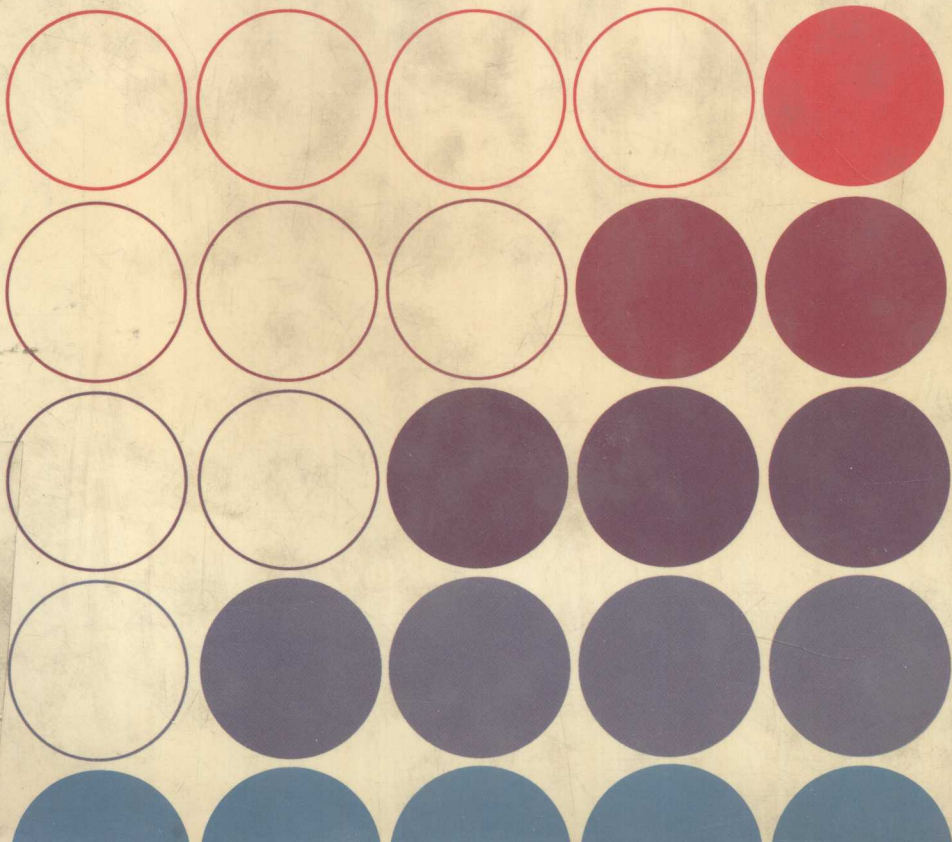
Hallucinogens: Neurochemical, Behavioral, and Clinical Perspectives

Volume Editor: Barry L. Jacobs



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Hallucinogens: Neurochemical, Behavioral, and Clinical Perspectives

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TO DIANE

Preface

Humans have been self-administering hallucinogenic drugs for many hundreds of years, and apparently in a few societies, for thousands of years. Historically, the use of these drugs was almost exclusively for religious and/or mystical purposes. More recently, however, especially within the past 60 or 70 years, the recreational use of hallucinogens has increased substantially. This trend peaked in the middle 1960s, when the use of hallucinogenic drugs reached what some have described as epidemic proportions. Coincident with this rising recreational use and possibly spurred by it, there has been a growing interest in the biologic bases or mechanisms of action of hallucinogenic drugs. Many answers to these questions have been elucidated as a result of recent technical advances in the fields of pharmacology and neuroscience.

In retrospect, two discoveries can be singled out as being seminal for advancing our understanding of the biologic bases of hallucinogenic drugs. First, in the early to middle 1950s, the monoamines norepinephrine, dopamine, and serotonin were found within the mammalian central nervous system and shown to be differentially concentrated in various brain regions. Based on this, it was proposed that these compounds might act as chemical neurotransmitters in the central nervous system. A second important advance was made about 10 years later. A group of Swedish investigators, utilizing fluorescence histochemistry, produced a detailed map of the localization of the cell bodies, efferent pathways, and axon terminal distribution of these monoamine-containing neurons. This "wiring diagram" provided other investigators with the basic information that allowed them to study or manipulate these neurochemically identifiable groups of neurons. This pioneering research in these two related areas set the stage for much of what is described in the experimental chapters in this book.

