routine pricing of our common-property environmental resources, which is probably a necessary development, we need to know much more than we do about the effects on health of various common pollutants. At the moment the main source of information is from statistical analysis of epidemiological data—scattered data at that (*5*). We need to know more than we do about the effects of air pollutants on the performance and lifetime of metal and other surfaces exposed to the air. We need to have some way of estimating the damage costs of stream pollution, including the value of lost recreational opportunities. We may even need to have some agreed way of putting a monetary value on clean buildings and unspoiled landscape. We must even estimate how many more people would wish to look at unspoiled landscape if we had more of it to look at. These sound like vague and almost foolish tasks, but we must take them seriously if we take our physical environment seriously.

There is also, I gather, much room for improvement in models of the circulation of water in river basins and coastal estuaries, and especially in models of atmospheric diffusion. Economists have little or nothing to contribute directly to this effort; but they may be indirectly helpful to the extent that the object is to construct models that illuminate the strategically important interactions of the physical environment and the economic system itself. What is meteorologically or hydrologically interesting need not coincide with what is economically important.

It is possible that here, at last, is a natural place for interdisciplinary work between the natural and social sciences. It would be very nice if, together, we could contribute a rational solution to a problem that concerns us all.

References and Notes

1. A. V. Kneese, "Environmental pollution: Economics and policy," *Amer. Econ. Rev.* (*Papers Proc.*) **61**, 153 (1971).
2. R. U. Ayres and A. V. Kneese, "Production, consumption and externalities," *Amer. Econ. Rev.* **59**, 286 (1969).
3. J. E. Hass, *Water Resour. Res.* **6**, 353 (1970).
4. E. S. Mills, *User Fees and the Quality of the Environment*, in preparation.
5. L. B. Lave and E. P. Seskin, *Science* **169**, 723 (1970).

NEWS AND COMMENT

Narcotic Antagonists: New Methods to Treat Heroin Addiction

The rising incidence of heroin addiction and the generally discouraging record of attempts to rehabilitate addicts has fostered the hope that modern chemical wizardry will provide some means of inoculating addicts or potential addicts against the effects of heroin, thereby preventing drug addiction. But if a drug to block heroin addiction could be developed, to what extent would it help solve the drug problem, and would it be beneficial, to the addict and to society, to administer it?

The questions are not hypothetical, because such drugs, known as narcotic antagonists, do exist; but neither are the answers obvious. Skeptics who doubt the clinical effectiveness of narcotic antagonists point out that drug addiction is a behavioral response to deep-seated emotional problems, and that administering yet another drug to "cure" those problems is a naïve and simplistic approach. Others think that blocking heroin use with the antagonists will only cause addicts to switch to different drugs and will leave untouched the deeper problem of drug-seeking behavior. Those who have used narcotic antagonists in treatment do not promote them as a cure for addiction, but they do believe that these drugs can be a useful adjunct to psychotherapy and a significant means of preventing heroin addiction, especially among adolescents. The whole issue is likely to receive much more attention; President Nixon's newly appointed coordinator for drug abuse prevention, Jerome Jaffe, has included antagonists on his list of potentially important treatment options. Funding for research on these drugs will apparently increase.

Narcotic antagonists are effective against heroin and other narcotics because they prevent those drugs from reaching the nervous system; antagonists differ, for example, from methadone, a synthetic narcotic, in that they themselves do not have narcotic effects and are not addictive.

The two narcotic antagonists now being used in experimental treatment programs are cyclazocine (a benzomorphine compound) and naloxone (*N*-allylnoroxymorphone). A daily dose of about 4 milligrams, given orally, of cyclazocine, which is the more widely used, will block both the habituating effects and the euphoria, or "high," from heroin for 24 hours. Patients are built up to this blocking dose gradually over a period of several weeks and in the early stages often experience dizziness, headaches, and other side effects—sometimes including hallucinations. Once established on the blocking dose, patients who miss their daily dose report experiencing headaches and sensations akin to "electric shocks." At two and three times the doses normally used in treatment, cyclazocine apparently can have an effect similar to LSD, only more unpleasant. Cyclazocine is slightly habituating, in the sense that mild withdrawal symptoms (the electric shocks) occur when its usage is discontinued; but neither it nor naloxone is addictive. The narcotic antagonists, unlike methadone, do not satisfy an addict's craving for drugs, and, despite side effects, treatment with these drugs is for the addict very much like being drug-free. In fact, many former addicts reportedly test the antagonist from time to time by injecting heroin, because they "don't feel anything" with the antagonist.

