Letters

Ascorbic acid and mental depression

To the Editor,

Recent initiative of the Public Health Campaign known as D/ART (Depression Awareness, Recognition and Treatment) has been reported in the July 15,1988 issue of *JAMA:* 309-310, by Dr. Raymond. I believe this training program very important because physicians are really the first line of defense against depression.

One of the most common problems facing pediatricians dealing with mental depression in children is drug treatment. In the last two decades great advances have been made in treating depressive disorders. A rapid rate of improvement is generally obtained by psychotherapy and the use of antidepressant drugs: tricyclic compounds, MAO (monoamine oxidase) inhibitors, lithium and phenothiazines. Although these drugs are generally effective and relatively safe, a variety of minor or even serious adverse effects occur, greatly limiting their use in children and in many different conditions in adults. Since depression appears to exist at all ages of childhood and ordinary antidepressant drugs are best reserved for severe depression, the availability of an effective and more safe drug is of primary importance. In 1980 we casually found that high doses of intravenous ascorbic acid (50 mg/Kg/day) relieved ACTH-induced depression in a child.[1] Since then additional patients, children, young adults and elderly subjects, who were affected by episodes of mental depression, were similarly resolved by courses of intravenous ascorbic acid therapy. On this safe and inexpensive therapeutic regimen psychic disturbances gradually subsided with complete recovery in almost all of them within three or four weeks. Most of these subjects were treated effectively on an outpatient basis. The initial clinical response to vitamin C may require from 6 to 8 consecutive days of treatment, and may not become maximal until the third or fourth week. If the patient does not show a clinical response in the first 3-4 weeks of ascorbic acid regimen, his condition should be re-evaluated and a second course should be considered in addition to the usual therapy.

Vitamin C may be said to possess few pharmacological actions. Acute administration of the compound in a single dose even greatly in excess of the physiological requirements causes few demonstrable influences upon the central nervous system. However, it must be remembered that in our cases only the chronic intravenous administration of large doses has been associated with some therapeutical effects. Ascorbic acid is absorbed in the intestine by an energy requiring a Na^+ dependent, carrier mediated transport system, and an inverse relationship exists between the size of the dose and the percentage of the dose absorbed. Due to this limited absorption capacity of ascorbic acid with oral intakes,[2] to increase vitamin C to suitable pharmacologic plasma concentrations, a parenteral route of administration is necessary.

In an article entitled *Orthomolecular Psychiatry,* Pauling[3] describes a method based on varying concentrations of substances normally present in the human body including ascorbic acid, that may be found to be of great value in treating many patients with mental symptoms, such as depression. The importance of ascorbic acid in neurobiology is suggested by the low levels of this vitamin in individuals with depressed mental states.[4] Mental depression is moreover the first clinical symptom of experimental scurvy in man.[5] The prominent biological role played by vitamin C in the onset of mental disturbances is suggested also by the depressive state that has been reported as a striking clinical feature of chronic scurvy, and the complete recovery after treatment with ascorbic acid.[6 7]

According to the catecholamine hypothesis of affective disorders,[8] depression may be associated with a relative deficiency of norepinephrine in the brain. Dixit[9] suggested that in chronic scurvy the lack of ascorbic acid leads to diminished activity

of the enzyme dopamine beta-monooxy-genase, a Cu^{2+} protein which requires ascorbic acid for activity. This enzyme catalyzes the reaction of molecular oxygen with dopamine and ascorbate to yield norepinephrine and dehydroascorbate.[10]

The results here reported, confirm the previous findings on antidepressant effect of ascorbic acid, but are insufficient at this time to formulate valid conclusions. However, the interesting clinical results obtained following administration of high doses of vitamin C, prompted us to continue this study, particularly in children and elderly individuals, owing to the complete safety of this treatment.

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Note

The usual dosage of sodium ascorbate (Redoxon^{0} Roche: 500 mg - 1 g vials) in mental depression in children and adults is 50 mg/Kg/day dissolved in 50 mL of 5% glucose solution administered by intravenous infusion at a rate of 30-60 drops/ minute.

Large doses of sodium ascorbate may be contra-indicated in subjects with underlying vascular hypertension, in recurrent stone formers, in patients with renal impairment and in patients on chronic hemodialysis.

References

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To the Editor,

In his article, *Family Tree Connection: How Your Past Can Shape Your Future Health — A Lesson in Orthomolecular Medicine* (Vol. 3, No. 3, pp. 123-134), Dr. Reading raises a good point and it certainly is not unknown that psychiatric patients have considerable nutritional deficiencies. Perhaps it would be useful for all of us to quantify what we find in our individual evaluations for our patients. For your readers I am including a table that I originally presented at the introduction of the Hoffer/Vickar Chair of Orthomolecular Psychiatry at Ben Gurion University in May of 1987. It is a summary of the lab results on schizophrenic patients done from January, 1985 to March of 1987. Some of the material was hard to obtain because the hospital data was not on computer and chart review was simply too unwieldy to get a more comprehensive evaluation. However, when these numbers were reviewed with the hospital pathologist, there were several impressions that struck him. I have included the table as I presented it and would draw attention to a

January 1985 - March 1987
Inpatients
Diagnosis: Schizophrenia
All Other Diagnoses Excluded

	Number	Above Norms	Below Norms
Magnesium	41	2%	12%
B,₂	55	20%	4%
Folic Acid	56	25%	11%
Copper	63	2%	30%
Zinc	67	0%	12%
Manganese	55	13%	7%
Kryptopyrolle Excretion	42	33%	0%

few findings. The numbers *below* the norms (that are standard norms that I suspect most hospitals use), were most impressive to the pathologist and certainly a surprise to me. Eleven percent folic acid deficiency is not an inconsiderable number, and four percent low on B_{12} has to be a consideration particularly since recent literature suggests that B_{12} supplementation may be appropriate even in the absence of physical signs of B_{12} deficiency. I think the fact that so few of the patients were above norms in zinc is of note. Whether this would be better explained if the numbers were broken down by sex and the copper/ zinc ratios reviewed has to be a consideration as well.

I do not make any further speculations as to the meanings of these numbers. They may simply be too small to lead to any conclusions, but I would certainly encourage others who run some of these evaluations to begin documenting the findings and perhaps there are patterns we can explain.

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