Abram Hoffer, MDF, PHD, FRCP(C)

Rose, my wife, was convinced that things do not happen by chance, that they are "beshared", meant to be. My good friend William Parsons who was the first physician to confirm our 1955 findings that niacin lowered cholesterol levels also uses the term "It was meant to be" when he talks about how my visit to the Mayo Clinic as a guest lecturer in 1956 and a chance conversation with Professor Howard Rome at our Saturday night dinner led to this very important work. For if the Mayo clinic had not undertaken that first study it might have never taken off to become the world's gold standard for lowering cholesterol and elevating high-density lipo protein cholesterol levels. Maybe they are both right. And it occurs to me that what happened in Saskatchewan in the spring of 1953 was beshared or meant to be. Whether it was meant to be or not to be it was one the most fortunate events in the history of psychiatry, at least, that is my view. In our niacin cholesterol discovery we were very fortunate to have William Parsons Jr[1] from a prestigious medical group like the Mayo Clinic corroborate our findings. Unfortunately in psychiatry no one equivalent to Dr Parsons has yet appeared.

One hot, dusty, summer day in Saskatoon, Saskatchewan, a strange constellation of events came together. I had been appointed Director of Psychiatric Research beginning in July 1, 1950. I would be given time to learn psychiatry. I had completed my Medical Degree, had my Ph.D. in Agricultural Biochemistry and one year general rotating internship and of course knew no psychiatry. That was a major advantage because I did not know enough about psychiatry to be convinced that one could not tackle such a serious topic as schizophrenia. There is a story about Irvine Langmuir, a very famous America physicist, He joined General Electric and was told he would be assigned the problem of the incandescent light bulbs that burned out too quickly. They forgot to tell him that this was not solvable, as they had told every previous new physicist. Langmuir solved it by evacuating the air from the bulbs so that the carbon filament did not burn up as quickly. He eventually became head of their research division. No one told me that the problem of schizophrenia could not be solved. The second condition was that I would be able to visit the major psychiatric research laboratories in Canada and the United States. After our tour, I was left with two main impressions. The first was that psychoanalysis was a bust and secondly that the only interesting things I heard were from Nolan DC Lewis, Chair, Department of Psychiatry, Columbia University and from Heinrich Kluver, Professor, University of Chicago who spoke about their research with mescaline. But I did not get any idea how we would start our research. Luckily I soon gave up an earlier idea to start psychosomatic research.

The second major event was Humphry Osmond's arrival. Humphry and his close friend and colleague John Smythies[2] had examined the psychotomimetic experience induced by mescaline and came to the conclusion that it resembled in many ways the experience induced in normal people by schizophrenia. They also discovered that mescaline is similar in structure to adrenalin and that

---

1 Parsons WB Jr Cholesterol Control Without Diet. The Niacin Solution, Revised, Expanded, Second Edition, Lilac Press, Scottsdale Arizona 85252-1356 2003

2 Osmond H & Smythies J Schizophrenia: a new approach J Mental Science 98;309-315:1952

led to their M hypothesis that perhaps the schizophrenic was suffering from an endogenous production of a compound like mescaline and somehow related to adrenalin. When they presented this view to the leaders in the field in England, especially at the Maudsley, they were rebuffed. Sir Aubrey Lewis was not impressed. Sir Aubrey knew that the problem was not solvable. Humphry was so frustrated that when Jane saw the Saskatchewan ad in the London paper she urged him to look into it. Humphry wanted to get as far away as possible from England and he thought that Saskatchewan was far enough. He thought that as clinical director he would be able to continue his research into mescaline.

During our first meeting Humphry told me about his research. I found it very interesting. It was the first new idea I had heard in psychiatry and it promised to provide us with a map to guide us in our research into schizophrenia. Schizophrenia was our major problem. Over half of our 5000 patients in our hospital system were schizophrenic. Humphry and I became close friends and colleagues that afternoon. At the end of the afternoon he left me his manuscript, which described his research and ideas for further research. This was published in the Journal of Mental Science, England in 1952. Our roles were clear. As Director of Research I would have to take on major responsibility to examine the hypothesis while Humphry had to undertake the very difficult task of bringing one of the worst hospitals in the world into the twentieth century. But from that moment we worked together and shared all our ideas very closely and with no hesitation. The idea Humphry and John Smythies had brought to me was excellent but we had to find a way to pursue it in our search for the schizophrenia toxin which we were convinced really was present in these unfortunate patients. We were convinced that they were physically sick.

There is a rule that chemicals with similar structure tend to have similar properties. I therefore decided to study the chemistry of every hallucinogen discussed in the literature. But before I did that Humphry and I laid down a rigorous definition of what was an hallucinogen. We excluded the anesthetics. Using our criteria I found about five natural compounds that were hallucinogens. We included pink or discolored adrenaline that in a few asthmatic medical students caused experiences that were similar to the mescaline experience. When I had finished gathering all the data I wrote down the formula of each one of these compounds except that of the discolored adrenalin. To my delight they were all indoles or like mescaline could theoretically be indolized in the body. In the meantime we applied to Ottawa for a small research grant to help us with our studies.

Our ideas were just as unpopular in Canada as they had been in England. When our proposal came before the committee it was rejected. Half of the members vetoed the idea and the other half supported it. The members who vetoed it were the three senior Professors of Psychiatry in Canada and the three who supported it were the scientific members of the committee. We were given that small grant only because the Chairman of the committee, Dr. C Roberts, sent it to Professor Nolan DC Lewis, Chair, Department of Psychiatry, Columbia University, for his opinion. After he read it he reported back that we must be supported not just for the two years we had requested but for many years. We got our grant not because our Canadian colleagues supported us but because one of the foremost US psychiatrists had the vision to see its potential. I had visited Dr Lewis when I was in New York in January of 1951 as part of my research tour of Canadian and US research establishments.

We organized the Saskatchewan Committee on Schizophrenia Research and had our first meeting in Saskatoon, in a small room at the back of the medical library. We spent the morning talking about schizophrenia, its clinical findings, its significance and how little we knew in treating it. Early in the afternoon I presented our hypothesis that indoles could be involved. After I had finished my talk Dr D Hutcheon asked us would we like to know what that pink stuff was in deteriorated adrenaline. We were electrified at his question. He told us it was adrenochrome. He was probably the only scientist in Canada who knew what it was. He had done research for his PhD with this compound in England with Professor Burns. It was an indole. Suddenly we had our adrenochrome hypothesis which was “Search the body of the schizophrenic patient for adrenochrome”, an indole derived from adrenalin. It was pink and similar in structure to the then known hallucinogens. The rest of the afternoon was very exciting as we discussed the implications and how we might tackle the problem. Professor V. Woodford told us that adrenochrome was an enzyme inhibitor of the Krebs cycle and since the B vitamins were involved in these reactions perhaps there was some connection. I did my PhD on thiamin in cereal grains and was familiar with vitamins and their properties. At this meeting the idea of using vitamins arose. Almost everything that originated from our research in Saskatchewan can be traced back to that original meeting and the adrenochrome hypothesis. If Humphry had not come to Saskatchewan it is likely that none of our research would have ever taken off and I would never have become orthomolecular.

