

The Abram Hoffer Orthomolecular Collection at the University of Saskatchewan

L. John Hoffer, MD, PhD¹

1. Lady Davis Institute for Medical Research, McGill University and Jewish General Hospital, 3755 Cote Sainte Catherine, Montreal, QC H3T 1E2. Telephone: 514-340-8222 ext. 5276. email: l.hoffer@mcgill.ca

Introduction

On February 3, 2012 my sister Miriam and I traveled from our homes in eastern Canada to attend a reception launching the Abram Hoffer Orthomolecular Collection at the Murray Library of the University of Saskatchewan in Saskatoon. On display were many historically interesting documents and books, not the least of which was Rose Hoffer's recipe book for orthomolecular muffins. On the back cover was her husband's ringing endorsement: "I have tried them, and they are good!" The reception was followed by the screening of a well-known documentary film, "Psychedelic Pioneers", which recounts the history of the birth of the psychedelic movement, in which Abram Hoffer and his colleague and close friend, Humphry Osmond, played the seminal role.

As Abram's son, and an academic physician myself, I commented on the historical significance of Abram's work and the potential for discovery within this large, diverse, and mostly unstudied collection of original scientific and personal documents that is now housed at the University of Saskatchewan. It may be of some interest to repeat and expand on some of the topics that were discussed.

Who was Abram Hoffer?

Born in 1917 in a farmhouse in southern Saskatchewan, Abram Hoffer seemed destined to become a farmer like his father, but his intellectual prowess took him instead to the University of Saskatchewan, in Saskatoon,

for bachelor and master of science degrees, to the University of Minnesota for a PhD in biochemistry with a focus on vitamin metabolism, to medical school at the University of Toronto, and finally back to Saskatchewan for a fellowship in psychiatry, where the chief of psychiatry saw in this young, biochemically trained psychiatrist a unique opportunity to investigate whether biochemical factors could play a role in mental illness. Abram was immediately made Director of Psychiatric Research for the Saskatchewan Department of Public Health, a post he held for approximately 15 fertile, rambunctious, and controversial years.

Here is a sampling of the original notions and ideas that emanated from this remote outpost of Canadian academic psychiatry between about 1952 and 1966:

Promulgation of a Conceptual Model for Investigating the Biochemical Aetiology of Schizophrenia

This model was originally the brain-child of two young British psychiatrists, John Smythies and Humphry Osmond, who joined Hoffer in Saskatchewan shortly after he took up his post. Humphry became Abram's closest friend and scientific collaborator in Saskatchewan. The metabolic "model of madness" postulates that an unknown toxic substance, generated in abnormal amounts in the brain (or inadequately metabolized) could generate the symptoms of schizophrenia. Under Abram's biochemically sophisticated scrutiny, this broad concept was

honed into a specific and, in principle, testable hypothesis. The adrenochrome hypothesis postulated that adrenochrome, a spontaneously generated oxidative metabolite of adrenaline (a hormone synthesized mostly in the adrenal glands and released into the general circulation, but now known also to be synthesized by white blood cells and in small amounts in the human brain as well), could be the toxic substance. Hoffer and his colleagues succeeded in synthesizing and crystallizing reasonable quantities of the highly unstable, red-hued molecule. They then administered tiny doses of it to themselves and others, and reported its psychotomimetic (psychosis-producing) properties. After a long and rancorous controversy, the psychotomimetic properties of adrenochrome were independently confirmed and scientifically accepted. Hoffer also reported that he had detected adrenochrome in the human bloodstream, but the claim was premature and incorrect. Adrenochrome is produced in such small quantities in the body, and so chemically reactive, that it remains impossible to isolate *in vivo* even with the best methods available more than 60 years later. The adrenochrome hypothesis was of great historical interest. It provided a striking practical example of biological thinking in the field of psychiatry, and it stimulated fundamental research on the pathways of catecholamine metabolism, especially by Julius Axelrod, who was eventually awarded the Nobel Prize for his work.

Investigation of the therapeutic properties of lysergic acid diethylamide

As Abram later explained, the reason he and Humphry administered lysergic acid diethylamide (LSD) to people suffering from alcoholism was to give them a harsh demonstration of the awful place continued drinking could lead them to. To their astonishment, many patients had a glorious experience that was charged with such sublime personal insights that they were motivated to stop drinking.

