3336

How LSD Originated†

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Dans les champs de l'observation le hasard ne favorise que les esprits préparés. – Louis Pasteur

Time and again it has been said and written that LSD was an accidental discovery. This is only partly correct, because LSD came into being in the course of systematic research, and only later in the game did the accident occur: when LSD was already five years old I experienced its unexpected effects in my own body; more correctly stated, in my own mind. Every discovery has its prehistory that shows in the end all that must happen before the discovery becomes possible.

When I look back in my thoughts to trace all the direction-giving events and decisions in my professional carrer that eventually steered my work into this field of research in which I synthesized LSD, I am led back to my choice of employment after I had finished my training in chemistry. Had I at any point chosen otherwise, then this substance, which has become world renowned under the designation LSD, might never have been created. If I wish to relate the story of the origin of LSD, I must therefore also describe briefly my career as a chemist in which the story is inseparably embedded.

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†Translated by Jonathan Ott from the forthcoming book *LSD: mein Sorgenkind* (Stuttgart: Klett-Cotta). This extract, the first chapter of Dr. Hofmann's book, along with the final chapter were read by the author in San Francisco on Saturday, 30 September 1978. Ott's translation of the entire book will be published under the title *LSD: My Problem Child.*

In the spring of 1929 at the conclusion of my chemical studies at the University of Zurich, I joined the pharmaceutical-chemical research laboratory of Sandoz in Basel as a co-worker of Professor Arthur Stoll, founder and director of the pharmaceutical department. I chose this position because it afforded me the opportunity to work on natural products, whereas two other job offers from the chemical industries of Basel had involved work in the field of synthetic chemistry.

FIRST CHEMICAL INVESTIGATIONS

My doctoral work under Professor Paul Karrer had already matched my predilection for the chemistry of the plant and animal world. With the aid of the gastrointestinal juice of the vineyard snail, I succeeded in the enzymatic degradation of chitin, the structural material of which the shells, wings and claws of insects, crustaceans and other lower animals are composed. The chemical structure of chitin could be derived from the cleavage product obtained by this degradation, a nitrogen-containing sugar. Chitin turned out to be an analog of cellulose, the structural material of plants. This important result, that required only three months of research, led to a doctoral thesis rated "with distinction."

At the time of my entry to the firm, the staff of the pharmaceutical-chemical department was yet rather modest. Four chemists with doctoral degrees worked in research, three in production.

In Stoll's laboratory I found employment that completely agreed with me as a research chemist. The objective upon which Professor Stoll had based the work of his pharmaceutical-chemical research laboratories was to isolate and prepare in pure form, by careful techniques, the intact active principles of known medicinal plants. This is particularly important in the case of medicinal plants whose active principles are unstable or whose potency is subject to great variation thereby making an exact dosage difficult to secure. But if the active principle is available in pure form, one has the prerequisite for the manufacture of a stable pharmaceutical preparation exactly quantifiable by weight. Out of such considerations, long-known valuable plant drugs like foxglove (*Digitalis*), Mediterranean squill (*Scilla maritima*) and ergot (*Secale cornutum*) that, owing to their instability and uncertain dosage had found only restricted medicinal application in the past, were placed under investigation by Professor Stoll.

The first years of my employment in the Sandoz laboratories were dedicated almost exclusively to the study of the active principles of Mediterranean squill. Dr. Walter Kreis, one of Professor Stoll's first co-workers, guided me in this field of research. The most important constituents of Mediterranean squill already existed in pure form. Their isolation and purification as well as that of the active agents of woolly foxglove (*Digitalis lanata*) had been carried out chiefly by Dr. Kreis with extraordinary experimental skill.

The active principles of Mediterranean squill belong to the group of cardioactive glycosides (glycoside = sugar-containing substance) and serve like those of foxglove in the treatment of cardiac insufficiency. The cardiac glycosides are extremely active substances. Their therapeutic (curative) and toxic (poisonous, leading to cardiac arrest) doses do not differ greatly, so that here an exact dosage with the aid of pure compounds is especially important.

