

Orthomolecular Treatment of Schizophrenia

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A. EVOLUTION OF THE CONCEPT

In 1968, Dr. Linus Pauling* stated, "I have reached the conclusion, through arguments summarized in the following paragraphs, that another general method of treatment, which may be called Orthomolecular therapy, may be found to be of great value and may turn out to be the best method of treatment for many patients." Immediately following this, Professor Pauling defined Orthomolecular psychiatric therapy as, "the treatment of mental disease by the provision of the optimum molecular environment for the mind, especially the optimum concentrations of substances normally present in the body."

In 1968, the Committee on Therapy of the American Schizophrenia Association consisting of around a dozen physicians all practicing, what was then called, megavitamin therapy for schizophrenia and other diseases, felt the need for a unifying concept. Dr. Linus Pauling's concept of Orthomolecular psychiatry seemed most appropriate at that time and still does because we all realized that we were, in fact,

* Pauling, Linus: Orthomolecular Psychiatry
Science, pages 160, 265-271, 1968.

This paper was presented at the joint meeting of The American Schizophrenia Association, The Canadian Schizophrenia Association and The Schizophrenia

Association of Great Britain; London, England,
September 28-30, 1971.

practicing a form of Orthomolecular medicine.

The historical roots of Orthomolecular psychiatry go back many years. One of the major roots began with the vitamin pioneers like Dr. Casimir Funk who first coined the term "vitamin." He was followed by a long line of distinguished vitaminologists and nutritionists. But a few have a special interest for us because they introduced the use of megavitamins into psychiatry. These are men like Goldberger, Sydenstricker and Joliffe and many others who did much of their work in mental hospitals. It includes psychiatrists like Cleckly, Medlicott, Sherill, Washburne, Thompson and Proctor. Gould completed very valuable work in England nearly twenty years ago.

The Adrenochrome Hypothesis of Schizophrenia

Another major root arose from the work that was started in Saskatchewan. With Osmond who recently arrived from England, I began to develop what was called the adrenochrome hypothesis of schizophrenia. We realized that the establishment of the adrenochrome hypothesis would require many decades and we were not prepared to wait patiently for this great day before

developing a therapeutic program. In 1952, there were no specific therapies for schizophrenia. If ECT or insulincoma did not work, we were helpless and our patients could look forward to many years of deprivation in totally inadequate institutions. We, therefore, made the assumption that our adrenochrome hypothesis might be correct and began to develop chemotherapy which could be used to counteract the production of the endogenous hallucinogens.

Water Soluble Vitamins

An examination of the chemistry involved suggested to us that the water soluble vitamins might be the most important factors in the treatment of schizophrenia. Of these, ascorbic acid, thiamin, riboflavin and nicotinic acid or vitamin B₃ seemed most relevant. The one that seemed the most promising was nicotinic acid. This was based upon the fact that a number of mental illnesses had already yielded to treatment with small doses of nicotinic acid. We also knew that pellagra, which had, at one time, been endemic around the Mediterranean Basin and Southern United States, was remarkably alike schizophrenia.

Megadoses of Nicotinic Acid

It also arose from observations that nicotinic acid in larger dosages had been used for the treatment of bromidism. We began to use megadoses because we were aware that if one or two grams a day of nicotinic acid had worked on chronic schizophrenics, this certainly would have been reported. We did not realize that due to error in philosophy, psychiatrists had prevented examination of the use of large dosages of vitamin for the treatment of chronic schizophrenia. When schizophrenic patients were given one gram of nicotinic acid per day and recovered, they were promptly rediag-nosed as pellagrin. This prevented proper examination of these dosages for chronic schizophrenics.

In addition, up until 1950 when most of this

work was done, nicotinic acid was very expensive and the idea of giving dosages of up to 30 grams a day could not have arisen, as it would have depleted most of the research budgets of these men.

We, therefore, decided to begin with at least three grams of nicotinic acid per day and to go up to 30 if necessary, in a carefully controlled research program. It was our hope that the use of this vitamin would effectively cut down the production of adrenochrome and adrenolutin and in this way would allow the normal, reparative processes of the body to become more effective.

