Chapter 16

TWENTY YEARS ON AN EVER-CHANGING QUEST

Alexander T. Shulgin

"Each man must look to himself to teach him the meaning of life. It is not something discovered: it is something moulded."
—Saint-Exupery

Millions of people have, at least once within their lifetimes, become aware of some form of psychedelic state. There have been many means employed: intentional ingestion of some drug; spontaneous rearrangements of internal chemistry; acts of physical excess, such as starvation or self-mutilation; or the quiet procedures of meditation or religious dedication. For some people, these have been one-time events which—if not disturbing enough to demand avoidance—have been of insufficient value to encourage re-exploration. For others, there has been a change in the flow of life-purpose, leading to an active search for further experiences, in order to build on the structures that have appeared. But few if any of these people would deny the impact, be it sacred or frightening, that such an experience has had on their view of themselves and others.

But this "change of life flow" capability seems not to be for everyone at all times. Unlike the rites of passage, practiced one way or another throughout the world, which are locked inexorably to adolescence by the biologic clock, the receptivity to psychedelic experience seems to require an emotional development that involves some entirely different timing mechanism. There must be an harmonious blend of attainment and dissatisfaction, something that is found, if ever, with the achievement of social maturity along with emotional honesty. Early psychedelic experiences that have the potential of affording transitions have too often and too tragically been wasted, like youth, on the young. Such exposures may have provided pleasure and entertainment, but they have also been correlated with the compulsive use of any accessible drugs. From such misuses have come

examples of social alienation and consequent isolation. Intense experiences, before their time, bid fair to be grasped at as escapes, and may not play the intended role in personal development.

But what is the time, the age, the state of emotional maturity that allows the power and potential of such experiences to be recognized and effective? The ego demands of each person the belief that his age, whatever it might be, is the optimum age for growth and understanding. And if a person finds that he has changed his life's course, he will usually convince himself of the correctness of the new direction. Successful (in retrospect) changes have occurred with adults in their teens, yet similar efforts have fallen on barren soil with others in their sixties. There are clues that might help define the necessary state of maturity, but they are difficult to observe in others. It is equally difficult to evaluate, objectively, the net long-term consequences of a psychedelic experience, one which has clearly set the subject on some change of life flow. Such perceptions and predictions are impossible to make in regard to oneself.

As illustration, let me outline briefly the histories of three people, each of whom had a cataclysmic experience with a psychedelic drug some 20 years ago. All were in their early thirties (an age which I feel is rarely sufficient for the achievement of that "personal development" I mentioned earlier). All three were, at the time of this experience, well educated, professionally competent, and highly respected by their peers. Each changed the direction of his life following his—in Maslow's terms—peak experience.

One, a professor of literature, underwent an intensely introspective evaluation (the drug was LSD) that demanded he look closely at the quality, the "lastingness" of his educational preparations; he saw them as simple machinery being constructed as a camouflage for his own unwillingness to acknowledge shallowness. He moved to Japan for 2 years, shifting from the role of teacher to one of student. He studied Zen philosophy, and felt that he was achieving both openness and self-awareness. On returning to this country, he entered and completed professional graduate school, and is presently a very successful administrator in a human-health oriented department of a major university. He felt that the single experience had been personally revelatory, and had led him towards his most productive niche, but he has never felt the need nor wish to repeat the experience.

The second person, an especially gifted neurologist, effectively disappeared from all social and medical contact following an intense LSD experience, one which truly showed him the hand and word of God. After 8 months he returned to his wife, family, and practice, with a 30-page tract that was the labor of love for this period, one which put into words the revelations whch had become so patently evident to him during the experiment. His subsequent 2 decades have been devoted to sharing, both medically and theologically, those insights that had so changed his personal attitudes. There has been modest experimentation with psychedelics during this period, but without the achievement of the transcendental state of enlightenment of that remarkable experience. Today he is living in a commune in the Midwest, dedicated to his practice of both medicine and religious teaching.

The third person was a biochemist, myself. I took a day from my professional work in industry to explore the catalytic effects of mescaline. The impressions of that experience are best expressed in the flow of events that followed that day. There began what might be called a quest of curiosity. I realized that the mind, and the senses that provide inputs to the mind, were all grossly underutilized faculties in the study of the world around us; and that it was irrational to ascribe to a small quantity of chemical the intrinsic power to provide this sensory augmentation. I found it hard to accept that such a simple, unsophisticated molecule, containing barely 30 atoms, could carry within its structure such complexities of thought patterns, of sensory license, of visual magic. It was inescapable that the molecule didn't do anything itself, but rather, allowed the human mind to make these changes. It could only serve as a catalyst, unleashing and promoting channels of mental processes that were native, that lay inculcate in the normal brain. And why should a modest cactus contain such an effective catalyst, expressible only in man?

