Orthomolecular Psychiatry: Past, Present and Future

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Abstract *Orthomolecular psychiatry is an approach to psychiatric therapy that aims to provide the optimum molecular environment for the brain, especially the optimum concentration of substances normally present in the body. This article reviews orthomolecular psychiatry's history, current status and possible future, both as a field of scientific and clinical endeavour and as a grassroots movement to increase awareness of the role that proper nutrition can play in the prevention and treatment of serious mental diseases.*

The Past

A half century ago, controlled clinical trials carried out in Saskatchewan by Abram Hoffer, Humphry Osmond and their collaborators indicated that the addition to best standard therapy of niacin (in one study, niacinamide) 1 gram three times daily plus vitamin C, 1 gram 3 times daily, improved the clinical outcome of patients suffering from an acute psychosis compatible with schizophrenia.[1-5] They also reported that this treatment was not effective in chronic schizophrenia, at least within a time frame practical for randomized clinical trials. Hoffer and Osmond considered patients to have "acute" schizophrenia if they had been psychotic for not longer than one, or at most two years. It was known that approximately one-third of people with a first acute psychosis recover on their own; what the new treatment did was double the recovery rate and prevent relapses.

This novel therapy for acute schizophrenia was introduced during the final years of what is now commonly referred to as the dark age of North American psychiatry. There were few treatment options for people with schizophrenia. Standard therapy was custodial care, barbiturate drugs, and electroconvulsive therapy.

Despite their publication in well-regarded research journals, the promising reports from Saskatchewan were disregarded by other psychiatric researchers. It is not hard to understand why. The studies were small, the treatment seemed suspect (academic physicians have traditionally been suspicious of vitamins when administered for any purpose other than to treat an overt deficiency disease), and at that time most psychiatrists had been taught that schizophrenia was a functional disorder rather than an organic disease that could be treated chemically. Perhaps most importantly of all, just as the Saskatchewan studies were being published the first generation antipsychotic drugs, starting with chlorpromazine, were in the process of transforming psychiatry. These new drugs rapidly controlled acute and chronic psychotic symptoms and improved severe mood abnormalities.[6] For the first time it seemed that many seemingly hopelessly psychotic people could recover, or at least become much better; there was real hope that a cure for schizophrenia was at hand. However, by

the late 1960s it had become clear that as invaluable as these drugs were at quickly suppressing psychotic symptoms, they were not so effective at eliminating them, and they brought with them a heavy burden of serious adverse and toxic effects.

We now know, after half a century of use, that even the latest generation antipsychotic drugs (the "atypical antipsychotics") brings about normalcy or near-normalcy for only a portion of schizophrenic patients. Thus, in a recent report of the 1- and 3-year outcomes of approximately 8,000 outpatients with schizophrenia who were treated with these drugs, at most one-half of them attained "minimally symptomatic" status after one year of therapy, and a substantial minority failed to attain it even after three years of therapy. Patients who did attain minimally symptomatic status had a 50% rate of relapse over the following two years.[7]

The first and second generation antipsychotic drugs also have significant and important side effects and toxicity, including the ultimate toxicity of an increased risk of sudden death.[8] As any person who has experience with them will testify, the atypical antipsychotics commonly induce serious weight gain, with obvious adverse psychological implications and a high rate of lipid disorders, diabetes, and an increased risk of cardiovascular disease. Tardive dyskinesia occurs, although at a lower frequency, even with these drugs.

By the late 1960s the inability of the antipsychotic drugs to produce actual recovery in many, if not most people with schizophrenia was clear to the patients and their families, and at a time when the importance of sound nutrition for health was becoming appreciated among the American public in general. The notion that vitamin and nutritional therapy could help many people with acute schizophrenia received a tremendous boost in 1968 after Linus Pauling published a lead article, entitled Orthomolecular Psychiatry, in the world's most prestigious scientific journal.[9] In his article, Pauling laid out a reasoned theoretical framework that supported the clinical plausibility of the niacin and vitamin C treatment of schizophrenia.[5,10] When his article was published, Pauling was America's most famous American-born scientific genius. If a biochemist with the knowledge and authority of Linus Pauling had determined that megavitamin treatment was worthy of careful examination, it was reasonable to assume it might indeed prove to be beneficial. A clamour arouse among patients and their families to examine this approach to schizophrenia treatment. Many practising psychiatrists were unsure how to respond. Leading academic psychiatrists were outraged at Pauling's intrusion into their field, and sought a remedy for what they perceived of as public misinformation and an intemperate assault on their authority.[5]

