Alternative Medicine Review Volume 13, Number 4 2008

Successful Treatment of Schizophrenia Requires Optimal Daily Doses of Vitamin B_3

For over 50 years Dr. Abram Hoffer has been educating clinicians about the need to correctly (optimally) dose schizophrenics with vitamin B_3 (niacin; niacinamide). For the past 10 years I have, likewise, educated numerous naturopathic and medical doctors about the very same thing. For some reason, both types of clinicians routinely treat schizophrenic patients with plenty of vitamins, minerals, and other natural health products, but they never provide enough vitamin B_3. In these authors opinions, schizophrenic patients cannot get well if not provided with optimal doses of vitamin B_3. This prevents the real acceptance of nutritional treatment since clinicians will not observe favorable results when inadequate treatment is provided; their schizophrenic patients will continue to suffer needlessly.

To understand the importance of vitamin B_3 treatment, some background information is needed. Schizophrenia is characterized by a combination of perceptual changes (e.g., hallucinations) and thought disorders (e.g., delusions).[1] These aberrant mental states, which can lead to psychotic behavior, cause a tremendous amount of emotional and psychological suffering. The cause of schizophrenia, the subject of much debate, is considered a biochemical imbalance, although certain genetic factors most certainly play a role.

The majority of scientists and psychiatrists subscribe to the dopamine excess theory of schizophrenia; i.e., that too much dopamine is largely responsible for the symptoms of psychosis. However, since 1952, Hoffer, the founding father of orthomolecular medicine, has researched, published, and expanded on the adrenochrome theory of schizophrenia.[1,2] He and his colleagues, Drs. Osmond and Smythies, arrived at this theory by studying and researching the effects of substances such as mescaline, lysergic acid diethylamide (LSD), and amphetamines – all of which can cause a clinical syndrome in normal individuals that would be clinically indistinguishable from schizophrenia.

Osmond and Smythies noted that mescaline had a similar chemical structure to that of adrenaline. Hoffer, Osmond, and Smythies concluded that since both can be converted to indoles in the body, the potential schizophrenic toxin might be an indole derivative of adrenaline with similar neurochemical properties to that of mescaline or LSD. They eventually deduced that the schizophrenic toxin was an oxidized derivative of adrenaline known as adrenochrome. Since the early 1950s, the adrenochrome theory has been validated by the following findings:

Alternative Medicine Review Volume 13, Number 4 2008

1. Adrenochrome and its close relatives – dopaminochrome (from dopamine) and noradrenochrome (from noradrenaline) – are present in the human brain.[3-5]
2. These compounds probably induce a combination of neurotoxic and mind-mood-altering effects.[3-5]
3. Reducing adrenochrome, dopaminochrome, and noradrenochrome is therapeutic for the treatment of schizophrenia.[6]

To reduce the production of adrenochrome, Hoffer and his team decided on the methyl acceptor vitamin B_3. This vitamin, previously used to treat pellagra (a disease clinically indistinguishable from schizophrenia) had relevant biochemical properties.[1,2] Hoffer and his team researched the metabolism of adrenaline. They knew that the reaction involving noradrenaline to adrenaline required the addition of one methyl group. Because vitamin B_3 was known to function as a methyl acceptor, Hoffer's team theorized that an optimum dose of niacin might decrease the amount of noradrenaline that would be converted to adrenaline. Since adrenochrome was thought to be an oxidized derivative of adrenaline, vitamin B_3 could help reduce the quantity of adrenochrome by simply limiting the production of adrenaline.

Hoffer and his team also discovered an additional biochemical property of vitamin B_3 that would help to explain its therapeutic efficacy. Vitamin B_3 is a precursor to nicotinamide adenine dinucleotide, which is present in both oxidized (NAD) and reduced (NADH) forms in the body. In the brain, adrenaline loses one electron to become oxidized adrenaline. If enough NAD and NADH are available then the oxidized adrenaline is reconverted to adrenaline. These back and forth processes continue to occur in the presence of sufficient vitamin B_3 coenzymes. However, in the absence of sufficient NAD and NADH, the oxidized adrenaline loses an additional electron and becomes adrenochrome. This last reaction is irreversible, and presumably occurs in much greater concentrations in the schizophrenic brain.

That being said, where is the proof? Can vitamin B_3 help in the treatment of acute and chronic schizophrenia? The first report on the therapeutic use of vitamin B_3 for schizophrenia was presented in 1952 at the Saskatchewan Committee on Schizophrenia. At this meeting, eight cases were presented, each demonstrating favorable effects from giving 1-10 g vitamin B_3, and, in the majority of cases, equal amounts of vitamin C.[1] After a more involved pilot study demonstrated excellent therapeutic responses to vitamin B_3,[1] the first North American double-blind, placebo-controlled experiment was undertaken to assess whether or not this vitamin was effective for schizophrenia. The study, which began in 1952 but was not published until 1957, involved 30 acute schizophrenic patients who were each randomized to placebo, niacinamide, or niacin.[1,2] They were given 1 g three times daily for 30 days, and then followed for one year. After one year, the patients given vitamin B_3 with the standard treatments at that time had more than double the recovery rate (80%) compared to patients in the placebo group (33%).[7]

