Agoraphobia

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PART I — AGORAPHOBIA: A NUTRITIONALLY RESPONSIVE DISORDER

Abstract

Agoraphobia (AGP), the most debilitating of all phobias is a complex psychophysiological disorder which manifests as severe anxiety and/or panic reactions, accompanied by a dread of being away from a "safe" place.

Data presented in this paper indicate that AGP might be called a somatopsychic disorder, i.e. a nutritional-biochemical imbalance which creates an emotional effect.

The term agoraphobia (AGP) is derived from the two Greek words "phobos", meaning fear, and "agora", meaning market place or place of assembly (Frampton, 1974).

The incidence of this disorder is significant and appears to be rapidly increasing. When studied in 1969, approximately one out of a hundred people had phobias disabling enough to seek professional help (Burns and Thorpe, 1977). The greatest percentage of phobias seen in clinical practice are agoraphobic (Burns and Thorpe, 1977).

Agoraphobia (AGP) was attended by multiple vitamin dependent enzymopathies in all of twelve clients tested. A genetic relationship is suggested in that pharmacological nutrient levels were necessary to eliminate the enzymopathies and reverse the symptomology.

The relationship of agoraphobia to disturbed metabolism is explored, particularly emphasizing carbohydrate metabolism. The relationship between allergy type reactions and agoraphobia is noted. The response of agoraphobics to a nutritional-biochemical approach has been dramatically successful, often resulting in complete recovery. Recovery in this context is defined as elimination of panic reactions and normal mobility.

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Introduction

The realization that agoraphobia (AGP) could be highly responsive *to* dietary manipulation occurred when a few clients of mine recovered after instituting an individually

determined nutritional regimen based in part on functional blood and urine tests for vitamin metabolism.

Currently I have seen over fifty AGP's and hundreds of people suffering with anxiety.

Such symptoms typically disappear or are markedly ameliorated via an orthomolecular approach.

Method

As part of my nutritional assessment I use a form called the Systems Review. It is a compilation of signs and symptoms which may be observed when various nutrients are undersupplied. See chart #1. (Note: a copy of the systems review may be requested from the author).

The form contains a total of 286 items which are reviewed and circled by the client if relevant. Among the items are such symptoms as headaches, anxiety, nausea, palpitation, dizziness, loss of balance, muscle tension, breathlessness, sense of impending doom, et al. Symptoms pertaining to all organ systems are assessed.

As a group, the AGP's have markedly more symptoms than my non-AGP clients. It was my contention that such symptoms are born of biochemical dysfunction and that biochemical function could be manipulated nutritionally.

In general, functional vitamin testing is deferred pending a trial of dietary manipulation (a supernutrition diet) with non-specific broad spectrum nutritional support in the form of various dietary supplements.

Progress is determined through client evaluation, repeat of the Systems Review, and through repeat of abnormal tests. Note that many clients in this sample had not completed individualized functional vitamin testing.

The category of TR (total recovery) was reserved for those AGP's in whom all panic and/or anxiety attacks were absent and who had returned to normal mobility.

The MI (marked improvement) category was applied when anxiety attacks, panic episodes and lack of mobility were *significantly* diminished from that experienced at the time of the initial intake interview. (No matter how improved, a client was not categorized TR unless totally free of panic attacks and fully mobile).

The SI (slight improvement) was applied to those agoraphobes who had a diminished number of symptoms and signs as per the Systems Review, which may or may not include diminution of the panic and/or phobic symptoms.

The NI (no improvement) category is reserved for those agoraphobes who've experienced little or no decrease in symptoms or signs on the Systems Review.

Follow-up visits generally occurred at six-week intervals. Many AGP's experienced marked improvement by the first six-week follow-up. See chart #1.

As a consequence of my belief that the

Chart #1

Total Sample — 23 Agoraphobics

Degree of Improvement within three months	**Number of Clients**
TR	7
MI	12
SI	4
NI	0
Dramatic Improvement (TR plus MI)	19
Complete Absence Panic Attacks	11

source of various common and chronic symptoms suffered by people might rest with defective enzyme activity from a long term disturbance in the dietary micronutrient/macronutrient ratio, I decided to measure vitamin-dependent enzyme reactions before and after stimulation with their respective coenzymes. Additionally, certain urinary metabolites can be used in performing functional tests of vitamin and mineral utilization (Sauberlich et al., 1977). Such tests have gained wide acceptance and are now considered the preferred method in assessing nutritional status, since they are sensitive and specific.

The following tests were done as a group on all subjects tested. The use of many of these tests for such assessment can be explored in the literature review by the CRC Press (Sauberlich et al., 1977). 1. Thiamine — TPP percentage uptake by erythrocyte transketolase

2. Pyridoxine — Erythrocyte glutamic pyruvate transaminase (EGPT) Index
3. Riboflavin — Erythrocyte glutathione reductase activity co-efficient
4. Niacin — Conjectured by N^1 methyl-nicotinamide in urine
5. Folic acid — Serum folate, (in some cases urinary FIGLU excretion and smear for hypersegmentation were utilized additionally)
6. Vitamin B-12 — Serum B-12 and urinary methylmalonic acid (MMA)
7. Serum A
8. Hair analysis — As a toxic metal screen

Additional tests were performed on various clients as individually indicated often including: iron and iron binding capacity; liver and kidney function tests; CBC; 24- hour urines for calcium, magnesium, phosphorus; free tryptophan (serum) and 24-hour urinary 5-HIAA; pyridoxal-5-phosphate (active coenzyme form of B-6.)

Chart #2

Incidence of Enzymopathy Total subjects — 12

Test Performed	**Vitamin Found Abnormal**	No. **of Clients**
TPP% uptake in erythrocyte transketolase activity	Thiamine	7
Erythrocyte glutathione reductase	Riboflavin	1
Erythrocyte glutamic — pyruvic transaminase	Pyridoxine	6
N^1 Methylnicotinamide	Niacinamide	3
Serum folate — FIGLU	Folic acid	2
Serum B-12 — MMA	B-12	3
Clients with more than one enzymopathy		10
Clients with more than two enzymopathies		2
Clients with more than three enzymopathies		1

Results

Among my 23 client AGP sample 12 have been tested for B vitamin disturbance. All were found to have abnormalities. See chart #3.

Disturbed thiamine metabolism was the most frequent abnormality with pyridoxine running a close second.

Dramatic improvements were observed in 83 percent of the sample. See chart #1.

Progress, as measured by client evaluation and the Systems Review, is remarkable. In one client, 47 of her original 80 presenting symptoms were gone in six weeks. In another client 28, out of an original 38 had disappeared, while 33 out of 44 were gone in another.

One severely obsessive-compulsive agoraphobic who at certain times wouldn't mobilize from a chair was completely recovered when in three months 44 of her 48 symptoms vanished! Her depression score on the Hoffer-Osmond psychological test was initially 13 on an 18-point scale. At a three-month follow-up her score was 1!

Discussion

It must be realized that these vitamin dependent enzymopathies can reflect, or create, genetic alterations. See chart #3. Note that such enzyme defects are more than simple dietary deficiencies, as correction of enzyme activity required pharmacological — not dietary levels of nutrients typically in the range of 200-500 mg of the various B complex factors.

