The Controversy Over Orthomolecular Therapy

John Hoffer

Introduction

Seventeen years ago, experimental results were published which showed that vitamin B3, used in combination with electroconvulsive therapy, was strikingly effective in the treatment of acute schizophrenia. Over the following few years a specific treatment method evolved which included vitamins B3 and C in amounts much greater than are usually used to treat vitamin deficiencies. This treatment was known as the "megavitamin" treatment for schizophrenia.

In 1968, the biochemist Linus Pauling published an article in which he outlined a new theoretical approach to the treatment of mental illness. He defined "Orthomolecular" psychiatric therapy as:

. . . the treatment of mental disease by the provision of the optimum molecular environment for the mind, especially the optimum concentration of substances normally present in the human body.

Pauling's concept well describes a therapy, based on megavitamin treatment, being developed by many psychiatrists in Canada and the United States. It is considered that schizophrenia is due to an imbalance in the biochemical pathways in the brain. By altering the diet and by providing some substances normally present in the brain (certain vitamins and minerals), the biochemical balance may be restored. Currently there is an intense controversy among psychiatrists about the effectiveness of the Orthomolecular therapy for schizophrenia. The American Psychiatric Association has recently published a "Task Force Report on Megavitamin and Orthomolecular Therapy in Psychiatry." The Task Force Report, purportedly an objective review of scientific evidence, is really a bitter attack on Orthomolecular therapy. The present paper has been written to review both the evidence and the claims made in the Task Force Report.

The Origins of Orthomolecular Therapy

In 1957 Hoffer, Osmond, Callbeck, and Kahan reported some results of the experimental use of vitamins B3 and C in the treatment of schizophrenia (11). Their conclusions were based on preliminary trials on individual patients; on a 30 patient, double-blind trial comparing the usual treatment of electroconvulsive therapy (ECT), barbiturates, and psychotherapy with the same treatment but including B3 in doses of 3 grams per day; and on a larger treatment trial over a four-year period, including 171 patients.

1 This will be available from the Canadian Schizophrenia Foundation, 2135 Albert St., Regina, Saskatchewan, S4P 2V1, in booklet form.


3 Vitamin B3 exists in two different forms: nicotinic acid also called niacin, and nicotinamide also called niacinamide. The numbers in parentheses indicate sources which have also been cited in the Task Force Report, where full references are given.
Another double-blind trial, published in 1962, included 82 patients (20, 32). A third double-blind trial was conducted by Denson (15). The results of all these trials indicated that the new treatment was much more effective for acute hospitalized schizophrenic patients than the conventional treatment without B3.

It is important to recognize that acute schizophrenia and chronic schizophrenia are different conditions, distinguishable on the basis of different symptoms as well as by some laboratory tests. Cases of acute schizophrenia may, over time, develop into chronic schizophrenia, and schizophrenia which has lasted more than a few years usually arrives at the chronic form. Very early in the research, in 1955, Dr. P.O. O'Reilly conducted an experiment on the use of B3 only in chronic schizophrenics, using 3 grams per day for eight weeks, and he found that his patients did not improve significantly with this treatment (47). Dr. O'Reilly was one of Dr. Hoffer's research associates. In 1957 Dr. Hoffer and Dr. Osmond confirmed this finding for the majority of chronic schizophrenics. The treatment was strikingly effective, however, for acute schizophrenics. Many patients who were not ill enough to require hospitalization responded to B3 alone, in doses of from 3 to 6 grams per day, with vitamin C frequently added. Those who required hospitalization usually responded to a combination of ECT, B3, and C. By 1962, a definite treatment procedure evolved (98) in which acute schizophrenics were divided into two groups, "Phase I" and "Phase II," while chronic patients were put into a "Phase III" group.

**Phase I Patients** were acute schizophrenics, ill less than a year, normally intelligent and cooperative, and not requiring immediate hospitalization. They were treated with 3 to 6 grams of B3, and vitamin C was frequently added in doses of 1 to 5 grams. If no substantial improvement was seen in one month or so, the patients were reclassified into Phase II.

**Phase II Patients** included all acute schizophrenic patients sick enough to require hospitalization. These patients received B3 and C and a short series of ECT. For these patients who required hospitalization, an interaction between B3 and ECT was clinically evident. In many cases B3 alone or ECT alone did not produce any results, while the combined treatment produced a recovery. Also many patients who did not respond to B3 in a dose of 3 grams per day responded when the dose was increased to 6 grams per day or more. Patients who responded to the treatment were discharged from the hospital and went home, where they continued to take B3 for at least a year.

**Phase III Patients** were chronic schizophrenic patients, and patients who had relapsed or failed to recover after Phase II treatment was completed. ECT, B3, and C were used for these patients as well.

It was found that the great majority of acute schizophrenics responded to Phase I and II treatments and many chronic schizophrenics responded to Phase III treatment. In all, over three-quarters of all patients treated were well or much improved - a much better response rate than for the traditional treatment. Follow-up studies published in 1963 and 1966 on patients treated many years before proved that patients who continued on the vitamin treatment tended to remain well, and gave strong support to the original findings (14, 19, 32).

By the late 1960s several improvements were made to the therapy, due to the contributions of Dr. A. Cott, Dr. D. Hawkins, Dr. C.C. Pfeiffer, and other Orthomolecular psychiatrists. Chief among these were the addition of vitamin B6, a new awareness of the importance of nutrition, and a new interest in trace metal metabolism. In 1973 laboratory and clinical contributions by 35 scientists and physicians involved in Orthomolecular therapy were published in the volume *Orthomolecular Psychiatry*. The following

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is a brief identification of the present components of
the Orthomolecular treatment for schizophrenia.5

1. **Vitamin B3.** The dosages required to have an
effect vary from patient to patient from a minimum
of 3 grams per day to (in a few cases) as much as 30
grams per day. The most frequently used dose
ranges from 3 to 9 grams.

2. **Vitamin C.** The first schizophrenic patient
successfully treated with B3 was also treated with 5
grams of vitamin C. While this vitamin was not
included in the double-blind trials published in 1957
and 1962 which used ECT and B3, it has
always been an integral part of the Orthomolecular
treatment. Lately, many experiments have shown
that vitamin C metabolism is abnormal in
schizophrenic patients. In 1963 a double-
blind study of 40 schizophrenics carried out in
England showed that there was a significant
improvement in those who received vitamin C over
those who received placebo.

3. **Vitamin B6 and other water-soluble
vitamins.** Vitamin B6 is used in doses of 0.25 to
0.50 grams or more. Dr. Cott first described the
effective use of vitamin B6, pantothenic acid, and
other B vitamins in the treatment of children with
mental illness. Dr. Rimland has published the results
of a study on the use of B3, B6, C, and pantothenic
acid in mentally ill children which showed that a
substantial proportion of the psychotic children were
benefited.