Psychological Investigation of the Personal and Perceptual Experience of Psychosis

In work that is astonishing in its prescient vision, Humphry and Abram endeavoured to

comprehend the world of psychotic people through their experiences. They developed a perceptual theory that could account for some of the specific symptoms of the disease. A person whose sense of smell is disturbed might logically wonder about poisonous gases. Someone unable to perfectly execute the very subtle, and largely unconscious skill of judging whether or not another person is looking at them, might logically entertain suspicious thoughts. Someone whose auditory cortex is subtly malfunctioning might misinterpret the significance of sounds, might mistake a change in the direction of the wind for a voice speaking to them, and so on. In hypnosis experiments, they rendered normal volunteer subjects either manic or depressed simply by suggesting a shorter or longer time interval between the beats of a metronome. One practical outcome of their research was the development of an award-winning architectural design for a patient-friendly psychiatric treatment facility.

Investigation and Promulgation of a Novel Treatment, Large Doses of the B Vitamin, Niacin, and Vitamin C, to Hasten Remission and Prevent Relapse in People with Acute Schizophrenia

This unusual therapy was largely a fortuitous discovery. The notion emerged from Hoffer's nutritional biochemistry training, which informed him that the deficiency disease caused by niacin deficiency, pellagra, commonly manifests as a psychosis or toxic delirium that, in some reports, occasionally required large doses of niacin to reverse. A few earlier psychiatrists, including the famous Canadian psychiatrist, Heinz Lehman, had published case reports indicating the value of administering large doses of niacin to patients with a variety of organic brain disorders. Hoffer and Osmond added vitamin C to the treatment on the speculative notion that its anti-oxidant activity might prevent the auto-oxidation of adrenaline to adrenochrome. However, as they frankly admitted in their clinical trial reports, they could provide no definitive explanation for the effectiveness of the treatment they had stumbled across;

what they observed, to their own great astonishment, was simply that it did work. They published their clinical trial results, and even more convincing, in my opinion, their long-term follow up data, in mainstream psychiatric and general medical journals during a time that is now known as the “dark age of psychiatry.” During that dark time, the leading academic psychiatrists in Canada and the United States confidently asserted that schizophrenia was a functional disease caused by unfortunate childhood experiences. It is now well understood that the authorities of the day were utterly mistaken, but in those dark years the assertion that schizophrenia could have a biochemical aetiology was ridiculed, and people who espoused it were academically punished. Hoffer, Osmond, Smythies, and a handful of other courageous and often brilliant biological psychiatrists kept on working in laboratories around the world. They are now recognized as the pioneers of the now well-established field of psychopharmacology.

Schizophrenics Anonymous

Through their relationship with the renowned British author, Aldous Huxley, Abram and Humphry befriended Eileen Garrett, a spiritualist, medium, and president of the New York based Parapsychology Foundation. (Eileen visited our house in Saskatoon and was thrilled by my brother Bill’s aura.) Abram met the co-founder of Alcoholics Anonymous, Bill W, at a foundation meeting in 1960, and the two iconoclasts became good friends. Bill W was intrigued by the prospect of using niacin to help alcoholics, and he inspired Abram to organize “Schizophrenics Anonymous” (SA), a peer-led empowerment group. SA meetings could be raucous. Participants occasionally exchanged the friendly greeting, “Salutations and hallucinations!”

Backlash from the Pharmaceutical Industry and Estrangement from the Medical Establishment

As a person, Abram was intensely intellectually curious, open-minded, and inventive. Although a shy man, he was enormously confident of the conclusions his ideas direct-

ed him to, as long as they were scientifically plausible and potentially important, even if unconventional or firmly rejected by other scientists. In this characteristic he was much like his famous later colleagues and friends, the Nobel Prize winning biochemists Albert Szent-Györgyi and Linus Pauling. In public, he was idea-sparking and inspirational. He founded a journal devoted to nutritional treatments for mental illness, and founded a non-profit foundation whose aim is to foster education and nutritional approaches for treating major mental illness. He published many scientific articles that expounded original and controversial notions. Regrettably, some of the claims were bolder than warranted by the volume and detail of the published evidence, and this got him into no end of trouble.