Vitamin C

Another root comes from the work of Dr. Irwin Stone who has been gathering the literature on vitamin C or, as he prefers to call it, ascorbic acid. It is Dr. Stone's thesis that over the course of millions of years certain essential nutrients which were manufactured within the body can no longer be made and species have become dependent upon external sources. Without ascorbic acid, man is one of the few species who will develop scurvy. Every person, therefore, suffers from a condition called hypoascorbemia which is kept in control only as long as that person is able to maintain his exogenous supplies of ascorbic acid.

Biochemical Individuality

Another major root was the work of Professor Roger Williams who has shown with remarkable clarity, the marked individuality of people. It is clear that there is sufficient biochemical individuality so that one day a proper examination of a person's enzymes would be enough to identify him.

Orthomolecular Medicine

Finally, a major historical root was the work of Professor Linus Pauling who, established a basis for the term orthomolecular

medicine with his pioneering work on sickle-cell anemia and its relationship to hemoglobin. Dr. Pauling, having examined all of these roots, developed his present concept of Orthomolecular medicine and showed how it would be possible for species of animals to drop certain enzymes and become more dependent upon external sources of nutrients.

Dr. Pauling concluded, "The functioning of the brain is affected by the molecular concentrations of many substances which are normally present in the brain. The optimum concentrations of these substances for a person may differ greatly from the concentration provided by his normal diet and genetic machinery. Biochemical and genetic arguments support the idea that Orthomolecular therapy, the provision for the individual person of the optimum concentration of important, normal constituents of the brain, may be the preferred treatment for many mentally ill patients." Then he goes on to say, "It is suggested that the genes responsible for abnormalities (deficiencies) in the concentration of vital substances in the brain may be responsible for increased penetrants of the postulated gene for schizophrenia and that the so called gene for schizophrenia may itself be a gene that leads to a localized cerebral deficiency in one or more vital substances."

B. THE ORTHOMOLECULAR PROGRAM

The present Orthomolecular program for treating schizophrenia was developed chiefly by members of the Committee on Therapy of the American Schizophrenia Association. Each physician uses essentially the same program although there are minor variations in dosages and in the adjunctive therapies which are used.

The program is based upon our philosophy that schizophrenia is a chronic condition which is more comparable as a model to diabetes which requires the continuous use of insulin and diet than it is to pneumonia which will

respond to one series of treatments of antibiotics.

The Orthomolecular Approach

In the Orthomolecular approach, we apply the simplest treatment first, then depending upon the response, apply more difficult and varied treatments until the patient has achieved either a full or near recovery. The program cannot be defined in terms of months or years. No trial is completed until at least five years have lapsed from the beginning of the treatment. Several patients have become well after seven years.

My treatment program is divided into phases. Phase I is the chemotherapy of schizophrenia without electro-convulsive therapy (ECT). It is usually given to acute schizophrenics who can cooperate with treatment as outpatients, or who have families who ensure that the medication is taken as directed. Patients who are so ill that they have to be admitted to hospital for treatment are not started on Phase I but go into, what I call Phase II, that is, they are given a series of ECT in combination with chemotherapy.

Phase I. Treatment

In Phase I, the patients are started on vitamin B₃ three or four grams per day. Vitamin B₃ is used to cover both nicotinic acid, the form which produces a flush the first few times it is taken and nicotinamide, which is not a vasodilator. I start with nicotinamide with all patients under the age of 21 simply because young people have a much harder time with the flush. With male patients over 21, I start with nicotinic acid because of the positive side effects, such as, the lowering of cholesterol levels and the decrease in the incidence of coronary disease as well as a decrease in the incidence of senility. With women who are concerned about the cosmetic effect of the

flush, I start with nicotinamide but otherwise will begin with nicotinic acid.

Chronic patients tend to do better with nicotinic acid, the reason being that it is possible to increase the dose to higher levels. There is a maximum dose beyond which one cannot go, not because it will produce any serious toxicity, but because it produces physiological reactions such as nausea and vomiting which severely limits further intake. As a rule, it is seldom possible to go beyond six or nine grams a day of nicotinamide, but it is quite possible to go up to 25 or 30 grams a day of nicotinic acid without developing nausea and vomiting.

In addition to the vitamin B₃, patients are also given ascorbic acid from one to three grams per day and other water-soluble vitamins. I use vitamin B₁ (thiamine) if there is a good deal of depression and vitamin B₆ (Pyridoxine) if there is a good deal of muscular hyper-activity, for example, in the hyperkinetic child or in the epileptic. For fatigue, I use vitamin B₁₂.