Naloxone has far fewer side effects than cyclazocine and apparently does not require a period of gradual accommodation. Pharmacologically, it is in many ways an almost perfect antagonist. It can be used to treat heroin overdose and has been licensed for this purpose by the Food and Drug Administration; * recovery from the effects of heroin overdose usually begins within a few minutes after naloxone is injected.

* Neither cyclazocine nor naloxone has been approved for the treatment of addiction, and both are available for this purpose as investigative drugs only.

For the treatment and prevention of addiction, however, the drug is not ideal because its antagonist effects do not last as long as those of cyclazocine; more than one dose per day, or clinical supervision during part of the day, is necessary. Naloxone is not very effective in oral form, thus doses of 1000 milligrams or higher must be used. According to those who have used it, the drug has a noxious taste that is impossible to hide.

Cyclazocine and naloxone are believed to work by attaching themselves to sites in the central nervous system known as morphine receptors. Because the antagonists have a greater affinity for these receptors than the narcotic drugs do, the latter are prevented from reaching the nervous system, and their effects are blocked. This blockade can be surmounted, but only by injecting extremely massive doses of narcotics. Several drugs other than cyclazocine and naloxone are known to have antagonistic properties, but many of them have unacceptable side effects as well. In contrast, the so-called pure antagonists, such as naloxone, have apparently no pharmacological properties in their own right except to block narcotics.

Clinical experience with narcotic antagonists at the present is limited—a consultant to the newly constituted Drug Abuse Prevention Office of the White House estimates that only about 200 persons have been treated with these drugs. Nor are the antagonists ideal, in the forms available today, because they have a relatively short active lifetime within the body. Other possibilities for blocking drugs may exist, and it may be possible to chemically modify cyclazocine and naloxone to obtain forms that will act longer. Even in their present form, the drugs can probably be packaged in a plastic time-release capsule or in some other preparation that would allow sustained action—from a few days to a month. But very little research has been done on these possibilities to date, in large part because of a lack of funds. The drug companies that developed the antagonists (Stirling–Winthrop for cyclazocine, and Endo Laboratories, a subsidiary of DuPont, for naloxone) are reluctantly making the drugs available for experimental use, and are doing some research as a "public service" and public relations gesture; but they have no great interest in narcotic antagonists because the potential market for these drugs is not large.

The federal government supports most current research on antagonists, although some state governments, notably New York, also finance research. In the fiscal year just ended, the National Institute of Mental Health (NIMH) funded some 32 research projects totaling $524,000, with the largest chunk of money devoted to clinical studies. More federal money is likely to become available, however, since the White House Drug Abuse Prevention Office, headed by Jerome Jaffe, is apparently going to recommend a major research and development effort aimed at finding a 30-day blocking drug for heroin, as well as expanded clinical trials.

But NIMH may lose some of its initiative and control over the research effort. By earmarking funds for specific purposes at the White House level, Jaffe and his staff will have a lot to say about how the research is done. One plan that is currently under discussion, for example, is to bring together several research groups, including some from the drug industry, and contract with them to develop the long-

Addict Treatment Programs

Clinical trials of narcotic antagonists in the treatment of heroin addicts are taking place in a number of small programs that usually involve no more than 15 patients at a time. At Kings County Hospital in New York City, for example, cyclazocine is administered on an outpatient basis, although patients must come in daily to take their dose. Before being admitted to the program, patients are required to attend group therapy sessions as part of an orientation and screening process to select likely candidates. Once admitted, they must spend 6 weeks in the hospital, being withdrawn from heroin with decreasing doses of methadone and then being gradually built up to the proper dosages of cyclazocine. Most dropouts from the program occur during this period, when patients try to face life without narcotics. Thereafter, they enter the outpatient program, which includes daily urine samples to check for drug use, counseling, and biweekly group therapy sessions in addition to the cyclazocine.