In their second double-blind, placebo-controlled experiment, Hoffer and his team used only niacin and placebo.[1,8] The study lasted 33 days and involved 82 patients (43 in the placebo group and 39 in the niacin group). Vitamin B_3 once again contributed significantly to the recovery of acute schizophrenic patients. In the niacin group, 79.5 percent improved compared to 41.9 percent in the placebo group. Other parameters evaluated by Hoffer and his team included the number of patients readmitted, the number of readmissions, the number of well or much improved patients, and the number of patients who were considered cured. This data involved the following groups of patients: (1) those who only took vitamin B_3 in the hospital and not in the community; (2) patients who did not take vitamin B_3 in the hospital but did take the vitamin when in the community; (3) patients who took vitamin B_3 in the hospital and community; and (4) patients who never took vitamin B_3. The results demonstrated that patients in the community who were taking niacin (groups 2 and 3) had more community years that were free of readmissions compared to patients not taking vitamin B_3 (groups 1 and 4) – 91 percent versus 62 percent of the community years free of readmissions. The entire niacin group (group 3) was readmitted 38 times for 67 readmissions (average 64 days per patient); whereas, the placebo/non-niacin group (group 4) was readmitted 36 times for 81 readmissions (average 147 days per patient). Once all the data was combined, the results revealed that the most five-year cures and best treatment responses were among the patients who took vitamin B_3 in the hospital and in the community.

Hoffer followed patients from 1953 to 1960, publishing a total of six double-blind, randomized controlled clinical trials. All trials confirmed the positive effects that vitamin B_3 had on the recovery of acute schizophrenic patients, and that the use of this vitamin substantially reduced patients' reliance on the health care system.[2]

In terms of treating chronic schizophrenic patients, Hoffer's early studies did not show a favorable response among chronic schizophrenic patients who were ill longer than one year. When Hoffer reviewed this problem more thoroughly, however, he discovered that the treatment duration was not long enough to have produced adequate results. Chronic patients required vitamin B_3 treatment for five or more years in order to derive observable benefits.[1,9]

In one study involving 32 chronic patients, no patient responded to vitamin B_3 after two years of use.[1] Nineteen patients discontinued the vitamin, while the remaining 13 patients continued with the vitamin treatment. Data was obtained for the years, 1956-1964. Of the patients not on niacin, the mean number of days spent in hospital was 691 compared to 79 in the niacin group. The proportion of time spent in the hospital was substantially less for the chronic patients who remained on the vitamin.

In a more recent analysis of 27 chronic schizophrenic patients who had been under treatment for at least 10 years, consistent treatment with vitamin B_3 produced the following results: 11 patients were able to work; two patients were able to marry and look after their families and homes; two patients were single mothers able to care for their children; and three patients were able to manage their own businesses.[9] These results are remarkable when one considers the state of these patients prior to receiving optimal doses

of vitamin B_3. The average age of these patients was 40, the majority of them were ill for seven years before they sought treatment from Hoffer, and all had been unresponsive to previous treatments.

The starting dose of niacin for adults is 1,000 mg three times daily. In our opinion, the daily dose should be slowly increased to 4,500-18,000 mg to achieve the best possible outcome. Patients must be educated about the flushing, heat, itchiness, pruritis, redness, and tingling that they will transiently experience. These benign cutaneous reactions usually begin 15 minutes after taking niacin for the first time, and are first noticed around the forehead, then descend to the thorax, and sometimes to the feet. These reactions typically abate 1-2 hours following the ingestion of niacin. Niacin causes such cutaneous reactions by inducing the production of prostaglandin D_2 in the skin, leading to vasodilation and a marked increase of its metabolite (9α, 11β-PGF_2) in the plasma.[10] Niacin is its own anti-flushing agent because taking it regularly depletes the skin of prostaglandin D_2 and prevents subsequent cutaneous reactions. At 3,000 mg daily, the flush and other symptoms will cease to be an issue following the first 2-3 days of treatment, and will practically disappear thereafter. If patients are not consistently taking these optimal doses throughout the day, they will continually re-experience cutaneous reactions and possibly discontinue treatment.

The concern over liver toxicity is very minor if immediate-release niacin preparations are used.[11,12] Timed-release preparations can cause liver toxicity and are not recommended for schizophrenic patients unless under very close supervision.[13] In Prousky's clinical experience, niacin is more effective and better tolerated than niacinamide for schizophrenia. Some patients prefer niacinamide since it does not cause flushing or other cutaneous reactions. Nausea and dry mouth are much more common with the use of niacinamide than with niacin. The daily dosages of niacinamide should not exceed 6,000 mg since the likelihood of nausea accompanied with vomiting is much greater.[14]

