2. Psychiatric Research with Hallucinogens: What have we learned?

Charles S. Grob, M.D.

Psychiatric research with hallucinogens has resumed. After two decades of virtual prohibition, formal authorization from federal regulatory agencies to conduct investigative studies in the United States with these unique mind altering substances has been successfully obtained (Strassman, 1991). The bitter and acrimonious debate that raged through the 1960s and 1970s and into the 1980s has largely subsided. Scientific and health policy makers have determined that these drugs, although possessing an inherent abuse potential, do have a safety profile of acceptable magnitude when compared to drugs currently the subject of formal research investigation as well as others actively dispensed in clinical practice. The U.S. Food and Drug Administration has therefore determined that formal and well controlled investigations designed to assess the risk-benefit ratio of particular hallucinogenic substances may now be pursued. However, for such studies to proceed successfully and for the much heralded (and often vilified) potential of the hallucinogens to be explored, it is imperative that we fully grasp the lessons of the past. For, to paraphrase Santayana, if we fail to understand our history, we will be condemned to repeat the patterns and reactions which will inevitably lead to yet another round of repudiation and rejection of this unique class of psychoactive substances, along with its inherent and inestimable potential for learning and healing.

Shamanistic Roots

Hallucinogens, throughout the breadth of time, have played a vital albeit hidden and mysterious role. They have often, in aboriginal and shamanic contexts, been at the absolute center of culture and world view (Dobkin de Rios, 1984). Opening up the doors to the spiritual planes, and accessing vital information imperative to tribal cohesion and survival, hallucinogenic plants became what some scholars have considered to be the bedrock of human civilization (Wasson, 1968; Wasson et al, 1978; Huxley, 1978). Within the context of shamanic society, these awe inspiring botanicals were utilized to facilitate healing, divine the future, protect the community from danger and enhance learning (e.g. teaching hunters the ways of animals) (Cordova-Rios, 1971). However, with the advent of stratified and hierarchical societies, such plant potentiators came to be viewed as dangerous to the commonweal and controls were placed on direct and revelatory access to the sacred (Dobkin de Rios and Smith, 1976). In some societies (e.g. Aztec civilization) use of psychotropic plants was restricted to the select castes of the religious priesthood. In others, including the progenitors of our own contemporary Euro-American culture, absolute proscriptions on the use of plant drugs for divine purposes were decreed.

Repression of Shamanistic Traditions

To fully understand the enormous resistances to these drugs and the unique experiences they induce, it would be revealing to examine some elements of our historical legacy. A poorly appreciated period from Fourteenth through Seventeenth Century European History has been the persecution of indigenous healers, predominantly woman, during the reign of the Inquisition, particularly in Northern and Western Europe. During a span of three hundred years several million women were accused of practicing witchcraft and condemned to die. The Medieval scholar Jules Michelet has explored the complicity between ecclesiastical and medical authorities in the subjugation of non-sanctioned healing, commenting on the attitude of the Church "that if a woman dare cure without having studied, she is a witch and must die" (Michelet, 1965). To have "studied" in this context is to have faithfully adhered to the precepts and moral authority of the Church, and to have forsworn receiving knowledge from Nature.

A rich heritage of plant lore and applied healing had been passed down from pagan and pre-Christian Europe, rivaling and often surpassing the demonstrated efficacy of Church sanctioned medical practitioners. Hallucinogenic plants with magical as well as healing properties were essential elements of this indigenous pharmacopoeia. Members of the *Solanaceae* family with their alkaloids atropine and scopolamine, including a great number of species of the genus Datura, as well as mandrake, henbane, and belladonna, had wide application as agents of healing and transcendence (Harner, 1973). In taking action against the indigenous use of psychotropic plants, the Church sought to eliminate a perceived threat to its oligarchic powers and reassert its monopoly on legitimate access to the supernatural (O'Neil, 1987). By casting the healer as a witch and the hallucinogenic plants as tools of Satan, the Church succeeded not only in eliminating competition to the elite physician class but also in

virtually eradicating knowledge of these vestiges of pagan and shamanic consciousness.

A second historical period whose examination may be pertinent to understanding our ingrained cultural resistances and aversion to hallucinogens is the European conquest of the New World. Shortly after arrival in Central and South America in the late Fifteenth and early Sixteenth Centuries, the invading Spanish Conquistadors observed an impressive array of psychoactive pharmacopoeia, including morning glory seeds (containing the potent hallucinogen, lysergic acid amide), peyote, and psilocybin mushrooms.

These extraordinary plants were utilized by the native inhabitants to induce an ecstatic intoxication and were an integral component of their aboriginal religion and ritual. As plant hallucinogens were attributed to have supernatural powers, they were quickly perceived by the European invaders as weapons of the Devil designed to prevent the triumph of Christianity over traditional Indian religion (Furst, 1976). An early Seventeenth Century Spanish observer of native customs, Hernando Ruiz de Alarcon, wrote of the idolatries he observed involving the consumption of the morning glory: "Olouihqui is a kind of seed-like lentils produced by a type of vine in this land, which when drunk deprive of the senses, because it is very powerful, and by this means they communicate with the devil, because he talks to them when they are deprived of judgment with the said drink, and deceive them with different hallucinations, and they attribute it to a god they say is inside the seed" (Guerra, 1971).

Identifying the threat not only to consolidating their power and control over the conquered peoples, but also the danger of lower caste immigrant Spaniards developing interest in native rituals and healing practices, The Holy Inquisition of Mexico issued in 1616 a proclamation ordering the persecution and excommunication of those who, under the influence of "herbs and roots with which they lose and confound their senses, and the illusions and fantastic representations they have, judge and proclaim afterwards as revelation, or true notice of things to come. . ." (Guerra, 1967). To continue to engage in native practices and utilize their traditional plant hallucinogens as agents of knowledge and healing would risk indictment of heresy and witchcraft, and inevitably the implementation of the cruelest punishments of the Inquisition, from public flogging to being burned alive at the stake. Unable to accept the indigenous utilization of such psychoactive substances as anything other than idolatry and a threat to their goals of domination and exploitation, the European conquerors denied them legitimacy, endeavoring to expunge their traditions and knowledge. Only by going deeply underground and maintaining their world view and shamanic practices in secret from the dominant Euro-American culture, has this knowledge survived.

Early Research with Hallucinogens

Interest in plant hallucinogens lay dormant until the second half of the Nineteenth Century when growing activities in the new fields of experimental physiology and pharmacology sparked efforts at laboratory analyses of medicinal plants. In the late 1880's German toxicologist Louis Lewin, often called the "father of modern psychopharmacology," received a collection of peyote samples from the Parke-Davis Pharmaceutical Company. Succeeding at isolating several alkaloids from the peyote, Lewin was unable to identify any of them as the psychoactive component through animal testing. The investigation was then taken up by Arthur Heffter, who characterized additional pure alkaloids from the cactus. By ingesting each of them he was able to identify the crucial one, which he named mescaline (Heffter, 1897).