These are the main events, which came together at our first meeting, an amazing series of coincidences.

1. A government, led by Premier T Douglas, interested in modernizing the mental hospitals and treating their patients better.
2. My presence with my peculiar background, my Ph D in vitamins and my ignorance of psychiatry.
3. Osmond’s presence with his unique hypothesis and interest in the hallucinogens. And the negative reaction he found in England.
4. Prof D Hutcheon who had studied adrenochrome.
5. No medical school. No one to tell us what we could not do.
6. At least 500 hundred miles away from the nearest medical school.
7. No committees on ethics or on research.
9. Total support from Dr G D McKerracher, Director of Psychiatric Services Branch, Department of Public Health.

The original M (for mescaline) hypothesis was developed by Osmond and Smythies. Hoffer Osmond and Smythies[3] formulated the adrenochrome hypothesis. After 1952 our research was based upon the hypothesis and its various derivatives and is a joint effort of Humphry Osmond and me. We each had our own areas of expertise.

---

3 Hoffer A, Osmond H & Smythies J. Schizophrenia: a new approach. II. Results of a year's research. J Mental Science 100;29-45: 1954.

The adrenochrome hypothesis of schizophrenia can be written as two simple equations[4].

Adrenalin → adrenochrome

Adrenochrome → schizophrenia

This hypothesis can only be supported if adrenochrome is made in the body, if it is an hallucinogen and if any substance which will neutralize its effect or inhibit its formation is therapeutic for schizophrenia. If these are not true the hypothesis is wrong. We therefore had to create research groups to test each of these sub postulates, a biochemical team to examine the chemistry of these reactions, a psychiatric team to study its hallucinogenic properties and a clinical team to test possible substances that would inhibit this reaction and be therapeutic. In our book *The Hallucinogens* we describe in detail our research.

Is adrenochrome made in the body?

After I discovered how to make pure crystalline adrenochrome our biochemical team led by Dr R Heacock studied its properties and the many reactions in which it participated. Dr Heacock became the world's expert on adrenochrome and its derivatives. Humphry was very pleased with the pure adrenochrome, beautiful crystals which were purplish red which formed a bright red solution which turned yellow when oxidized by the oxygen in the air. I gave him a small amount of the crystals. It was so stable it could be stored at room temperature. Humphry had a subtle sense of humor and enjoyed teasing some of our international biochemical colleagues. At meetings he would have the vial in his pocket. He would talk about adrenochrome and after the colleague had finished telling him that it could not be made stable, could not be crystallized and could not be made in the body because of its remarkable instability he would pull out the little vial of crystalline adrenochrome and show it to the discomfited authority. Before that the preparations were very unstable and the first one made for us had to stored at minus 40 Degrees Centigrade. But one day when I was in Vancouver at the faculty club University of British Columbia I had lunch with an English organic chemist and I discussed with him the problems with unstable adrenochrome. He replied that usually unstable organic chemicals were not pure. That was the answer. I suddenly realized that the silver used in converting adrenalin to adrenochrome had not been removed. I immediately wrote a note to my chemist (not Dr Heacock who had not yet joined us) to take the adrenochrome and to pour a solution of the adrenochrome through a carbon column to strip all the silver out. When I came home I went to the lab to see what had happened and discovered that my chemist had not done it. I was very angry. That afternoon he came to me and showed me the first ever pure crystals. Taking out all the silver had made it stable. Later we sent samples to Prof Mark Alchule of Harvard and McLeans Hospital in Boston and to Dr S Udenfriend of NIMH in Washington DC. Later when NIMH was so anxious to prove us wrong Dr Seymour Kety reported at one of the meetings I attended that Dr Julius Axelrod proved that adrenochrome could not be made in the body. He described with glee how his friend and colleague who later got the Nobel Prize for some of his other work had asked Udenfriend for a small

---

4 Hoffer A & Osmond H: The Hallucinogens. Academic Press, New York, 1967.

sample of our adrenochrome. He did not know how to make it himself. Udenfriend would not do so. That did not stop him and Axelrod stole some of the adrenochrome crystals from Udenfriend's laboratory. Kety thought that was hilarious.

Another laboratory developed an assay method for adrenolutin, a reduced derivative of adrenochrome in blood. Adrenochrome is recognized as a constituent of the body and its role in schizophrenia, Parkinson's disease, and other degenerative diseases and in heart dysfunction is being examined. This is described by Foster and Hoffer[5]. On a positive note it is an inhibitor of cell division and is being used for treating cancer.

Our laboratory also discovered kryptopyrrole in the urine of schizophrenic patients and to a lesser degree in other patients. We called it the mauve factor. I will discuss this later.

Is adrenochrome an hallucinogen?

Professor D Hutcheon synthesized our first few milligrams of adrenochrome and tested its toxic properties in animals. We were then ready to start our psychological studies. Humphry, our expert in hallucinogenic reactions, volunteered to be the first. I injected him subcutaneously with a few micrograms of adrenochrome. There was no reaction and about one hour later Humphry injected me with double that dose. Again there was no reaction and it was his turn to receive double my dose. Eventually we both reacted. Humphry developed minor changes similar to those induced by LSD. I became depressed and paranoid for two weeks. We then decided to be much more careful because of this prolonged reaction. The experiences are described in our book *The Hallucinogens*. A group in Czechoslovakia, using our method for making adrenochrome, conducted double blind controlled studies and confirmed our findings. Since then every animal given adrenochrome has shown toxic changes in behaviour from pigeons, rats, cats, to spiders and more.

Will compounds that inhibit adrenochrome formation or are antidotes to its toxic effect be therapeutic?

Humphry and I understood that most medical hypotheses turn out to be wrong. But we were desperate to have a better treatment for our patients. We hoped that the hypothesis was reasonably correct and considered how we might reverse the reaction in the body using substances that were safe and could be taken for long periods of time. Schizophrenia is a chronic disease and needs chronic prevention and treatment. At our first meeting of the Saskatchewan Committee on Schizophrenia Research Professor Vernon Woodford told us about the essential role B vitamins played in cell biochemistry. Vitamin B-3, nicotinic acid and nicotinamide, like all B vitamins, are extraordinarily safe. It prevents and treats pellagra and had been used sporadically to treat a number of other psychiatric problems, including depression, with some success. It is a methyl acceptor and theoretically could decrease the formation of adrenalin from nor adrenalin by decreasing the methyl groups available for adding to nor adrenalin. Later we found that nicotinic acid given intravenously to epileptic patients who had been first injected with

---

5 Foster HD and Hoffer A: The two faces of L-dopa: benefits and adverse side effects in the treatment of Encephalitis lethargica, Parkinson's disease, multiple sclerosis and amyotrophic lateral sclerosis. Medical Hypotheses 62; 177-181:2004.

adrenochrome reversed the abnormal EEG pattern induced by the adrenochrome. It was an effective antidote in these studies. We obtained supplies of pure nicotinic acid, nicotinamide, ascorbic acid. Vitamin B-3 is a component of the pyridine dinucleotide cycle which is involved in at least 200 reactions in the body. It takes part in oxidation-reduction reactions.