4. **Electroconvulsive Therapy.** This treatment is
used for Phase II, acute hospitalized patients, and for
chronic patients (Phase III). Previously, ECT gave
unpredictable and only transient improvements when
used in the treatment of schizophrenia. Dr. Hoffer
and Dr. Osmond found that when ECT and B3 are
used together, patients respond better than they
would to ECT alone. Furthermore, patients who
continue taking B3 afterwards tend to remain well, while it is
well known that conventionally-treated patients
who respond to ECT alone frequently relapse after a short while

5. **Antihypoglycemia diet.** Reactive functional
hypoglycemia occurs almost universally in patients
with emotional problems. This is now known to be
true of schizophrenics. Though it has never been
determined whether the altered carbohydrate
metabolism of emotionally disturbed patients is a
cause or a result of their illness, experience with the
antihypoglycemia diet has shown that when the diet
is corrected a substantial proportion of the patients
improve. Many schizophrenics consume large
amounts of refined carbohydrates and sugar. This
tends to make hypoglycemia worse. In Orthomole-
cular therapy, patients are placed on the high-
protein, low-carbohydrate, frequent-feeding diet
which is used in the treatment of functional
hypoglycemia.

6. **Trace Metals.** Dr. C. C. Pfeiffer discovered
that schizophrenics may be divided into groups of
patients who have too little blood histamine and
groups who have too much. In his experience the
histadelic (high-histamine) group, comprising about
15 percent of his patients, respond well after several
weeks to supplements of zinc and manganese. He
also has found a therapeutic interaction between
zinc and vitamin B6.

7. **Conventional Psychiatric Drugs.** These
include the neuroleptic tranquilizers commonly
used in conventional psychiatry, the sedatives, and
the antidepressants. They are used in much smaller
doses than in conventional psychiatry to keep
severe symptoms under control until the other
components of the treatment are able to act, and
they are discontinued as early as possible.

**Replications**

For many years, Orthomolecular therapy
attracted little attention from the medical
establishment, despite the fact that the results
obtained with it are superior to
those being obtained with conventional tranquilizer therapy. In the last few years there has been much more interest and this has prompted a number of independent studies. There has also been a great deal of misunderstanding and a fierce controversy about the effectiveness of Orthomolecular therapy in the treatment of schizophrenia.

Some recently published studies have been interpreted by critics of Orthomolecular therapy as finding that it was ineffective. This interpretation is disputable. In the studies a treatment of 3 grams of B3, along with the conventional drug therapy, was compared to a treatment consisting of the drug therapy alone. In many cases, there were marked clinical improvements in the patients receiving B3 compared to those who were not, while in some others there was no difference in the responses of the B3-treated and the control patients. These findings will be discussed later in detail. Much more relevant is the fact that none of the studies used Orthomolecular therapy.

There is no controversy on this point; the Task Force Report, in its discussion of these studies, agrees that the procedures of Orthomolecular therapy were not followed. However, it maintains that the results obtained are still relevant to Orthomolecular therapy. Clearly, it is important to understand whether recent studies used appropriate procedures and whether adherence to the procedures of Orthomolecular therapy is really important.

First, the early double-blind trials which formed the basis of Orthomolecular therapy used B3 and ECT in the treatment of acute, hospitalized schizophrenics (Phase II patients). Most of the trials conducted later by others dealt only with chronic patients (Phase III), and they did not include ECT. Yet the studies of O'Reilly and of Hoffer and Osmond had shown by 1957 that a treatment consisting of B3, in a dose of 3 grams per day, and ECT does not usually improve chronic patients. Trials conducted later, which dealt only with chronic patients and merely confirmed the earlier finding by Dr. O'Reilly, are not relevant to the therapy for acute schizophrenia.

Only three studies have dealt with the appropriate type of patient, that is, with acute hospitalized patients. However, none of these studies adhered to the procedure used in 1957 for none of them used ECT. With regard to the failure to replicate the procedure of the original studies, the Task Force Report states on page 46:

Electroconvulsive therapy, specifically advocated for hospitalized patients (Phases II and III patients), has especially not been replicated because it has generally fallen out of favor for the treatment of schizophrenia since the advent of the phenothiazines and butyrophenones.

Since most of the tests showing no value of nicotinic acid have dealt with Phases II and III patients and precise replication has not been carried out, it is barely possible that some of the other aspects of the treatment program (e.g. the ECT) may be the crucial variables in failing to confirm the positive results. If this should prove to be the case, then ECT may again deserve a place in the conventional treatment of schizophrenia. But if it is the case, then megavitamin or Orthomolecular treatment is a misnomer, for ECT is certainly neither. The last statement suggests the committee has some omniscient knowledge not generally available to psychiatrists. Since the mode of action of ECT is unknown, one cannot rule out the possibility ECT does help restore biochemical function of the brain - the aim of Orthomolecular therapy. On page 10 the Report states:

Although the usage of B3 remains the constant factor, and in the view of its advocates the crucial factor, this obviously does not necessarily mean that NA (nicotinic acid) or the amide is actually the single most important aspect of the total treatment program. For example, ECT might be an equally significant variable. However, as megavitamin proponents so emphatically claim that it is the crucial factor, attempts at
replication of the nicotinic acid work have usually dealt with the single addition of nicotinic acid or the amide to other specific treatment procedures.

In fact, this is not true. Orthomolecular psychiatrists do not claim that B3 is the single, crucial variable; they have never advocated treating Phase II or III patients with B3 alone. The trials published in 1957 and 1962 showed that acute schizophrenics respond exceptionally well to a treatment in which ECT and B3 are used. No claim is made about B3 alone for these hospitalized patients except that alone it is much less effective, especially in low dosages such as 3 grams, than when it is used with ECT.

The Task Force Report appears to maintain that the failure to adhere to the original procedure, while "barely possibly" the reason for the failure to obtain similar results, is really not important. This attitude is incorrect, for the published data indicate the contrary. No one who designed the experiments which omitted ECT and none of the authors of the Task Force Report have had any personal experience with Orthomolecular therapy; they have no grounds on which to determine which factors in the procedure are more or less important. The fact that ECT was omitted is a likely explanation for failures to obtain comparable results.

However, there is a more important consideration about Orthomolecular therapy: it is very different now from the simple combination of ECT and B3 which was used in the early successful trials. Psychiatrists interested in verifying its effectiveness should not confine their procedures to the ones used 15 years before. Yet most of the studies published recently by non-orthomolecular psychiatrists have been restricted to B3 alone in small, fixed dosages. Thus not only have they failed to use the procedures of the earliest B3 studies, they are completely irrelevant to current Orthomolecular therapy.