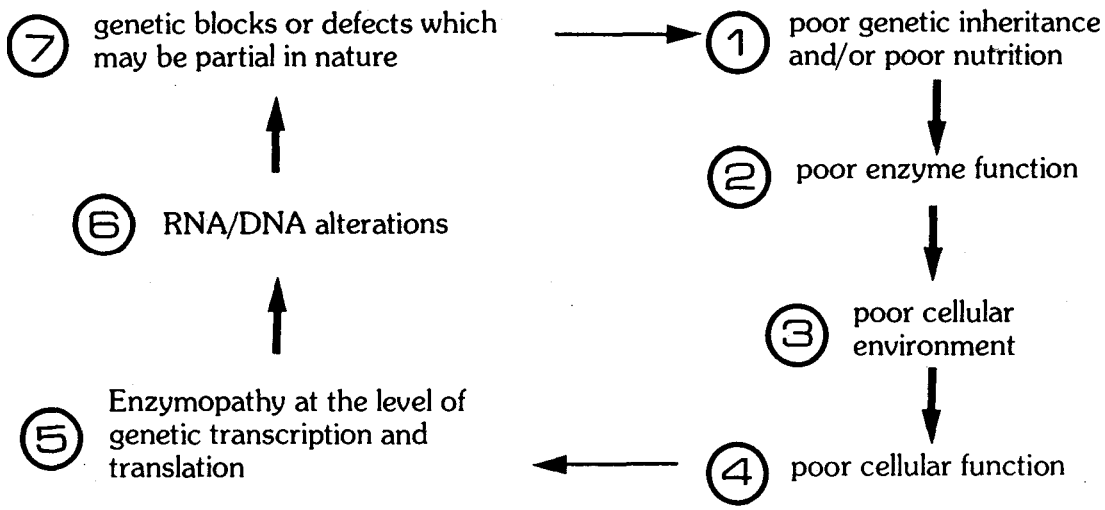
Vitamin dependent genetic disease is gaining attention from geneticists since the incidence of such disorders is proliferating rapidly (Rosenberg, 1970 and 1974).

A.D. Hunt and associates are credited with the discovery of the vitamin-dependent disorders. They administered pharmacologic doses of pyridoxine to successfully eliminate seizures in two infant siblings. Forty other documented cases have been demonstrated and in all the inherited, and therefore genetic character, was established (Rosenberg, 1970 and 1974).

I'd like to emphasize that with considerable frequency I have observed evidence of defective enzyme activity where the coenzyme precursor (vitamin) was perfectly normal in serum and in fact, on some occasions, elevated. **Elevations in serum vitamins may reflect a failure of the vitamin to be properly metabolized due to various enzymopathies beyond the absorption level.** Thus they accumulate in the blood. This has been observed in the relationship between B 12 and folate. When a thiamine deficiency exists, B 12 and folate levels often rise in serum. Administration of thiamine generally results in a drop in such abnormal serum vitamin levels (Personal observation and verbal communication via Derrick Lonsdale).

As one example, I frequently observe methylmalonic aciduria (MMA) in people with normal or high serum B 12 levels who respond to pharmacological doses of B 12 orally with a decrease in symptomatology

Chart #3



and cessation of MMA production. This may explain the so-called placebo effect of B 12 in those people without pernicious anemia who insist they feel better on high doses of the vitamin. Vitamin B 12 is the vitamin cofactor for methylmalonyl CoA mutase which drives the conversion of methylmalonyl CoA to succinyl CoA.

In Babior's text, **Cobalamin,** MMA is noted as a reliable and sensitive indicator of vitamin B 12 deficiency, "except in the rare cases in which it is due to an inborn error of metabolism."

My data suggest that the inborn error of metabolism, to which he refers, is anything but rare. I frequently see MMA without serum B 12 depletion which is indicative of enzymopathy, not simple deficiency. What is rare is a total block in the conversion of a methylmalonyl CoA to succinyl CoA. Partial blocks (as a result of "leaky genes") in varying degrees probably are not uncommon. This phenomenon is discussed by biochemist Roger Williams in his discussion of genetic gradients in the treatise **Biochemical Individuality** (Williams, 1956).

All AGP's tested suffered multiple vitamin responsive enzymopathy. Further establishing the genetic connection is a familial trend reported by some AGP's. In one family, grandma, daughter, and granddaughter all had it. In another, mother and daughter suffered.

The idea that agoraphobia might be a sequel to disturbed carbohydrate metabolism presented itself when I noted that many of the symptoms suffered by agoraphobics were identical *to* those commonly presented in hypoglycemia**.**

The characteristically excessive and diverse symptoms which hallmark the AGP syndrome are reminiscent in nature and scope to those commonly experienced by hypoglycemics.

The theory that AGP might represent a sequel to disturbed carbohydrate metabolism began to take shape.

The dietary and laboratory data were consistent with the possibility of disturbed carbohydrate metabolism.

As a group, the diets of AGP's are among the worst I've ever seen. There are exceptions, however. The majority virtually subsist on "foods" consisting primarily of refined carbohydrates with large amounts of caffeine.

The average American derives roughly one-third of his calories from refined grains or white flour products. Such products, devoid of the bran and germ of the grain, are on the average 80 to 85 percent deficient in mineral and trace elements and significantly lacking in some vitamins as well. (Schroeder, 1975).

Based on national consumption studies, refined sugars supply one-sixth of our day's calories — most of which is found in processed foods as an additive. Sugar is devoid of virtually all micronutrients (Yudkin, 1972; Schroeder, 1975).

Thus, an average American gets a full 50 percent of his calories from refined sugar and refined flour which contains only 15 to 20 percent of the previous mineral content.

Many of the AGP's I see get up to three-fourths of their calories from processed foods — usually junk carbohydrates.

Consumption of such refined carbohydrates creates enzymopathies by virtue of the lack of micronutrients in such foods. Such enzymopathies result in disturbances of carbohydrate, protein, and fat metabolism.

Enzyme systems incorporate (in addition to apoenzymes) coenzymes and metal-ions as metaloproteins or metaloenzymes, which are derived respectively from dietary vitamins, minerals, and trace elements. These latter items, collectively known as the micronutrients, are depleted in processed foods in general, sugar and white flour in particular.

It is important to understand that for optimal biochemical function beyond a certain minimal level, the requirement for various micronutrients is not a fixed numerical value, but rather a range, in that the levels of various micronutrients are needed in proportion to the amount of a given macronutrient (carbohydrate, protein, fat) upon which the micronutrient dependent enzymes must act.

One dramatic example of a disturbance in macro vs. micronutrient ratio was reported by pediatric geneticist and noted thiamine researcher Derrick Lonsdale of the Cleveland

Clinic. Thiamine deficient chow was fed to two groups of animals. One group was permitted to feed naturally while the other group was force-fed the thiamine deficient ration. The force-fed group actually died faster than the others! (Unpublished Address to the Society for Orthomolecular Medicine — East, 1978). Symptomology and ultimately clinical disability may result from a decrease in enzyme product formation or from the toxic effects of accumulated substrate as a sequel to enzymopathy.

The relationship of thiamine to carbohydrate metabolism was first established by Peters in 1930 (Wolstenholme and O'Connor, 1967).