I think it is very important in testing new treatments that the first one comes out positive. This encourages the investigator to keep on trying. Our first case was positive. I had just received four fifty-pound barrels each containing the vitamins we wanted to test. I took some of that precious niacin to Humphry in Weyburn. As we were visiting the head psychiatrist came in and told Humphry that Kenneth was dying. A few catatonic schizophrenic patients died and at autopsy no reason was found. Kenneth had insulin coma and ECT, which had not helped. I suggested that we should give him the two vitamins I had brought with me, niacin, vitamin C. We rushed to the ward and found Kenneth in a coma. We promptly put in a stomach tube and poured in 10 grams of niacin and 5 grams of vitamin C. The next day he sat up and drank the mixture and thirty days later he was so well his parents insisted on taking him home. I tracked him down about fifteen years later and found that he could not remember having been in the hospital. He was a contractor and had been Chairman of the Board of Trade of his small community.

We treated 8 schizophrenic patients in pilot trials using 1 gram of vitamin C after each of three meals. Two were treated under my care at the Munro Wing, General Hospital, Regina, Saskatchewan and six by Humphry at the Saskatchewan Hospital, Weyburn. All eight responded with recovery. There were no toxic reactions. We then completed six double blind controlled, randomized trials between 1953 and 1960 on adults and two on children and showed that we doubled the two years recovery rate from 35 to 75 percent. These were the first double blind trials conducted by psychiatrists. It led eventually to orthomolecular medicine and psychiatry, which is beginning to flourish and is used world wide but only to a small degree.

Reducing substances will inhibit the oxidations of adrenalin to adrenochrome. Ascorbic acid has been used to stabilize adrenalin solutions but it does not do this very well. We did not conduct any double blind controlled studies with ascorbic acid but I use it routinely for all my schizophrenic patients and am convinced that it adds to the quality of the recovery. In 1952 a woman dying from breast cancer was admitted psychotic with a serious infected ulcerated breast area followings mastectomy. Her psychiatrist was going to start her on ECT for her schizophrenic psychosis. I asked him to wait for a few days and he agreed to wait for two days. I gave her ascorbic acid 1 gram every hour. She started on Saturday morning and on Monday when she had been given 45 grams her psychiatrist found her mentally normal and discharged her. Her ulcerated lesion had started to heal. In this case there is no doubt that the ascorbic acid cured her psychosis. She died 6 months later but remained mentally normal.

Other reducing natural compounds ought to have similar properties. This includes glutathione, N acetyl cysteine, and vitamin E. There are indications that they are helpful but no controlled trials have been reported. Recent studies show that schizophrenic patients have low blood levels of the antioxidants albumin, uric acid and bilirubin.

The adrenochrome hypothesis generated a tremendous amount of criticism and hostility from the establishment led by the National Institute Mental Health, Washington DC, and the American Psychiatric Association. They claimed

that adrenochrome could not be made in the body, that it was not an hallucinogen and that vitamin B–3 had no merit in treatment. These powerful institutes were wrong on all three counts but their opposition effectively suppressed research into this area for the last 30 years and only now is it beginning to come out of the shadows into which it was forced by these associations.

The following anecdote illustrates the American Psychiatric Association reaction to our niacin schizophrenia claims. In 1960 I was made a Fellow in the APA because that year Dr. Ewen Cameron was President of the APA, of the Canadian Psychiatric Association and the World Psychiatric Association. The APA was holding its annual meeting in Montreal. It was politically wise to upgrade Canadian members. But I played no role in the APA. In 1971 I received a letter from the President of APA advising me that a complaint had been registered against me by a member that I was promoting a treatment not recognized by the APA. Their committee on Ethics had instructed him to reprimand me and to ask me to cease and desist. This annoyed me but was not a threat as I did not have to be a member to practice. I wrote requesting the name of the complainant and reason for their complaint, which the APA would not give me. I pointed out that before they had judged me I should have had the opportunity of appearing before them and I demanded a hearing before their committee. The president replied that they were short of money and that the meeting could not be held for another year. Eventually they agreed to meet with us in Washington, DC. We met with their committee, which included their legal council. At the onset I opened the meeting by telling them that they had no jurisdiction over what we wrote or did and that the correct committee to have considered the issue was the committee on therapy and not the committee on ethics. They replied that they were wearing two hats. One hat was as the committee on ethics and the other hat was that they were simply our colleagues and were interested. I answered that in that case I only accepted the collegial hat and we were prepared to spend the whole day discussing our work with them. We debated all morning. It was obvious that they had not done any of their homework. They had not read our papers, and they knew nothing about vitamins but I did discover that the complainant, still unnamed, had objected to a paper I had written called Five California Schizophrenics[6] in which I gave the case histories of five patients, who having failed to get well on the best standard treatment, recovered when they are given orthomolecular treatment. At the end of the morning they asked us to wait for a few minutes while they would decide what to do. They came back much later and announced that they had not been able to come to a decision and would let us have it in two weeks. I still have not heard from them. They realized they had no case that their action had been inappropriate but they were intelligent enough not to give us an answer because had they announced that we had been ethical we could have used this against our critics. But APA did not forget and eventually in their infamous task force report destroyed for four decades the possibility of improved treatment for schizophrenic patients. I resigned my fellowship in the APA on the basis that its action had been inappropriate, unethical and an attempt to censure papers long after they had been published.

The adrenochrome hypothesis has been and still is very fruitful in developing new ideas in many fields in medicine, not only in schizophrenia.

---

6 Hoffer A: Five California schizophrenics. J Schizophrenia 1;209-220:1967.

Research with the hallucinogens

Dr John Smythies and Humphry began to correspond with Aldous Huxley. Aldous wanted to experiences the reacton to mescaline. We had not yet started to work with LSD. The American Psychiatric Association was holding its annual meeting in Los Angeles in 1952 and Humphry and I were there. Rose and I went to Hamilton,Ontario, picked up a new car through my brother-in-law Ed Vickar and drove down route number 66 to Los Angeles. Humphry had agreed to give Aldous some mescaline at his home after the meeting was over and Rose and I left the city. While we were there we had dinner with Aldous and Maria in their lovely home on one of the hills in Los Angeles. Also present was the great hypnotist Dr. Milton Erickson. The result of that experience is now known world wide and culminated in the two famous Huxley books. In his book *Doors to Perception* Aldous Huxley referred to our work in a little footnote. When Rose and I toured Great Britain in 1954 to visit research centers my name was already fairly well known just by that little reference.