Along with Lewin's published work, interest in plant hallucinogens was encouraged by increasing dissemination of knowledge of the Native American Indian use of peyote, a phenomena of increasing prevalence as the century drew to a close. Obtaining a sample of peyote from the South-Western plains, physician and founder of the American Neurological Association Weir Mitchell, conducted an experiment using himself as the subject. Although overwhelmed with the aesthetic power of the experience, describing that the peyote revealed "a certain sense of the things about me as having a more positive existence than usual," Mitchell expressed alarm that such a profound experience might not be successfully integrated within his contemporary context: "I predict a perilous reign of the mescal habit . . . The temptation to call again the enchanting magic of my experience will, I am sure, be too much for some men to resist after they have once set foot in this land of fairy colors where there seems so much to charm and so little to excite horror or disgust" (Mitchell, 1896).

Inspired by reports of Mitchell's self-experimentation, the prominent English physician Havelock Ellis decided to pursue a similar encounter with the plant hallucinogen, which he later reported as an experience of unparalleled magnitude, asserting that to "once or twice be admitted to the rites of mescal is not only an unforgettable delight but an educational influence of no mean value" (Ellis, 1897). Such unqualified praise of a drug with as yet no proven medical application, however, provoked harsh censure from the editors of the British Medical Journal who

expressed grave concern of peyote's injurious potential and reprimanded Ellis for irresponsibly "putting the temptation before the section of the public which is always in search of new sensation" (British Medical Journal, 1898). Such a vituperative response to Ellis' naive efforts at publicizing and perhaps promoting auto-experimentation with magical plants is an early harbinger of the conflict that mired and paralyzed the field of hallucinogenic research some seventy years later.

Interest in the unusual psychogenic effects of peyote and, following its synthesis in 1919, mescaline, continued through the 1920's. Activities included further exploration of the unique visions induced by the drug by a variety of literary figures and scholars introduced to its exotic phenomena, although when William James experienced a severe gastro-intestinal reaction upon attempting to swallow a segment of peyote he is alleged to have stated: "Henceforth, I'll take the visions on trust" (Stevens, 1987). A comprehensive survey of the effects of mescaline was published by Karl Beringer, a close associate of Hermann Hesse and Carl Jung, in his massive tome "Der Meskalinrausch" (The Mescaline Inebriation) in 1927, followed a year later by Heinrich Kluver's Mescal: The "Divine" Plant and Its Psychological Effects, the first attempt at formal classification and analysis of mescaline visions (Kluver, 1928). And heralding the next phase of hallucinogen research, mescaline was touted by psychiatric researchers as a putative biochemical model for major mental disturbances, particularly schizophrenia (Guttman and Maclay, 1936; Stockings, 1940).

Dr. Hofmann's Serendipitous Discovery

The modern era of hallucinogen research began in the laboratory of Dr. Albert Hofmann, a senior research chemist for the Sandoz Pharmaceutical Company in Basel, Switzerland. In mid April, 1943, Hofmann was engaged in work to chemically modify alkaloids from the rye ergot fungus, *Claviceps purpurea*, in an effort to develop a new analeptic agent (a respiratory stimulant). Acting on a premonition that earlier tests had missed something, he returned to and prepared a fresh batch of a compound he had previously synthesized in 1938, but which had proved at that time to have what were considered to be uninteresting results in animal testing. The chemical compound he had decided to return to after this five year hiatus was the twenty-fifth in a series of lysergic acid amides, and had previously received the designation of LSD-25.

While working with a modest quantity of this compound for further study, Hofmann complained of restlessness and feeling dizzy and decided to return to his home to rest. He subsequently would write that upon reaching home and lying down with his eyes closed he experienced an "extreme activity of the imagination . . . there surged upon me an uninterrupted stream of fantastic images of extraordinary plasticity and vividness and accompanied by an intense kaleidoscope like play of colors. After about two hours, the not unpleasant inebriation, which had been experienced while I was fully conscious, disappeared" (Hofmann, 1983).

Concluding that he had probably accidentally absorbed a small quantity of the compound through his skin, Hofmann set out three days later, on April 19, 1943, to replicate the phenomena by self administering what he considered to be an extremely small and cautious dose, 250 micrograms. Intending to record his subjective experiences of what he had assumed to be a very low dose of the peculiar substance, less than an hour later Hofmann began to feel the onset of what was to be a powerful and indeed frightening altered state of consciousness, and again felt compelled to return to his home. Hofmann would later report "On the way home, my condition began to assume threatening forms. . . Everything in my field of vision wavered and was distorted as if seen in a curved mirror. I also had the sensation of being unable to move from the spot. Nevertheless, my assistant later told me that we had traveled very rapidly. . . My surroundings had now transformed themselves in more terrifying ways. Everything in the room spun around, and the familiar objects and pieces of furniture assumed grotesque, threatening forms. They were in continuous motion, animated, as if driven by an inner restlessness… Even worse than these demonic transformations of the outer world, were the alterations that I perceived in myself, in my inner being. Every exertion of my will, every attempt to put an end to the disintegrations of the outer world and the dissolution of my ego, seemed to be wasted effort. A demon had invaded me, had taken possession of my body, mind and soul." Shortly thereafter, Hofmann would describe, "the climax of my despondent condition had passed. . . the horror softened and gave way to a feeling of good fortune and gratitude. . . now, little by little I could begin to enjoy the unprecedented colors and plays of shapes that persisted behind my closed eyes. Kaleidoscopic, fantastic images surged in on me, alternating, variegated, opening and then closing themselves in circles and spirals, exploding in colored fountains. . . Exhausted, I then slept, to awake next morning refreshed, with a clear head, though still somewhat tired physically. A sensation of well-being and renewed life flowed through me " (Hofmann, 1983). Dr. Hofmann's shocking experience of madness and transcendence, precipitated by an

infinitesimally low dose of what would soon be recognized as the most potent psychoactive substance known to man, heralded the advent of a new era of psychiatric research committed to uncovering the mysteries of the mind and revealing the basis of mental illness.