On the basis of their own research as well as that of others, most authors in this volume have concluded that of all the brain neurotransmitters studied to date, none plays as crucial a role in drug-induced hallucinogenesis as serotonin.

The major focus of the present volume is to provide an up-to-date account of current research on the mechanisms of action of hallucinogenic drugs. The approach is a multidisciplinary one that, hopefully, avoids many of the pitfalls inherent in a dependency on any single experimental methodology.

The book begins with introductory chapters on the natural history of hallucinogens and on the effects of these drugs in humans, followed by two chapters on the behavioral effects of hallucinogens in animals, with one focusing on unconditioned, and the other on conditioned effects. The next section deals with neurochemical studies of hallucinogenic drug action in which structure–activity relationships and receptor binding are examined. This is followed by

two chapters in which the neurophysiologic aspects of the action of these drugs is examined at the single unit level, *in vitro* and in anesthetized rats, and in freely moving cats. The book concludes with an overview and speculations about future research in this field.

This book will be of interest to students and professionals in the fields of neuroscience, psychology, physiology, pharmacology, and psychiatry.

B. L. Jacobs

Acknowledgments

When Sam Enna, the series editor, wrote and asked me to edit a book on hallucinogenic drugs, I told him I would do it if one critical condition was met: I would have to obtain the agreement of the leading scientists in this field to contribute chapters. If even as few as two or three refused to undertake writing yet another chapter, the project, at least with me as editor, would be dropped. I am happy to say, and as the reader can plainly see from the list of contributing authors to this volume, that most of the scientists that I contacted agreed.

Many outstanding investigators who have made important contributions to the study of hallucinogenic drugs are not included among the authors in this volume for two reasons: First, this volume represents the field from my own scientific interest and perspective. Thus all research areas may not be represented. Second, in several of the content areas covered in this volume, there are considerably more than one or two excellent researchers. Space limitations and danger of overlapping subject coverage forced us to confine ourselves to nine chapters.

Two unique aspects of this book are worthy of mention. First, the reader will note that three of the chapters have authors from two different institutions. It was an expediency that saved me from having to choose between excellent scientists, and, more important, it fostered and encouraged a give-and-take dialogue between the coauthors. Second, this volume is not simply nine individually contributed chapters. In initial conversations and letters with many of the authors before they began their writing, we attempted both to cover the specific fields comprehensively and to insure that there would be little overlap between chapters. The attainment of these objectives was bolstered by having each author send me an initial draft of the chapter, which was then edited and sent back for revision. Much of this was time-consuming and I would like to thank both Sam Enna and Raven Press for their patience with me and confidence in this project.

I would also like to thank the Psychology Department at Princeton University and the National Institute of Mental Health for various forms of support which made this project feasible. I owe a special debt of gratitude to Ms. Arlene Kronewitter for her good humor and outstanding secretarial skills.

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The Natural History of Hallucinogens

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Wandering about in the planetary garden, botanists have encountered more than 700,000 species of plants. Many plants provide sources of food; others provide materials for clothing and shelter; still others yield medicines and poisons. Among this latter group, 91 species have been identified as hallucinogenic plants. These plants are unique: sometimes "magic," "mystical," or "religious." They are actually complex chemical factories that produce compounds capable of inducing hallucinations. These compounds are referred to as hallucinogens.

Experiences with hallucinogens have puzzled and intrigued man for centuries. They have given him "sights" to see, "voices" to hear, "thoughts" to ponder, and "altered states of consciousness" to explore. They have generated conditions that can only be described by such global terms as ecstacy or madness. It is not surprising that man has given these drugs numerous descriptions varying widely in precision. A study of these historic descriptions adds greatly to a definition of hallucinogens. In the following section, the definitions used in early historic works are examined in an effort to explain the conceptual grouping of some drugs as hallucinogens.

