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Abram Hoffer's 60 Years of Research and Discovery of the Orthomolecular Approach to Psychiatry

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(OMNS Jan 17 2019) Abram Hoffer, PhD, MD, had a remarkable career. Before becoming a physician, he developed a keen interest in chemistry. In the 1940s, he studied biochemistry, and acquired in-depth knowledge about metabolism, enzymes, and essential nutrients, including vitamins. Hoffer graduated from medical school in 1949, choosing psychiatry as his specialty. He became interested in psychiatric research. He considered biochemical causes of patients' symptoms, developed restorative treatments and helped thousands of patients.

Applying his knowledge of biochemistry to psychiatric research, Hoffer made a number of ground-breaking discoveries. Starting in Saskatchewan during the 1950s, he collaborated with colleagues in schizophrenia research. They improved treatments and developed a promising clinical approach that involved the use of supplements of essential nutrients. Linus Pauling coined the term 'orthomolecular medicine' to describe this use of essential nutrients -- natural molecules used in the body-- to prevent and reverse disease.

For decades, Hoffer shared his findings and wrote books and articles to educate the public. His legacy is more than 35 books and hundreds of journal articles that explain his biochemical approach, the underlying concepts, his clinical experience, his research and discoveries. Hoffer's insights, experiments, clinical regimens, reports and methods are still relevant and important today.

Hoffer's hypotheses, research, discoveries

Dr. Hoffer was consulted by hundreds of desperately ill psychotic and depressed patients, and wondered how a newly-qualified psychiatrist could help them. Apparently, most of them had no hope of recovering. Hoffer questioned the efficacy of then-current treatments such as inducing comas and seizures, brain surgery or electric shock, as a rationale for the cure was not evident.

Hoffer's knowledge about biochemistry and research methods gave him an advantage over most physicians and psychiatrists. Curious about the root causes of serious mental illnesses, Hoffer took detailed histories and wondered whether underlying medical and/or biochemical disorders could cause severe mental illness. While taking patient histories, Hoffer noted a range of symptoms including hallucinations and mood swings, and underlying issues such as malnourishment, chronic infections, or problems with alcohol. He resolved to help his psychotic patients stabilize and recover.

Dr. Hoffer and his team focused on schizophrenia, documenting the first double-blind placebo-controlled research studies in psychiatry, describing their hypotheses, discoveries and treatment regimens. By the late 1950s, the team reported that a subset of psychotic patients improved while taking optimal doses of vitamins and other nutritional supplements which helped to restore and maintain normal brain function. Malnourished patients were encouraged to improve their diets, and alcoholic patients were encouraged to moderate their drinking.

Over six decades, Abram Hoffer networked with a series of physicians and psychiatrists. His early books explained how he and his team researched psychosis, studied disorders of metabolism, and developed restorative therapies. The books written for clinicians encouraged health professionals to consider the root cause(s) of each patient's episodes before prescribing treatments. Books written for the lay public shared patients' recovery stories. However, in spite of Hoffer's marathon efforts to educate the public about his research, restorative treatments, and patients' recoveries, his biochemical approach was dismissed by the sceptical caretakers of mainstream psychiatry. This was partly based on research ostensibly attempting to duplicate Hoffer's studies, in which patients were often given fixed dosages of niacin, too small to have any effect. Hoffer had found that the dosage needed for each patient had to be individually determined and could be as high as 10 grams per day or more, while replicate studies used far lower dosages and did not titrate until beneficial effects were found, as Hoffer had suggested.

Hoffer's scientific memoirs, *Adventures in Psychiatry* (2005) present his early experiences as a psychiatrist. In those years, the sickest patients went to asylums; some stayed for decades. Treatments in the Weyburn, Saskatchewan facility included insulin coma therapy, metrazole-induced seizures, analyses of childhood experiences, lobotomies and ECT (electro-convulsive shock therapy). Noting that few psychotic patients improved, Dr. Hoffer nevertheless believed that at least some psychotic patients could recover if they received better quality care, safer treatments relevant to each patient's underlying medical, metabolic and/or nutritional condition.

Considering the Chemical Basis of Psychosis

Meanwhile, thousands of miles away in England, Dr. H. Osmond and Dr. J. Smythies theorized that a disorder of catecholamine metabolism could cause psychosis in some patients. After that possibility was dismissed by senior psychiatrists in the U.K., Dr. Osmond emigrated to Saskatchewan where he met Dr. Hoffer. Dr. Hoffer found the ideas of Osmond and Smythies intriguing and agreed to collaborate and study the biochemical bases of psychosis, hoping to improve the quality of care. Studying their patients' case histories, they noted that certain underlying conditions appeared to cause or contribute to depressed and anxious moods, as well as episodes of psychosis, perceptual distortions, and hallucinations. They reasoned that any underlying "co-morbid" conditions could affect patients' brain chemistries.