The Psychotomimetic Model

Albert Hofmann's discovery of LSD soon led to a period of intense interest and activity designed to explore its utility as a model of understanding and treating psychotic illness. Such a direction was consistent with earlier investigations equating the mescaline catalyzed altered state of consciousness with the subjective experience of schizophrenic patients (Guttman and Maclay, 1936; Stockings, 1940). Tayleur Stockings had described the similarities between the two states: "Mescaline intoxication is indeed a true 'schizophrenia' if we use the word in its literal sense of 'split mind,' for the characteristic effect of mescaline is a molecular fragmentation of the entire personality, exactly similar to that found in schizophrenic patients… Thus the subject of the mescaline psychosis may believe that he has become transformed into some great personage, such as a god or a legendary character, or a being from another world. This is a well-known symptom found in states such as paraphrenia and paranoia" (Stockings, 1940). Noting the enormity of perceptual disturbances induced by LSD, coupled with the sensation in some subjects of losing their mind, as had transiently been the case with Dr. Hofmann, Sandoz in 1947 began actively marketing LSD to psychiatric researchers and practitioners as a tool for understanding psychoses. Not only was LSD experimentation in normal subjects proposed as a viable model for studying the pathogenesis of psychotic illness, but psychiatrists were encouraged to self-administer the drug so as to gain insight into the subjective world of the patient with serious mental illness (Stevens, 1987). For a young field struggling to gain credibility as a medical science, this model of chemically controlled psychosis emerged as a propitious sign for the future.

Preoccupation with the hallucinogen induced psychotomimetic model continued through the 1950's. The psychotomimetic position was summarized by one its leading proponents, Harvard psychiatrist Max Rinkel: "The psychotic phenomena produced were predominantly schizophrenia-like symptoms, manifested in disturbances of thought and speech, changes in affect and mood, changes in perception, production of hallucinations and delusions, depersonalizations and changes in behavior. Rorschach tests and concrete-abstract thinking tests showed responses quite similar to those obtained with schizophrenics" (Rinkel and Denber, 1958)., it became increasingly apparent, however, that although an impressive array of psychiatric researchers and theoreticians had elucidated and elaborated upon the startling degree of resemblance between schizophrenia and the hallucinogenic experience, a growing consensus was emerging that the dissimilarities between the two states essentially obviated the value of the chemical psychosis model (Grinspoon and Bakalar, 1979). Speaking at the First International Congress of Neuropsychopharmacology in 1959, the legendary Manfred Bleuler enunciated the central argument in opposition to the psychotomimetic model. He stated that it was the gradual and inexorable progression of a symptom complex that included disturbed thought processes, depersonalization and auditory hallucinations, evolving into a generalized functional incapacitation that was characteristic of schizophrenia. He concluded with the demonstrative declaration that although the psychotomimetic drugs may have strengthened our conceptual understanding of organic psychoses, they have "contributed nothing to the understanding of the pathogenesis of schizophrenia" (Bleuler, 1959).

Hallucinogen Research and the Role of the CIA

Following the end of World War II, as relations with our former ally the Soviet Union began to deteriorate and Cold War tensions heightened, a program was initiated by the U.S. Central Intelligence Agency to develop a speech inducing drug for use in interrogations of suspected enemy agents. Such a search was in part stimulated by knowledge of prior, albeit unsuccessful, efforts by Nazi medical researchers at the Dachau Concentration Camp to utilize mescaline as an agent of mind control (Marks, 1979). By the early 1950's the CIA had acquired from Sandoz Pharmaceutical a large quantity of the highly touted psychotomimetic, LSD, and had begun their own extensive testing program. Early experiments often involved the furtive "dosing" of unwitting subjects, including employees of the CIA and other intelligence organizations, soldiers and customers solicited by prostitutes in the service of the CIA. Given the ill-prepared mental set of the victim, the often adverse setting in which the "experiment" occurred, and the lack of therapeutic aftercare, it is no surprise that highly deleterious outcomes, including suicide, did occur. Although knowledge of this irresponsible and ethically suspect association between the CIA and hallucinogenic substances remained suppressed for the next twenty years, knowledge of such activities was ultimately obtained through the Freedom of Information Act

(Marks, 1979; Lee and Schlain, 1985).

Through the 1950's, as Cold War fears escalated, the CIA began to developed an affinity for the psychotomimetic model then in vogue. In order to further their own goals of investigating the mind control potentials of hallucinogenic drugs, the CIA began to recruit and fund a number of distinguished psychiatric researchers. Included among these was Ewen Cameron, elected President of the American Psychiatric Association in 1953 and first President of the World Psychiatric Association. Capitalizing on the CIA's preoccupation with LSD's purported ability to break down familiar behavior patterns, Cameron received funding to develop a bizarre and unorthodox method for treating severe mental illness. The treatment protocol began with "sleep therapy", where patients were sedated with barbiturates for a several month period, and was followed by a "depatterning" phase of massive electroshock and frequent doses of LSD designed to obliterate past behavior patterns. Patients were then once again heavily sedated, and subsequently subjected to a prolonged "psychic driving" reconditioning phase where they received constant auditory bombardment from speakers under their pillows repeating tape recorded messages, with some patients hearing the same message repeated a quarter of a million times. Given the gross excesses in all modalities of this "treatment", inevitably severe neuro-psychiatric deterioration was incurred by many of Cameron's unconsented subjects (Marks, 1979; Lee and Schlain, 1985). Ultimately, the efforts of the CIA and their contract psychiatrists came to naught as their ill-advised collaboration with hallucinogens yielded little of value to support either the CIA's mind control theories or the psychotomimetic investigations of psychiatric researchers.

The Psycholytic Treatment Model

Early experimentation in Switzerland following Albert Hofmann's discovery in the 1940's had discerned a phenomena quite different than that of the much heralded yet bizarre psychotomimetic mental experience. In subjects given a relatively low dose of LSD, there appeared to occur a release of repressed psychic material, particularly in anxiety states and obsessional neuroses. By allowing this otherwise repressed and threatening material to flow effortlessly into consciousness, investigators surmised that low dose LSD treatment could facilitate the psychotherapy process (Stoll, 1947). Application of the low dose model in Europe as well as the United States ascertained that psycholytic treatment had particular value with patients with rigid defense mechanisms and excessively strict superego structures. By facilitating ego regression, uncovering early childhood memories, and inducing an affective release, psychiatrists claimed to have achieved a breakthrough in reducing the duration and improving the outcome of psychotherapeutic treatment (Chandler and Hartmann, 1960). Problems arose with the psycholytic paradigm, however, as critics noted that the content of regressed material released from the unconscious was extremely sensitive to the psychiatrist's own analytic orientation, in most cases Freudian or Jungian. Questions arose over whether the phenomena observed in the psychotherapeutic sessions, including the often positive treatment outcome, were not simply attributable to the presence of heightened powers of suggestibility. Moreover, with psycholytic treatments, care had to be taken to utilize sufficiently low dosages of the hallucinogen that the patient's ego would not be overwhelmed to the point where verbal analysis would be inhibited. When in the course of psycholytic psychotherapy higher dosages were utilized, the resultant experience could no longer be contained within the intended theoretical framework, thus necessitating delineation of an entirely new paradigm.