At the beginning of my investigations, a pharmaceutical preparation with *Scilla* glycosides had already been introduced into therapy by Sandoz; however, the chemical structure of these active compounds, with the exception of the sugar portion, was yet largely unknown. My main contribution to the *Scilla* research, in which I participated with enthusiasm, involved the elucidation of the chemical structure of the common nucleus of *Scilla* glycosides, showing on the one hand their differences from the *Digitalis* glycosides, on the other hand their close structural relationship with the toxic principles isolated from skin glands of toads. In 1935, these studies found a temporary conclusion.

In search of a new field of research, I proposed to Professor Stoll to continue the investigations on the alkaloids of ergot that he had begun in 1917, and that led directly to the isolation of ergotamine in 1918. Ergotamine, discovered by Stoll, was the first ergot alkaloid obtained in pure chemical form. Although ergotamine quickly took a significant place in therapeutics, under the trade name Gynergen®, as a hemostatic remedy in obstetrics and as a medicament in the treatment of migraine, chemical research on ergot in the Sandoz laboratories was abandoned after the isolation of ergotamine and the determination of its empirical forumula. Meanwhile, at the beginning of the thirties, determination of the chemical structure of ergot alkaloids had commenced in English and American laboratories. Moreover, a new water-soluble ergot alkaloid had been discovered, which could also be isolated from the mother liquor of ergotamine production. It therefore seemed timely to me to again take up chemical investigations on ergot alkaloids, if Sandoz did not want to run the risk of losing its leading role in this field of medicinal research.

Professor Stoll was in agreement with my request but remarked, "I warn you of the difficulties that you will encounter in working with ergot alkaloids. These are exceedingly sensitive, easily decomposed substances, their stability being completely different from the compounds with which you have worked in the cardiac glycoside field. But, if you wish, you may try it."

With this the switches were thrown that led me into a field of study that would become the main theme of my professional career. I still remember completely the feeling of creative joy – full of anticipation – that I felt with regard to the planned investigations in the field of ergot alkaloids, at the time yet little researched.

ERGOT

Here some background information about ergot is needed.[1] Ergot is produced by a lower fungus (*Claviceps purpurea*) that grows parasitically on rye, but also to a lesser extent on other species of grain and on wild grasses. The kernels infested with this fungus develop into light brown to violet-brown curved pegs (sclerotia) that push forth from the husk in place of normal grains. Ergot is described botanically as a sclerotium, the form of the ergot fungus that passes the winter. It is ergot of rye (*Secale cornutum*) that is used medicinally.

Ergot has, more than any other drug, a fascinating history, in the course of which its role and significance has inverted: once dreaded as a poison, in the course of time it has been recognized as a rich storehouse of valuable remedies. Ergot first appeared on the stage of history in the early Middle Ages as the cause of

epidemic-like outbreaks of mass poisonings to which thousands of people at times fell victim. The illness, whose connection with ergot was for a long time obscure, appeared in two characteristic forms: a gangrenous form (*ergotismus gangraenosus*) and a convulsive form (*ergotismus convulsivus*). Designations of the disease, such as "mal des ardents," "ignis sacer," "heiliges Feuer" or "St. Anthony's fire" refer to the gangrenous form of ergotism. The patron saint of ergotism victims was St. Anthony, and it was the Order of St. Anthony that above all undertook care of these patients. Until recent times epidemic-like occurrences of ergot poisoning have been recorded in most European countries and also in certain areas of Russia. With improvements in agriculture and with the understanding that was attained in the 17th Century that ergot-containing bread was the cause of ergotism, the frequency and extent of ergotism epidemics diminished considerably. The last great epidemic occurred in certain areas of southern Russia in the years 1926-1927.[2]

The first mention of a medicinal application of ergot, namely as an ecbolic (a medicament to precipitate childbirth), is found in the herbal of the Frankfurt city physician, Adam Lonitzer (Lonicerus), from the year 1582. Although ergot, as in the above citation, was used even since olden times by midwives, it was not until 1808 that this drug found entry into academic medicine, based on the work by the American physician, John Stearns, entitled "Account of the pulvis parturiens, a remedy for quickening childbirth." The use of ergot as an ecbolic did not, however, endure. The great danger for the child that lay above all in the uncertainty of dosage, which when too high led to uterine spasms, indeed became known early. From then on the use of ergot in obstetrics was confined to the stopping of post-partum hemorrhage (bleeding after childbirth).