Wendel and Beebe studying glycolytic activity in schizophrenia reported on the association of anxiety with lactic acid production in neurosis (Pauling and Hawkins, 1973). During a glucose tolerance test it had been observed that symptoms of anxiety became prominent when the blood glucose dropped below the fasting level. They decided to measure blood lactate, pyruvate and ATP concentrations during the GTT. Their observations were most interesting. Lactate concentrations were markedly increased during the 3rd, 4th, and 5th hour post-glucose in anxiety prone patients but not in the non-anxiety psychiatric patients (Pauling and Hawkins, 1973, p. 289). Further, with respect to pyruvate concentrations, only the anxiety patients showed a high production of lactate in relation to pyruvate or a high L/P ratio (Pauling and Hawkins, 1973, p. 293). ATP concentrations were significantly lower in the blood of anxiety patients in the first, second and third hours following a glucose challenge, whereas non-anxiety patients had no change.

Alterations in blood lactate, pyruvate, ATP and the L/P ratio indicate a profound disturbance in transformation of chemical to kinetic energy in the anxiety prone patients. (Pauling and Hawkins, 1973., p. 295) In such patients symptoms of anxiety may occur when there is a requirement to mobilize energy rapidly. Since these patients exhibit a marked shift from aerobic to anaerobic metabolism, their production of energy is markedly reduced.

The relationship between lactic acid and anxiety has been explored by a number of researchers other than Beebe and Wendell.

Pitts and McClure (1967) reported on the experimental production of anxiety attacks in patients suffering anxiety neurosis by blood infusions of the lactate ion. Patients reported they experienced symptoms from the lactate infusion that were identical to those they experienced in spontaneous anxiety attacks.

In 1950, Cohen and White summarized the then current knowledge of neurocirculatory asthenia also referred to as anxiety neurosis, neurasthenia, and effort syndrome.

The chief symptoms of anxiety neurosis, as noted by Cohen and White, are breathlessness, palpitations, nervousness, fatigability, headaches, irritability, dizziness, chest pain, paresthesias and episodes of extreme tearfulness referred to as anxiety attacks.

The disorder is characterized by the appearance of many symptoms but few signs (Cohen and White, p. 834). Blood lactate was found to be twice as high in neurocirculatory asthenia as in controls. (Cohen and White, p. 847).

Cohen and White found many measurable abnormalities in the response of the anxiety patients to muscular work. These abnormalities which included low oxygen consumption are consistent with a defect in aerobic metabolism and a high anaerobic metabolism. (Cohen and White, p. 847).

A characteristic of both disorders is breathlessness or air hunger which is particularly evident in crowded or stuffy atmospheres. Cohen and White noted that sufferers report avoidance of churches or movie theatres due to such smothering feelings. The overdevelopment of this avoidance pattern (phobia) in response to the various symptoms classified as an anxiety reaction is the essence of what differentiates agoraphobia from simple anxiety and panic reactions.

Differences in the tolerance for inspired carbon dioxide between normal subjects and those with anxiety neurosis were observed (Cohen and White). The oft described feeling of choking or smothering in crowded places led to a study in which

increased percentages of carbon dioxide were inhaled by study subjects. Approximately 80 percent of the anxiety group experienced symptoms similar or identical to those experienced during anxiety attacks, including a feeling of fear.

Cohen and White concluded that **under laboratory induced stress striking biochemical abnormalities were noted in anxiety patients,** (p. 863), including elevated blood lactate levels, decreased tolerance for carbon dioxide, and decreased ventilatory capacity via a decrease in oxygen consumption.

Not just subjective, but objective and quantitative abnormalities were demonstrated in response to various stimuli and stressors. In addition to those mentioned, additional abnormal responses were noted to pain, cold, noise, and anticipation in those patients classified as having anxiety neurosis (Cohen and White, p. 864).

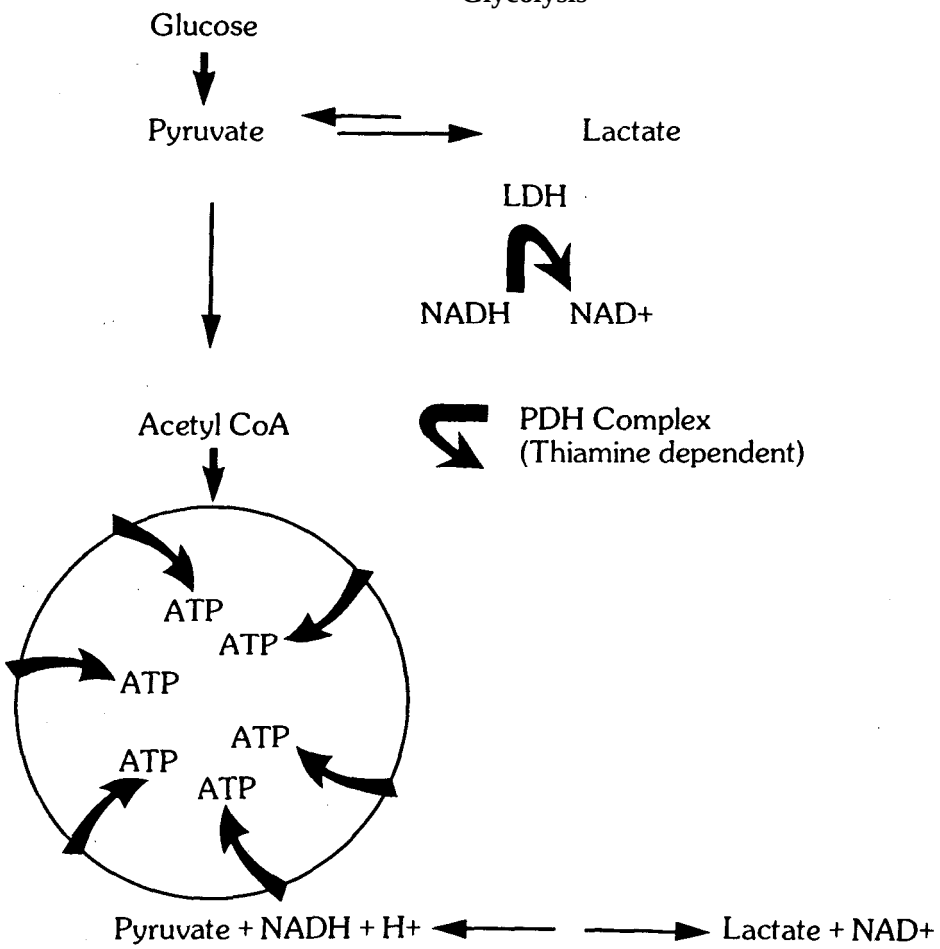
These determinations appear to have been undiscovered or disregarded by the many clinicians who accept the premise that anxiety reactions are purely psychogenic — born of personality factors rather than somatogenic — deriving from biochemical factors.

Since lactic acid metabolism is related to activity, exploring the biochemistry of glycolysis and its sequel, the Kreb's cycle, may shed some light on biochemical lesions involved in the genesis of anxiety.

Essential for the conversion of pyruvate to acetyl CoA (the beginning of the Kreb's cycle) is the pyruvate dehydrogenase complex in which thiamine pyrophosphate (TPP) is a coenzyme.

Undersupply of the TPP coenzyme due to deficiencies or malabsorption of thiamine or failure of thiamine or TPP binding to appropriate sites on the enzyme could result in accumulations of pyruvate with

Chart #4
Glycolysis



diminished synthesis of ATP (via Kreb's cycle). See Chart #4. Both diminished ATP and accumulated pyruvate could manifest in profound disturbances in energy due to the shift to anaerobic metabolism.