The Psychedelic Treatment Model

Psychiatrists utilizing the higher dose model on their patients, as well as self-experimenting on themselves, quickly realized that they had accessed an entirely new and novel dimension of consciousness. As Dr. Hofmann had experienced during his own exploration, this unexpected level of awareness could alternately be rapturous or terrifying. The first psychiatrist to explore this paradigm was the Canadian researcher Humphrey Osmond. Utilizing first mescaline, and later LSD, Osmond devoted his studies to the treatment of alcoholism, a notoriously difficult and refractory condition. Noting that some alcoholics were only able to cease their pathological drinking behaviors after they had experienced a terrifying, hallucinatory episode of delirium tremens during alcohol withdrawal, Osmond set out to replicate this state through utilization of a high dose hallucinogen model. Observing that what distinguished his treatment successes from his treatment failures was whether a transcendent and mystical state of consciousness was attained, Osmond recognized the strong resemblance to states of religious conversion, bringing to mind William James' old axiom that "the best cure for dipsomania is religiomania." Dissatisfied with the prevailing jargon, and arguing that his model demonstrated that hallucinogens did much more than "mimic psychosis", Osmond introduced at the 1957 meeting of the New York Academy of Sciences the term psychedelic, explaining that the "mind manifesting" state did not necessarily produce a predictable and

pathological sequence of events, but rather could catalyze an enriching and life changing vision. And in presaging the cacophonous debate that would shortly fall upon the infant field of hallucinogen research, Osmond concluded that the psychedelic model not only allowed us to escape "Freud's gloomier moods that persuaded him that a happy man is a self-deceiver", but would soon come to the aid of humanity's imperiled existence and "have a part to play in our survival as a species" (Osmond, 1957).

The Prohibition of Hallucinogen Research

With the evolution to the psychedelic model, hallucinogens moved beyond the bounds of control of the medical elite (Neill, 1987). No longer could they be confined to investigations of a model psychosis, nor could they be contained within the framework of conventional psychiatric therapies with implicit prescribed roles for doctor and patient. By blurring the boundaries between religion and science, between sickness and health, and between healer and sufferer, the psychedelic model entered the realm of applied mysticism. As word of the astounding phenomenon induced by the psychedelic model spread into the culture at large, the inevitable backlash occurred. Horrified that this extraordinary investigative probe had been appropriated from their control, the leaders of the psychiatric profession directed harsh criticism at their irrepressible and increasingly evangelistic colleagues. Roy Grinker, the first editor of the prestigious Archives of General Psychiatry, in a 1963 editorial castigated those psychiatric researchers who had become preoccupied with administering "the drug to themselves, and some, who became enamored with the mystical hallucinatory state, eventually in their 'mystique' became unqualified as competent investigators" (Grinker, 1963). And a year later, in the Journal of the American Medical Association, Grinker charged researchers with "using uncontrolled, unscientific methods. In fact, these professionals are widely known to participate in drug ingestion, rendering their conclusions biased by their own ecstasy…The psychotomimetics are being 'bootlegged', and as drugs now under scientific investigation they are being misused" (Grinker, 1964). In moving beyond the boundaries of conventional scientific inquiry, the hallucinogens had "become invested with an aura of magic" (Cole and Katz, 1964), and thus could no longer be provided the status and protection of their elite profession. The covenant had been broken. The hallucinogens, along with the proponents of their continued exploration, were cast out, becoming pariahs in a land and a time that increasingly viewed them as threats to public safety and social order.

By the mid-1960's, the secret was out. Growing interest in hallucinogens had catalyzed, and was catalyzed by, profound cultural shifts. Along with the social upheaval surrounding opposition to an increasingly unpopular war in South-East Asia, hallucinogens assumed a central role in a movement that began to question many of the basic values and precepts of mainstream Euro-American culture. The populace, fueled by sensational media accounts, grew to identify hallucinogens as a prime suspect in inciting the accelerating state of cultural havoc. Along with the drugs themselves, adherents of the experimental and treatment models became increasingly identified as part of the problem. Such circumstances were in no way improved by the rash pronouncements from the radical wing of what had rapidly become identified as an hallucinogen-inspired political movement. The leaders of one notorious research group in particular drew public ire and aroused anxiety and panic by such proclamations as: "Make no mistake: the effect of consciousness-expanding drugs will be to transform our concepts of human nature, of human potentialities, of existence. The game is about to be changed, ladies and gentleman. . . These possibilities naturally threaten every branch of the Establishment. The dangers of external change appear to frighten us less than the peril of internal change. LSD is more frightening than the Bomb!" (Leary and Alpert, 1962).

In response to escalating fears that hallucinogens had become an out of control menace to public safety and cultural stability, the government moved to restrict access to these potent agents of change. Psychiatric leaders, gravely concerned by the threat to public mental health, and perhaps to their professional image as well, vehemently urged government regulating agencies to tighten their controls. Roy Grinker, illustrious psychiatrist and President of the American Medical Association, issued an urgent warning to his colleagues that greater damage lay ahead unless usage of these hazardous chemical agents was contained. Going beyond merely calling for the psychiatry profession to take action against this growing peril, which would include denouncing the renegades within its own ranks, Grinker castigated the government for having been woefully lacking in vigilance and having neglected its duty: "The Food and Drug Administration has failed in its policing functions. The drugs are indeed dangerous even when used under the best of precautions and conditions" (Grinker, 1964).

Driven into action by increasingly lurid media and law enforcement accounts of widespread hallucinogen use among the young, amidst dire warnings that this insidious threat would erode the values and work ethic of future generations, government regulators had no

choice but to act. In 1965 the Congress passed the Drug Abuse Control Amendment, which placed tight restrictions on hallucinogen research, forcing all research applications to be routed through the FDA for approval. In April, 1966, succumbing to mounting adverse publicity, Sandoz Pharmaceuticals ceased the marketing of what their esteemed research chemist Albert Hofmann would come to call "my problem child" (Hoffman, 1983). Also during the spring of 1966, Senator Robert Kennedy called for Congressional Hearings on the problem. Kennedy, whose wife Ethel had reportedly received psychiatric treatments with LSD, expressed concern that potentially vital research was being obstructed, questioning: "Why if they were worthwhile six months ago, why aren't they worthwhile now?… I think we have given too much emphasis and so much attention to the fact that it can be dangerous and that it can hurt an individual who uses it. . . that perhaps to some extent we have lost sight of the fact that it can be very, very helpful in our society if used properly" (Lee and Schlain, 1985). Kennedy's pleas went unheeded, as over the next few years more and more stringent restrictions were imposed on hallucinogen research, culminating in the Bureau of Narcotics and Dangerous Drugs (the predecessor to the Drug Enforcement Agency) decision to place the hallucinogens in the Schedule I class, reserved for dangerous drugs of abuse with no medical value. Research ground to a virtual halt. Government, civic and medical leaders had all responded to their call to duty, permanently expunging, they hoped, what President Lyndon Johnson had declared in his State of the Union address in January, 1968, "these powders and pills which threaten our nation's health, vitality and self-respect" (Stevens, 1987).