The history of the drugs that are defined as hallucinogens is explored through the natural history of their development among the flora and fauna of the planetary garden. From early uses by primitive peoples to later experimentation, hallucinogens followed a natural path dictated by certain chemical properties and behavioral possibilities. First, the common botanical origins of these plant drugs are discussed in terms of the production of alkaloids which had unusual consequences for browsing animal life. These accidental encounters were observed by early man, who quickly discovered the unique properties of the hallucinogenic plants. The story of primitive experimentation with five representative groups of hallucinogenic plants is then told. Such experimental use appeared to be chiefly concerned with perceptual changes, and the history of the experimental analysis of these phenomena is briefly described. The discussion is then concluded by an outline of theoretical speculations and future developments in this natural history.

DEFINITIONS AND HISTORIC WORKS ON HALLUCINOGENS

Succinctly defined, the word hallucinogen refers to substances capable of producing hallucinations. Hallucinations, in turn, comes from the Latin *alucinatio,* meaning a wandering in mind, idle talk, prating. To the extent that substances produce a wandering in mind or attention, most psychoactive drugs might qualify as hallucinogens. However, hallucinations have more commonly referred to visions and apparitions. The first use of the word in the English language was by Lavater (1572), who used the term to refer to "ghostes and spirites walking by nyght" (32). Accordingly, hallucinogens become substances that produce false sensory perceptions in the absence of an actual external stimulus. These false perceptions can occur in any of the senses.

The definition remains far from precise. While the 91 plant hallucinogens, and a greater number of synthetic hallucinogens, are capable of producing hallucinations, other drugs may also produce these false perceptions, particularly when taken in toxic or lethal dosages. Conversely, the classic plant hallucinogens often produce nonhallucinatory effects as well as experiences lacking in false perceptions. In order to circumvent this difficulty, Hoffer and Osmond (15) offer the following broad and generally accepted definition:

> Hallucinogens are then chemicals which in nontoxic doses produce changes in perception, in thought, and in mood, but which seldom produce mental confusion, memory loss, or disorientation for person, place, and time.

This contemporary definition is reminiscent of the description offered by French psychiatrist Jacques Moreau (23) in the first book on hallucinogens in 1845. Although Humphrey Davy (5) had published a 600-page book on nitrous oxide and its hallucinatory effects in 1800, Moreau's work was the first to include other hallucinogens. Moreau claimed that one could study mental illness by provoking it artificially through the ingestion of hashish (*Cannabis*), which possessed the characteristics of plunging one into an hallucinatory state while preserving the ability to observe and report events. Moreau described hallucinations as being similar to dreams wherein imagined visual, auditory, and tactile stimuli appear to be part of reality. He noted that the psychologic phenomena of hallucinations were basically the same whether induced by nitrous oxide, *Datura stramonium, Atropa belladonna, Hyoscyamus niger,* or a variety of other hallucinogens. With uncanny insight into what future neurophysiologic research would reveal, Moreau believed that the hallucinatory state resulted from excitation of the brain, which enabled imagined thoughts and memories to become transformed into the sensory impressions of visions and sounds:[1]

> . . . the hallucinating person hears his own thoughts as he sees, hears the creations of his imagination as he is moved by his memories . . . and, what is even more extraordinary, certain combinations of thought are transformed into sensory impressions—that is to say, are endowed with the property of acting physically upon our senses in the manner of exterior stimuli.

[1] Translated from the original by R. K. Siegel.

After experimenting on both himself and his patients, Moreau tried to persuade his colleagues at the Hôpital de Bicetre to try hashish for themselves. His medical friends were hesitant to accept Moreau's notion of "objective experimentation" with a hallucinogen, but the Bohemian artists and writers of 19th century Paris were more receptive. Among them were several writers who formed the Club des Haschichins. Its members included Theophile Gautier, Honore de Balzac, Charles Baudelaire, Alexander Dumas, and Victor Hugo. Their writings emphasized various aspects of the hashish-induced hallucinatory experience, including an overwhelming joy.