Perhaps the largest and oldest cyclazocine program in the country is that at the Metropolitan Hospital in New York City. After a hospital stay for detoxification, medical treatment, evaluation, and accommodation to the cyclazocine, the patients are treated on an outpatient basis. Patients come in only two or three times a week, rather than daily, and urine samples are spot-checked on the average of once every couple of weeks. The length of time required to build up to the prescribed dose is shortened to 4 days, by treating the initial side effects of cyclazocine with naloxone. But because it is still an experimental rather than a treatment program, patients commonly are kept in the hospital a total of 3 to 9 weeks.

One of the narcotic antagonist programs using naloxone is that at the Connecticut Mental Health Center in New Haven. The program gets around the problem of naloxone's limited period of action by operating as a day-patient facility. The patients, adolescents in this case, take part in therapy and vocational and recreational activities; at the end of the day, they receive their naloxone and leave for the night. But the antagonist is not the only method of treatment. The program relies heavily on what its director calls psychosocial intervention—the attempt to replace the drug culture for the addict by making available to him alternative life styles, goals, and opportunities.

Although essentially all of the existing antagonist programs are still experimental in character and design, many of them report encouraging results. In some cases, patients who are still being treated with cyclazocine are working and living an apparently drug-free existence some 2 years after entering the program. The patients themselves appear to be satisfied that treatment with an antagonist is a good thing—those contacted by *Science* expressed fears about being on the street again and said that they were glad to have that extra bit of security.—A.L.H.

acting forms of the antagonists. Contract research, although common in other areas of research, would be a novelty in the pharmaceutical field. Several major drug firms have indicated an interest in the project, even though nothing definite has been agreed upon yet.

Supply Problems

The new drug office in the White House will also have to contend with a variety of problems in supplying the narcotic antagonists. For example, one constraint on any operational program using naloxone is its expense and lack of availability. Naloxone is derived from thebine, a chemical present in small amounts in opium; it is correspondingly expensive, and, according to most investigators, hard to come by. It took one New York research group some 18 months to obtain sufficient quantities from DuPont for a clinical trial. Federal officials insist that adequate supplies are available for experimental use, and officials at the Bureau of Narcotics and Dangerous Drugs, which establishes production quotas for investigative use, maintain that closing the Turkish poppy fields will not make it impossible for individual companies to get enough raw materials in the future. But difficulties in obtaining a supply of opium may well provide companies with another disincentive to produce naloxone and similar compounds and a convenient excuse for not doing so.

Some research into new narcotic antagonists is already under way, with promising early results. One compound being studied is closely related to naloxone and is also derived from thebine, but it appears to have some advantages over both naloxone and cyclazocine. The new drug, known as EN-16-39 (*N*-cyclopropylmethylnoroxymorphone), is undergoing preliminary tests at the Addiction Research Center (ARC) of NIMH in Lexington, Kentucky, where the use of antagonists for the treatment of narcotic addition was first suggested and tried. The compound has already been tested in animals at Endo Laboratories on Long Island and is being tested in human subjects during the current ARC trials. According to William R. Martin of ARC, the drug is about twice as long-acting as naloxone, and, although it does have some side effects, they appear to be far fewer and less severe than those associated with cyclazocine. Because it is also more effective orally than naloxone, the required dose (and the cost of the drug) appears to be about one-twentieth that of naloxone.

