New Look at Heroin Could Spur Better Medical Use of Narcotics

The Carter Administration this month officially decreed that medical research with so-called dangerous drugs, namely heroin and marihuana, should no longer be impeded by prejudiced notions about their potential for abuse, and that the drugs should be evaluated on the same basis as any others.

This move is an attempt to break away from the antiquated attitudes toward drugs of abuse that have held sway since the days of Harry Anslinger, the first commissioner of narcotics and the man who branded marihuana the "killer drug." It also is in response to increasing public agitation over inadequate management of the pain of terminal cancer.

The fact is, pain is a major health problem in this country. Not acute or short-term pain, but chronic, "intractable" pain. More particularly, the kind of pain that afflicts a substantial portion of cancer victims.

John J. Bonica of the University of Washington School of Medicine, an anesthesiologist and an international authority on pain, estimates that the disease causes severe pain among 70 to 90 percent of hospitalized cancer patients. According to experts in the study and treatment of pain, the suffering from terminal cancer is poorly handled almost everywhere. There are few or no data to support this belief because nobody has thought to compile statistics; nonetheless, anecdotal evidence alone makes it clear that the problem is more extensive than most doctors would care to admit. In fact, fear of pain is one of the main reasons that fear of cancer has attained the proportions of a national phobia.

Only in the last few years have professionals and citizens begun to organize to come to grips with the problem. Three years ago the International Association for the Study of Pain was formed, chapters of which are now being organized in this country. The society, which has launched a new journal called *Pain*, held a world symposium on management of cancer pain in Italy in 1975, and another meeting, to be the largest ever held on cancer pain, is planned for next May. "Cancer pain is badly managed throughout the world," says Bonica. Now, he believes, we are seeing the beginning of a "major worldwide movement" on pain.

In this country there is the beginning of a popular movement to better the lot of terminal cancer patients. Those involved, led primarily by nurses and members of the clergy, are interested in establishing hospices—homelike places, modeled on English hospices, where people can spend their final days in a peaceful, caring atmosphere with enough narcotics to keep them continuously pain-free (*Science*, 30 July 1976). Only last summer a group of people in Washington, D.C., organized a national Committee on the Treatment of Intractable Pain, headed by American University law professor Arnold Trebach. The committee has made as its first specific goal the legalization of heroin for treatment of pain. Last spring Trebach petitioned the Attorney General to have heroin categorized as a Schedule II drug, giving it the same medical status as morphine.

Although the overwhelming stigma attached to heroin has prevented much research on it, public pressure is now beginning to outweigh political timorousness on the subject. The new Administration policy was masterminded by Carter's special assistant for health, psychiatrist Peter Bourne, who last month sent a moemorandum to health undersecretary Julius Richmond directing that dangerous drugs be evaluated on an equal footing with any other drugs for potential medical benefits and that appropriate investigations be carried out not by drug abuse agencies but by the National Cancer Institute (NCI) and others engaged in medical research. Bourne was scheduled to meet with top NCI officials on 16 November to discuss implementation of the policy. "Fifty years of policy have been reversed in terms of the government being willing to evaluate heroin on the same terms as any other drug," he says. The same goes for marihuana, which, in addition to showing promise for the treatment of glaucoma, has been found helpful in relieving nausea from cancer chemotherapy.

Although heroin is not the panacea that some fancy it is, the drug at the moment appears to supply a dramatic focus for public concern about cancer pain.

There are very few scientific data on the relative benefits of morphine and its derivative diacetylmorphine (diamorphine, or heroin). The major study that addresses these two drugs in the treatment of cancer pain was recently completed by R. G. Twycross at St. Christopher's Hospice in London. Twycross conducted a fairly limited study comparing the effects of morphine and diamorphine when taken orally in the Brompton mixture, a concoction that includes cocaine, phenothiazine, and alcohol. Those at the hospice had long had the impression that heroin was preferable for several reasons: that it caused less nausea, was less constipating, helped the appetite, was less soporific, and was a better mood enhancer. However, Twycross concluded from his study that there was practically no difference between the two, except when they were injected. Then, he said, heroin's greater solubility made it preferable to morphine, particularly when large doses are required. (Heroin is thought to be two to four times as potent as morphine when injected; therefore less than half as much is needed to achieve the same analgesic effect.)