Nicotinamide Adenine Dinucleotide (NAD) formation requires Adenosine Triphosphate (ATP) and ATP formation requires NAD, which is to say that the reactions are coupled (Pauling and Hawkins, p. 300). Therefore, disturbances originating with either ATP or NAD synthesis will affect energy metabolism.

Disturbed thiamine biochemistry could theoretically be one mechanism participating in elevation of the L/P ratio.

A partial block in the conversion of pyruvate to acetyl CoA via defective pyruvate dehydrogenase activity (thiamine pyrophosphate activated) could result in greater proportions of lactic and pyruvic acids. The equilibrium between lactate and pyruvate favors lactate.

In the conversion of lactate to pyruvate, nicotinamide adenine dinucleotide (NAD) is reduced. The reaction must be driven which requires an excess of NAD (Pauling and Hawkins, p. 283). Without an excess of NAD it would therefore appear that lactate would rise in proportion to pyruvate.

With the reduction in ATP synthesis engendered by defective pyruvate dehydrogenase (PDH) activity, the synthesis of NAD could be correspondingly reduced and thus lack the excess NAD needed to drive the conversion of lactate to pyruvate. Therefore the L/P ratio could rise, which as noted before was characteristic of anxiety patients (but not of controls).

Another pathway for lactic acid disposal is through gluconeogenesis. This process also requires ATP which if undersupplied due to the failure of oxidative metabolism would retard the clearance of lactic acid. This could also contribute to raising the L/P ratio.

Lacticacidemia following PDH underactivity as a result of thiamine dependency was reported by Schweizer and Baumgart-ner in 1977. Such dependency had previously been suggested by Lonsdale, Faulkner et al. in 1969. Further discussion and a summary on the regulation of the PDH complex
and its relation to neuromuscular disease can be found in the paper by Ngo and Barbeau (1978).

Insufficient NAD, by inhibiting the conversion of lactate back to pyruvate, would also contribute to a high L/P ratio and therefore to anxiety.

Again, the formation of NAD requires ATP. Niacin, as a precursor of the NAD compound is derived through diet directly and by conversion of pyridoxine dependent enzymes from tryptophan.

Disturbances in tryptophan metabolism have been related to anxiety reactions. Formation of serotonin, also derived from tryptophan, depends on pyridoxine-dependent enzyme reactions. See chart #5 Animals depleted in serotonin have been used as experimental models of anxiety (Hoes et al., p. 7) Disturbances in pyridoxine metabolism could therefore affect the formation of serotonin and/or niacin via the tryptophan pathway, both of which could ultimately manifest in anxiety.

Obsessive-compulsive anxiety disorders have been successfully treated with tryptophan. This has been documented by Yaryura-Tobias (1977). Since disturbances in pyridoxine metabolism could affect the formation of serotonin and/or niacin via the tryptophan pathway it too can contribute to anxiety. See chart #5.

Six of the twelve AGP's on whom functional vitamin tests were carried out had disturbances in pyridoxine metabolism. See chart #2. A higher percentage may actually have B 6 disturbance, as in later data, when measurements of pyridoxal-5-phosphate were done (in addition to the EGPT) more B 6 dependencies were detected.

Hoes et al. (1981) reported on treatment of "hyperventilation syndrome" (HVS) with tryptophan and pyridoxine. Among those patients with HVS demonstrating abnormal xanthurenic acid (XA) excretion, all responded clinically as well as by normalizing of the XA excretion to the administration of pyridoxine and tryptophan.

One of my clients, in whom abnormal pyridoxine metabolism was isolated, failed to respond to the orthomolecular program as anticipated. Upon rechecking her previously abnormal tests all were found to be

normal, including the EGPT enzyme (this B 6-activated enzyme was previously abnormal) for which she had been placed on 500 mg of B 6 daily. After reviewing Dr. Wm. Philpott's work on defective conversion of pyridoxal-5-phosphate, the active coenzyme form of B 6, I decided to measure serum pyridoxal-5-phosphate additionally along with free tryptophan in the blood and the major serotonin breakdown product 5-hydroxyindoleacetic acid (5-HIAA) in a 24-hour urine before a tryptophan load. This was followed by another 24-hour urine for 5-HIAA after a five-gram tryptophan load the next day (Philpott, 1979).

Results were most interesting. Serum free tryptophan was significantly elevated *before* the tryptophan load and serum pyridoxal-5-phosphate was almost nonexistent! Note this lady was taking 500 mg of B 6 daily. After the tryptophan load there was a very small increase in 5-HIAA which suggested that tryptophan was not being converted efficiently to serotonin. After beginning a supplement of the phosphorylated form of B 6 known as pyridoxal-5-phosphate, in addition to 1000 mg of regular B 6 and L-cysteine there was a rapid reduction in her constant anxiety. She is now completely free of panic attacks and highly mobile.

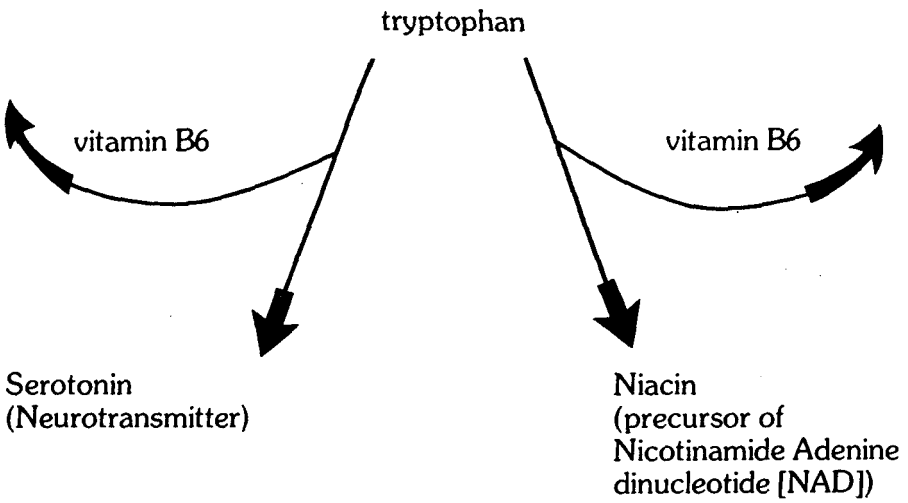
Pyridoxine is necessary to synthesis of the inhibitory neurotransmitter gamma aminobutyric acid (GABA), (Wurtman and Wurtman, 1980; Rosenberg, 1974) which appears to be intimately involved with the regulation of anxiety. The relationship of GABA facilitation with anxiety reduction was noted in a 1979 editorial in **Psychological Medicine** entitled, "Anxiety and the Brain."

Thus, it can be seen how disturbances in thiamine, pyridoxine, and niacin biochemistry could participate in the genesis of anxiety through increased production of lactic acid relative to pyruvic acid, through failure to synthesize adequate brain serotonin, and possibly through underproduction of GABA, the inhibitory neurotransmitter.

Orthomolecular approaches have been highly productive in resolving intractable anxiety. Pharmacological rather than dietary levels of nutrient supplements were required to correct enzyme activity in my AGP client sample.

