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Tom Spies Memorial Lecture
Niacinamide: A Most Neglected Vitamin

William Kaufman, Ph.D., M.D.

TOM DOUGLAS SPIES (1902-1960), an outstanding clinician, researcher and teacher in nutrition and metabolism who pioneered many aspects of nutritional and vitamin therapy of pellagra and other nutritional deficiency diseases.

WILLIAM KAUFMAN, Ph.D., M.D., recipient of the Tom Spies Memorial Award presented by the IAPM in 1978. Dr. Kaufman was associated with Kemther Advertising, Inc. Prior to joining Klemmer, Dr. Kaufman, a Diplomate of the American Board of Internal Medicine, did research and taught at the University of Michigan Medical School and Yale University School of Medicine. He practiced internal medicine in Bridgeport, Connecticut with emphasis on nutrition, food allergy and psychosomatic aspects of illness. He has written more than 80 scientific and medical papers and served as American Editor-in-Chief of the International Archives of Allergy and Applied Immunology. He has served as President of the Academy of Psychosomatic Medicine and chaired other national and international medical committees.

Dr. Kaufman is a Fellow of the American College of Physicians, the American College of Allergists (and a 1951 recipient of its Award of Merit), the Royal Society of Medicine (London), the American Association for the Advancement of Science, New York Academy of Medicine (and member of its Nutrition and Geriatric Sections), American College of Nutrition, Gerontological Society, and a Life Member of the National Association of Science Writers. In addition to numerous monographs, Dr. Kaufman has written many articles, book reviews and two major books on niacinamide deficiency diseases and joint dysfunction.

INTRODUCTION

As health professionals interested in preventive medicine, we all owe a great debt to the late Dr. Tom Douglas Spies, eminent teacher, clinician and researcher, for his numerous outstanding contributions to the understanding and treatment of pellagra as well as other nutritional and metabolic diseases.

In a sense, my clinical work is both an extension and a departure from Dr. Spies’ basic contributions in the field of human nutrition. I have been able to demonstrate through objective methods that with adequate nutritional therapy some very important accompaniments of so-called normal aging such as impaired joint mobility, impaired muscle strength, impaired maximal muscle working capacity, impaired balance sense and certain geriatric mental syndromes can be reversed to a considerable degree. I shall discuss the clinical evidence for this at some length.

HISTORICAL BACKGROUND

My first awareness of the metabolic functions of niacinamide was in 1935 when Warburg and Christian found that coenzyme II, now called nicotinamide adenine dinucleotide phosphate, contained nicotinic acid amide, and von Euler, Albers and Schlenk found that niacinamide also formed an important part of coenzyme I now called nicotinamide adenine dinucleotide. Today, we know that these two coenzymes control in excess of 200 different metabolic reactions. While particularly abundant in brain, kidney, heart, liver, and muscle, both these coenzymes are a vital part of the metabolic machinery of every living mammalian cell. This basic concept proved very important in shaping my therapeutic decisions when I first started to practice medicine in 1941.

My first personal experience with nicotinic acid was in 1938. After reading Spies, Cooper and Blankenhorn’s classic paper which described the safety and efficacy of nicotinic acid in the treatment of pellagrins. I took 200 milligrams to experience the flush they described. I not only flushed but I also experienced a severe, prolonged idiosyncratic reaction. As a result for the first two years of my private practice, I insisted that each patient take the first dose of niacinamide (or niacin) in my presence and be observed by me for the following hour for possible adverse reactions. This enabled me to make observations on the clinical syndrome of aniacinaminosis and its earliest response to oral niacinamide therapy that otherwise could never have been made. During the first two years of my practice I dispensed
niacinamide in my office. This made it possible for me to check the patient's clinical response against placebo from time to time.

From the beginning of my practice, I took unhurried, complete histories that allowed each patient adequate time to tell me about past and present health problems. In addition to doing an internist's physical examination I also did a careful neurological and psychological study of each patient.

After a few months of practice, seeking objective data. I began verbatim recording of everything that was said during an office visit, did biomicroscopic examinations of the conjunctivae, lips, gums, tongue, and skin, and took color pictures of these as well as of the cervix. I soon added measurements of the patient's Joint Range Index, his strength, maximal muscle working capacity and balance sense. An initial office visit would take from three to five hours. Subsequent check-up visits would take from one to two hours. Most patients also kept a monthly food-symptom-daily events diary which made it possible for me to examine their daily food intake and detect inadequacies in dietary, food-induced allergic and psychosomatic reactions, all of which contributed to their ill-health.

Aniacinamidosis

I have defined aniacinamidosis as a multisystem syndrome of ill-health caused by the lack of niacinamide in adequate amounts for optimal functioning of all the cells of the body. The multisystem symptoms and signs of aniacinamidosis 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.

Thus, aniacinamidosis encompasses the whole range of pellagrous disease. It includes severe, potentially lethal, florid pellagra as well as the less severe and more chronic forms which cause protracted ill-health and which have been called pellagra sine pellagra, atypical pellagra, pre-pellagra, subclinical pellagra, incipient pellagra, subacute pellagra and prodromal pellagra.

In my view, aniacinamidosis is a much better descriptor than any of these terms. It emphasizes not the presence or absence of a rough skin, but rather the lack of niacinamide which is the cause. If other vitamins are prominently deficient, as may be the case in florid pellagra, the disorder can be designated as aniacinamidosis with ahaminosis and arboflavinosis indicating that these three vitamins are of etiologic importance for that patient.

The Early 1940's

Certain kinds of malnutrition were widespread in the United States during the 1930's and early 1940's. I quote from the Bulletin of the National Research Council No. 109, dated November 1943, entitled "Inadequate Diets and Nutritional Deficiencies in the United States: Their Prevalence and Significance." "All the data from numerous surveys among persons of all ages in many regions are entirely in accord in showing that deficiency states are rife throughout the nation. Relatively few are the traditional severe, acute types. Most are milder in intensity and gradual in their course. Predominantly they are subacute or chronic states; some marked, but very many mild or moderate. From this evidence, it is clear that there is both a preventive and a corrective problem."

When I began practicing in Bridgeport, Connecticut in 1941, such deficiency states were rife not only there but also in distant localities from which many of my patients came.

Multisystem Aniacinamidosis

From December 1940 to about March 1943, most patients I saw had this multisystem, niacinamide-responsive syndrome of aniacinamidosis. The various symptoms and signs varied in intensity and extensiveness from patient to patient. Minor variations on a fundamental pattern of niacinamide deficiency disease.

The syndrome included impairments of nervous system functioning as evidenced by anxiety, depression, personality changes, excessive startle reaction to noise, excessive fear of being hurt, impaired balance sense, paresthesias and other sensory impairments. Dermal changes consisted of an excessive tendency to calluses, often pigmented yellow to brown, and prolonged retention of sun-tan: derangement of gastrointestinal functioning: adverse changes in lingual mucous membrane and lingual muscles; liver enlargement and tenderness, both in non-users and users of alcohol; excessive fatigability, impairment of muscle strength and maximal muscle working capacity; metabolic edema; impairment of joint mobility; periosteal and cartilage tenderness to digital pressure, and, in women, a reddened, swollen and often tender vaginal mucous membrane. All these components of the common form of aniacinamidosis were ameliorated by adequate niacinamide therapy and recurred when treatment was stopped and the patient subsisted solely on his or her usual diet.