On page 8, referring to experiments which only used three grams of B3, the Task Force Report states:

Arguments that these studies are not relevant because they do not address themselves to the complete therapeutic program as it is employed in 1972 would appear to have little merit because the claims made for the newer procedures are not based upon rigorously controlled studies and have not been published in careful detail.

Also, it is argued:

Orthomolecular psychiatrists constantly protest that failures to replicate results stem from inappropriate selection of patients and from the failure to utilize all of the components of their present program. The latter claim is probably correct because it is virtually impossible to replicate studies in which each patient receives a highly individualized therapeutic program with from one to seven vitamins in huge doses, plus hormones, special diets, other drugs and ECT, which are added or subtracted not on the basis of proved biochemical abnormalities but rather on the basis of the clinicians' individual judgment as to the patient's needs.

Orthomolecular therapy, like other therapies in medicine, requires a knowledgeable, experienced physician who can judge the dosages of vitamins, minerals, and drugs to prescribe, according to each patient's needs. Each patient is treated as an individual, but there is nothing variable or arbitrary about the overall approach to the therapy, which is quite straightforward. It is probably much less complicated than conventional psychiatric treatment methods, which use a wide assortment of sedatives, antidepressants, anticholinergics, hormones, ECT, and tranquilizers, often in enormous dosages. What the Task Force Report is doubtless referring to, when it states that replicating Orthomolecular therapy is "virtually impossible," is double-blind, placebo-controlled experiments.

Their argument can be more plainly put as follows. The double-blind - a method of experimentation in which neither the
patients nor their doctors know which patients are taking the active medication and which are taking placebos - is only amenable to testing simple treatments which are not individualized. Orthomolecular therapy is individualized, and without knowing what dosages of vitamins and other substances a patient is receiving, it is impossible to judge the correct amount he ought to be given to treat him effectively. The amounts required will differ from patient to patient, and it would be virtually impossible to arrive at the correct dosage for each patient in a double-blind setting.

Implicit in the Task Force's argument is the assumption that the double-blind method is the only one that can produce useful clinical evidence. Actually there are a number of valid alternatives, and the double-blind is by no means the only way of testing new treatments, nor is it invariably the best. Dr. Louis Lasagna has recently written:

I am sorry that so many people have overbought the concept of the controlled trial and that other valid ways of acquiring evidence have been neglected. L-dopa is an example of how a drug can be rated as ineffective on the basis of poor double-blind controlled trials, several of which were done early in its history. Because inadequate dosages were used for inadequate periods of time, there was no significant effect. It was on the basis of uncontrolled trials of L-dopa ... that one came to the conclusion, and rightly so, that this drug was a dramatic therapeutic advance. We have only to remind ourselves that all sorts of highly important psychoactive agents such as barbiturates, meprobamate, chlorpromazine, imipramine, etc. were discovered by ways other than the formally controlled trial.6

Since Orthomolecular therapy cannot be fitted, into the design of a double-blind experiment, it is a mistake to alter the treatment to try and fit the device which is testing it. Alternate testing methods, some of which will be mentioned below, must be employed.7 There is another important reason why the double blind is a poor method to use for Orthomolecular therapy: the inhomogeneity of schizophrenia. It is now generally believed by psychiatrists that schizophrenia is a group of different mental diseases which have a similar expression. In double-blind studies in which a single component of Orthomolecular therapy is used, some of the patients may well respond to it, but the finding could go undetected in the overall results because many other patients treated with this single component will not improve. Combining their response with that of the patients for whom the treatment is effective, the averaged-out figure for the treated group's improvement might not be significantly different from the figure for the control group.8

Dr. JR. Smythies has recently written an article in which he criticized on just these grounds the double-blind studies described in the Task Force Report. He advises that the large double-blind experiments be abandoned and replaced by screening trials and by longitudinal studies of individual patients who respond to Orthomolecular treatment.9 Dr. T.A. Ban, a co-author of the Task Force Report in discussing the question of orthomolecular therapy and the lack of homogeneity in schizophrenia, has written (not in the Task Force Report):

...(N)o clinical trials in carefully selected populations, employing biochemical indicators, have been completed as yet. Without the results of these studies the therapeutic potential of nicotinic acid in Psychiatry cannot be considered fully evaluated (57).


7 Many others have pointed out situations where the double blind is not applicable, yet valuable results may be obtained. See, for instance, the remarks of Sir Austin Bradford H9: The Clinical Trial. Practitioner. 190:85, 1983.

8 J.R. Wittenborn's study, discussed later, is an example of this.

The controversy over orthomolecular therapy

Before it can be predicted from biochemical or other tests precisely which patients are likely to respond to specific components of Orthomolecular therapy, it does seem apparent that double-blind trials are uninformative and wasteful. There is one simple, conclusive method by which research psychiatrists can verify the effectiveness of the Orthomolecular approach within the setting of a clinical trial:

*It is hoped that investigators will one day start with a cohort of schizophrenics and carry them through the entire procedure together with a control cohort who would not receive any vitamins. In this way improvement with megadoses of vitamin B3 would be apparent within two years (13).*

Using this method, the Orthomolecular procedure will be carried out in full, with consultation from an experienced orthomolecular psychiatrist. If the program is of no value, this will be demonstrated. On the other hand, if the orthomolecular-treated group is significantly improved over the conventional group, the difference will be obvious. The patients who respond to the Orthomolecular treatment can be studied individually and biochemically along the lines described by Dr. Smythies.

In fact, many psychiatrists have used essentially this approach on their own, and they have reported highly favorable results (10, 16, 17, 33, 34, 35, 38, 39, 40). The authors of the Task Force Report discount the findings of these psychiatrists who found that Orthomolecular treatment is effective on the grounds that they were not based on double-blind experiments.

The fact remains that experiments cited as contradicting the findings of Orthomolecular psychiatrists have not used the procedures either of the early successful trials or of modern Orthomolecular therapy.

They have all been double-blind experiments, and most of them have been conducted on chronic patients. As it happens, the results of these studies are mixed. In many of them, the use of 3 grams of B3 alone in a double-blind setting produced significant improvements in schizophrenics. It is important to examine these studies carefully. The finding that B3 alone may benefit many schizophrenics is strong support for Orthomolecular therapy, which uses B3 as one of its main components.

The Canadian Mental Health Association Collaborative Study

In 1968 the Canadian Mental Health Association (C.M.H.A.) set up a series of studies to obtain information on the effectiveness of Orthomolecular therapy. Twelve studies were planned, of which five have now been completed. Unfortunately, none of them used the procedure of the 1957 and 1962 research involving the interaction between B3 and ECT. Despite this, several of the studies have shown significant improvements in patients treated with low dosages of B3 over control patients. All five of the C.M.H.A. studies will be considered in this paper.

