For many years I had problems finding quality care. Misdiagnosed and mistreated by a succession of health professionals, I got worse taking prescription medications. While ill with a bipolar II mood disorder and other problems, I read about psychiatry, orthomolecular medicine and other specialties. Gradually, I learned about disorders of metabolism. I wrote this article to outline one patient’s perspective on the past, present and future of orthomolecular psychiatry. Before trusting my life to orthomolecular medicine, a little-known alternative, I wanted to learn how it works. Abram Hoffer’s books enlightened me. I read 26 of Dr. Hoffer’s 36 books and some of his references. For ten years, I corresponded with Abram Hoffer. He kindly encouraged me to read, restore my health and tell my recovery story. Here’s what I learned.

Drs. Hoffer, Osmond and Smythies Applied Biochemistry to Psychiatry

When they worked together in the UK, Dr. H. Osmond and Dr. J. Smythies proposed a biochemical basis for psychosis. Dr. Osmond brought his research papers when he moved to Saskatchewan where he met Abram Hoffer. In the early 1950s, Dr. Hoffer and Dr. Osmond had hundreds of schizophrenic patients but no ‘restorative’ treatments. In those days, few patients recovered.

Abram Hoffer’s memoirs, Adventures in Psychiatry, explain how they researched schizophrenia and discovered that a disorder of catecholamine metabolism can cause episodes of psychosis, anxiety and depression. Before becoming a physician and starting his research in psychiatry, Dr. Hoffer obtained a PhD in biochemistry. That advanced degree helped him review the scientific and medical literature and study the metabolism of catecholamines, particularly adrenalin (also called epinephrine).

Hoffer and Osmond Linked Indoles to Schizophrenia - The Adrenochrome Hypothesis

Hoffer and Osmond found 1937 and 1940 reports by Richter and Green, British scientists who studied a lesser oxidation pathway of catecholamine metabolism and discovered adrenochrome, an indole byproduct. (See also Graham.) Sitting at his kitchen table, Abram Hoffer had a eureka moment when he sketched the chemical structures of several hallucinogens on a napkin and suddenly realized that those compounds were all indoles. Could a disorder of adrenalin metabolism produce too many indoles until a vulnerable patient hallucinated? Hoffer and Osmond decided to study the effects of adrenochrome.

In the 1950s, the two doctors took adrenochrome under controlled conditions. They soon experienced the same symptoms as their psychotic patients. Their detailed accounts of these experiments on themselves make fascinating reading. Reasoning that some patients may produce too much adrenochrome (or other indoles), Hoffer and Osmond wondered if a methyl acceptor and an antioxidant could help. In the first double-blind placebo-controlled experiments ever done in psychiatry, they tested therapeutic doses of niacin and ascorbic acid (vitamins B3 and C). Seventy-five percent of their patients recovered.

Hoffer and Osmond designed the Hoffer-Osmond Diagnostic Test to diagnose patients with schizophrenia if they had perceptual and thinking problems. They tested vitamin regimens and noted which patients recovered. Hoffer and Osmond researched disorders of catecholamine metabolism, designed a series of scientific experiments to test their ‘adrenochrome hypothesis’ and performed double-blind placebo-controlled clinical trials. They began to develop safe and effective treatments for schizophrenia.

In 1958, Hoffer, Osmond and Smythies wrote “Schizophrenia: A New Approach” for Psychopathology, A Source Book. Their powerful and prescient chapter explains how they applied biochemistry to research psycho-
sis and why they believed that a disorder of adrenalin metabolism could cause schizophrenia. Hoffer and Osmond also wrote chapters for the 1958 book, *Chemical Concepts of Psychosis* and in 1960 they detailed their theories about disorders of adrenalin metabolism in *The Chemical Basis of Clinical Psychiatry* (supported by hundreds of references).

Year after year, Dr. Hoffer wrote papers and articles for medical journals. His 1962 book, *Niacin Therapy in Psychiatry*, teaches us that (1) niacin (also called vitamin B₃ or nicotinic acid) has healing capabilities; (2) Hoffer and Osmond did double-blind experiments; and (3) vitamin therapy helped many of their first patients. Dr. Hoffer outlined the properties of nicotinic acid and presented a case series of 60 patients.

