

Remembering Humphry Osmond: A Pioneer in Orthomolecular Medicine

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Humphry Osmond
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Humphry Osmond, good friend and colleague for the past 52 years, died quietly at home surrounded by his family. Since then several obituaries have appeared, some of what I have contributed to. He was featured in the *National Post*, Toronto, the *Washington Post*, the *New York Times*, the *LA Times*, and the *Guardian*, on BBC radio and in Google under Images. Of course some of the information appeared in dozens of smaller and less notable news media. Collegium Internationale Neuro Psycho-pharmaco-logicum (CINP) newsletter will also carry one.

This report will not be another obituary. I am writing not to mourn his death, as we all do, but to celebrate his half century of creativity and scientific productivity. Humphry changed my life, the life of thousands of schizophrenic patients who are today well; his work is beginning to change the entire field of

psychiatry and medicine. What follows is an account of the relationship between the two of us.

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. If the Mayo clinic had not undertaken that first study, niacin might never have taken off to become the world’s gold standard for lowering cholesterol and elevating high-density lipoprotein cholesterol levels. Maybe Rose and Bill are right. It occurs to me that what happened in Saskatchewan in the spring of 1953 was *beshared*. Whether it was meant to be or

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not, it was one of the most fortunate events in the history of psychiatry, at least 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.

Saskatchewan, 1950s

One hot, dusty, summer day in Saskatoon, Saskatchewan, a strange constellation of events came together. I had been appointed Director of Psychiatric Research beginning July 1, 1950 with two conditions. The first condition was that 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 area as schizophrenia. There is a story about Irvine Langmuir, very famous American physicist, who 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: that psychoanalysis was a bust and that the only interesting things I heard were from Nolan 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 next major event was Humphry Osmond's arrival. The chief of Psychiatric Services Branch, Saskatchewan, had been in England interviewing psychiatrists for employment in Saskatchewan. After talking to 70 he was finished, tired and ready to come home but as he was leaving the office of the Saskatchewan Commissioner in London he was told that there was one more he would have to see. Eventually and very reluctantly he said he would see him for ten minutes. He and Humphry finished their conversation three hours later and he hired Humphry to be clinical Director of the Saskatchewan Hospital at Weyburn.

Humphry and his close friend and colleague, John Smythies,¹ 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 led to their M hypothesis that perhaps the schizophrenic person 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, he knew that the problem was not solvable. Humphry was so frustrated that when his wife 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 the 5,000 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. 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. Before I did that Humphry and I laid down a rigorous definition of what was an hallucinogen. We excluded the anaesthetics. Using our criteria, I found about five natural compounds that were hallucinogens. We included pink or discoloured 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 discoloured 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. Roberts sent it to Professor Nolan 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 American psychiatrists had the vision to see its potential. Fortunately, I had visited Dr. Lewis when I was in New York in January, 1951, as part of my research tour of Canadian and USA research establishments.

Adrenochrome Hypothesis

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. Humphry and I planned this very carefully. We had to get our colleagues really interested in a subject about which they knew nothing. 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. Hutcheon asked us if would we like to know what that pink stuff was in deteriorated adrenaline. We were electrified by his question. He told us it was adrenochrome, an indole. He was probably the only scientist in Canada who knew what it was. He had done research for his Ph.D. with this compound in England with Professor Burns. 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 Ph.D. 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. That was the major initial contribution Humphry made. The work he and Smythies did made it possible for us to develop 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." None of the subsequent contributions that followed Osmond's and Smythies's original observation could have occurred if the hypothesis had not travelled from England to Saskatchewan.

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

1. A government, led by Premier Tommy 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 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.
8. Total support from Dr. McKerracher, Di-

rector of Psychiatric Services Branch, Department of Public Health.

The original M (for mescaline) hypothesis was developed by Osmond and Smythies. Hoffer, Osmond and Smythies³ 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 I. We each had our own areas of expertise. We met very frequently, spent many hours on the telephone, met in our homes and in other places, travelled thousands of miles together seeking funds and going to meetings and we published many joint papers. (Humphry Osmond's complete bibliography is available at http://www.doctoryourself.com/biblio_osmond.html)

Of course we did not work alone. We inspired and directed the research in Saskatchewan and depended upon the lead investigators: Dr. Heacock in chemistry; Dr. Agnew in psychology; Dr. Smith as assistant director of Research; M.J. Callbeck R.N., in charge of research nursing and Irwin Kahan who was in charge of community follow up and later first director of the Canadian Schizophrenia Foundation. I will not list all the workers who contributed; they are listed in the many publications arising from this research. As Director of Psychiatric Research I asked each head to contribute fifty percent of their time to the general research objectives and fifty percent of the time to pursuing ideas of their own. My name only appeared on publications to which I had made a major contribution. Had I put my name on every paper coming from our research, a common practice in research institutions, my bibliography would have become much more unwieldy. The research I will describe from here on is therefore the result of the joint effort of many dedicated people all working together toward a common objective, to improve the fate of our patients. The main and overriding objective of the research as long as I was Director was clinical, to improve the lot of all our patients. Humphry and I

shared all ideas freely. I will indicate as I write this the areas in which we each took primary responsibility.

