Hallucinogens and narcotics alarm public

Hallucinogens rarely used medically but opioids are best pain killers, thus search continues for strong but nonaddictive analgesic

Of all the drugs popularly abused in the United States today, probably none are viewed with more alarm by the general public than are hallucinogens and narcotic analgesics. Heroin is the most widely used example of the latter category.

Hallucinogens are drugs that stimulate sensory perception having no basis in physical reality. Hallucinations may be visual, auditory, gustatory, olfactory, or tactile, but more often than not, hallucinogenic drugs are taken for their visual effects. Some of the more popularly abused hallucinogens are LSD (D-lysergic acid diethylamide—usually as the tartrate), mescaline (3,4,5-trimethoxyphenethylamine), psilocybin (3-[2-(dimethylamino) ethyl]-indol-4-ol dihydrogen phosphate ester), STP or DOM (2,5-dimethoxy - 4 - methylamphetamine), DMT (N,N-dimethyltryptamine) and its diethyl analog, DET.

Narcotic analgesics include the naturally occurring opium alkaloids, semisynthetics, and a number of synthetic compounds with morphinelike activity that may or may not be structurally similar to opium alkaloids. The term narcotic analgesic is commonly used interchangeably with opioid, and embraces such compounds as morphine, heroin (diacetylmorphine), codeine (methylmorphine), methadone (6-dimethylamino-4,4-diphenyl-3-heptanone), meperidine (N-methyl-4-phenyl-4-carboxyoxypiperidine), and propoxyphene (4-dimethylamino-3-methyl-1,2-diphenyl-2-butanol propionate).

The interest of the scientific world in the hallucinogens has been intimately bound with their use to produce experimental psychoses. Mescaline, the first hallucinogen to be studied in this context, is found in the peyote cactus (Lophophora williamsii) and had been known to primitive New World peoples in pre-Columbian history. Interest in the subjective effects of mescaline by psychologist Havelock Ellis during the late 1800's sparked further research into the hallucinogenic potential of that drug. The alkaloid was isolated in 1896 from plant material, but the structure was not determined until 1918. The structural similarity between mescaline and epinephrine has continued to intrigue investigators.

Mescaline is effective in oral doses of about 5 mg, per kg, of body weight. Effects begin 30 minutes to an hour after ingestion and typically include colorful geometric hallucinations or fluid distortions of familiar objects. Auditory or tactile hallucinations may also be present. Tremors, anxiety, exaggerated reflexes, and electroencephalogram abnormalities have also been reported. The effects of the drug usually last about 12 hours. The mescaline user typically reports that he is aware that hallucinations do not represent reality and generally feels that he is in touch with the real world, although paranoia or extreme anxiety has been reported in schizophrenic patients given the drug.

LSD. Like mescaline and psilocybin, LSD is capable of producing profound perceptual alterations. LSD is semisynthetic in origin, lysergic acid being derived from Claviceps purpurea, the ergot fungus that attacks some grains. Its hallucinogenic effects were first described by the Swiss chemist Albert Hofmann after he accidentally ingested some of the compound in his laboratory in 1943.

By the 1950's, the compound was being intensively investigated as an adjunct to psychotherapy. Claims for its efficaciousness ranged all the way from its ability to elicit model psychoses or remove deep-seated psychological blocks, to a suggestion in recent years that with the drug, terminal cancer patients might be better able to cope with impending death. It is estimated that about 3000 papers on LSD have been published in primary journals, although, as has been the case with most pop drugs, a sizable portion of these fail to withstand rigorous scientific scrutiny.

LSD is an experimental drug. It has not been approved for medical use by any official agency. Only the d-isomer is active. An oral dose of 20 to 30 micrograms elicits psychological responses in sensitive individuals, although "trip" doses of 200 to 250 micrograms are more typical.

The effects of LSD are usually apparent within an hour following ingestion, and the spectacular effects last for about 12 hours. Milder reactions may persist for an additional 10 to 12 hours.

LSD acts largely on the central nervous system. Numerous and diverse mechanisms of action have been proposed, but as yet no satisfactory mechanism can be agreed upon. Physiological effects include elevated blood pressure and increased heart rate, dilated pupils, elevated body
Narcotic analgesics are widely abused

Morphine

Codeine

Heroin

Methadone

Meperidine

Temperature, increased blood glucose levels, and changes in the electroencephalogram.