First, Study No. 12, by Ananth, Ban, Lehmann et al. is entitled "Nicotinic Acid in the Prevention and Treatment of Artificially Induced Psychopathology in Schizophrenics" (54). It consisted of a study on chronic, schizophrenics (Phase III) in which half the patients were given nicotinic acid in a dose of 3 grams per day and half were given placebos, for two weeks. The neuroleptic tranquilizer therapy which all the patients had been on was withdrawn. As might be expected, the patients receiving placebos deteriorated significantly when the tranquilizers were withdrawn. However, the patients receiving 3 grams of B3 showed a marked, statistically significant improvement.
All the patients were then given very large doses of methionine, 20 grams per day, along with their continued medication of 3 grams of B3 or placebos. The hypothesis tested in this experiment was that methionine, which has been shown to worsen the symptoms of schizophrenia, might exert this effect because it is a methyl group donor. B3, on the other hand, is a methyl group acceptor. It was hypothesized that the effectiveness of B3 in schizophrenia results from this characteristic of the molecules of B3; that is, B3 might remove methyl groups from some methylated compounds in the body which could be causing the mental illness. After the administration of 20 grams of methionine per day, all the patients showed a pronounced worsening of their symptoms. The Task Force Report has interpreted this as showing that nicotinic acid does not neutralize the methyl-donating effect of methionine in worsening schizophrenia. This conclusion, however, is not justified, because there was a serious flaw in the experiment. The patients were given 20 grams of methionine per day, but only 3 grams of nicotinic acid. Over 16 grams of nicotinic acid are required to accept the methyl groups donated by 20 grams of methionine. The experiment was bound to fail.

This flaw was acknowledged in the original published research report as well as in an official summary of it. The flaw is not acknowledged or even mentioned in the Task Force Report. The only valid finding emerging from this study is that B3 not only forestalled the deterioration anticipated when tranquilizer medication was withdrawn, but it produced a significant improvement in the patients treated with it. This finding is not mentioned in the Task Force Report.

Methionine binds Pyridoxine which is essential for the conversion of tryptophan into coenzyme one, nicotinamide adenine dinucleotide (NAD). The injurious effect of methionine is therefore easily explainable.


It would be almost a miracle if any quantity of vitamin B3 could compensate for a methionine-induced Pyridoxine deficiency.

Second Study No. 1 of the C.M.H.A. studies, by Ananth, Vacaflor, Kelhwa, et al. (58) dealt with 30 acute hospitalized schizophrenics (Phase II). The patients were divided into three groups, one group receiving nicotinic acid, one group nicotinamide, and the third group placebos. Neuroleptic tranquilizers were administered to all the groups on a restricted scale. It was intended to investigate the patients for two years, but only six patients completed the entire period. Nevertheless, 25 patients spent the first three months in hospital, and at the end of this period their clinical status was assessed by means of the Brief Psychiatric Rating Scale (BPRS).

It was found that there were statistically significant improvements in the total BPRS scores for all three groups. However, Table 3 of the research paper shows that out of 15 BPRS items, the patients receiving nicotinic acid improved in 11 items and the patients receiving nicotinamide improved in 12 items, while the patients receiving placebos improved in only six items. Thus both the B3-treated groups scored improvements in approximately twice as many items of the BPRS as the placebo-treated group. The published paper also includes clinical assessments of the patients at the end of the two-year study. There were improvements in 10 out of 15 items in both the nicotinic acid and the nicotinamide-treated groups, but improvement in only six items in the placebo-treated group. Because 80 percent of the patients dropped out of the study before its completion, these results are much less reliable than the ones obtained at the end of the three-month period in hospital, when few patients had dropped out. However, the same general picture is obtained as at the end of the three-month period; that is, both the nicotinic acid and the nicotinamide-treated

12 This difference is statistically significant at the .05 level. P<.05.\textsuperscript{2} = 6.007. Hypothesis of Homogeneity with 2 degrees of freedom.
groups improved in many more BPRS items than did the placebo group.

The summary of this study given in the Task Force Report doesn't mention these results. Instead, it points out that the average number of days in hospital during the two-year period was 214 days in the placebo-treated group, 214 days in the nicotinic acid-treated group, and 353 days in the nicotinamide-treated group, showing that the length of time spent in hospital was not significantly different for the B3-treated groups compared to the control group. The conclusion to be reached about the study depends on whether one takes the average number of days spent in hospital as the critical variable, or whether one takes the number of symptoms of mental illness alleviated in the course of the treatment as the critical variable. The latter is by far the more reliable.

The Task Force Report has interpreted this study as demonstrating that (page 15): . . . The overall therapeutic efficacy of nicotinic acid as the sole medication in newly admitted schizophrenic patients is not superior to the overall therapeutic efficacy of an inactive placebo.

This conclusion is based on the insignificant differences in average duration of hospital stays. The evidence derived from actual psychiatric evaluation of the patients, which showed a definite superiority of both the groups receiving B3 over the control group, is not even mentioned.

**Study No. 7** of the C.M.H.A. studies, by Ananth, Ban, and Lehmann, is entitled "Potentiation of Therapeutic Effects of Nicotinic Acid by Pyridoxine in Chronic Schizophrenics." It was intended in this experiment to test the finding of Orthomolecular psychiatrists that B3 and B6 (Pyridoxine), when combined, have an enhanced effect in the treatment of schizophrenia. A 48-week double-blind study was conducted in which one group of patients received nicotinic acid, one group Pyridoxine, and a third group received a combination of nicotinic acid and Pyridoxine. All the patients were chronic schizophrenics. The Task Force Report summarized the results of this study as follows (page 15):

**From Study No. 7:** the overall therapeutic efficacy of combined administration of nicotinic acid and Pyridoxine as an adjuvant medication in chronically hospitalized schizophrenic patients is inferior to the overall therapeutic efficacy of the component drugs.

This summary is a completely inaccurate description of the actual findings in the study. The results which were actually obtained and reported in the published research paper were the following:

In this 48-week placebo-controlled study, the therapeutic effect of a combination of nicotinic acid and Pyridoxine was compared with that of treatment with either nicotinic acid or Pyridoxine alone. Of the three indices of therapeutic effects, global improvement in Psychopathology (BPRS and NOSIE) scores was seen in all three groups; the number of days of hospitalization during the period of the clinical study was lower in both the nicotinic acid and the combined treatment group; and only in the combined treatment group was the daily average dosage of phenothiazine medication decreased. Thus, improvement in all three indices was noted in the combined treatment group.