Treat the Symptom or the Cause?

Initially, I found myself in a therapeutic quandary when as a result of careful clinical study I elicited all these symptoms and signs and many more. I pondered, "How should I approach the treatment of the patient's problems? Should I treat
anxiety with a sedative-tranquilizer? Should I treat the depression with an antidepressant? Should I add atropine to allay gastrointestinal symptoms; prescribe emollients to soften the calluses; prescribe douches and antibacterial drugs to control the vaginitis; advise extra rest to control the asthma; do liver function tests to determine the cause of tenderness and enlargement and perhaps order liver biopsies too; give diuretics to rid the patient of edema; salicylates to reduce the bone and joint discomfort?" I considered all these therapeutic options. And, I rejected them all.

The reason was this. I recognized that the multi-system symptoms and signs I elicited were pellagrous in origin and based on a single etiology - the lack of adequate amounts of niacinamide in all the bodily cells of the patient. As a consequence, I chose niacinamide as the sole therapeutic agent.

I started aniacinamidototic patients on what I now know to be very low doses of niacinamide, 50 to 100 milligrams, three times daily. What happened in response to niacinamide therapy offended my sense of reality.

When a single oral dose of 100 milligrams of niacinamide was administered while I was observing the patient, the metabolic edema began receding in 10 to 15 minutes at which time measurable improvement in muscle strength and maximal muscle working capacity could often be recorded. Balance sense sometimes improved as early as 30 to 60 minutes after ingestion of niacinamide but might take weeks to months of constant therapy with niacinamide alone or combined with other vitamins to reach a normal level. Within a few days, anxiety, depression, "erisible" sole of the foot paresthesias disappeared as did digestive complaints. Usually, at the end of a week or two, and rarely taking as long as two to three months, liver enlargement and tenderness could no longer be demonstrated. Vaginal redness and tenderness vanished by the end of two to ten days of continuous niacinamide therapy. Although long retained sun-tan pigmentation took several weeks to disappear, excess callusing with or without pigmentation took three to six months to resolve. Periosteal and cartilage tenderness to digital palpation took about a week to ten days to disappear. The tongue might be reduced in redness and swelling within a week, but in most instances it took years of continuous niacinamide treatment to restore lingual papillae to anything resembling near normal and to heal to some degree lingual fissures. Atrophy of lingual muscle was slowly reversible, taking three months to several years to be accomplished. Even with these small oral doses of niacinamide, I could observe measurable improvement within a week to a month in some joint ranges whether the patient had hypertrophic or rheumatoid arthritis or whether he just had impaired joint mobility without any external evidence of arthritis. As I learned gradually, much higher doses of niacinamide - a total of 1,500 to 4,000 milligrams a day in divided doses throughout the day - were necessary to bring about maximal improvement in impaired joint mobility provided that (a) the patient's diet was adequate in protein and calories, (b) his joints were not being excessively traumatized by overuse, repetitive minor injuries, excessive muscle tension, or major injuries, and (c) his joints were not so severely damaged previously by trauma or arthritis that little or no recovery was possible. Since obesity is a significant contributory cause of trauma to the weight-bearing joints, overweight persons must have their weight reduced before an optimal response to niacinamide therapy can be obtained in improved joint mobility. Food and drug allergies that adversely affect articular tissues may slow or greatly impede niacinamide-induced recovery of joint mobility until the allergenic factors are eliminated.

The widespread deficiency states that had been reported throughout our country gave impetus to increase the nutritional value of bread. From 1941 to early 1943, the program of enrichment of bread and flour was voluntary. However, early in 1943, war regulation required compulsory enrichment of bread but only for the duration of World War II.

Of course, the amounts of added nutrients used to enrich bread on an absolute basis would be considered trivial by health professionals accustomed to thinking in megavitamin doses. But in relative terms, enrichment provided huge increases in the intake of thiamine, niacin, riboflavin and iron in the daily diet of those who ate bread in adequate amounts.

As a consequence, the incidence of florid pellagra was greatly reduced. Concurrently, many of the niacinamide-responsive symptoms and signs of the pre-1943 common form of aniacinamidosis immediately lessened in severity and extensiveness and, depending on the year, only 5 to 10% of new patients had the complete pre-1943 syndrome of aniacinamidosis. To what degree the one-a-day-vitamin supplementation that became so popular after 1945 contributed to the reduction of niacinamide-responsive signs and symptoms cannot be pinpointed by my own studies.

The niacinamide-responsive signs and symptoms that largely disappeared soon after compulsory enrichment of bread early in 1943 were: anxiety, depression, changes in personality, startle reaction to unexpected sounds, excessive fear of being hurt, "erisible" paresthesias of the soles of the feet, metabolic edema, gastrointestinal symptoms, liver
tenderness and enlargement, periosteal and cartilaginous tenderness to digital pressure, callusing in response to minor pressure, prolonged retention of sun-tan pigment, and finally, vaginal redness, swelling and tenderness.

But what was equally important was that certain other signs and symptoms of the pre-1943 pattern of the common form of aniacinamidosis persisted. These included adverse changes in the lingual membrane, impaired muscle strength, impaired maximum muscle working capacity, impaired joint mobility, impaired balance sense and in persons over 55, a mental syndrome consisting of mild depression or agitation and hyperkinesis.

Variable Tissue Demand
What did all this mean? It proved conclusively that some tissues needed less additional niacinamide in the diet than others in order to function at greatly improved levels. It also showed that somatic muscles, movable joints, lingual mucosa, the long tract in the posterior portion of the spinal cord important to the integrity of balance sense and, in the over-55 age group certain parts of the brain, all required much more niacinamide than was provided by diet alone including enrichment of cereal products and bread.

If I had not done such careful studies of patients with the pre-1943 form of aniacinamidosis, I would never have realized that impaired joint mobility in persons with or without visible arthritis, impaired muscle strength, impaired maximal muscle working capacity, impaired balance sense, chronic changes in the lingual mucous membrane and certain mental syndromes in the over-55 age group could be greatly ameliorated by adequate continuous therapy with niacinamide used alone or in combination with other vitamins.

From 1943 to 1964 during which time I made these observations, over 95% of my patients had some degree of impaired joint mobility and chronic lingual changes; 65% had impaired strength or impaired maximum muscle working capacity, 40% had impaired balance sense, about 10% of the over-55 year age group had mild depression and agitation, and 8% had hyperkinesis.

Post-1943 Aniacinamidosis
I shall discuss each of these manifestations of post-1943 aniacinamidosis and leave for last a discussion of my most original and important contribution to nutritional medicine, the ameliorative effect of adequate niacinamide therapy on impaired joint mobility.

The post-1943 lingual membrane changes were mild chronic changes, occasionally with an acute overlay. Since these changes in lingual mucosa and their response to niacinamide as seen with the biomicroscope have been described by H.D. Kruse in minute detail. I shall not review this subject here except to say there is slow improvement morphologically. While there is evidence of repair and improvement in the lingual mucosa, this exists side by side with unresolved chronic changes. While some tissues heal, many do not even after decades of intensive therapy. Atrophic tongue muscle, especially in the elderly, slowly responds to niacinamide therapy.

