

# THE EFFECTIVENESS OF TARGETED NUTRIENT THERAPY IN TREATMENT OF MENTAL ILLNESS

## A PILOT STUDY

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### ABSTRACT

In a pilot study aimed at investigating the effectiveness of targeted nutrient therapy, the clinical progress of 567 patients with a range of mental illnesses receiving established medical treatment in conjunction with a targeted nutrient program were assessed by clinical outcome after 12 months.

492 of the 567 patients interviewed commenced treatment and of these 382 complied for one year.

The verified diagnoses included Autism Spectrum, ADHD, Asperger's Syndrome, Anxiety, Bipolar Disorder, Depression, Schizophrenia and Obsessive Compulsive Disorder (OCD).

Of the total treatment group, 110 (23.6%) failed to complete one year treatment, 221 (44.9%) noted major improvement, 91 (18.5%) noted partial improvement, and 70 (14.2%) noted nil improvement in 3 nominated quality of life outcomes. These outcomes were compared to a comparison group (26) not receiving the equivalent nutrient treatment of which 5 (19%) noted major improvement, 5 (19%) noted partial improvement, and 16 (62%) noted nil improvement. Hospital admission was substantially lower in the treatment group.

### INTRODUCTION

The emergence of the pharmacological age of more effective drugs to treat mental illness may result in the under-valuation of the effectiveness of nutritional treatment.

The nutritional treatment of mental illness is not a new area and pioneers in this field such as Abram Hoffer and Carl Pfeiffer<sup>1,2,3</sup> quoted success in treating mental illnesses using high doses of selected nutritional supplements. In particular, the work of Pfeiffer centred on three key areas.

The **first** was the observation that most people with mental illness were low or deficient in zinc or had a copper-zinc imbalance. This finding has been duplicated by many researchers<sup>4-8</sup> including the corresponding author, and is a key focus of this paper.

The **second** observation was that many sufferers of mental illness had malfunction of their methylation pathway. Pfeiffer coined the terms 'histadelia' or high histamine and 'histapenia' or low histamine and observed a very different set of personality traits in these two groups before the development of their illness. Some years later, William Walsh (one of the authors) realised that high histamine was likely to be indicative of undermethylation and histapenia of overmethylation. Aberrations of methylation status in mental illness have also been observed by many other researchers<sup>9-17</sup>.

The **third** key observation was that urinary pyrrole excretion was higher in people with mental illness than those without and that this also correlated with a certain pattern of character traits.

The current study was therefore aimed at examining the use of targeted nutrient therapy in conjunction with conventional treatment to produce a better long term outcome in patients with a range of mental illnesses.

### MATERIALS AND METHODS

#### Design, setting and patients

A clinical outcome assessment was performed on 567 consecutive patients followed up for one year after initial consultation. The data covered patients interviewed between March 2004 and June 2007. Established diagnoses included Autism, ADHD, Asperger's, Anxiety, Bipolar Disorder, Depression, Schizophrenia and OCD. All patients had an established verifiable diagnosis and most were receiving conventional pharmacological therapy. Patients were instructed not to change any treatment (pharmacological or physical) unless on the instruction of their usual treating practitioner. Treating practitioners were also informed of the additional targeted nutrient program.

All patients (and/or carers) were initially interviewed for up to 1 hour. This process centred on making a clinical diagnosis of an underlying biochemical imbalance with respect to the methylation process, oxidative stress, and copper/zinc ratio (see Table 1). In order to have an outcome assessment pertinent to

from page 3

the variety of disorders, each patient (and/or carer) was required to nominate the three clinical issues in which improvement was most desirable. At 3, 6 and 12 month interviews they were asked if they had made major improvement, partial improvement or nil improvement in all three aspects nominated as most important at the initial contact. This was used as the outcome assessment.

Considerable emphasis was given to the clinical diagnosis, as the biochemical markers are sometimes imprecise and the therapeutic decision may be made on the clinical diagnosis.

In cases where there was a discrepancy between the clinical and biochemical diagnoses, initial treatment decisions were made according to the biochemical diagnosis.