Now, at last, Americans are going to conduct their own study, the first of its kind, to evaluate heroin in relation to other narcotic analgesics in cancer. The National Institute on Drug Abuse (NIDA) earlier this year awarded the Sloan-Kettering Institute for Cancer Research (SKI) a $1.9-million grant for an exhaustive 5-year research program that will also include detailed studies of the pharmacokinetics (how the drug moves through the body) of several natural and synthetic opiates, and clinical studies of endorphins, the morphine-like substances manufactured by the brain.

While the British study documented subjective reports by patients and side effects such as nausea and grogginess, the SKI study will rely in addition on a great deal of chemistry, studying blood samples and other biofluids to determine how the drugs break down into metabolites, and where and how various effects take place in the body. Heroin will be evaluated every which way. (Ironically, since the manufacture of heroin is prohibited in this country, the researchers will be working with heroin that has been confiscated by the Drug Enforcement Administration and has to be purified for research.) Intramuscular injections of heroin will be compared to those of morphine in patients who have already built up a tolerance to narcotics and those who haven't. Oral heroin will be compared to intramuscular heroin (the potency ratio of heroin goes down when it is orally administered because it is deacetylated—turned back into mor-

Pain Control with Hypnosis

Much has been learned in recent years about the power of the mind to affect involuntary bodily processes in very specific ways, including the brain's perception of pain. Manifestation of this power is often dismissed as the placebo effect because it is unpredictable, usually temporary, and no one knows how to harness it in a systematic fashion.

Yet hypnosis is a technique that can do just that, according to Paul Sacerdote, a New York psychiatrist associated with the oncology service of Montefiore Hospital. Now in his seventies, Sacerdote is one of the most experienced and resourceful hypnotherapists in the country. Unlike most practitioners, he has worked extensively with pain patients, particularly those suffering from pain of cancer and its treatments.

In a conversation with *Science*, Sacerdote said that "at a very minimum one in four people with cancer will respond very well to hypnotherapy for relief of pain." This means that many can do without narcotics altogether and others can have their medication significantly reduced. Sacerdote says it is possible to teach a person how to become hypnotized in only a few sessions; thereafter the patient can hypnotize himself when necessary. He believes almost anyone can derive some benefit from hypnosis, although light trances are hardly different from a simple relaxation state. But many are able to achieve a state so deep as to resemble a stupor.

It is in the in-between states that a therapist can achieve the most creative results. There is literally no limit to the things people can be trained to do and train themselves to do to manipulate their pain when hypnotized. They can displace their pain to another part of the body; change the sensation to one that is not painful; use images, such as switching electric circuits on and off, to control the pain; disassociate themselves from the part of the body that hurts; create images and hallucinations to replace reality; experiment with time distortion as though under the influence of psychedelic drugs. A patient who can succeed in achieving effects like these not only enjoys decreased pain, but has side benefits such as improved sleep and appetite and a happier emotional environment which prolongs hope and, very likely, life.

Despite reports from Sacerdote and others such as Stanford psychologist Ernest Hilgard, there is not much medical interest in hypnosis (the National Cancer Institute is funding two projects on hypnosis with cancer pain). Sacerdote says part of the problem is that most doctors have heard of hypnosis only casually and do not know much about psychology. He related a case where a dying cancer patient in a hospital requested hypnosis; the physician refused to take the responsibility for allowing the therapist to come in, and the buck was passed up to the hospital's medical director, who denied permission on the grounds that "hypnosis is a parlor game."

Most doctors, however, probably share the attitude of those at Sloan-Kettering who, on being asked whether they were interested in hypnosis, said they felt that too few people were able to benefit from the technique and that success was too heavily dependent on the personality of the therapist. Sacerdote believes that medical resistance is also related to the reluctance of physicians to become emotionally involved with their patients, particularly those who are dying.