Muscle Strength and Maximum Muscle Working Capacity
This severely neurosthenic women's behind shows marked pigmented callusing which resulted from sitting in a secretary's chair. (Figure 1). One should immediately think of aniacinamidosis as a possible cause. Actually, both her severe neurasthenia and her pigmented callusing disappeared in response to adequate niacinamide therapy.

![Figure 1](image)

Because this patient and so many other pre-1943 aniacinamidotic patients had muscle weakness, decreased maximum muscle working capacity and greatly increased fatigability, and because these symptoms were so swiftly responsive to adequate niacinamide therapy, I introduced simple methods for testing of strength and maximum muscle working capacity into my practice. I measured strength with a gripmeter (See Figure 2). The maximum hand grip measured in pounds per square inch was an excellent index to the patient's overall strength. Figure 3 is a graph showing the age distribution of right and left grip strength in men and women. The normal range for hand grip strength for women is about 50 to 70 pounds per square inch and for men 80 to 120 pounds per square inch.
To assess the time when muscular fatigue first becomes evident, as indicated by slowing of the rate of working, one can read the moving dial at 15-second intervals during the one-minute test of maximum muscle working capacity. Here, too, the time of onset of muscle discomfort or pain is noted since it does not occur in normal persons.

Here are some examples of initial improvement in maximum muscle working capacity in response to niacinamide in aniacinamidotic patients.

CASE HISTORIES: PRE-1943

This 52-year-old aniacinamidotic woman had below normal strength (right 40 and left 36 pounds per square inch). She complained of excessive, uncomfortable fatigue on doing housework and of needing frequent rest periods to overcome her exhaustion.
At baseline (A on Figure 5) her total strokes per minute were 175 or 20% below the lower limit of normal for the tally register test. In addition, starting at 10 seconds, she began developing muscle discomfort in her right forearm which by 30 seconds became extremely severe cramping muscle pain and continued for the rest of this one-minute test.

Thirty minutes after ingestion of 100 milligrams of niacinamide (B on Figure 5), her total score was virtually unchanged, but for the first 30 seconds she had no muscle discomfort and for the last 30 seconds she had mild muscle discomfort. This, in itself, was a remarkable improvement in muscle working capacity in the sense that this working rate no longer caused extremely severe cramping muscle pain.

One hour after ingestion of niacinamide, her total score rose to 188 painless strokes per minute, an increase of only 5.6% above baseline (C on Figure 5). Even this improved score was 14.5% below the lower limit of normal for this test.

After six weeks of maintenance therapy on 100 milligrams of niacinamide, three times daily, this woman performed the tally register test and obtained a score of 280 strokes per minute with no discomfort or pain. This was at the very upper limit of maximum muscle working capacity. She told me that in less than a week she had lost her need for extra rest; she was no longer easily tired by housework, had no feelings of painful exhaustion and had greatly expanded her physical activities to now include bowling. In addition, she also lost her pattern of other aniacinamidotic symptoms. Thus, a woman who might easily have been labeled a neurasthenic or psychasthenic was restored to greatly improved health through the use of niacinamide.

Another patient is a 24-year-old, athletic, pre-1943 aniacinamidotic man with high normal grip strength. He complains of excessive fatigue playing tennis and also when he exerts himself physically in other ways.

Figure 6 shows that at baseline, his maximum muscle working capacity was 196 (11% below the lower limit of normal for this test). He had no muscle pain or discomfort with this test or subsequently.

Ten minutes after the ingestion of 100 milligrams of niacinamide, his score rose to 205 strokes per minute; in 15 minutes, it went up to 234 strokes per minute; in 30 minutes, it hit a high of 250 strokes per minute (a score at the upper range of normal) and he maintained this high level of performance for the next 90 minutes when his score declined within a few hours to baseline.

It is notable that the 10- to 15-minute period of rapid rise in his maximum muscle working capacity reflected rising niacinamide levels in the bloodstream and corresponded to the time patients often spontaneously smile and say they are feeling better and when there is initial visible recession of the metabolic edema of aniacinamidosis.

Within a week of taking 100 milligrams of niacinamide three times daily, this man lost all complaints of fatigue and had great improvement in many of his niacinamide-responsive symptoms and signs. Because this man seemed robust and athletic, his original complaints of easy fatigability might easily have been considered a sign of hypochondriasis by many a physician.

Pre-1943 aniacinamidotic patients' responses were somewhere between these two examples. Those who had below normal strength generally had improvement of this parameter. Those who had muscle discomfort and pain on doing muscular work lost this in response to niacinamide therapy. Those who had low maximum muscle working capacity scores had great improvement in this area.

But what about the post-1943 patients?

CASE HISTORIES: POST-1943

The next patient is a 60-year-old woman who complained of excessive fatigability but had high normal strength. She also had mild chronic lingual mucosal changes, impaired joint mobility, impaired balance sense and as the test showed impaired muscle working capacity.

Her graph (Figure 7) shows her tally register performance read at 15-second intervals before and one-half hour after the ingestion of 300 milligrams of niacinamide. These data are displayed in three ways.

Notice in the upper graph how much she improved in her muscle working capacity one-half hour after taking 300 milligrams of niacinamide orally.
Before niacinamide ingestion, her total score was 25% below the lower limits of normal for the tally register test. One-half hour after 300 milligrams of niacinamide, she performed close to the upper limit of normal, reaching 48.2% above her pretreatment score, an enormous improvement in her maximum working capacity.

The left lower chart gives the total individual scores for each successive 15-second interval before and after the ingestion of 300 milligrams of niacinamide. The lower right graph displays her successive 15-second scores in terms of percentages of her final total one-minute score before and after the ingestion of 300 milligrams of niacinamide. In each of these two graphs, if there were no fatigue experienced, then the score and percentage score for each 15-second interval would be equal and the graph would form a straight line parallel to the X-axis. By following the slope of the lines before niacinamide ingestion and after the ingestion of 300 milligrams of niacinamide, you can see how rapidly she fatigued prior to niacinamide ingestion and how within 30 minutes of the ingestion of 300 milligrams of niacinamide, the graph approached a no-fatigue level for the first three quarters of the test and showed slight fatigue only during the last quarter of the test.

In response to maintenance niacinamide therapy at the level of 300 milligrams every three hours for six doses each day, a total of 1,800 milligrams a day, the 60-year-old woman lost her excessive fatigability and also had improvement in her joint mobility, balance sense and lingual mucosal morphology.