He was not exactly a team player. An insightful story about Abram, published in the May 14, 1966 issue of *Macleans Magazine*, reported that “Doctors are slow to try his treatment for schizophrenia because, he says, ‘Most psychiatrists have been brainwashed.’” Such language is hardly likely to earn warm feelings and cooperation from other psychiatrists, especially those alongside him in the faculty of the University of Saskatchewan’s tiny medical school, or those practicing in the isolated prairie community of Saskatoon. His friendships or research co-publication with renowned figures like Aldous Huxley, Sir Julian Huxley, and Ernst Mayr made things all the worse. The “brainwashing” Abram was referring to in 1966 was the highly prevalent Freudian theory that schizophrenia is a psychological disorder. The brainwashing that psychiatry is now accused of is, of course, on the part of the pharmaceutical industry to the effect that the only effective treatment for schizophrenia is life-long provision of the drugs they manufacture and profit from.

I never directly asked my father why he took such a pugnacious approach. But knowing him so well, and having discussed his ideas with him for many years, I know what his answer would be. He would say that there was no point being conciliatory, because conventional psychiatry’s rejection, even of the possibility of testing nutritional approaches

for treating mental illness, was total. Indeed, Abram and Humphry started out conventionally, publishing in the best psychiatry journals, and were completely ignored. They could choose to continue the quiet, team approach, and count on being disregarded and forgotten, or they could speak out boldly. They chose the latter.

Because of this boldness (their critics would say rashness), Abram and Humphry made bitter enemies in the medical establishment. Abram told me of instance after instance in which other psychiatrists in Saskatoon and around the country warned their patients about him—actually forbidding them to see him—on the grounds that he was dishonest, a fool, and a quack. But these patients were interested in Abram Hoffer for an important reason: conventional care was not getting them better. So they came anyway, because Hoffer offered something their psychiatrists could not provide and which they desperately needed: hope. For his part, nothing gave Abram more delicious pleasure than recounting the recovery stories of such patients, and there were many of them.

The era of the antipsychotic drugs began in the mid-1950s and was ramping up by the mid-1960s, thus coinciding with, and eclipsing, the vitamin research in Saskatchewan. It is hardly surprising that it did so. The antipsychotic drugs work rapidly and reasonably effectively to reduce and often completely eliminate psychotic symptoms caused by a wide variety of brain disorders. “Megavitamin” therapy involved taking a lot of vitamin pills, following a prudent diet and lifestyle, and could take months to show an effect brought about, not by symptom repression, but through brain healing. (The term used nowadays to describe this therapeutic concept is “neuroprotection.”) Also, unlike the vitamins, the antipsychotic drugs, being highly profitable, were aggressively promoted by the pharmaceutical industry.

Modern antipsychotic drug therapy has been a godsend for people with major mental illness. But these drugs do not cure schizophrenia, and their too-frequent ineffectiveness, disabling side effects, and metabolic tox-

icity are real problems. The credo of modern psychiatry is that schizophrenia is a chronic, life-long disease for which the only option is life-long antipsychotic drug therapy, tailored to achieve the maximum benefit with the minimum of side effects and toxicity. Abram’s view of schizophrenia was radically different. It is not good enough to control the symptoms of schizophrenia, he asserted. The proper goal should be nothing less than a cure. He worked empirically, inventively and tirelessly with his patients with that goal in mind.

What is Orthomolecular?

Linus Pauling coined this term in a lead article published in 1968 in the journal *Science*. When the article was published, Pauling was probably the most renowned and revered scientist in the world, certainly so in the United States, where Americans were justly proud of their two-time Nobel prize-winning native son. Pauling was one of the greatest scientific geniuses of the century. He produced highly original concepts, and coined new scientific terms. “Molecular biology” is a term coined by Pauling to describe the field he pioneered in the late 1940s. In his 1968 article, “Orthomolecular Psychiatry,” Pauling outlined a scientific framework for thinking about therapeutic hypotheses. He suggested that there could be great value in testing treatments that deliberately provide (or restrict intake of) a molecule that participates as a substrate in (or regulator of) biochemical pathways in the brain to leverage metabolite flow rates and tissue concentrations for the benefit of the patient, either by making something work better or by rebalancing a pathologically altered pathway. This concept included the use of naturally occurring antioxidants like vitamin C. The connection between Pauling and Hoffer and Osmond was that Pauling’s entire line of thinking had been triggered by reading their popular and scientific articles, and he formally credited them in his wide-ranging article.