Clinical Symptom	Under-methylation	Over-methylation	Pyrrroluria	Elevated Serum Cu/Zn
High academic achievement	+			
Competitive	+			
Addictiveness	+			
Eating disorder	+			
Obsessive Compulsive	+			
Perfectionism	+			
Inner tension	+			
Ritualism	+			
Ruminate	+			
Psychosis	Catatonic	Active		
Hirsute	N	Y		
Pain threshold	Low	High		
Responds to SSRI drugs	Yes	No		
Responds to Benzodiazepines	No	Yes		
Tinnitus		+		
Poor organisation		+		
Food/chemical sensitivity		+		
Poor sleep		+		+
Paranoia		+		
Anxiety/panic attacks		+		
Grandiosity/religiosity		+		
Racing thoughts		+		
Auditory hallucinations		+		
Poor dream recall		+	+	
Nervous		+	+	
Aversion to breakfast			+	
Crave spicy foods			+	
Self esteem	High		Low	
Keeps same friends		Yes	No	
Sensitive light, noise, smells			+	
Moodiness			+	
Tan easily			No	
Fears			+	
Poor short term memory			+	
Worrier			+	
Visual hallucinations			+	
Aggressive, assaultive			+	+
Poor concentration				+
PMS				+
Sensitive to tight clothes, tags				+

**Table 1.** Table of typically associated clinical symptoms

## Pathology

### Zinc

Serum zinc was used for zinc analyses. Potential sources of error using this technique are known, thus achieving consistency for these tests was paramount. This was achieved through use of standardised collection protocol and assigned venepuncturists. Incorrect collection technique tends to give artificially elevated results.

### Whole Blood Histamine

Histamine is formed by the decarboxylation of histidine and is metabolised by the enzymes histamine-N-methyl transferase and diamine oxidase. Histamine is therefore methylated for its metabolism, which enables its use as an inverse indicator of the methylation status of an individual. For example, relatively high histamine suggests under-methylation and low histamine over-methylation.

For the purpose of this study, whole blood histamine was used as an indirect marker of methylation with a narrow range of

histamine [0.4-0.6mm/l] representing normal methylation.

More reliable biochemical indicators of methylation are available for research purposes. Methylation status can be better measured by either serum methionine or the ratio of s-adenosyl methionine [SAMe] to s-adenosyl homocysteine. These assays were not available commercially during the treatment phase of this trial.

### Urinary Pyrrole/Mauve Factor

Pyrroles are ubiquitous waste products. Increased excretion of these products is a common feature of many behavioural disorders (also referred to as Pyrroluria<sup>19,20,21</sup>). The product measured is hydroxyhemopyrroline-2-one (HPL). Increased excretion of HPL can result either from a genetic disorder affecting haemoglobin synthesis or from the oxidative degradation of heme. Whilst HPL itself has low toxicity it binds irreversibly to pyridoxine (B6) and zinc rendering both inactive. Biochemical pathways requiring these nutrients as cofactors are thus hindered.

Second morning void specimens were collected into vials containing preservative and then snap frozen (-30°C). Samples remained frozen and protected from direct light until analysis. Through co-operation from a national pathology service, it was possible to standardize the collection and transport of samples for HPL analysis both nationally and internationally. Results were corrected for hydration status and the working range for urine HPL levels were as follows:

[HPL] under 10 micgr/dl: Normal

[HPL] between 10-20 micgr/dl: Borderline (considered high if clinical correlation)

[HPL] over 20 micgr/dl: High

Clinically accurate measurement of urinary HPL concentration was therefore a useful bio-marker for oxidative stress.

### Cu/Zn Imbalance

In some patients there was no evidence of methylation abnormality or of high pyrrole excretion. The serum copper to zinc ratio in some cases was nearly 2/1 whereas the accepted normal is near 1/1.

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from page 5

### Targeted Supplementation

Compounds were individualized for each patient according to the nature of the imbalance, the degree of deficiencies and the age and size of the patient. Doses were well in excess of recommended daily allowances.

Decisions were generally made according to the biochemical profile but in cases where this was indistinct, decisions were made on the clinical diagnosis. Note from the schematic representation of the methylation pathway (see Figure 1) there may appear to be some logic in using methionine, or SAME, in under-methylators and B3, folate and B12 in over-methylators. It is noted that 'over-methylation' may not necessarily be a literal overactivity of methylation but alternatively a block in the adjacent folic acid pathway. The two enzymes implicated are Methylenetetrahydrofolate reductase and Cathchol-O-Methyltransferase

Patients exhibiting symptoms and pathology correlating with under-methylation were administered Vitamins C and B6, Pyridine-5-Phosphate (P5P), Methionine, Calcium, Zinc and Magnesium. Those exhibiting symptoms and pathology correlating with over-methylation were prescribed Vitamins B3 (Niacinamide), B6, B12, C and E, P5P, Folic acid and Zinc. Patients exhibiting elevated urinary pyrroles (and symptoms of Pyroluria) were prescribed Vitamins C, B6, P5P, and Zinc, while patients exhibiting Copper/Zinc imbalance were prescribed Zinc alone or in combination with Vitamin C.