Some psychotic patients were malnourished or sensitive to certain foods. In the US in the early 1900s, a disease called pellagra (symptoms include dermatitis, diarrhea and dementia) killed thousands of patients. Research done by Goldberg in the 1920s and Elvehjem et al in the 1930s eventually linked pellagra to corn-based diets, deficient in vitamins, particularly vitamin B3. Patients only recovered if they ate a more nutritious diet or received adequate doses of vitamin B3, or its precursor tryptophan found in corn properly processed with alkaline treatment. Pellagra became a largely forgotten diagnosis after wheat was fortified with niacin and other vitamins in the 1940s. However, we now know that secondary pellagra can still develop after consuming too much alcohol or when receiving kidney dialysis without vitamin supplements.

Patients with untreated syphilis eventually became psychotic. If those patients were committed to asylums without ever getting tested for sexually-transmitted diseases or treated with penicillin, their infections could progress and cause even worse episodes of psychosis. If they did not receive appropriate treatments for their infections, they could die.

Some patients had overindulged in drinking alcohol until they became psychotic. Still other patients had taken hallucinogenic herbs or compounds such as LSD which at the time was legally available. The early treatments for mental illness could not help or heal the biochemical disorders caused by

excessive drinking or drug-taking. Those patients needed detox and rehab programs as well as supportive nutrition.

Apparently, nutritional deficiencies, infections and intoxicating substances could interfere with patients' brain chemistries and trigger psychotic episodes. However, a subset of Hoffer and Osmond's early patients did not have those problems. That knowledge suggested a review of Osmond's and Smythies' hypothesis that a disorder of adrenalin metabolism could make some patients hallucinate.

Disorders of Metabolism Can Produce Hallucinogenic By-products: The Adrenochrome Hypothesis

As a part of his research, Abram Hoffer reviewed a list of hallucinogenic compounds including mescaline, peyote and ibogaine. His book, *The Hallucinogens*, published in 1967, makes fascinating reading for anyone who wants to know what sorts of compounds can cause people to hallucinate, become delusional, psychotic, depressed and/or anxious. When Hoffer reviewed the chemical structures of hallucinogenic compounds, he noticed a common feature - "indole backbones." Recalling Osmond's and Smythies' hypothesis, Hoffer wondered whether some indole-based metabolite(s) of catecholamines (biochemical precursors to neurotransmitters in the brain) could cause psychosis. When he analyzed the by-products of adrenalin metabolism, Hoffer noted that both adrenochrome and its metabolite adrenolutin had a similar indole chemical structure. However, another metabolite of adenochrome, leucoadrenochrome, had a calming effect. Evidently, some patients would accumulate adrenolutin and become psychotic while other patients metabolized most of their adrenochrome to leucoadrenochome (remaining calm and rational). Several disorders of metabolism can cause or contribute to psychosis, depression and other "mental" episodes. For example, porphyria, a disorder of hemoglobin biosynthesis, can cause hallucinogenic by-products.

Hoffer and Osmond wondered whether some of their patients might have a previously-unknown disorder of adrenalin metabolism. They reasoned that a minority of patients metabolize adrenalin to adrenolutin, making them vulnerable to episodes of psychosis, anxiety and depression. Hoffer and his colleagues synthesized adrenochrome and adrenolutin, and within the context of their research studies, they took those compounds themselves and administered them to test subjects. After learning that very low doses of adrenochrome and adrenolutin could cause psychosis and depression, Hoffer and Osmond hypothesized how best to treat those patients.

Developing Restorative Treatments for Psychosis

Hoffer, Osmond and their team read that previous studies had shown that optimal doses of certain vitamins had helped some patients recover from delirium and pellagra. Recalling his PhD studies in agricultural chemistry at the University of Minnesota in the 1940s, Hoffer knew that vital amines (i.e. 'vitamins') were essential nutrients. This knowledge suggested that adequate doses of vitamins and other essential nutrients could help psychotic patients recover from hallucinogenic byproducts of adrenalin metabolism such as adrenolutin.

Hoffer reasoned that vitamin B3, a methyl acceptor, could moderate the production of adrenalin. He also hypothesized that vitamin C, an antioxidant, could suppress the oxidation of adrenalin to adrenochrome. Hoffer proposed that divided daily doses of vitamin B3 and vitamin C could reduce psychotic patients' levels of adrenochrome and adrenolutin without causing problematic side effects.

One concern with niacin (a form of vitamin B3) was its tendency to cause brief, harmless "skin flushes." However, Dr. Hoffer noted that most psychotic patients did not flush when they took niacin -- suggesting that they had a greater intrinsic need for this vitamin. Even so, some patients preferred

other forms of vitamin B3 such as niacinamide or no-flush niacin (inositol hexanicotinate, also known as hexaniacinate). Hoffer and Osmond reported that optimal doses of vitamins B3 and C could help 75% of psychotic patients to recover. Their evidenced-based double-blind placebo-controlled research was published in medical journals, but was widely ignored by mainstream psychiatrists who relied on antipsychotic medications that dampened symptoms but caused troublesome side effects.