Hoffer and Osmond's 1966 book, *How to Live with Schizophrenia*, was well received by patients and families who needed information, help and hope. It sold more than 100,000 copies. Their 1967 book, *The Hallucinogens*, analyzed compounds which cause hallucinations and compared adrenochrome experiences with hallucinations caused by other indole compounds such as mescaline and lysergic acid diethylamide.

Unfortunately, mainstream psychiatrists disputed Hoffer and Osmond’s idea that a disorder of adrenalin metabolism could cause schizophrenia. A succession of mental health professionals dismissed their research. Rather than study the research reports and read Hoffer and Osmond’s books, skeptics either claimed (falsely) that vitamin therapy could not possibly help psychotic patients and or claimed (falsely) that Hoffer never did any double-blind placebo-controlled experiments.

Orthomolecular vs. Standard Psychiatry: Tension, Bias, Progress and Public Education

After reading the *How To* book, Linus Pauling, PhD revised his earlier term “molecular medicine” into “ortho-molecular medicine.” In his 1968 article, “Orthomolecular Psychiatry,” published in *Science*, Pauling, a Nobel prize winner (chemistry and peace), described Hoffer and Osmond's restorative approach as “orthomolecular” psychiatry. “Ortho” means “correct” and “molecular” refers to chemistry so Pauling's word means “correct the chemistry.” “Orthomolecular psychiatry” aptly describes the practice of prescribing optimum doses of vitamins (and other supplements) to restore normal metabolism. Abram Hoffer quickly accepted the word “orthomolecular.” When combined with the name of any medical specialty (such as “orthomolecular psychiatry”) or as “orthomolecular medicine,” the resulting phrase helps patients, families, researchers and clinicians understand the process of diagnosing biochemical disorders, prescribing nutritional supplements and helping patients recover. Although useful to many people, Pauling’s well-intentioned but complicated term also caused tension and confusion. The phrase “orthomolecular psychiatry” provoked scorn and skepticism from many psychiatrists.

In the 1950s and 1960s, psychiatry used various treatments including Freudian analysis, talk therapy, insulin comas, electric shocks or the newly-developed antipsychotic (neuroleptic) medications such as chlorpromazine. Psychiatrists trained to use talk therapy or psychopharmacology did not accept Dr. Hoffer’s vitamins-as-therapy paradigm. Hoffer and Osmond’s research, progress and success in treating schizophrenia “restoratively” did not impress close-minded psychiatrists who ignored biochemistry, dismissed vitamin therapy and continued prescribing drugs, talks or shocks or trusting patients’ lives to therapeutic nihilism (doing nothing but watch and wait). Mainstream psychiatry misunderstood the ‘orthomolecular’ concept. A 1973 report by an American Psychiatry Association Task Force advised its members not to consider vitamin therapy as an alternative to the usual treatments.

Pauling’s excellent term “orthomolecular” highlighted the gap between the quick and efficient approach commonly used in modern psychiatry (i.e., label and medicate) and the orthomolecular approach which diagnoses metabolic disorders and complements other treatments with nutritional
supplements. Few doctors had the time or the motivation to learn orthomolecular regimens. Their bias against the restorative approach meant that many psychiatrists and physicians withheld “orthocare” from millions of patients. The rejection and exclusion of “orthomolecular” medicine by his own profession did not stop Abram Hoffer from launching a public education campaign to bring orthomolecular information, help and hope directly to the public. For six decades, while seeing thousands of patients in his clinical practice, Dr. Hoffer somehow found the time to write and network with colleagues, patients and families as he planned his campaign to educate the public about orthomolecular medicine. He wrote books, articles and editorials, organized meetings and spoke at conferences, around the world. Dr. Hoffer taught the orthomolecular approach to open-minded physicians and he encouraged recovered orthomolecular patients, like this author, to share our recovery stories.

Over ten years, I spoke at 20 public meetings and volunteered at orthomolecular conferences in Toronto, Vancouver, Ottawa and Montreal. Few people in Toronto know about “orthomolecular” medicine. Where I live, mental patients or their families rarely hear a psychiatrist say that a restorative approach can complement other treatments, safely and effectively. I kept studying and learning, hoping to find additional information to share with patients and families.