I met Aldous several times after that but our relationship was primarily through Humphry and by correspondence. But through Huxley Humphry met Bill Wilson cofounder of Alcoholics Anonymous. I first met Bill W. at a New York meeting. He was sitting on my right and Humphry was on his right. Humphry and I were experimenting with leukoadrenochrome. This is a nontoxic reduced derivative of adrenochrome which Dr. R Heacock made in our laboratory. We wanted to study its properties. I cannot remember our reasoning but I am fairly certain we felt it was not an hallucinogen. We made up 3 milligram tablets and decided to use it sublingually. We tested it on a number of friends and colleagues and it either did nothing or had remarkable anti-anxiety properties. We even interested one of the major drug companies who made a batch using our formula and we ran a long series of tests. But they eventually would not take it on because its action was not predictable. Drug companies like drugs that always do something even if it is bad and undesirable for then they are sure it has activity. Our research is described in our book *The Hallucinogens.*

As we were sitting listening to the proceedings Bill W remarked to Humphry that he was very tense and we could see that he was not comfortable. Humphry promptly gave Bill one of these 3 milligram tablets. Bill placed it under his tongue and about 20 minutes later he turned to Humphry and said, “Now I know what you are talking about when you say you are relaxed.” It had a remarkable effect on him. We left him a substantial supply and he used it for several months but eventually we ran out and decided that we could not pursue it any further. Bill was once more in trouble with his moods. By then the three of us had spent many hours talking about our research, about Alcoholic Anonymous, about our use of LSD for treating alcoholics and our use of niacin which was beneficial for many of the patients. Bill was very impressed and he began to take 1 gram of niacin after each meal. Two weeks later he was free of his chronic tension and depression. He remained on this vitamin until he died. He was so enthusiastic that he began to hand it out to his friends in AA who also suffered many symptoms of mood disorder even though they were not drinking. One evening when I was visiting Bill at his hotel he suddenly produced thirty charts and he said that he wanted to show me the results of his research. I was surprised and pleased. He told me that he had given the niacin to 30 members of AA. After one month ten were. After two months another ten were well but the last ten had not responded. This was remarkably like the data I had been seeing. Bill W. outlined the value of our work with niacin as a treatment to members of the International Doctors in AA and that spread the idea throughout AA. Bill W had to do this outside of his

association with the International Board because they were violently opposed to Bill talking about vitamins[7]. One of the doctors on the board was violently opposed to the idea that niacin could be helpful but their main concern was that Bill was not a doctor.

Bill wrote two pamphlets called A Communication to A.A. Physicians, the first one in 1965(green cover). It had a limited circulation and was followed by the second one in 1968 (yellow cover) and the last one (white cover) by Drs. Edwin Boyle Jr, David Hawkins and Russell F Smith. Dr E Boyle was one of the first American physicians, then working at NIH, who helped plan the Coronary Drug Study which established niacin as the gold standard for lowering cholesterol levels. David Hawkins and Linus Pauling co authored the classical book *Orthomolecular Psychiatry*. The first clinical meeting on orthomolecular psychiatry was held in Long Island at Brunswick Hospital where he was in charge of the department of psychiatry. Russell Smith was clinical director of a large hospital in Detroit which specialized in treating alcoholics. In the introduction they wrote “Bill’s first inspiration had a profound impact throughout the world as evidence no only by the growth of AA itself and its affect on the field of alcoholism, but also its impact on the field of mental health in general, with AA type group therapy having become the foremost successful treatment modality. Bill and those close to him felt that he had a second inspiration when he recognized the importance of certain vitamins in returning the brain of some alcoholic to normal functioning. It was Bill who saw the far reaching implications of this discovery and brought it into awareness. This again is already having an impact on the entire field of mental health. The scientific importance of this discovery was recognized by the brilliant Nobel Prize Winning Professor, Linus Pauling, who termed this new development, Orthomolecular Psychiatry”

Because of Bill’s interest many AA doctors became powerful advocates of orthomolecular medicine. Bills ideas were rejected by the AA International Headquarters because not being a doctor he had no right to talk about vitamins. To help him the Huxley Institute of Biosocial Research gave him a small grant to pay for secretarial and other expenses. The AA doctors decided to test our claims, and without any demand for double blind controlled studies they created a committee. Each member of the committee tried niacin on themselves and the result was so beneficial they approved its use. Bill W. with his enormous influence was a major player in the development of orthomolecular medicine. He even resurrected the name Vitamin B-3 to replace niacin and niacinamide. While preparing his material for distribution he asked us whether there was another name for it. He did not think that using the current names would help. I remembered that in 1937 when I took my first class in biochemistry professor Roger Manning had discussed the vitamins in the order in which they had been discovered. The first was vitamin A, then vitamin B. But it turned out that vitamin B consisted of a number of vitamins. The first was thiamin, the second riboflavin and next in line was niacin, which was number, three. I suggested he call it vitamin B-3. This is now the accepted common term.

Bill Humphry and I were involved in an unusual series of events. Humphry was the Director of the Bureau of Research in Neurology and Psychiatry, New Jersey Neuropsychiatric Institute, Princeton, New Jersey and lived in one of the buildings while Jane remained in England. Whenever I went

---

7 Hartigan F: Bill W: A biography of alcoholics anonymous cofounder Bill Wilson St. Martins Press, New York 2000.

east I would slip down to Princeton and visit with Humphry for a few days. One evening we met with Bill at his hotel. I had invited the medical director of a company to come as well. This physician had asked me to be a consultant on a product for which they had the patents called NAD. It was specially formulated so that it was not digested and destroyed in the stomach. The company had been exploring it as a treatment for alcoholism and had applied for a patent but the data needed a lot of work. As soon as I learned that such a compound was available I became very interested, not in using it for alcoholics but in using it for treating schizophrenia. I had been dreaming about it for a long time but was never able to obtain any and the pure product taken by mouth was not active. The company agreed to provide me with adequate supplies.

The results on our patients were remarkable. It would produce the kind of response in several days that I would expect in several months from vitamin B-3. Eventually the company decided that the new patent would be very valuable and decided that I was no longer needed. We terminated our relationship. I sent them my final report and informed them that I would briefly refer to NAD in my talk to be given at the Waldorf Astoria on the mechanism of action of the hallucinogens. I was going to insert one sentence as part of my argument. I told the company. They wanted me to eliminate that sentence stating that it would be an infringement of their trade secret. They offered to pay me an enormous sum of money if I would keep quiet.

After visiting Humphry I went back to New York to prepare for my talk. That morning the company's lawyer called my hotel. He said he was with the Richard Nixon firm and wanted me to come to their office on Wall Street to discuss the matter. Fortunately I called the lawyer for the nascent American Schizophrenia Association instead. He advised me to come to his office, which was across the street from the Richard Nixon firm. My lawyer and the company lawyer debated the issue vigorously for half a day and eventually the company lawyer consulted with the company president who ordered him to withdraw the action. Had I gone to their office I would have been served with a subpoena forbidding me from giving my talk at the hotel. I discovered later that process servers were waiting at each entrance to their building. They really had no grounds for action. My lawyer then advised me to hide until my lecture. He said that the Nixon firm was honorable and would keep their word but there was nothing to prevent the company from seeking another firm and starting again. I immediately called Bill at his hotel and asked him to get me a room. I called Humphry who was coming in that afternoon and asked him to go to my hotel to pick up some things for me and bring it to Bill's hotel room. Humphry thought this was great. Then my lawyer escorted me down into some subterranean tunnel with a private door into the subway. Once I mingled with the crowds I was safe. In true spy fashion Humphry watched very carefully to see if he was being followed. He walked around the block which housed my hotel, the Roger Smith on Lexington Ave, three times before entering, its treatment and so on. I called John Osmundsen, Humphry's good friend who was senior science editor for the New York Times. I told John that I would be speaking and that there was a chance that I would be served with a subpoena before I could give my lecture. John promised he would be there. I think he was excited by the prospect I might be prevented from talking. John A Osmundsen was a journalist who had worked for the New York Times, Life and Look Magazines, on Public Broadcasting Television and many other institutions. He was senior science editor for the Times.