And:
*On balance, these results suggest that the addition of Pyridoxine may potentiate the actions of nicotinic acid. Thus Pyridoxine seems to be a useful adjunct to nicotinic acid therapy.*

The Task Force Report summary of the C.M.H.A. **Study No. 3** by Ramsay et al.

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(53) also gives a false representation of the actual findings. On page 15 the Task Force Report states:

*From Study No. 3: the overall therapeutic efficacy of nicotinic acid as an adjuvant medication in newly admitted schizophrenic patients is inferior to the overall therapeutic efficacy of an inactive placebo.*

In fact, the addition of nicotinic acid, in the dosage of 3,000 mg per day, to the regular phenothiazine treatment - in a placebo controlled six months study with 30 patients - prolonged the duration of hospital stay and increased the amount of neuroleptic medication required in treatment.

The results of this study do not show that patients receiving nicotinic acid were made worse because of it. The difference in the average duration of hospital stays was not significant. The difference in the average amounts of neuroleptic tranquilizers administered to the different groups is of doubtful significance. The drugs were prescribed for more than half the duration of the study on the basis of short, outpatient interviews by resident psychiatrists (psychiatrists in training). Even among experienced psychiatrists, the dosages of these drugs given to acute schizophrenics are highly variable. The dosage of a tranquilizer drug prescribed for a psychotic patient is a very crude and very indirect indication of his clinical status, and it can be influenced by a multitude of extraneous factors.

The direct and obvious method of assessing the condition of patients is by observing them. If B3 had worsened the patients, it would be detectable by a worsening of their symptoms. In fact, it was found that the B3-treated groups improved significantly. The research paper states:

*Of the three, the nicotinamide-treated group showed statistically significant therapeutic improvement on more individual items (9) of the BPRS than either the nicotinic acid or the placebo groups; the latter two groups showed significant improvement on six and eight items respectively (53).*

One may conclude that the B3-treated groups in this study did not, in the overall assessment, improve more than the control groups. This has little relevance to Orthomolecular therapy, in which B3 would not be used alone and in such small dosages. There is no evidence that B3 worsened the condition of the patients who were treated with it.

The final C.M.H.A. collaborative study was conducted on 30 chronic schizophrenic patients. In this study one group of patients was treated with 3 grams of nicotinic acid, one group with 3 grams of nicotinamide, and the third group was given placebos. The Task Force Report's summary of the results of the study is as follows:

*From Study No. 4: the overall therapeutic efficacy of nicotinic acid - in the dosage of 3000 mg per day - as an adjuvant medication in chronically hospitalized schizophrenic patients is inferior to the overall therapeutic efficacy of an inactive placebo. In fact, in a one-year placebo-controlled study with 30 patients, the active treatment groups fared worse than the placebo group by all measures of assessment. The least improvement and the greatest amount of deterioration was seen in the nicotinic acid group. Moreover, it was shown that patients in the placebo group required less increase in their concomitant phenothiazine medication than patients in the two active treatment groups.*

The actual published data 16 show that

*16 T.A. Ban. op.cit.*
THE CONTROVERSY OVER ORTHOMOLECULAR THERAPY

ey every statement in this summary is false. In the study, three methods of clinical evaluation were used: the Clinical Global Impression Scale (CGI), the Nurses Observation Scale for Inpatient Evaluation (NOSIE), and the Brief Psychiatric Rating Scale (BPRS). The patients were rated on these scales before the study began and after its conclusion, and the results are these: the changes in all three evaluation scales before and after treatment were insignificantly small for the patients in the two B3-treated groups and in the placebo group. There was no improvement and no deterioration in any group.

It is clear that a treatment of 3 grams of B3 per day did not benefit these chronic patients. This is a result to be expected on the basis of the studies by Dr. Hoffer and Dr. Osmond and by Dr. O'Reilly, who had already reported that chronic patients, like the ones in this study do not respond to 3 grams of B3 alone.17 At the same time, contrary to the claims in the Task Force Report, there is absolutely no evidence that the administration of B3 worsened the condition of the patients who received it. It can easily be shown that the numerical variations in the clinical scales which were observed are small, random fluctuations which are due to the inexactness of the evaluation methods. For example, on the CGI scale, the nicotinic acid-treated group went from a pre-treatment score of 4.1 down to 3.9 after treatment, an improvement of 0.2 points. The placebo group went from 4.2 down to 3.7 - an improvement of 0.5 points. The nicotinamide group also improved by 0.5 points (4.7 to 4.2). On the basis of this the Task Force Report states that the nicotinic acid group "had the least improvement and the greatest amount of deterioration." Yet the CGI scale in this experiment is inexact by a minimum of 0.6 points; any change less than that is equivalent to no change at all. The nicotinic acid group's "improvement" by 0.2 points is not less than the placebo and nicotinamide groups' "improvements" of 0.5 points - all these changes are too small to have any significance.

The Task Force Report states: "... the active treatment groups fared worse than the placebo group by all measures of assessment." This is false, for the nicotinamide group "improved" on the BPRS by 1.3 points (improving from a pre-treatment 45.9 to 44.6 after treatment), while the placebo group "deteriorated" by 1.6 points (rising from 37.8 to 39.4).

As it happens, BPRS was imprecise by at least 10 points, so these changes, too, are not significant. The differences in the average dosages of the tranquilizers administered to the patients before and after treatment were also insignificantly small. There was no evidence that the patients in the placebo group required less increase in their tranquilizer medication than the B3-treated patients; the statement to this effect in the Task Force Report is wrong.

In summary, three of the five C.M.H.A. studies provide evidence to support the findings of Orthomolecular psychiatry. The Task Force Report's description of every study is biased and misleading. It is remarkable that the authors of the Report make incorrect claims that B3 is worse than a placebo, putting the most negative possible interpretation to some equivocal research findings, while not even mentioning the research findings that showed B3 was of clear definite benefit18

The Studies by Wittenborn and McGrath

Only two other double-blind trials have been carried out dealing with acute schizophrenics. The first of these is the study by McGrath et al. (51) who studied 265 consecutive admissions for schizophrenia, both acute and chronic. Half the subjects were given placebos and half were given 3 grams of nicotinamide, in

17 Nevertheless, in studies 7 and 12 chronic patients did improve significantly, so the picture is not so clear. Apparently some chronic patients may respond to B3 alone.

