TREATMENT OF ARTHRITIS BY NICOTINIC ACID AND NICOTINAMIDE

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INTRODUCTION

NICOTINIC ACID and nicotinamide have been used successfully in treating patients with acute schizophrenia. If the illness is well established, they can still be useful when combined with electroconvulsive therapy (ECT). Unfortunately, they are of little value for treating chronic patients in mental hospitals.[5, 10] In addition, nicotinic acid is the most effective substance (cheapest, safest, least interference in dietary habits, freedom from side effects) yet discovered for lowering cholesterol levels. In sharp contrast, nicotinamide is not effective.[1]

These vitamins are now being used in substantial quantities in Saskatchewan for the treatment of schizophrenia and for normalizing cholesterol levels. These observations suggested that nicotinic acid by its hypocholesterolæmic activity ought to be useful for improving the health of aged people. In 1954, I prescribed one gram of nicotinic acid per day for an elderly woman who had started to decline physically (subject H.C., described later). A few months later, she reported that she was better and that the osteoarthritis of her hands which had troubled her was much improved. Since then, I have observed its antirheumatic effect in six cases with uniformly excellent results. Since my interest is psychiatric research, I did not search the literature very thoroughly to see whether anyone had made similar observations. In August 1957, after our paper on nicotinic acid and schizophrenia was published, I received a letter from Dr. William Kaufman.† He kindly informed me of his interest in our work, told me about his use of nicotinamide for the treatment of arthritis since 1941 and sent me his two major publications.‡

Dr. Kaufman in a letter of October 24, 1957, wrote: "Ever since 1943 I have tried to call my work on niacinamide to the attention of leading rheumatologists, nutritionists and gerontologists through conversations with them, by sending them copies of my monographs and papers on this subject, and by two talks given on the usefulness of niacinamide and other vitamins which I gave at International Gerontological Congresses in 1951 and 1954. I think that two factors have made it difficult for doctors to accept the concept that continuous therapy with large doses of niacinamide could cause improvement in joint dysfunction and give other benefits: (a) the advent of cortisone, and (b) the fact that my use of the vitamins was such a departure from the recommended daily allowance for vitamins by the National Research Council."

Kaufman first used niacinamide in large doses in the treatment of his private patients in 1941. In his initial monograph (1943) reporting his observations, made before compulsory enrichment of refined cereal products with vitamins and iron in the United States in 1943, he stated that when niacinamide was administered orally in amounts from 400 to 1000 mg. per day in divided doses, it improved joint function (increasing joint mobility and decreasing joint stiffness, swelling, deformity and pain), in addition to conferring other benefits on 30 patients with clinically obvious hypertrophic and rheumatoid arthritis.

After devising a simple, objective method of determining joint mobility through routine measurements of joint movements made on each patient on each visit, Kaufman in a detailed monograph (1949)[7] summarized his use of niacinamide as a therapeutic agent to improve joint mobility and function in 342 patients; in 1953, he reported results on 606 patients,[8] and in 1955, on 663 patients.[9] Since 1943, the range of niacinamide dosage he prescribed as oral medication has been from 900 to 4000 mg. per day in divided doses (alone or in combination with other vitamins).

The results of Kaufman's cumulative experience over a period of 18 years can be summarized thus: Without exception, those patients who took adequate amounts of niacinamide continuously, experienced clinically significant, measurable improvement in joint mobility and joint function—and often such additional benefits as improvement in muscle strength and working capacity, decreased fatigability, improved sense of equilibrium, and relief of certain mental syndromes, including depression. These patients included those who had clinically obvious rheumatoid arthritis or hypertrophic arthritis, or those who had the stiffness of increasing age which had not as yet developed clinically to the degree where it would be diagnosed on casual examination as hypertrophic arthritis. Joint deformities often lessened in severity or disappeared. Elevated sedimentation rates, such as seen in rheumatoid arthritis, tended to become and remain normal, and some hæmoglobin levels which were initially low were restored to the range of normal. The benefits of therapy continued for as long as niacinamide was used. Reduction in the amount of niacinamide taken by the patient per day, from the prescribed amount to lesser amounts, resulted in decrease in benefits. Cessation of niacinamide therapy resulted in a slow, moderate or even rapid return to the pre-treatment status, including a return of joint stiffness, swelling, discomfort and decreased joint mobility. Reinstitution of adequate niacinamide therapy resulted in the reinstatement of all the improvements pre-

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‡The Common Forms of Joint Dysfunction, E. L. Hildreth and Company, Brattleboro, Vermont, 1949, and The Common Form of Niacinamide Deficiency Disease: Aniacinamidosis, Yale University Press, New Haven, Conn., 1943.

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viously listed, including the beneficial effects on joint function and other aspects of the patient's health.