Even as academic psychiatry refused the invitation to explore nutritional approaches for treating schizophrenia, Abram Hoffer – who retired in 1966 from his academic positions to fully devote himself to patient care and advocacy[11] – was joined by a cadre of innovative psychiatrists and general physicians interested in exploring this new approach to treating schizophrenia and other mental illnesses, using (as a supplement to antipsychotic medication at the lowest effective dose) a wide variety of empirical approaches that included the use of vitamin B_6, essential fatty acids, zinc, manganese, fasts and food elimination diets while continuing to use antipsychotic drugs at the lowest effective dose.[12] Hoffer continued to advocate a treatment regimen for acute schizophrenia that included daily niacin (usually in a dose of 3 - 6 grams or more) or niacinamide (3 grams) along with vitamin C (3 grams) and commonly vitamin B_6 (250 to 500 mg), which with over time expanded to include a junk food-free, low-carbohydrate diet and the empirical use of other B vitamins and zinc.[13-15] The aim of therapy was to be control or eliminate psychiatric symptoms at the lowest possible dose of antipsychotic medication, thereby limiting its side effects and toxicity, improving compliance, and minimizing the risk of relapse.

Hoffer was impressed, both by reports and his personal clinical experience, that

some schizophrenic patients – especially those with chronic symptoms – improved greatly after they eliminated certain food items such as wheat or dairy protein from their diet.[14] Hoffer called these reactions "cerebral allergies."[16] The specific mechanism and prevalence of serious neuropsychiatric reactions to specific foods is not known, and the notion that they occur at all is rejected by mainstream medicine except in cases of celiac disease.

Although chronic schizophrenia did not respond rapidly to niacin, vitamin C and other vitamin therapies, Hoffer patiently treated such patients as he did people with acute schizophrenia, but counseled higher doses of niacin (but not niacinamide) combined with an empirical nutritional approach which he described over and over again in his many articles and books. In these publications he described many individual cases in which important and sometimes complete remissions of symptoms occurred.

From the beginning, Hoffer advocated a respectful, supportive and professional approach with all patients. The notion that simple respect and attention to basic well-being are humane and sensible when dealing with schizophrenia seems self-evident, but this aspect of care is sometimes neglected in conventional medicine and psychiatry. Thus, a small clinical trial was recently published indicating that massage can greatly improve the symptoms of anxious, psychotic patients.[17] Hoffer would have considered this an example of applied common sense, but it is also science based. As Hoffer realized, but contrary to what is often taught about schizophrenia, marked improvement or complete recovery is possible for a sizeable proportion of patients, and it is fostered by a supportive, hopeful and optimistic treatment approach.[18]

There are both strengths and weaknesses in the way orthomolecular psychiatry developed. It is a strength that the new approach fostered creative thinking and the empiric examination of nutritional approaches that, until very recently, were completely ignored by mainstream psychiatry. On the other hand, Pauling's basket concept of "the right naturally occurring molecule in the right concentration" is capacious enough to accommodate almost any nutritional approach. The concept of orthomolecular psychiatry is simply that: a thought framework for capturing and analysing diagnostic and therapeutic possibilities that remain to be tested for robustness, both biochemically and in the clinic. Approaches like herbal therapy and diets that eliminate cerebral allergies may sometimes be effective, but they are not properly classified as examples of orthomolecular psychiatry as Linus Pauling defined it, and considering them to be so misunderstands his conceptual formulation. On the other hand, the mere fact that a potential therapy can be accurately termed "orthomolecular" and its originator finds it exciting doesn't mean it actually works for patients.

Within the rubric of orthomolecular psychiatry one can encounter a bewildering variety of tests and treatments, sometimes offered without reliable information about what the tests actually indicate, their accuracy, and the impact of their use and related treatments on actual patient outcomes. Costly nutritional therapies could be slickly marketed to psychiatric patients on the basis of claims that go well beyond what is justified by the available clinical data. Vendors may refuse to disclose the ingredients in their products, which might merely consist of a combination of vitamins available in a pharmacy a fraction of the cost.

