

Is Vitamin B₃ Dependency a Causal Factor in the Development of Hypochlorhydria and Achlorhydria?

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Introduction

It is well known by many clinicians in the field of complementary and alternative medicine that vitamin B₃ has numerous therapeutic indications. The many review articles, case reports, and books authored by Hoffer fully elucidate the known and theoretical benefits of vitamin B₃ administration for the treatment of AIDS, alcoholism, arthritis, cancer, cardiovascular disease, childhood learning and behavioral disorders, longevity, post-traumatic stress disorder, schizophrenia and senility.¹⁻⁷ Despite the breadth of Hoffer's work, there has been no direct description regarding the usefulness of vitamin B₃ for the treatment of hypochlorhydria and achlorhydria conditions denoting a lack and absence of stomach (gastric) acid secretion.

Role of Hydrochloric Acid in Hypochlorhydria and Achlorhydria

When hydrochloric acid (HCl) secretion is insufficient, the gastric pH will not be sufficiently acidic, digestion will be impaired, and signs and symptoms of hypochlorhydria will be apparent. The common signs and symptoms of hypochlorhydria have been well described by Kelly.⁸ Accordingly, hypochlorhydria is a condition where the parietal cells of the stomach secrete insufficient amounts of HCl when stimulated by the presence of food or other known stimulators such as fasting,⁹ caffeine,¹⁰ alcohol,¹⁰ and calcium carbonate.¹⁰ Achlorhydria is simply a more severe form of hypochlorhydria where the parietal cells no longer function and acid secretion does

not occur. The consequences of hypo- and achlorhydria involve an increased susceptibility to gastric bacterial overgrowth,¹¹ enteric infections,^{12,13} hypergastrinemia that may lead to enterochromaffin-like cell hyperplasia and neoplasia,¹⁴⁻¹⁷ and malabsorption of various nutrients and amino acids.^{8,18} Thus, the proper release of HCl is essential for optimal health as it renders the stomach sterile against pathogens, prevents fungal and bacterial overgrowth of the small intestine, facilitates the flow of bile and pancreatic enzymes, and enables the proper absorption of protein and a variety of nutrients.

Gastric pH

Various investigators have used fasting pH values above 3.5,^{19,20} 6.0,^{21,22} 7.0,²³ or 8.2²⁴ to establish a diagnosis of achlorhydria. This has created much confusion as to the exact pH that clearly defines the diagnosis, and the pH that would help to differentiate achlorhydria from hypochlorhydria. Fasting pH was found to be a sensitive method for diagnosing "true" hypochlorhydria in a study by Feldman and Barnett,⁹ but these investigators failed to distinguish between hypochlorhydria in terms of pH from achlorhydria. For these reasons, no pH values will be presented in this paper to clearly define hypo- and achlorhydria.

HCl Production Does Not Necessarily Decline with Age

While several studies have demonstrated that HCl production apparently decreases with advancing age,²⁵⁻²⁷ the Feldman and Barnett study demonstrated that an elevated basal pH had the same clinical significance regardless of the age of the subject. A study by Hurwitz et al demonstrated that with advancing age

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there is not a decline in HCl production.²⁸ The study assessed the prevalence of basal gastric acidity and atrophic gastritis in 248 Caucasian male and female subjects aged 65 years or older. The results revealed that only 16% of the study subjects were deficient in their ability to secrete stomach acid, and that this compared almost equally to the 14% frequency that occurs among a much younger (mean age, 30 years) population group. Furthermore, the incidence of achlorhydria among the study participants did not exceed 11%, which evidently does not differ significantly when compared to younger people either.

In summary, HCl secretion does not necessarily decline with advancing age as the prevalence of impaired HCl secretion appears to affect the elderly and young population groups equally. If age is not the most important factor to be considered, there must be another reason to account for impaired HCl secretion. It is my belief that vitamin B₃ dependency, if not corrected, is a causal factor in the development of hypochlorhydria, and, in severe cases, achlorhydria. Furthermore, one of the early manifestations of vitamin B₃ dependency is hypochlorhydria.