The second book on hallucinogens, *Die narkotischen Genussmittel und der Mensch* by Ernst Freiherr von Bibra (37) in 1855, referred to the hallucinogenic plants as *Genussmittel,* meaning "medium of enjoyment." In the same year, James Johnston, in his two-volume masterpiece *The Chemistry of Common Life* (19), referred to these plants as "narcotics." Johnston wrote that man uses narcotics to "multiply his enjoyments, intellectual and animal, and for the time to exalt them" (vol. II, p. 7). Included in his extensive discussion of narcotics were *Cannabis, Datura,* and *Amanita.* Here, as in later books on hallucinogens, the word narcotic was used in its broadest sense, meaning to benumb or to stupefy. Thus a narcotic was viewed as any substance which, when taken into the body, induced drowsiness, sleep, stupefaction, or insensibility. Certain stages of intoxication resulting from hallucinogens, such as *Cannabis,* and even stimulants, such as coca, were seen as depressive enough to qualify for the classification of narcotic.

The next book on hallucinogens, *The Seven Sisters of Sleep* by British mycologist M. C. Cooke (4), continued the narcotic labeling but suggested that the hallucinations and stimulating effects of drugs, such as *Cannabis,* make them qualitatively different from opium and the other "sisters of sleep." Several texts were subsequently published in both Europe and the United States, and these retained either the narcotic or *Genussmittel* classifications. Among these, Hartwich's 1911 opus *Die Menschlichen Genussmittel* (14) is noteworthy in that it added new drugs to the list of those capable of producing hallucinations. In 1907, De Veze (6) made the daring attempt to separate psychoactive substances into narcotic plants (opium) and magical plants (*Cannabis* and other hallucinogens), but his classification system was not adopted widely.

The definitions did not change substantially until the publication of Louis Lewin's *Phantastica* (22) in 1924. An influential German toxicologist and early psychopharmacologist, Lewin classified narcotic and stimulating drugs into five subgroups: euphorica, phantastica, inebriantia, hypnotica, and excitantia. His definition of phantastica is a definition of hallucinogens:

> Phantastica; hallucinating substances. This series comprises a number of substances of vegetable origin, varying greatly in their chemical constitution, and to these belongs in its proper sense the name Phantastica, or Drugs of Illusion. The representatives of this group, such as mescal buttons (*Anhalonium lewinii*), Indian hemp (*Cannabis indica*), and the plants which contain tropines, bring about evident cerebral excitation in the form of hallucinations, illusions, and visions. These

> phenomena may be accompanied or followed by unconsciousness or other symptoms of altered cerebral functioning.

While Lewin's term phantastica did not survive in the literature, his separate classification of hallucinating substances did. Various alternative labels have been applied to these drugs, including deliriants, delusionogens, eidetics, hallucinogens, misperceptinogens, mysticomimetics, phanerothymes, phantasticants, psychedelics, psycotics, psychoticants, psychogens, psychosomimetics, psychodysleptics, psychotaraxics, psychotogens, psychotomimetics, and schizogens. Of these terms, three have persisted in the contemporary literature. Several texts (e.g., ref. 7) use the term psychotomimetic, which Hollister (16) defines with five criteria:

> (a) In proportion to other effects, changes in thought, perception and mood should predominate; (b) intellectual or memory impairment should be minimal with doses producing the above mental effects; with large doses these may occur; (c) stupor, narcosis or excessive stimulation should not be an integral part of the action; (d) autonomic nervous system side-effects should be neither disabling nor severely disconcerting; (e) addictive craving should be minimal.

Objections to the use of psychotomimetics have been raised on the grounds that the term is pejorative, limiting, and misleading. For example, Grinspoon and Bakalar (12) note that the symptoms of the drug reaction at times resemble the symptoms of functional psychoses, but most investigators agree they are not the same. Alternatively, these authors adopt the popular term psychedelic, a term coined by psychiatrist Humphrey Osmond in a correspondence with novelist Aldous Huxley in 1956, meaning "mind manifesting" or "mind revealing." The term psychedelic has acquired numerous value-laden cultural meanings, however, which compromise its utility in academic or scientific discourse.