The next morning I delivered my talk. The following day the New York Times carried a full page story on the first page of the second section

describing my paper. That event marks one of the major turning points in orthomolecular psychiatry. For within a few days both Humphry and I were receiving enormous numbers of letters, first from the east coast, then from places further west and in a few days from the far east. I received as many as three hundred letters per week and had to hire another secretary to handle the load. Humphry and I kept these letters and later when we were organizing the American Schizophrenia Association we sent an appeals letter to all the people who had written to us. Within a few weeks we received about $70,000. This was a remarkable 6% yield. With this money we were able to establish the American Schizophrenia Association.

Bill W. was convinced that niacin should be an essential element of the AA program because it healed the members of their chronic tensions, depression, pain and fatigue. Probably these symptoms were the main reasons why they became alcoholics in the first place. He told Humphry and me about a home in Detroit called Guest House. This was a treatment center for alcoholic Catholic priests. It had been the private home of a very wealthy Detroit resident. We asked Bill whether it would be possible to visit Guest House. He arranged this and sometime later we and Bill were guests of this lovely home for a couple of days. The priests were all members of AA. One of the priests, a faculty member of Fordham University, was delighted to meet us. He had suffered from severe Migraine all his life but soon after he started taking niacin his migraine headaches were gone. He immediately became a convert and began to proselytize niacin even more than Bill W. He was called Father Niacin and they called me Doctor Niacin. I was more closely identified with niacin than Humphry was because I was more closely involved in the clinical trials. I was so well known in Canada that one day a letter arrived addressed to Doctor Niacin. The post office had re-addressed it. Guest House was described in the book Fannie Kahan wrote for both of us called *New Hope for Alcoholics*, University Books, New York, 1966.

Father Niacin later arranged a meeting at Fordham University to discuss the use of niacin in treatment. At that time we had an active schizophrenics anonymous group in Saskatoon. Two of their members came to the meeting and using the usual AA format told the audience about their own recovery from schizophrenia.

Osmond and Smythies first studied the mescaline experience because they wanted to know more about schizophrenia. After A Hofmann discovered lysergic acid diethylamide (LSD) studies of its hallucinogenic properties quickly spread through North America and Western Europe. It was used to mimic psychosis and was called psychotomimetic. That is how we first used it in Saskatchewan. Every volunteer who took it exposed himself to a transient short lived psychosis which could be terminated quickly when necessary by giving them niacin either intravenously when it worked more quickly or orally. Osmond was our senior expert in these studies. In order to study the phenomenon more intensively we called for volunteers, mostly University students. A few scientists also came, as did some journalists. They were much more enterprising than were psychiatrists but several of our psychiatric colleagues in Saskatchewan also volunteered. Volunteers were not paid. They were selected very carefully. After they volunteered they were examined carefully to make sure they were not schizophrenic as we did not want to give it to anyone who was or might become schizophrenic. We also excluded relatives who had first order schizophrenic relatives. After this examination they were advised to think about it for one month and if they still wanted to do it they would be accepted and given the experience in a controlled

setting, usually a hospital. This is probably why we had no major adverse after effects in the ten years or so that we were studying these compounds.

My first call for volunteers was made in Regina in 1953. Neil Agnew, research psychologist, was the first volunteer. We invited a number of junior members of the Regina Board of Trade to come to the hospital. I outlined what we were doing and why. To my amazement every one volunteered. From that study Agnew and I published a report with evidence that we could terminate the experience using either niacin or niacinamide.

Our policy was not to give these drugs to patients. Schizophrenic patients have enough trouble with their illness and we saw no need to make them worse. This is in sharp contrast to studies in New York state where LSD was given to schizophrenic patients. But eventually we became interested in treating our alcoholic patients. One day after a long, tiring and boring noisy flight from Saskatoon to Ottawa in an old North Star with Rolls Royce engines, Humphry and I arrived at our hotel exhausted and nearly deaf and I had a severe cold. Many years later I diagnosed myself more accurately as having had allergic reaction to milk and after that discovery have had no more colds. I could not sleep that night. At 4:00 AM it occurred to me that perhaps we might help alcoholics by giving them a controlled dts experience. In Alcoholics Anonymous it was accepted that hitting bottom was often a prerequisite but natural dts was dangerous with a high death rate. No drugs were then available. The problem with natural dts was that too often after they recovered they remembered little of what had happened. I thought that if we could induce a terrible, a real psychotomimetic experience, which might resemble dts, they would recover from the experience with a perfect memory of what happened and that this might get them ready to join AA. When Humphry awoke I immediately talked to him about it and we both agreed it was an idea worth trying. Humphry had several alcoholic patients in his hospital that had been committed. We wanted to induce a psychotomimetic transient experience using LSD. We found that we had to use 200 micrograms whereas normal volunteers responded to 100 micrograms.

After Humphry had treated about five patients he told me that they were having difficulty giving their patients this terrible experience. Some of the patients were having an unusually pleasant experience. This had occurred so frequently that Humphry concluded it was a new phenomenon and that it needed a name. He had given Aldous Huxley mescaline in his home in California in 1953. I think watching what happened to Huxley and his own experience with mescaline and LSD sensitized Humphry to this different type of experience. Almost everyone believed that LSD made everyone psychotic. Humphry finally concluded that the term psychedelic best expressed what was happening. He announced the name and described the experience in his paper to the New York Academy of Science in 1957. Since then he is best known internationally for the name and for having been the pioneer.

Psychedelic therapy was taken up very quickly by many centers and flourished until governments shut it down. Humphry and I advised our government not to do so but they preferred to listen to the advice of our naysayers and critics who had never studied the phenomenon. The result was that we all stopped treating our alcoholics this way. It became impossible to get LSD and to use it responsibly except of course on the streets where it has always been available and not in the pure form that Sandoz provided. But it is not fair to Osmond to consider only his work with psychedelics. His most important work originated from his original idea that he seeded in the hospitable research soil in Saskatchewan in 1952. This was the impetus for

the major research we all did culminating in orthomolecular psychiatry, the new paradigm. The literature on psychedelics is vast and growing quickly and the BBC and the National Film Board, Canada, made videos describing its history. It is slowly coming back into use in the United States, against immense opposition.

Our LSD studies in Regina created an opportunity to study the Native American Church of North America. In the mid 1950's while I was still working at the General Hospital in Regina, Sask., I got a call from the local paper The Leader Post. The reporter told me that the CCF MP from Prince Albert had asked a question in the House of Commons in Ottawa about the Native American Church of North America and that the Minister of Health had replied that the government of Canada was going to take immediate action to deal with this dangerous practice of these Indians. He asked me what my opinion was about this. I knew about the church in the United States whose members used the Peyote Button (which contains mescaline) as part of their sacrament and the history in the United States of trying to suppress this religion and I was in agreement with the Native Americans that this practice was not dangerous and should not be harassed nor suppressed. I replied to the reporter the action of the government was nonsense. The next day I was quoted all across Canada, giving me the first taste of notoriety for speaking what I considered to be the truth. At the same time I wrote to Tommy Douglas in Ottawa complaining about his member Mr. Max Campbell for raising the issue and I was not very complimentary to Mr. Campbell. The government did not do anything but I doubt my statement had much to do with that. They probably had second sober thoughts about the issue. Later Mr. Campbell and I became good friends. He had been given a loaded question by the Department of Health who wanted to suppress the use of Peyote and they needed someone to ask the question for which they had already prepared their answer. Max realized he had been used.