### TABLE 1

**One-Minute Tally Register Test Performed by a 67-Year-Old Man Taking 300 mg of Niacinamide Every Three Hours for Six Doses a Day**

<table>
<thead>
<tr>
<th>Strokes cumulated every 15 seconds</th>
<th>Strokes for each 15-second interval</th>
<th>Percentage of total strokes per each 15-second interval</th>
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<tr>
<td>67</td>
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<td>235</td>
<td>40</td>
<td>17.0%</td>
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**One Week Later: One Minute Work, Four Minutes Rest For Eight Successive Trials**

<table>
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<tr>
<th>Strokes cumulated every 15 seconds</th>
<th>Strokes for each 15-second interval</th>
<th>Percentage of total strokes for each 15-second interval</th>
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<tr>
<td>61</td>
<td>61</td>
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<tr>
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<td>26.1%</td>
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<tr>
<td>183</td>
<td>61</td>
<td>26.1%</td>
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<tr>
<td>234</td>
<td>51</td>
<td>21.8%</td>
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<tr>
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<td>192</td>
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<td>240</td>
<td>32</td>
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<td>60</td>
<td>25.5%</td>
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<td>234</td>
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<tr>
<td>234</td>
<td>46</td>
<td>18.7%</td>
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Table 1 shows the post-1943 maximum muscle working capacity of a 67-year-old male on a maintenance schedule of 300 milligrams of niacinamide every three hours every day for a total dose of 1,800 milligrams per day.

This patient performed the one-minute tally register test, then rested four minutes and repeated the cycle for eight successive trials. You will note that his maximum muscle working capacity in the eight tests varied narrowly from 234 to 243 strokes per minute. Fatigue was minimal and occurred during the last 15 seconds of the test, a normal finding.

DISCUSSION

Not all patients receiving niacinamide alone had improvement in muscle strength and working capacity. However, in some of these patients, the addition of thiamine and riboflavin to the niacinamide therapy caused prompt improvement in muscle function. Others required, additionally, choline dihydrogen citrate in divided doses totaling 2.4 grams a day. Those benefiting from the addition of choline, who had flabby muscles prior to therapy, developed muscle turgor and tone approximating what one would expect in persons doing heavy work.

In 30% of patients, no type of vitamin therapy overcame muscle weakness. Fatigability or improved impaired grip strength or impaired maximum muscle working capacity after an adequate three-month trial of therapy with niacinamide alone or in combination with other vitamins.

BALANCE TESTING

Uncertainty of balance sense and often some degree of ataxic gait are common findings in the pellagrous syndromes as noted by Spiers, Field, myself and others. Such patients do not have vertigo as a usual finding. They do at times lose balance when changing position, stagger, often bump themselves severely enough to develop black and blue areas and sometimes have nasty falls. Yet, they may be able to stand in perfect balance in the Romberg position with eyes open or closed but not when a more strenuous test is made of their balance sense.

In 1941, I devised a strenuous test of balance sense. In this, I have the patient keep his hands by his sides, stand on his right foot, place the heel of his left foot one inch in front of his knee cap and stand as long as he can with his eyes open. The test is then repeated with his eyes closed. The length of time he can stand in this position with eyes open or closed is determined. Then, the test is repeated with the patient assuming a symmetrical position while standing on his left foot (Figure 8).
walk in the dark since this favors falls with all the possible serious consequences.

**DISCUSSION**

In response to adequate niacinamide therapy, many patients regain normal balance sense. If recovery is to occur, it will be evident in the first three months of therapy. In some persons, thiamine and pyridoxine orally and B12 parenterally may be needed in addition to niacinamide to restore normal balance sense. Once restored, stopping niacinamide alone or in combination with the other vitamins will cause the impairment in balance sense to recur. Especially in some older persons, no amount of vitamin therapy will restore normal balance sense even when such persons benefit greatly from treatment with the above vitamins in other ways.

**DEPRESSION, AGITATION, HYPERKINESIS**

Most of the over-55-year-old patients who had mild depression, agitation or hyperkinesis recovered after a week or two of adequate niacinamide therapy and this improvement continued as long as such treatment was maintained. Some patients required in addition to niacinamide such other B-complex vitamins as B1, B6, and B12 to recover. There were patients with these mental syndromes who were not helped by prolonged massive vitamin therapy of the sorts noted above even though they benefited in other ways.

**NIAVINAMIDE AND JOINT MOBILITY**

Now I will discuss my most important contribution to nutritional medicine, the finding that adequate niacinamide therapy can ameliorate impaired joint mobility in persons of all ages with or without visible arthritic deformities provided that they also ingest adequate protein and calories provided that their joints are not so deteriorated by arthritis prior to niacinamide therapy that little or no recovery is possible, and provided the joints are not subjected to repetitive minor injuries, overuse, excessive muscle tension or major injuries.

In 1941, I first began studying the effect of niacinamide on joint mobility when I initially discovered to my astonishment that niacinamide used for the treatment of a pellagrous syndrome, eniacinamide, simultaneously caused significant improvement in impaired joint mobility so that stiff joints became more flexible.

I immediately began studying the maximum ranges of joint movement in all patients prior to and during niacinamide treatment. In order to gain objective evidence, I devised or adapted goniometers with which to measure maximum joint movement before and during treatment.

In addition, I used photography to document some important data. For example, in my study of Heberden's nodes, I found that the normal range of joint movement of the distal interphalangeal joint was as illustrated in Figure 9. When the proximal interphalangeal joint was flexed so that the middle finger bone was at right angles to the proximal finger bone, the distal phalanx could be moved so that the finger pad would easily touch the skin overlying the upper middle phalanx.

Various degrees of hypertrophic or degenerative arthritis of the distal interphalangeal joint caused various degrees of impaired movement of this joint with maximal impairment when the Heberden's node deformity was present. Impaired mobility in the distal interphalangeal joints often could be demonstrated in an age group that was two or more decades younger than the group in which the Heberden's deformity was evident, implying that it took a longer period of distal interphalangeal joint microtrauma to induce this deformity.

Figure 10 illustrates the limitation of motion of the distal interphalangeal joint of a 25-year-old woman who does not have Heberden's nodes but does have degenerative joint disease of the terminal interphalangeal joint. When her middle finger bone is held at right angles to the proximal finger bone, the skin of the finger pad covering her distal finger bone cannot be made to touch the skin overlying the middle finger bone.

**JOINT RANGE INDEX**

To make joint measurement a practical clinical procedure rather than a research undertaking, I selected 20 separate joint ranges which could easily be measured and were likely to show the earliest impairment of joint mobility. I devised a weighted average of these joint measurements which could be easily calculated to give a single number which I call the Joint Range Index or JRI. When done with strict attention to detail, the entire procedure was accurate, reproducible on any given visit with no more varying of the JRI than plus or minus 0.3 of a JRI unit. The entire procedure took less than three minutes to perform.
Calibrated Collar Used in the Measurement of Lateral Neck Rotation

(a)  (b)  (c)  (d)  (e)
Measurement of Lateral Neck Rotation Using the Graduated Collar

Gravity-Type Goniometer Showing Calibration

(a)  (b)  (c)
Measurement of the Knee Joint Extension

(a)  (b)  (c)
Measurement of Hip Abduction

(a)  (b)  (c)
Measurement of Flexion and Extension of the Wrist with the Graduated Wrist Plate

(g)  (h)  (i)
Measurement of Extension of the Metacarpophalangeal Joints

Figure 11.
The actual method of measuring the 20 joint ranges and the computation of the JRI are described in detail in a previously published monograph, "The Common Form of Joint Dysfunction." (Kaufman, 1949).