But even if medical practice encouraged hypnotherapy, it would probably be found that able practitioners are rare. It requires conviction in the worth of the technique, highly developed intuitive capabilities, and a close empathic rapport with the patient.

How hypnosis works remains a mystery. Sacerdote believes that it may make the gate control mechanism in the central nervous system that can short-circuit pain messages to the brain more accessible to the patient's control, and that it may release endorphins, the morphine-like substances manufactured in the brain.

Sacerdote wants to conduct a study testing the effect of hypnosis on the pain and survival rates of lung cancer patients (almost all of whom die within 1½ years of diagnosis). But, as he has written, a double-blind study would be just about impossible—"We cannot test 'hypnosis' versus some 'placebo,' because hypnosis may be in many ways the most powerful of placebos."—C.H.

phine—faster by various organs before it gets to the brain). Then intravenous heroin will be compared with intravenous morphine. Finally, the Brompton mixture will be introduced and compared with either heroin (if that is found better than morphine) or oral methadone.

"Ten years ago it would have been virtually impossible to conduct a study like this" because of the red tape involved, says Raymond Houde, the chief investigator who heads the analgesic studies section, the base of SKI's pain team.

But while the SKI people welcome the opportunity to look at this long-ostracized drug, they made it clear in a discussion with *Science* that the real problems in managing cancer pain stem from ignorance and prejudice on the part of medical people rather than from lack of effective analgesics. Although doctors have been roundly criticized for overprescribing drugs and oversedating hospital patients, it appears they more often have the opposite problem when it comes to administering narcotics for cancer pain. The causes range from fear of legal sanctions (the Harrison Narcotics Act of 1914 imposes severe penalties for administration of narcotics for other than medical purposes) to remnants of the Puritan concept that suffering is good. They are concerned about side effects, and worry that too many narcotics will hasten death. Some doctors are so terrified of addicting their patients that they stay their hands even with people who are clearly dying anyway. And sometimes the existence of the pain is denied by the physician—Kathleen Foley, a doctor of the SKI pain team, says, "Chronic benign patients give cancer patients a bad name." (Narcotics are not advisable for chronic conditions such as lower back pain, and chronic pain patients tend to suffer from so many emotional complications that there is now a growing movement to get them off medication and teach them other ways to alleviate their pain.)

Houde and Bonica (who was visiting Houde at the time) pointed out that doctors understand very little about most drugs in general, and less still about pain. (Houde pulled a fat tome called *Cancer Medicine* off his shelf and found only a few pages devoted to the subject of pain.) There is little comprehension of the fundamental difference between acute and chronic pain: the former may be a useful symptom of an underlying pathology, whereas the latter is pointless and deserves to be treated as a primary problem rather than a symptom.

Another distinction doctors fail to note is the difference between tolerance and addiction. "They think that if you want

another dose after 2 hours you must be peculiar or addicted," says Bonica. Yet patients vary widely in the way they metabolize the drugs, and the inevitable buildup of tolerance does not necessarily mean physical or psychological addiction. Foley adds that doctors have a peculiar double standard when it comes to handling psychoactive drugs. "They will give you 20 grams of gentamicin that cures the infection but ruins your kidneys," but they eschew bold use of narcotics for fear of making a patient a "slave" to drugs, impairing his "free will," and so forth—this despite the fact that pain is the greatest enslaver and personality-destroyer of all.

It becomes clear in discussions with pain experts that the availability of heroin would probably offer only marginal benefits. The real value of opening the issue would more likely be in leading doctors to more sophisticated use of narcotic analgesics.

The extent of the problem can only be guessed at. "If you ask the NCI the incidence of cancer pain," says Bonica, "they have not one piece of datum." That is supposed to change. Bonica wants to conduct an epidemiological study to gather information on the types of cancer that pose the worst problems, the treatments commonly given, and the effectiveness of treatment. The NCI, which is now putting $650,000 of its $800 million budget into pain research, is currently developing a Request for Proposals to conduct such a study.