At the same time I learned that the Red Pheasant tribe was members of this church. I thought this would be a marvelous opportunity to learn more about it from first hand observation. Humphry was equally interested. I wrote to their headquarters in the United States. Six months later Mr. Frank Takes Gun answered and wanted to know why I was interested. He thought at first that I was working for the federal government that I might be a spy. I reassured him that my interest was entirely research and had nothing to do with the government views. He agreed and sometime later the Native American Church of North America invited me to come and participate at one of their all night Saturday sessions. Humphry and I planned this carefully. About four of us went including Humphry, Duncan Blewett, Professor of Psychology, Dr T Weckowitz and I. I decided to be an observer with a tape recorder. Humphry volunteered to take the peyote and to become a member of the group. We spent the night with them. I was not as observant as I should have been and slept part of the time but Humphry remained wide awake. He found the experience fascinating and very educational. I do remember that at midnight the Chairman Frank Takes Gun said that being midnight when all the whites were asleep was a good time to pray to God for he would be more apt to hear them. The total experience reinforced my earlier conclusion that the way these native Canadians practice their church using Peyote was benign, safe and certainly very valuable to them. Later my sister Fannie Kahan studied the literature on the use of the hallucinogen Peyote, summarized it and wrote up the entire experience with chapters by Osmond, by me, by Blewett, but we have not been able to find anyone willing to publish the result of that interesting night.

To test the therapeutic efficacy of any treatment, one must have ways of determining whether there has been a change and how much. This can be done

by clinical examination but this is notoriously incomplete and inexact and one should use more objective tests. Osmond and I asked Dr N Agnew to cull the psychological literature and pull out any available tests that we could use. After several years of investigation and a lot of money Agnew finally concluded that there were no psychological tests. During our discussion he remarked that the reason was that psychiatrists could not agree on diagnostic criteria nor how to use them. In other words there was too much diagnostic inconsistency for any psychological test to be developed. He was of course correct. His conclusion forced me for the first time to think about the process of diagnosis. I came to the conclusion that it was simply a matter of asking the correct question which could be answered yes or no, a binary system. This being true one could do as well by using cards containing the correct questions which would be scored into true or false, Yes or No categories. Humphry agreed that this was a good idea, and drawing upon our accumulated knowledge of the schizophrenic experience, drafted 145 questions that we thought would explore the experential world of our patients. This became the HOD test, the Hoffer Osmond Diagnostic test[8]. It fully fulfilled our expectations. We tested thousands of patients at all of our units and found that it picked out schizophrenic patients from all other diagnostic groups very efficiently, very simply and was very acceptable to our patients. We are not psychologists and therefore did not follow the usual psychological methods but later when Humphry was in Princeton he and his psychologist Dr. M El Meligi developed a much more sophisticated test they called the Experiential World Inventory (EWI). This was much superior. We gave thousands of my patients both of these tests and eventually if my diagnostic skills were not adequate and if the HOD did not help I used the EWI, which was very helpful. Unfortunately the EWI was never used on a large scale while the HOD was avoided by psychologists and psychiatrists. The HOD test is very useful in evaluating progress with treatment. There was a high correlation between high HOD scores and the presence of the mauve factor and response to vitamin treatment. Irrespective of the clinical diagnosis, patients with high scores and mauve factor in their urine generally responded very well to orthomolecular treatment. Many chiropractors in Southwest United States are using the HOD test in this way.

Does inhibiting the reaction to adrenochrome help patients?

We hoped to inhibit this reaction by slowing down the formation of nor adrenalin from which adrenalin is made in the body by adding methyl groups and by adding antioxidants (reducing compounds such as vitamin C) to slow the oxidation of adrenalin to adrenochrome. All the natural antioxidants ought to be effective but glutathione should be especially effective because it neutralizes adrenochrome. Vitamin B-3 increases the natural production of glutathione in the body. We looked at the reactions that led to adrenalin from noradrenalin and on to adrenochrome. We thought that nicotinic acid, vitamin B-3, which is a methyl acceptor, might decrease the methylation of noradrenalin to adrenalin. This vitamin also had many other advantages. It was available, was safe, could be taken forever and had been used in large doses to treat chronic pellagra when the usual small vitamin doses had failed to do so. It had one major disadvantage. It could not be patented. We conducted the first double blind controlled prospective randomized therapeutic trials and showed that we doubled the 2-year recovery rate when

---

8 Hoffer A, Kelm H & Osmond H: The Hoffer-Osmond Diagnostic test. RE Krieger Publishing Co. Huntington, New York, 1975.

this vitamin was added in optimal doses to the treatment program of these years, mostly ECT. This became the basis of orthomolecular psychiatry. After Linus Pauling joined us and published his paper in Science in 1968, this led to orthomolecular psychiatry.
The data which shows how effective this treatment is voluminous and widely published but still ignored. There are no drug companies pushing niacin, as it cannot be patented.

An offshoot of our niacin studies was the discovery by Altshul, Hoffer and Stephen[9] that this vitamin in large doses lowered cholesterol levels. Since then it has been found that it also elevates high density lipoprotein cholesterol and lowers triglycerides as well as lipo A, all very important. It normalizes blood lipid levels and is the gold standard and much superior and safer than the statins. This 1955 niacin report of the effect of niacin on cholesterol is considered the first major paper to initiate the new vitamin paradigm in medicine. The old paradigm gradually being replaced is the vitamins-as-prevention paradigm. It is being replaced by the vitamin-as-treatment paradigm. Niacin is the first vitamin released by the FDA in large or mega vitamin doses. They looked upon it as a drug for lowering cholesterol.

Orthomolecular treatment has expanded much beyond its first use in treating schizophrenic patients. It is a full scope treatment for every aspect of psychiatry and medicine. In my opinion orthomolecular theory and practice is the major contribution that has come from our Saskatchewan research.

Involving the community

One of the first conclusions made by Dr DG McKerracher in the late 1940's was that the mental hospital had been moved too far from the community from which these patients came. He established the Saskatchewan Plan for building smaller hospitals all across the province so that no one need travel more than 50 miles to visit their relatives. Humphry and I considered this a very good plan and had a small part in its development. But we went somewhat further and started to involve the public by creating the American Schizophrenia Association, later called the Huxley Institute for Biosocial Research, and following that in Canada the Canadian Schizophrenia Foundation now known as the International Schizophrenia Foundation. These associations were created to provide accurate information about the disease and its treatment. We are the only organization in North America still doing so. We support the best treatment available, which is orthomolecular. Humphry and I were founding members; we were on the board and officers at various times. We also traveled together a lot looking for funds to further our research and went to meetings together. This gave us ample time to talk about our mutual activities and interests.