Vitamin B₃ Deficiency and Vitamin B₃ Dependency

Before I elaborate on my hypothesis the difference between a vitamin B₃ deficiency and a vitamin B₃ dependency should be clarified. A vitamin B₃ deficiency occurs when the minimal amounts of the vitamin are not obtained due to an inadequate diet. If the minimal amounts are not met (somewhere between 5.5-13 mg per day),²⁹ within 1-2 months the tissues become depleted, biochemical abnormalities occur, and clinical features of vitamin B₃ deficiency (pellagra) eventually develop.³⁰ The 3Ds, diarrhea, dermatitis and dementia characterize the clinical manifestations of pellagra. Pellagra can be a fatal disease, and shortly after the 3Ds become clinically apparent,

death occurs.³⁰ Pellagra is considered rare today since the average Western diet supplies approximately 1 gram of tryptophan daily.³¹ Tryptophan is converted into niacin within the body, and for every 60 mg of tryptophan derived from dietary sources, 1 mg of niacin is produced.³¹ Furthermore, the niacin made from tryptophan does not include preformed niacin obtained from other dietary sources.³¹ Based on these facts, the development of vitamin B₃ deficiency is extremely rare.

By contrast, a vitamin B₃ dependency denotes an increased metabolic need for the vitamin. The definition of a vitamin dependency has been well described in many publications.^{1,3,32} The cause of a vitamin B₃ dependency probably stems from long-term environmental-genetic stresses that impair biochemical processes dependent upon a constant supply of the vitamin. Individuals with a vitamin B₃ dependency do obtain the minimal amounts necessary to prevent frank pellagra. Corrective treatment for a vitamin B₃ dependency requires very large doses (megadoses) of the vitamin in order to normalize the underlying metabolic dysfunction. These doses would need to be far greater than what would normally be obtained through diet alone. Individuals having a vitamin B₃ dependency tend to have disturbances in mood (e.g., anxiety, depression and fatigue), and vague somatic complaints,³ but do not manifest the same clinical features of the pellagrous disease. The primary somatic complaints of individuals with vitamin B₃ dependency are be gastrointestinal disturbances with hypochlorhydria presenting as one of the early clinical signs of the vitamin dependency. The only way to confirm a clinical suspicion of a vitamin B₃ dependency is to provide optimal doses of the vitamin, and see if the clinical problems improve or resolve.

To reiterate then, a vitamin B₃ deficiency occurs when the intake of the vitamin is below a known minimal amount that guards against pellagra. A vitamin B₃ de-

pendency occurs when there is an increased metabolic need for the vitamin requiring treatment with megadose amounts.

Aniainamidosis and Symptoms Suggestive of Impaired HCl Production

Evidence in support of my hypothesis comes from the work of Kaufman, who was likely the first clinician to describe on clinical grounds an association between symptoms of hypochlorhydria with an insufficient intake of the amide form of vitamin B₃ (niacinamide).³³ He used the term aniainamidosis to denote a “multisystem syndrome of ill-health caused by a lack of niacinamide in adequate amounts for optimal functioning of all cells of the body.”³⁴ He elaborated further on his definition by stating the following: “The multisystem symptoms and signs of aniainamidosis are ameliorated when the patient is treated with adequate amounts of niacinamide and recur when the patient again subsists solely on his or her diet.”³⁴ It is interesting to note Kaufman’s definition of aniainamidosis is consistent with the previous definition of vitamin B₃ dependency.

Kaufman’s description of aniainamidosis was based on his clinical observations of 150 private patients seen over the course of one year (approximate time period from September 1941 to September 1942), which culminated into a monograph on aniainamidosis.³⁵ While sifting through his detailed clinical observations, it became apparent to me that many signs and symptoms of the aniainamidosis syndrome were suggestive of hypochlorhydria - e.g. digestive upsets, an occasional sense of fullness when only small amounts of food are eaten, heartburn, frequent belching, indigestion, abdominal discomfort or pain, loose stools up to three times per day or constipation, glossitis, and general malaise.³³ Kaufman’s work showed that as little as 50-100 mg of niacinamide three times per day was all that was required to com-

pletely ameliorate the troublesome signs and symptoms of aniainamidosis.³⁶ His work demonstrated that no one is immune to the aniain-amidosis syndrome, as it occurs in children and adults, and that the subtle progressive deterioration of mental and physical health is often “attributed mistakenly by the patient and his associates to be part of the natural aging process.”³⁷ This also implies that hypochlorhydria, as part of the aniainamidosis syndrome, is not a function of aging, but rather a consequence of vitamin B₃ dependency.

In a later publication, Kaufman stated that with the enrichment of flour and bread with B vitamins (thiamin, niacin and riboflavin) and iron, many of the niacinamide-responsive symptoms (including the gastrointestinal symptoms) afflicting his patients in the pre-1943 time period disappeared.³⁴ What remained post-1943 was mainly clinical dysfunction of the musculoskeletal system.³⁴ Even though Kaufman noted an absence of gastrointestinal symptoms post-1943, I believe many people continue to suffer from gastrointestinal symptoms suggestive of hypo- and achlorhydria as a result of a vitamin B₃ dependency.

