# Niacinamide As a Therapeutic Agent: A Memoir

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## Introduction

When I was in medical school in the 1930s, there were no automated blood chemistries of blood counts. There were no CAT, PET, MRI or ultrasound scans, The electrocardiographic chest leads were just being invented. Coronary artery catherization had not yet been attempted. There was no cardiac angiography. There were no coronary artery by-pass grafts. In cataract patients, there were no intraocular lens implants. There were no flexible gastro-scopes and no colonoscopies. There were no antibiotics. Sulfanilamide had just been tried as an antibacterial agent which proved to be mostly ineffective. There were no thiazide diuretics, no beta blockers, no calcium channel blockers. There were no renal dialysis centers. There was no cortisone. There were no tranquilizers, anti-psychotic agents or anti-depressents. There were no oral contraceptive agents.

## The New Vitamins as Treatment Paradigm

The newest and most exciting development in the 1930s was the identification, structural analysis, synthesis and the ensuing commercial availability of such vitamins as ascorbic acid, thiamin, riboflavin, pyridoxine, pantothemic acid, nicotinic acid, nicotinic acid amide, vitamin K1, and alpha tocopherol.[1] In addition, there were those derived from natural sources such as vitamin A, vitamin D and vitamin E complex which also were available commercially. As a result, the 1930s saw an explosive increase in research on animal and human nutritional deficiencies.[2] The frequency and scope of animal and clinical nutritional research resulted in large numbers of publications by the end of 1940. This can best be appreciated by scanning the bibliographies and references in some of the books dealing with the diagnosis and treatment of nutritional deficiency diseases in animals and humans that were published during the late 1930s and early 1940s.

I was a fortunate beneficiary of all this burgeoning activity in nutritional research. In my Junior and Senior years at the University of Michigan Medical School in Ann Arbor (1936–1938), the curriculum gave a new emphasis to nutrition. The Pathology Department gave intensive lectures on nutritional deficiency diseases including their histopathology at various phases of their development and severity. The Departments of Physiological Chemistry, Internal Medicine, Pediatrics, Neurology and Psychiatry, all gave detailed lectures on nutritional deficiency diseases from the point of view of their speciality. They also assigned readings of then current articles dealing with the diagnosis and treatment of nutritional deficiencies. In addition, I was able to take an elective program dealing with nutrition from the point of view of the dietitian.

Although I had intended to become a cardiologist I was fascinated by the power of nutritional therapy in ameliorating serious nutritional deficiencies. In addition to the assigned readings in nutrition, I read as much as I could of non-assigned, then current nutritional literature. I also began collecting and reading old books on nutritional deficiency diseases. I became very interested in pellagra and the many attempts to find its cause and cure.

## Nicotinic Acid

In 1937, Elvejhem and his associates found nicotinic acid and in 1938, that nicotinic acid amide could cure canine

1.Deceased, August 24, 2000, Inducted into the Orthomolecular Medicine Hall of Fame, 2006

black tongue, an analogue of human pellagra. Thus, by the accident of the earlier discovery of its possible anti-pellagra activity, nicotinic acid was used in the therapy of pellagrous patients months before nicotinic acid amide was, In 1938, I took 200 mg of encapsulated nicotinic acid, a dose described as safe. In addition to the anticipated flushing, I experienced an extremely severe, acute, idiosyncratic adverse reaction.[3] This is why when I finally started my private practice of internal medicine, I always gave the patient an oral test dose of nicotinic acid in my office if I planned to use nicotinic acid for therapy, a thing I rarely did. I would then observe for the next hour to be sure that he or she did not experience a life threatening reaction to it as I did. If the patient had no early adverse reaction to it (excluding the anticipated flush) only then would I prescribe nicotinic acid in his or her therapy. In the latter part of 1938, I developed the courage to take a 200 mg oral dose of nicotinic acid amide and experienced no adverse side effects

In the course of my reading, I learned of an interesting ailment, "pellagra sine pellagra". The term pellagra comes from the Italian "pelle" and "agra" meaning "rough skin." People suffering from "pellagra sine pellagra" had the symptomatology of pellagra but not its skin rashes (Casal's necklace and the florid dermatitis on skin surfaces exposed to sunlight). This syndrome sometimes also was called "prepellagra," "incipient pellagra," "atypical pellagra" and "sub-clinical pellagra." But as you will soon see from my description of this syndrome, there was nothing subclinical about "pellagra sine pellagra."