In addition to adjusting the vitamins, they are placed upon a nutritious diet which means reducing the intake of refined foods, such as flour and sugar, increasing the frequency of feeding and of course, increasing the proportion of protein.

Attention must also be given to the use of minerals such as zinc, calcium, magnesium, iodine.

Many early cases of schizophrenia will not require anything more than this nutritional approach. I have a series of several hundred who have never received any other chemotherapies commonly used in psychiatry. However, if the patient is severely disturbed or severely depressed, it may be essential to use the tranquilizers, etc. I use moderate quantities of tranquilizers on out patients because the vitamin approach tends to improve the efficiency of these substances. Patients admitted to the hospitals where I work are treated with heavy

dosages of tranquilizers because it is important to bring them under control within 48 hours.

At the initial interview, the patients are given perceptual tests. The one that I commonly use is the Hoffer-Osmond Diagnostic Test which has proven to be a very efficient diagnostic aid, not only for diagnosing but also for monitoring treatment. It also has great value in determining when relapse is occurring. Another test is the EWI test developed by Dr. El Meligi and Dr. Osmond which is a much more skillful and sophisticated test.

After the patient has been on this program for a reasonable period of time, say about a month, he is reevaluated. If he is much improved, he is continued on the same program until he has made a complete recovery. By recovery I mean that he is free of signs and symptoms, that he is functioning well in the community, that he is getting along well with his family or at least as well as he did before he got sick, that he is a productive member of society. In other words, this patient, if examined by the most objective psychiatrist, would not show any evidence of residual disability.

The dosages of vitamin B₃ may have to be varied in order to achieve this state; between three to 30 grams a day for nicotinic acid and usually between three to nine grams a day for nicotinamide. However, once the patient has recovered, the dosages are slowly reduced until a proper maintenance is obtained. This is usually well under nine grams per day although a few cases have been higher. Tranquilizers, etc. are slowly removed from the program.

Phase II. Treatment

If the patients do not respond in a reasonable period of time to Phase I treatment, he becomes a candidate for Phase II treatment, that is, he will receive a series of ECT either as an outpatient or as an inpatient in addition to the chemotherapy.

Over the past four years, I have been using a modification of standard bilateral ECT called unilateral ECT for some patients. This has been a great improvement because it has allowed me to treat a large number of patients as outpatients and because it has reduced the average day in hospital over the past four years to fourteen days. In comparison, the University of Saskatchewan, University Hospital, Department of Psychiatry, averages around 18 to 21 days including what are called emergency admissions who are discharged after 48 hours. The patients are given anywhere from five to 20 ECT but the mode tends to be around eight to 12 ECT.

After the ECT, if the patients are substantially improved, they are discharged on the same chemotherapy.

Phase III. Treatment

If the patients have not responded, they are Phase II failures. I consider them Phase III treatment problems and will continue to work with them trying out various forms of chemotherapy and often adding to the therapeutic program penicillamine, known commercially as cuprimine, up to one gram per day. Penicillamine is a copper chelating agent which picks up extra quantities of copper from the body.

In Phase III, a five year program is laid down which might include bringing them back into the hospital every six to twelve months for a short series of ECT and for the application of various chemicals which might be of some help to them. They are special research cases. I do not give up unless the patient is taken away from me either by his own wish or by going to one of the local mental hospitals who will usually immediately discontinue the megavitamin program that they had been following. In most cases, however, as soon as they are discharged, they come right back to me. In this stage, one will also use more sophisticated techniques, for example, injectable vitamins.

Expected Results

One can expect the following results. If one were to start with a cohort of schizophrenic patients ill for one year or less, coming from the community but who have not been injured by residing in a chronic mental hospital, one would expect over a two year period to achieve over ninety percent recovery rate. The other ten percent will be better and none will have been made worse.

If, however, one started with a cohort of patients who have been sick between one and ten years but who have not been injured by residing in a chronic mental hospital, one would expect perhaps 70 per cent recovery or better.

If one were to start with a chronic population who have been treated in chronic mental hospitals for anywhere from one to 20 or more years, the recovery results are very much less and I would be surprised if one could get more than 25 per cent recovery. However, even with these chronic cases most of them will be vastly improved and will be able to function in the community to a limited degree.

