

# The search for a heroin 'cure'

Scientists concur that chemicals alone are not the answer

by Joan Lynn Arehart

Now that heroin is an economic and social blight on American society, the drums are beating loudly for a heroin substitute, or "cure."

In November, Rep. Claude Pepper (D-Fla.) called for a crash program to find a "heroin cure," and for allocation of \$50 million of public funds in fiscal 1972 for this purpose. In December the Senate passed a bill establishing, by statutory authority, the Special Action Office for Drug Abuse Prevention which President Nixon set up by executive order last June (SN: 6/26/71, p. 433). The House passed a similar bill this February. The Senate and House then met in conference; the compromise bill was signed into law by the President on March 22. In addition to placing statutory authority behind the drug abuse office, the law authorizes \$1 billion for drug abuse prevention in fiscal 1972, 1973, 1974 and 1975. A hefty \$75 million is earmarked for the office's scientific research in 1973, 1974 and 1975—specifically "to create, develop and test nonaddictive, synthetic analgesics to replace opium and its derivatives in medical use and to look for long-lasting, nonaddicting blocking or antagonistic drugs or other pharmacological substances for treatment of heroin addiction and detoxification agents which, when administered, relieve the physical effects of heroin addiction." In short: to find a chemical substitute for heroin. All these funds, whether fully or partially appropriated, will sweeten a healthy \$70 million already budgeted for such research in fiscal 1973.

However emotionally appealing the idea of a heroin surrogate, many responsible heroin authorities see grave flaws in the concept. They believe the public should not be led to consider a heroin substitute a panacea for the heroin problem.

The first object of the critics' attack is the widespread notion that any problem can be solved with a drug, even

addiction to a drug. As James Allen, a former heroin addict and director of Harlem's Addicts Rehabilitation Center says, "Don't Americans always substitute one problem for another?" The medical profession also perpetuates the notion that problems dissolve with drug treatment, admits a physician working on a potential heroin substitute. "Drugs are the art of medicine these days," he says, "and this situation isn't liable to change any time soon."

Second, a substitute for heroin already exists: methadone. Methadone maintenance consists of transferring an addict from heroin to methadone. During the past seven years, since methadone maintenance has progressed from a controversial research program into clinical treatment for thousands of addicts in every major city in the United States, the heroin addiction problem has become worse, if anything. The creator of the concept of methadone maintenance, Vincent Dole of Rockefeller University, told SCIENCE NEWS he is particularly disturbed that four out of every five persons in the "Tombs" (New York City jail) are on drugs, most of them being blacks or Puerto Ricans. "They lie on the floor and vomit," he says. "It's absolutely medieval." And if the white middle class thinks it is being spared, Dole and others report that the heroin epidemic is spreading to the suburbs.

Methadone maintenance eliminates the physiological craving for heroin. By maintaining an even "high"—by not creating sporadic euphorias and stupors—methadone allows an addict to function in society. Methadone can be taken orally, it is not needed in increasingly larger doses like heroin, and it is far less expensive. A study carried out by Dole's group at Rockefeller University claims that of 14,000 addicts who stayed with methadone maintenance, two-thirds to three-fourths returned to society as productive members. The director of the Washington,

D.C., Narcotics Treatment Administration, Robert L. DuPont, cites statistics as evidence that the crime rate can be reduced in proportion to the increase in the number of heroin addicts who undergo methadone treatment.

But according to a study published recently in the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, most of 100 methadone maintenance subjects followed up eventually reverted to heroin use. Also, because of its narcotic kicks and low cost, methadone is rapidly seconding heroin as a black-market product. Dole is troubled by this mushrooming market. He attributes it to the shortage of methadone maintenance facilities. Some 15,000 addicts are awaiting admission in New York City alone. Harlem's James Allen, though, suspects that most of the addicts seeking illegal methadone are more interested in highs than in returning to society.

In fact youngsters are dying in the ghettos from methadone overdoses. The New York Times recently reported 11 deaths in one weekend. Young children, JAMA reports, have been seriously poisoned, to the point of death, by ingesting methadone in households where one of the members is on methadone maintenance.

In an effort to answer some of the questions and solve some of the problems created by methadone use, the Government announced new guidelines for methadone-maintenance programs on April 3 (SN: 4/8/72, p. 229). The more than 450 programs will be reviewed; methadone will be reclassified to take it out of the hands of private practitioners and pharmacies, and then the methadone-maintenance system will be greatly expanded.

"There are bad sides to this whole picture," Dole acknowledges. Advantages and disadvantages of methadone aside, though, he considers the mounting thrust for still another heroin substitute to be an ill-conceived political

football. The instigators, in his view, are primarily Rep. Pepper and the National Institute of Mental Health.

Apart from the social and political issues, there are scientific obstacles blocking the discovery of an ideal heroin substitute. Most of the work is being conducted by drug companies. On March 28 the Pharmaceutical Manufacturers Association's Special Task Force on Drug Abuse issued a report to Rep. Paul G. Rogers (R-Fla.) on research progress in this area. John Adams, the physician who heads up the PMA task force, says the report represents some progress. But talks with scientists conducting the research turn up other, less favorable impressions.

For example, the PMA report emphasizes five potential heroin "antagonists." An antagonist is a drug that blocks the physiological effects of another compound in the body. The compounds are cyclazocine from Winthrop Laboratories, naloxone from Endo Laboratories, chemical cousins of naloxone from Endo and Bristol-Myers and another compound from Ciba-Geigy. One of the drugs is still being tested on animals; the other four have moved into clinical tests. And since the PMA report was drawn up, the Ciba antagonist has been found clinically ineffective, a Ciba scientist told SCIENCE NEWS.