As previously stated, deficiency of vitamin B₃ is extremely rare although a dependency on the vitamin is not. Many people living in our highly industrialized society suffer from “affluent malnutrition,” a term coined by Hoffer.³ This term presumes that present day food practices and habits (i.e., processed foods, unnatural synthetic food compounds, too many refined sugars, and too much saturated fat) promote malnutrition and/or disrupts the *in vivo* conversion of dietary tryptophan into a sufficient amount of niacin. Even though these individuals will not exhibit clinical features of vitamin B₃ deficiency, they will probably manifest hypochlorhydric symptoms early in the course of their dependent state. In his article, *Vitamin B₃ Dependency: Chronic Pellagra*, Hoffer states that any “chronic gastrointestinal syndrome will

probably lead to one or more vitamin dependencies,"³ with vitamin B₃ being one of them. In the *Encyclopedia of Human Nutrition*, achlorhydria is listed as one of the clinical features of the pellagrous disease.³⁸ Perhaps many patients having achlorhydria simply suffer from a chronic form of advanced vitamin B₃ dependency that has persisted for many years.

The following are two patient reports demonstrating the potential role that vitamin B₃ may have for the treatment of suspected hypochlorhydria. These patients have been courteous enough to write about their experiences with vitamin B₃, and have given me permission to include their personal accounts in this paper.

Case #1

"I was asked by Dr. Prousky to describe my experience with niacin. I am a 28 year-old Caucasian male of Jewish descent. After consulting with Dr. Prousky about the possible therapeutic effects of niacin treatment, I decided to give the vitamin a try. Faced with tiredness due to long school hours, in February, 2001, in addition to my multivitamin, I began a regimen of niacin 100 mg/day, and steadily increased my dosage to 1,200 mg/day in divided doses. After a few days of treatment I began to notice that my energy had increased substantially. However, what was more surprising was that the abdominal bloating I had frequently experienced after eating had diminished greatly, and at times was completely absent. After some research into the subject matter, it became apparent that histamine release caused by the niacin might have influenced a greater release of HCl from the gastric parietal cells.

After 1 month I also added a B-complex to my regimen, as well as biotin (600 mcg/day). The biotin seemed to control a chronic dandruff problem. My bloating remained fairly in control until April 9 when I took a vitamin hiatus due to the holiday of Passover. I then experienced abdominal

pain, bloating, and blood in the stools for several days, as well as a return of my dandruff problem. Perhaps this was due to the holiday foods, or perhaps due to the rapid withdrawal of all supplements, including the niacin. I do not think it was the holiday foods since in previous years I never experienced such problems. Needless to say, after the Passover week, I returned to my supplement regimen and normal eating habits, and my abdominal pain, diarrhea, and blood in the stools went away. This time, however, my bloating did not remain in control as much as it had before. This might have been due to the tremendous stress of finals, which continued for one month.

I did notice another interesting phenomena during my exam period - when I was overly tired, due to all-night study sessions, I did not flush at the usual dosage. Perhaps we need more niacin when our adrenals are stressed. At present, June 5, 2001, I am still experiencing occasional burping and abdominal fullness following meals. I think that my current dose of niacin is inadequate since I am only taking 750 mg once every morning."

Case #2

"I am a 28-year-old male Caucasian of European ethnicity. My height is 170 cm and my weight is currently 168 pounds. My weight has fluctuated between 160 lbs and 170 lbs each year for the past ten years with the most dramatic weight loss occurring during the spring and summer months. My family history includes paternal heart disease, high blood pressure and high cholesterol and maternal hypothyroidism, rheumatoid arthritis and leukemia.

Prior to the age of 21, I was physically active engaging in various sports such as TaeKwonDo and cycling both at a semi-professional level. I have attempted to maintain a moderate level of exercise during the last seven years while attending post-secondary studies on a consecutive

basis. Bloating of my abdominal region has existed for approximately fifteen years. Upon physical examination, the bloating was dismissed as unexplainable or resulting from a lack of whole wheat in my diet. Even prior to fifteen years ago, I experienced severe local abdominal pain, which upon examination was dismissed as idiopathic. In both cases no dietary or pharmaceutical intervention was made.