18 For a striking example of this, read on page 16, in reference to Study No. 12: "In fact, during the two weeks of methionine (20,000 mg per day) administration, there was a considerably greater increase in psychopathological symptoms ... in the nicotinic acid group than in the placebo-treated group." This difference was of no statistical or clinical significance. The highly significant improvement observed two weeks earlier in the nicotinic acid group (P<.02) is nowhere acknowledged.
addition to the regular tranquilizer and rehabilitation program. One can infer from the information given in the published research paper that between 30 and 57 percent of the patients were acute schizophrenics, while between 43 and 70 percent were chronic. When McGrath et al. compared the response of the patients who received 3 grams of nicotinamide with the response of the control patients, they found no significant difference between them. Considering that the treatment was inadequate and that more than half the patients in the study were chronic, this result was to be expected. In referring to this study, the Task Force Report states (page 11):

No improvement was noticeable either after 30 days of treatment or after one year in either the acute or chronic patients.

This statement is seriously misleading, for it leaves the impression that the responses of the acute and chronic patients were observed separately. In fact, the McGrath et al. report made no distinction between acute and chronic patients, and all the figures presented in the research paper were based on the results of the total group. Even if a significant number of the Phase II (acute) patients did respond to McGrath's treatment of 3 grams of B3, the significance was not detected because of the large number of unimproved chronic patients.

The only other study which included acute schizophrenic patients is the one by Wittenborn et al. (52). As in other studies, the treatment chosen was inappropriate for these Phase II hospitalized, acute schizophrenics, consisting only of 3 grams of nicotinic acid. Despite this, the study provided strong evidence that this treatment with only a part of the Orthomolecular program was of significant benefit to a certain proportion of the patients.

Based on the overall results, Wittenborn et al. found that there was no significant difference, over 24 months, between the nicotinic acid-treated group and the control group (52). However, a certain subgroup of the patients, making up about one-third of all the patients, did respond well to the treatment of 3 grams of nicotinic acid per day.¹⁹

Each patient entering the study was examined carefully before the treatment was started. From social data so obtained, several factors discriminated between the patients who responded to 3 grams of nicotinic acid and those who did not respond, as the study progressed. The patients who responded well to nicotinic acid were ones whose past history before becoming psychotic had involved strong elements of interpersonal participation. Such patients comprised 35 percent of the whole group being investigated. These "high predictive score" patients fared much differently during the experiment, depending on whether they received nicotinic acid or placebos. The B3-treated group scored approximately two times better than the placebo-treated group on all the clinical assessment scores. When outpatient adjustment was studied, it appeared that the patients with high positive predictive scores who were treated with B3 resumed a constructive quality of adjustment outside the hospital. The same type of patients (high positive predictive score) who received placebos did not show any reconstructive trends and did not do particularly well:

The present post hoc treatment of the data reveals that persons whose premorbid history suggested a participatory life style tend to return to a participatory pattern of living after a year or more treatment with high levels of niacin. No such reconstructive trend was indicated for the control patients, however.²⁰

There is a further interesting aspect of this study. Because of the heterogeneity of the patients, the significant improvement of one subgroup of them was statistically hidden, and overall there was no

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²⁰ Wittenborn, J.R. op.cit.
significant difference between the total B3-treated group and the control group. This is one of the faults of the large double-blind trials. Had Wittenborn’s analysis been less detailed, the important result obtained would have gone undetected. It might be compared to treating with vitamin B12 a group of anemic patients, only one-third of whom have a vitamin B12-deficiency anemia. Since only one-third of the group given B12 will respond, there might be no overall statistically significant difference between the groups treated with B12 and placebos.

The authors of the Task Force Report choose to downplay the importance of Dr. Wittenborn’s findings; indeed, they appear almost disconcerted by them (page 13):

*The analysis of the data continues, but none of Wittenborn’s findings encourage the expectation that vitamin B3 is an effective treatment for the great mass of schizophrenics who are hospitalized for this disorder. Although Wittenborn considers his data to be consistent with the possibility that as many as 1/4 of his schizophrenic population (those with good premorbid adjustment) might be benefitted by the addition of niacin to the psychotropic drug treatment, the fact that he finds no significant difference between the total control group and the total vitamin group implies that a fraction of his experimental group may have had their progress impeded by the vitamin addition. Wittenborn also questions the aptness of the schizophrenic designation for those patients with the good premorbid history that are identified as improving with the vitamin.*

There is no evidence from the results of the study that patients had their progress impeded because they were treated with B3. It is true that two-thirds of the special patients benefited from 3 grams of B3, while there was no statistically significant difference between the total control group and the total B3 group. But as is well known in statistics - this does not permit the inference that some of the B3-treated patients were harmed.

The Task Force Report correctly points out that Dr. Wittenborn questioned the adequacy of the schizophrenic designation for the subgroup of patients who responded to 3 grams of B3. In fact, he suggested that they might not be "schizophrenics," but rather persons suffering from "dissociative psychotic episodes suggestive of schizophrenia."21 This possibility is of great importance. It will be the first time a group of schizophrenic patients have been identified who respond specifically to small dosages of B3, in the absence of the other components of Orthomolecular therapy; clearly one should split this group away from the main group of schizophrenics. It is only through attempts of this sort that the inhomogeneous group of "schizophrenias" will be broken down into specific diseases which will respond to specific biochemical (and other) treatments.

It is important to recognize that the clinical symptoms of the subgroup of patients who responded to B3 were the same as those of the other patients; the characteristic that is different about them is that they had good personal relationships before becoming ill. The natural course of their illness also is the same as that of the other patients for if they received tranquilizers only (without B3) they did not do well.

The Task Force Report, by not amplifying its statement, "Wittenborn also questions the aptness of the schizophrenic designation for those patients . . . improving with the vitamin," may leave the impression that these patients have a more benign disease. The results of the study show the contrary: they are just as ill, and have just as poor an outlook if treated conventionally, as all the other patients. This finding, along with the possibility that such patients may make up about one-third of all mental hospital admissions diagnosed as acute schizophrenia,22

21 Wittenborn, J.R. op.cit.
22 The Task Force Report quotes the figure 25 percent. The high predictor group comprised 35 percent of the total sample; two-thirds of this group responded to B3.
emphasizes the importance of following up Dr. Wittenborn's findings.

This study together with two of the C.M.H.A. studies are the only ones which dealt specifically with acute, hospitalized schizophrenics. None of the three were replications of the treatment method used in the double-blind studies published in 1957 and 1962, and none of them used methods which resemble current Orthomolecular therapy. Yet the results of two of the three studies using B3 alone demonstrate a distinct benefit in many acute schizophrenics receiving this single component of the entire Orthomolecular procedure. Other investigators have conducted trials where B3 or vitamin C were used in the treatment of acute and chronic schizophrenics. It was found in these trials, as well, that certain components of Orthomolecular therapy are of value even when used alone (46, 48).