Since enzyme synthesis is controlled genetically and allosterically (Wurtman and Wurtman, 1980) enzymopathies may reflect genetic change as a result of mutant genes. Genetic change need not manifest in gross metabolic defects or deformity because

Chart #5



such changes can be heterozygous or recessive (Reed, 1964).

Wagner and Mitchell state, "although mutation is a sudden event, it can produce almost any degree of effect from those barely detectable by known means to those too extreme for the cell to survive." Altered enzyme activity as may arise from dietary nutritional insufficiency will ultimately affect cell function. Thus the genetic code contained within the cell nucleus can be altered to produce partial genetic blocks often referred to as "leaky" genes, (Williams, 1956, p. 11; Roe, 1978, p. 70-91; Goodhart & Shils, eds., p. 1191-1219). See chart #4.

Chronic symptomology even without objective signs must be taken seriously as a sign of biochemical disturbance.

In my experience with a total of one hundred thirty-six highly symptomatic patients (comprised of agoraphobic and non-agoraphobic clients) on whom functional vitamin testing was performed, only five people failed to show abnormalities in any of those nutrients assayed. Five out of one hundred thirty-six! In all such clients low megadose levels of B-vitamins failed to correct the symptomatology and the enzymopathy. Pharmacological doses of vitamins given for the individually determined abnormalities eliminated or markedly reduced symptomatology, and in all patients retested the enzymopathy was corrected when the symptoms were eliminated.

This suggests that partial blocks in some enzymes' activities are being compensated for with the addition of more coenzyme. This compensatory ability is often possible because many enzymes are not saturated with coenzyme under physiological conditions (Wurtman and Wurtman, 1980; Goodhart and Shils, 1980, p. 1198).

Under certain circumstances, massive levels of vitamins (coenzyme precursors) can increase coenzyme synthesis which in turn increases the maximum velocity (Vmax) and the Michaelis Constant (Km) of an enzyme.

Conclusion

A working understanding of enzyme kinetics clarifies the value of so-called mega-vitamin therapy in the treatment of agoraphobia. The dramatic claims made for the efficacy of orthomolecular or megavitamin therapy by both professional and lay as-cribers, often branded by skeptics as purely placebo effect, receive support through this data identifying and eliminating clinically measurable enzymopathy via megavitamins.

Increasing the percentage of functioning apoenzymes will override a partial enzyme block and, by increasing the Vmax and Km, increase product formation.

The fact that signs aren't always apparent or are of lesser number should make us no less concerned about reporting on the presence of symptoms since many researchers have commented that clinical or biochemical lesions may precede histologic changes (National Academy of Sciences, 1977).

The idea that neurosis characterized by many symptoms with few signs is a purely emotional disorder psychogenic in origin is an outmoded concept not supported by the latest data in biological-nutritional research.

The value and importance of ortho-molecular therapy lies in minimizing the effects of genetic or biochemical damage, but perhaps more important and far more exciting is the prevention of hereditary damage to offspring. Cotzias et al., 1972 demonstrated in a strain of mutant mice with a congenital defect of manganese transport into the brain that the ataxia which resulted from this defect could be prevented in themselves by supplementing with much larger than normal dietary levels of manganese. Further the pregnant mice in this mutant strain so supplemented gave birth to completely normal offspring, free of the genetic defect!!

The real concern which must be extracted from all this is that a population with increasing persistent symptoms and signs is suffering genetic damage and that such damage can result largely from dietary abuse, particularly in depletion of many vitamins, minerals, and trace elements as a consequence of consuming refined and processed foods thereby disturbing the macro-nutrient-micronutrient ratio. This ultimately results in enzymopathy and finally genetic damage.

We have only to note the fertility problems and sudden infant death syndrome to suspect that dietary genocide may be the ultimate outcome of the standard American diet.

References

BABIOR, B.M., Ed.: Cobalamine Biochemistry and Pathophysiology. John Wiley and Sons, New York, pp. 386,387, 410, 1976.

BURNS, L.E. and THORPE, G.L.: The Epidemiology of Fears and Phobias. J. Int. Med. Res. 5, Supplement (5), p. 2-3,1977.

COHEN, M.E. and WHITE, P.D.: Life Situations, Emotions and Neurocirculatory Asthenia. A Research Nerv. and Ment. Dis. Proc. 29,832-869,1950.

COTZIAS, G.C.: Geochemistry and the Environment, The Relation of Other Selected Trace Elements to Health and Disease. Vol. 2, pp. 32-34,1977.

EDITORIAL.: Anxiety and the Brain; Not by Neurochemistry Alone. Psychological Medicine 9,605-609, 1979.

FRAMPTON, M.: Overcoming Agoraphobia. St. Martin's Press, N.Y., p. 15,1974.

GOODHART, R.S. and SHILS, M.E. Eds.: Modern Nutrition in Health and Disease. Philadelphia, Lea and Febiger, pp. 1193-1219,1980.

HOES, M., COLLA, P. and FOLGERING, H.: Hyperventilation Syndrome, Treatment with L-Tryptophan and Pyridoxine; Predictive Values of Xanthurenic Acid Excretion. J. of Orthomolecular Psychiatry 10, 1, pp. 7-15,1981.

LONSDALE, D., FAULKNER, W. et al.: Intermittent Cerebellar Ataxia Associated with Hyperpyruvic Acidemia, Hyperalaninemia, and Hyperalanura. Pediatrics 43, 6, pp. 1025-1034, June, 1969.

National Academy of Sciences: Geochemistry and the Environment. The Relation of Other Selected Trace Elements to Health and Disease. Vol. 2, pp. 32-34, 1977.

NGO, T.T. and BARBEAU, A.: Regulation of Brain Pyruvate Dehydrogenase Multienzyme Complex. The Canadian Journal of Neurological Sciences 5,2, 231-238, May, 1978.

PAULING, L. and HAWKINS, D, Eds.: Orthomolecular Psychiatry — Treatment of Schizophrenia. San Francisco, W.H. Freeman & Co., 1973.

PHILPOTT, W.: New Evidence Showing Lack of Conversion of Vitamin B-6 into the Active Coenzyme Form in Patients with Chronic Degenerative Disease . Presented at Fourteenth Annual Mtg. Society for Clinical Ecology, San Diego, Ca. October 28, 1979.

PITTS, F.N. and McCLURE, J.N.: Lactate Metabolism in Anxiety Neurosis. New England J. of Med. 277,25 1329-1336,1967.

REED, S.: Parenthood and Heredity. John Wiley & Sons, N.Y., 1964. ROE, D.A.: Drug Induced Nutritional Deficiencies. Conn. The AVI Publishing Co., 1978.

ROSENBERG, L.E.: Vitamin-Dependent Genetic Disease. Medical Genetics. Eds. Kusick, J. and Claiborne, R. H.P. Publishers, N.Y., pp. 73-78,1970.

ROSENBERG, L.E.: Vitamin-Responsive Inherited Diseases Affecting the Nervous System. Brain Dys function in Metabolic Disorders. Ed., F. Plum, Res. Publ. Assoc. Nerv. Ment. Dis., Vol. 53, Raven Press, N.Y. pp. 263-264, 1974.

SAUBERLICH, H., DOWDY, K. and SKALA, J.: Laboratory Tests for the Assessment of Nutritional Status. CRC Press, Ohio, p. 177, 1977.