There were no adverse side reactions or allergic, toxic or idiosyncratic effects from niacinamide therapy in the dosage range from 900 to 4000 mg. per day in divided doses—and a considerable number of the patients whom Kaufman studied and treated have taken such doses for 10 to 15 years without interruption.

Since his first publication on niacinamide as a therapeutic agent, Kaufman has had many personal communications indicating that other doctors using the larger doses of niacinamide he recommended also noted the same beneficial effects on joint function and the patient's sense of well-being. Several surgeons whose progressive hypertrophic arthritis of the hands had made surgical work difficult noted that as a result of adequate niacinamide therapy they had increased flexibility of the finger joints which resulted in greater ease in operating. However, apparently in the past 18 years no systematic investigation has been undertaken or reported by others on the use of niacinamide as a therapeutic agent for impaired joint mobility such as exists in the arthritis of aging (hypertrophic arthritis) or in rheumatoid arthritis. Despite the fact that no extensive clinical trials have been made, some rheumatologists on *a priori* grounds continue to state categorically that vitamins have no place in the treatment of arthritis.

Nicotinic acid or its amide benefited my six cases. I hope by publishing a brief clinical report confirming Kaufman's findings to stimulate those who work with arthritics. I believe that a proper clinical trial of the effect of large doses of these vitamins in arthritic illnesses is long overdue.

Patients sometimes object to the severe flushing which follows the ingestion of nicotinic acid, while others complain about its acidity. Slow-release[11] and buffered preparations[2] have overcome these difficulties. Some patients feel that the flush is beneficial. Because of this, one person in this series (Case 5) refused to change from nicotinic acid to nicotinamide. In my opinion, nicotinamide would be preferable for uncomplicated rheumatic disease while nicotinic acid, because of its hypocholesterolæmic action, is preferable for aged patients or patients who have a raised blood cholesterol.

CASE REPORTS

CASE 1.—Mrs. H.C., aged 68 in 1954, had recently experienced severe and prolonged stress due to a severe and lingering illness of her husband. In February 1954, I observed a rapid and disheartening change in her physical and mental status. She began to age very rapidly and complained of severe neuritis (pain in both arms), failing vision in one eye, insomnia, and pain and restricted movement of her hands. On examination, her skin had developed the parched and crinkly appearance of old age. Her hands were becoming deformed and showed marked ulnar deviation, well-marked Heberden's nodes on all fingers, and severe pain on movement. In March 1954, she was started on 1 gram nicotinic acid per day in two divided doses. She has continued on this medication until the present report. About three months later (July 1954) I again examined this patient. There was a marked improvement, mentally and physically. She no longer complained of neuritis; her vision became normal and has not failed her since. The ulnar deviation of her hands vanished, as did the Heberden's nodes. These nodes went through an interesting change. In random order they first enlarged somewhat, then receded in size until today they are barely visible. Her hands became normally mobile. The skin regained its previous elasticity and tone. For the remainder of the year and over the next two years, she continued to be subjected to severe stress and during that interval suffered the loss of her husband, some difficulty with the estate, etc. She has remained mentally and physically normal. It would have been easy to blame the onset of her arthritis on stress. However, the stress became even more severe but the arthritis was reversed by nicotinic acid.

CASE 2.—C.M., aged 14 in 1952. This boy was well until 1952, when he developed pain and restriction of movement in his knees. Tuberculosis was suspected but not found. He was in hospital for five weeks in June and July 1953. There he received 80 grains of acetylsalicylic acid per day and physiotherapy. He had to use crutches for some time, being very weak and stiff. By the fall of 1953, he was much improved. During the winter his condition became worse. He continued to receive acetylsalicylic acid as well as hot wax baths and physiotherapy. In the summer of 1954 he spent one month receiving mineral baths and massage which did not improve him in any way.

In October and November 1954, he was away from school and in bed five weeks with severe hip pain. On examination, he complained of severe pain in his back and in the joints of his foot. His physician did not give him cortisone because of his age. About the first part of December, he was started on 2 grams of nicotinic acid per day in two doses and 1 gram of ascorbic acid per day as well as his acetylsalicylic acid. Five days after, he returned to school somewhat improved. He has continued to improve since that time.

By June 1955, his feet, which had been swollen to a size E shoe, were reduced in size to a C width. His fingers were less swollen and more mobile. He discontinued physiotherapy in 1955, as it did not benefit him. The dose of acetylsalicylic acid was reduced to 40 grains. In 1956 it was reduced to 20 grains. By 1957 his condition had steadily continued to improve. He reported that during these two years he missed less school than any year since 1953. He still had pain in his back, which was slightly stiff. His legs gave him trouble if he walked an excessive distance, i.e. one-half mile. In 1957, the nicotinic acid was reduced to 1 gram per day. He reported that he had voluntarily reduced the vitamins several times but this was immediately followed by a return of stiffness. He was now able to walk fairly well. His erythrocyte sedimentation rate became normal this year.