The third term in current use, hallucinogens, is the one Osmond himself selected after discarding psychedelic for scientific writings (15). The term hallucinogen perhaps overemphasizes the perceptual effects, but its continuing use as the classification of choice in science has served to deemphasize perceptual effects and give balanced attention to changes in thought and mood. It is also the term adopted by anthropologists (e.g., ref. 11), botanists, and chemists (e.g., ref. 26), as well as psychiatric workers studying drug-induced hallucinations (e.g., ref. 9). As these scientists are fond of noting, from their botanical origins, it was precisely the overemphasized perceptual effects that led to the discovery, identification, and use of hallucinogenic plants.

BOTANICAL ORIGINS

Hallucinogenic species occur among the highest evolved flowering plants (angiosperms) and in one division (fungi) of the simpler plants. As a general rule, these plants are rich in bitter-tasting alkaloids that act as extremely effective feeding deterents. Alkaloids also have a wide range of physiologic activity, including psychologic, teratogenic, and toxic effects. Indeed, it has been argued

that many of the naturally occurring hallucinogenic plants are evolutionarily justified in terms of the maladaptive effects that they could have on herbivores (29). The initial effects of such plant browsing—bitterness, nausea, emesis, and dizziness—give animals clear warnings to avoid continued feeding. Interestingly, most of the angiosperm hallucinogens evolved at roughly the same time the giant dinosaurs began to disappear. Swain (36) has noted that these reptiles, unlike the birds and mammals that followed, failed to evolve effective mechanisms with which to detect and/or detoxify these alkaloids. Subsequently, changes occurred in the thickness of dinosaur egg shells; there was an increase in the size of their hypothalamus; and their fossils have been found in contorted positions suggestive of alkaloid poisoning. It may be speculated that alkaloid poisoning contributed to the ultimate demise of at least some dinosaurs.

Today, perhaps 65 million years later, veterinarians are well acquainted with the contorted bodies of grazing horses, cattle, and other animals that have accidentally ingested lethal amounts of highly toxic hallucinogenic plants, such as *Datura* (33). Similar accidents have occurred in man. For example, a group of soldiers, sent to Jamestown in 1676 to quell Bacon's Rebellion, ate the young shoots of *Datura* as a pot green and became severely intoxicated for several days. *Datura* (containing scopolamine, atropine, and hyoscyamine) has since been known as "Jamestown" or jimson weed. Anthony's legion had a similar *Datura* accident during a retreat in 38–37 B.C.

Periodic ingestions of the fungus *Claviceps purpurea,* which attacks rye and other small grains or forage plants, caused the convulsive or gangrenous death of many grazing animals. This fungal disease is known as ergot, meaning "spur," and refers to the sclerotium or fruiting body of the fungus which parasitically replaces the grain kernel. The pharmacologically active constituents of ergot include ergoline alkaloids, mainly derivatives of lysergic acid. When the fungus-infected rye kernels were milled into flour, periodic outbreaks of ergotism occurred, resulting from eating the poisoned bread. Epidemics occurred in France as far back as 857 A.D. and as recently as 1951. In 944 A.D., 40,000 people died of the disorder. In many such cases, the death of dogs and other animals fed on the rye fungus was equally unavoidable and dramatic.

There are two types of ergotism: gangrenous and convulsive. Gangrenous ergotism was known by a number of names, including *ignis sacer,* the holy fire, or St. Anthony's fire, in reference to the feverish hallucinations of fires and devils. This condition is usually characterized by dry gangrene of the extremities, followed by the falling away of the affected portions of the body. Convulsive ergotism is characterized by symptoms including crawling sensations in the skin, tingling in the fingers, vertigo, tinnitus aurium, headaches, disturbances in sensation, hallucinations, painful muscular contractions leading to epileptiform convulsions, vomiting, and diarrhea. Muscle fibers are involuntarily contracted, and mental disturbances, including mania, melancholia, psychosis, and delirium, occur.

Symptoms of convulsive ergotism were conspicuous in the Salem witchcraft records of the 17th century. The sudden onset of the condition was considered

symptomatic of demonic possession rather than disease. In her 1976 study of the Salem witch trials, Caporael (3) notes that "the content of hallucinations and other perceptual disturbances would have been greatly influenced by the state of mind, mood, and expectations of the individual." Accordingly, victims who experienced visions of undulating objects and lights tended to interpret them as specters of accused witches or agents of the devil in animal form. Spanos and Gottlieb (35), however, have argued that hallucinations, such as are to be expected from ergot, were conspicuously absent from these reports.