In 1994, I was diagnosed with gastroesophageal reflux. Each experience would last from hours to days with no incidence of nocturnal occurrence. The typical symptoms experienced were bloating of the abdominal region (in addition to the existing abdominal bloating), belching, a mild sensation of heat throughout the body and the regurgitation of stomach acid. The monthly occurrence since the initial attack has been on average four flare-ups per month. Each flare-up appeared to be initiated from intense stress and/or the consumption of a fatty diet. Pharmaceutical intervention consisted of Zantac® and Gaviscon® (both only relieved the symptoms). An attempt to modify my diet appeared to have the greatest positive effect.

Three years ago I was diagnosed with elevated levels of cholesterol including elevated Triglycerides, LDL and Total Cholesterol/HDL Ratio. No pharmaceutical intervention occurred.

I began taking niacin approximately three months ago at a dosage of 1 g, three times per day under the supervision of Dr. Prousky. The consistency of my dosage varied between two to three grams per day. The intentions were to lower Total Cholesterol, decrease LDL and Triglycerides and increase HDL. Upon my initial intake of niacin (one gram), I experienced intense flushing of my entire body accompanied by a feeling of itchiness. Occasionally, I experienced a feeling of nausea upon the initial intake of niacin for that day. This nausea was not experienced each time I consumed the niacin. These symptoms of flushing and

itchiness greatly diminished upon the second and third doses of the day.

Since I have been taking niacin I have not experienced any reoccurrence of gastroesophageal reflux symptoms. Belching and abdominal bloating have both decreased by roughly 50%. These findings may also be the result of a diet lower in saturated fats and higher in fruits and vegetables. Also, I have been taking a combination of two multi-vitamins, zinc (30 mg daily), vitamin C (1000 mg daily), biotin (900 mcg daily) and vitamin E (400 IU daily). An observation was made when I consumed niacin during a period of stress (exam period), I did not experience the intense flush as I have in other less stressful states.”

Summary of Cases

The first patient had a response to niacin treatment that was impressive, even though he was not taking optimal doses (1 gram three times daily) of niacin. Had he taken niacin in optimal doses, his symptoms suggestive of hypochlorhydria would likely have resolved, and he would have noticed a greater sense well-being. It is unclear if niacin had any impact on his chronic dandruff problem since biotin is an excellent anti-dandruff (anti-dermatitis) agent as well.³⁹ The fact that he was under a considerable amount of stress, combined with a lack of sleep, would certainly increase his metabolic need for vitamin B₃. This might be the reason why he exhibited diminished flushing and a partial resumption of gastrointestinal symptoms during the stressful time period.

The second patient had symptoms of gastroesophageal reflux, abdominal bloating, and belching, all of which are strongly suggestive of hypochlorhydria. This patient also demonstrated a therapeutic response to niacin. His gastro-esophageal reflux completely resolved while on niacin, and his abdominal bloating and belching diminished by 50%. Like the first patient,

he noticed an absence of an intense flush when under more stress.

Stress, Diminished Flushing, and Increased Need for Vitamin B₃

By reviewing vitamin B₃'s mechanism of action, in regards to stress and hypochlorhydria, it will be evident why these patients had success with niacin treatment. Vitamin B₃ is involved in some 200 enzymatic reactions, involving mostly dehydrogenases, that require NAD (nicotinamide adenine dinucleotide) and NADP (nicotinamide adenine dinucleotide phosphate).⁴⁰ Niacin, as well as niacinamide, can be absorbed in the stomach, but are more appreciably absorbed within the small intestine.⁴¹ Within the intestinal lumen the concentration of the vitamin dictates how it is absorbed. At low concentrations the vitamin is absorbed through sodium-dependent, carrier-mediated, facilitated diffusion, while absorption is through passive diffusion at high concentrations.⁴¹ The absorption of niacin is efficient as 85% of a 3-gram or greater dose will be excreted into the urine.⁴² When placed directly into the upper ileum levels peak in the blood plasma within 5-10 minutes.⁴² Transport of niacin between the liver and intestine occurs within the body, with the liver being the major site where niacin gets converted to the nicotinamide nucleotide coenzymes.⁴³ Even though the liver contains the highest concentration of the nicotinamide coenzymes, all metabolically active tissues contain these vital metabolic products.⁴³

When an individual is stressed, their requirements for vitamin B₃ will need to increase, due to increased amounts of adrenalin (epinephrine) being released from the adrenal medulla, creating more oxidized adrenalin.⁴⁴ To convert the increased oxidized adrenalin back to original adrenalin, the reducing ability of NAD is necessary, and thus the need for more vitamin B₃.⁴⁴ Perhaps the lack of or reduced flushing among these patients was due to

an increased metabolic need for vitamin B₃ (i.e., a more rapid conversion of vitamin B₃ to NAD within the body), necessitated by heightened periods of stress.