Discounting Hallucinogen Research

Hallucinogens, in the guise of an experimental probe into the mysterious world of mental illness, had burst on the scene during the infancy of psychiatric research. They had not only unleashed a firestorm of controversy as a highly touted therapeutic intervention, but had greatly contributed to the development of the exciting new specialty of laboratory neurochemistry research. Access to these unique agents for animal research has been permitted to continue unimpeded, and they have contributed greatly to our understanding of neurotransmitter systems, brain imaging techniques and behavioral pharmacology (Jacobs, 1984; Freedman, 1986). And yet, human research with hallucinogens had, until now, vanished from the scene. Discounted for ever having held value or potential, it is as if they had never been with us. A source of embarrassment and shame, hallucinogen research became a non-issue, virtually disappearing from the professional literature and educational curriculums. By the early 1970's, psychiatric researchers and academicians had perceived that to continue to advocate for human research with hallucinogens, or even to be identified with past interest in their therapeutic potential, might seriously jeopardize their future careers. Difficult decisions had to be made. From the mid 1960's onward, a split began to appear in the ranks of psychiatric hallucinogen researchers. For those who would maintain their enthusiasm for the potentials of these singular substances, a path of professional marginalization would follow. For those who would take a stand against their perfidious threat, accolades and professional advancement would be forthcoming. For most, however, it was to be a process of quietly disengaging, often from what had been a passionate interest, and re-directing their careers towards tamer and less disputable areas. With very few exceptions (Grinspoon and Bakalar, 1979; Grinspoon and Bakalar, 1986; Strassman, 1984), a veil of silence had descended over the putative role of hallucinogen research in psychiatry.

The Future of Hallucinogen Research in Psychiatry

Where are we to go with this most unusual class of psychoactive substances? Some would say it is best to let sleeping dogs lie, that the hallucinogens only brought discord and controversy to the ranks of psychiatry and their re-examination can only lead to further turmoil and acrimony. Psychiatry has moved far beyond the time where hallucinogens were viewed as being on the cutting edge of research investigation. Many psychiatrists graduating from training programs in the last decade are not even aware of the role hallucinogens once did play in the arena of legitimate research. The conventional point of view is that these drugs are potential substances of abuse, nothing more. Within mainstream, academic psychiatry forums for discussion of the relative merits of resuming inquiries into this area have been restricted. What was once a roar of often vituperative debate has receded to barely a whisper.

Perhaps this twenty-five year period of quiescence and retreat into relative obscurity has been necessary to finally give the question of hallucinogens a fair hearing. We have seen in a prior epoch of investigation a playing field painfully polarized between ardent advocates and fervent foes of the hallucinogens' putative role as agents of discovery and healing. The truth has always rested somewhere in between the dichotomous poles of panacea and toxin. The protagonists of the past, whose careers and integrity so often appeared to be interwoven

with the content and outcome of their fierce debate, are exiting the arena. Rumblings of renewed interest are being heard within the halls of academic psychiatry. A new dialogue is slowly starting to emerge. Hopefully, the lessons of the past will be appreciated, and utilized to forge a partnership and collaboration where divergent perspectives will be given a fair and open hearing, and the true potential of the hallucinogens may finally be illuminated.

As the sleeping giant of hallucinogen research emerges from its twenty-five year slumber, it will perceive that the world of psychiatry has vastly changed from when it was put to rest. The once reigning rulers of psychoanalysis have receded to positions of relative obscurity as the field has become progressively dominated by the adherents of biological reductionism. The insights gleaned from the individual case study, once the standard of psychoanalytic investigation, have been devalued and supplanted by the rigorous methodological research design of modern psychiatry. In the future, the putative value of hallucinogens in psychiatry can no longer rest on claims deriving from anecdotal case studies, as inspiring as they may be, but rather must evolve out of the findings of well-structured, controlled, scientific investigation. To achieve relevance and be accepted as a reputable field of study, hallucinogen research must satisfy the standards of contemporary psychiatric research. To maintain an iconoclastic insistence that the very nature of these substances transcends standard research designs would be to prolong their marginalization and deny the opportunity finally to explore their potential utility.

The knowledge base of biological psychiatry and the neurosciences has exploded over the last two decades, facilitated in part by probes and techniques developed with hallucinogen research in animals (Jacobs, 1984; Freedman, 1986). The potential for further advances in our understanding of the mechanisms of brain function has been recognized and enunciated at a technical meeting of the National Institute on Drug Abuse (NIDA) in July, 1992, that concluded that it is now time to move beyond pure animal research into the realm of human investigation. We are now on the threshold of initiating studies utilizing state of the art research techniques, including sophisticated brain imaging scans, neuroendocrine challenge tests, and receptor binding studies in human subjects. The strategy of pursuing such biological investigations will likely not only yield valuable new information in the neurosciences, but facilitate the re-legitimization of human research with hallucinogens and ultimately become a prelude to the re-exploration of their effects on perception, cognition, and emotion.

One of the most controversial arenas of hallucinogen research during the 1950s and 1960s, and persisting as an alluring hope, has been their putative role in alleviating mental suffering. During a mere fifteen year period, over a thousand clinical papers were published in the professional literature discussing the experiences of 40,000 patients treated with hallucinogens (Grinspoon and Bakalar, 1979). While many of these reports were presented in the form of descriptive case studies and are attributed little value by contemporary research standards, they can help point the way for future investigations. A wide variety of psychopathological phenomena were subjected to intervention with hallucinogens, often leading to encouraging reports of positive clinical outcomes. Unfortunately, examining these stimulating accounts in retrospect reveals notable flaws in their design, including primitive and by today's standards deficient measures designed to evaluate therapeutic change, lack of outcome follow-up and unwillingness to utilize appropriate control subjects. As the debate over hallucinogens intensified, it also became apparent that from both warring camps investigators' biases (whether conscious or unconscious) were confounding their results. From our current vantage point, it is often difficult to ascertain the true significance of this past research other than to appreciate that sufficient clinical change appears to have been catalyzed that further investigation is merited. And as we prepare to delve into the question of the hallucinogens' application to treatment models, it will be essential that we control for the flaws that made a previous generation of research suspect. State of the art research methodology must be utilized, including proper attention to set and setting, control populations and measures of short and long term treatment outcome. An atmosphere of active collaboration among investigators with contrasting perspectives needs to be established, avoiding at all costs the schism which led to the collapse of earlier efforts.