The Present

More than fifty years after its introduction into psychiatry, orthomolecular psychiatry remains a marginal therapy with little or no impact on psychiatric practice. This is not to say that people may not benefit from it. Practitioners who prescribe specific versions of orthomolecular psychiatry and the patients who try them have a personal interest and responsibility to find out what works and doesn't work for themselves. But we cannot forget that Abram Hoffer's aim, and the aim of the International Schizophrenia Founda-

tion (ISF), has always been to inform and to increase interest in developing and testing this approach, with the eventual goal of determining its most effective elements and fostering widespread acceptance of them.

At present few psychiatrists and medical doctors practice orthomolecular psychiatry. Current practitioners largely comprise a heterogenous mix of naturopaths, osteopaths, chiropractors, and other unclassified therapists. In most cases the specific approaches used, the reasons for the formulations, and the outcomes of their use, are undocumented. How many people claiming to practice orthomolecular psychiatry actually use niacin to treat schizophrenia, or if they do, in the doses that were reported to be effective in the early clinical trials?

Challenges to Modern Psychiatry

Even as orthomolecular psychiatry is confronted by challenges of identity, validation and mainstream acceptance, modern psychiatry has its own set of challenges. The pernicious influence of the pharmaceutical industry on the attitudes and clinical practice of many physicians and psychiatrists is a well-documented and serious concern. The great majority of clinical trials of new treatments for schizophrenia and other major mental diseases are funded by the pharmaceutical industry to obtain regulatory approval to market new drugs. In the recent past large pharmaceutical companies have misrepresented the results of clinical trials of their drugs, censored completed trials when they failed to show effectiveness, and lobbied physicians to use drugs for "off-label" indications; that is, for indications that have not been approved by regulatory agencies because evidence is lacking as to their safety and effectiveness.

This is not to say that the pharmaceutical industry is all bad, for it is not. For obvious reasons, the pharmaceutical industry is very interested in discovering drugs as effective or more effective than clozapine without the risk of agranulocytosis, and drugs that are highly effective at suppressing or reversing psychotic and mood disorders without excessive sedation or weight gain. The pharmaceutical industry could well discover and develop such drugs, at least for some forms of schizophrenia.

At its best, medical and psychiatric practice involves the thoughtful and rational application of evidence derived from clinical trials and well-documented clinical experience. Modern conventional psychiatry is seriously flawed in this regard, however.[19,20] It is a serious problem that the best available antipsychotic drugs are of such limited effectiveness and have such serious side effects and toxicity, and that basic questions about their correct use remain without adequate answers. Large clinical trials provide a sound basis for broad therapeutic approaches, but can be surprisingly unhelpful at guiding individual treatment decisions. Thus, the design of clinical trials designed to obtain regulatory approval for a drug, including the way in which average clinical responses are scored, may have little bearing on the way psychiatrists use it in actual practice. Which if any particular antipsychotic drug is superior in a given situation? What is its optimum dose? What is the appropriate measure of response to use? How much time should be allowed before changing the drug or its dose?[19] In practice, skilled psychiatrists continue to base clinical decisions on personal judgment, personal bias, their training experience, the prevailing culture of the centre they are working in, and on their continuing systematic and unsystematically gathered personal experience.

Things could be better. For example, it has been pointed out that clinical trials would be far more useful if they provided clinically meaningful measures of response rather than merely percentage changes on rating scales or percentage differences from the average response in the placebo group; yet these are the standard parameters used in clinical trials. It would seem far more useful to assess globally how patients are actually doing, and to develop clinical global impression scales that are more in line with how clinicians and their patients actually understand improvement and wellness.[19]

Too few patients with schizophrenia have an excellent response to antipsychotic drug therapy and too many experience serious side effects, so it is understandable why psychiatrists resort to polypharmacy. Yet little evidence exists to guide the use of combinations of antipsychotic drugs, antidepressants, anxiolytics, anticonvulsants, and lithium in this situation. Certainly, in the absence of good quality evidence, skilful psychiatrists rely on the most reliable information they can find, including information from case reports and low-quality clinical trials, and on acute observation and good judgment when selecting the combination of drugs and doses they hope will bring about the best possible outcome with the least toxicity. When considered in this light, good clinical psychiatry starts to sound something like good orthomolecular psychiatry, except that, unlike in orthomolecular therapy, psychiatrists prescribe costly and potent drugs with important side effects and toxicity, whereas orthomolecular practitioners advocate sound diet, healthy lifestyle, and micronutrient supplements.