**Nutritional Deficiencies in the USA**

June 1938, I left the University of Michigan with a Master's degree in Chemistry (1932), a Ph.D. in Physiology (1937) and an M.D. (cum laude). I completed a rotating medical Internship at Barnes Hospital in St. Louis (1938-39); then an assistant residency and residency in private medicine at New York's Mount Sinai Hospital (1939-40) and next held post-graduate fellowships for two years in the Physiology Department of Yale School of Medicine (1940-42) joining a research group dedicated to researching the origins of the electrocardiogram. In addition, some mornings, I also taught students in Yale's medical outpatient department.

At the end of December 1940, I decided that in addition to continuing with my electrocardiographic research and medical outpatient teaching at Yale, I would begin my private practice of internal medicine in Bridgeport, Connecticut I planned to see patients some afternoons, some evenings and week-ends. I would accept only those patients who wanted complete physical examinations. By the end of 1942, I practises full time.

Without knowing what had been happening nutritionally to the American population in the 1930s, it may be difficult for you to understand how "pellagra sine pellagra" and other nutritional deficiencies I may refer to in this memoir could have existed in such abundance even during the early 1940s. To give you an overview, I call your attention to the very important November, 1943 report of The Committee on Diagnosis and Pathology of Nutritional Deficiencies of The Food and Nutrition Board of the National Research Council entitled *Inadequate Diets and Nutritional Deficiencies In The United States; Their Prevalence and Significance.* The distinguished committee chaired by the late Dr. H.D. Kruse (who taught me nutritional biomicroscopy) concluded that in the previous decade that malnutrition was widespread in the United States.

However, the extremely severe classic nutritional deficiencies such as beri-beri, pellagra, scurvy, xerophthalmia were relatively uncommon. The most frequent

nutritional deficiencies were the milder, less acute, more moderate, more chronic forms. These abounded in the United States. Over the ten years preceding 1943, these nutritional deficiencies adversely affected persons of all ages in many locations and without exception led to the conclusion that a significant number of the diets were more than 50% deficient in the RDAs of several essential nutrients and most of the diets were less than 50% deficient. Accordingly, there is widespread prevalence of moderately deficient diets. "All the data from numerous surveys with new methods among persons of all ages in many regions are entirely in accord that deficiency states are rife throughout the nation."

The severe economic depression of the 1930s played an important part of reducing the quality of the diet for many families. They could not afford to buy much meat, fresh fruit or even fresh grean or yellow vegetables. Bread was the "staff of life." The majority of people ate large amounts of white bread. Milling procedures then used robbed the white flour of much of its vitamin, trace mineral and roughage content. Many families could barely afford to buy adequate amounts of milk for their children and thus had to forgo drinking milk themselves. It is clear how such inadequate diets could lead to various nutritional deficiency syndromes.[4]

But even the well-to-do families also had nutritional deficiency disorders arising from their poor habits of food selection. Many preferred meat, potato and apple pie suppers. These meals sometimes included green and yellow vegetables, There was always snacking on fresh fruit when these were in season. The favourite fruit was probably canned peaches in heavy syrup. Breakfasts may have started with a glass of orange juice and often included bacon, eggs and fried potatoes followed by buttered white bread toast, some jam and coffee, heavily sugared and loaded with heavy cream; The lunch often was a hamburger–white bread sandwich and more coffee. Adults might sometimes have a strong cheese with their apple pie or have the pie *a la mode* but they rarely drank milk. Yet, they insisted that their young children drink plenty of milk. Although these people were financially well off, they too developed a variety of nutritional deficiencies, obesity, and over time some of their potential medical complications.

**Aniacinamidosis**

I bad decided that before I began my private medical practice at the end of December 1940, I would want to make a careful clinical study of "pellagra sine pellagra" including the response of patients to nicotinic acid amide therapy. To best accomplish this, I wanted to dispense this vitamin and have look-alike placebos to use as controls. I also decided to rename "pellagra sine pellagra" "niacin amide deficiency disease" and later "aniacinamidosis". Pellagra would then become "aniacinamidosis" with skin rash. If there was a coexisting thiamin deficiency, I would add "athiaminosis" to the diagnosis. If there was a co-existing riboflavin deficiency I would also add "ariboflavinosis" to the diagnosis.