### RESULTS AND DISCUSSION

#### Zinc Pathology

The mean serum zinc in this target group was initially at the 3rd percentile of the pathology quoted ranges (see Figure 2), indicating that low to deficient zinc levels seem to be a major and likely significant nutritional imbalance in a range of mental illnesses.

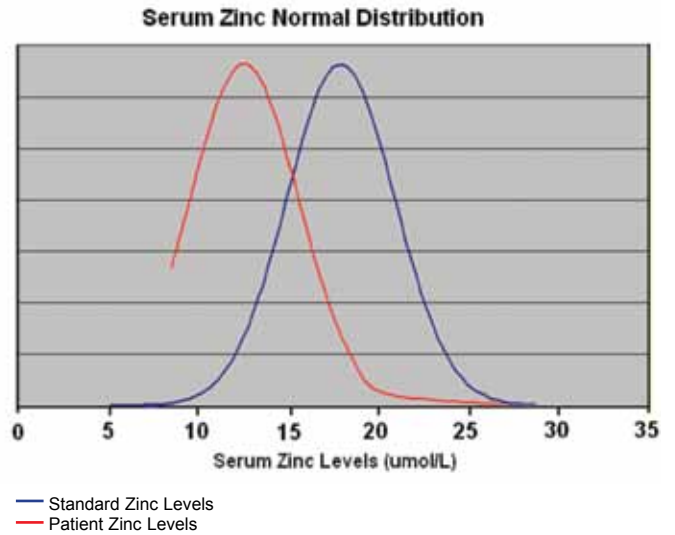


Figure 2. Serum zinc distribution of study patients compared with standard pathology ranges.

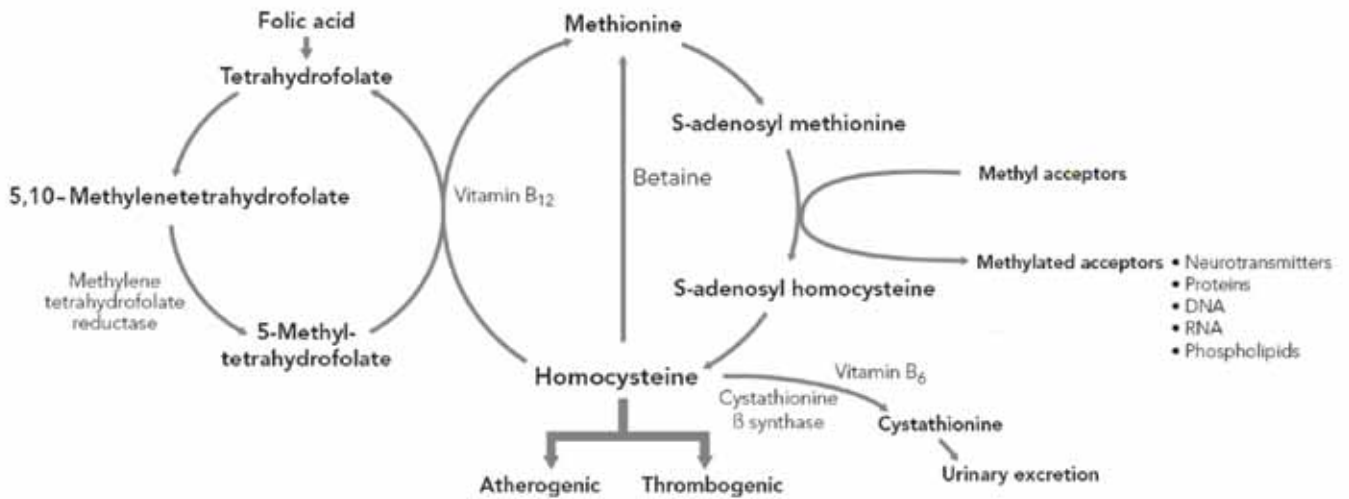
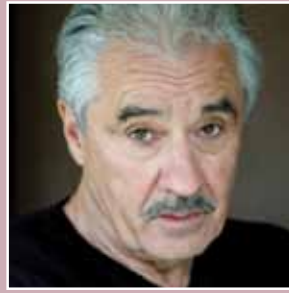


Figure 1. Schematic representation of the methylation pathway.



### Outcome Measures

The interview process for the treatment program began with 567 patients of whom 492 commenced treatment with 382 complying for 12 months. 110 discontinued for a range of reasons (22.4% non-compliance). 75 of those interviewed did not commence the program and respondents to a questionnaire in this group were assigned to the comparison group. Of the 382 that completed one year of the program, 221 (57.9%) stated major improvement, 91 (23.8%) partial improvement and 70 (18.3%) nil improvement.