The Relevance of the Past

We are on the threshold of initiating explorations which may have considerable ramifications for our future. There is much at stake and much to learn. But in order to take full advantage of this opportunity we must fully understand our past, including that which we know from cultures distant to our own place and time. Plant derived hallucinogens once played a vital, albeit poorly appreciated role in our pre-historical lineage (Furst, 1976; Dobkin de Rios, 1984). While psychiatry has traditionally held a disparaging and pathologizing view towards shamanic belief systems and practices (Devereux, 1958), evidence supplied by transcultural anthropological investigators (Jilek, 1971; Noll, 1983)

demonstrates that shamanic practices may actually be conducive to high levels of psychological health and functioning. To move beyond the commonly held psychiatric viewpoint that shamanism is nothing more than primitivism and the prehistorical wellspring of mental illness, would allow for receptivity to learning from a paradigm that has incorporated for thousands of years the utilization of hallucinogens as a vital facet of belief systems and healing practices (Bravo and Grob, 1989). If we are to assess optimally the true clinical efficacy and safety of the hallucinogens, it is imperative that we be conscious of the critical extrapharmacological variables that we know to be integral to the shamanic model. Ample attention and sensitivity must be given to the preparation for the hallucinogen experience, the powerful expectation effects directed toward predetermined therapeutic goals, the formalized structure of the session and the integration of the altered state experience in the days, weeks and months following the experience. The failure to adhere to any of these aspects of the shamanic paradigm would be to deny hallucinogen research the full opportunity to test its true value.

What removes the shamanic world view so far from our own, and consequently presents the greatest challenges when attempting to incorporate its insights into contemporary research methodology, is the belief that the plant hallucinogens are sacraments of divine origin. However, it is this reverential and spiritual utilization of psychoactive substances that so pointedly distinguishes the practices of tribal and shamanic peoples from our own contemporary profaned and pathologized context of drug abuse. Hallucinogens in the shamanic world have traditionally played a critical role in rites of initiation, providing personal regeneration and radical change, and are perceived as essential to the process of growth and maturity and the acquisition of meaning (Grob and Dobkin de Rios, 1992; Zoja, 1989). They are not mis-used or abused, and are not agents of societal chaos and destruction. Their use is fully sanctioned and integrated into the mainstream of society, and commonly utilized in ritually prescribed and elder facilitated ceremonies. The hypersuggestible properties of the hallucinogens, utilized within a highly controlled set and setting, achieves a powerful effect, reinforcing cultural cohesion and commitment. These apparent beneficial effects of shamanic hallucinogen use contrast markedly with the destructive outcomes often observed in our own contemporary contexts (Dobkin de Rios and Grob, 1993).

An Illustrative Model

One of the most exciting areas of investigation from the past era of hallucinogen research was the treatment of severe, refractory alcoholism. In the 1950s psychiatric researchers had identified the similarities between the spectrum of the LSD experience and the phenomenology of delirium tremens (Osmond, 1957; Ditman and Whittlesey, 1959). As alcoholism was notorious for its lack of responsiveness to conventional treatment approaches, great interest and energies were directed towards this area of study. Highly impressive short term results of treatment with hallucinogens (Chwelos et al, 1959; MacLean et al, 1961; Van Dusen et al, 1967) gave impetus to a surge of enthusiasm that a dramatic and effective intervention had finally been found. Additional support was forthcoming from Bill Wilson, the founder of Alcoholics Anonymous, who revealed that his own carefully supervised experiences with LSD had not only been a highly valuable personal experience, but were also fully compatible with the tenets of the movement he had started (Grof, 1987). However, as the level of discord within the psychiatric profession and the degree of alarm in the public heightened, resistance to accepting the hallucinogen model for alcoholism intensified. As mainstream psychiatry could no longer stand idly by in the face of threatened radical upheaval, so the Board of Trustees of Alcoholics Anonymous felt compelled to reject their creator Bill Wilson's proposed endorsement.

It soon became apparent that the methodological shortcomings of the research alleging to demonstrate unequivocally positive results in the treatment of alcoholism would undermine progress in the field. Poorly controlled research design, with questionable measures of change and inadequate follow-up led to charges that hallucinogen advocates had been blinded by their own enthusiasm and had mis-interpreted and mis-represented their findings. Opponents of the hallucinogen treatment model would subsequently conduct their own clinical trials, designed to refute what they perceived as dangerous and exaggerated claims of therapeutic success (Smart et al, 1966; Hollister et al, 1969; Ludwig, Levine and Stark, 1970). These studies, which purported to demonstrate an entire lack of treatment efficacy of models utilizing hallucinogens, were received by the psychiatric establishment with great relief. In fact, the Ludwig, Levine and Stark study provided such reassurance to a profession so shaken by its own iconoclasts, as well as satisfying contemporary formal medical research standards with such aplomb, that it was awarded the prestigious Lester N. Hofheimer Prize for Research from the American Psychiatric Association.

Nevertheless, the investigations designed to provide the last word on the "failed" hallucinogen treatment model have themselves come under scathing attack. Not only have the investigators' lack of appreciation of set and setting, failure to adequately prepare their patients for the experience and refusal to allow for follow-up integration been identified (Grinspoon and Bakalar, 1979), but the capricious nature of medical research has itself been implicated. "At a time when LSD was popular, Levine and Ludwig (1967) had reported positive results… When LSD fell out of favor and the positive results became politically unwise, they obtained negative results. Unconsciously or consciously they built into their study a number of antitherapeutic elements that guaranteed a therapeutic failure" (Grof, 1980).

The discussion of the potential role of hallucinogens in the treatment of alcoholism, and by inference its application to other psychiatric disorders as well, would not be complete without an examination of the role of the plant hallucinogen, peyote, in the treatment of Native American Indians. Evidence exists that peyote was in widespread use in Central America and revered as a medicine and religious sacrament as early as 200 B.C. (Furst, 1976). After the American Civil War, the use of peyote moved north of the Rio Grande River and quickly spread to dozens of native tribes throughout the United States and Canada. During the 1870s and 1880s a peyote vision religion developed in reaction to the inexorable encroachment of non-native peoples onto the Indian lands and the associated, deliberate destruction of native culture. With the defeat and subjugation of the Native American people, alcoholism became epidemic. Although until recently faced with unrelenting political repression by the U.S. government, the Native American Church, a syncretistic church combining elements of traditional Indian religion and Christianity and utilizing peyote as its ritual sacrament, has been recognized by anthropologists and psychiatrists as being the only effective treatment for endemic alcoholism (Schultes, 1938, La Barre, 1947, Bergman, 1971, Albaugh and Anderson, 1974). Karl Menninger, a revered figure in the development of American Psychiatry in the 20th Century, has stated: "Peyote is not harmful to these people; it is beneficial, comforting, inspiring, and appears to be spiritually nourishing. It is a better antidote to alcohol than anything the missionaries, the white man, the American Medical Association, and the public health services have come up with" (Bergman, 1971).