After the assimilation of ergot into various pharmacopoeias during the first half of the 19th Century, the first chemical work toward isolating the active principles of the drug began. The numerous researchers that concerned themselves with this problem during the first 100 years did not, however, succeed in identifying the actual substances possessing therapeutic activity. In 1907, the Englishmen, G. Barger and F.H. Carr, were the first to isolate an active alkaloidal preparation that they named ergotoxine because it produced more of the toxic than therapeutic properties of ergot. (This preparation was not homogeneous, but was a mixture of several alkaloids, as I was able to show 35 years later.) Nevertheless, the pharmacologist, H.H. Dale, discovered for ergotoxine, besides the uterotonic effect, an antagonistic activity on adrenaline in the autonomic nervous system, an important feature in the therapeutic use of ergot alkaloids. Only with the aforementioned isolation of ergotamine by Stoll did an ergot alkaloid find entry and widespread use in therapeutics.

At the start of the Thirties, a new era of ergot research opened commencing with the determination of the chemical structure of ergot alkaloids in English and American laboratories. By chemical cleavage, W.A. Jacobs and L.C. Craig of the Rockefeller Institute of New York succeeded in isolating and characterizing the nucleus common to all ergot alkaloids. They named it lysergic acid. An important development, as much from the chemical as medicinal perspective, later brought the isolation of the specifically uterotonic, hemostatic principle of ergot, which was published simultaneously by four institutions, independently of one another, among them the Sandoz laboratories. It concerned an alkaloid of comparatively simple structure that was named ergobasine (syn. ergometrine, ergonovine) by A. Stoll and E. Burckhardt. By chemical degradation of ergobasine, W.A. Jacobs and L.C. Craig obtained lysergic acid and the aminoalcohol propanolamine as cleavage products.

I set as the first goal of my new field of research the problem of preparing this alkaloid synthetically through chemical linking of the two components of ergobasine, lysergic acid and propanolamine. The lysergic acid necessary for these studies had to be obtained by chemical cleavage of some other ergot alkaloid. Since only ergotamine was available as a pure alkaloid and was already being produced in kilogram quantities in the pharmaceutical production department, I wished to use this alkaloid as the starting material for my investigations. When I tried to obtain 0.5 g of ergotamine from ergot production and the internal requisition lay before Professor Stoll for his countersignature, he appeared personally in my laboratory. He reproved me angrily: "If you wish to work with ergot alkaloids, then you must familiarize yourself with the techniques of micro-chemistry. It is not acceptable that you consume such a large amount of my expensive ergotamine for your investigations."

In the ergot production department, along with ergot of Swiss origin from which ergotamine was obtained, Portuguese ergot was also extracted, which yielded an amorphous alkaloidal preparation that corresponded to the already mentioned ergotoxine first produced by Barger and Carr. This less expensive starting material I now used for the preparation of lysergic acid. The alkaloid obtained from the production department had to be yet further purified before it would be suitable

for cleavage to lysergic acid. During the purification process, I made observations that indicated that ergotoxine could be a mixture of several alkaloids rather than one homogeneous alkaloid. I will come to speak later of the far-reaching sequelae of these observations.

Here some remarks about the working conditions and techniques of that time seem appropriate. They should be of interest to the present generation of research chemists in industry who are accustomed to better conditions. Individual laboratories were considered to be a rare extravagance. During the first six years of my employment with Sandoz, I shared a laboratory with two colleagues. We three chemists each worked with an assistant, all in the same room, on three different projects: Dr. Kreiss on cardiac glycosides; Dr. Wiedemann, who joined Sandoz almost at the same time as I, on the leaf pigment chlorophyll; and I ultimately on ergot alkaloids. The laboratory was equipped with two fume hoods (compartments supplied with outlets), whose ventilation by gas flames was hardly effective. When we expressed the wish to replace these by ventilators, this request was refused by the chief with the reason that this type of ventilation had sufficed in Willstätter's laboratory.