I sent out my announcements December 1940 that I was opening my office for the practice of internal medicine in Bridgeport, Connecticut to community doctors. I was astonished to get so many patient referrals from physicians who told me that I could keep the referred patients as my own. Only some years later, a doctor friend who was one of the referring physicians told me that he and a small group of his doctor friends (who later also became my friends) saw a way they could get rid of their most complaining, most difficult to get along with, most obnoxious patients by sending them to me and they

waited to enjoy hearing me complain that I found these referred patients very difficult to manage medically. It was a sort of a medical hazing ceremony and an initiation rite into the brotherhood of physicians. The majority of the referred patients had unrecognized aniacinamidosis. The comic outcome came into being because I could recognize, diagnose, and successfully treat aniacinamidosis, while at that time the referring physicians could not.

It was not easy to establish rapport with the patients during the initial part of their first visit, they frowned, scowled, looked and acted tired, anxious and worried. They were circumloquacious, repetitive and generally unfriendly. I treated these referred patients with kindness, respect and adequate niacinamide and they soon became easy to take care of medically. In a matter of days, they also had astonishing improvements in their health. They were basically good and decent people and not ogres. Because of their spectacular medical response to niacinamide therapy, some of their friends and neighbours sought appointments with me. Not long thereafter some of their relatives living in distant states (California, Georgia, Illinois, Indiana, Massachusetts, New Jersey, New York, Rhode Island and even from Montreal) made appointments for medical consultations and returned at intervals so that I could check on their progress.

My patients with aniacinamidosis had not felt well for many years, They were mainly middle-aged, one third more women than men, many more elderly than children or teenagers in the group. Most adults were in the middle income class. Most had at least a high school education. All had some occupation and daily responsibilities.

**Practising Medicine in the 1940s**

The first visit generally took three hours, sometimes longer. Spending this amount of time was possible because the new patient was either the only patient I saw that day or was the last patient I saw that day. This first visit was dedicated to getting acquainted with the patient, his health problems and what medications he was taking, his family problems, his business or work problems, his economic worries and lastly what he expected from any medical treatment I might prescribe. Thus, this first visit included unhurried but detailed history taking, inventorying the patient's eating patterns, a brief psychological survey, a careful physical and neurological examination, a careful examination of the skin, conjunctivae, lingual and buccal mucosa, lips, gums, and in women, the uterine cervix under magnification for possible signs of nutritional deficiencies, some laboratory tests, a discussion of the patient's health problems and my recommendations for treatment and followup.

Early in the course of the first visit, most patients realized I was taking their complaints seriously, that I was not hurrying them to make their visit fit a limited time frame and that when I questioned them I was truly trying to understand their health problems, their dietary problems, their family and business problems, their life style and what they wanted to achieve healthwise from any medical treatment I might prescribe. Please remember that by December 1940, the United States had made considerable recovery from the depths of the great economic depression of the 1930s. This meant that most families were better off financially than they had been since the early 1930s and that more people could afford to eat a nutritionally good diet even if they did not do so. However, I did not make any recommendations that they change their diets. I wanted to observe what treatment with niacinamide alone (or sometimes combined with other vitamins) would do for them healthwise.

Then, I made suggestions that some modifications of their usual pattern of eating might provide additional benefits.

**Symptoms of Aniacinamidosis**

Here is a description both of the symptomatology and of the coexisting clinical signs of aniacinamidosis based on my study of over 150 patients with this syndrome who consulted me between the end of December 1940 through March, 1943 when bread was "enriched." Of course no patient had all the symptoms or all the clinical signs, but most had enough symptoms to make it easy to conclude that their ailment fitted into the pattern of aniacinamidosis especially when correlated with the coexisting physical signs. The final test was that most of the symptoms disappeared with normal maintenance therapy and that simultaneously, most of the physical signs of aniacinamidosis were ameliorated to a significant degree and some vanished altogether. However, cessation of oral niacinamide maintenance therapy lead to recurrences of the entire syndrome in a relatively short time.

Aniacinamidosis was independent of family income. No patient had the florid dermatitis of pellagra, nor dementia. Most had normal bowel movements. Some tended to be constipated. A minority had two or three loose stools a day.