It is understood that there are methods to 'objectify' improvement by questionnaires designed specifically for some of the diagnostic groups, but there are none that would encompass all the diagnostic groups in this study. The outcomes according to diagnosis are represented in Table 2.

### Clinical Notes:

- There was a marked reduction in hospital admissions during the 1st year of treatment as compared with the year prior to nutrient treatment.
- There was a reduction in doses of prescription medication in 22.3% of the patient group. Antidepressants and anxiolytics were occasionally withdrawn but antipsychotics were not.
- Most patients with the best results used a combination of both pharmacological and nutritional interventions.
- The relative percentages of improvement and non-improvement were remarkably similar in each of the three groups.

Diagnosis	Major Improvement	Partial Improvement	Nil Response	Total
Autism	49 (45.4%)	38 (35.2%)	21 (19.4%)	108
Aspergers	2 (28.6%)	2 (28.6%)	3 (42.8%)	7
ADHD	16 (57.1%)	3 (10.7%)	9 (32.1%)	28
Anxiety	43 (65.2%)	14 (21.2%)	9 (13.6%)	66
Bipolar Disorder	17 (68.0%)	5 (20.0%)	3 (12.0%)	25
Depression	53 (63.9%)	16 (19.3%)	14 (16.9%)	83
Schizophrenia	30 (61.2%)	11 (22.5%)	8 (16.3%)	49
Other*	11 (68.8%)	2 (12.5%)	3 (18.7%)	16
Totals	221 (57.9%)	91 (23.8%)	70 (18.3%)	382

\*This group was comprised of Obsessive Compulsive Disorder and Oppositional Defiance Disorder.

**Table 2.** Survey results after 1 year targeted nutritional treatment

### Comparison Group

As this was a pilot study, the comparison group consisted of patients who underwent an initial interview, but subsequently did not commence the targeted nutrient program. These patients were contacted to ascertain whether they had found clinical

improvement elsewhere, what the treatment was and whether they assessed the improvement as major or partial. Table 3 lists their responses. Although this group is small it does represent a comparison with the treatment group.

Major Improvement	Partial Improvement	Nil Improvement	Total
5 (19.2%)	5 (19.2%)	16 (61.6%)	26

**Table 3.** 1 Year follow-up on those interviewed but who did not start the program.

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The proportions of improvers and non-improvers differed markedly from the treated group. More surprisingly, and suggestive of substantial potential cost savings of nutrient therapy, the comparison group of 26 patients had a combined total of approximately 650 hospital days. This was more than double the total hospital days of the 382 patients who began the targeted nutrient supplement program.

### Compliance

Of interest to the authors is the lack of comprehensive trials or clinical outcome studies of nutrient therapy in the literature. In this study 382 (77.6%) of the 492 who began the program complied for one year. This is considered a high compliance rate when compared to compliance in studies of pharmaceutical products. For example, in a recent study looking at antihypertensive compliance by Simons et al<sup>18</sup>, only 42% of those prescribed calcium channel blockers and 62% of those prescribed ACE inhibitors were compliant at 12 months.

### CONCLUSIONS

Much of the published literature in this field documents the presence of nutritional deficiencies and imbalances in a higher percentage of those with mental illness than those without mental illness. There are however, no randomized, blinded, placebo-controlled studies and few, if any, outcome studies.

The purpose of this paper is to highlight targeted nutritional correction in mental illness, and to present outcome data collected for one year after initial interview, demonstrating a considerable subjective improvement in more than 60% of patients. This compared favourably with the conventionally treated comparison group.

One of the startling findings is the vast difference in inpatient hospital days between the treatment and control groups.

The weaknesses inherent in this study are recognized. These include multiple clinical diagnoses, the subjective nature of the follow-up, lack of a placebo arm, and lack of randomisation. The results however suggest that further, better constructed studies of nutrient therapy in mental illness are needed.

The results of the above study point towards the following conclusions:

- Relative zinc depletion is probably endemic in our community.
- The majority of those with mental illness have some nutritional deficiencies or imbalance.
- Correction of these leads to a clinical improvement in a high proportion of cases than standard treatment.
- A huge reduction in the number of days spent in hospital was observed in patients following this program.
- Targeted nutritional treatment is a worthwhile addition to pharmacological treatment, as a combined pharmacological and nutritional approach gave the best results.
- Further studies are needed in this area.

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