During the last years of the First World War, Professor Stoll had been an assistant in Berlin and Munich to the world-famous chemist and Nobel Laureate Professor Richard Willstätter and with him had conducted the fundamental investigations on chlorophyll and the assimilation of carbon dioxide. There was scarcely a scientific discussion with Professor Stoll in which he did not come to speak of his revered teacher Professor Willstätter and his work in Willstätter's laboratory.

The working techniques at the disposal of chemists in the field of organic chemistry, in those days at the beginning of the Thirties, were in essence about the same as those that were already employed by Justus von Liebig 100 years earlier. The most important development achieved since then was the introduction of microanalysis by B. Pregl that made it possible to ascertain the elemental composition of a compound with only a few milligrams of substance, whereas earlier a few centigrams were required. All of the other physical-chemical techniques that are at the disposal of the chemist today, which have made research faster and more effective and have created entirely new possibilities, above all for the elucidation of structure, did not yet exist in those days.

For the investigations of *Scilla* glycosides and the first studies in the ergot field I still used the old separation and purification techniques from Liebig's day: fractional extraction, fractional precipitation, fractional crystallization, etc. The introduction of column chromatography, the first important step in modern laboratory technique, was of great value to me only in later investigations. For structure determination, which today can be conducted rapidly and elegantly with the help of spectroscopic methods (UV, IR, NMR) and X-ray crystallography, we had at our disposal in the first fundamental ergot studies only the old laborious methods of chemical degradation and derivatization.

LYSERGIC ACID AND ITS DERIVATIVES

Lysergic acid proved to be a rather unstable substance and its rebonding with basic radicals posed difficulties. In the technique known as Curtius' Synthesis, I ultimately found a process that proved useful for combining lysergic acid with amines. Utilizing this method I produced a great number of lysergic acid compounds. By the combination of lysergic acid with the aminoalcohol propanolamine, a compound was obtained that was identical to the natural ergot alkaloid ergobasine. With that, the first synthesis (that is, artificial production) of an ergot alkaloid was accomplished. This was not only of scientific interest as confirmation of the chemical structure of ergobasine, but also of practical significance because the specifically uterotonic, hemostatic principle ergobasine is present in ergot only in very trifling quantities. With this synthesis it now became possible to convert the other alkaloids existing abundantly in ergot to ergobasine, valuable in obstetrics.

After this first success in the ergot field, my investigations progressed further in two directions. First I attempted to improve the pharmacological properties of ergobasine by variations of its aminoalcohol radical. Together with my colleague, Dr. J. Peyer, a process was developed for the economical production of propanolamine and other aminoalcohols. Indeed, by substitution of the propanolamine contained in ergobasine with the aminoalcohol butanolamine, an active principle was obtained that even surpassed the natural alkaloid in its therapeutic properties. This improved ergobasine has found worldwide application as a dependable uterotonic and hemostatic remedy under the trade name Methergine® and is today the leading medicament for this indication in obstetrics.

I further employed my synthetic procedure to produce new lysergic acid compounds for which uterotonic activity was not prominent, but from which, on the basis of their chemical structure, other types of interesting pharmacological properties could be expected. The 25th substance in this series of lysergic acid

derivatives was lysergic acid diethylamide, abbreviated LSD-25 (LysergSäure-Diäthylamid) for laboratory usage, which I first produced in 1938. I had planned the synthesis of this compound with the intention of obtaining a circulatory and respiratory stimulant (an analeptic). Such stimulating properties could be expected for lysergic acid diethylamide because it shows similarity in chemical structure to the analeptic already known at that time, namely nicotinic acid diethylamide (Coramin®). During the testing of LSD-25 in the pharmacological department of Sandoz, whose director at the time was Professor Ernst Rothlin, a strong effect on the uterus was established. It amounted to some 70 percent of the activity of ergobasine. Furthermore, it was remarked in the research report that the experimental animals became restless during the narcosis. The new substance, however, aroused no special interest in our pharmacologists and physicians; further tests were therefore ceased.