These are the 20 joint ranges I routinely measured for incorporation into the JRI: lateral rotation of the neck to the right and the left; extension and flexion of the wrist joint of each hand; extension of the metacarpophalangeal joints of each of the four fingers of both hands; circumduction of each shoulder joint; abduction of each hip joint with the thigh maintained in a plane perpendicular to the trunk; extension of the right and left knee joint when the thigh is maintained perpendicular to the trunk.

JOINT DYSFUNCTION

I use the term "joint dysfunction" to indicate that the patient has measurable evidence of impaired mobility of his joints whether or not he has visible hypertrophic or rheumatoid arthritic deformities.

Determination of the patient's Joint Range Index is useful in many ways (See Table 2). Firstly, it helps classify the patient's clinical joint status in terms of degree of joint dysfunction or no joint dysfunction. For example, a JRI of 50 to 100 indicates no joint dysfunction; 60 to 95 equals slight joint dysfunction; 71 to 85, moderate joint dysfunction; 55 to 70, severe joint dysfunction; or less, extremely severe joint dysfunction.

The JRI is also an index to the level and frequency of niacinamide administration required to improve the patient's impaired joint mobility; at each level of joint dysfunction. What is extremely important is that the patient's initial pretreatment JRI indicates the level of niacinamide therapy he should have throughout the entire treatment program rather than the rising JRI which results from successful niacinamide therapy. The lower his initial JRI, the more damaged are the articular surfaces. Even though such sick joints may develop improved mobility, to maintain such improvement requires treatment with the amounts of niacinamide indicated by the patient's initial joint range index. My long-term experience with niacinamide therapy teaches this important lesson.

Table 2, reprinted here with the permission of the Journal of the American Geriatric Society, provides the needed data about dosage levels and their distribution throughout the day. The JRI also allows one to judge if the rate and degree of improvement in joint mobility in response to niacinamide therapy are adequate. A satisfactory response occurs when the JRI rises from 6 to 12 JRI units the first month of therapy and subsequently increases from one-half to one JRI unit per month thereafter. In addition, the JRI helps detect regression which results from the patient's reducing niacinamide intake, stopping niacinamide, or taking the right total daily dose but taking it in fewer doses than prescribed. It helps indicate the degree to which joint trauma overcomes the body's ability to improve joint mobility. Patients tend to have more joint complaints with decreasing JRI's; i.e., with worsening joint mobility. Females tend to have more joint complaints for any level of joint dysfunction than males.

The Sedimentation Rate Index (SRI) was determined by making readings of the fall of red blood cells in a Wintrobe Sedimentation Tube every five minutes, plotting these values, and then

<table>
<thead>
<tr>
<th>Joint Range Index</th>
<th>Clinical Status</th>
<th>Oral Dosage Schedules of Niacinamide Per Day</th>
<th>Range of Total Mg of Niacinamide taken per 24 hrs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>98-100</td>
<td>No joint dysfunction</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>86-85</td>
<td>Slight joint dysfunction</td>
<td>150-250 mg every 3 hrs. for 6 doses</td>
<td>900-1500</td>
</tr>
<tr>
<td>71-85</td>
<td>Moderate joint dysfunction</td>
<td>250 mg every 3 hrs. for 6 doses; or 250 mg every 2 hrs. for 8 doses</td>
<td>1500-2000</td>
</tr>
<tr>
<td>55-70</td>
<td>Severe joint dysfunction</td>
<td>250 mg every 2 hrs. for 8 doses; or 250 mg every 1½ hrs. for 10 doses</td>
<td>2000-2500</td>
</tr>
<tr>
<td>55 or less</td>
<td>Extremely severe joint dysfunction</td>
<td>250 mg every 1½ hrs. for 10 doses; or 250 mg every hr. for 16 doses</td>
<td>2500-4000</td>
</tr>
</tbody>
</table>

ascertaining the 20 minutes of fastest fall in millimeters. This value was divided by 20. The SRI then was given in millimeters per minute. This was a much more sensitive test than one in which the sedimentation rate was given in millimeters per hour. The better a patient's JRI's, the lower his SRI's. Figure 12 shows that for groups of patients the SRI rises as joint dysfunction worsens.

![Graph](Image)

**WINTROBE SEDIMENTATION RATE INDEX IN MILLIMETERS PER SECOND**

**SLIGHT MODERATE SEVERE EXTREMELY SEVERE**

**JOINT DYSFUNCTION**

Figure 12. F = average for females in each class of joint dysfunction; M = average for males in each class of joint dysfunction; T = average for the total number of patients in each class of joint dysfunction.

**TREATMENT**

In the treatment of joint dysfunction, niacinamide is not an analgesic although many patients have marked decrease in joint discomfort and pain as recovery progresses. Niacinamide does not have a corticosteroid nor a non-steroidal anti-inflammatory action although inflammation is often reduced in response to adequate therapy. Niacinamide, among other therapeutic capacities, favors repair of damaged articular surfaces such as occurs in degenerative or hypertrophic joint disease and in this sense exerts a potent anabolic action. Niacinamide works slowly and gently. Unless you measure joint mobility on each visit, you might not be aware of significant improvement in joint mobility.

For niacinamide therapy to be effective, the patient's diet must have adequate protein and calories. Excessive joint trauma must be avoided since it can overcome the reparative effects of niacinamide. Many articular surfaces are so severely damaged by arthritis prior to niacinamide therapy, that the full range of joint mobility can never be recovered and in many instances there can be no recovery or improvement in joint mobility of specific joints. But only a long trial of niacinamide therapy in severe joint mobility impairment can determine if such joints can recover to any degree.

The half life of niacinamide is relatively short and its renal clearance is relatively high. For this reason, it must be given in divided doses, administered at frequent but regular intervals during the day. If table 2 suggests 250 milligrams to be taken every three hours for six daily doses, the same therapeutic effectiveness cannot be achieved by giving 300 milligrams of niacinamide three times daily even though the total daily dose is identical. The thicker the patient's joints, the higher and more frequent schedule of niacinamide therapy the patient will require for recovery.

**A Review of Joint Pathophysiology**

Today, rheumatologists believe that chemical abnormalities impair cartilage metabolism in degenerative joint disease which in its later stages manifests itself as osteoarthritis. The earliest microscopic lesions include decreases in articular cartilage's metachromatic material, reduction of chondrocytes, fatty degeneration, adverse changes in collagen fibrils with resulting irregularities of articular surfaces. Soon there are localized cartilage softenings, surface flaking and fibrillation. Bennett, Waite and Bauer demonstrated that judged by the gross and microscopic changes in articular cartilage surfaces of the knee joints of patients of various ages who never had joint complaints or evidence of arthritis on physical examination, everyone beyond the second decade had evidence of some degree of degenerative changes in articular cartilages. Ordinary joint movements, and more so those that use great force, further abrade the fibrillated articular surfaces. This causes additional loss of articular cartilage with exposure of subchondral bone at the margin of the cartilage. With ensuing ulceration of articular cartilage, new bone formation is stimulated at the margins of the degenerated articular cartilage and these osteophytes are visualized as spurs in X-rays. Lowman has shown that by the time a population reaches 40 years of age, ninety per cent show minimal X-ray signs of osteoarthritis, mostly without any accompanying symptoms. As degenerative joint disease progresses, cysts of various sizes form beneath the articular surface and there is considerable remodeling of subchondral bone. Thus, adverse changes in articular cartilages are in part the result of aging, wear and tear and the body's metabolic mobility to successfully compensate for the degenerative changes by complete repair. The trauma of ordinary and extraordinary wear and tear causes the metabolic activity of chondrocytes to increase but their ability to continue to replicate and form...
new articulating cartilage matrix for repair is very limited. Whenever wear and tear of articulating cartilage exceeds the body's ability to repair it, degenerative joint disease ensues. But what is important with niacinamide therapy is that it seems to induce metabolic changes in articulating cartilage cells (chondrocytes) which enhance the ability of cartilage to repair itself and better fend off the adverse effects of joint wear and tear and aging than when the patient subsists on diet alone. When adequate niacinamide therapy is stopped, in a few weeks the gains are dissipated. Thus, continuous maintenance therapy with niacinamide is necessary to sustain improvements in joint mobility.

