LYSERGIC ACID DIETHYLAMIDE: An Historical Perspective

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The ergot alkaloids are a group of drugs obtained from the fungus ergot, which grows on rye and gives rise to a great number of medically useful compounds, such as ergonovine and ergotamine. These latter compounds are used to contract the uterus after child birth, and for the treatment of migrane headaches. LSD was first synthesized in 1938 as an intermediate leading to the synthesis of ergonovine. Its profound psychological effects were completely unknown at that time.

In 1943, Dr. Albert Hoffman, who was one of the people involved in the original synthesis, began working with LSD again. This time he was seeking a stimulant using lysergic acid (which is the base of all the ergot alkaloids) in combination with a chemical similar in structure to nikethamide, a central nervous system stimulant.

One day when he was working with this drug he began to have some peculiar psychological effects which he described as follows:

"In the afternoon of April 16, 1943, when I was working on this problem, I was seized by a pecualiar sensation of vertigo and restlessness. Objects, as well as the shape of my associates in the laboratory, appeared to undergo optical changes. I was unable to concentrate on my work. In a dream-like state I left for home, where an irresistable urge to lie down overcame me. I drew the curtains and immediately fell into a peculiar state similar to a drunkenness, characterized by an exaggerated imagination.

"With my eyes closed, fantastic pictures of extraordinary plasticity and intensive color seemed to surge toward me. After two hours this state gradually wore off."

He thought that the psychological effects he had experienced were due to ingestion of some of the compound he was working with, and the next day he went back and purposely took what he considered to be an extremely small dose of the drug, 250 micrograms. (In fact, LSD can exert its psychological effects in a dose as small as 35 micrograms). He again developed these unusual psychological effects and, in fact, found they were now stronger because he apparently had taken a larger dose the second time.

Physiologically this compound acts as a sympathomimetic agent. The pupils dilate after taking LSD, the blood pressure rises slightly, and the pulse quickens. The acute physiological effects are minor when compared to the profound psychological effects that occur however, and at present there is concern over the chronic physiological toxicity which may take place with repeated LSD ingestion. Certain clinicians have reported persistent alterations

in E.E.G. patterns in chronic LSD users. These brain wave changes might suggest chronic brain damage, but at present there is no documented evidence of brain "organicity" with LSD. In addition, certain investigators have reported chromosomal alterations in peripheral white blood cells secondary to LSD in both in-vitro and in-vivo situations. There are also isolated reports of teratogenesis in rats when LSD is injected in the first trimester of pregnancy. There is no documented proof of human teratogenesis, but it seems quite clear that LSD is contraindicated in pregnancy because of its unknown effects on fetal development and because of its well known uterine stimulant properties.

When someone ingests an average dose of LSD, (150-250 micrograms) nothing happens for the first 30 to 45 minutes, and then after the sympathetic response the first thing the individual usually notices are illusions (objects in his sensory environment changing shape and color. Frequently he notices that the walls and other objects seem to move. Then he might notice that colors are looking much brighter or more intense than they usually appear and, in fact, as time goes on these colors can seem exquisitely intense and more beautiful than any colors he has seen before. Also, it is common for individuals to see a halo around lights, with a rainbow effect. The ordinary white light looks much brighter, and one can see numerous colors surrounding it.

Hallucinations, (a false sensory perception without a basis in external reality) are rather rare with LSD. What is more common is the phenomena of pseudohallucinations, where the individual may see something but at the same time he also knows his perception doesn't have a basis in external reality. For example, he may see geometric forms of figures or brilliant colors, but he realizes that they don't really exist out there.

There is another kind of perceptual change which occurs with LSD intoxication referred to as a synesthesia. One type of sensory experience is translated into another, so that if one is listening to music, for example, one can sometimes feel the vibrations of the music in one's body, or one can sometimes see the actual notes moving or the colors that he is seeing will beat in rhythm with the music so that we have a translation of one type of sensory experience into another type of experience.

There is a marked emotional liability and the changes in emotion are very frequent. Early in the LSD experience, one is often noted to be euphoric and when the individual is asked, "Why are you laughing", the person says, "I don't know, really, but I just feel like laughing." This laughter can very rapidly change to sadness and crying with very small changes in the environment. For example, one could be looking out and seeing green grass and blue sky, and the green grass looks more green than he has ever seen it before, and the blue sky is more intense, and he has an ecstatic feeling over the beautiful colors. Then perhaps the sun will go behind a cloud, and it gets gray, and suddenly he feels very blue and very sad, and it seems that everything in the whole world is turning gray. This is what is meant by marked emotional lability and the accentuation of mood.

Another area where an individual sees changes is the area of cognitive functioning or value judgment formation. When one is under the influence of LSD there is no loss of consciousness. He is fully conscious and usually remembers most of what happens. Thoughts move much more rapidly than usual, and one doesn't necessarily think in the same logical way or on the basis of the standard causal relations. Things that are ordinarily thought of as being opposite can now exist together and not appear as opposites.

