Editorial

A. Hoffer, M.D., Ph.D.[1]

MEGA AMINO ACID THERAPY

Orthomolecular psychiatry derives from the use of large doses of one vitamin, B3, in the treatment of schizophrenia. Humphry Osmond and I did not stumble into the use of this vitamin; our decision arose from the adrenochrome hypothesis of schizophrenia which we first reported to the Dementia Praecox Committee of Scottish Rites Mason, at the Waldorf Astoria Hotel in 1952. This was the committee created by Dr. Nolan D.C Lewis, the first and best-known Director of the Psychiatric Institute, New York. Dr. Lewis created this committee as a way of keeping biological psychiatry alive at a time when there were few funds for psychiatric research and when the winds of psychoanalysis began to scorch U.S.A. psychiatry.

Once we had enunciated our hypothesis any competent clinician would have concluded, as we did, that the logical substance to try to reverse the effects of aberrant adrenalin — adrenochrome — metabolism would be Vitamin B3 and, in a subsidiary role, ascorbic acid. Our decision to use this vitamin was not serendipitous. Using statistical language we could have used a one tailed test for significance instead of the usual two tailed test.

We were the first psychiatrists to use double blind methods for testing the therapeutic effects of drugs. We do not know of any previous double blind controlled studies in any field of medicine in North America. If there have been any we would be happy to be so informed. This method started in England where it was called the double dummy method since tablets containing the drug were compared with tablets which were inert. The latter were dummy tablets. In North America the term placebo became popular and there was even a brief, minor movement in North American psychiatry called "placedology." We used double blind experiments because we were advised to do so by Dr. Bud Fisher, a biostatistician, with Department of Health and Welfare, Ottawa. When he made this suggestion we quickly saw the merits of this method, but we also felt that our chance of being awarded a research grant would be enhanced. Soon after, each application form for research grants in Canada carried a question about what method would the applicant use and how would it be analyzed statistically. Researchers quickly caught on and the golden era of double blind methodology began. Since then we have also become aware of the problems created by double blinds. For the first time vitamin B3 was used to treat schizophrenics by a new method never before used in North America, with perhaps only two previous studies in England in physical medicine. Perhaps the association of a new treatment

3-A 2727 Quadra Street, Victoria, B.C., V8T 4E5

arising from a new theory and introduced by a new experimental method doomed it to a long arduous uphill struggle.

Since this early work Orthomolecular has been associated with the use of large doses of vitamins commonly called 'megavita-mins'. Of course, there is no megavitamin. The term refers only to the use of doses considered optimum by Orthomolecular therapists, but considered large by those who have had no practical experience in their use; except for nicotinic acid which has been used widely in large mega doses to lower blood fat levels. Other vitamins are being used in mega doses including vitamin A to restore immune defensive systems in the body; thiamine to repair the ravages of excessive alcoholism, for multiple sclerosis and depression; pyridoxine for infantile autism, other children with learning and behavioral disorders, and for schizophrenics (especially for pyroluriacs). Vitamin E used as an antioxident, for cardiovascular disease. Ascorbic acid is used for a large variety of conditions including virus diseases, cancer and many others. Folic acid and vitamin B 12 are also used, especially for senility and for some schizophrenics. It is highly probable that eventually each vitamin will be found to be necessary in high doses for some patients. They will be found in that group of chronic illnesses who do not respond to current treatment.

The purpose of this editorial is to bring attention to the expansion of Orthomolecular therapy to the use of amino acids in large doses, to mega amino acid treatment. Why should only the vitamins and minerals be required in high doses by a few patients? In fact there is already evidence that a few patients require amino acids in large quantities. More amino acid dependent patients will be discovered once we begin to search for them seriously.

All twenty amino acids are essential for life; they must all be present at about the same time at the correct level. The required pattern of amino acids is unique to individuals. Each individual can start with a pattern available in food and by degrading some and making others can obtain the pattern best suited to its cellular needs. This process is called "justification" by Bessman. Only eight amino acids are said to be essential since they can not be made in the body; they must be ingested. One essential amino acid, l-tryptophane, is already coming into common use for insomnia and for depression to a lesser degree. A few preliminary studies I have done suggest it may be very helpful in clearing skin eruptions frequently found in schizophrenic patients. Tryptophan has been popularized by the finding it can control brain levels of a neurohormone, serotonin. We already have mega tryptophan therapy, one of the eight essential amino acids.