In adults, rheumatoid arthritis is always superimposed on some degree of degenerative joint disease involving articulating cartilages. In some adults with rheumatoid arthritis, niacinamide (alone or in combination with other vitamins) will significantly ameliorate rheumatoid arthritis in both its articular and systemic aspects and cause a marked reduction in the patient's Sedimentation Rate Index. In some patients with rheumatoid arthritis who experience some degree of clinical improvement in response to niacinamide therapy (alone or in combination with other vitamins) but who continue having certain acute or chronic systemic and articular symptoms and signs which are allergic in origin, identification of these allergens and their elimination from the patient's diet, medication and environment will markedly improve the patient's rate of recovery from arthritis. In some patients with rheumatoid arthritis, a three month trial with adequate niacinamide therapy (alone or in combination with other vitamins) will not cause significant benefits as far as the joints are concerned.

**CASE HISTORY**

The joint record of a 77-year-old woman with degenerative arthritis, also known as osteoarthritis and hypertrophic arthritis, is shown in Table 3. She is greatly crippled by this disorder. Her pretreatment JRI is 55.7. A mite better than extremely severe joint dysfunction. Taking 250 milligrams of niacinamide every hour and a half for ten doses a day, her JRI shows satisfactory improvement until her fifth visit. One month before, contrary to my advice, she decided to take 500 milligrams of niacinamide every three hours for 5 doses a day. As previously indicated, although her total daily dose was the same as I prescribed for

<table>
<thead>
<tr>
<th>TABLE 3</th>
<th>Joint Range Index Data</th>
<th>Female</th>
<th>No. 83</th>
<th>Age 77</th>
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<tbody>
<tr>
<td>Neck Rotation</td>
<td>R.</td>
<td>40</td>
<td>45</td>
<td>50</td>
</tr>
<tr>
<td>Neck Rotation</td>
<td>L.</td>
<td>40</td>
<td>45</td>
<td>50</td>
</tr>
<tr>
<td>Shoulder</td>
<td>R.</td>
<td>50</td>
<td>100</td>
<td>80</td>
</tr>
<tr>
<td>Shoulder</td>
<td>L.</td>
<td>50</td>
<td>50</td>
<td>55</td>
</tr>
<tr>
<td>Wrist Flexion</td>
<td>R.</td>
<td>90</td>
<td>90</td>
<td>75</td>
</tr>
<tr>
<td>Wrist Extension</td>
<td>R.</td>
<td>75</td>
<td>95</td>
<td>100</td>
</tr>
<tr>
<td>Wrist Flexion</td>
<td>L.</td>
<td>70</td>
<td>70</td>
<td>70</td>
</tr>
<tr>
<td>Wrist Extension</td>
<td>L.</td>
<td>70</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>Fingers</td>
<td>R1.</td>
<td>80</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>70</td>
<td>90</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>60</td>
<td>90</td>
<td>90</td>
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<td></td>
<td>4</td>
<td>80</td>
<td>90</td>
<td>100</td>
</tr>
<tr>
<td>Fingers</td>
<td>L1.</td>
<td>90</td>
<td>95</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>80</td>
<td>95</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>80</td>
<td>80</td>
<td>90</td>
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<tr>
<td></td>
<td>4</td>
<td>80</td>
<td>90</td>
<td>100</td>
</tr>
<tr>
<td>Hip</td>
<td>R.</td>
<td>33</td>
<td>35</td>
<td>55</td>
</tr>
<tr>
<td>Hip</td>
<td>L.</td>
<td>30</td>
<td>55</td>
<td>55</td>
</tr>
<tr>
<td>Knee</td>
<td>R.</td>
<td>58</td>
<td>60</td>
<td>80</td>
</tr>
<tr>
<td>Knee</td>
<td>L.</td>
<td>48</td>
<td>75</td>
<td>85</td>
</tr>
<tr>
<td>Joint Range Index (JRI)</td>
<td><strong>55.7</strong></td>
<td><strong>70.1</strong></td>
<td><strong>75.4</strong></td>
<td><strong>80.2</strong></td>
</tr>
<tr>
<td>Days</td>
<td>0</td>
<td>25</td>
<td>227</td>
<td>385</td>
</tr>
</tbody>
</table>
her, the larger dose taken less frequently was about half as effective as the dosage schedule I prescribed for her. When she returned to the original dosage regimen for the next month her JRI rose again. (See Table 3.)

From 10/16/45 to 10/26/48, her chart showed that with niacinamide treatment she had progressed from the lowermost range of severe joint dysfunction to the middle range of moderate joint dysfunction; i.e., from being severely crippled by osteoarthritis to being ambulatory and free from arthritis symptoms. This chart also showed how individual joints fared during treatment. Overuse of the fingers and wrists in crocheting, knitting and tatting interfered with full improvement in mobility. Thus, even as the overall JRI improves with niacinamide therapy, there is considerable variation in the rate and degree of improvement of individual joint mobility and to some degree this is conditioned by the amount of overuse the joint receives. Some joint ranges improve, some stay stationary, some regress. Joint dysfunction is a dynamic process with a constant battle between the forces of repair and the forces of wear and tear. In this patient, for the most part, the processes of repair stimulated by adequate niacinamide therapy held dominance as indicated by rising Joint Range Indexes except for the month when she deliberately changed her niacinamide regimen in the manner described above.

**DISCUSSION**

So far I have merely talked numbers. But what about the quality of her life?

When I first saw this decrepit, depressed elderly patient, she could not get into or out of a chair, onto or off the toilet seat, into or out of bed without the help of a strong person. Once helped into the standing position, she had trouble standing, walking, keeping her balance. To maintain stability in the erect position, she had to use two canes which she clutched with all her might; this greatly traumatized her finger joints which became very painful. She fatigued easily. She could not negotiate the stairs. She could not comb her hair. She wept frequently and was chair-bound and virtually house-bound.

In response to the initiation of adequate niacinamide therapy, the patient’s family noted beginning improvement by the end of the first week. By the third month, the patient had regained her strength, was no longer excessively fatigued and had normal balance sense. She was no longer depressed or weepy. She was able to sit down and get up from a chair or the toilet and into and out of a bed without assistance. Her joint mobility had improved enough so that she was fully ambulatory.