He has continued on this medication until today. There is very little disability. He has very slight stiffness of his back but this is hardly noticeable. His scholastic career continues uninterrupted but medication cannot be stopped.

CASE 3.—Mrs. S.T., aged 44, first developed rheumatoid arthritis of her right shoulder in 1939. For the next eight years there were recurrences followed by remissions. Between 1948 and 1956, relapses became more frequent. She received physiotherapy, salicylates and cortisone. In the winter of 1956-57, movement of her shoulder joint became very painful with limited excursions. Cortisone was not effective. She was then started on 3 grams of nicotinic acid per day, which later was changed to nicotinamide in the same dosage. By June 1958, movement had been much improved and there was only occasional discomfort. She discontinued vitamin medication about this time. A few months later, her arthritis began to return and her husband, a physician, immediately placed her on nicotinamide medication which again controlled the arthritis. At present, she remains well so long as she takes nicotinamide.

CASE 4.—Mrs. C.J., aged 34 in 1957, was admitted to hospital in August 1957, complaining of pain and joint stiffness. The illness started five weeks before admission with chills, sharp pain in her joints, etc. The pain was severe in all joints and was accompanied by generalized swelling in almost all parts of the body. She was bedridden at home and unable to move for bodily functions. Much of the time she was fed by tube. She was then admitted by ambulance to hospital.

On examination, her extremities were swollen and hot, with pain and stiffness in all the joints except her hips. The left ankle was inflamed. A neurological examination was not possible owing to her stiffness. The hæmoglobin value was 12 grams per 100 ml. Total W.B.C. was 11,500. Sedimentation rate was 60 mm. in one hour. No radiological changes were found. After the start of this acute attack she received salicylates and cortisone. There was no clinical improvement. She developed hairiness of her upper lip, and her breasts decreased in size. Her mental condition was deteriorating rapidly and there was some question of a cortisone psychosis developing.

On August 19, 1957, she started on 3 grams of nicotinamide per day. On August 20, her total W.B.C. was 5700 and sedimentation rate was 67 mm. In about 10 days there was a marked improvement and physiotherapy was started. On August 21, she felt much better. On September 12, her condition was much improved. She was able to move her legs without any difficulty but her arms were still sore when she moved. Her appetite was good. On September 20, she was much improved but there was still some limitation of movement of her arms. The right elbow and shoulder were sore occasionally. On September 24, there were no complaints of discomfort. She was discharged on September 25. The final diagnosis was rheumatoid arthritis. The sedimentation rate was still high—55 mm.

By June 1958, her recovery was excellent. She exercised regularly and had good movement in all the joints. There were rare twinges of pain. There was still slight swelling of the ankles and she became fatigued readily. However, she managed the household very well and her nervous condition was much improved. Anxiety symptoms were greatly decreased. After the cortisone was stopped on August 19, 1958, the hairiness disappeared and her breasts became normal.

On February 28, 1959, she was seen and reported that there was no arthritic disability. All joints were normal. She was in good spirits and humour. She had discontinued nicotinamide several times but discovered that within a few days joint stiffness started again.

CASE 5.—Mrs. R.H., 37, first developed pain in her left shoulder in 1947, diagnosed as "nervous arthritis". In the same year, she had a baby and remained free of pain until 1955. In July 1955 the pain reappeared after prolonged cough. In the spring of 1958 she was admitted to hospital with the diagnosis of obsessive compulsive neurosis, quickly changed to schizophrenia. She received 3 grams of nicotinic acid per day for one month. As she recovered, her diagnosis was changed back to obsessive compulsive neurosis. (She was not under my care then.) She continued on one gram of nicotinic acid per day. The pain in her shoulder continued for one month as her mental condition improved, then quickly eased. By September 1958, there was hardly any pain at all. This patient has remained mentally and physically well. She believed that the heat due to the vasodilatation "went right into the sore areas" and refused to change to nicotinamide.

CASE 6.—Mrs. M.T., aged 58 in 1958, had for five years been troubled with recurrent local swellings on her arms and legs. These gradually enlarged and became sore and inflamed and itchy. They then broke open and slowly healed with scar formation. Her ankles were swollen and indurated with pitting œdema. She was able to achieve some control by using 100 mg. cortisone per day.

Early in May 1958, she began to take 3 grams of nicotinic acid per day and decreased the cortisone dose to 25 mg. per day. On May 30, she reported a marked improvement. The lumps were coming on much less frequently. In March 1959, she reported that she was much improved but that when she was very tired and had been up for some time, both feet swelled. By morning, they were normal. She takes 25 mg. cortisone per day, rarely 50 mg. per day, to control the œdema of the feet. She was diagnosed as having vascular nodulitis. This condition is of course not an arthritis but is included in this account as another interesting response of a condition which had responded poorly to cortisone.