According to Hoffer, schizophrenia may be an evolutionary defense against severe stress.⁴⁴ Untreated schizophrenic patients may therefore manifest the clinical picture of schizophrenia as result of homeostatic survival mechanisms.⁴⁴ These patients require optimal doses (usually 3 grams or more per day) of vitamin B₃ in order to prevent adrenalin from undergoing two oxidation reactions, leading to the production of the toxic-hallucinogenic compound known as adrenochrome.^{44,45} Furthermore, a subpopulation of schizophrenic patients (24-59%) do not flush when given niacin, although the percentage might even be greater, given the fact that studies conducted to date have had a lack of reproducibility (i.e., they differed in dose, route of administration, and methodology used to assess the flush).⁴⁶ The untreated schizophrenic patient under a state of extreme stress will likely not flush when given niacin due to the increased metabolic need/dependency on the vitamin. Similarly, the non-schizophrenic patient on vitamin B₃, who experiences heightened periods of stress, might not flush and have a relapse in his symptoms due to the increased metabolic need for the vitamin. In terms of biological survival and homeostasis, it makes more sense for the human organism to preserve adrenalin by reducing the amount of oxidized (non-active) adrenalin when under periods of heightened stress. Humans have the ability to increase adrenalin through the deconjugation of the adrenalin-sulfate storage pool, in order to increase the amount of free adrenalin available.⁴⁷ The increased utilization of vitamin B₃ to NAD may be another important mechanism for allowing the human organism to meet the demands of increased stress.

The Physiology of HCl Secretion

In addition to the absence of flush, the patient first suffered a reoccurrence of his abdominal bloating under increased stress—a response likely due to the increased metabolic need for vitamin B₃. Both patients had a therapeutic response to niacin. The first patient's symptom of abdominal bloating ameliorated when on 1200 mg/day of niacin, and then reappeared when he was taking a lesser dose of daily niacin. The second patient's seven-year history of gastroesophageal reflux ameliorated while on niacin, and his abdominal bloating and belching decreased by 50%. My hypothesis can be understood by examining the physiology of HCl secretion,⁴⁸ although the exact mechanism has not been completely elucidated.

The acid-forming gastric (oxyntic) glands secrete HCl, pepsinogen, intrinsic factor and mucus. These glands line the surfaces of the body and fundus of the stomach, comprising the proximal 80% of the stomach. The pyloric glands, located at the antral portion of the stomach, which secrete mucus, some pepsinogen, and the hormone gastrin, line the remainder of the stomach. The oxyntic glands contain three types of cells – mucus neck cells, peptic (chief) cells, and parietal (oxyntic) cells. HCl secretion from the parietal cells is mediated by the neurotransmitter-hormonal substances acetylcholine, gastrin, and histamine. All of these substances, originating in the brain (especially the limbic system) or the stomach, by way of vagal stimulation and local enteric reflexes, bind to receptors that activate secretory processes. Acetylcholine stimulates the release of all the secretory cells, including the secretion of pepsinogen by the peptic cells, HCl by the parietal cells, mucus by the mucus cells, and gastrin by the gastrin cells. Both gastrin and histamine primarily stimulate the secretion of HCl from the parietal cells.

Although histamine promotes HCl secretion, the small amounts that are con-

tinually produced by the gastric mucosa's mast cells cause very little HCl secretion. Histamine, a paracrine hormone, stimulates the type II (H₂) receptors located on the parietal cells to secrete HCl.⁴⁹ The parietal cells may also secrete histamine since they contain histaminocytes, which is where histidine is decarboxylated to form histamine₅₀—an autocrine effect. Only when the other neurotransmitter-hormonal substances (acetylcholine and gastrin) are present will the available histamine enable a strong release of HCl production to occur. Histamine is by far the most important of the three mediators. When H₂-receptor antagonists such as cimetidine block the effect of histamine, acetylcholine and gastrin cannot produce adequate amounts of HCl secretion. Therefore, the stimulus for HCl secretion depends upon histamine being present with acetylcholine and gastrin.

Adequate HCl Secretion Requires Optimal Amounts of Vitamin B₃

Niacin is a potent stimulator of histamine and PGD₂ (a vasodilator).^{51,52,53} When administered orally in amounts of 100 mg or greater, there is a release of histamine from storage sites (e.g., mast cells and basophils) through a complicated process of degranulation, and the release of PGD₂ from dermal macrophages. There is evidence that the niacin flush is not mediated by the release of histamine from mast cells or other storage sites.⁵² Researchers discovered that niacin caused a markedly increased release of PGD₂, but there was no concomitant release of histamine from mast cells (as would have been suggested by an increase in plasma levels of a histamine metabolite). They concluded that the niacin-induced vasodilation was primarily mediated by the release of PGD₂.