The Future

Despite the challenges that confront orthomolecular psychiatry and conventional psychiatry, there are reasons to be confident about both of their futures, and more importantly, about the future for people suffering from schizophrenia.

The notion that excellent nutrition and orthomolecular supplements have the potential to improve body and brain makes sense to most literate people, and is no longer anathema to much of mainstream medicine. The vitamin D phenomenon dramatically illustrates the kind of change now taking place in medical thought. Only a handful of years ago most nutrition experts regarded 200 IU of supplemental vitamin D as ample. The evidence is now overwhelming that optimum vitamin D nutriture – from sunlight or supplements – requires at least ten times that much, and that some people require substantially more than this. It now appears that perhaps one third or more of apparently well people in Canada and the United States are nutritionally insufficient in vitamin D. The implications of the modern, correct understanding of human vitamin D nutrition and physiology is forcing medical authorities to revise long-held, archaic notions about vitamin deficiency and sufficiency, for if the requirement for health of this one vitamin has been so vastly underestimated for decades, why not for others? The prolific molecular and biochemical research carried out by B. N. Ames suggests that some individuals may indeed require much higher than average intakes of several vitamins for optimum physical and mental health.[21,22] Since the human brain is rich in vitamin D receptors,[23] questions about vitamin D sufficiency are certainly pertinent to people with mental illness. A recent study demonstrated vitamin D deficiency in 60% of psychiatric in-patients, but only 30% of healthy control subjects.[24]

Modern young psychiatrists are somewhat more open-minded than their predecessors. The visceral contempt felt by earlier generations of psychiatrists for vitamin and nutritional therapies doesn't have the same force among young staff psychiatrists and residents. Like other members of society, they have no problem with the notion that good nutrition is relevant to health, including brain health, and are open to the idea that vitamin supplements can play a role in guaranteeing optimum health. This is not to say that they are particularly interested in prescribing nutritional supplements to their patients! In many cases, however, younger psychiatrists are willing to go along with a reasonable therapeutic trial of orthomolecular psychiatry if they respect the integrity of the practitioner, and as long as they don't personally have to go out on a limb, or have to do extra work or study. After all, nutritional therapy for mental illness is foreign to their training and culture, and questions about vitamins won't appear on their certification exams.

Even though academic research on nutrition in schizophrenia is definitely on the back burner, some promising, innovative

research is nevertheless being carried out in a few forward-looking academic centres, especially in the study, treatment and prevention of first-episode psychosis.[25-28] One very promising research tool is structural and dynamic brain imaging to gain biological insight, diagnose variants of psychotic diseases, and identify potential beneficial changes brought about by candidate treatments.

Insights have emerged from the study of first-episode and early psychosis that tend to validate the contention by Hoffer and Osmond that the early acute phase of psychosis is biochemically different from its chronic phases, thus exposing the error mainstream psychiatry committed when it rejected the possibility that niacin/vitamin C therapy could help patients with acute schizophrenia on the grounds it was ineffective in chronic schizophrenia. Paradigms of mental illness are now emerging that were anticipated 50 years earlier by Hoffer and Osmond.

The discovery, in 2003, that many cells have a G protein-linked receptor with high affinity for niacin (but not niacinamide) has important implications in biochemistry, medicine, pharmacology and, potentially, psychiatry.[29] Activation of this receptor in skin cells stimulates prostaglandin synthesis, triggering niacin's benign skin flush. Activation of the receptor in fat cells helps explain niacin's potent triglyceride- and LDL-cholesterol lowering action, first reported by the Saskatchewan research team. Hoffer's observation that the skin flush response to niacin is diminished in many people with schizophrenia led to the development of a skin patch test which appears to represent the first specific biological marker for some forms of schizophrenia.[5] The patch test is more reliable than the rather variable flush that occurs after oral ingestion of the vitamin.[30] Since many people with acute schizophrenia (but not those with chronic schizophrenia) have a reduced or absence skin reaction to niacin, could the niacin receptors in their brains also be abnormal? Could high-dose niacin treatment restore normal niacin receptor-activated signalling in the brains of these patients? If so, then niacin therapy would represent a classic example of orthomolecular psychiatry.