Two of the essential amino acids, leucine and isoleucine, are involved in the etiology of pellagra and may be involved in schizophrenia as well as in other similar conditions. Pellagra is caused by a monotonous diet which depends primarily on corn. Corn is low in l-tryptophane, low in vitamin B3 which is present in a tightly bound form from which the human body can extract little, and it is too rich in leucine compared to isoleucine. leucine increases the loss of vitamin B3 into the urine. In India it has been shown that pellagrins made normal by giving them Vitamin B3 quickly become psychotic by giving them leucine; it increases the loss of the vitamin. But if isoleucine is given, the psychosis is promptly reversed. Isoleucine shuts off the loss of vitamin B3. Perhaps this is an explanation for the presence of a novel endorphin called leu endorphin in the blood of schizophrenics. If the presence of this substance is confirmed it will open up this area of the relationship of leucine and isoleucine to schizophrenia. In a few pilot studies about ten years ago I found that 3 grams per day of isoleucine rapidly cleared schizophrenic symptoms in a few acute outpatient schizophrenics, doing in a week what vitamin B3 would do in several months. Unfortunately it was impossible to obtain adequate quantities *or* to have access to the vast sums of money required to satisfy the legal requirements of FDD (Canada) or FDA (U.S.A.). The combination of isoleucine and vitamin B3 would be a powerful one. The isoleucine would

enhance the effect of the vitamin so that lower doses could be used.

The remaining twelve so-called "non-essential" amino acids may be essential for some. This means that in a few people they have not acquired the ability to convert one of the eight essential amino acids to one of the remaining twelve. The twelve are considered not essential because they can be synthesized in the body from the essential eight. But all are essential and if one can not be made it becomes an essential one for that individual. There are two examples:

Cystine is one of the twelve unessential amino acids as it is made from one of the essential amino acids, methionine. But premature infants have not yet developed the biochemical apparatus for making cystine from methionine. This is why human milk is so much better than cows' milk for babies; it contains cystine. Are there adults who fail to make enough cystine? We will not know until studies have been done.

Over the past decade Bessman (1979) has pointed his finger at tyrosine as another non-essential amino acid which is essential for some. In most people enough phenylalanine is converted into tyrosine by an enzyme called phenylalanine hydroxylase. The phenylalanine simply piles up in the body while the body suffers from a deficiency of tyrosine. This is the genetic defect which is behind the disease called phenylketonuria (PKU), which is associated with retardation in infants and schizophrenia in adults. The first cases of PKU were found in the chronic wards of a Norwegian mental hospital by Foiling nearly fifty years ago. Bessman considers PKU to be a tyrosine deficiency disease. In normal people 95 percent of the phenylalanine is converted into tyrosine. If not, phenylalanine will accumulate in the body. An individual with two genes for PKU (homozygous) can convert little or no phenylalanine to tyrosine. The average food supplies less than about one-third of the amount required. A person with only one gene for PKU (heterozygous) will convert about half of the phenylalanine to tyrosine; this, plus the tyrosine in food supplies them with about two-thirds of the normal amount.

Heterozygotes (example — mothers of PKU children) have more phenylalanine and less tyrosine in their blood than do normal subjects.

There is a significant association between intelligence and the ability to make enough tyrosine; the less conversion, the lower the I.Q.

Since heterozygotes can not make as much tyrosine they are more dependent on tyrosine in their food; for them tyrosine is an essential amino acid and PKU is a tyrosine deficiency or dependency. Such people are therefore much more dependent upon having a diet high in tyrosine, i.e. in proteins rich in tyrosine. A potential PKU may be normal on a high protein diet and ill on a low protein diet.

Bessman has examined the impact of his theory on the field of retardation in general. Between 60 and 90 percent of all retardation is non-specific, meaning we don't know why. But in the major suspected associated conditions — renal disease, hypertension, eclampsia and pernicious vomiting of pregnancy, protein deficiency is common. Mothers may be severely protein deficient because they are ill and can not eat, because they are unaware protein is essential or because they are too poor. In the U.S.A. and Canada the main reason must be our typical low fiber, high sugar diet with the heavy consumption of processed and junk foods. Also, more and more early teenage girls are having and keeping their babies. They come from our generation brought up on junk food, a generation which considers chips, a soft drink and a hamburger a perfectly adequate diet. Many leave home to live in poverty. The combination of ignorance and poverty produces an appalling state of nutrition.

Bessman's views must be examined very seriously. I recommend to readers of this journal that an examination of the relationship of tyrosine deficiency to learning disorders will prove very fruitful. A large proportion of children with learning and behavioral disorders, especially the hyperactive group, are blondhaired blue-eyed boys. Is this due to their inability to convert phenylalanine to tyrosine? Tyrosine

is essential for the formation of all pigment in skin, hair and in the eye. Will tyrosine help these children?

Finally Bessman recommends that pregnant women who are homozygous for PKU (very rare but will become more common) should be given 2 grams per day

of tyrosine while heterogyzotes should get 1 gram per day. It is safe; in pregnant rats given 2 grams to 3 grams per kilogram per day (I gram per pound or 50 grams per day in an adult woman) it was toxic. One to 4 grams per day should be safe.

Other non-essential amino acids are being examined in the same way. With Bessman's data before medicine it is likely the search for new amino acids deficiency disease will accelerate. Orthomolecular therapists will be in the forefront of this exciting new development.

REFERENCE

BESSMAN, S.P.: The Justification Theory: The Essential Nature of the Nonessential Amino Acids. Nutrition Review, 37,209-220,1979.