**Inborn Errors and Disorders of Metabolism**

By reading scientific and medical books, I learned that other specialists also treat disorders of metabolism. In his 1908 Croonian lecture, Dr. Archibald Garrod introduced the concept of Inborn Errors of Metabolism. Dr. Garrod studied disorders of tyrosine metabolism such as alkaptonuria. He inspired many doctors to research disorders of metabolism and develop effective treatments. Over the years, the list of known metabolic disorders has grown to include several hundred; most are rare. Like Dr. Hoffer, these researchers applied biochemistry to discover that disorders of metabolism typically involve lesser or blocked pathways, inherited metabolic disorders, genetic polymorphisms, deficiencies, excesses, toxins, enzyme inefficiencies, antimetabolites, and biological antagonists. Some patients with metabolic disorders respond to customized treatments using vitamins or other supplements. According to medical professionals who see patients with disorders of metabolism, treatments can include substrates (amino acids) and/or enzyme co-factors (vitamins and minerals), byproducts, hormones or even dietary adjustments. A disorder of metabolism may be inborn (i.e., inherited) or it can appear following an infection, inflammation or ingestion of toxins. Medical conditions, even auto-immune disorders (such as celiac disease) can affect metabolism. Internists, endocrinologists, gastroenterologists and pediatricians routinely look for disorders of metabolism when they see patients with certain patterns of symptoms.

**Identifying and Treating Disorders of Metabolism**

Books about orthomolecular medicine and books about other medical specialties which also treat disorders of metabolism teach us that researchers have discovered disorders of metabolism, developed diagnostic tests and recommend restorative treatments which use vitamins, minerals, amino acids and other substances normally present in the human body. Treatments for metabolic disorders have to be customized based on each patient’s differential diagnosis and biochemical individuality. In volume 25 #2, 2010 of the *Journal of Orthomolecular Medicine*, L. John Hoffer, MD, PhD, a professor of medicine, offered his views as a “cautious clinical researcher” on the past, present and future of orthomolecular psychiatry and in 2008, he wrote that some schizophrenic patients actually have disorders of metabolism. “It is currently popular to regard schizophrenia as a ‘multiple-hit’ neurodevelopmental disorder; equally plausible is the older hypothesis of a toxic psychosis triggered by an abnormal [level of an] endogenous metabo-
literate. Organic brain disorders indistinguishable from schizophrenia may be induced by certain drugs and by neurological, metabolic, inflammatory and infectious diseases. Such disorders account for approximately 5% of cases initially diagnosed as first-episode schizophrenia by expert psychiatrists. Wilson’s disease, unrecognized adult phenylketonuria, pellagra and celiac disease can induce brain disorders indistinguishable from schizophrenia... Although known metabolic disorders and neurologic injury only rarely cause clinical schizophrenia, their very existence is good reason to search for the abnormal molecules, enzyme activities and markers of brain injury that may eventually reveal its cause or causes. Examples of orthomolecular therapy include dietary phenylalanine restriction in phenylketonuria, high-dose pyridoxine therapy in pyridoxine-responsive variants of homocysteinuria, and the treatment of pellagra psychosis with niacin...”

**Do Patients Want Labels, Meds, Talks and Shocks or Guideline-Quality Care?**

Hundreds of thousands of mental patients risk deteriorating if they get substandard care. Unfortunately, few modern psychiatrists diagnose or treat disorders of metabolism, or recommend restorative treatments. Many psychiatrists prescribe antidepressants, anxiolytics, antipsychotics or anticonvulsants. These medications do not heal disorders of metabolism but they do suppress symptoms. Psychiatrists also recommend talk therapy such as cognitive behavioral therapy (CBT). While CBT may encourage patients to improve their patterns of thinking, feeling and responding, talk therapy does not diagnose or treat underlying metabolic disorders. The American and Canadian practice guidelines of psychiatry encourage psychiatrists to note mental status, take medical and mental histories, order lab tests, examine patients carefully and diagnose underlying medical conditions [such as disorders of metabolism]. Psychiatrists could follow their practice guidelines when they examine patients, order blood tests and make differential diagnoses before recommending appropriate treatments. Even if conventional psychiatrists do not believe in the orthomolecular approach, they could consult specialists who know how to diagnose and treat disorders of metabolism.