Psychologists might be able to dissect the nature of the changes, and physicians might be able to define the sites of action, but my background in chemistry and biochemistry limited me to the atoms and bonds of this catalyst, and the compelling inquiry into their function by the simple strategy of changing them, observing the changes in effect that resulted. I felt that by providing in a single process both the structural change and the subjective evaluation of the results of such change, a pattern might emerge that would tie together the definitions of the catalyst and the process being catalyzed.

A first step in this direction had already been taken by Hey and Smithies, and other Canadian workers, who blended together the molecules of mescaline and amphetamine. The result was TMA, and in the late 1950's they found it to be similar in action to, and more potent than, mescaline. This observation, in effect, dispelled the myth that natural products were the *only* truly effective psychedelics. This was a blend of the natural and the man-made, and it historically launched the studies that followed. It is still true that the most potent, though not necessarily the most interesting drugs have this amphetamine skeleton, and often have alphabetic abbreviations ending in "A."

But nature and her botanicals were still to contribute to the development of this area. The oils of several plants (nutmeg, parsley, dill) have had checkered reputations as intoxicants. In these extracts there are unusual chemicals which resemble amphetamine, except that the elements of ammonia are lacking. In a series of studies, these natural plant products were fractionated into their components, and I converted them separately into biologically acceptable amines. Safrole gave rise to MDA, which had been first explored and reported by Gordon Alles several years earlier as a sensory enhancing agent. Elemicin yielded the base TMA. Myristicin gave rise to MMDA, which had been synthesized and found to be psychedelically active by both Alles and myself, at about the same time but independently of each other. We had coincidentally given it the same alphabet name and had found it through the same line of reasoning. (During the month before our first intended meeting, Alles died, and the

work that has followed in the subsequent 20 years could be appropriately dedicated to his curiosity and impetus.) MMDA was a "natural" product, in that it was derived from natural sources, but, being some three times more potent than mescaline, showed that indeed man could improve upon nature. The heart of this is the finding that the arrangement "MD" (methylenedioxy) exceeded in both potency and virtue (pleasantness of experience with fewer physical side-effects) the "DM" (dimethoxy) arrangement to be found in analogs.

The third principle of structure *versus* activity was the result of a complete chemical and psychopharmacologic study which I made of all possible arrangements within these molecules. I found that the "natural" orientation was exceeded in potency by a factor of 10, by the "unnatural" 2,4,5-substitution pattern. This is now the universally accepted basis of most currently known psychedelic drugs. The magical "four position" was shown completely to control the character of a drug's effects. It was thought that placing a metabolically inert group at this position might lead to an inactive, thus possibly prophylactic, antagonist to related drugs. It might be a therapeutic agent against endogenous schizophrenia.

But the product (DOM, also known as STP) proved to be an exceptionally potent psychedelic, perhaps a hundred times more potent than mescaline. This compound escaped into the street scene in the late 1960s and contributed to the polarization of opinions concerning paramedical drug use. From the viewpoint of my own understanding of the whys and wherefores of drug action, this proved to be a major breakthrough. Virtually any substituent at this "four position," as long as the rest of the molecule was left intact, led to some form of psychedelically active drug. The comparative potencies might vary, as one could expect, but the range and variation of effect was the rich, unpredictable reward of such modifications. At this position, going from one carbon to two carbons, a structurally trivial modification, produced DOET, a drug that has been found by several research groups to facilitate the unblocking of imagination and creativity.

Replacing this one carbon atom with the halogens, bromine and iodine, produced DOB and DOI, both extremely potent (with the active forms requiring about one molecule to do the task of 1,000 molecules of mescaline) and allowing an exceptionally long-lasting, rich, visual and sensory experience. Replacing the one carbon atom with a sulfur atom produced the first of a still largely unexplored "aleph" series, which bids fair to evoke the richness and introspection of LSD, with the added possibility of teasing out specific aspects of action for emphasis.

The last principle, interestingly, closed the circle on the first. The amphetamine chain has served the role of fine-tuning the substitution nature of the psychedelic catalyst, but it has been discovered that by returning to the simple phenethylamine skeleton found in mescaline and in the vital neurotransmitters of the brain, this richness of potential comes home in logical proximity to natural biochemistry. The neurotransmitter-analog related to DOB is 2C-B, which allows a luxury of sensory enhancement (visual, sexual, gustatory) with a minimum of introspective demands. The analog related to DOET is 2C-E, which permits extraordinary fantasy, both factual (childhood reliving) and insightful. The analog related to

mescaline but with sulfur in place of oxygen at this same four-position is thiomescaline, which disorganizes the logical patterning of thought processes, with surprisingly little visual or sensory modification.