SCHROEDER, H.A.: The Trace Elements and Man. Connecticut, Devin-Adair, 1975.

WILLIAMS, R.J.: Biochemical Individuality. Texas Univ. Press, 1956.

WOLSTENHOLME, G.E.W. and O'CONNOR, M., Eds.: Thiamine Deficiency: Biochemical Lesions and Their Clinical Significance. Ciba Foundation Study Group, No. 28, Little, Brown & Co., Boston, 1967.

WURTMAN, R. and WURTMAN, J., Eds.: Nutrition and the Brain. Raven Press, N.Y., p. 142, 1980.

YARYURA-TOBIAS, J. and BHAGANAN, H.: L-Tryptophan in the Treatment of Obsessive-Compul sive Disorders. American J. of Psychiatry 134, 11, Nov. 1977.

YUDKIN, J.: Sweet and Dangerous. Bantam Books, N.Y., p. 17,1972.

Part II — Thiamine, Neurotransmitters, and Agoraphobia: A Discussion

Abstract

Thiamine biochemistry was abnormal in seven out of twelve agoraphobics tested. Exploring the biochemistry of beriberi may identify the metabolic factors related to agoraphobia since there is a similarity of symptoms between the two disorders. The thiamine deficiency disease, beriberi, is characterized by a large number of symptoms, many of which reflect neuronal dysfunction.

Possible mechanisms by which thiamine depletion might affect neurotransmission are explored. Agoraphobics experience a dramatic response to nutritional intervention as determined by a Systems Review.

The most common enzymopathy observed among the agoraphobia test sample was the abnormal erythrocyte transketolase (see chart #3), a thiamine dependent enzyme.

Derrick Lonsdale reiterated the discovery by Peters that thiamine is required in proportion to the amount of carbohydrate consumed (Lonsdale and Shamberger, 1980)

Large scale consumption of refined carbohydrates, particularly sugar (there is no thiamine in refined sugar) will create metabolic abnormalities associated with autonomic nervous system dysfunction, (beriberi has been described as the prototype of autonomic dysfunction). Changes in vasomotor function have been observed, such as an exaggerated response to adrenalin injection resulting in tachycardia, elevated blood pressure, substernal oppression, nausea and vomiting with derangement of energy metabolism (Lonsdale, 1980).

The exaggerated adrenal response is particularly interesting when one looks at the classical symptoms that are part of the agoraphobic process which I'll discuss shortly.

When reviewing the world literature on beriberi, (Shimazono and Katsura, 1965; Lonsdale, 1975; Wolstenholme, 1967) I was amazed to discover that much of the symptomology was virtually the same in agoraphobia (AGP) although the signs were not identical.

The nature and abundance of symptoms presenting in AGP and hypoglycemia are suggestive of autonomic nervous dysfunction. Beriberi has been described as the prototype of autonomic dysfunction, (Lonsdale and Shamberger, p. 208).

Autonomic nervous system effects are best seen as vasomotor changes. It has been observed that injections of adrenalin caused an exaggerated response of the nervous system resulting in tachycardia, elevated blood pressure, substernal oppression, nausea, and vomiting (Shimazono and Katsura, p. 35) in beriberi patients.

Cardiovascular symptoms are among the most important clinical signs in beriberi. Palpitation, dyspnea with exertion, and mental excitement are symptoms commonly described as part of the AGP syndrome.

Also noted in beriberi is vertigo and instability or ataxia, (Shimazono and Katsura, p. 40), sensory and motor nerve afflictions, respiratory symptoms in the form of dyspnea and digestive symptoms including full sensation in epigastrum, heartburn and constipation. The blood picture is found to be within normal limits. (Shimazono and Katsura, p. 43). Note again that such symptoms are classically described by the agoraphobic.

In 1928 Kawatara found that blood lactic acid was increased in beriberi and in experimentally induced vitamin B deficiency. (Shimazono and Katsura, p. 51). This was confirmed in the same year by Inawashiro who emphasized that the increase in blood lactic acid was more striking upon physical exertion. Note that an increase in lactic acid upon exertion was reported by Cohen and White in their study of patients with anxiety neurosis.

It was stressed at the Princeton Ciba conference (Wolstenholme, 1967) that thiamine deficiency and beriberi are not synonymous terms. Folles was quoted in 1958 saying that the inter-relation of various nutrients is of great importance in the production of pathological changes of one type or another (Wolstenholme, p. 137).

Therefore while AGP, defective glucose metabolism, and beriberi are different disorders they all demonstrate symptomatology of disturbances in the glucose-oxidative pathway.

A relationship between thiamine depletion and serotonin metabolism has been examined and reported by Plaitakis et al. (1978) in a short communication in the Journal of Neurochemistry. Increased brain concentrations of 5-HIAA were found in the PT (pyrithiamine is a vitamin Bl analog.) treated rats with no alteration of serotonin or tryptophan levels noted. This suggested an increased in vivo turnover of serotonin in the brain of PT-treated animals.

Due to this increased turnover of serotonin, any disturbances in serotonin metabolism would be aggravated by a thiamine deficiency. Niacin deficiency may lead to depression of serotonin synthesis since tryptophan will be diverted away from serotonin synthesis to synthesize niacin. Both niacin and serotonin synthesis from tryptophan require B 6 dependent enzyme reactions for their synthesis. Thus, disturbed B 6 metabolism can inhibit synthesis of serotonin and formation of niacin via the tryptophan pathway.

In experiments by Plaitakis et al., in 1978, a selective inhibition of serotonin uptake was demonstrated only by the cerebellar synaptosomes. Kinetic studies on pyrithia-

mine treated rats in this study indicated a 50 percent decrease in the Vmax and a 40 percent decrease in the Km for serotonin. The uptake of GABA, glutamic acid, norepinephrine, and choline were not affected. This work suggests a selective involvement of serotonergic activity in the development of neurological manifestations following thiamine deficiency.

Glucose metabolism has a key position in the synthesis of the putative amino acid transmitters, glutamic acid, aspartic acid and GABA (Hamel et al., 1979). Diminished PDH activity may be critical for regions of the brain in which an excess of enzyme activity is minimal, since Reynolds and Blass had shown that PDH activity is not evenly distributed in the brain (Hamel et al.). Thus, alterations in amino acids and neurotransmitters may be the result of reduced PDH activity in response to thiamine deficiency or dependency. Such alterations could lead to the neuronal dysfunction associated with disturbed thiamine biochemistry.

I'd like to emphasize the relationship of caffeine and disturbed carbohydrate metabolism to neurotransmission and ultimately agoraphobia.

In fact, in one housebound agoraphobic, the entire symptomology was reversed by just the elimination of a daily ten-cup coffee habit.

Most of the agoraphobics I've encountered have been heavy caffeine consumers in the form of coffee, tea, chocolate, and cola beverages. Caffeine stimulates the adrenal glands, thus raising the level of circulating hormones, (Bolton, Null and Pressman) Lonsdale reported (1975) that blood pyruvate is increased as a response to adrenalin, thus stressing the oxidative pathways.

Note that, as previously mentioned, in beriberi there is a hyper-response of the nervous system to injected adrenalin.

Thus, caffeine may result in increased adrenalin which in a thiamine deficient-dependent state could result in further disturbance in oxidative metabolism with accumulations of lactate and pyruvate. In the biochemically impaired agoraphobic any adrenal stimulant or stressor, including emotions and caffeine, may initiate a hyper response of the auto-nomic nervous system manifesting in symptomology which triggers or is characteristic of, panic attacks.