A related discovery by Hoffer, the use of niacin to lower LDL cholesterol, was published in 1954, and was verified by Dr. Parsons of the Mayo Clinic. That became a standard of care for optimizing cholesterol levels, although later studies have shown that moderately high blood cholesterol is not a cause of heart disease. In spite of this, the pharmaceutical industry has developed a multi-billion industry selling statin drugs to lower even perfectly normal blood cholesterol levels.

Dr. Hoffer was ahead of his time. Few doctors or psychiatrists among his peers had degrees in chemistry. Hoffer had a PhD and had studied the biochemical pathways important in the brain. Mainstream physicians denied the existence of adrenochrome, dismissed vitamin supplements and withheld orthomolecular treatments from patients. Adrenochrome was reported in 1937 by Richter and Green along with an enzyme that can produce adrenochrome from adrenalin. In 1960, a research scientist named Julius Axelrod looked for adrenochrome when he studied the metabolism of adrenalin, and reported finding that metabolite and its responsible enzyme in 1964.

Over decades, other researchers used scientific methods to test for adrenochrome and adrenolutin and other metabolites of catecholamines. The scientific literature has verified the existence of indole-based compounds including adrenochrome and other aminochromes in our biological metabolism. It is currently believed that a subset of patients can be dramatically improved with supplements of niacin -- they are considered to be "niacin-dependent."[1,2]

60-Year Marathon to Educate the Public about Orthomolecular Medicine

In 1966, Hoffer had collaborated with Dr. Osmond to write a book called *How to Live with Schizophrenia*, a layman's guide to educate patients and families. In his memoirs, published as *Adventures in Psychiatry*, Hoffer said that that book was the prompt that inspired Linus Pauling, PhD to add 'ortho' to Pauling's 'molecular' medicine concept thereby defining Orthomolecular Medicine. One of Hoffer's previous books, *Niacin Therapy in Psychiatry* (published in 1962), explained how niacin therapy can help some patients and shared 60 case reports (many of those patients recovered after taking optimal doses of vitamin B3 and vitamin C). Current research has confirmed Hoffer's original ideas, and niacin therapy is now known to prevent psychotic episodes in a subgroup of schizophrenic patients.[1]

Because of Hoffer's growing clinical practice and public education marathon (writing, speaking, networking and teaching), he needed help. In the Spring 2018 issue of the *Journal of Orthomolecular Medicine (JOM)*, Steven Carter recalled meeting Abram Hoffer in 1987 for a job interview.[2] Carter was offered two jobs - editor of the *Journal of Orthomolecular Medicine (JOM)* and executive director of the Canadian Schizophrenia Foundation.

For more than thirty years, Steven Carter cooperated with Abram Hoffer to publish the *Journal of Orthomolecular Medicine (JOM)*. They encouraged scientists and clinicians to research, apply the orthomolecular approach, and publish the results of their clinical work helping patients who had schizophrenia, psychosis, attention deficit and hyperactivity disorders, autism, depression, anxiety, bipolar disorder, alcoholism, age-related cognitive issues, arthritis or cancer. As editor of the JOM, Steven Carter encouraged Dr. Hoffer and the other co-founders of orthomolecular medicine to share

their discoveries by writing books and articles. Hoffer and Carter operated the ISF foundation and ISOM (International Society of Orthomolecular Medicine) for several decades. They also organized Orthomolecular Medicine Today conferences to educate the public about orthomolecular research, discoveries, clinical progress and success.

Orthomolecular medicine involves 3 steps:

1. Test and diagnose the root cause(s) of each patient's symptoms,
2. Consider the "biochemical" factors involved with chronic mental and physical conditions including nutritional deficiencies, sub-optimal diets, infections, drug and alcohol consumption, disorders of metabolism and biochemical individuality.
3. Prescribe/administer optimal doses of vitamins, minerals, amino acids, energy and enzyme co-factors to complement other treatments and help patients restore and maintain their health.

From 1949 to 2009, Abram Hoffer and his colleagues researched, developed and applied the orthomolecular approach. They helped thousands of psychotic, depressed and anxious patients to stabilize, recover and live well. Unfortunately, most psychiatrists today still don't utilize "restorative care." They typically offer prescription medications, talk therapies and ECT (shock treatments). Therefore, most patients today still do not receive orthomolecular treatments.

We believe that the orthomolecular approach could become a standard of care. The scene is set for modern psychiatrists to rediscover Hoffer's methods, learn the orthomolecular approach, consider and test for chemical factors involved with psychosis and other mental illness, diagnose underlying medical, metabolic and nutritional conditions and compliment other treatments by prescribing restorative regimens.

Over Abram Hoffer's remarkable 60-year career, his public education marathon produced more than 35 books and 600 articles for scientific and medical journals. We encourage readers to search out Hoffer's publications and learn how he treated his patients. Readers of the *Journal of Orthomolecular Medicine*, recovered patients, and families and friends of orthomolecular medicine can continue Abram Hoffer's public education marathon by sharing orthomolecular books, articles and recovery stories.

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A selection of books written by Abram Hoffer and colleagues

(Dr. Hoffer's complete nutrition bibliography is posted at http://www.doctoryourself.com/biblio_hoffer.html)

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