Throughout this early work, I was absorbed primarily with how much of a chemical it took to achieve an effect, rather than with the nature of the effect achieved. In my notes the term "psychedelic effectiveness" reflected only the potency. I left to others the task of determining the qualitative aspects of the effects of these drugs, and their potential values. It was around this time that I became aware that I was trying to answer a complex question with a hopelessly restricted vocabulary. I needed a fundamental understanding of many other aspects of the functioning of the human animal. I entered medical school to learn the mechanics of these functions; the search for their purpose and meaning was begun at this same time, through the study of philosophy and literature. But it must also, sadly, be called the time of my quest for camouflage. These were the years of paranoia and extreme opinions on any topic that embraced the word "psychedelic."

A public conference on the subject of LSD, scheduled for the University of California in Berkeley, was abruptly disavowed by the faculty, and frantically transferred to San Francisco. It was attended by many hundreds of people, who seemed divided into rabid proponents of the use of psychedelic drugs—largely representing the "flower-child" movement in San Francisco, euphemized by the term "Haight-Ashbury"—equally extreme antagonists, representing the academic establishment voicing fear of the unknown, and a battalion of the quiet ones, participating only with tape recorders and cameras, probably representing the Bureau of Narcotics, the FBI, and possibly the press.

Some time later, and some 10 blocks away, a second circus took place: the hearings of the House Select committee on Crime, chaired by Senator Claude Pepper, which were also devoted, in large measure, to psychedelic drug use.

By keeping a low profile, one could avoid allying oneself with either extreme. Replacing the term "psychedelics" with "psychotomimetics," researchers in the field locked themselves into the then prevalent clinical concept that LSD and related drugs had value only in the generation of a "model psychosis," but they were able to continue their investigations. This was, throughout the western world, a period of little progress in the field, since every discovery—if it were to be reported at all—had to be phrased in terms of mental illness. Industrial laboratories restricted their psychopharmacology research to the development of tranquilizers and antidepressants. The academic institutions maintained interest in this area, but confined themselves to the more negative questions of neurological damage and addiction. This period of repression gave caution to many investigators who were widely published and thus widely known, but gave assurance of professional survival to others who (wisely) chose to continue their searches with circumspection.

With the passage of the Uniform Substances Control Act, the extent, but also the limits, of the "drug evil" were defined. This allowed academic scientists to continue their studies in areas that could be rationalized as conforming to the popular ethic. (But outside were to be found the anti-

nomians who listened to a different drummer.) The well known "drugs of abuse" had been explicitly defined; LSD, STP, mescaline, psilocybin, and some three score relatives were condemned by these statutes. A modest wealth of discovery in several research environments throughout the world began uncovering the generality of psychedelic drug structures and, much more important to the studies that stemmed from this, a wealth of qualitative distinctions and values which can be found within them.

Here was the start of my quest of caring. I began the study of these drugs, not from the viewpoint of classification and simple assignment of potency, but inquiring into the values of human interaction that can result from their study in terms of personal development. I became aware that it was of little merit merely to observe what a drug does to the human nervous system, unless one also observes how it permits a person to interact with others, and especially, how it allows him to acknowledge himself. Some of the most complex psychedelics will achieve, in persons who are psychologically well centered and personally on terms with their internal anger, little more than an adventure in sensory release, with an occasional insight which reminds them of their humanness. Yet, with some of the simplest materials, ones which will normally yield nothing more than a simple opening "window" effect in most subjects, an occasional abreactive bubble is brought to the surface, brought completely and inescapably to conscious awareness with the concomitant acknowledgement that prepares the ground for progress. However, the assignment to a drug of a position on the continuum between "simple" and "complex" depends as much on the situation as it does on the chemical. Within such research, I feel that there are several requirements that must be met before any generalized statement of properties can be ascribed to a psychedelic drug.

First, there must be complete confidence on the part of the experimenter that there are no toxicological or physically threatening properties that might color the responses evoked. This means, simply, that the observer must be completely aware of the potency and the potential quality of the effects to be experienced before there is any interaction whatsoever with a subject. In this regard I have used the term coined by Gordon Alles, of "double conscious" protocols. In the evaluation of a new drug, the rubric of the medical community is that, for the sake of objectivity, both the subject and the experimenter must be unaware of the presence or absence of an active component being used in a trial, and that the nature of the expected action should also be hidden. In the area of psychedelic drugs, this is both unethical and absurd. If the potential exists for the upheaval of a person's "change of life flow," then it is unprofessional, if not criminal, to fail to advise him of this potential outcome. And if you, yourself, as the investigator, are uncertain of the potential ramifications of such an experiment, then you are remiss in exposing others to that with which you are not personally familiar. One must personally know the experience to understand properly another's experience. Humphry Osmond states this well in his analogy:

> "A eunuch could write an authoritative book on sexual behavior, but a book on sexual experience by the same author would inspire less confidence."