"As the knowledge concerning the biochemical pathology of genetically determined metabolic disorders accumulates, important inter-relationships between various vitamins, cofactors, and essential substances seem to emerge, further complicating an already obfuscated field." (Gubler, Fujiwara, Dreyfus, 1976, p. 380-381).

Much can be done to correct faulty biochemistry and to ameliorate symptoms and signs. Even genetic changes can be reversed in some situations as reported by Cotzias (1977).

Agoraphobia, characterized by a tremendous number of symptoms and few signs would appear to be a sequel to dysfunction of metabolism and most particularly carbohydrate metabolism. The multitudinous and diverse symptoms of agoraphobia, so much like those of early beriberi, accompanied by multiple vitamin dependent enzyme defects suggest the need for a massive dietary overhaul.

References

BOLTON, S., NULL, G. and PRESSMAN, A.H.: Caffeine: Its Effects, Uses and Abuses. J. Applied Nutrition 33, 1, pp. 35-53, 1981.

COTZIAS, G.C.: Geochemistry and the Environment; The Relation of Other Selected Trace Elements to Health and Disease 2, pp. 32-34, 1977.

GUBLER, C: Effect of Thiamine Deprivation and Thiamine Antagonists on the Level of Aminobutyric Acid and 2-OxogIutarate Metabolism in Rat Brain. J. of Neurochemistry 22, pp. 831-836, Pergamen Press, Gr. Britain, 1974.

HAMEL, E., BUTTERWORTH, R. and BARBEAU, A.: Effect of Thiamine Deficiency on Levels of Putative Amino Acid Transmitters in Affected Regions of Rat Brain. J. of Neurochemistry 33, pp. 575-577,1979.

LONSDALE, D.: Thiamine Metabolism in Disease. CRC Critical Review in Clinical Laboratory Science, Jan. 1975.

LONSDALE, D. and SHAMBERGER, R.: Red Cell Transkeltolase as an Indicator of Nutritional Deficiency. American J. of Clin. Nut. 33,205-211,1980.

PLAITAKIS, A., VAN WOERT, M.H., HWANG, E. and BERL, S.: The Effect of Acute Thiamine Deficiency on Brain Tryptophan, Serotonin and 5-Hydrooxyindoleacetic Acid. J. Neurochemistry 31, pp. 1087-1089, 1978.

SHIMAZONO, N. and KATSURA, E.: Review of Japanese Literature on Beriberi and Thiamine. Vitamin B Research Com. of Japan, pp. 51,52,1965.

WOLSTENHOLME, V.: Thiamine Deficiency; Biochemical Lesions and their Clinical Significance. Ciba Fdn. Study Group 28, Little, Brown & Co., Boston, 1967.

Part III Agoraphobia and Allergy

For many, the association of allergy and agoraphobia may appear an odd one at best.

The avoidance and/or neutralization treatment of substances to which the agoraphobic is found to be allergic or hypersensitive often results in a rapid and dramatic reduction in the various agoraphobic symptoms.

In some agoraphobics avoidance of reactive substances is of primary importance in symptom relief, whereas in other agoraphobics defective nutrient metabolism is more central to their symptoms. Invariably both areas are involved and in general both areas should be assessed unless attention to either aspect singularly resolves all symptoms.

Following are some of the outstanding examples of agoraphobics in whom substance reactivity was a major contributor (but not the only contributor) to their symptomology.

N. W., Baltimore, Md. — intense anxiety experienced after ingesting milk . . . fully mobile - panic free;

J. A., Newark, N.J. — exposure to dogs produced nausea and ataxia, sugar and wheat resulted in pronounced anxiety, depression and headaches . .. fully mobile -panic free;

M. A., Ohio — housebound from panic attacks and paranoid - total elimination of symptoms by elimination of daily ten-cup coffee habit. . . fully mobile - panic free;

S. L., New Jersey — severe obsessive-compulsive behavior, accompanying panic attacks at various times, wouldn't move from a chair ... sugar, mushrooms, squash primary allergens . . . significant symptom reduction following elimination of these foods .. . fully mobile - panic free;

M. S., Princeton, N.J. — severe panic attacks and eczema virtually produced at will by consumption of potatoes to which it was discovered he was allergic . . . fully mobile - panic free;

E. G., Florida — panic, sweats, irregular heartbeats produced by milk. Much improved - still in process.

S. A., Trenton, N.J. — panic attacks, breathing difficulty, choking sensations determined to be provoked by exposure to yeast.. . fully mobile - panic free.

Substance reactivity may manifest in very diverse symptoms. An individual's target organ is a function of his biochemical individuality. Thus, various substances may produce G.I. symptoms in one individual, cardiac irregularities in another, behavioral or mood problems in yet another, and so forth.

The term cerebral or neuroallergy is often applied to apparently emotional or mental symptoms induced by a reactive substance. The reader is referred to the work of Theron Randolph, Marshall Mandell, Doris Rapp, Joseph Miller, William Philpott, et al. in the field of Clinical Ecology for further exploration and understanding of this phenomenon.

Some techniques for assessing allergy-hypersensitivity reactions include food avoidance and challenge testing, the cytotoxic test, the provocative intradermal serial dilution titration technique, (Miller technique), RAST, and PRIST tests.

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Part IV Two Case Studies

Case #1

On December 17,1979, S. M., a 30 year-old agoraphobic woman, somewhat overweight at 130 lbs., 5'2", when first seen in my office, presented with daily headaches, dizziness, fatigue, chest pains, and numbness in her left arm. She suffered episodes of what she called "visual field shrinking," as well as "shakes" (which she referred to as seizures), and stated rapid movements would provoke these.

Medical evaluations had been done which included neurological, cardiac, and psychiatric workups. The working diagnosis was severe anxiety, more specifically agoraphobia.

She was in weekly treatment with a psychiatrist for her panic attacks and phobic condition.

Due to the multiplicity and severity of her symptoms, her brother reported he often literally carried her into and out of her psychiatrist's office.

In addition to the previously mentioned symptoms, she had a large number of rather typical nutritional signs such as periodontal problems (bleeding and receding gums), muscle spasms, skin problems, poor hair quality, etc.

Her self-image was very poor. Her response to the systems review question, "Do you like yourself?" was, "No, I always feel ugly and sick."

A required detailed three-day chronological food/symptom diary demonstrated very poor nutritional practices, such as large scale consumption of foods high in sugar, fat, salt, caffeine, including coffee and carbonated beverages. She was also a smoker.

Functional nutritional testing was done which demonstrated abnormal activity of the erythrocyte transketolase and erythrocyte glutamic pyruvate transaminase (EGPT) enzymes. This established a functional deficiency or dependency for vitamins B 1 and B 6, respectively.

Hair analysis demonstrated low zinc, chromium, and iron.

She was also sent for food allergy screening via the Bryan method of leukocyte cytotoxic testing and found to be multiply allergic. Of particular significance were mushrooms, rice, rye, tobacco, fructose, and brussels sprouts. She had slight reactions to most foods tested.

She was placed on a nutritional regimen which included a rotational diet (no food repeated more than once in five days).