Miller and Dulay measured the expression of the high affinity HM74A (niacin) receptor and, as a control, that of another, HM74 receptor with low affinity for niacin in postmortem brain tissue of schizophrenic patients, bipolar patients and people without mental illness.[31] They chose the anterior cingulate lobe for study, since this region of the brain is thought to be disrupted in psychosis. Protein mass of the control HM74 receptor was the same in all groups, but the protein mass of HM74A – the niacin receptor – was significantly decreased in the brains of people suffering from schizophrenia even though its RNA transcript was significantly increased, thus revealing a striking dysregulation between gene transcription and final protein product. No abnormalities in this receptor or its expression were present in the bipolar group. These highly novel results suggest the possibility there is a block in the genetic signal to synthesize skin and brain niacin receptors in schizophrenia.[31]

In 2005 the likely natural ligand for the niacin receptor was identified as the ketone body beta-hydroxybutyric acid, whose concentration rises in the circulation and brain during fasting (or the consumption of a ketogenic diet) to levels sufficient to activate the receptor.[32] Many years ago the orthomolecular psychiatrist Allan Cott reported that a prolonged fast was effective at clearing psychosis in many patients with treatment-resistant schizophrenia.[33] Could this treatment have acted, in part, by activating brain niacin receptors?

Wood and colleagues[34] used magnetic resonance spectroscopy to noninvasively measure glutathione concentrations in the medial temporal lobes of the living brain of normal people and 30 people with a first-episode psychosis, while also determining their skin patch response to niacin. One-half of the psychotic patients had a subnormal niacin skin patch response, and only these patients demonstrated an increase in temporal lobe glutathione. The implications of these findings are far from clear, but they suggest an important role of glutathione metabolism

in acute psychosis, and suggest that abnormalities in the amount of niacin receptors in the skin and brain are somehow involved in the pathogenesis of some forms of acute psychosis.[34]

Abnormalities in glutathione metabolism may be important in some forms of schizophrenia. In a small clinical trial, Berk and others found that treatment with the glutathione precursor, N-acetylcysteine, in the modest dose of 1 gram twice daily[35] was clinically beneficial for patients with chronic schizophrenia.[36] Recent studies suggest that high-dose vitamin B_6 ameliorates tardive dyskinesia.[37] Finally, a most interesting recent development in nutritional psychiatry is the accumulation of promising evidence that appropriate treatment with certain omega-3 fatty acids are of benefit in some mood disorders and play a role in the treatment[38] and prevention[39] of first-episode psychosis. It is worth noting that this work was anticipated many years earlier by the orthomolecular pioneer, D. O. Rudin.[40]

Action

What can people interested in orthomolecular psychiatry do to foster the goals of the ISF and improve treatment for people with schizophrenia? What are the proper mission and activities of orthomolecular psychiatry researchers and practitioners? What is the most useful role for orthomolecular advocates, educators, and activists? What can patients and their families who are interested in orthomolecular psychiatry do to help themselves?

I suggest that the future of orthomolecular psychiatry rests on 3 pillars: rational and innovative clinical practice; accurate, comprehensible and effective teaching, and first-class pragmatic clinical research.

How to Gain the Interest of Academic Psychiatry

At present there are few academic centres of psychiatric excellence with a formal interest in orthomolecular psychiatry, with the notable exception of the Department of Psychiatry at Ben Gurion University in Beersheva, Israel, where there is a chair in orthomolecular psychiatry. Young psychiatrists coming down the training pipeline don't even know orthomolecular psychiatry exists. What can non-academic practitioners do to promote a research agenda for orthomolecular psychiatry?

One way to foster academic research in orthomolecular psychiatry is for the ISF to garner funds and make them available to academic psychiatrists for simple, but sophisticated pilot projects, including Phase I and II clinical trials, especially trials that incorporate structural and dynamic brain imaging in patients with first episode psychosis or acute schizophrenia. But simply making funds available is not enough. First class clinical scientists are, by their nature, busy people who have ideas of their own to test. Those of us with an interest in orthomolecular psychiatry need to marshal arguments that will persuade talented and open-minded academic researchers that orthomolecular psychiatry is worth their attention.