In his account of the 1951 ergotism epidemic in France, Fuller (10) describes the presence of classic drug-induced hallucinations among the victims:

> A common vision among the sick was that of fireballs coming toward them, then receding and coming back again. *Zoopsie,* hallucinatory visions of animals, was rampant among the victims . . . patients talked of the astonishing, brilliant, vivid, intense, and unbelievable colors—orange, red, brilliant white, moving in spirals, glowing from objects—that encompassed all their surrounding. Others described the conviction that they had been in a vast room, where the ceiling descended and the walls closed in on them, ready to crush them to death. Or there were those who described the feeling that their arms were pulling into their bodies, their knees telescoping up into their shoulders and chests. Auditory hallucinations—the noise of a clock, music, voices—were rare but noted by some. Three of the victims were absolutely sure they were witnessing their own funerals and actually invited the fatigued volunteers to take part in the obsequies. Nearly always the same hallucinations returned to each individual, varying little from the one that struck the victim at the beginning. Some patients were in helpless confusion, knowing neither time nor space. Some were not even able to perceive heat when they were so tested. Often the tetanuslike convulsions would seize the patients and throw them into uncontrolled paroxysms, usually at the times the hallucinations began again.

Ingestion of hallucinogenic plant alkaloids and allied compounds does not always result in death. Many grazing animals display paresis, ataxia, dullness, and a tendency to isolate themselves from the herd. Some animals appear to act bizarre. Observations of such animal-plant interactions could have provided man with much information about hallucinogens.

Even when ingestion of plant hallucinogens did not result in death or even intoxication of the animals, it did contribute to the dispersal of these plants throughout the world. For example, horses and cattle constantly swallow spores of hallucinogenic fungi (e.g., *Psilocybe* spp.) in the grass they eat and pass them in a germinating condition. Other plants ingested and dispersed by animals throughout the world include: *Cannabis* (insects, birds, rodents), *Datura* (goats, cattle, horses, ants), *Atropa belladonna* (birds, pigs), *Claviceps purpurea* (flies), and *Amanita muscaria* (deer, rodents, insects).

DISCOVERY OF HALLUCINOGENS BY OBSERVATIONS ON ANIMALS

Not all man's encounters with naturally occurring hallucinogens were accidental. Ritual, magic, religious, or medicinal uses of these drugs date back into

the early history of both Old and New World peoples. Anthropologists have traced the use of hallucinogens as far back as paleolithic Europe and neolithic Asia Minor. Archaeologically, hallucinogen use has been dated to 8500 B.C. in the New World. Throughout recorded history, there are abundant instances of such plant use being surprisingly discriminative and efficacious. Early man learned much of this basic psychopharmacology from observations on animal-plant interactions.

Folklore and mythology are replete with examples of man's discovery of these hallucinogenic plants through observations on animals (27). For example, *Tabernanthe iboga,* a tropical West African shrub containing the hallucinogen ibogaine, was reportedly discovered by boars, porcupines, and gorillas. According to one anthropologist: "Several accounts mention that the natives saw boars dig up and eat the roots of the plant, only to go into a wild frenzy, jumping around and perhaps fleeing from frightening visions" (29). In Eastern Europe, a folktale tells that the avidity with which grasshoppers and leafhoppers jump about the *Cannabis* plant suggested its properties as a strong and stimulating plant. The story is probably related to the Polish custom of dancing or jumping to promote the growth of the plant. The hemp dance, as it is called, is modeled after movements of these creatures and is marked by high jumps with much excitement and enjoyment. Even the ancient Greeks and Scythians were reported to have adopted the habit of eating seeds from the *Cannabis* plant after watching finches pick at them with a remarkable passion. The Greek physician Galen (130–200 A.D.) wrote that it was customary to give hemp seeds to the guests at banquets as a promoter of hilarity, enjoyment, and passion.