The prognosis for the majority of schizophrenic patients is bleak, especially if they only receive contemporary medical treatments. About 90 percent will remain unwell and nonfunctional for the rest of their lives despite receiving the most advanced drugs and social services currently available.[15] Estimates of first episode schizophrenics are a little more optimistic and indicate that of five recently diagnosed patients, one will recover sufficiently to live an almost normal life without medication or with very low doses of medication.[16] The economic costs of schizophrenia to society are enormous, amounting to approximately two million dollars for each schizophrenic patient over a 40-year course of the illness.[17] In a recent publication examining the economic burden of schizophrenia in Canada, the direct and indirect health care costs associated with this disease were estimated to be 2.02 billion Canadian dollars in 2004.[18] In addition, when these figures were added to the high unemployment rate with additional productivity, morbidity, and mortality losses, the estimate reached 4.83 billion Canadian dollars, for a total cost estimate of 6.85 billion Canadian dollars in 2004. The authors of this report arrived at the following conclusion: "Despite significant improvements in the past decade in pharmacotherapy, programs, and services available for patients with schizophrenia, the economic burden of schizophrenia in Canada remains high."

As clinicians we need to offer restorative care to patients who suffer with schizophrenia, a severe and usually chronic mental illness. The only reasonable conclusion to be made from this data is that all schizophrenic patients, including both acute and chronic patients, need to be treated with vitamin B_3 as quickly as possible and for the duration of their lives. Vitamin B_3 treatment offers significant hope of a reasonable quality of life among patients who would otherwise remain incapacitated and in and out of hospitals for the remainder of their lives. Some might improve so much that they achieve clinical remission. Since not enough clinicians utilize optimal doses of vitamin B_3 with their schizophrenic patients, we hope that the information presented here persuades other clinicians to adopt this very effective and safe treatment.

Respectfully,
Abram Hoffer, MD (retired), PhD
Jonathan Prousky, ND

Abram Hoffer, PhD, MD, FRCP(C), ROHP – President, Orthomolecular Vitamins Information Centre; professor psychiatry, 1955-1967; Director Psychiatric Research, Department Health, Saskatchewan, 1950-1967; President Emeritus, International Schizophrenia Foundation; Editor, *Journal Orthomolecular Medicine*; 2007 winner of Dr Rogers Prize; pain in the neck to orthodox psychiatry. Correspondence address: 2727 Quadra Street, Suite 3A, Victoria BC, V8T 4E5

Jonathan E. Prousky, BPHE, BSc, MSc, ND – Chief Naturopathic Medical Officer and professor of clinical nutrition, Canadian College of Naturopathic Medicine.

References

1. Hoffer A. *Vitamin B-3 & Schizophrenia. Discovery, Recovery, Controversy*. Kingston, ON: Quarry Press, Inc; 1998:28-76.
2. Hoffer A. *Adventures in Psychiatry. The Scientific Memoirs of Dr. Abram Hoffer*. Caledon, ON: KOS Publishing Inc; 2005:50-99.
3. Smythies J. Endogenous neurotoxins relevant to schizophrenia. *J R Soc Med* 1996;89:679-680.
4. Smythies JR. Oxidative reactions and schizophrenia: a review-discussion. *Schizophr Res* 1997;24:357-364.
5. Smythies J. The adrenochrome hypothesis of schizophrenia revisited. *Neurotox Res* 2002;4:147-150.
6. Hoffer A. The adrenochrome hypothesis and psychiatry. *J Orthomol Med* 1999;14:49-62.
7. Hoffer A, Osmond H, Callbeck MJ, Kahan I. Treatment of schizophrenia with nicotinic acid and nicotinamide. *J Clin Exp Psychopathol* 1957;18:131-158.
8. Hoffer A. *Niacin Therapy In Psychiatry*. Springfield, IL: Charles C. Thomas; 1962;35-71.
9. Hoffer A. Chronic schizophrenic patients treated ten years or more. *J Orthomol Med* 1994;9:7-37.
10. Morrow JD, Parsons WG 3rd, Roberts LJ 2nd. Release of markedly increased quantities of prostaglandin D_2 *in vivo* in humans following the administration of nicotinic acid. *Prostaglandins* 1989;38:263-274.
11. Hoffer A. Vitamin B-3 and schizophrenia. *Townsend Lett Doctors Patients* 2001;213:20-23.
12. Paterson ET. Vitamin B_3 and liver toxicity. *Townsend Lett Doctors Patients* 2001;207:23.
13. Mullin GE, Greenson JK, Mitchell MC. Fulminant hepatic failure after ingestion of sustained-release nicotinic acid. *Ann Intern Med* 1989;111:253-255.
14. Hoffer A. Vitamin B-3: niacin and its amide. *Townsend Lett Doctors Patients* 1995;147:30-39.
15. Hoffer A. *Healing Schizophrenia*. Toronto, ON: CCNM Press Inc; 2004:7-21.
16. Horrobin D. *The Madness of Adam and Eve*. London, England: Corgi Books; 2001:149-151.
17. Hoffer A. Treating chronic schizophrenic patients. *J Orthomol Med* 2002;17:25-41.
18. Goeree R, Farahati F, Burke N, et al. The economic burden of schizophrenia in Canada in 2004. *Curr Med Res Opin* 2005;21:2017-2028.