*Skin:* Many patients had prolonged retention of sun-tan for five or more months after the last exposure to the sun, There was a tendency toward excessive, localized callusing in areas subjected to even mild recurrent pressure or rubbing. Many had calluses on the skin overlying their Achilles' tendons from the rubbing of the back of their shoes in this area. Nearly all had corns on several of their toes of each foot. Nearly all had calluses on the soles of their feet. Those who did manual labour also had marked occupational calluses on their hands. A secretary who sat a great deal of her working time in the office had callusing on her buttocks and skin overlying her sacrum which she pressed against the back of the chair as she sat. The calluses were pigmented a dark shade of yellow and sometimes a deep brown. Middle aged patients tended to have the wrinkled, reticular skin pattern of a much older person.

*Muscle:* Many complained of excessive fatiguability. A goodly number of patients talked about muscular weakness. Some complained of muscle aching after relatively mild physical activity. Simple instruments made it easy to confirm that the patients had measurably increased fatiguability, impaired muscle strength and impaired maximal muscle working capacity. Many complained that when I pumped up the blood pressure cuff, it hurt them a great deal. This suggests that their muscles were tender to this kind of squeezing.

*Psychological Characteristics.*[5] The patient says he feels tense, is restless, frequently changes sitting position in the consultation room facing me as I ask questions.

Seems calm but as we talk he or she often tell me that they are seething with resentment. They hate feeling so bad. They hate doctors who have not been able to help them and there is often a litany of other resentments against members of their family, friends, and people they work with. Can't relax. They often seem apathetic. They complain of mental sluggishness. Thoughts are slowed. Feel as if they are in a mental fog. Attention is easily distracted. Delays making decisions. Difficult to concentrate. The response to questions I ask is often delayed although hearing sense is normal. Not always sure he understands what he hears. May have to re-read an item in a newspaper or other reading material to get the meaning. Doesn't read as much as he did. Increased irritability. Frequently has unwarranted,

prolonged anxieties which he can't get rid of. Some patients feel "nervous" and are tense and anxious all the time. Excessive worry and tension about small and often unimportant matters. Often feels that there is something drastically wrong with him and that's why he feels so bad. Can't shake his worries he may have cancer or is going to get a stroke or heart attack or die. Has recurrent feelings of other impending troubles. Has uncertainties about what his future will hold for him. He sometimes loses his former interest and pleasure in work, family, friends, hobbies. Adjusts poorly to unanticipated adverse life situations. Lacks initiative. Often uncooperative. Routine duties become particularly burdensome. Procrastinates. Often with a burst of enthusiasm, he starts projects which he never finishes. Frequently feels and acts opinionated, vindictive, quarrelsome, mean, unreasonable and intolerant. Tends to act impulsively without considering the possible consequences of what he does. Emotional instability. Easily startled when I make a sudden movement to pick a pen off my desk. Flares "off the handle" when their feelings are hurt by trivial but reasonable criticism of some of his actions. Women and some men often feel like crying but hold back. Both men and women sometimes burst into tears and sob for no reason they can explain. Tearful or not, both sexes tend to become belligerent at the least challenge to their *amour propre*. Many tend to have a poor self-image. Tends to scowl or frown during our interview. Rarely smiles. Tends to be repetitive in his complaints.

Some patients occasionally become quite unhappy for short intervals (for less than an hour) without apparent cause. Some are mildly depressed much of the time, don't enjoy their work as they formerly did. Often feels aggrieved and unappreciated by their employer or family. Some complain that they have not been themselves for years and that their personalities have changed for the worse. Many felt they were aging too fast. A surprising number were afraid of being hurt when their blood pressure was taken or when a venipuncture was done. Many apologized after expressing their fear of being hurt by saying, "I guess I'm just a big baby."

Most had sleep problems. It was difficult to fall asleep. They turn, toss twist at night They waken at intervals not because they need to urinate. They dream a lot but generally they have troubling dreams. Generally doesn't feel rested when he wakens. After an intermittently wakeful night, in the morning when he has to go to work he feels that if only he could sleep a little longer he would be rested. Barbiturates help put him to sleep but when he wakens in the morning he feels groggy. In a short time, sleeping pills are no longer very effective and again does not have restful sleep and wakes up tired and groggy.

Many have been told by one or more doctors they consulted that there was nothing wrong with them excepting they were neurotics. They were given a sedative, generally phenobarbital, advised to take a rest cure, or just to "snap out of it". Some were referred to distant famous name clinics for diagnosis and treatment. The pattern of treatment generally was that the patient should rest as much as possible, (never walk when they can sit never sit when they can lie down). They were to take a barbiturate (to calm their nerves) and belladonna (to relax their stomach and intestines) three or four times a day. That was the total treatment.