In 1957 we flew to Zurich, Switzerland, to participate in the Second International Congress of Psychiatry. Dr C Jung was the Honorary Chair of our section. The Collegium Internationale Neuro-Psychopharmacology was formally inaugurated at that meeting with Professor E Rothlin the first President.

---

9 Altschul R, Hoffer A & Stephen JD: Influence of nicotinic acid on serum cholesterol in man. Archives Biochemistry Biophysics. 54; 558-559: 1955.

Humphry and I were there as founding members. It was an interesting meeting. We met Dr Jung, also spoke to Professor Rothlin who advised us both to spend as much time as possible on our research and as little as possible traveling to meetings. Those were heady years and investigators were spending a lot of time traveling to each other's meetings using travel funds from each other's grants and saying the same thing over and over. Rothlin's advice was very good and we did take it. On the way home we visited Dr. Tiselius, Nobel Laureate for his work with chromatographic analysis. He was encouraging. We had an hypothesis that could be used. Many had asked him to become involved in the search for the schizophrenic toxin and in every case he would ask his biochemical staff and how do we start. How does one look for one of perhaps 50,000 compounds that might be present in the body. No one had ever discussed with him any way of finding out what might be the schizophrenic toxin. Humphry and I were encouraged by this visit.

Dr Donald Johnson and *How to Live With Schizophrenia*

Involving the community also meant providing it with information. This is why we wrote our book *How to Live with Schizophrenia*[10]. This was published by Dr. Donald Johnson MP, conservative member. When I was searching for all the known hallucinogens I ran across a pamphlet written by Dr Johnson called *The Hallucinogens*. It was a review of the effects of hash. I wrote to Dr Johnson and he immediately sent me a copy. This started our correspondence and later when I was in England he invited me to have tea with him in the members' lounge overlooking the Thames. His story was intriguing. He had given up the practice of medicine to take law. Later he gave that up as well and became an innkeeper. In the meantime he had run for parliament on several occasions for the conservative party and had not won election. One day at the inn a wine salesman offered him some wine to taste. He broke one of the cardinal rules of tasting wind from a stranger; never drink from an open bottle. This time he did. As he was about to take his first sip his wife came in and he offered her a drink. She took about one third and he finished the rest. That evening he became psychotic while his wife felt ill. She called for help and he was committed to a mental hospital. On admissions he was told by the admitting psychiatrist that he had schizophrenia and that he would never leave hospital. But Dr Johnson recovered in a few days without medication. The current drugs were then not available. The hospital would not release him until he slipped notes under his door which eventually found their way to his lawyer. The whole episode puzzled him because he'd never been ill before and could not believe that he had a short lived episode of schizophrenia. So he began to search the literature and eventually concluded that the wine salesman had placed a hallucinogen in his wine. He reported this to the police but they ignored the whole episode. He then gave up his inn, became a book publisher and ran for parliament and this time he was elected. During our talk he suddenly asked me if I would write a book for him. Surprised I asked him what about. He replied about anything. I replied that I had nothing in mind but then it occurred to me that we did need a book directed to schizophrenic patients and their families. It was almost impossible for families to find any information except the old text books

---

10 Hoffer A & Osmond H: *How to Live With Schizophrenia*. University Books, New York, NY, 1966. Also published by Johnson, London, 1966. Written by Fannie Kahan. New and Revised Ed. Citadel Press, New York, NY, 1992. Revised. New Title *Healing Schizophrenia* CCNM Press, Toronto, ON 2004.

which describe only the worst chronic cases and are very discouraging. I was reminded of a young man who had been treated at University Hospital in Saskatoon for schizophrenia but had not been told his diagnosis. After discharge he was followed by his family doctor. During his first follow up interview his doctor was called out and the young man looked up his file and read that he had schizophrenia. He did not know what it meant but when he got home he looked it up in the dictionary and read that it was a hopelessly incurable chronic disease. He shot himself with a rifle narrowly missing his heart. In hospital I saw him, started him on vitamins and explained what the condition was. Had he been given proper information at the hospital in the first place he probably would not have made the attempt on his own life. I told Dr. Johnson that I would discuss this with Humphry Osmond and let him know. It occurred to me that Humphry and I would write the first drafts of this book and that I would ask Fannie Kahan, my sister, to rewrite it. I asked her if she would be interested in writing it so that the average 12 year old could understand. When I told my family what I was planning, John suggested that we use the title "How To" because How To books were becoming popular. Humphry and I divided the book into sections that we would each do and after we were satisfied with the work we turned it over to Fannie and she rewrote the entire book. We wanted to have three author on the title but DR Johnson adamantly refused saying that he wanted only doctors as authors. I was sorry about this but had I insisted there would not have been any book. Since then this book has been republished several times and present sale must be over 100,000. It was never a best seller but did sell slowly and steadily and it did save many people's lives. The present version is mine alone and is called *Healing Schizophrenia*. Humphry was not able to write after his stroke over 10 years ago. My sister Fannie Kahan wrote the final version of this book but the publisher would not publish with her name on the cover. The royalties were split three ways. This was one of the first medical How To books and the first one written for patients and their families. It has sold since then at a slow but steady pace. The new revised edition is now available. We also worked together to create the Journal published by the Canadian Schizophrenia Foundation, now the International Schizophrenia Foundation and we shared authorship for many papers and books. Humphry's writing skills were invaluable and I learned a tremendous amount from him. We also organized the American Schizophrenia Association, later renamed the Huxley Institute of Biosocial Research. The HIBR trained hundreds of doctors who attended weekend meetings all across the United States.

Huxley Institute of Biosocial Research

About 1959 Humphry called me from Princeton. A middle aged man landed on the hospital grounds in a helicopter. He told Humphry about his son who had been schizophrenic from childhood. He had become wealthy entirely on his own effort, taking law while driving a cab and eventually he bought the furniture factory where he had once been a worker. Humphry told him to call me and soon he did. He wanted me to take his son in for treatment. I had a few beds of my own and in those years we were not so desperately short of beds as we are today. As I was working full time for the Government I could not charge him. He insisted he would have to give me something and soon a set of outdoor furniture arrived made in his factory. Forty-five years later it is still in excellent shape even though it has been outdoors in the winter and summers in Saskatchewan and since 1976 in Victoria BC.

Humphry had been corresponding with Mrs. Miriam Rothschild in London. I met her in 1954 when Rose and I were on our Rockerfeller Foundation sponsored

tour. Before driving west to Wales we had dinner with her and with Dr. Dereck Richter. Dr Richter had once considered the indole theory of schizophrenia but had concluded that not enough indoles could be formed in the body. He had also looked at adrenochrome and had concluded that it was not made in the body. Mrs. Rothschild was a biochemist who was studying the biochemistry of insects. Humphry had written her about the need for an organization for schizophrenic patients that would do for them what the cancer society was doing for cancer patients. Mrs. Rothschild replied that if we could organize an International Schizophrenia Society she would ask her brothers to contribute. Following up this idea we spoke to the father about organizing such a society in the United States. He agreed and gave us 25,000 dollars with which to start. Fortunately about that time a New York investigative journalist, Cal Samra, had contacted me and on learning about the vitamin program became very interested. He was very intelligent and a very good writer. Humphry and I decided that he would be our first director, the father would be the Chairman of the Board of the American Schizophrenia Association and both Humphry and I would be founding members of the board. Cal Samra knew a law firm in New York and they agreed to act for us pro bono. One day Humphry and I and Cal met in New York in a walk up apartment with our lawyer. We drafted our constitution and we were on our way.