I suggest that the ISF maintain and increase its effort to attract the interest of mainstream psychiatrists in orthomolecular psychiatry. Without implying any prejudice against complementary and alternative medicine, I view orthomolecular psychiatry as "alternative medicine" only in that it is ignored by mainstream medicine. Orthomolecular psychiatry concepts lie well within the biomedical model, even though, no doubt, the clinical practice is on the outer edges of what is known. Yet conventional psychiatrists commonly practice in the unknown, since so many of their standard approaches are unsupported by reliable evidence from well conducted randomized clinical trials.

Orthomolecular Psychiatry Practitioners as Clinical Scientists

It is no easy matter to maintain an efficient clinical practice while meticulously documenting one's observations and actions with an eye to publishing high-quality case reports. Most conventional physicians don't have the time for it. Yet I suggest that practitioners of an envelope-pushing treat-

ment like orthomolecular psychiatry should aspire to learn from every treatment experience and lucidly report what they find out. An organization like the ISF could help by developing documentation guidelines and evaluation aids, and by providing structure in the form of a system for convenient information exchange. Although others may disagree, I believe that the present state of orthomolecular psychiatry is such that appropriately designed and suitably powered prospective clinical trials would be premature even if they were practical, which they are not. Accurate, skilfully drafted clinical case reports and case series can be an important component of evidence-based medicine, especially when, as is true in the case of orthomolecular psychiatry, there is little or no reliable information available from randomized clinical trials. Two recent examples of this approach can be cited, the first published in the inaugural 2010 issue of the *Journal of Orthomolecular Medicine*[41] and the second a case report from the Duke University Medical School. The authors of the latter article report in detail the case of an elderly woman with chronic schizophrenia that had failed to respond to high dose lithium, olanzapine, ziprasidone, ariprazole, lamotrigine, and quetiapine but who promptly became well after she was placed on a carbohydrate- and wheat-free ketogenic diet.[42]

Orthomolecular psychiatry practitioners can have an impact beyond their own practice. First, however, they have to agree to treat people with schizophrenia! Treating psychotic people is a time consuming and often frustrating business that requires commitment, patience, and trust, but it can also be very gratifying. Patients and their families who seek orthomolecular psychiatry are most often those with a potentially better outlook, simply because they are motivated and have a social support system in place. Patients with acute psychosis are the most likely to provide dramatic results.

Since few current orthomolecular psychiatry practitioners are psychiatrists, orthomolecular psychiatry practitioners who treat psychiatric patients will be most effective if they can form a working partnership with the treating psychiatrist. Many modern psychiatrists are open to such a partnership if it is offered in a rational, conciliatory and non-threatening way. A foundational role of the orthomolecular practitioner is to make explicit the importance of a nutritious diet with minimal amounts of sugary junk food, avoidance of illicit drugs and alcohol, and the entrainment of a structured, healthy lifestyle for recovery of an ailing brain.

Schizophrenic patients I have seen in my small, hospital-based internal medicine practice were people who wanted to try orthomolecular psychiatry and who were, at my insistence, formally referred to me by the treating psychiatrist. It is my practice to send the referring psychiatrist a consultation report that summarizes the salient clinical details, including general health issues, in the process demonstrating my command of the patient's dossier. The letter includes a brief summary of the scientific principles of orthomolecular psychiatry as they apply to the case. It points out that good nutrition is important for all people and perhaps could be even more important for people whose brain is functioning suboptimally and who are prone to metabolic complications from their antipsychotic drugs. I point out that the nutritional and vitamin regimen being proposed is "off-label," but that it will be supervised by me for safety and effectiveness, while leaving decisions about the choice and dose of antipsychotic drugs between the treating psychiatrist and patient. I commonly suggest, as an empirical off-label approach, large doses of niacin and vitamin C, omega-3 fatty acids, a high-dose B complex vitamin, and adequate vitamin D for a period of 6 to 12 months of continuous therapy. In light of recent reports I will probably now include N-acetylcysteine. I commonly suggest natural vitamin E 400 IU three times daily with food as a plausible strategy to prevent tardive dyskinesia. I send a copy of the letter to the patient. I send the treating psychiatrist succinct progress reports, also usually copied to the patient. The goal of orthomolecular psychiatry therapy is to identify, when pos-

sible, a suitable signal symptom (or symptoms) that can be monitored for effect. The treatment goal is disappearance of the signals of the ongoing psychotic process such as thought disorder, paranoia, hallucinations, and negative symptoms, and the prevention of relapses. When symptoms improve, a gradual reduction in the dose of the antipsychotic drug is appropriate and prudent to mitigate its side effects and toxicity.