There is a chance, of course, that one of the others might prove to be effective. But as one of the investigators admits, the idea of a heroin antagonist, like that of an alcohol antagonist, is not new, and "work to date has been a bust." The essential problem is that the screening of existing compounds for antagonist potential is both tedious and expensive. The ideal way to find a heroin antagonist, notes another drug company researcher, would be to design one chemically. But first scientists would have to understand how narcotics act at the physiological and biochemical levels. All they know now is that narcotics somehow affect the central nervous system.

Even if an effective antagonist is found, scientists researching promising compounds or substitutes concur that an antagonist will never erase the mental craving for heroin. Says Sidney Spector, pharmacologist-biochemist at Hoffmann-LaRoche's Institute of Molecular Biology: "An antagonist is not the answer."

Asserts a scientist working on an antagonist: "Even the most superior substitute would never be enough without supportive moral and psychological support." Charles E. Becker, chief of detoxification at San Francisco General Hospital, reports that some of their patients who successfully switched from heroin to methadone still had a psychological craving for drugs, and then turned to alcohol. Although the PMA report emphasizes progress with antagonists, several drug companies are also working on heroin detoxifiers—drugs to help an addict get off heroin. A detoxifier is used temporarily, unlike a maintenance drug, which is taken indefinitely.

One of these compounds, from G. D. Searle & Co., prevents morphine withdrawal symptoms in animals without producing symptoms of its own. Details were being presented this week at the annual meeting of the Federation of American Societies for Experimental Biology in Atlantic City. But as Mary Jane Kreek, a physician colleague of Dole, points out, methadone has been used successfully for detoxification purposes for a long time—longer, in fact, than for methadone maintenance. If methadone is used correctly, she says, it produces no symptoms of its own. Hence any advantages of the Searle compound over methadone are doubtful. In fact as a top scientist at Searle admits, "I am not at all sure that our compound would prove any better for detoxification than sedatives."

The other detoxifier drug is haloperidol (SN: 5/15/71, p. 331) from McNeil Laboratories. It has helped several hundred addicts get off heroin. But it has serious side effects of its own, tremors and muscle rigidity. And as

one of the McNeil investigators working on this compound says, "A detoxifier is not that crucial to heroin withdrawal anyway. Alcoholics and barbiturate addicts can die from drug withdrawal. This rarely happens to heroin addicts."

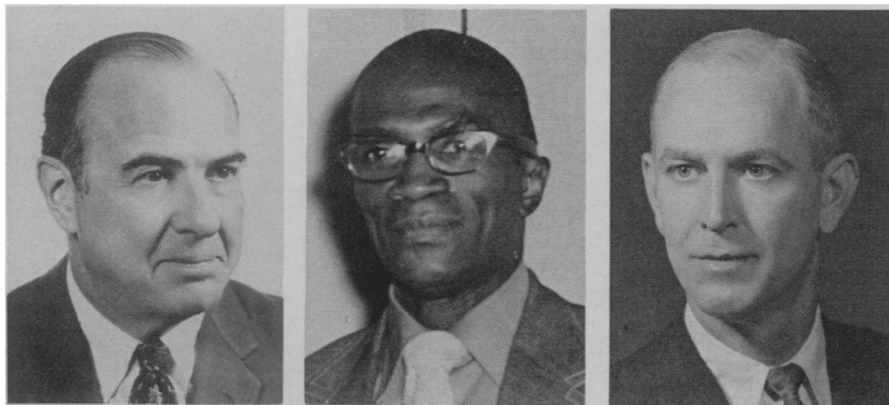
Aside from haloperidol, McNeil Laboratories is also working on another potential surrogate for heroin—a revulsion drug. When given to monkeys for some time and then discontinued, the compound makes the animals violently ill upon the injection of morphine. The PMA report cites this compound as a novel approach to heroin abuse. But the idea of a revulsion drug is not new. Ayerst Laboratories has marketed a drug for some time that, when ingested by alcoholics, makes them violently ill if they take a drink. But Ayerst has never been overwhelmed by Antabuse sales, and a heroin revulsion drug probably wouldn't be any more popular.

As for the possibilities of finding a good, nonaddicting analgesic (sedative), the pharmaceutical industry has been looking for one for years without success, says PMA's John Adams.

In fact, if anything looks as if it might be an ideal heroin substitute, it is not an antagonist, detoxifier, revulsion drug or analgesic, but immunization. At first blush the idea sounds outlandish. But Hoffmann-LaRoche's Sidney Spector has actually built antibodies to heroin. He is now trying to determine, in rodents, whether the antibodies might modify euphoric and physical dependency effects of heroin. Nonetheless Spector cautions that the chances of developing a heroin vaccination are slim.

In fact, as far as any scientific effort to find an ideal chemical replacement for heroin is concerned, Thomas M. Rauch, chairman of the board and president of Smith Klein & French Laboratories testified before Congressional hearings on the subject last August: "We do not see the miracle drug to cure addiction as a near-term possibility."

Weighing all the practical, logical, political and scientific ramifications of seeking a magic substitute for heroin, then, one cannot help but wonder whether the thrust for a heroin replacement might not be called off, or at least toned down. Some scientists such as Vincent Dole think so. Others, such as John Adams and Charles Becker, do not. But what they all tend to agree on is that a chemical replacement for heroin will never be more than a stop-gap to an overwhelmingly complex problem. The PMP stressed this point before Congress. Jerome Jaffe, the physician who heads up the Special Action Office for Drug Abuse Prevention, holds similar convictions. □



Rockefeller Univ. Bill Carter PMA  
Dole, Allen, Adams: Some precautions about emphasis on a chemical 'cure'.