She could comb her hair and walk up and down the stairs for the first time in many years. She was free from discomfort and pain in her joints. What pleased her the most was that she had recovered sufficiently so that she could resume her social and church activities.

All these improvements persisted with continued niacinamide therapy. The only time her Joint Range Index declined was on her fifth visit because she failed to take her niacinamide in the manner I prescribed. Her JRI recovered its upward course when she resumed niacinamide therapy in the manner I had prescribed.

On her last visit, this spry, cheerful, physically active 80-year-old woman kissed me on the cheek as she said, “You liberated me from the prison of my arthritis.”

**OVERVIEW OF NIACINAMIDE THERAPEUTICS: INDIVIDUAL CASE HISTORIES**

Next, I show a number of graphs which depict various patients’ responses to niacinamide therapy. These cases were taken from that portion of my total study which concerned itself with trying to find out what the lowest amount of niacinamide was that would permit a favorable rate of improvement in the Joint Range Index and, thus, in the patients’ overall joint mobility. I shall not give particulars about each case history because I wish to concentrate on the rate of improvement in Joint Range Indexes in response to niacinamide therapy.

Figure 13A illustrates the response of joint dysfunction to treatment with niacinamide alone. Patient No. 431, a 37-year-old female with moderate joint dysfunction, and patient No. 325, a 63-year-old female with severe joint dysfunction, each received 150 milligrams of niacinamide orally every three hours for six doses a day - a total of 600 milligrams of niacinamide per 24 hours. Patient No. 416, a male aged 68 with severe joint dysfunction, ingested 150 milligrams of niacinamide every two hours for a total of eight doses a day - a total of 1,200 milligrams of niacinamide per 24 hours. In each instance, the pattern of improvement in joint dysfunction was similar as evidenced by the rising values of the patient’s Joint Range Index.

Figure 13B shows the response of two patients who in addition to niacinamide received thiamine, riboflavin and ascorbic acid.

Patient No. 427, a 45-year-old male with severe joint dysfunction, received capsules containing 150 milligrams of niacinamide, 5 milligrams of thiamine, 7 milligrams of riboflavin and 200 milligrams of vitamin C every three hours for six doses a day - a total of 900 milligrams of niacinamide, 30 milligrams of thiamine, 42 milligrams of riboflavin and 1,200 milligrams of vitamin C per 24 hours.
Patient No. 413, a 61-year-old male with severe joint dysfunction, took capsules containing 162.5 milligrams of niacinamide, 3 milligrams of thiamine, 7 milligrams of riboflavin and 225 milligrams of vitamin C every three hours for six doses a day for a total of 975 milligrams of niacinamide, 18 milligrams of thiamine, 42 milligrams of riboflavin and 1,350 milligrams of vitamin C.

Figure 13A. The three patients received only niacinamide therapy. Compare the Joint Range Index response of this group to the two patients in Figure 13B who received niacinamide plus thiamine, riboflavin and ascorbic acid. The additional vitamins neither augmented nor retarded the niacinamide effect on the JRI.

When the JRI improvements of patients in Figure 13B are compared to the JRI improvements of the patients in Figure 13A, the response of joint dysfunction as indicated by the rising values of the Joint Range Index has a pattern of improvement almost identical with that observed in the three patients who received niacinamide alone. Thus it would appear that the addition of thiamine, riboflavin and vitamin C neither augmented nor retarded the rate of recovery from joint dysfunction. In other patients who received pyridoxine and calcium pantothenate in addition to niacinamide, thiamine, riboflavin and ascorbic acid, recovery from joint dysfunction was identical with what would have occurred if the same dose of niacinamide had been the sole therapeutic agent.

This 78-year-old woman (# 339) (See Figure 14) had severe joint dysfunction caused by severe rheumatoid arthritis. Note that in addition to improvement in her JRI, her Sedimentation Rate Index declined markedly as her joint mobility improved. This improvement in the Sedimentation Rate Index signaled improvement in the inflammatory aspects of her rheumatoid arthritis and was paralleled by improvement in her strength.
Figure 15 is taken from that part of my study which determined the least amount of niacinamide that will cause improvement in patients' JRI's.

The upper chart for patient No. 336, a 29-year-old female, shows the effect of niacinamide therapy in improving her Joint Range Index. The pre-treatment level, and with resumption of niacinamide therapy, again marked improvement was seen.

The lower chart for patient No. 309, a 26-year-old female, shows the effect of niacinamide therapy in improving her JRI: the effect of gradually tapering off niacinamide intake and then stopping it entirely for a short period of time. This was repeated. Because she tapered off niacinamide and stopped intake for a short time, her JRI on day 460 was lower than the last measured JRI value before dosage reduction. It was higher than her pre-treatment JRI.

These findings emphasize the need for continuous adequate niacinamide therapy if improvements in the JRI induced by niacinamide are to be maintained over the longer term.

The next graph, reprinted here with the permission of the Journal of the American Geriatric Society (Figure 15) shows the improvement in five women in response to niacinamide and ascorbic acid in four, and to niacinamide alone in one. All had improvements in JRI as well as in grip strength. The first three women also had remarkable improvement in their maximal muscle working capacity. The statin register test could not be done in one 78- and 80-year-old women because of the still persisting severe hand deformities of rheumatoid arthritis.


OVERVIEW OF NIACINAMIDE THERAPEUTICS: LARGE PATIENT POPULATION

So much for individual patients. Now, I wish to show the impact of niacinamide on a large patient population. The next graph (See Figure 17), reprinted with permission from the Journal of the American Geriatric Society, shows the age distribution of the male, female and the total population studied.

Figure 18 shows the linear decline in the Joint Range Index for the untreated population. Each successive point represents the average of the JRI's for each successive five-year age period.

Figure 19. Effect of niacinamide therapy on decline in JRI with age. J. Am. Geriatr. Soc. Reprinted with permission.

Figure 20 shows data plotted according to the patients' pre-treatment and post-treatment JRI's for various periods of treatment, some as short as a month. You will note massive movement from the severe joint dysfunction categories into the less severe categories.

Patients slowly develop progressive impairment of joint mobility as they age, going from slight to moderate to severe joint dysfunction. This is in keeping with folk wisdom that our joints stiffen as we age.

Figure 19 shows how niacinamide therapy improves joint mobility. The treated patients had varying periods of therapy and include both good and poor compliers. Improvement from pre-treatment levels takes place in all age groups. Remember, the larger doses of niacinamide are used in the treatment of the more severe degrees of joint dysfunction.
severe categories. Thus, in the treated group there are far fewer patients with extremely severe, severe and moderate joint dysfunction - most moved to the slight joint dysfunction category.

DISCUSSION

The statistical graphs you have just seen deal with persons who have had from a few months to as much as three years of niacinamide therapy. One may well ask whether niacinamide therapy can support improved joint mobility for longer periods of time, let us say a decade or more. Here are a few examples of what can happen with up to 20 consecutive years of niacinamide therapy.

But first consider a start-and-stop woman (See Figure 21). In a decade she has started, stopped and resumed niacinamide therapy four times. Each time she starts, her JRI improves; each time she stops, her JRI declines almost to about what it would have been if she had never had niacinamide therapy.

Figure 21.  