Integral to the positive treatment outcome with peyote has been its sacramental utilization within the ritual context of mystical-religious experience. The Native American Church is a clear contemporary example of the successful application of the shamanic model to the treatment of severe, refractory illness. Although the Native American Church applies to a circumscribed and relatively homogenous population, it provides a valuable lesson on the importance of the shamanic model and the need for attentiveness to set and setting, intention, preparation and integration, as well as group identification. If we are to develop optimal research designs for evaluating the therapeutic utility of hallucinogens, it will not be sufficient to adhere to strict standards of scientific methodology alone. We must also pay heed to the examples provided us by such successful applications of the shamanic paradigm. It will only be then, when we have wedded our state of the art research designs to the wisdom accrued from the past, that we will adequately appreciate what role hallucinogens may have in our future.

Conclusion

After a twenty-five year period of virtual prohibition, formal psychiatric research with hallucinogenic drugs has resumed. This article has reviewed the process by which hallucinogens came to be viewed as beyond the pale of respected and sanctioned clinical investigation, and has directed attention to the importance of fully understanding the lessons of the past so as to avoid a similar fate for recently approved research endeavors. The shamanistic use of hallucinogenic plants as agents designed to facilitate healing, acquire knowledge and enhance societal cohesion were brutally repressed in both the Old and New Worlds by the progenitors of our own contemporary Euro-American culture, often with complicity of the medical professions. Knowledge of the properties and potentials of these consciousness altering plants was forgotten or driven deeply underground for centuries. It was not until the late 1800s that German pharmaceutical researchers investigating the properties of peyote re-discovered the profound and highly unusual effects of these substances. A dispute anticipating the virulent controversies of the 1960s ensued, however, pitting proponents of this new model of consciousness exploration against those who questioned the propriety of their colleagues enthusiasm for self experimentation and penchant for sweeping proclamations. The history of hallucinogen research in the 20th century has revolved around this regrettable polarization, and as such has impeded the evolution of the field.

Developments in the second half of the 20th century were catalyzed by the remarkable discoveries of the Swiss research chemist, Albert Hofmann. In the

wake of his synthesis of the extraordinarily potent psychoactive substance, lysergic acid diethylamide, a period of active investigation ensued. Notable gains were accomplished utilizing the psychotomimetic model for understanding mental illness and the low dose psycholytic approach for the treatment of a variety of psychiatric conditions. It soon became apparent however, that these models possessed inherent limitations when applied to the orthodox psychiatric constructs then in vogue. The implementation of the high dose psychedelic model, in spite of its apparent utility in treating resistant conditions such as refractory alcoholism, presented even greater difficulties in conforming to the boundaries of conventional theory and practice. Acceptance of hallucinogens as reputable tools for investigation and agents for treatment were dealt a further and near fatal blow when they became embroiled in the cultural wars of the 1960s. Together with revelations of unethical activities of psychiatric researchers under contract to military intelligence and the CIA, the highly publicized and controversial behaviors of hallucinogen enthusiasts led to the repression of efforts to investigate formally these substances. For the next twenty-five years research with hallucinogens assumed pariah status within academic psychiatry, virtually putting an end to formal dialogue and debate.

We now have before us the opportunity to resurrect the long dormant field of hallucinogen research. However, if the debacle of the past is to be avoided, it is imperative that we learn from the lessons of prior generations of researchers who saw their hopes and accomplishments dissipate under the pressures of cultural apprehension and the threat of professional ostracism. It is essential that the mistakes of the past not be replicated. Definitive steps to end the protracted period of silence and inactivity have been initiated. Contemporary investigators will need to proceed tactfully however, and with respect for the anxieties that this work may provoke in their colleagues. Serious effort must be taken to facilitate active dialogue and collaboration. Current and accepted models of research design must be rigorously adhered to, for to disregard the state of contemporary scientific investigation would ultimately undermine the goals of fully exploring the rich potential of these substances. It will also be critical to learn from the wisdom accrued over the ages in cultures with world views quite different from our own. Although much of the knowledge of the shamanic utilization of plant hallucinogens has been lost with the passage of time, investigators must appreciate the vital role that set and setting have on determining outcome, and incorporate such parameters in their research designs. An opening now exists to explore this fascinating yet poorly understood class of psychoactive substances. Whether we can successfully take advantage of this opportunity will depend ultimately on how well we have learned the lessons of the past.

References

Albaugh, BJ (1974) Peyote in the treatment of alcoholism among American Indians. *Am J Psychiatry* 131, 1247-1250.

Bergman, RL (1971) Navajo peyote use: Its apparent safety. *Amer J Psychiatry* 128, 695-699.

Berringer, K (1927) Der Mescalinrausch. Springer, Berlin.

Bleuler, M (1958) Comparison of drug-induced and endogenous psychoses in man. In, PB Breatly, R Deniker, Raduco-Thomas,D (Eds): Proceedings of the First International Congress of Neuropsychopharmacology. Elsevier, Amsterdam.

Bravo, G, Grob, C (1989) Shamans, sacraments and psychiatrists. *J Psychoactive Drugs* 21, 123-128.

Chandler, AL, Hartman, MA (1960) Lysergic acid diethylamide (LSD-25) as a facilitating agent in psychotherapy. *Arch Gen Psychiatry* 2, 286-299.

Chwelos, N, Blewett, DB, Smith, CM, Hoffer, A (1959) Use of d-lysergic acid diethhylamide in the treatment of alcoholism. *Quarterly J Studies Alcohol* 20, 577-590.

Cole, JO, Katz, M (1964) The psychotomimetic drugs. *JAMA* 187, 182-185.

Cordova-Rios, M (1971) The Wizard of the Upper Amazon. Atheneum, New York.

De Rios, MD, Smith, DE (1976) Using or abusing? An anthropological approach to the study of psychoactive drugs. *J Psychedel Drugs* 8, 263-266.

De Rios, MD, Grob, CS (1993) Hallucinogens, suggestibility and adolescence in cross-cultural perspective. Yearbook of Ethnomedicine 3, 113-132.

Devereux, G (1958) Cultural thought models in primitive and modern psychiatric theories. *Psychiatry* 21, 359-374.

Ditman, KS, Whittlesey, JRB (1959) Comparisons of the LSD experience and delirium tremens. *Arch Gen Psychiatry* 1, 47.