*Nervous System:* Patients complained of impairments in balance sense. This resulted in bumps into furniture or walls, severe enough to cause black and blue marks on the arms or legs. There were also many episodes of near falls on level ground. This was not associated with dizziness or vertigo.

Some also complained of awkward-

ness or clumsiness in the use of their hands and of dropping things. The explanation I received was that their fingers suddenly stopped holding the object that they dropped. I devised a simple test for detecting impairment of balance sense. With eyes open, the patient stood on one foot and elevated the other foot and positioned it so that its heel would be two inches in front of the knee of the contralateral leg. The patient would have to be able to remain in this position for at least 30 seconds. This maneuver was repeated with the patient standing on his other limb. Then, this entire test was repeated with the patient's eyes closed. If a patient had impaired balance sense, I could ascertain if it was a one sided or bilateral impairment of balance and if it was elicited both with eyes open and closed or only occurred with eyes closed. It was surprising how often the impaired balance sense was unilateral and only with eyes closed. In this case, the black and blue marks from bumping occurred only on the side that showed imbalance. Caution: In conducting this test of balance one must have attendants beside the patient ready to prevent a fall from impaired balance sense.

The patients who tended to drop things from their hands often could not perform the finger-to-nose test accurately. This awkwardness could be unilateral or bilateral. It could occur only with eyes closed or open. When the sole of a patient's foot was stroked to elicit a plantar reflex, most patients experienced a persistent, disagreeable linear after-sensation on the sole lasting as long as ten minutes. However, simply passing my palm over the patient's sole would immediately "erase" these unpleasant sensations. I called this phenomenon "erasable paresthesias." Many patients had spontaneous paresthesias mainly on the distal portions of the upper and lower limb and occasionally on the cheeks and around the mouth. These were in areas where there was significant decrease in light touch sensitivity but not of pain or temperature.

*Gastro-intestinal:* Many patients ate because they knew they had to, to sustain life. They did not have a good appetite. Food did not taste as good as it used to. Many ate small portions of food throughout the day, having six or seven small meals. They did this because regular sized meals filled them up too much and made them feel uncomfortably distended. Some talked about their many digestive upsets. By this they meant that they did not feel well after eating, had water brash, belching, bloating, heart burn, indigestion, upper abdominal pain.

Many had loud intestinal rumbling and associated abdominal discomfort. Most patients had normal bowel movements.

Liver enlargement and tenderness was almost universal in both persons who never used alcohol and in those who drank social amounts. The liver edge was down one to two (rarely more) centimetres below the costal margin in the right midclavicular line and was soft and very painful to palpation. The lingual membrane showed adverse changes in its morphology exhibiting some degree of atrophy of all of its papillae. This differed in degree of severity in different patients. In some patients there was additional increased redness at the tip and sides of the tongue. Sometimes the sides of the tongue bad an indented pattern made by the sides of the patient's teeth and the tongue itself seemed swollen and larger than normal. Some of these patients reported that when they were tense and didn't want to say something that might hurt another person's feelings, they would almost automatically press their tongue forcefully against their front teeth while their mouth was shut. In some, the lingual muscles had undergone some degree of atrophy and in these patents the tongue seemed smaller than normal and there was the most advanced atrophy of the lingual papillae.

*Metabolic Edema:* Virtually all patient's had a specific type of non-dependent metabolic edema that affected non-articular cartilage including the aural, nasal, costal cartilages as well as the long bone's periosteum. All these swollen structures were very tender to digital pressure. (This edema also affected articular cartilages. Evidence for this will be given later). In addition, it also probably affected all tissues of the body to some degree. This metabolic edema was unique in that it would disappear upon the administration of a single oral 100 to 200 mg dose of niacinamide starting within 10 to 15 minutes of administration.

This was accompanied by a diuresis as copious as one would expect from a 40 mg oral dose of Lasix. Then, this metabolic edema would reaccumulate starting within 90 minutes of the time that the niacinamide tablet was ingested. Niacinamide has a half life of about 90 minutes. If niacinamide was taken at intervals during every three hours during the day, this metabolic edema would not recur. The dosage pattern of niacinamide intake will be discussed in some detail later.