Pauling’s public endorsement of “megavitamin therapy” for acute schizophrenia created an enormous controversy in Canada and

the United States. Patients and their families clamoured for what seemed like a plausible and natural therapy for schizophrenia with little risk and few side effects, especially in view of the emerging evidence that the antipsychotic drugs were falling short of the promise of “cure” that had been anticipated for them. Why not give nutritional therapy an honest and rigorous empirical evaluation? An outraged psychiatric establishment struck back at what it perceived as a threat to its credibility, with position papers and committee investigations aimed more at discrediting orthomolecular therapy and stamping out a dangerous brush fire than seriously addressing the possibility that these ideas were promising and merited examination. The nub of the problem was that claims that orthomolecular therapy was effective for most patients, while interesting and provocative, went beyond the existing evidence, whereas the claim by the psychiatric establishment that the whole approach was nonsense and quackery didn't ring true either, especially at a time when awareness of the importance of nutrition in health was on the upswing, and awareness of the inadequacies and side effects of the antipsychotic drugs was all too apparent to patients and their families, if not always to the psychiatrists looking after them.

Regrettably, what ought to have been a productive scientific exchange almost immediately became a political and cultural war (couched in scientific language) between proponents of conventional drug therapy and advocates of the empirical use of orthomolecular therapies. As the most credible, and hence most dangerous of their opponents, Hoffer was the lightning rod for criticism in the thunderstorm that erupted. In the years that followed, “orthomolecular medicine” failed to gain traction on the scientific front, and seems to have evolved on the cultural front into a scientific-sounding rallying cry for “natural” approaches to medical therapy; a push back against the firm embeddedness of conventional psychiatry in a pharmaceutical culture that disregards other avenues to wellness and healing, such as diet,

natural products, lifestyle, movement, awareness, meditation, and so on.

Abram saw this occurring, and he was not opposed to it. He was open-minded to a fault. He believed in trying out new ideas as long as they were safe and supported by biological plausibility. He and Humphry endorsed the credo of the famous 19th century physiologist, Claude Bernard: Among the experiments that may be tried on man, those that only harm are forbidden, those that are innocent are permissible, and those that may do good are obligatory.

Even if the message was blurred, Abram argued, it was getting out. But there were disadvantages. One problem, from the research standpoint, is that if “orthomolecular” is a rallying cry, how is it different from “natural medicine”? Are orthomolecular and natural medicine the same thing? Is every therapy that is natural (or orthomolecular) inherently good, and likely to be effective, whereas anything developed by the pharmaceutical industry is bad, or harmful? Well, of course not, at least not from a scientific, rather than a philosophical or moral standpoint.

In the last few years of his life Abram told me about the disillusionment he felt, not only about mainstream psychiatry, but with the chaotic direction “orthomolecular psychiatry” seemed to have taken. One day, to my astonishment, he told me that he regarded the traditional Freudian psychiatrists with real respect. These were the very people that we, as children, had heard roundly and regularly criticized at the dinner table! Why the change of heart, I asked. Because, Abram replied, unlike too many modern psychiatrists, whose encounters with their patients seem to be limited to the few minutes required to adjust their drug dosages, the Freudians listen carefully to their patients and seriously try to “cure” them. He was especially disappointed that the treatment for acute schizophrenia that had been so carefully worked out and studied, high-dose niacin, is now little used by orthomolecular practitioners, who tend to adopt a wide, eclectic and often idiosyncratic variety of unvalidated and poorly rationalized analyses and nutritional supplements.

Why is the Orthomolecular Collection Valuable?

The Controversies are Still Alive

Nutritional therapies for schizophrenia and other major mental illness were unheard of when Abram Hoffer embarked on his research program in the early 1950s, but even 60 years later, and despite the accumulation of an enormous amount of biochemical understanding that makes such approaches increasingly more plausible, they continue to be drastically under-investigated. Contrary to what is often claimed, the vitamin therapy for acute schizophrenia developed in Saskatchewan has never been properly tested, and remains neither verified nor refuted. (In my view, the most impressive evidence, and greatest promise of the nutritional approach may be in preventing relapse, a huge problem in schizophrenia.) Hoffer and his colleagues clearly saw the promise of LSD as a psychotherapeutic adjunct. They argued strenuously for its availability in the hands of intelligent and skilled therapists, but widespread irresponsible use of it led the Canadian government make the possession of LSD a crime and shut down all clinical investigation using it. But investigation continued at a low rate in other countries. A recent meta-analysis of carefully conducted clinical trials appears to confirm the considerable promise of this approach for dealing with alcoholism. Information about all of these issues is available in the collection.