**Hostile Bias of the Task Force Report**

The Task Force Report strongly criticizes the research in which it was found that the Orthomolecular therapy produced a significant improvement in acute schizophrenics; however, many of the criticisms are incorrect. For instance, the report criticizes the studies by Dr. Hoffer and Dr. Osmond on the grounds of a "non-random selection of small numbers of the total population at risk;" of a "lack of clearly specified initial clinical diagnosis or systematic rating of patient behaviour;" and of a failure to clearly explicate the criteria of patient improvement.

In fact, the double-blind studies were randomized and the patients were representative of the population at risk. It is wrong to claim that the number of patients in the studies is small, since the number of patients in the first double-blind study was 30, the same number of patients as in each of the C.M.H.A. studies, while the number of patients in the 1962 study was 82, almost the same number of patients as was used in Dr. Wittenborn's study. These other studies have not been criticized on the grounds of a small number of patients.

The criteria for improvement in the second double-blind study and in its follow-up study have been criticized, but they were identical to those used in the McGrath et al. study; that is, Not Improved, Improved, Much Improved, and Well. The diagnostic assessment of patients was clearly explained in the paper of Hoffer et al. (11), and included the Bleuler criteria as well as a scoring on 10 factors characteristic of schizophrenia, such as delusions, speech and mental blocks, hallucinations, ideas of reference and control, seclusiveness, and so forth. The 10-year follow-up study has been criticized on the grounds of a small number of patients, yet the survey included a total of 518 patients, of whom 169 were on the megavitamin treatment and 349 on other treatments (14).

It is evident that the Task Force Report is harshly critical of any research which supports Orthomolecular treatment, while it supports anything which might be used to discredit it. For instance, on page 45 a claim is made with regard to the treatment of Phase I patients:

*It is suspected that a substantial number of ambulatory patients (Phase I) for whom the best results are obtained may not actually have been schizophrenic and represent a group for whom the spontaneous recovery is high.*

23 See also the following:


24 "All patients diagnosed as schizophrenic by the clinical staff were assigned to the research project. They were then given a series of psychological tests and assigned at random to one of three treatments, that is, administration of a placebo, nicotinic acid, or nicotinamide using a double-blind procedure" (11).
There is no evidence to support this claim. In fact, the only possible support is Dr. Wittenborn's suggestion that perhaps the particular type of patient in his study who responded to 3 grams of nicotinic acid per day might not be schizophrenic, but suffering from dissociative psychotic episodes suggestive of schizophrenia. However, this could not represent a group for whom the spontaneous recovery is high for Dr. Wittenborn found that, in contrast to the patients receiving B3 who made marked clinical improvements, the patients taking placebos did not improve at all. The spontaneous recovery rate in this latter group of patients was not high; it was very low.

The hostile bias is evident in other areas as well, to the extent that the authors make dogmatic statements which they contradict by their remarks in other publications. For example, there is the criticism of the Adrenochrome Hypothesis originated by Dr. Hoffer and Dr. Osmond, a hypothesis that a substance called adrenochrome may be formed in abnormal amounts in the tissues of schizophrenics and cause the mental illness. On page 6 it is claimed, "Not only is there no evidence for adrenochrome formation in vivo, but the psychotomimetic properties of adrenochrome have not been replicated." The psychotomimetic ("psychosis-producing") properties of adrenochrome, originally reported by Dr. Hoffer and Dr. Osmond, have indeed been replicated, as Dr. Ban, a co-author of the Task Force Report, has acknowledged elsewhere.25

Another example is related to the use of nicotinamide adenine dinucleotide (NAD) in the treatment of schizophrenia. NAD is not vitamin B3 but is one of the molecules which B3 forms in the body. It was found to be effective in the treatment of a group of acute and chronic schizophrenics by Dr. Hoffer and Dr. Osmond in a study published in 1966. A number of other scientists tried to repeat these results, but did not find NAD to have any significant effect in their experiments. These different findings have not been explained, though it is known that there is great variability in the quality of commercial NAD because it is a very unstable molecule. Furthermore two different groups of patients were used. The original NAD study was made on patients who were acute, subacute, and chronic, but most had not spent many decades in mental hospitals. The attempts to confirm used chronic deteriorated schizophrenics of the back ward type. Even so, of the eight patients from Kline's study who were able to complete the HOD test the scores of the four on NAD became normal while the scores of the four on placebo remained at their original high levels.

The Task Force Report has used the differing experimental findings to attack the credibility of Dr. Hoffer and Dr. Osmond. It states on page 22, with regard to the use of NAD as a treatment for schizophrenia: "The total failure to obtain positive findings when the therapeutic procedure was attempted by other investigators diminishes the credibility of niacin advocates as critical clinical researchers."

The Task Force Report also claims that:

. . evidence that NAD is effective has been refuted clinically and evidence of an NAD deficiency in schizophrenia lacks both biochemical and clinical support.

These statements are contradicted by Dr. Ban in another publication in which he reviewed the theoretical and biochemical basis for NAD therapy in schizophrenia in a favorable manner. Referring to the NAD trials, Dr. Ban writes:

In spite of the challenging theoretical considerations based on animal pharmacological studies, and Hoffer's (7966) positive therapeutic results, the unsuccessful attempts to replicate his findings have resulted in a decrease of interest in the nicotinamide adenine nucleotide question.

25 In: Nicotinic Acid in the Treatment of Schizophrenias, Canadian Mental Health Collaborative studies. Introduction, 1971, Dr. Ban wrote, "After a considerable dispute, however, the psychotomimetic properties of adrenochrome were confirmed."
The NAD problem was brought into a different light, however, by the systematic studies of Pfeiffer and his collaborators (7968). In combining the clinical with the electroencephalographic method, Pfeiffer and his group were able to demonstrate that an enteric coated NAD preparation does exhibit a therapeutic action ... Pfeiffer et al's (7968) findings indicate that the claims about the clinical effectiveness of NAD therapy need to be further investigated with contemporary methods.26

There is both clinical and biochemical evidence to suggest that an elevation of the NAD concentration in the tissues of schizophrenics may alleviate their disease, but the evidence, some of which a Task Force member cited in a different paper, is not acknowledged in the Task Force Report. The following are further examples of the hostile bias in the Task Force Report. On page 43, in a discussion of the side effects of nicotinic acid, it states:

*Dermatological: the initial flush upon ingestion of NA has been found not to subside (as claimed by Hoffer) but to become chronic in 30 to 59% of patients.*

The statement implies that Dr. Hoffer claimed the initial flush experienced when first taking nicotinic acid is only transient. But this is quite true, and generally speaking, after a few days, one no longer experiences the strong flushing as long as it is taken regularly. This is not a claim made only by Dr. Hoffer; it has been well recognized by physicians for decades. The other part of the statement, that the initial flush becomes chronic in 30 to 59 percent of cases, is quite incorrect. The statement is based on the findings in two studies; however, the researchers in those studies were referring to something quite different from the initial flush. Thus the authors of one of the studies write:

> By the phrasing of a sentence, and by adding "as claimed by Hoffer," the impression is left that the nicotinic acid flush is more severe than it really is and that Dr. Hoffer made a false claim about it.