I have for the past five years been following about 25 chronic schizophrenics whose average duration of stay in hospitals had been around 25 years. They have been on the megavitamin approach. I have been astonished at the remarkable improvement in some of them although none will ever be considered well. I am positive that had these unfortunate schizophrenics been started on the program 20 years ago most of them today would be well.

C. EVIDENCE THAT THE ORTHOMOLECULAR PROGRAM WORKS

It is the fashion today to depend upon double-blind control experiments to establish new treatment in psychiatry. I really

cannot complain about this because Dr. Osmond and I directed the first double-blind control experiment in the history of psychiatry in 1951 in Saskatchewan. The first experiment was a controlled study of the effect of certain yeast nucleotides. The second double-blind experiment was a study comparing the efficacy of nicotinic acid, nicotinamide and placebo in each case using three grams per day.

Double-blind Study of Thirty Acute Schizophrenics

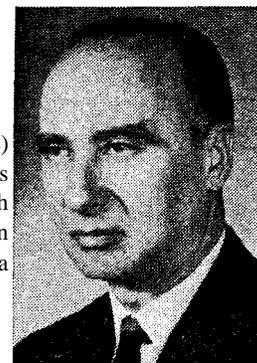
This study was started at the Munroe wing, General Hospital in Regina, Saskatchewan. Thirty acute schizophrenic patients admitted to this hospital and diagnosed by their own clinicians were randomized using random numbers into three groups of roughly ten each. All of the 30 patients received the usual psychotherapy given at this unit which was very dynamic and gave each patient about three hours per week of psychotherapy.

In addition, each therapist gave his patient ECT if this was indicated. Insulin coma was not used and the tranquilizers had not been introduced. Ten of the patients received nicotinic acid three grams per day. This group would be betrayed by the flush due to the nicotine acid and therefore, could not be considered a proper control group. However, a second group was given nicotinamide which does not produce any flush, while the third group received placebo.

The clinical and nursing staff were informed that there would only be two medications in this trial—placebo and nicotinic acid. They would assume that all of the patients who flushed were receiving nicotinic acid and that the others were on placebo. In fact, half of the non-flushers were on nicotinamide. The patients were all evaluated before the treatment by a team of psychologists and clinicians. The study ran 33 days at the end of which time the

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medication was discontinued and the patients were reevaluated.

One Year Follow Up

We decided not to use discharge criteria alone because it had become obvious that whether or not a patient was discharged did not depend primarily upon his own clinical state. It depended much more upon what the psychiatrist felt about him. The patients were followed up for one year by a trained worker who did not know what treatment they had had in the hospital. Patients were recalled at three-month intervals. At the end of twelve months, after the last patient had been treated, the code was broken and the results were evaluated.

Evaluation of the Study

It turned out that of the ten or so patients receiving nicotinic acid seven had remained well over that year. Of the ten or so nicotinamide patients, seven or eight had remained well, while of the ten placebo patients only three had remained well. Around 75% of the patients receiving vitamins had remained well, whereas, only one-third of the patients receiving placebo had remained well. It is important to remember that about two-thirds of all the patients had also received ECT so that this was a study of the combination of ECT plus megavitamins.

Double-blind Study of Eighty-two Schizophrenic Patients

The results of the study were relatively clear cut, but it seemed very important to us, not to report this until we repeated the study on a larger scale, to make sure there had been no hidden errors. We, therefore, started the second double-blind clinical experiment using the same design except that this time we did use nicotinic acid and placebo while informing the staff that we were going to follow the previous design. With our second study, we were able to treat 82 patients. The results were very similar.

Additional Studies with Schizophrenic Patients

In the meantime, I encouraged a psychiatrist working on our staff to run a study on a group of chronic schizophrenic patients using three grams per day. We proved to our own satisfaction that this dose was inadequate for this group of patients since none of them got well. (P.O. O'Reilly 1955*).

Additional evidence is based from the combined experience of the Committee on Therapy who have a total experience of 15,000 schizophrenic patients or more. We have compared notes every year for the past five years. There is no doubt that we are all obtaining similar results.

Schizophrenic Twins

Recently, I reviewed a series of 11 identical schizophrenic twins. Of these 11 identical twins which are the subject of a separate paper, every twin treated with the megavitamin B₃ approach recovered, whereas, every twin treated by the standard, that is, tranquilizer approach, is still ill. The most striking pair are a couple of

* O'Reilly, P.O.: Nicotinic Acid Therapy and the Chronic Schizophrenia. Dis. New System, pp. 16, 67-72, 1955.

women who were so identical at birth that their parents could not tell them apart and who were able to confuse their teachers and their boyfriends for a long time.

