public officials desperate for alternatives. Snyder remembers a telephone call last autumn from an aide to Representative Silvio O. Conte (R–MA), who had heard about the possibility of cocaine medications and wanted to know more. "We literally spent hours talking about the basic scientific background, the progress that had been made, why we thought that the medical approach could work, and what we could do with adequate funding," says Snyder. As a result, Conte put $10 million into NIDA's fiscal year 1989 appropriations bill, together with another $10 million of internal NIDA funds that became the seed money for the Medications Development Program.

Second, the fact that the AIDS virus is transmitted by intravenous drug users provides a huge incentive for mounting a medical attack on drug abuse. Indeed, says Sny-

* The 198th National Meeting of the American Chemical Society, 10 to 15 September 1989, Miami, Florida.

Magic Bullets for Addiction?

The prospects for new addiction-fighting medications are not just theoretical: a number of particularly promising compounds have come to light in recent years. Two of them were reported at the American Chemical Society's recent drug abuse symposium in Miami.

Buprenorphine is an opioid drug that has been marketed as an injectable analgesic since the early 1970s. About 3 years ago, however, Yale University psychiatrist Thomas R. Kosten and his colleagues began studying the compound as an alternative to methadone in the detoxification of heroin addicts. It worked—and to their astonishment, led their subjects to spontaneously give up cocaine as well. About 70 to 80% of heroin addicts are also hooked on cocaine, said Kosten. Methadone will typically cut that figure in half, whereas buprenorphine gets it down to about 3%. A Harvard group has recently found a similar effect in cocaine-addicted rhesus monkeys (*Science*, 25 August 1989, p. 859).

Buprenorphine is particularly exciting, said Kosten, because whatever it is doing—its mechanism is still unclear—it does not seem to be directly affecting the dopamine pathways implicated in cocaine addiction. "We think it is offering a unique direction, perhaps opening up a whole new class of compounds," he said.

Buspirone, a new type of anti-anxiety agent that partially blocks certain of the brain's seratonin receptors, was first marketed by the Bristol-Myers Company about 2 years ago. Even then, however, it was already showing promise in the treatment of alcoholism. As Bristol-Myers senior researcher Duncan P. Taylor reported, buspirone sharply reduces the voluntary alcohol intake of addicted monkeys and rats. In humans, it alleviates many of the symptoms of alcohol withdrawal, such as anxiety, depression, clouded sensorium, and reduced cognition—without impairing such tasks as driving. And in recent preliminary double-blind trials on chronic alcoholics, it sharply reduced the craving, enabling about twice as many subjects to remain in the study after 6 weeks than those receiving a placebo. Buspirone's impact on cocaine addiction is not yet known, said Taylor, but tests are under way. ■ **M.M.W.**

der, the final $7 million of his first-year funding is AIDS money.

Third, he says, the increase in on-the-job urine screening means that more and more people are going to be entering mandatory drug treatment programs at a relatively early stage of their addiction. And that, he says, is when the drug companies start to get interested. When the addicts are motivated—by a desire to keep their jobs, if nothing else—when they are candidates for long-term treatment, and especially when they (or their health plans) are able to pay, then addiction starts to look as profitable as any other chronic disease.

And finally, says Snyder, "there's been incredible progress in the last 15 years in our understanding of the brain mechanisms of addiction." There is even hope that maybe, just maybe, a few common pathways can be found that underlie *all* addiction. "We're anticipating that some of the new medications, because they target the fundamental mechanism of addiction, may be useful in fighting more than one drug," he says.

With these factors in mind, says Snyder, the new NIDA program is designed to get the pharmaceutical houses and the research community alike more deeply engaged. In addition to providing individual research grants, for example, NIDA has set up a series of contracts with laboratories around the country where chemists can send in promising compounds for animal tests.

Meanwhile, in an effort to lower the development risk for the pharmaceutical companies, NIDA has set up six different treatment research units. If a company comes up with a promising new compound, says Snyder, "we'll work with them to do patient recruitment and perform clinical tests. In exchange, when we enter into a formal agreement, the company will take on the responsibility to get the medication through the FDA approval process."

However, he says, even that final hurdle has been lowered: "We now have an agreement in principle with the FDA to 'Fast Track' these drugs" under the new system recently set up for testing AIDS treatments.

Eventually, says Snyder, NIDA plans to have about eight products in clinical trials at any given time. That will not be cheap: Snyder estimates the cost at some $100 to $200 million per year. However, he also says he has already gotten indications of strong support from such figures as Senators Sam Nunn (D–GA), Joseph Biden (D–DL), and Daniel Patrick Moynihan (D–NY). Nothing is guaranteed, with the federal deficit being what it is. "But when we can justify the expenditure," says Snyder, "they say they will do their best."

■ M. MITCHELL WALDROP

The Epilepsy "Cure": Bold Claims, Weak Data

A peer-reviewed article stirs a furor among neuroscientists and raises questions about how journals handle such claims

EARLIER THIS MONTH, the *International Journal of Neuroscience* (*IJN*)* published an article that looked on the face of it as though it would raise something of a stir. It was entitled "Localization and cure of epileptic foci with the use of MEG measurements." The authors, Phodios A. Anninos and N. Tsagas, asserted that "we have cured 20 pathological subjects suffering from focal and general epilepsies by using an electronic device which we invented recently."

This remarkable claim—and the decision by a peer-reviewed journal to publish it—raise several troubling questions about the role that such journals, their editors, and reviewers play in establishing scientific truths. Who is responsible for controlling the quality of articles? Should standards be relaxed for laboratories outside the wealthy industrial nations? What are the dangers of lowering standards? How representative is this case of the selection process at other journals? It is apparent from the wide range of opinion *Science* encountered among those who know of the epilepsy "cure" article that on these issues there is no consensus.

In their article, Anninos and Tsagas, who are members of the Department of Medicine and Polytechnic School at the Democrition University of Thrace in Alexandroupolis and Xanthi, Greece, claim to have done as follows: They first mapped the brain activity of epileptic patients with magnetoencephalograms (MEGs) and determined the focus of the seizures. Then they adjusted their "electronic device" to beam back into the patients' skull a magnetic field of the same intensity and frequency as that emitted by the focus. According to Anninos and Tsagas, the two fields destructively interfered with each other on the analogy of the Young double-slit experiment ("by which under certain conditions light plus light gives darkness"), and the patients were "cured."

Once in circulation, the article drew a swift and vehement response from mainstream U.S. neuroscientists. "I don't know how it got into a journal," says William Southerling of the Department of Neurology at the University of California, Los Angeles. "It's so appallingly bad," says Timothy Pedley of Columbia University, "that when I first read it I thought that it must be some kind of joke." "It's the worst thing I have seen in a scientific journal," says Lloyd Kaufman, a leader in the field and a member of the *IJN* advisory board. Indeed, Kaufman and another board member sent the editor a scathing attack on the article and announced their intention to resign if no action was forthcoming. Their criticisms have been accepted and will appear in a future issue. But the question remains: should an article claiming that an unknown technique "cured" a major disease—an article regarded by leaders in the field as unsubstantiated—be published in a scientific journal in the first place?

The claim of Anninos and Tsagas "has no basis of reason in the current historical development of the field."

—Dominick Purpura

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