On pages 42 and 43 the Task Force Report is highly critical of statements made by Dr. Hoffer and Dr. Osmond.

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regarding the relative lack of toxicity of B3. It quotes a number of phrases, taken out of their context, to the effect that B3 is "remarkably safe," "among the least toxic of all medications used in psychiatry," and so forth. These statements are true. The administration of B3 has never resulted in a death or in any irreversible side effects, contrary to most of the other drugs used in psychiatry. The lethal dose for rats and mice would be equivalent in an adult human to about 420 grams or about a pound of pure nicotinic acid powder. The report continues (p. 42),

Most surprising of all is Hoffer's claim in this same paper - in flat contradiction to his earlier statements cited above - that he never stated that B3 was nontoxic. "This," he says, "obviously would have been a foolhardy and erroneous claim."

The Task Force Report does not dispute B3's relative lack of toxicity, though it has reservations about some possible long-term effects (page 43):29

While finding that B3 does appear to be "relatively harmless," the available evidence seems to indicate that far more caution should be exercised in its long-term administration than the megavitamin proponents seem to recognize.

In fact, Dr. Hoffer has claimed that B3 is "relatively non-toxic" (13, page 499). There is no substance, water included, which is completely nontoxic or completely safe, and this has never been stated about B3. The authors of the Task Force Report may dispute the relative safety of B3 compared to other substances, but it is dishonest to manipulate quotations, as has been done, in order to imply that Dr. Hoffer claims B3 is "completely safe" when the claim actually made is that it is "relatively safe."


Summary

The Task Force Report concludes that Orthomolecular therapy is not scientific, that it is not effective, and that even the possibility of a small subgroup of patients responsive to the therapy "appears to be minimal" (page 47). On the basis of some double-blind studies in which a dose of 3 grams of B3 was used and none of the other components of Orthomolecular therapy were included, the Report suggests that enough evidence has been gathered to diminish "the credibility of all present and future claims which are offered" by Orthomolecular psychiatrists. These negative conclusions are not supported by the facts. The following statements are offered as a more accurate summary of the state of knowledge about Orthomolecular therapy:

1. The claims for effectiveness of Orthomolecular therapy are based on double-blind controlled trials and other trials, including long-term follow-up studies, and on many years of clinical experience with thousands of patients in whom consistent results have been obtained by many different psychiatrists. The claims are that specific procedures of treatment for different types of patients (Phases I, II, III) will improve schizophrenics significantly more than the conventional treatment methods can. The treatment is most effective for acute schizophrenia (Phases I and II), and less effective in chronic schizophrenia (Phase III). The original double-blind controlled trials used B3, together with ECT, for Phase II (acute hospitalized) patients and obtained significant positive results using this treatment, but Orthomolecular therapy now includes other components which increase its effectiveness.

2. The components of Orthomolecular therapy include correction of the diet to reduce the intake of refined starches and sugar, certain vitamins, certain minerals, and short courses of ECT, in addition to supportive
psychotherapy and, in moderate amounts, the tranquilizer drug therapy used in conventional psychiatry. Each patient is treated as an individual, with consideration of his chronicity, clinical status, and response to previous therapy. Responses to therapy are followed up at short intervals early in the treatment, and adjustments are frequently made on these occasions. At present, the therapy is empirical because it cannot yet be predicted which patients will respond to B3 alone and in which dosage, or to B3 plus C, or B3 plus B6 plus C, and so forth; therefore a broad approach is used. Such an approach cannot be incorporated into the design of a double-blind trial. The double blind, then, is not the appropriate method to use in verifying the results of Orthomolecular therapy, and other, more valid approaches will have to be used. Some of these have been suggested in this paper. Without exception, experiments which have been cited as obtaining negative results while claiming to be using Orthomolecular therapy have not used the procedure of Orthomolecular therapy. All such experiments used a small fixed dosage of B3, and none of the other components, usually in the treatment of chronic schizophrenic patients in whom it was already established that B3 alone will not usually be effective. Only three studies have been published which dealt exclusively with the Phase II (acute hospitalized) patients for whom Orthomolecular therapy is primarily effective. One of them obtained overall negative results. A second obtained results that may be considered controversial: while the average number of days spent in the hospital was not significantly different for the treatment and control groups, the group of patients receiving nicotinic acid and the group receiving nicotinamide both improved in approximately twice as many symptoms of mental illness as did the group receiving placebos. The third study, while not demonstrating an overall benefit for the group of patients receiving 3 grams of B3 per day, did show that a certain subgroup (about one-third of the patients) responded significantly to this treatment, while their counterparts receiving placebos did not improve.

4. The C.M.H.A. Collaborative Study is still in progress. Of the five studies completed, two of them dealt with acute schizophrenics and three with chronic patients. Three of the studies provided clear-cut evidence that components of Orthomolecular therapy are effective in treating many cases of acute and chronic schizophrenia.

5. The components of Orthomolecular psychiatry are very safe, compared with other treatments used in psychiatry. Vitamin B3 is not free of side effects, and it should be given under the supervision of a doctor who can effectively control unpleasant side effects, should they appear. On the whole, with regard to toxicity, B3 appears to be "relatively harmless," and while it is thus "very safe," it would be incorrect to describe it or any other substances as "completely safe."

6. The Task Force Report on Megavitamin and Orthomolecular Therapy in Psychiatry cannot be considered an accurate, objective review of the status of Orthomolecular therapy. It is a mistake to use it as a reference source in evaluating Orthomolecular therapy, because it is more a source of misinformation than a source of information.

Pauling (1973)30 rejected the negative conclusions of the A.P.A. Task Force Report which contained scientific errors.

errors of omission from the literature, and errors arising from obvious bias. "The A.P.A. report," he said, "shows the same sort of negative attitude as that shown by the authorities toward ascorbic acid in relation to the common cold. There seems to be a sort of professional inertia that hinders progress." Pauling concluded, "There is evidence that an increased intake of some vitamins, including ascorbic acid, niacin, Pyridoxine and cyanocobalamin, is useful in treating schizophrenia, and this treatment has a sound theoretical basis. The A.P.A. Task Force Report on megavitamin and Orthomolecular therapy in psychiatry discusses vitamins in a very limited way (niacin only) and only one or two aspects of the theory. Its arguments are in part faulty and its conclusions are unjustified.

REFERENCES