Advocacy and Education

By training and inclination I am a cautious clinical researcher, but this personal orientation does not blind me to the fact that orthomolecular psychiatry and the ISF were historically energized by the grass roots enthusiasm of patients and their families, nor to the conviction that its future continues to lie in their hands. In our current information age, orthomolecular psychiatry advocacy and education are more important than ever, and they have to be continual, smart, sophisticated, and passionate. There comes to mind a remark made by the Scottish philosopher, John Stuart Mill in 1861: "One person with a belief is a social power equal to ninety-nine who have only interests."

There is an unavoidable tussle and tension between the cautious, dispassionate, "interest-focused" approach necessary for sound clinical investigation and the "belief-focus" of the activist. Both attitudes are possible, and both are necessary. For good reasons one senses that it must be true that sound nutrition is vital for mental health. The multitude of reports of patients with mental illness who recovered with orthomolecular therapy, while anecdotal, is sufficient to convince those who have seen it happen or experienced it themselves of the importance of this movement.

The large drug companies have to be kept accountable for the way they promote their psychiatric drugs to physicians and the public. Good advocacy also keeps close watch on and hectors conventional narrow-minded, drug-company influenced psychiatric thinking.

Advocates can help foster a culture which no longer regards it as normal, or acceptable, to ignore malnutrition. They can expose the numb, irrational thinking some over-busy clinicians lapse into when their efficiency or authority is threatened by puzzling or seemingly intractable problems. In his account of the denial, by uncurious physicians, of rampant vitamin C deficiency among the Australian aborigines, Archie Kalokerinos, referred to this phenomenon as "mumbo jumbo thinking."[43] Doctors are neither perfect nor idiots. Most of them are doing the best they can with a heavy patient load and a deluge of medical information of varying reliability. The remedy for mumbo jumbo thinking is evidence-based medicine.

It is a real problem that so little of mainstream clinical psychiatry is based on modern evidence-based medicine, and indeed that too few psychiatrists and their patients seem to understand the principles of evidence-based medicine and how they apply to individual clinical practice. Although they seldom realize it, most psychiatrists who resist plausible nutritional approaches for treating schizophrenia do so because the approaches are foreign to the culture of their training and practice and hence evoke emotional disquiet. Advocates of orthomolecular psychiatry may gently point this problem out. It is entirely within the framework of evidence-based medicine to empirically use a safe and inexpensive off-label therapy like orthomolecular psychiatry if it is plausible, in keeping with the best available biochemical, anecdotal, and clinical evidence and complies with the wishes and preferences of the patient.[44] The reciprocal responsibility of the orthomolecular practitioner is to explain to the patient that the treatment is off-label, point out potential problems and side effects, offer the best possible prediction about what might be achieved and document the clinical situation, the treatment, and its results. The use of large doses of potentially dangerous antipsychotic drugs, and especially polypharmacy, has limited support from well conducted randomized clinical trials, and hence is also off-label, and carries with it the potential for serious side effects, toxicity, and even death.[8]

Finally, advocates can work to empower people with schizophrenia. A recent analysis once again documented the high death rate associated with schizophrenia.[45] There is need for a change in social attitudes about mental illness. According to the authors of the report, "The increased frequency of physical diseases in schizophrenia might be on account of factors related to schizophrenia and its treatment, but undoubtedly also results from the unsatisfactory organization of health services, from the attitudes of medical doctors, and the social stigma ascribed to the schizophrenic patients."

Patients and Families

Patients and families can respectfully and calmly insist on proper norms of clinical practice. They should not hesitate to have the psychiatrist clarify when an off-label treatment is being prescribed, but without being surprised how often it is justified given the inadequacy of the available on-label ones. They can bring up issues about good nutrition and a healthy lifestyle. When the patient is ready to embark on a change in diet and lifestyle they should ask for a referral to a reliable orthomolecular practitioner.

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