Marijuana "Justifies Serious Concern"

New Institute of Medicine report suggests cannabis has some potentially harmful effects, some possible therapeutic uses

"Marijuana has a broad range of psychological and biological effects, some of which, at least under certain conditions, are harmful to human health. . . . What little we know for certain about the effects of marijuana on human health—and all that we have reason to suspect—justifies serious national concern." So concludes a new report on marijuana issued in February by the Institute of Medicine of the National Academy of Sciences.* The report was prepared by a panel of 22 scientists chaired by Arnold S. Relman, editor of the *New England Journal of Medicine*. The panel members "all were experts in the relevant disciplines," the report says, but "only a few had previously been involved in the study of marijuana or had taken public positions on the subject."

The panel was convened in September 1980 at the request of the Secretary of the Department of Health and Human Services and the director of the National Institutes of Health to take a fresh look at the evidence about marijuana. The principal goals of the $450,000 study were to analyze existing evidence about the potential health hazards of marijuana, to assess possible therapeutic benefits, and to identify the directions in which U.S. research on the drug should proceed. The panel carried out a systematic review of all relevant literature published since 1975 and a selective review of earlier literature. It also solicited public comments and consulted experts in each field.

Because of this approach, there were few surprises in the study—although a few highly publicized reports of hazards were dismissed as inconclusive. In general, the report occupies the solid middle ground between those who argue that marijuana is safe and those who claim it is a serious hazard. Says Relman, "Our committee found the present truth of the matter to lie somewhere in between the two extremes, so we give no comfort to those with strong positions on either side of the argument."

The panel's conclusions and recommendations can be broken down into six major areas.

Patterns of use. Since 1971, the number of individuals who have used marijuana at some time during their life has doubled in every age group between 12 and 24. Overall, more than 50 million Americans have used marijuana at least once. It is the most commonly used illicit drug among adolescents, although alcohol and tobacco are the most commonly used of all drugs.

Surveys directed by Lloyd Johnston and Jerald Bachman of the University of Michigan show that the number of high school seniors reporting daily use of marijuana rose from 6 percent in 1975 to a peak of 11 percent in 1978, before declining to 9.1 percent in 1980. A new report by Johnston and Bachman issued only days before the Academy report indicates that daily use among this group further declined to 7 percent in 1981—perhaps, they say, because of an increased perception of hazards.

The number of seniors reporting daily use of alcohol has remained constant at about 6 percent throughout this period. But the use of alcohol and most other drugs takes place after school and on weekends, whereas much marijuana use occurs during school sessions. This pattern is "particularly disturbing" because of the drug's effects on behavior, short-term memory, communication skills, and learning ability.

The report also concludes that "marijuana users perform more poorly in school, are less religious, have performed more delinquent acts, are more often in trouble with the law, have more traffic accidents, and use more illicit drugs than nonusers." Many of these factors, however, preceded the use of drugs. There is, furthermore, "no evidence to support the belief that the use of [marijuana] will inevitably lead to the use of any other drug." In fact, most individuals who use drugs began with tobacco or alcohol; only slightly more than one-quarter of those who worked their way up from these drugs to marijuana proceeded on to other drugs, and only a very small percentage of those are current users. The single strongest factor influencing adolescents toward use of marijuana is its use by their peers.

Heart and lungs. The smoking of cannabis causes changes in the heart and circulation that are characteristic of stress, but there is no evidence that this is harmful to healthy individuals. "This rise in workload [does pose] a threat to patients with hypertension, cerebrovascular disease, and coronary atherosclerosis." These individuals should avoid the drug.

Short-term use of marijuana produces dilation of the bronchial passages, but persistent use leads to significant increases in resistance to airflow. Heavy users often develop such respiratory problems as pharyngitis, sinusitis, bronchitis, and asthma. The most severe problem in the respiratory system, however, is the potential to produce carcinoma of the lung.

With the exception of the cannabinoids in one and tobacco alkaloids (nicotine) in the other, tobacco and marijuana smoke are qualitatively similar; marijuana smoke, however, contains about 50 percent more carcinogenic hydrocarbons. Δ-9-Tetrahydrocannabinol (THC), the primary psychoactive ingredient of marijuana, is not itself mutagenic, but extracts of marijuana smoke ("tar") produce mutations in both bacterial and mammalian test systems. A series of experiments by Cecile and Rudolph Leuchtenberger of the Swiss Institute for Experimental Cancer Research in Lausanne shows that marijuana smoke produces abnormal proliferation and malignant transformation of cultured hamster lung cells within 3 to 6 months. Exposure of cultured human lung cells to the smoke produces the early changes characteristic of malignancy. Preliminary results from Forest S. Tennant, Jr., and his colleagues at the University of California Medical Center at Los Angeles suggest that exposure to combined marijuana and tobacco smoke produces more harmful effects than are produced by either alone.

There have not yet been any cases of human lung carcinoma attributable solely to smoking cannabis—"possibly because marijuana has been widely smoked in this country for only about 20 years, and data have not been collected systematically in other countries with a much longer history of heavy marijuana use."