*Impaired Joint Mobility:* Patients had varying degrees of impaired joint mobility which could be documented by measurements of maximal joint ranges of various moveable joints.[6]

I began when I was still a student collecting some of the names which had been used to describe pellagra. These included *formes fruste* of pellagra, subclinical pellagra, pellagra sine pellagra, atypical pellagra in addition to names used in European countries including *mal de la rosa* used by Casal in 1730 in Spain when he described pellagra and *pella agra* a term used by Frapolli in Italy in 1771 plus 41 other names used in various provinces of various European countries to describe the nutritional deficiency disease we today call pellagra but should call aniacinamidosis. The reason for all the European names was because pellagra was endemic in large areas of Italy, Spain and France and some of the Balkan countries.

I was carried away by reading about the superb results various investigators were having in the treatment of pellagra, a potentially fatal disease, using niacin. When I read an article by Spies and his associates in the *JAMA,* 110: 461, 1938, I couldn't rest until I, myself, took 200 mg of nicotinic acid, a supposedly safe dose, to see what the flushing that this substance caused was like. Within 15 minutes, I flushed and itched but I was also violently ill with uncontrollable alternate contraction of the large flexor and extensor groups of muscles in my arms and legs and periods of chest spasm creating apneic periods because I could not overcome the muscle spasm by willing to breathe.[3] This episode lasted about a half hour, was terrifying. A few years ago, I tried the same dose of nicotinic acid, and had exactly the same violent reaction. However, this reaction never occurred with 250 mg of nicotinic acid amide taken every three hours for six doses a day. It was then that I first realized that niacin was not an innocuous material even though it was well tolerated by many. It made me feel that any patient given niacin should be given in gradually increasing amounts if it is used at all. And, that there was no point in subjecting a patient to the flushing, itching and other reactions that nicotinic acid could cause when nicotinic acid amide would not cause such untoward effects and be just as therapeutic. As we now know from the pioneer work of Altschul, Hoffer and Stephen, large divided doses of nicotinic acid will lower blood cholesterol in those with hypercholesterolemia whereas nicotinic acid amide will not do this. However, my major adverse reaction to nicotinic acid was not completely in vain. I noticed quite to my astonishment that the areas in which I flushed were exactly the major areas where the rash of pellagra occurred.

I had planned to become a cardiologist and in my senior year in medical school worked in Dr. Frank N. Wilson's Laboratory with Franklin Johnston as my collaborator. Dr. Wilson suggested that I intern at Barnes Hospital, Washington University Medical School's teaching hospital, in St. Louis. I did so. Strangely, there was relatively little interest in the newer research using the vitamins. However, Robert Elman was researching the intravenous use of protein hydrolysates in surgical patients and was one of the pioneers who helped develop current total parenteral nutrition.

Because of recurrent infectious mononucleosis, (I had had two severe episodes of this in Ann Arbor), I switched from an 18 month straight medical internship to a 12 month rotating internship in medicine which included considerable work in the medical clinics and in radiology.

I rotated through the arthritis clinic and was horrified how little could be done for these sufferers. You could provide aspirin or other salycilates, hot paraffin dips, occasionally hyperthermia treatments in the "hot box", more rarely helpful physiotherapy. Sometimes surgical ankylosis of painful joints helped relieve the pain but made the joint totally unmovable. I recommended losing weight, not injuring joints through daily activities, resting painful joints, applying heat and sometimes elevation to knee joints and taking aspirin to the a level that gave substantial relief without causing serious side effects.

In the x-ray department, I sat in at the reading of all the films that came through in a three month period and I kept seeing all sorts of arthritic changes and developed some skill at interpreting such films.

One of the important learning experiences at Barnes Hospital was taking histories of patients for Dr. David Preswick Barr who wanted to use them in his lectures to demonstrate certain clinical syndromes and diseases. When I took the routine history on ward patients, it was the conventional medical history that went into the basic medical aspects of the patient's past and present health problems. But when I had a great deal of time to spend with the special patients who were to be used in the teaching sessions, I was able to ask questions which gave me a very broad view of the patient in his milieu at home, at work, at play and of his social status, his economic problems, his inter-family problems, and the impact of his ill health on his life and that of his family. It was astonishing how many health problems that would have escaped attention in the taking of a routine medical history became evident when more time was spent with the patient and a wider range of questions were asked.