The fact that niacin markedly improved symptoms suggestive of hypochlorhydria in these two patients indicates that niacin can be used therapeutically to in-

crease functionally the secretion of HCl from parietal cells. It is conceivable that the niacin-induced release of PGD₂ leads to the binding of this prostaglandin to receptors on parietal cells stimulating the release of HCl. This would mean that there is a gastric source of PGD₂ other than dermal macrophages, and that the parietal cells contain receptors for PGD₂. There is no current evidence addressing the niacin-induced prostaglandin-mediated release of HCl. More likely, niacin ingestion causes the release of PGD₂ from dermal macrophages and the release of histamine from gastric mast cells. The histamine release might be mediated by some of the niacin that gets absorbed within the stomach. The histamine released from gastric mast cells would then be available to bind to the H₂ receptors on the parietal cells, thus stimulating the release of HCl.

Doses of niacin, such as 2-3 grams per day, will deplete histamine storage sites after a few days of continued use, and the flush typically goes away. If the histamine storage sites become depleted with continued use, how then does niacin benefit individuals with hypochlorhydria? Niacin and niacinamide are precursors to coenzymes that participate in a few hundred enzymatic reactions in the body, but their involvement in mitochondrial functioning may explain how both forms of vitamin B₃ optimize HCl secretion. Both forms of vitamin B₃ are precursors to NAD⁺, which is then converted to the energy-rich reduced coenzyme, NADH, that plays a critical role in complex I of the mitochondrial respiratory chain.⁵⁴ Half the parietal cell volume is occupied by mitochondria,⁵⁵ making the parietal cells the largest storehouse of mitochondria among all eukaryotic cells.⁵⁶ Basic biochemistry has revealed to us that the free energy produced by oxidative phosphorylation within the mitochondria is used to produce ATP. A report by Spenney,⁵⁵ elucidating the mechanisms of HCl secretion, has shown it to be an ATP-dependent

process. The ATP synthesized from mitochondrial energy, once stimulated to breakdown, mediates HCl secretion, and provides the necessary fuel that facilitates the exchange of K⁺ for H⁺ occurring within the canalicular membrane of the parietal cell.⁵⁵ Chloride ions are also actively transported into the lumen of the parietal cell where they combine with hydrogen ions to form HCl.^{57,58} The therapeutic use of niacin seems to restore the functional ability of the parietal cells by a mechanism of action unrelated to histamine. Like niacin, niacinamide has been shown to correct symptoms suggestive of hypochlorhydria, even though niacinamide's pharmacologic actions do not involve the release of histamine from storage sites. The coenzymes formed from vitamin B₃ allow for optimal mitochondrial functioning, leading to the production of ATP, and the necessary fuel to drive the process of releasing HCl from the parietal cells.

Vitamin B₃ May be More Responsible for the Development of Hypo- and Achlorhydria than Helicobacter Pylori Infection

Cater has written a very interesting article⁵⁹ describing Type A and B gastritis and the role that *Helicobacter pylori* (*H. pylori*) plays in not only being the primary cause of Type B or antral gastritis, but is also etiologic for chronic persistent hypochlorhydria. Type A gastritis is atrophic throughout, is autoimmune in nature, and is related to pernicious anemia. Type B gastritis is characterized by patchy areas of varying degrees of histological involvement, along with normal (uninvolved) areas, and the antrum is typically more affected than other regions of the stomach. While both of these disorders cause hypo- and achlorhydria (i.e., they significantly affect gastric acid secretion) and are considered to be subtypes of non-erosive gastritis, the Type B gastritis has been clearly associated with *H. pylori*,^{59,60,61} whereas the Type A^{59,62} has not. Acute gastritis has also been associated with *H. pylori* infection, but

the concomitant hypochlorhydria tends to be self-limited.^{59,63} HCl renders the stomach environment sterile and is very much involved in non-immunological defenses that protect against the development of *H. pylori* infection.^{8,64} A deficiency in HCl production will inevitably favor the colonization of *H. pylori*. Vitamin B₃ is critical for the maintenance of optimal parietal cell function and is integral for the production of ATP that drives HCl secretion. An uncorrected vitamin B₃ dependency could lead to histological changes among the parietal cells, a weakened gastric defense system, leading to gastric mucosal damage, the development of acute and/or chronic gastritis, hypo- and achlorhydria, and *H. pylori* infection.