They both became psychotic about 25 years ago, and over the next 20 years each one suffered frequent relapses. They went into a mental hospital at least once a year for between one and three months and between their admissions to hospital were barely able to function. About five years ago, one of these twins consulted her family physician for backache. He diagnosed her schizophrenic, started her on the megavitamin B₃ and she recovered. Her identical twin had a similar history except that she was not permitted to start on the megavitamin by her psychiatrist. The control twin, therefore, not receiving therapy but receiving expensive psychotherapy and tranquilizer therapy has in the past three years been readmitted to a psychiatric ward at least a dozen times.

The Evidence is Conclusive

Looking over the evidence, I have concluded that every physician who has used the Orthomolecular approach, as described, with care, skill and industry, has gotten identical results. On the other hand, every physician who has not used the program, as described, has been disappointed in its results. This should not be very surprising.

A few papers have appeared recently with claims that the results of the megavitamin approach have not been obtained. When these papers are examined carefully, it is obvious that they have not followed the Orthomolecular approach because of ineffective low doses without ECT and without the other nutrients.

D. EXPANSION OF THE ORTHOMOLECULAR CONCEPT

One of the greatest but perhaps least well known psychiatrist was Dr. John Conolly who worked in England at Hanwell Hospital

over 130 years ago. Dr. Conolly had a modern conception of psychosis which he described as a perceptual disease. I am at a loss to understand how this brilliant work by Dr. Conolly has been so totally submerged in British psychiatry and only now is beginning to emerge. It is ironic that the first hospital to be called the John Conolly Hospital is now being built in New Jersey by Dr. Jack Ward and his associates.

Dr. Jack Ward, many years ago, became aware that a large number of patients, not schizophrenic but with many perceptual changes and high scores on the HOD* test, responded very quickly to megavitamin B₃. His concept was taken up by Dr. Bella Kowalson who wrote a brief paper describing a disease she called metabolic disper-ception. Most of her patients were schizophrenic but she felt that her term was not only more accurate but was much safer for her to use since as a general practitioner she did not want to argue with her psychiatric colleagues about her right to diagnose schizophrenia. In any event, we are now aware of a large number of patients who do suffer major perceptual changes which can be diagnosed by the clinical interview but which can be done more economically by the use of the HOD and EWI tests. They do respond very well on the megavitamin or Orthomolecular approach.

Effective Treatment for Alcoholic Patients

Another large group of patients are alcoholics. It has been found that they too will respond effectively. Some of the pioneers in this work are Dr. David Hawkins and Dr. Russell Smith. This work was encouraged by Mr. Bill Wilson, formerly known as Bill W. and whom you might know as the co-founder of Alcoholics

* The HOD test is a simple card sort test developed by Hoffer and Osmond (1961), Kelm, Hoffer and Osmond (1967), for assisting in the diagnosis of schizophrenia. High scores indicate severe Psychopathology. Normal scores are as follows: Total score 0—30; Perceptual score 0—3; Paranoid score 0—3; Depression score

0—3.

Anonymous. Bill W. who was one of my closest friends had watched our program with great care for many years and when he saw many alcoholics recover, he became excited, began to think about it, began to look at the evidence and eventually, depending upon data produced by men like Dr. Hawkins and Dr. Russell Smith, prepared a memo which he distributed to physicians interested in the treatment of alcoholics.

This work was primarily responsible for the present major use of the Orthomolecular approach in the treatment of alcoholism. Just to illustrate the kind of results which might be obtained, Dr. Russell Smith has been treating over 500 chronic alcoholics who had failed to respond to the best previous program including membership in Alcoholics Anonymous. Dr. Smith follows an AA program. Over the past five years he has treated these people with megadoses of nicotinic acid, ascorbic acid and with other adjuncts.

Today, 85% of these alcoholics have been abstinent for the past three years. Many of them, at first, continued to have relapses which gradually became less severe and did not last as long until the alcoholic was able to discontinue his alcohol. His work had an unexpected consequence because there was a major decrease in the highway traffic fatality rate which dropped in one county from approximately 150 to about 80 per year.