Now for the next four patients' graphs. Please keep in mind that with growing older, for untreated patients one would expect a progressive decline along the average path shown by the thick black line which represents the average decline in the JRI's of a general aging population.

Figure 22.  

Figure 23 is of a 32-year-old male who had improvement from moderate joint dysfunction which continued as he took niacinamide as prescribed for the next 17 years. His JRI hovered between slight joint dysfunction and no joint dysfunction during this long period of time.

Figure 23.  

Figure 24 is of a 65-year-old golf enthusiast who also did hard work with his hands. His JRI at the beginning of treatment indicated severe joint dysfunction but he managed to achieve moderate joint dysfunction despite the continuing trauma from these two sources to his joints. This benefit continued for more than 15 years.

Figure 24.
Figure 25 presents a 71-year-old patient with severe joint dysfunction who responded to niacinamide with an improvement to moderate joint dysfunction - and maintained her improvement for more than 12 years.

![Graph showing improvement over time](image)

**Figure 25.**

Now plotting the JRI’s (See Figure 25) of these four patients on a single chart (which also show the decline of the JRI’s with increasing age - the straight lines we observe at a glance their long-term status. Each person had considerable benefit in terms of hitting an equilibrium point which was higher than his or her part of the aging line showing the decline of the JRI in the untreated population. Remember, the JRI in some measure, is the balance between wear and tear and the body’s ability to repair and each of these patients subjected his or her joints to quite different degrees of trauma. If these persons had had less joint trauma, they all might have been somewhere between slight joint dysfunction and no joint dysfunction.

![Graph showing JRI values](image)

**Figure 26.**

Thus, maintenance niacinamide therapy is able to support improved joint function as indicated by an elevated JRI for as long as 20 years. There is no reason to suppose that such benefits could not be maintained for a lifetime.

**CONCLUSION**

Just imagine for a moment what things might be like today if patients now “warehoused” in nursing homes and geriatric hospitals had received (starting two, three or four decades earlier) the benefit of adequate niacinamide therapy either alone or in combination with other vitamins. They would now have improved joint mobility, improved strength, improved maximum muscle working capacity, improved balance sense and freedom from certain mental syndromes.

I am convinced, on the basis of my large clinical experience, that there would have been extraordinary human benefits and comparable economic benefits to the individual and society. The whole syndrome of old age as we know it today would have been modified for the better. Geriatric persons would have been able to be independent much longer, would have developed fewer and less severe infirmities and would have required much less professional and professional medical care than is now the case.

In closing I now want to report an ophthalmoscopic finding I first became aware of in 1941-1942. As people age, retinal arterial walls tend to become less transparent and more opaque presumably as part of the progression of atherosclerosis. After several months to a year of adequate niacinamide therapy, I noted a slow, progressive tendency for the walls of retinal arteries to become less opaque and more transparent. Furthermore, the incidence of stroke in such persons was far below what I would have expected in their age groups.

Funduscopic color photographs taken at intervals of every six months would be required to provide objective data. If the development of the films will give true color, then any changes in the retinal arterial walls toward a more transparent and less opaque wall would corroborate my clinical impressions. I hope that other investigators will be able to undertake this type of clinical research. If my observations are confirmed by this objective technique, it would be important evidence that another concomitant of so-called normal aging is reversible to a significant degree.

I have not mentioned side effects because niacinamide used according to the game plan I devised was not associated with adverse side effects.

I now quote Dr. Andres Gocht, an eminent and respected pharmacologist, who has expressed in his textbook, Medical Pharmacology, a view held by most physicians: “In most cases, however, vitamins are used by the medical profession and the laity under the mistaken impression that larger amounts than the minimal daily requirement will promote
optimal health. This feeling has been further promoted by popular statements concerning the inadequacy of our modern manufactured foods with regard to vitamin and mineral content. It is believed by critical authorities that most of the widespread use of vitamins by the population is wasteful and that the benefits claimed by many persons must be due to a placebo effect.

I have demonstrated with objective measurements that niacinamide alone or combined with other vitamins can improve joint mobility as expressed by a rising JRI. I have improved impaired muscle strength and maximum muscle working capacity, and by an objective test, it can also improve balance sense. Repeated observation indicates that niacinamide alone or in combination with other vitamins will also ameliorate certain mental deficiencies found in the over-55 age group.

I am aware that some will say that my findings are not all placebo controlled. From 1941 through 1942, a limited number of placebo studies were done. More than a score of patients were treated first with niacinamide and then with placebo and a similar number were treated first with placebo and then with niacinamide. Placebos could not sustain niacinamide-induced improvement in joint mobility and placebos could not cause significant improvement in joint mobility. However, such placebo controls could not be done on a large scale in private practice and basically were never really necessary for the following reasons:

With respect to diet alone, eleven stubborn patients insisted that I prescribe only the best diet I could devise and for periods up to a year they subsisted on such a diet without any clinically significant improvement in joint mobility.

Furthermore, the therapeutic response to adequate niacinamide therapy was predictable within a quantitative range as previously indicated provided the patient had adequate protein and calories in his diet; did not subject his joints to overuse, repetitive or major injuries; and, provided that his joints had not been so deteriorated by previous arthritis or trauma prior to niacinamide therapy that little or no recovery of joint mobility was possible.

When patients experiencing clinically significant improvement in joint mobility decided to stop adequate niacinamide therapy, their JRI's declined to pre-therapy values within a few weeks. Patients with improved joint mobility in response to adequate niacinamide therapy sometimes decided to reduce their intake of niacinamide to inadequate levels and as a result their JRI's declined markedly. Patients taking adequate niacinamide therapy who substituted a one-a-day vitamin containing only 20 mg of niacinamide had their JRI's return to pre-treatment values despite the patients' conviction that the one-a-day vitamin would be the therapeutic equivalent of 250 mg of niacinamide taken every 3 hours for six doses a day. Because of the relatively short half-life of niacinamide, 500 mg of niacinamide taken three times a day is about half as effective as 250 mg of niacinamide taken every 3 hours for 6 doses a day in causing improvement in the patient's JRI even though the total daily dose of niacinamide is identical.

For all these reasons, there is no doubt that the observed improvements in joint mobility in response to adequate niacinamide therapy result from the therapeutic action of this vitamin.

In closing, I wish to say my only research associate was my wife, Charlotte. Although not a physician, she helped with certain aspects of patient care, helped in gathering and analyzing data and in the enormous task of accurate record-keeping. She also provided valuable editorial assistance. In response to some questions already asked, we received no outside financial aid from individuals, pharmaceutical companies, foundations or government to support my clinical studies.

If Dr. Spies were alive today, I think he would agree with me that niacinamide is not a panacea, nor will it create a race of supermen or superwomen. But properly used, I believe it could greatly improve the health of millions of people of all ages. I have already shown how it can ameliorate some of the common accompaniments of the so-called normal aging process. These include impaired joint mobility, impaired strength and impaired maximum muscle working capacity, impaired balance sense and certain mental deficiencies in the over-55 age group. Yet, today it is not used for such purposes. As a consequence, it is a most neglected vitamin. My hope for the future is that health professionals will interest themselves in applying niacinamide therapy to help patients of all ages achieve greatly improved health.

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