Second, the experimenter should enter the experiment along with the subject, with the same chemical and at the same dosage. The classic arguments of objectivity *versus* subjectivity are not applicable here. The barriers of distrust, a familiar hurdle to be overcome in psychiatric interactions, have thus been lowered. Otherwise, the "subject," feeling himself without defenses in interaction with an "observer" who has all of his own defenses intact, may feel alienated and inhibited. Openness must be reciprocal. Two unmarked and equal capsules can dispel dramatically any anxieties that might arise during an experiment.

Third, the setting must be familiar and benign. Two (unintentionally) parallel studies bear witness to this need. One, in Los Angeles several years ago, was conducted with some hundred subjects taking LSD in a clinical environment, with medical back up, blood pressure measurements, and thorazine at the ready. Many of the subjects had a difficult time within the experiment, and most stated that they would not choose to repeat the experience. The other study took place in New York at about the same time, with a similar number of subjects and the same drug and dosages, but in a private home with support and personal interaction. This produced a largely positive result and a sustained interest in further exploration.

There is really a fourth consideration, in addition to the trilogy above. One must have a genuine curiosity about new directions of personal growth and the fabric of psychedelic insight and discovery, rather than just a wish for sensory entertainment or escape. There should be dedication of purpose or recognition of need.

In my own case, I had culminated some 10 years of academic curiosity with a personal experience of mescaline, in early 1960. The 20 years since then have been invested in a search that may not yet have its final direction. Now, the quest is assuming a different character. There is a need for integration. There are literally hundreds of psychedelic "catalysts" currently at hand that run the gamut of potencies and qualitative characteristics. But now it is becoming apparent to me that these materials, rather than being simply flowers in an expanding anthology, could have value beyond their present acceptance as sensory disinhibitors. Two or three are especially noteworthy, partly for the specificity of their effects, and partly for the consistency of action.

One of the most thoroughly studied, with hundreds of clinical trials, is the material known as MDMA. It has proven to be of remarkably consistent chronology (the duration of action is about an hour) and dosage requirements (the effective dosage is 100-150 mgs. orally). In most aspects, it is deceptively simple in action, leading to a sensory and verbal disinhibition, a state of mutual trust and confidence between subject and therapist, but without the distractions of visual distortion or compelling introspection. This "window" effect is almost always graciously accepted, and the consistent short duration of action gives assurance of gradual but certain re-establishment of a "normal" baseline. It is, on one hand, the ideal introductory experience for the naive subject, yet it allows a flow of communication (intra- as well as interpersonal). Some experienced psychiatrists and psychologists insist that it has reduced to a day the labors that might have normally taken months. With its use there have been occasional abreactive crises, but these have usually been understood and

acknowledged in terms of repressed personal history. With some people, there appears to be no need to dip deeper into the psychedelic pharmacopoeia. With others, the openness serves to dispel anxieties concerning alteration in states of consciousness, and access can then be attempted with more moving and commanding substances. These materials are indeed catalysts which work at the levels of fundamental processes of emotion and perception.

Very little, however, has been learned about the actual processes being catalyzed. The striking similarity between many of these substances and vital biochemicals found in and about the central nervous system suggests that there might be a mechanism that involves disruption or augmentation of these biochemicals with a concomitant unbalancing or rebalancing (temporarily) of the nervous system. The hows and whys of the action of this fascinating family of compounds is still a mystery, but some unorthodox speculations are tempting. Our cultural heritage requires the initial conclusion that these transient yet potentially enduring changes of states of consciousness are unnatural or abnormal. But perhaps they reveal the "normal" state through some disinhibition of an evolutionarily imposed safeguard. Perhaps these chemicals, by themselves, or through the *in vivo* conversion to some intrinsically appropriate metabolite, may serve a neurotransmitter role at some synaptic network, restoring certain neurological functions that have been lost through evolution. To many people, the states of awareness that are experienced are not "abnormal," but rather, familiar territory that had been lost in some primal amnesia.

Perhaps. But if these states are the human heritage, it cannot be forgotten that they represent, unless explored with caution, honesty, and preparation, serious threats to survival in a hostile but stable world. It is one thing to uncover the means of exploring the unlimited sensory reality about us, but quite another to divest the innocent of the learned biases and thought patterns which allow him acceptable behavior in a "normal" world. The zealous proselytes who talk of "turning on the world," without thought of the chaos that would certainly ensue, are in fact antisocial in their messages. There is much potential for mischief, even for physical and psychological damage, in these chemical catalysts. But the enriching growth potential that they also contain demands continuing study and attempts to understand them.