Most of the treatment programs using narcotic antagonists (see box) are restricted to patients who appear to be highly motivated to stop using drugs. But even with these patients a wide variety of problems are often encountered, including high dropout rates during the early stages of treatment and the use of other drugs. One of the chief causes appears to be that patients are compelled to face their problems and to deal with the realities of their social situations, however impossible. This may well be beyond the capability of large numbers of addicts, many of whom presumably use narcotics to avoid just those situations.

For how many addicts, then, are the antagonists likely to be useful? Methadone, because of its narcotic effect, is more appealing to many addicts, and the relaxed, jovial atmosphere of a methadone ward contrasts sharply with the tension, frustration, and anxiety that characterize a cyclazocine ward, according to one psychiatrist who has worked in both. Since there are more patients needing treatment than there are facilities available, antagonist therapy and methadone maintenance are not competitive methods of treatment at present. Yet it is still uncertain how many addicts can be induced, in the long run, to seek the more demanding type of treatment.

Three major roles have been proposed for narcotic antagonists in the treatment of heroin addiction. They might be useful in a preventive role in the treatment of the casual user of heroin who has a high likelihood of becoming addicted. They might be useful in the rehabilitation of addicted individuals who do not wish to be maintained on methadone—both those who want to end a period of methadone maintenance and those just entering treatment for whom neither methadone nor a therapeutic community is acceptable. In this regard, antagonists might be a significant option in combination with a therapeutic community, perhaps making possible a shift to nonresidential programs. Third, the narcotic antagonists might be used prophylactically, more or less as a vaccine, in high drug risk areas during a crisis. An example of such a use would be to vaccinate large numbers of teenagers at a high school that was experiencing an epidemic of heroin use. Large-scale prophylactic use of antagonists in the armed forces has also been proposed—as a kind of social experiment.

A number of objections have been raised to the use of narcotic antagonists, either in treatment or in the prevention of heroin addiction. Multi-drug use appears to be an increasingly common practice, even among heroin addicts, and the effect of widespread administration of antagonists might be to switch heroin users to amphetamines, cocaine, alcohol, or other drugs. Barbiturates, in particular, seem to be the drug of choice for many who would otherwise "mainline" heroin, because the calming, sedative effect is somewhat similar. But barbiturates are more addictive than heroin, and withdrawal much more dangerous—apparently the mortality rate for unassisted withdrawal is as high as 15 percent.

Conflicting Views

There appear, in fact, to be two basic points of view among those who work with the drug problem. Critics of both the antagonists and methadone believe that the attempt to treat drug addiction medicinally, rather than by educational preventive measures and other "soft social programming," is characterized more by a concern for the welfare of society than for the welfare of the patient. Psychologists and ex-addicts involved with therapeutic communities have charged that the therapy provided in the antagonist programs amounts only to hand-holding, and that the addict's basic problems are rarely tapped and dealt with. (The situation is complicated by the tendency of many partisans of a particular rehabilitative approach to be so committed to their own method that they cannot see the value of any other approach.) Some observers fear that antagonists, especially in their long-acting forms, will have a high potential for being used in socially irresponsible ways, whether or not those who developed them intended it.

Supporters of the narcotic antagonists believe that the urgency of the drug problem does not admit of waiting for ideal solutions and that the antagonists can provide help—if not a cure—for many who desperately need it. The psychiatric director of at least one antagonist program, while admitting that the cyclazocine and supportive therapy that she administers is little more than a crutch for the patient, points out the practical advantages—the addict is not down in

the gutter, not narcotized past the point of coping with daily problems, and not compelled to steal. Others point out that, while antagonists as presently administered will not stop those who want to use heroin, they can help prevent the impulse "fix," which may be of particular help to the adolescent in resisting peer-group pressure to use drugs.

Antagonists are not the solution to the drug problem. But since the problem seems unlikely to go away, the antagonists, as is true of other methods, can play a potentially important role in treatment. They can be, as one addict put it, "like having a friend in your pocket."—ALLEN L. HAMMOND

Health Radicals: Crusade to Shift Medical Power to the People

Not long ago, critics of health care in America routinely blamed everything that was wrong with medicine in America on the American Medical Association. Liberal doctors and others would rhetorically agonize over the AMA's artificial maintenance of physician scarcity, its exclusion of minorities, and its preoccupation with large profits. The government's inattention to many of the glaring inequities in medical service was frequently blamed on the AMA's well-heeled lobbying efforts.