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 a 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 our research in detail.

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. 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 on.

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—pigeons, rats, cats, spiders—given adrenochrome has shown toxic changes in behaviour.

Will Compounds that Inhibit Adrenochrome Formation or Antidote 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 assumed 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. The effect of the B vitamins on cell biochemistry had been brought forward

at our first meeting of the Saskatchewan Committee on Schizophrenia Research. Vitamin B₃, 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 noradrenalin by decreasing the methyl groups available for adding to noradrenalin. Later we found that nicotinic acid given intravenously to epileptic patients who had been first injected with 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 B₃ is a component of the pyridine dinucleotide cycle which is involved in at least 200 reactions in the body, including oxidation-reduction reactions.

I think it is very important in testing new treatments that the first one has a positive outcome. This encourages the investigator to keep on trying. Our first case was positive. I had just received four fifty pound barrels containing the vitamins we wanted to test. I took some of that precious niacin to give Humphry in Weyburn. As we were visiting the head psychiatrist came in and told Humphry that Kenneth was dying. A few schizophrenic patients in a catatonic state died and at autopsy no reason was found. Kenneth had had insulin coma and ECT, which had not helped. I suggested to Humphry that we should give him the two vitamins I had brought with me, niacin and 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 parent 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 Chair of the Board of Trade of his small community.

We treated eight schizophrenic patients in pilot trials using 1 gram of vitamin B₃ 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 four 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 oxidation 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 remained mentally normal until she died six months later.

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, D.C., 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 B₃ had no merit in treatment. These powerful institutes were wrong on all three counts but their opposition effectively suppressed research into this area for 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 Humphry and me 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 were 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 know 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 the APA did not forget. Eventually, their infamous task force report destroyed the possibility of improved treatment for schizophrenic

patients for four decades. 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.

Offshoots of the Hypothesis

The adrenochrome hypothesis has been and still is very fruitful in developing new ideas in many fields in medicine, not only in schizophrenia. I will refer to them briefly.

Treatment: The Need to Understand 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 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 student. 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 any one 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.

Treating Alcoholism

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. However, 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 an allergic rhinitis 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 control over their delirium tremens experience. In Alcoholics Anonymous it was accepted that hitting bottom was often a prerequisite but natural delirium tremens was dangerous with a high death rate. No drugs were then available. The problem with natural delirium tremens was that too often after patients recovered they remembered little of what had happened. I thought that if we could induce a terrible, a real psychotomimetic

experience, which might resemble delirium tremens, 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.

The Psychedelic Experience

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 every one 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 word and for having been the pioneer. Aldous Huxley introduced Humphry to Eileen Garrett, President, Parapsychology Foundation in New York and through her we both met Bill W., co-founder of Alcoholics Anonymous. Bill W. outlined the value of our work with niacin as a treatment to members of the International Physicians Association 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, who was not an M.D., talking about vitamins.⁷

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 though 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 films describing its history. It is slowly coming back into use in the United States, against immense opposition.

In our book, *The Hallucinogens*, we described in careful detail the experiences induced by LSD. B Stefaniuk, psychologist working with Dr. Osmond in Weyburn, collected this information.

Effect on Psychiatrists and Nurses

Understanding schizophrenia was not just an intellectual need. It was also very useful in improving the quality of care by psychiatrists and nurses. A few of our psychiatric colleagues and psychiatric nurses also volunteered to have the experience. In my opinion they were much better psychotherapists and nurses thereafter. Patients have much more confidence in their doctors who are not afraid to discuss their hallucinations and delusions with them. The experience also improved their diag-

nostic skills. I continue to be surprised at the number of schizophrenic patients I see, who have been under care from other psychiatrists for a long time, who have not told them about these symptoms. When I ask why, they reply they had not been asked.

Methods of Evaluating Change-The HOD Test

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. 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. Drawing upon our accumulated knowledge of the schizophrenic experience, we drafted 145 questions that we thought would explore the experiential world of our patients. This became the HOD test, the Hoffer-Osmond Diagnostic test.⁸ It completely 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 there-

fore did not follow the usual psychological methods but later when Humphry was in Princeton he and his psychologist Dr. El Meligi developed a much more sophisticated test the 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 South West United States are using the HOD test in this way.

Housing for Patients

Why would anyone allow patients to live in totally inadequate shelters when they themselves, when given a choice, prefer healthier places in which to live? Given a free choice, how many people would choose to live in the slums or on the streets? Yet this is what patients in all mental hospitals were exposed to. Over 150 years ago the Quakers established small homes housing no more than 12 patients and providing decent shelter, food and humane care. They found a fifty percent recovery rate. The adrenochrome hypothesis is consistent with this. Stress increases the secretion of adrenalin and therefore adrenochrome production. Relieving stress by proper housing is therefore very important. Osmond, in charge of one of these totally inadequate warehouses of humanity, was keenly aware of the need to modernize and improve the quality of care. This required better administration and to achieve this he worked with Professor Tom Paterson,