All refined carbohydrates, caffeine, and tobacco were to be strictly eliminated. For general health purposes and due to her significant hypersensitivity reactions she was also to avoid additives, preservatives, and chemicals as much as possible.

Her nutrient program consisted of special low allergy vitamin brands free of soy, yeast, wheat, lactose, corn, etc.

She was placed on six grams of vitamin C, a multi-vitamin, 500 mg thiamine (B1) O.D., 200 mg pyridoxine (B 6) O.D., 800 mcg folic acid B.I.D., 400 i.u. Vitamin E (soy and wheat free), 500 mg calcium, 250 mg magnesium, 50 mg zinc (chelated), 17 mg manganese (chelated), 30 mg iron (chelated), 1,000 mg choline, 1,000 mg inositol, and 300 mg methionine.

At the three-month follow-up she was dramatically improved. Visual blurring and focusing difficulties were gone as were her frequent ear infections. Her periodontal signs and symptoms were much improved. Her muscle spasms were gone. Persistent nasal stuffiness was gone. Chest pain, headaches, dizziness, lightheadedness, trembling

hands, numbness and tingling in her extremities were gone. The "visual field shrinking" and "shakes" were gone. Sluggishness and fatigue had disappeared. Her phobias were almost gone as was her anxiety. Occasional mild episodes would still occur at times in shopping malls or in cars. She evaluated herself as 95 percent improved. Happily her self concept improved right along with the decline in her symptoms.

The abnormal enzymes were retested and found normal, establishing functional adequacy of thiamine and pyridoxine.

Provocative intradermal testing, particularly for petrochemical reactivity, was suggested due to a mild persistence of reactions in shopping malls and automobiles. However, she declined to pursue this as she was more than happy with her progress.

In September, 1980, I watched her slim, beautifully tanned body rise to leave my office. Her eyes sparkled and her hair shone as she flashed a smile that said it all. . . the beauty of health.

Case #2

J. A., a very determined lady of 51, told me that I was her last hope. She handed me a two-page summary of her medical history pertinent to the agoraphobia and rather significant depressions. Repeat hospitalizations for depression had occurred. She'd had trials on many psychotropic drugs, none of which had helped her and some of which had provoked significant adverse reactions.

She told of the hell her life had become and of the virtual prison that was once her home. She was mobilizing from her home in a limited way only when accompanied by her husband. The caring between her husband and herself, though obvious, was severely stressed. His dreams for travel during retirement appeared shattered.

Pride in her once independent and optimistic nature now taken from her left her with one way out — suicide. She would give this approach every chance, but if she continued in this spiral of depression, fear, and incapacitation, she stated she would terminate her life.

Thankfully, she had an immediate response to the elimination of all refined sugars, white flour, and caffeine. Her depression although still present, had lifted significantly. She began to feel hopeful.

The Bryant method of cytotoxic testing was done. She was placed on a five-day rotary diet combined with initial avoidance of major offending foods.

She was placed on a broad spectrum orthomolecular nutrition program. Digestive enzymes, bulking agents, and mucolytics were included to successfully eliminate her chronic constipation. (Note: she had been moving her bowels approximately once in four days.)

Initially she was receiving: VM-75 Formula, once daily O.D.; 1,000 mg Calcium Ascorbate power T.I.D.; B-100 Complex with 400 mcg folic acid O.D.; Vitamin E, 400 I.U., wheat and soy free O.D.; Choline, 330 mg B.I.D.; Inositol, 330 B.I.D.; Methionine, 100 B.I.D.; GTF Chromium, 200 mcg T.I.D.; Chelated Copper, 2 mg O.D.; Chelated Zinc, 50 mg O.D.; Calcium, 330 mg O.D.; Magnesium, 150 mg O.D.

Her progress was remarkable. Her depressions were dramatically reduced in both frequency and intensity. Anxiety was markedly diminished and she was mobilizing both with and without her husband with greater frequency.

She was very subject to food related depressions. Even small diversions from her rotary diversified diet would manifest in major shifts and anxiety.

Due to food reactions and to a persistence of some disturbing symptoms, including a history of chronic vaginal infections as assessed by the systems review, it was decided that she would begin allergy testing and treatment by the provocative intradermal serial dilution titration technique (Miller technique).

My procedure has been to have all of the individual's commonly eaten foods tested (foods normally consumed more frequently than once in five days), stressing foods that are difficult to rotate.

At a minimum, the following foods are generally included in the testing: milk, corn, wheat, yeast, tomato, sugar beet and sugar cane, onion, soy, beef, and egg. Many other foods are commonly tested, such as potato, chicken, garlic, rice, peanut, orange, etc.

Common inhalants and substances such as housedust, mites, molds, yeast, try-chophyton, epidermophyton, Candida albicans, and ethanol (synthetic hydrocarbon test for petrochemical hypersensitivity) are tested routinely. Grasses, trees, and pollens are often tested based in part on history and seasonality of symptoms. Pets or animals are included when indicated by exposure.

Neutralization doses (end points) for each allergen, when determined, are generally combined in one vial and injected subcut-aneously twice weekly. Patients with high end points for Candida albicans and/or significant histories of vaginal infections or cutaneous itching are generally treated with the fungus suppressing agent Nystatin in addition to neutralization. Acidophillus capsules taken orally as well as added to a douche solution are also helpful.

J. A. had strong reactions to the Candida albicans skin test as suspected by her history of vaginal infections and hormonally related anxiety and depression. She was reactive to many other substances tested. She was placed on Nystatin 777 QID and neutralization therapy.

J. A. responded beautifully to neutralization and Nystatin; so well, in fact, that even before all allergy testing had been completed, she was able to take an airplane trip from New Jersey to Florida for a ten-day vacation with her husband! To her delight, her last remaining symptom, a periodic feeling of lightheadedness, accompanied by some mild ataxia, disappeared altogether during the trip, only to return again on arrival at her home.

Was it the air, the water, the plant life? Her last round of allergy tests told the story. It was her dog. Intradermal injection of dog extract produced immediate lightheadedness and ataxia. Her end point for dog extract was higher than for any other allergen tested. The neutralization dose relieved the induced symptoms immediately. This reaction treatment response was reproduced three times to the amazement of all. Simultaneously with allergy testing and treatment, functional vitamin studies were done.

Multiple disturbances were identified. The EGPT index was high indicating a functional deficiency of vitamin B 6. She was excreting methylmalonic acid (MMA) in her urine, indicating a functional deficiency of vitamin B 12. Urinary levels of formiminoglutamic acid (FIGLU) were elevated and can occur with a functional deficiency of either vitamin B12 or folic acid. Therefore, assessment for FIGLU was performed after correcting the functional B 12 deficiency as indicated by the elimination of methylmalonic aciduria.

Her vitamin program was adjusted to include more folic acid, B12, and B 6. Due to yeast allergy she was switched to hypoaller-genic yeast-free brands of vitamins.

The previous vitamin abnormalities were all corrected, except urinary FIGLU, which was significantly reduced.

Folic acid was increased a second time and when recently encountered in a shopping mall she reported virtually the complete elimination of her nervousness and ataxia. She commented, "The extra folic acid made a notable difference within 48 hours."

On vitamin-mineral orthomolecular therapy, dietary modification, and allergen neutralization injections, J. A. is now totally recovered, i.e., fully mobile and free of any panic attacks, independent, and happy again.