For the next five years nothing happened with the substance LSD-25. Meanwhile, my work in the ergot field advanced further in other directions. By the purification of ergotoxine, the starting material for lysergic acid, I obtained the impression that this alkaloidal preparation was not homogeneous but was rather a mixture of different substances. This doubt as to the homogeneity of ergotoxine was reinforced when, in its hydrogenation (introduction of hydrogen), two distinctly different hydrogenation products were obtained, whereas the homogeneous alkaloid ergotamine under the same condition yielded only a single hydrogenation product. Extended, systematic analytical investigations of the supposed ergotoxine mixture led ultimately to the separation of this alkaloidal preparation into three homogeneous components. One of the three chemically homogeneous ergotoxine alkaloids proved to be identical with an alkaloid isolated shortly before in the production department which A. Stoll and E. Burckhardt had named ergocristin. Both of the other alkaloids were new. The first I named ergocornin, and the second, the last to be isolated having long remained hidden in the mother liquor, I gave the name ergokryptin (kryptos = hidden). Later it was found the ergokryptin occurs in two isomeric forms which are differentiated as α- and β-ergokryptin.

The solution of the ergotoxine problem was not merely of scientific interest but also of great practical significance. A valuable remedy arose from it. The three hydrogenated ergotoxine alkaloids that I produced in the course of these investigations, dihydro-ergocristin, dihydro-ergokryptin and dihydro-ergocornin, displayed medicinally-useful properties during testing by Professor Rothlin in the pharmacological department. From these three substances, the pharmaceutical preparation Hydergine® was developed, a medicament for improvement of peripheral circulation and cerebral function in the control of geriatric disorders. Hydergine® has proven to be an effective remedy in geriatrics for these indications. Today it is the most important Sandoz pharmaceutical product. Dihydro-ergotamine, which I likewise produced in the course of these investigations, has also found application in therapeutics under the trade name Dihydergot® as a circulation- and blood pressure-stabilizing medicament.

While today research on important projects is almost exclusively carried out as teamwork, the investigations on ergot alkaloids described above were conducted by myself alone. Even the further chemical steps in the evolution of commercial preparations remained in my hands, that is, the preparation of greater amounts of substances for the clinical trials, and finally the perfection of the first procedures for mass production of Methergine®, Hydergine® and Dihydergot®. This even included the analytical controls for the development of the first galenical forms of these three preparations: ampules, liquid solutions and tablets. A laboratory assistant, a laboratory helper, and later a second laboratory assistant and a chemical technician, were at that time my aides.

THE DISCOVERY OF THE PSYCHIC EFFECTS OF LSD

All these fruitful studies that developed out of the solution of the ergotoxine problem, only briefly described here, were unable, however, to fully push the substance LSD-25 into oblivion. A peculiar presentiment, that this substance could possess properties other than those established in the first investigations, induced me, five years after the first synthesis, once again to produce LSD-25 in order to give it again to the pharmacological department for further tests. That was in a way uncommon, for experimental substances were as a rule definitely stricken from the research program, if they were once found uninteresting from the pharmacological aspect.

In the spring of 1943, I then repeated the synthesis of LSD-25. This involved, as in the first synthesis, the production of only a few centigrams of this compound. In the final step of the synthesis, during the purification and crystallization of lysergic acid diethylamide in the form of a tartrate (tartaric acid salt), I was interrupted in my work by unusual sensations. I take the description of this incident from the report that I sent at the time to Professor Stoll.

> Last Friday, April 16, 1943, I was forced to interrupt my work in the laboratory in the middle of the afternoon and proceed home, as I was seized by a remarkable restlessness, combined with a slight dizziness. At home I lay down and sank into a not-unpleasant intoxicated-like condition that was characterized by an extremely stimulated imagination. In a dream-like state, with eyes closed (I found the daylight to be unpleasantly glaring), an uninterrupted stream of fantastic pictures of extraordinary plasticity with intense, kaleidoscope-like play of colors surged in on me. After some two hours this condition faded away.

The nature and course of this remarkable experience aroused the suspicion that it resulted from an external toxic influence and I surmised a connection with the substance with which I had just worked, lysergic acid diethylamide tartrate. I could indeed not rightly explain how I could have absorbed some of this material, since I was accustomed, because of the known toxicity of ergot substances, to meticulously neat work. But possibly a bit of the LSD solution had contacted my fingertips during crystallization and a trace of the substance became absorbed through the skin. In the event that LSD-25 had been the cause of the incident described, then it would have to be a substance of extraordinary potency. With the objective of getting to the bottom of this, I decided on a self-experiment. In order to be cautious I therefore began the planned series of experiments with the smallest quantity with which a definite effect could just barely be expected, considering the activity of the ergot alkaloids known at the time, namely with 0.25 mg (one-quarter of a thousandth of a gram = 250 micrograms) lysergic acid diethylamide tartrate.