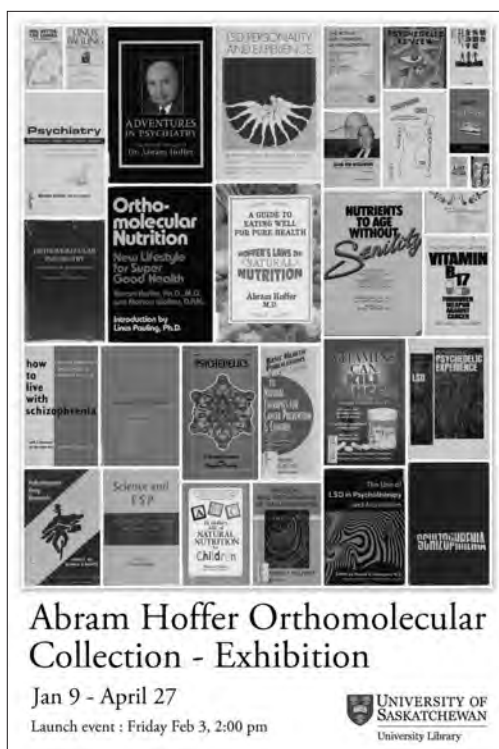
Nutrition, Medicine and Psychiatry

The relationship between nutrition and medicine is complex and intriguing, and it has a fascinating cultural history. The birth of orthomolecular psychiatry in Saskatchewan in the 1950s and 1960s is but one, inadequately documented theme in a tumultuous period in the history of psychiatry which included the development and expansion both of psychopharmacology and the anti-psychiatry movement. According to anti-psychiatry, mental illness does not exist except as way to label non-conformist behaviour and exert social control. Hoffer and Osmond regarded the anti-psychiatry movement with a mixture of horror and bemusement. For their parts, Freudian psychiatry, psychopharmacology-oriented academic psychiatry and anti-psychiatry could all agree on one thing: that Hoffer and Osmond were fools and quacks.

Movements, Medicine and Nutrition

Even though it earned him the enmity of the psychiatric establishment, Abram's direct appeal to the grassroots—to people suffering from serious mental illness—may

well have contributed to beneficial change in culture and attitude, even among psychiatrists, regarding the role nutrition can play in preventing mental illness and mitigating its symptoms. It is worth noting that Linus Pauling found out about the Saskatchewan research not from the academic literature, but by coming across a copy of the popular book, *How to Live with Schizophrenia* (1966), which he read from cover to cover in a single evening, only afterwards turning to the scientific



The poster created for the entrance to the Collection displays covers from many of Abram Hoffer's published books.

articles in the *Journal of Mental Science* and the *Journal of Clinical and Experimental Psychopathology*. Regrettably, I never discussed the point with Abram, but I have often wondered at the irony that he and the famous American psychiatrist, Loren Mosher, were actually more spiritual allies than the mutual enemies they took themselves to be. Hoffer and Osmond were well aware that acute schizophrenia has a natural remission rate of about 33%; indeed, their knowledge of this potential for natural remission fuelled their therapeutic efforts. Hoffer and Osmond combined the skillful use of antipsychotic drugs, nutrition, and lifestyle to facilitate remission and prevent relapse with the lowest possible dose of antipsychotic

medication. Although Mosher appears to have been completely unaware of the importance of nutrition and lifestyle, he did demonstrate in his clinical research that with psychological and social therapy many schizophrenic people could go into remission and may not need antipsychotic drugs to remain well. Mosher's promulgation of this concept put him in conflict with a psychiatric establishment that had whole-heartedly invested in anti-psychotic drug therapy, and, to his embitterment, his research program at the National Institute of Mental Health was shut down. The question arises, how many more of Mosher's patients might become well, and avoid relapse, with careful attention to nutrition and lifestyle?



The ISF documentaries *Feed Your Head* (2010); *Masks of Madness: Science of Healing* (1998); and *The Psychedelic Pioneers* on display.



John Hoffer presenting at the opening of the Collection



The opening of the Abram Hoffer Orthomolecular Collection was well attended.