Does Vitamin B_3 Really Reduce Adrenochrome?

Until his death, Dr. Abram Hoffer educated clinicians for over 50 years about the need to correctly (optimally) provide schizophrenics with vitamin B_3 (niacinamide or niacin). For over 13 years I have, likewise, educated numerous naturopathic and medical doctors about the very same thing. Schizophrenic patients are less likely to get well if not provided with optimal doses of vitamin B_3.

To understand the importance of vitamin B_3 treatment, some background information is necessary. Beginning around 1952, Hoffer researched, published, and expanded upon the adrenochrome theory of schizophrenia.[1,2] He and his colleagues, Drs. Osmond and Smythies, came to 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.

Hoffer noticed that mescaline had a similar chemical structure to that of adrenaline, and 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. He conjectured that the schizophrenic toxin was an oxidized derivative of adrenaline known as adrenochrome. To reduce the production of adrenochrome, Hoffer and his team decided upon the methyl acceptor, vitamin B_3. This vitamin had previously been used to treat pellagra (a disease clinically indistinguishable from schizophrenia), and 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 thought 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 might help to 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 it is a precursor to nicotinamide adenine dinucleotide, which is present in both oxidized (NAD) and reduced forms (NADH) in the body. In the brain, adrenaline becomes oxidized and 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 is believed to occur in much greater concentrations in the schizophrenic brain.

Over the past 15 years, Smythies, Hoffer's former research colleague, noted that:

1. Adrenochrome's close relatives–dopaminochrome (from dopamine) and noradrenochrome (from noradrenaline)–are present in the human brain.[3-5]

2. Adrenochrome and its close relatives induce a combination of neurotoxic and mind-mood-altering effects.[3-5]

While there are clinical studies and reports demonstrating that vitamin B_3 does indeed help in the treatment of acute and chronic schizophrenia,[1,2,6-8] the available data is insufficient in proving that it mitigates schizophrenic symptoms by lowering adrenochrome concentrations in the brain. Adrenochrome might be present in the blood[9] of normal human subjects or it might not be.[10] Even though its presence in the blood has been the subject of much debate, none of this proves it is in the blood (or brains) of schizophrenic patients and that it is responsible for schizophrenic symptoms. A urine study found N-methylmetanephrine, a metabolite of N-methylepinephrine, in 3 of 18 psychotic children.[11] This might suggest some increased

build-up of epinephrine (i.e., adrenaline) metabolites in the blood, but this does not prove the presence of adrenaline metabolites in the brain. Data that loosely suggests the possibility that adrenochrome might be present in the human brain comes from an animal experiment that identified aminochrome (i.e., a mixture of adrenochrome and noradrenochrome) in the rat brain.[12]

The majority of supportive data on the psychotomimetic properties of adrenochrome came from studies where normal and/or psychiatric patients were given adrenochrome experimentally.[5] For example, the first-generation antipsychotic medications reduce schizophrenic symptoms by blocking dopamine-type 2 receptors within the brain. They are not, however, correcting for an overproduction of dopamine within the brain. Likewise, vitamin B_3's beneficial therapeutic effects do not prove that it counteracts adrenochrome's psychotomimetic properties by diminishing its production and/or the double oxidation of adrenaline. Conclusions drawn from these sources of data have not proven anything causal, except that adrenochrome might be implicated in some aspect of the disorder, or adrenochrome might not be. We must entertain the possibility that vitamin B_3's therapeutic effects might have nothing to do with adrenochrome alteration.

Vitamin B_3 remains an important asset to those practicing orthomolecular medicine. Without Hoffer's dedication, perseverance, and prolific writings, the therapeutic uses of vitamin B_3 would likely have been forgotten. Vitamin B_3 definitely has value in helping to assuage the devastation of schizophrenia. I believe it is therapeutic precisely because of its global physiologic (i.e., likely increases brain vasodilatation) and metabolic effects (i.e., enhances oxidative phosphorylation) – some of which oppose several side effects induced from first and second generation antipsychotic medication (e.g., cognitive impairment, fatigue, hypercholesterolemia, and weight gain). On the other hand, newer publications have discovered intriguing links between niacin status, tryptophan metabolism and schizophrenia.[13,14] Until more research is done on the adrenochrome hypothesis of schizophrenia, we should seriously consider alternative viewpoints into vitamin B_3's mechanism of action.

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