The following is a translation of the entry for this experiment in my laboratory journal of 19 April 1943.

SELF-EXPERIMENTS

4/19/43 1620: 0.5 cc of ½ promil aqueous solution of diethylamide tartrate orally = 0.25 mg tartrate. Taken diluted with about 10 cc water. Tasteless.

1700: Beginning dizziness, feeling of anxiety, visual distortions, symptoms of paralysis, desire to laugh.

Supplement of

4/21/43 Home by bicycle. From 1800 – ca. 2000 most severe crisis. (See special report.)

Here the notes in my laboratory journal cease. The last words could be written down only with great effort. It was now already clear to me that LSD had been the cause of the remarkable experience of the previous Friday, for the altered perceptions were of the same type as before, only much more intense. Only with the greatest difficulty could I still speak intelligibly. I asked my laboratory assistant, who was informed of the self-experiment, to escort me home. On the way home by bicycle (during wartime automobiles were available only to a few privileged people) 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 travelled very rapidly. Finally, however, we arrived at home still safe and sound, and I was just still capable of asking my companion to summon our family doctor and to ask for milk from the neighbors. In spite of my delirious, bewildered condition, I could think clearly and effectively for brief periods – I thought of milk as a non-specific antidote for poisoning.

The dizziness and sensation of fainting became so strong at times that I could no longer hold myself erect and had to lie down on a sofa. My surroundings had transformed themselves in more terrifying ways. Everything in the room spun around and the familiar objects and pieces of furniture assumed grotesque, mostly threatening forms. They were in continuous motion, animated, as if impregnated by an inner restlessness. The neighbor woman who brought me milk – in the course of the evening I drank more than two liters – I scarcely recognized any longer. She was no longer Mrs. R., but rather a malevolent, insidious witch with a colored mask. 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, to put an end to the disintegration of the outer world and the dissolution of my ego, seemed a wasted effort. A demon had invaded me and had taken possession of my body, mind and soul. I jumped up and screamed in order to free myself from him, but then sank down again powerless on the sofa. The substance, with which I had wanted to experiment, had vanquished me. It was the demon that scornfully triumphed over my will. A dreadful fear grasped me that I was becoming insane. I was taken to another world, another place, another time. My body seemed to me to be without sensation, lifeless, strange. Was I dying? Was this the transition? At times I believed myself to be outside my body and then perceived clearly, as an outside observer, the complete tragedy of my situation. I

had not even taken leave of my family (my wife had travelled that day to visit her parents in Lucerne with our three children). Would they ever understand that I had not experimented thoughtlessly, irresponsibly but rather with the utmost caution and that such a result was in no way foreseeable? My fear and despair intensified, not only because a young family should lose its father prematurely, but also because I thought of having to break off unfinished my work as a research chemist, which meant so much to me, in the midst of fruitful, promising development. Also, the reflection emerged, full of acrimonious irony, that I was now to be compelled to leave this world behind prematurely through the effect of this lysergic acid diethylamide that I had brought forth into the world.

As the doctor stepped in, the climax of my despairing condition had already passed. My laboratory assistant informed him about my self-experiment, as I myself was not yet able to formulate a coherent sentence. He perplexedly shook his head, after I had attempted to refer to my supposed mortally-threatened bodily condition, for he could ascertain no abnormal symptoms other than extremely dilated pupils. Pulse, blood pressure and breathing were normal. He therefore prescribed no medicaments. He conveyed me into my bedroom and watched over me on my bed. Slowly I again returned from a weird, unfamiliar world to familiar everyday reality. The horror softened and gave way to a feeling of fortune and gratitude, the more normal perceptions and thoughts returned and my assurance increased that the danger of insanity was conclusively past.