Ellis, H (1897) Mescal: A new artificial paradise. Annual Report of the Smithsonian Institution, pp. 537-548.

Freedman, DX (1986) Hallucinogenic drug research - if so, so what?: Symposioum summary and commentary. *Pharmacol Biochem Behav*: 24, 407-415.

Furst, PT (1976) Hallucinogens and Culture. Chandler and Sharp, Novato, CA.

Grinker, R (1963) Lysergic acid diethylamide. *Arch Gen Psychiatry* 8, 425.

Grinker, R (1964) Bootlegged ecstasy. *JAMA* 187, 192.

Grinspoon, L, Bakalar, JB (1979) Psychedelic Drugs Reconsidered. Basic Books, New York.

Grinspoon, L Bakalar, JB (1986) Can drugs be used to enhance the psychotherapeutic process? *Amer J Psychotherapy* 40, 393-404.

Grob, C, De Rios, MD (1992) Adolescent drug use in cross-cultural perspective. *J Drug Issues* 22, 121-138.

Grof, S (1980) LSD Psychotherapy. Hunter House, Pomona, CA.

Grof, S (1987) Spirituality, addiction, and western science: *ReVision* 10(2), 5-18.

Guerra, F (1967) Mexican phantastica - A study of the early ethnobotanical sources on hallucinogenic drugs. *Br J Addict* 62, 171-187.

Guerra, F (1971) The Pre-Columbian Mind. Seminar Press, London.

Guttman, E, Maclsy, WS (1936) Mescaline and depersonalization: Therapeutic experiments. *J Neurol Psychopath* 16, 193-212.

Harner, MJ (1973) The role of hallucinogenic plants in European witchcraft. In, Harner MJ (Ed): Hallucinogens and Shamanism. PP. 125-150. London, Oxford University Press.

Heffter, A. (1897) Uber Pellote. *Arch. Exp. Path. Pharmakol* 40, 418-425.

Hofmann, A (1985) LSD - My Problem Child: Reflections on Sacred Drugs, Myasticism, and Science. J.P. Tarcher, Los Angeles.

Hollister, LE, Shelton, J, Krieger, G (1969) A controlled comparison of lysergic diethylamide (LSD) and dextroamphetamine in alcoholics. *Amer J Psychiatry* 125, 1352-1357.

Huxley, A (1977) Moksha: Writings on Psychedelics and the Visionary Experience. J.P. Tarcher, Los Angeles.

Jacobs, BL (1984) Hallucinogens: Neurochemical, Behavioral and Clinical Perspectives. Raven Press, New York.

Jilek, WG (1971) From crazy witchdoctor to auxiiary psychotherapist: The changing image of the medicine man. *Psychiatrica Clinica* 4, 200-220.

Kluver, H (1928) Mescal: The 'Divine' Plant and its Psychological Effects. Keegan-Paul, London.

LaBarre, W (1947) Primitive psychotherapy in native American cultures: Peyotism and confession. *J Abnormal Soc Psychol* 42, 294-309.

Leary, T, Alpert, R (1962) The politics of consciousness. Harvard Review 1(4), 33-37.

Lee, MA, Shlain, B (1985) Acid Dreams: The CIA, LSD and the Sixties Rebellion. New York, Grove Weidenfeld.

Levine, J, Ludwig, AM (1967) The hypnodelic treatment technique. In, HA Abramson (ed), The Use of LSD in Psychotherapy and Alcoholism. New York, Bobbs-Merrill.

Ludwig, AM, Levine, J, Stark, LH (1970) LSD and Alcoholism: A Clinical Study of Treatment Efficacy. Springfield, Illinois, Charles C. Thomas.

Maclean, JR, Macdonald, DC, Byrne, UP, Hubbard, AM (1961) LSD in treatment of alcoholism and other psychiatric problems. *Quarterly J Studies Alcohol* 22, 34-45.

Marks, J (1979) The Search for the "Manchurian Candidate". New York, Dell.

Michelet, J (1965) Satanism and Witchcraft: A Study in Medieval Superstition (1862). Translated by A.R. Allinson. New York, Citadel.

Mitchell, SW (1896) Remarks on the effects of Abhelonium lewinii (the mescal button). *Br Med J* 2, 1625-1629.

Neill, JR (1987) "More than medical significance": LSD and American psychiatry 1953-1966. *J Psychoactive Drugs*, 19, 39-45.

Noll, R (1983) Shamanism and schizophrenia: A state-specific approach to the "schizophrenia metaphor" of shamanic states. *American Ethnologist* 10, 443-459.

O'Neil, M (1987) Magical healing, love magic and the Inquisition in late sixteenth-century Modena. In, S. Haliczer (Ed): Inquisition and Society in Early Modern Europe, pp. 88-114. Croom Helm, London.

Osmond, H (1957) A review of the clinical effects of psychotomimetic agents. *Ann NY Acad Sci* 66, 418-434.

Rinkel, M, Denber, HCB (Eds) (1958) Chemical Concepts of Psychosis. McDowell, New York.

Schultes, RE (1938) The appeal of peyote (Lophophora williamsii) as a medicine. *American Anthropologist* 40, 698-715.

Smart, RG, Storm, T, Baker EFW, Solursh, L (1966) A controlled study of lysergide in the treatment or alcoholism. *Quarterly J Studies Alcohol* 27, 469-482.

Stevens, J: Storming Heaven (1988) LSD and the American Dream. Harper and Row, New York.

Stockings, GT (1940) A clinical study of the mescaline psychosis, with special reference to the mechanism of the genesis of schizophrenia and other psychotic states. *J Mental Science* 86, 29-47.

Stoll, WA (1947) Lysergaure-diathylamid, ein phantastikum aus der mutterkorngruppe. *Schweizer Archiv fur Neurologie und Psychiatrie* 60, 279-323.

Strassman, RJ (1984) Adverse reactions to psychedelic drugs: A review of the literature. *J Nervous Mental Disease* 172, 577-595.

Strassman, RJ (1991) Human hallucinogenic drug research in the United States: A present-day case history and review of the process. *J Psychoactive Drugs* 23, 29-37.

Van Dusen, W, Wilson, W, Miners, W, Hook, H (1967) Treatment of alcoholism with lysergide. *Quarterly J Studies Alcohol* 28, 295-304.

Wasson, RG (1968) Soma: Divine Mushroom of Immortality. Harcourt, Brace and World, New York.

Wasson, RG, Ruck, CAP, Hofmann, A (1978) The Road to Eleusis. Harcourt, Brace, Jovanovich, New York.

A slightly abbreviated version of this article first appeared in the Yearbook for Ethnomedicine and the Study of Consciousness 3:91-112, 1994