Cal eventually became president and put himself wholeheartedly into our association. We published a newsletter which he edited and wrote and we began our first drive for money. We sent a letter to every person who had ever contacted Humphry and me and to our amazement took in about 70,000 dollars. We were at last firmly launched. We held our second scientific meeting in Ireland. Our benefactor owned a castle near Shannon Airport and offered it to us for the meeting. But several years later we and our benefactor parted but on condition that the 25,000 he had given us be given to a Psychiatric Hospital for a biochemical study which I considered totally wasteful but we had no choice. We were on our own. That year I invited Mr. Ben Webster to join us as our treasurer. Later we became the Huxley Institute of Biosocial Research with the approval of the Huxley family. Humphry was a very active member on our board and at our meetings until the HIBR collapsed some years ago due to lack of interest and money. This was one of the objectives of the NIMH who considered us a major irritant and a burr under their saddle. NIMH had US government money and the United States psychiatric establishment depended on them for their research monies.

Our executive director, after Cal Samra left, arranged for some of us to meet with a small representation from NIMH. We met in Washington, DC. On our side we had Linus Pauling, Humphry Osmond, our executive director and for the NIMH Dr Morris Lipton, who had chaired the remarkable Task Force of the American Psychiatric Association which had roundly denounced our work and had published a most remarkable document, remarkable for its totally dishonest account of what we had been doing and claiming. The most rabid republican in the United States would probably have done a more honest job in attacking the Democratic Party. Humphry and I replied to this corrupt document but few paid any attention[11]. It became the holy writ, the bible, for the anti orthomolecular movement.

---

11 Hoffer A and Osmond H. Megavitamin Therapy. In Reply To The American Psychiatric Association Task Force Report on Megavitamin and Orthomolecular Therapy in Psychiatry. Canadian Schizophrenia Foundation, August 1976.

The morning was not pleasant. Seymour Kety and Dr. Loren Mosher were present. Without any notice Dr. Kety introduced our benefactor who got up to talk about how my treatment had not helped his son. In fact after I had him with me for a month he was very much better and his mother was very pleased with the outcome. But our benefactor could not find any physician who would carry on the treatment after his son came home and he slowly relapsed. I could not describe the case because I had been his doctor. Kety had used our benefactor as a tool and I suspect had been instrumental in the split that occurred between him and the rest of our board of the ASA. Morris Lipton maintained that he was a biochemist because he had done research work in the laboratory where Elvehjem had proved that niacin was vitamin B-3. But he knew little chemistry and when he made a statement that even a first year chemistry student should not have made, Pauling, the world's greatest chemist, the two-time Nobel winner, the first for chemistry, roundly berated him for his ignorance. Mosher was equally hostile. He told us that in his view even if every psychiatrist in the United States used orthomolecular treatment he would still not believe it had any value. Mosher was Director of the Schizophrenia Section of NIMH. This I thought was very appropriate since he did not believe such a disease existed and he was totally opposed to any form of chemical intervention. This meeting did not resolve any of our difficulties and NIMH remained solidly opposed to everything that we did. Lipton told me privately that he would never publish any paper of mine no matter how good it was and as Associate Editor of the *American Journal of Psychiatry* he remained true to his word. Recently Dr. Mosher told one of my acquaintances that the only reason I had gotten good results was because I had carefully preselected only those patients who would have gotten well anyway. I know no one so skillful that he could preselect the ones who were going to get well. And our placebo control group, which is supposed to eliminate bias, showed that only one third of this group was well two years later. This was the unreasonable and hostile criticism that was applied to our work.

The Mauve factor (kryptopyrrole) test[12], [13]

We were treating alcoholic patients with the psychedelic experience using LSD. It occurred to me that in the same way that LSD reproduced some of the characteristics of schizophrenia as was pointed out by Osmond and Smythies that there might be a similar change in their biochemistry. We tested this idea by collecting their urine before and after they had taken the LSD. In the first patient we tested we found a new biochemical on the paper chromatogram that had not been present in the base line sample of urine. After we showed it was not LSD, we studied the urine of a large number of patients in our three research hospitals and found that it was found chiefly in schizophrenic patients but to a smaller degree in other patients. It was found rarely in normal subjects but was found in patients under severe stress from cancer. Because it stained mauve we called it the mauve factor

---

12 Hoffer A & Mahon M: The presence of unidentified substances in the urine of psychiatric patients. J. Neuropsychiatry 2; 331-362: 1961.

13 Hoffer A & Osmond H: The relationship between an unknown factor (US) in the urine of subjects and HOD test results. J Neuropsychiatry 2; 363-368:1961.

and the condition in which it was found we called Malvaria[14]. Later we identified it as a kryptopyrrole but that was only partially correct and recent research is revealing its true identity.

After ten years at Weyburn in Saskatchewan, Dr Osmond became Director of The Bureau of Research in Neurology and Psychiatry in Princeton. This bureau had been organized by Dr Nolan DC Lewis, the great American psychiatrist, Chair, Columbia University. Dr CC Pfeiffer in Osmond's research group developed a quantitative test which has been very fruitful. Today the study of this mauve factor has been expanded as it is found in nearly half of the cases of infantile autism. It is a marker for oxidative stress. It binds both zinc and pyridoxine and produces a double deficiency.

We found that patients who excreted this factor resembled our schizophrenic patients more than they did non-schizophrenic patients. They scored in the schizophrenic range using the HOD test and responded well to megavitamin therapy. This suggests that we are really looking at a homogeneous disease. Carl Pfeiffer called it pyrroluria.

A good hypothesis in science is very rare. By good I do not mean correct. Hypotheses tend to be evanescent and are modified as new information accumulates. Good means that it directs useful research and leads to useful discoveries. The original toxin M hypothesis by Osmond and Smythies is one of these rare good hypotheses. Newer and better ones will replace its follow up hypothesis by Hoffer, Osmond and Smythies.

The New York Times summarized an amazing paradigm shift in hypothesis about heart disease. The current belief is that plaque is responsible and for that reason mechanical methods have been used to remove the obstruction, replace vessels, and enlarge them with balloons and to use stints. But evidence is developing that these methods are no better in increasing longevity than are methods for lowering cholesterol. Had the investigators used niacin as the cholesterol-lowering agent they would have found a significant improvement compared to the surgical techniques. In the New York Times Sunday March 28,2004, under the title The Limits of Opening Arteries the editorial laments "This profound change in thinking about cardiovascular problems makes us yearn for the day when there can be much wider testing of one therapy against another to identify those that work best from those that may be oversold." In the same edition Thomas L Friedman concludes that 9/11 was not a failure of intelligence. It was a failure of imagination. If these two views had been followed orthomolecular medicine would by now be well established. Due to the lack of imagination and failure to run comparison trials we are still struggling to have it established.

Go back to Orthomolecular.org – Dr. Hoffer's page

14 Hoffer A & Osmond H: Malvaria: a new psychiatric disease. Acta Psychiatrica Scandinavica 39; 335-366:1963.