The names given by early man to hallucinogenic plants also reveal much about their observed effects on animals. The etymology of such terms provides us with an instructive lesson in the natural history of animal use of these drugs. Many plants were named for their apparent aversive properties. Henbane (*Hyoscyamus niger,* containing atropine and scopolamine) seems to have derived its name from the baneful effects its seeds have upon poultry. When eaten by man, henbane produced sleepy and drowsy behavior and thus acquired the alternative name "insana." Fly-agaric (*Amanita muscaria*) killed the flies that landed on it. Wormwood (*Absinthium* spp., containing thujone, which is similar to tetrahydrocannabinol found in *Cannabis*) drove away insects and insect larvae. Flea bane (marigolds, including the hallucinogenic *Tagetes lucida*) repulsed fleas and other insects. Other plants were identified by the attraction that animals displayed toward them. Catnip (*Nepeta cataria,* containing the hallucinogen nepetalactone) attracted cats that eagerly ingested it. Pigeon candy was an early vernacular name for *Cannabis* seeds because of its stimulating effects on pigeons.

EARLY EXPERIMENTATION BY MAN

Despite the benefit of animal observation, early man developed experience with hallucinogenic plants far beyond that obtained by animals. Cultural uses of hallucinogens established efficient methods for harnessing the specific psy-

choactive properties of these plants. Experimentation with *Amanita* resulted in patterns of recycling active ingredients that passed into the urine. Controlled usage of the deadly ergot alkaloids from *Claviceps* and other plant sources contributed greatly to religious ecstasy among both ancient Greeks and Aztecs. *Cannabis* was found to be effective via inhalation of the burning plant. Resin from the bark of *Virola* trees and beans from *Anadenanthera peregrina* trees were found by South American Indians to be effective hallucinogens when administered intranasally as snuffs. Peyote (*Lophophora williamsii*) was employed by Indians in Mexico who discovered it to be an effective medicine and ceremonial hallucinogen when orally ingested or administered as an enema. Several members of the Nightshade family of plants (mainly *Hyoscyamus niger, Atropa belladonna,* and *Mandragora officinarum*) were employed by medieval witches who experimented with topical applications and discovered the broom as an effective vaginal applicator for their hallucinatory ointments.

Amanita

Fly-agaric, or *Amanita muscaria,* a mushroom native to Europe, Africa, Asia, and America, is perhaps man's oldest hallucinogen. The initial discovery may have been prompted by animal use. The native peoples of the Asian forest and tundra regions in Siberia, who employ fly-agaric in shamanistic practices, have observed their reindeer browsing the mushrooms. This browsing results in the reindeer becoming unmanageable and suffering "profound mental disturbances" (38). The natives may have copied this behavior only to discover the hallucinatory effects they later employed in their shamanism. The most expressive account of *Amanita* intoxication is given by anthropologist Waldemar Jochelson who traveled among the Koryaks in Siberia (38):

> Like certain other vegetable poisons, as opium and hashish, the alkaloid of fly-agaric produces intoxication, hallucinations, and delirium. Light forms of intoxication are accompanied by a certain degree of animation and some spontaneity of movements. Many shamans, previous to their seances, eat fly-agaric in order to get into ecstatic states. . . . Under strong intoxication, the senses become deranged; surrounding objects appear either very large or very small, hallucinations set in, spontaneous movements, and convulsions. So far as I could observe, attacks of great animation alternate with moments of deep depression. The person intoxicated by fly-agaric sits quietly rocking from side to side, even taking part in the conversation with his family. Suddenly his eyes dilate, he begins to gesticulate convulsively, converses with persons whom he imagines he sees, sings, and dances. Then an interval of rest sets in again.

The Koryaks were also urine drinkers. They rapidly discovered that the active principles of fly-agaric are excreted unchanged in the urine and practiced saving their postmushroom urine for additional intoxications. Ceremonial urine drinking is also mentioned in the Rig-Veda, a 3,500-year-old collection of hymns celebrating Soma, the god-narcotic of ancient India. Called soma, this most ancient of all hallucinogens has now been identified as *Amanita.* It has also