**Abram Hoffer Differentiated Psychoses from Syphilis, Pellagra, Celiac Disease and Redox Disorders**

As a research psychiatrist and a clinician, Dr. Hoffer believed in examining patients carefully, testing their blood, making a differential diagnosis and determining the cause(s) of patients’ symptoms before recommending treatments. If he tested a patient’s blood and found that the patient had a spirochetal infection, but was labelled “schizophrenic” after an episode of psychosis during an advanced stage of syphilis, Dr. Hoffer would treat that infected patient with antibiotics. If a patient experienced psychosis after becoming ill with pellagra, Dr. Hoffer understood that some starving patients needed niacin and tryptophan, as well as balanced diets. Hoffer also believed that some processed foods were so depleted of essential nutrients that even non-starved patients could develop nutritional deficiencies and show signs and symptoms of metabolic disorders. If a patient had poor absorption of nutrients during episodes of celiac disease, Dr. Hoffer knew that the patient could benefit from nutritional supplements as well as a gluten-free diet.

In the 1950s, Hoffer and Osmond began to identify a group of psychotic patients who did not have infections, inflammations or gluten sensitivities. These patients had redox disorders. The irreversible oxidation of catecholamines (adrenalin, noradrenalin and/or dopamine), using a lesser oxidative pathway, increased their levels of aminochromes, (halucinogenic indoles such as adrenochrome, adrenolutin or other quinone metabolites). The doctors’ research showed that these patients could recover on vitamin therapy if they received optimum doses of a methyl acceptor (niacin or niacinamide) along with...
an antioxidant (ascorbic acid).\textsuperscript{2,6,7,9, 10,11} Dr. Hoffer proposed an “adrenochrome hypothesis” when he wrote about the metabolic form of schizophrenia which he sometimes called hyperaminochromia. \textit{Adventures in Psychiatry: The Scientific Memoirs of Dr. Abram Hoffer} tells us about his career and his schizophrenia research. The bibliography lists Hoffer’s 36 books and 600 articles that he wrote for medical journals.\textsuperscript{3} Dr. Hoffer’s book: \textit{Psychiatry: Then (1950) and Now (2007)} compares conventional psychiatry with the restorative orthomolecular approach.\textsuperscript{30,31}

**Conclusion – Mental Patients can Recover and Live Well on a Restorative Program**

The orthomolecular approach helped me recover from a bipolar disorder, safely and effectively. I wrote this article because I believe that the public needs to know that orthomolecular medicine has a solid scientific foundation consistent with other medical specialties that also treat patients who have metabolic disorders. Skeptics may question how supplementing vitamins, trace minerals, amino acids, energy and enzyme cofactors, antioxidants, methyl acceptors or hormones can help patients recover from episodes of serious mental illness. Readers of this journal learned from Dr. Hoffer and other contributors that the restorative approach can help patients who have psychosis or acute schizophrenia (perception and thought disorders), depression, anxiety or bipolar (mood disorders), ADHD, autism or Asperger’s syndrome (attention disorders), hyperaminochromia (a metabolic disorder), and stroke, dementia or Parkinson’s disease (aging and neurological disorders). The public also needs to know that a succession of researchers and clinicians studied Hoffer and Osmond’s experiments, verified their discoveries and used the orthomolecular approach (vitamins, minerals and other supplements) to help thousands of their patients. \textit{Orthomolecular Psychiatry: Treatment of Schizophrenia}, ed. by Hawkins and Pauling, published this evidence, in 1973.\textsuperscript{32} Recent advances have been documented in medical books.\textsuperscript{33,34,35,36}

**Abram Hoffer Asked Us to Continue Project H.O.P.E. to Help Orthomolecular Public Education**

After decades of research, progress and success, Dr. Hoffer and his colleagues left the world a substantive educational legacy. Their important books and papers still read fresh and clear so their discoveries and their reports can continue to inspire scientific and medical professionals. In his ninetieth year, speaking at a 2007 dinner to honour his lifetime achievements, Dr. Hoffer encouraged us to continue his marathon project to help orthomolecular public education. We can tell our families and friends about orthomolecular medicine; we can expect new discoveries, monitor progress and cooperate with researchers who study disorders of metabolism and support clinicians who prescribe restorative regimens to help patients recover and live well. On behalf of thousands of recovered orthomolecular patients, I am pleased to say, “Thank you Dr. Hoffer!” and “Yes we will continue Project H.O.P.E.”

—Robert Sealey, BSc, CA

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