later Dean, Department of Industrial Administration, University of Strathclyde, Scotland, one of the world's experts in administration. Humphry had read *Glasgow Limited. A Case study in Industrial War and Peace* by Paterson and was very impressed. He worked with Joe Izumi, one of Canada's best and imaginative architects to design hospitals. Joe volunteered to take LSD and to spend time in the hospital to study first hand the effect of his experience. He took it at the University Hospital in Saskatoon, at that time the best hospital in Saskatchewan and he took it with Osmond in Weyburn, at that time the worst Hospital. They then designed the circular hospital and two were built in Saskatchewan, at Yorkton and later at Prince Albert. They were designed to house patients until they were well enough to be discharged and to remain in the community. They were to be true hospitals, not first-aid stations. Unfortunately, the introduction of the tranquilizer drugs altered the function of these hospitals to the point that they need not have been built. Patients were admitted, medicated and discharged with little attention to whether they had been given enough time to recover. With modern tranquilizer treatment the same results of treatment can be obtained no matter what the quality of the housing. The recovery of schizophrenia cannot be rushed. It takes the body a long time to stop making excess adrenochrome and to clear the effect of this toxic compound that has been present for so many years. The hospital at Yorkton won the silver medal for design from the American Psychiatric Association.

Humphry was also interested in the impact the disease had on interpersonal relationship using space as the environment to be studied. With Dr. R. Sommers he explored this important relationship. It is certainly clear that schizophrenic patients have a different concept of body space than when they are well. This is also apparent under the influence of LSD.

With Dr. T. Ayllon, Humphry studied the behaviour of chronic schizophrenic patients on the wards. This led to administrative behaviour which improved the life of these patients. For example one of the chronic female wards housed up to 27° C females of all ages living on a huge ward with concrete floors. These patients would not keep their clothes on so the temperature was kept at around 27° C. The administration was worried about the high cost of buying new dresses. But Osmond observed with Ayllon that these clothes were the cheapest the hospital could buy, very flimsy, very unattractive and were of such quality that there was no incentive to keep them on. Against the opposition of the business manager they persuaded administration to buy much more attractive clothing made from better quality cloth and to everyone's surprise, except Osmond's and Ayllon's, they stopped tearing up their dresses and kept them on. The total cost for dress replacement went down. It seems so simple but at that time it was thought that one of the symptoms of chronic schizophrenic patients was that they did not want to keep their clothes on. They showed that this was an artifact produced by the inhumane way in which they were treated. This became known as behavioural therapy but one of the evil outcomes was that in other hospitals cigarettes were given as a reward and the incidence of smoking went up.

Does Inhibiting the Reaction to Adrenochrome Help Patients?

We hoped to inhibit this reaction by slowing down the formation of noradrenalin from which adrenalin is made in the body by adding methyl groups and by adding anti-oxidants (reducing compounds such as vitamin C) to slow the oxidation of adrenalin to adrenochrome. All the natural anti-oxidants ought to be effective but glutathione should be especially effective because it neutralizes adrenochrome. Vita-

min B₃ increases the natural production of glutathione in the body. We looked at the reactions that led to adrenalin from nor adrenalin and on to adrenochrome. We thought that nicotinic acid, vitamin B₃, which is a methyl acceptor, might decrease the methylation of noradrenalin to adrenalin. This vitamin also had many other advantages. It was available, safe, could be taken indefinitely 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 two year recovery rate when this vitamin was added in optimal doses to the treatment program of those years, mostly ECT. After Linus Pauling joined us and published his paper in *Science* in 1968, this led to orthomolecular psychiatry.

The data which shows the effectiveness of this treatment is voluminous and widely published but still ignored. There are no drug companies pushing niacin, as it cannot be patented.

Niacin Lowers Cholesterol

Another offshoot of our niacin studies was the discovery by Altshul, Hoffer and Stephen⁹ 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, superior to 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-vita-

min 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 spectrum 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. D.G. McKerracher in the late 1940s 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 the International Schizophrenia Foundation (ISF). These associations were created to provide accurate information about the disease and its treatment. The ISF is 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 travelled 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. 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 travelling to meetings. Those were heady years and investigators were spending a lot of time travelling 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, Noble 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.

Involving the community also meant providing it with information. This is why we wrote our book *How To Live with Schizophrenia*.¹⁰ 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 sold at a slow but steady pace. The new revised edition is now available. We also worked together to create the *Journal of Orthomolecular Psychiatry*, now the *Journal of Orthomolecular Medicine*, published by 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.

Development of Diagnostic Tests: The HOD Test, the Mauve Factor (kryptopyrrole) Test^{11,12}

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 on 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 others 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 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, Osmond became Director of The Bureau of Research in Neurology and Psychiatry in Princeton. This bureau had been organized by Dr. Nolan Lewis, the great American psychiatrist, Chair, Columbia University. Dr. Carl 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.

Conclusion

Humphry had many other interests. He was interested in poetry, in writing plays, in Carl Jung's theories of personality, to name some of these.

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. Its consequent Adrenochrome Hypothesis by Hoffer, Osmond and Smythies will be replaced by newer and better ones.

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, enlarge them with balloons and to use stents. 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 con-

cludes 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.

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