From Barnes Hospital, I went directly to an assistant residency and residency in private medicine at New York's Mt. Sinai Hospital and took care of the patients of many of the outstanding medical leaders of our time including such physicians as Dr. George Baehr, Dr. Burrill Crohn, Dr. Bela Schick, Dr. Arthur M. Masters, and leaders in neurology, surgery and surgical specialties. It was a very good experience even though I was plagued by attacks of recurrent infectious mononucleosis. When my residency was completed, July 1940, I started my Dazian Foundation and my concurrent Emanuel Libman Fellowships in the Physiology Department at the Yale University School of Medicine working in experimental canine electrocardiography with Drs. Louis Nahum and Hebbel Hoff and spent time teaching in the medical clinics. At the end of 1940, I was licensed to practice medicine in Connecticut and started seeing private patients. What astonished me was that nearly all of the patients I saw had the form of niacinamide nutritional deficiency disease that Dr. Field had been talking about in his lectures.)

At that time, I did not have any idea why there was so much niacinamide deficiency around that was not classic end stage

pellagra. It was only in 1943 and finally in 1950, that I had a good idea why so many people I saw as patients had nutritional deficiency diseases, primarily lacking niacinamide. And, the results of treatment with niacinamide were absolutely astonishing because really sick people suddenly developed a high degree of wellness and maintained this as long as they continued taking niacinamide and relapsed when they stopped.

*Vagina:* Some women complained of dysparunia. Vaginal tissue was unusually red and tender to vaginal examination. No type of fungal, bacterial, or trichamonal infection could be demonstrated in most of these women. The syndrome disappeared with adequate oral niacinamide therapy.

*The Chief Complaint:* The chief complaint might be "I'm tired all the time", "I don't feel good," "I've got arthritis," "I think I'm losing my mind," "I'm very nervous and jittery," "I have stomach trouble," "It hurts me to give my husband his rights," meaning a tender and spastic vagina.

Careful, considerate questioning could elicit the symptoms and pattern of the patient's ill-health. The physical examination will contribute other data. The beneficial response of the patient to oral niacinamide therapy will contribute other data that will make it very likely that patient's illness was aniacinamidosis. Cessation of niacinamide therapy (or the administration of a placebo) will cause the niacinamide-induced improvements to disappear.

**Notes by Abram Hoffer, M.D., Ph.D.**

1.The golden age of vitamin discovery occurred between 1930 and 1940 with several Noble prizes awarded for these discoveries. Dr. W. Kaufamn was caught up in the excitement of those heady days in nutrition. The vitamins-as-prevention paradigm had finally become established and had made it possible to identify, isolate and synthesize these vitamins. And non of these nutrients were captured by companies because they were not patentable. According to this paradigm vitamins were only useful to prevent the occurrence of the vitamin deficiency diseases such as beri beri, pellagra and scurvy and were to be used only in very small doses for these conditions after they had been diagnosed. This paradigm still reigns over most of the world but is being rapidly eroded in North America. Dr. Kaufman was not aware that his work was one of the major blows against this early paradigm since he used very large doses of a vitamin for conditions not considered to be deficiency diseases.

2. This was amazing. Compare it with any medical school today. Canadian Medical schools may provide their students as much as 1 or 2 hours of academic nutrition but never any instruction in clinical nutrition and how it is used to fight disease. In 1949-1950 in my fourth year medicine in the course on therapeutics the professor spent at least one third of the time discussing nutrition for each disease he was covering.

3. Dr. Kaufman's reaction must have been intense indeed. This does occur with a very small proportion of patients and they all have to be told in advance all about the flush. However, it is not life threatening and no one has ever died from the niacin flush. With very sensitive patients it is a good idea to start with small doses and gradually increase them. Niacin is safe and today is used to decrease cholesterol levels, to increase high density lipoprotein cholesterol and to decrease triglycerides. It is the gold standard of cholesterol lowering agents. It also decreases mortality and increases longevity. Doctors skilled in the use of niacin have no difficulty with their patients and there are many ways of dealing with this. It is in most cases a nuisance or irritant, not a major side effect or complication.

4. This is an excellent description of most modern diets.

5. This could have been written for any modern text on psychiatry describing many of the syndromes psychiatrists must deal with. It is really unfortunate that modern medicine did not take seriously the fact that vitamin $B_3$ deficiency can produce syndromes that mimic so much of modern psychiatry.

6. Dr. Kaufman became interested in the use of vitamin $B_3$, mostly niacinamide, for treating arthritis. This is how his interest developed.

**Brief Bibliography for William Kaufman**


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