Now I gradually began to enjoy the unprecedented colors and plays of shapes that persisted behind my closed eyes. Kaleidoscope-like fantastic images surged in on me, alternating, variegated, opening and then closing themselves in circles and spirals, exploding in colored fountains, rearranging and hybridizing themselves in constant flux. It was particularly remarkable how every acoustic perception, such as the sound of a door handle or a passing automobile, became transformed into optical perceptions. Every sound generated a vividly changing image, corresponding in form and color.

Late in the evening my wife returned from Lucerne. Someone had informed her by telephone that I had sustained a mysterious breakdown. Leaving the children behind with her parents, she had traveled home forthwith. I had by now already recovered myself sufficiently that I could relate what had happened.

Exhausted, I then slept and awoke the next morning refreshed with a clear head, even though still somewhat tired physically. A sensation of well-being and renewed life flowed through me. Breakfast tasted delicious and was an extraordinary pleasure. When I later walked out into the garden, in which the sun shone now after a spring rain, everything glistened and sparkled in a fresh light. The world was as if newly created. All my senses vibrated in a condition of highest sensitivity that persisted for the entire day.

This self-experiment showed that LSD-25 behaved as a psychoactive substance with extraordinary properties and potency. There was to my knowledge no other substance known that evoked such profound psychic effects in such extremely low doses and that engendered such dramatic changes in consciousness and experience of the inner and outer worlds.

It also appeared to me to be of great significance that I could remember the experience of LSD inebriation in every detail. That could be explained only by the fact that the recording function of consciousness was not interrupted even in the climax of the LSD experience, in spite of the profound breakdown of the normal world view. For the entire duration of the experiment, I was even aware of being in the midst of an experiment, but in spite of the recognition of my condition, I was unable to shake off the LSD world with every exertion of my will. Everything was experienced as completely real, as alarming reality; alarming, because the picture of the other, the familiar everyday reality was still fully preserved for comparison in the memory.

What I found further surprising about LSD was its ability to produce such a far-reaching, powerful, inebriated condition without leaving a hangover. Completely to the contrary, on the day after the LSD experiment I felt myself to be, as already described, in excellent physical and mental condition.

I was aware that LSD, a new active compound with such properties, would have to be of use in pharmacology, in neurology and especially in psychiatry and that it would arouse the interest of concerned specialists. But at that time I could not imagine that the new substance would later also come to be used beyond medical science as an intoxicant in the drug scene. Since in my first self-experiment I had experienced LSD in its terrifying, demonic aspect, it had to be the farthest thing from my mind that this substance could ever find application as a pleasure drug, so to speak. Also, I recognized the meaningful connection between LSD inebriation and spontaneous visionary experience only later after further experiments, which were carried out with much lower doses and under different conditions.

On the next day I wrote the aforementioned report to Professor Stoll about my extraordinary experience with LSD-25 and sent a copy to the director of the

pharmacological department, Professor Rothlin. As expected, my report first provoked incredulous astonishment. Instantly a telephone call came from the management; Professor Stoll asked, "Are you certain that you have made no mistake in the weighing? Is the stated dose really correct?" Professor Rothlin also called and posed the same questions. I was certain of this point for I had executed the weighing and dosage with my own hands. The expressed doubts were justified to some extent, for up until then no substance was known that had displayed even the slightest psychic effect in fraction-of-a-milligram doses. An active compound of such potency seemed almost unbelievable.

Professor Rothlin himself and two of his colleagues were the first to repeat my self-experiment, with only one third of the dose utilized by me. But even at that level, the effects were still extremely impressive and fantastic. All doubts in the statements of my report were eliminated.

NOTES

1. Those more deeply interested in ergot should refer to the monographs of G. Barger, *Ergot and Ergotism* (London: Gurney & Jackson, 1931) and A. Hofmann, *Die Mutterkornalkaloide* (Stuttgart: F. Enke Verlag, 1964). In the former book, history of the drug finds its classical presentation, in the latter the chemistry stands in the foreground.

2. The mass poisoning in the southern French city of Pont-St. Esprit in the year 1961, that has been attributed to ergot-containing bread in many publications, actually had nothing to do with ergotism. It rather involved poisoning by an organic mercury compound that was utilized for the disinfection of seed corn.