For example, black and white become equal, or good and bad frequently become equal. A person can feel heavy and light at the same time, so there is a breakdown of our ordinary way of logical thinking; but again if the person is asked to do something, he usually can perform the task although he may be annoyed. If you ask him to write his name or take a psychological test, he may say, "I know I can do this, but don't bother me now. I just want to go on having my experience." Time orientation is frequently affected and past, present and future may merge; special orientation is also altered and the individual may describe himself as being "spaced".

An interesting feature is that anything that happens while one is under the influence of LSD frequently assumes an increased sense of meaning and/or increased sense of importance. When in the LSD state one begins to feel that certain things which are usually regarded as trivial are now much more important. For example, when under LSD, one might look at a rose and feel this is a vision of true beauty, and the answer to "what is meaningful in life". Unfortunately such drug-induced insights are transcient, but at least under the influence of LSD, "a rose may be more than a rose".

What the individual experiences while under the influence of LSD is greatly dependent on his personality structure, his set or attitude prior to the experience, and the setting or envisionment surrounding the drug experience. Variation in any of these parameters can greatly alter the individual drug experience.

In the early days after LSD's psychological effects were discovered it was felt that LSD simulated a model psychosis; psychological symptoms seen in certain types of psychoses, such as schizophrenia. Some people expressed the idea that perhaps this drug could be used as a tool that would induce a model psychosis, and in this way we could learn more about schizophrenia and also could perhaps use it as a tool in drug screening so that if we brought about this model psychosis with LSD we might then try other drugs which would reverse the effects and thus have a screen for drugs that might be useful in treating psychoses.

We no longer think that LSD produces a model psychosis. While some of the psychological effects it produces are seen in some forms of mental illness, there are many differences that are noted. Therefore, most people do not believe that the model psychosis notion was valid. Along the way people began searching for endogenous compounds which were like LSD

and which might be responsible for causing illnesses like schizophrenia, but at the present time no such endogenous circulating compound has been found.

While the "model psychosis era" of LSD use was slowly losing momentum, the popular era was just beginning. In 1957, Aldous Huxley wrote "The Doors of Perception" relating his psychedelic experiences utilizing mescaline, a compound which has similar psychological properties to LSD. Soon after, Leary and Alpert, at Harvard, gave birth to the "psychedelic cult" which included a group of intellectuals in Cambridge who felt LSD enhanced their powers of creativity. The media spread the news of the psychedelic cults' mystical experiences throughout the nation, and today we see the use of psychedelic chemicals increased by geometrical proportions, so that in certain subcultures such as the Haight-Ashbury, use approaches 100%. In later articles the social significance of such widespread use of powerful psychedelic chemicals will be discussed.

As to the present medical status of LSD: It is considered an investigational new drug by the Food and Drug Administration. That means that there hasn't been demonstrated for the drug either the requisite safety or efficacy with regard to its treatment utility to warrant its being made available on a prescription basis.

At the present time there are a number of studies in progress to evaluate the usefulness of the drug as a possible therapeutic agent in the treatment of chronic alcoholism, psychoneurosis and of autism in children. Some individuals have also found that in cases of terminal illness, which some patients have a great difficulty in accepting, treatment with LSD helps them to accept the terminal illness.

In properly supervised circumstances, with subjects who have been previously medically and psychiatrically screened, the incidence of adverse reactions is extremely low. In circumstances where there is not the proper supervision and where individuals are not screened before they take the drug the incidence of adverse effects is significantly higher.

The adverse effects of LSD are largely psychologic in nature and can be divided into acute immediate effects and chronic after-effects.

First of all, an individual can knowingly take the drug and then feel that the drug has gotten away from him, and he is being controlled, or that he can no longer control the psychological effects that are happening to him. Under this circumstance some individuals panic and become frightened. They want to be taken out of this state immediately. They sometimes try to flee the situation which they are in. At other times they become quite paranoid and suspicious of other people who are with them. They begin to feel these other people are doing something to them or may do something to them, and

they may actually lash out at them. Thus, we have the acute panic states in which the individual either tried to flee the situation or actually lashed out.

Secondly, the individuals under LSD can show what, under ordinary circumstances, we would say is very poor judgment. For example, they can have the feeling that they are very light, that they really can fly, and under these circumstances they can actually go out windows. Individuals have been reported as walking out into the ocean, feeling they were "just part of the universe." Individuals have talked about having a feeling of invincibility, such as, "It doesn't matter if my body dies; my spirit will live," and this mind-body dissociation leads to a variety of problems, including inadvertant suicide. Following adverse reactions or "bad trips" a wide variety of long-term psychological problems can develop.

These chronic psychological after-effects of LSD can be divided into three categories.

1. The long term schizophrenic reaction: this usually occurs in people who were disturbed prior to the LSD usage.

2. The long term depression, recurrent panic reactions; these usually occur in an acute panic reaction.

3. The long term perceptual and recurrent hallucinosis or "flash-back" phenomena.

In summary: If a person is given LSD under properly supervised circumstances and is screened medically, the drug is relatively safe; but when a person who has not been screened medically and psychiatrically takes LSD of unknown purity in unknown quantity, in unsupervised circumstances, it can be an extremely dangerous drug. Unfortunately in the United States at present, this latter circumstance predominates and is largely responsible for the high incidence of adverse reactions to LSD now being seen.