The Treatment of Hypo- and Achlorhydria with HCl Supplements

In addition to non-erosive and acute gastritis, many other diseases and medical conditions (e.g., Addison's disease, asthma, systemic lupus erythematosus, osteoporosis, and Sjogren's syndrome) are associated with hypo- and achlorhydria as well.⁸ It is my contention that as the human organism attempts to maintain homeostasis in response to the stress of any pathophysiological process, the body's requirements/metabolic needs for vitamin B₃ correspondingly increases. Hypo- and achlorhydria ensues since there would be less vitamin B₃ coenzymes available for maintaining parietal cell function and gastric acid secretion. For the treatment of hypo- and achlorhydria, many clinicians have utilized HCl supplements (either betaine HCl or glutamic acid HCl with or without pepsin). This method requires the use of increasing doses of HCl supplements with meals until gastric tolerance is reached.⁶⁵ Gastric tolerance occurs when the patient experiences warmth or a slight burning sensation in the stomach. At this point, the patient would know the total dose of HCl supplements required per meal. Whenever gastric toler-

ance occurs, the patient would reduce the total dose by one. The patient would be instructed to use fewer capsules with smaller meals and the therapeutic dose (the dose below gastric tolerance) at larger meals.

The theory behind this method is that as the patient regains his functional ability to secrete adequate amounts of HCl, he will require smaller doses of HCl supplements, and will occasionally be able to completely wean off the HCl supplements. In my clinical experience with this method, patients have usually required daily maintenance doses of HCl supplements in order to properly digest their food and feel well. Only in a few cases have patients been able to completely wean off the HCl supplements. My suspicion is that supplementing with HCl does not ameliorate the underlying vitamin B₃ dependency that may be the primary factor involved in the pathogenesis of hypo- and achlorhydria. Vitamin B₃ may be an excellent complement to HCl supplementation, and should be given in optimal doses in order to correct the metabolic dysfunction associated with patients' gastrointestinal symptoms.

Other Nutritional Treatment Considerations Implicated in Vitamin B₃ Dependency

Even though I consider vitamin B₃ to be the primary treatment for hypo- and achlorhydria, other nutritional interventions may be necessary as part of an optimum orthomolecular treatment plan. For instance riboflavin (vitamin B₂) and/or pyridoxine (vitamin B₆) dependencies can impair the biosynthesis of tryptophan into niacin. Riboflavin is the coenzyme for kynurenine hydroxylase and pyridoxine is the coenzyme for kynureninase – both enzymes enable the *in vivo* conversion of tryptophan to niacin.³¹ If a dependency of any one of these vitamins exists, clinical features of vitamin B₃ dependency may manifest with hypochlorhydria being the first sign of such a problem. Vitamin B₃ should

still be the primary method of treatment, but should be complemented with a B-complex (50 or 100) supplement taken two to three times each day.

In addition to pyridoxine and riboflavin dependencies, another nutritional factor may be related to the development of hypochlorhydria. Rudin has proposed that an omega-3 essential fatty acid (EFA) deficiency may lead to "substrate pellagra" even when the diet contains adequate amounts of tryptophan and B vitamins.⁶⁶ Bearing in mind that the modern diet rarely contains 20% of omega-3 EFAs, substrate pellagra may develop in susceptible individuals. Good sources of omega-3 EFAs are green leafy vegetables, flaxseed oil, cod liver oil, and fish oil. Substrate pellagra is characterized by alterations in thought (schizophrenia), in mood (manic-depressive psychosis), in neurotic fears (agoraphobia), and is also marked by symptoms of irritable bowel syndrome, dermatitis, tinnitus, and fatigue. Minerals, antioxidants and B vitamins (especially pyridoxine), in conjunction with optimal amounts of omega-3 EFAs, catalyze the conversion of omega-3 EFAs into necessary prostaglandins that can improve or reverse the clinical presentation of substrate pellagra.⁶⁶

Rudin is correct about the lack of omega-3 EFAs in the modern diet. The ratio of omega-6 EFAs to omega-3 EFAs in the modern diet ranges from 20:1 to 14:1, instead of 1:1 that presumably was the ratio among Paleolithic human beings.⁶⁷ This has profound effects on human metabolism, particularly with respect to prostaglandin production. Considering gastrointestinal symptoms are part of the substrate pellagra complex, hypochlorhydria may precede the development of other symptoms early in the course of this clinical entity. I believe substrate pellagra to be less common than vitamin B₃ dependency. For more than 50 years Hoffer has successfully treated thousands of schizophrenic patients with vitamin B₃ therapy.⁶ Omega-3

EFA supplementation has not been the primary method of treatment during this time period. Hoffer's success indicates that human beings have probably adapted to or are less affected by an omega-3 EFA deficiency compared to a dependency on vitamin B₃. When a patient is not having an effective therapeutic response to vitamin B₃ and B-complex therapy, I recommend the addition of omega-3 EFAs (e.g., 1 tablespoon of cod liver oil daily) to the orthomolecular treatment plan.