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One controversial subject related to the lungs is paraquat, an herbicide sprayed on cannabis plants in Mexico by the government to kill them. Growers harvest marijuana immediately after such spraying before the herbicide can take effect; it is estimated that as much as a quarter of the marijuana entering the United States is thereby contaminated with paraquat residues. Large doses of paraquat by mouth or inhaled in aerosols can cause severe lung damage, particularly pulmonary fibrosis, "but no cases in human beings have yet been proved to result from paraquat-contaminated cannabis." Furthermore, "few cannabis smokers are expected to be exposed to the large amounts of paraquat known to cause severe lung damage." Exposure to paraquat may be increased, however, as a result of the recent decision by the U.S. government to spray cannabis fields in this country.

Reproduction and other biological systems. In men and male animals, marijuana suppresses the production of male hormones, decreases the size and weight of the prostate and the testes, and inhibits sperm production. These effects are reversible, and "there is no proof that it has a deleterious effect on male fertility."

There have been few studies on women of childbearing age because most investigators are reluctant to administer the drug to them. Studies in rats, mice, rabbits, and rhesus monkeys show that marijuana blocks ovulation, probably by its effects on the production of hormones. Crude marijuana extracts and THC are both teratogenic (produce birth defects) in animals, but "there is no evidence yet of any teratogenic effects of high frequency or consistent association with the drug"—at least partially because of confounding by the mothers' use of other drugs. THC does cross the placental barrier, so there is the potential for harm to the fetus. It can also be secreted in breast milk and could be toxic to infants ingesting it.

Contrary to some earlier, highly publicized studies, the committee concluded that neither cannabis nor THC causes chromosome breaks, which are thought to be an indicator of genetic damage. The panel also concluded that THC and some of its analogs can produce a mild, transient suppression of the immune system. This could produce a slight increase in infections among normal users, but could be "dangerous" for cancer patients and others whose immune systems are already suppressed. There is also evidence that marijuana can interfere with the regulation of body temperature; in hot environments, particularly, it causes inhibition of sweating and a consistent rise in body temperature.

Nervous system and behavior. "We can say with confidence that marijuana produces acute effects on the brain. . . . [It] impairs motor coordination and affects tracking ability and sensory and perceptual functions important for safe driving and the operation of other machines; it also impairs short-term memory and slows learning." The effects of marijuana on driving ability are thus comparable to those produced by alcohol, and the effects of the two drugs are additive. But Herbert Moskowitz and his colleagues at the Southern California Research Institute have recently shown that the impairment produced by cannabis lasts for 4 to 8 hours after the feeling of intoxication is over, much longer than is the case with alcohol.

Peter Arnold

The panel concluded that the so-called amotivational syndrome—whose effects include apathy, loss of ambition, loss of effectiveness, diminished ability to carry out long-term plans, difficulty in concentrating, and a decline in school or work performance—does exist among marijuana users. Such symptoms can also occur in the absence of marijuana, however, and they may predispose an individual to use of drugs, which would then accentuate the behavior.

There has been much controversy about whether marijuana causes changes in brain structure. The late A. M. G. Campbell and his colleagues at the British Royal United Hospitals in London had reported atrophy in the brains of ten heavy marijuana users observed by a technique known as air encephalography—in which air is injected into the brain cavity prior to taking x-rays. Robert G. Heath and his colleagues at Tulane University have reported "dramatic" changes in the structure of the brain in monkeys that have received heavy doses of marijuana.

But both studies, the panel argues, "suffer sufficiently from methodologic and interpretation defects that their conclusions cannot be accepted." In particular, the panel cites more recent studies by John Kuehnle and his colleagues at Harvard Medical School and by a team headed by Donald W. Goodwin of the University of Kansas School of Medicine in which computed tomography, a noninvasive diagnostic technique, showed no gross changes in brain morphology. As in the other areas, the panel concludes that "much more work is needed to settle this important point."

Therapeutic potential. Preliminary studies suggest that marijuana and its derivatives might be useful for lowering intraocular pressure in glaucoma, in the control of severe nausea and vomiting caused by cancer chemotherapy, and in the treatment of asthma. One constituent of marijuana, cannabidiol, might also be useful for treating certain types of epileptic seizures and other diseases of the nervous system. Other studies, in contrast, show that cannabis will probably not be useful as an antianxiety agent, antidepressant, analgesic, or antitumor drug.

The psychotropic and cardiovascular effects of cannabis, however, could limit use of the drug in treating older patients. The panel therefore urges that greater effort be made to find analogs that retain the therapeutic function without these side effects. Counterbalancing this problem is the observation that "cannabis seems to exert its beneficial effects through mechanisms that differ from those of other available drugs," so that marijuana and its derivatives would be complementary to other agents.

Research funding. "Well-designed studies on human beings are relatively few. . . . The federal investment in research on the health-related effects of marijuana has been small, both in relation to the expenditure on other illicit drugs and in absolute terms." In 1981 dollars, expenditures for marijuana research have remained relatively constant for the last 5 years at just over $4 million. Last year, they represented only 8.2 percent of the budget of the National Institute on Drug Abuse. "The committee considers the research particularly inadequate when viewed in the light of the extent of marijuana use in this country, especially by young people. We believe there should be a greater investment in research on marijuana."

—THOMAS H. MAUGH II