Teratogenic potential. Such physiological concomitants are considered of small clinical importance by members of the Canadian Commission of Inquiry into the Nonmedical Use of Drugs, and physiological toxicity appears to be low. There have been no recorded human deaths directly attributable to overdose. Research into the teratogenic potential of LSD has yielded confusing results, the commission says in its report. High doses taken early in pregnancies variably produce deformations in newborn of some animals but not in others. The possibility of chromosome damage in humans has also been explored, but the results are often contradictory.

LSD is concentrated in the liver after absorption from the gastrointestinal tract. Relatively little of the compound reaches the brain despite the fact that LSD easily penetrates the brain and readily crosses the placenta in pregnant females. LSD is essentially completely metabolized by the liver to 2-oxo-LSD (an inactive compound) and excreted.

Physical dependence on the hallucinogens does not develop, and periods of weeks or months may separate trips by even the most avid users. Tolerance to LSD develops rapidly, however, and a period of several days is needed to re-establish response in a tolerant individual. Cross-tolerance between LSD and mescaline, psilocybin, or other lysergic acid derivatives may develop, in which tolerance to one drug bestows upon the individual tolerance to other drugs having similar effects.

Narcotic analgesics. Like many of the hallucinogens, narcotic analgesics were first isolated from plant material. The major narcotic is derived from the opium poppy—Papaver somniferum— indigenous to parts of Asia. The dried juice from the unripe seed pod of this plant is opium—a mixture of several alkaloids. Morphine—a major constituent of opium powder—was isolated in 1805, followed in the next 50 years by codeine and papaverine. Heroin, a semisynthetic morphine derivative, was first produced in 1874. Since then, a variety of synthetic drugs with opiumlike activity (methadone, meperidine, and others) have been prepared and have found widespread application.

The opioids are unsurpassed in their ability to relieve moderate or severe pain. Unfortunately, pharmacologists have been unable to divorce addiction potential from the analgesic properties of these drugs. Although much research continues to be directed toward finding a strong analgesic without the attendant addiction liability of the opioids, morphine remains the standard against which other strong analgesics are measured.

Heroin, which is not considered medically useful in the U.S., is several times more potent than morphine. When it was first developed, heroin was not thought to produce addiction, the Canadian commission notes, but it has since become the drug of choice among chronic opiate abusers in the lay population. Addicts in the medical professions seem to prefer morphine or synthetics like meperidine.

The physiological effects of opioids in therapeutic doses are not particularly remarkable. Respiration and cardiovascular activity are somewhat depressed, the pupil is constricted, and body temperature may be elevated. Gastrointestinal disturbances are frequently reported. Nausea or vomiting may occur and decreased intestinal motility may cause constipation. In higher doses, respiration may be severely depressed. Toxic effects of overdose are coma, shock, and respiratory failure leading to death.

Sterile drugs. Contrary to popular misconception, chronic opioid addiction in itself is not incompatible with normal, productive life, according to University of Chicago's Dr. Jerome H. Jaffe. Individuals who can afford to maintain their addiction with sterile drugs show little direct, physical damage from opioids. Such individuals are rare, Dr. Jaffe hastens to add, and life expectancy among opioid addicts is considerably diminished by poor hygiene, adulterated samples, faulty nutrition, and secondary infections—such as tetanus or hepatitis spread by unsterile hypodermic needles. Overdosing among addicts with little access to controlled-potency opioids is frequent.

Morphine is metabolized by conjugation with glucuronic acid. Other narcotics are N-demethylated and excreted. Small amounts of free morphine are detectable in the urine, as is the conjugated form. Codeine is also metabolized by the liver and excreted in inactive form, but a small amount may be demethylated to form morphine that is metabolized by conventional pathways. Heroin is hydroyzied to monacetylmorphine. This compound in turn is hydrolyzed to morphine, which is excreted either in free or conjugated form.

Occasional use of opioid narcotics does not produce tolerance, the Canadian commission finds, although with chronic use, tolerance develops to the sedative, respiratory depressant, and analgesic effects. Tolerance to the gastrointestinal effects and to pupil constriction is slower to develop.

Physical dependence is related to dose and frequency of use. At higher chronic doses, a full-blown abstinence syndrome develops upon withdrawal, including severe and painful physiological responses. The syndrome resembles that produced by abrupt discontinuation of barbiturates, although it is not physically as dangerous. Considerable cross-tolerance and cross-dependence to the various opioids exists, and these phenomena may be exploited in easing the withdrawal syndrome. Methadone, for example, may eliminate the heroin withdrawal syndrome at doses that do not produce euphoria. Addicts may thus be maintained on methadone while undergoing detoxification in rehabilitation programs. Although methadone, too, is a narcotic, it may be possible for an addict to draw support from such maintenance therapy while undergoing re-habilitation.