The results of these few trials are summarized in Table I.

TABLE I.—RESPONSE OF PATIENTS TO NICOTINIC ACID OR NICOTINAMIDE

Patient	*Sex*	*Age*	*Diagnosis*	*Treatment started*	*Present state*
H.C.	F	68	Osteoarthritis	March 1954	Normal
C.M.	M	14	Rheumatoid arthritis	Dec. 1954	Nearly normal
S.T.	F	44	Rheumatoid arthritis	Nov. 1956	Normal
C.J.	F	34	Rheumatoid arthritis	Aug. 1957	Normal
R.H.	F	37	Schizophrenia, arthritis	April 1958	Normal for both conditions
M.T.	F	58	Vascular nodulitis	May 1958	Much improved

DISCUSSION

Although I have shown that nicotinic acid and its amide controlled arthritis of varying degree of severity in five patients and markedly alleviated one case of vascular nodulitis, this does not imply that it will be generally successful in treating these illnesses. My purpose has been only, by providing some confirmation, to draw attention to Kaufman's earlier and much more thorough work. I am not a rheumatologist and can only say that my results have been uniformly good and that some cases have been followed for four years. The vitamin must be taken continuously and so cannot be considered curative in the strict sense. But nicotinic acid and the amide are easy to take, have few side effects, and are non-toxic, easy to administer and fairly cheap. In a very large series of schizophrenic patients given these vitamins in similar quantities for as long as five years, there were no toxic reactions.[5]

We do not know why these substances should act favourably in rheumatism. Nicotinic acid shares with salicylates and benzoates the ability to combine with glycine. It may act in this way, and this would suggest some disorder of glycine metabolism – possibly an excess. But since nicotinamide which is just as effective does not bind glycine, its removal cannot be a main variable. Further, nicotinamide does not lower cholesterol levels, so that improved vascular efficiency can hardly be a main variable. Perhaps these massive quantities of vitamin force some improvement in intracellular oxidative respiration, as nicotinamide is an important component of diphosphopyridine nucleotide, one of the respiratory enzymes.

Nicotinic acid decreases the excretion of uric acid.[4] For this reason, I suggested that it be tried for the treatment of gout, but no trials have as yet been reported.

I would recommend to physicians who deal much with various forms of arthritis that they give these vitamins an adequate therapeutic trial. In this treatment, nicotinic acid and nicotinamide are not being used as vitamins. A daily dosage of about one gram per 50 lb. body weight is necessary. Any trial should run for at least one month.

CONCLUSION

Nicotinic acid and nicotinamide in massive doses can produce remissions in various forms of arthritis. The excellent response observed in a small series of patients provides confirmation of Kaufman's extensive observations.

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RÉSUMÉ

L'auteur rapporte les excellents résultats qu'il a obtenu dans le traitement de diverses formes de rhumatismes avec l'acide nicotinique. Ses observations corroborent celles publiées antérieurement par le Dr. W. Kaufman. Les doses employées varient de 400 à 4000 mg. par jour. Cette posologie fut très bien tolérée par plusieurs malades pendant des périodes s'étendant de 10 à 15 ans. La vitamine agit aussi bien dans la polyarthrite chronique évolutive que dans les rhumatismes chroniques dégénératifs. Elle améliore aussi l'état général du malade.

Ces constatations n'ont pas suscité chez les rheumatologues l'intérêt qu'elles semblaient mériter. L'évolution clinique de six malades sous traitement est rapportée dans le texte. L'auteur présente un plaidoyer en faveur d'une évaluation plus approfondie de cette forme de thérapie qui à l'heure actuelle semble pleine d'avenir.

RENAL TUBERCULOSIS IN A NATIVE POPULATION*

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IT IS WELL KNOWN that tuberculosis is a common disease in our native Canadian population, both Indian and Eskimo. The present series is a review of 104 cases of renal tuberculosis in patients admitted to the Charles Camsell Hospital in Edmonton, Alberta, from 1946 to 1958 inclusive.

This hospital draws patients from Alberta, the Yukon and the North West Territories. The great majority of admissions are of non-tuberculous patients. During the review period, 6559 patients have been admitted to hospital and 104 cases of renal tuberculosis have been found, an incidence of 1.6%. This series of cases have all been proven tuberculous by at least one positive urine culture for acid-fast bacilli before initiation of treatment. In addition to positive urine culture, further proof has been obtained in the majority of patients in the form of intravenous, and in many cases retrograde, pyelograms, as well as histological proof in those cases which came to nephrectomy or necropsy.

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