Treatment of Emotional and Behavioral Disorders in Children

The third major area where this work has expanded is in the treatment of emotional and behavioral disorders in children. I have corroborated everything that has been reported by Dr. Cott and Dr. Hawkins. A large majority of hyperkinetic children or children with learning disabilities will respond to this treatment. I have recently reviewed 140 children under the age of 14

treated with this technique. Of the total number who were maintained on the program, most are well today.

Schizophrenia an Orthomolecular Disease

I have concluded after reviewing all of this material that schizophrenia is one of the Orthomolecular diseases.

If a person consumes a diet too low in vitamin B₃ and if his average requirements are normal, he will develop pellagra. This is a condition which is so like schizophrenia that they are easily confused. If, however, the person has an average diet containing average quantities of vitamin B₃ but due to some defect in his chemistry requires quantities of vitamin B₃ which are not provided by the diet, he will suffer from exactly the same deficiency but he is said now to have a dependency condition since the error is in his body and not in the diet. It is my contention that schizophrenia is a vitamin B₃ dependency condition.

It is also my contention that this vitamin B₃ dependency condition can strike at any time from infancy to senility. If it strikes, or becomes apparent before puberty, then it will take on any of the forms of learning and other behavioral disabilities.

Study of Thirty Children with Learning or Behavioral Disorders

I am completing a study on about 30 children who were all either learning or behavioral disorders. I was not concerned about their diagnosis but merely about the fact that they were not doing well at home or at school and had been referred to me by their family physician. They were all placed upon Orthomolecular treatment and in every case where this was followed, recovered. There were a very small number where treatment could not be continued due to factors beyond my control. After these young patients had recovered, they were given placebo instead of

nicotinamide and in every case, within one month had relapsed to their previous condition. When they were again placed upon nicotinamide, they once more recovered but in many cases it took a much longer period of time thereafter, as if one major relapse had had a gravely pathological effect on their need for vitamins thereafter.

Childhood Vitamin B₃ Dependency

In my opinion, the majority of childhood illnesses of this nature, where there are perceptual and behavioral changes, which can be measured using perceptual tests or behavioral tests are instances of vitamin B₃ dependency.

During adolescence this takes the form of rebellion, hostility, excessive use of drugs like LSD, marijuana and more recently, heroin and methadone. These young children also suffer from a variety of perceptual disturbances which, by and large, are ignored by psychiatrists who deal with them and who are not aware that these are there.

Adulthood Schizophrenia

If the condition should express itself during adulthood, then, of course, we have the more typical cases of adulthood schizophrenia. We, however, run into the difficulty of diagnoses in that various countries use different diagnostic criteria and people who are considered schizophrenic in Canada and the United States might be considered not to have schizophrenia in London. These discrepancies in diagnosis will disappear as soon as all of the psychiatrists begin to use proper perceptual tests to aid them in their diagnosis.

If the condition should strike after the age of 60, these patients may be diagnosed senility. I have a fair number of so called senile patients who have been treated with the Orthomolecular approach and who are now normal.

Many Need More Essential Nutrients

Finally, there is a most important expansion of this program to include most people. According to Dr. Linus Pauling, there are at least 40 to 50 essential nutrients and perhaps 50,000 enzymes in the body. It is quite obvious that we are all different and it makes sense to believe that a large number of people may require extra quantities of one or more of these essential nutrients. At the moment, there is no scientific way of determining which of these nutrients are lacking, although a beginning has been made in this area. Dr. Arthur Robinson working with Dr. Linus Pauling, has shown that schizophrenic patients tend to retain more ascorbic acid, nicotinic acid and pyridoxin than do normal controls. When they are given a test dose of these vitamins, much less appears in their urine than it does in normal people. Their theory is that a body which requires these vitamins will tend to excrete less. This technique might one day be developed to determine which of these nutrients, any one of

us might lack. There is, however, a practical way, which is for each one of us, to run experiments on ourselves, with the essential nutrients, none of which are toxic. By trying out these nutrients, one after the other and measuring our own response, we could soon, discover whether or not, we do suffer from these Orthomolecular but perhaps, minor diseases.

CONCLUSION

I have outlined the evolution of the Orthomolecular approach where various historical streams of research have come together and have been combined into a major stream that we call Orthomolecular psychiatry. Orthomolecular therapy in psychiatry has been proven more effective for treating schizophrenia than standard therapy. It is coming into use very rapidly for treating learning and behavioral problems in children, for alcoholics and for other patients with many perceptual difficulties.

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