While the AMA is still the object of great scorn, from many directions, the elevation of health care to the stature of a full-blown national crisis has left the doctors' organization just one of the many combatants in the current free-for-all over health care. The now familiar and depressing statistics detailing American infant mortality, distribution of services, rising medical costs, and declining life expectancy (which were once offered by the liberals as evidence against the AMA) are now listed by both the Nixon Administration and Senator Kennedy as reasons for enacting their particular national health insurance plan. Indeed, countless politicians and special-interest groups have their own ideas of what needs to be done about health care in America, and most of them are talking in terms of vaster reforms than bringing to its knees an AMA that now counts fewer than half of the nation's doctors in its membership.

Among the more notable forces emerging in the health care battle of the 1970's is a coalition of radical professionals, students, health workers, and community activists, which might be called, for lack of a better term, the radical health movement. Its members range from vaguely dissatisfied doctors and medical students to committed revolutionaries, and, until now, no organization on the national level has represented the movement. Last month, however, the Medical Committee for Human Rights (MCHR), a 7-year-old organization with some 20,000 members in 40 local chapters across the country, embarked on a "National Health Crusade" in the hope of providing the movement with a national focus.

Begun as a group of mostly young, white, male doctors who offered money and medical assistance to the civil rights movement—its members provided aid, for example, on the long march from Selma to Montgomery—MCHR at first abstained from any direct political involvement, fearing such activities would compromise its professional influence. Eventually, however, the organization evolved first into "the voice of humanist medicine" that spoke out from time to time against the AMA and then into a more radical group whose members, particularly at the local level, carried out a wide range of activities from the staffing of community controlled free clinics to confrontations with established health care institutions. Each new step of political advocacy taken by MCHR has led to the attrition of some of the doctor-members who thought the action to be "unprofessional," with the result that MCHR now consists largely of house staff, medical students, and young middle-level health professionals such as nurses and laboratory technicians. And in its current national crusade MCHR hopes to recruit an increasing percentage of nonprofessional health care critics.

"What we're trying to do in the health crusade," Quentin Young, a Chicago internist and the organization's director told *Science*, "is show the ubiquity of the health care problem—so that the coal miner in Appalachia and the slum resident in a big city can see that their health problems have a common origin." According to a recent pamphlet, MCHR will "Begin educational programs in schools, neighborhoods, unions and hospitals; conduct letter writing campaigns; collect petitions; and go to radio, television and the press in our fight."

Unlike the politicians who seek to reform the health care system with plans for national insurance, health radicals challenge many of the basic assumptions underlying American medicine. The radicals seek primarily to give the recipient of health care a voice in controlling the institutions that deliver health care. This in turn has implications for the nature of professionalism, the uses of technology, and the distribution of social and economic power. Although for the most part the health radicals are aiming peashooters at well-entrenched fortresses of political strength, they've already exerted influence far out of proportion to their numbers. Typically, the radicals heap equal scorn on the private practitioners and their AMA, the more liberal hospital- and university-based physicians, as well as almost every other element in the established health care system. In the words of the staff of the Health Policy Advisory Committee (Health–PAC), a group which has offered a good deal of analysis in support of the radical health movement:*

> Traditionally, liberals have explained that America is not a healthy place to live, in either a medical or a social sense, simply because health and other social services are low priority items in a nation whose resources are committed to military and economic expansion. "If only we could spend all the money we spend in Viet Nam on hospitals, housing, schools . . ." goes the refrain.
>
> So we have reasoned. But on looking

* This quote is from Health–PAC's book *The American Health Empire: Power Profits and Politics* (Random House, New York, 1970). The organization also publishes a monthly bulletin. Subscriptions are $7 per year, from Health–PAC, 17 Murray Street, New York 10007.