Assessing the Patient: Gastric pH and Other Factors

It would be best if assessments of gastric pH were performed prior to any therapeutic intervention, during treatment, and at some determined endpoint. Any patient with suspected hypo- or achlorhydria should be given a thorough medical examination including diagnostic studies to rule-out pathologies such as *H. pylori*, peptic ulcer disease, and gastric cancer. Non-invasive methods, such as the Gastro-Test⁶⁸ or Heidelberg pH Capsule Gastric Analysis⁶⁹ are available and could assist the clinician with gastric pH analysis. A useful indirect measure of hypo- and achlorhydria is the presence of increased urinary indican,^{70,71} although this test is not specific for these pathologies.

Mycotoxins deplete tissue stores of vitamin B₃ and may play a role in the development of gastrointestinal symptoms.³¹ An excess of dietary leucine inhibits kynureninase, and depletes the formation NAD.³¹ An imbalance of leucine due to an excessive intake will further deplete NAD synthesis as it is a competitive inhibitor of tryptophan for tissue uptake.³¹ Estrogen metabolites are competitive inhibitors of kynureninase, whereas progesterone or its conjugates may reduce the activity of kynurenine hydroxylase.⁷² Hormonal imbalances may precipitate vitamin B₃ dependency and cause chronic gastrointestinal symptoms. Carcinoid syndrome, a tumor of

the enterochromaffin cells of the gastrointestinal tract, diverts most of the tryptophan from being available for NAD synthesis to that of serotonin synthesis.⁷² Inborn errors of metabolism and drug-induced nutrient depletion can also be factors in vitamin B₃ dependency.⁷² The clinician needs to be mindful of these factors when evaluating patients for vitamin B₃ dependencies so that these contributing factors do not remain unrecognized.

The Treatment of Hypo- and Achlorhydria and *H. Pylori* Infection with Vitamin B₃

For those patients who have been identified as hypersecretors, HCl augmentation is contraindicated. In newly diagnosed (early cases) where hypochlorhydria is suggested by symptomatology the use of 100-500 mg of niacinamide per meal may be the only therapy required to correct the underlying metabolic problem responsible for the gastrointestinal symptoms. For advanced cases, I recommend HCl supplementation to gastric tolerance, and the addition of 500-1000 mg of niacin per meal. Even though vitamin B₃ therapy has not been studied as a treatment for *H. pylori*, doses of niacin that will not chronically deplete histamine stores (e.g., 100-400 mg with each meal) might be able to re-sterilize the gastric environment and eradicate *H. pylori* infection. The addition of HCl supplements with niacin may be even more effective against *H. pylori* than using niacin alone, especially when there is irreversible damage to the parietal cells. The use of niacin may be more therapeutic than niacinamide due to its functional ability to indirectly stimulate the release of HCl from parietal cells. Both forms of vitamin B₃ appear to restore "health" to the parietal cells in a manner that is related to mitochondrial function.

Conclusion

When taken with meals, vitamin B₃ can markedly improve and possibly eradicate

symptoms of hypo- and achlorhydria. One of the first clinical features vitamin B₃ dependency may be hypochlorhydria. The treatment of hypochlorhydria may also require optimal doses of other nutrients (riboflavin and pyridoxine) and omega-3 EFA supplementation. Excessive leucine and non-nutritional factors such as hormonal imbalances, prescription drug use, carcinoid syndrome, and inborn errors of tryptophan metabolism need to be considered when evaluating the patient. Two patient accounts were presented demonstrating the effectiveness of vitamin B₃ therapy for suspected hypochlorhydria. Future case reports and studies should help to clarify vitamin B₃'s role in the maintenance of parietal cell function and in the optimization of gastric acid secretion. The remarkable therapeutic index of vitamin B₃ allows for megadose amounts.^{73,74} This makes it an excellent first line of treatment for hypo- and achlorhydria, and possibly *H. pylori* infection.

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