Meanwhile, Arnold Trebach of the intractable pain committee was recently found sitting in a borrowed office amid hundreds of unanswered letters—from sufferers, nurses, widows, and even a few hospitals—that came in response to an article in *Parade* magazine. "I'm stunned by the response," he says. "I didn't know how bad the problem was. A lot of these letters would make you cry. I don't know what to tell these people. I have a full course load to teach. I don't have the time. We don't have any staff. I'm overwhelmed." Although the pain committee's primary emphasis is on heroin—"it's obscene that our doctors and patients don't have the choice," says Trebach—he said he guessed the most realistic goal was to "educate the public on what they have a right to demand from the medical profession." The consumer movement has taught citizens to speak up for themselves. Now they are speaking up for their right not to die in pain.—CONSTANCE HOLDEN

Minerals and Mining: Major Review of Federal Policy Is in Prospect

President Jimmy Carter may soon call for a major interagency review of nonfuel minerals policy. Elaborate plans for such a study have, at White House direction, been under preparation for several months now and they are expected to be presented to the President within the next week or two.

Many of the mining state congressmen who have been pushing for such an initiative see it partly as a means of reversing what they regard as a tendency of the federal government to put more and more of the public lands off limits to mining and to impose increasingly onerous environmental regulations on the domestic mining and minerals-processing industries. But, according to present plans, the study would be broadly framed and would take into account environmental as well as industry concerns.

Moreover, despite the alarms sounded by industry about an increasing U.S. dependence on insecure foreign sources of certain minerals, the study would weigh the importance of the American market to other mineral-producing nations and the advantages as well as disadvantages to the United States of this "dependence."

During the past several decades, proposals to develop a national minerals policy have appeared repeatedly on the Washington agenda. Yet, apart from some studies and reports (of which the most famous was the 1952 report of the Paley Commission, appointed by President Truman), nothing much has come of them. This is not to say, however, that the mining industry has been without friends or influence in government circles. At least until fairly recent years, the policies governing most of the federal domain lands in the West have been liberal and permissive with respect to mineral exploration and the patenting and development of mining claims. Under the Mining Law of 1872, which remains the basic statute even today, holders of valid claims pay no royalties to the government, however profitable the mineral deposits may be.

The current policy study initiative is traceable to a letter sent to President Carter last February by Representative Jim Santini (D-Nev.) and 42 other House members (most of them from western states where mining is important) and to a meeting subsequently held at the White House. Santini, a 40-year-old Italian-American from Las Vegas now in his second term, is a lively and evidently persuasive congressman who is emerging as an important member of the House Committee on Interior and Insular Affairs and its mines and mining subcommittee. The letter, which he drafted, declared that the need for a national minerals policy is urgent. It said in part:

> New [mineral] exploration and production are stifled as the majority of our public lands have been withdrawn from mineral entry. Simultaneously, the small miner and prospector, who account for most new exploration, are entombed with never-ending federal regulation. The net effect has been that we have become dependent upon unreliable foreign imports for numerous survival minerals, which has left our country vulnerable and threatened, our national stockpiles notwithstanding. Mr. President, even a cursory review of the record will illustrate that our nation is in a state of foolish oblivion about this grave resource issue, and we are in desperate need of a balanced mineral policy to direct us out of this dilemma.
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> Administrative avenues must be developed which would insure that a mineral policy be effectively administered and implemented. Such avenues do not presently exist. . . . The U.S. Bureau of Mines and the U.S. Geological Survey [agencies within the Department of the Interior] both play an important minerals role; however, both entities are part of an organizational structure where a host of conflicting concerns precludes the minerals side of the story from being given a fair hearing. The Bureau of Land Management, which regulates mineral development on the public lands, plays a major role in the development of mineral resouces, and yet the BLM is directed by biologists whose primary stewardship is over the surface and renewable biological resources. Thus the sub-surface mineral resource voice in existing structures is neither independent nor objective. . . .

Santini and his cosigners—they included both Morris Udall (D-Ariz.), chairman of the Interior Committee, and Abraham Kazen (D-Tex.), chairman of the mining subcommittee—called for not