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Niacinamide Treatment of Arthritis, with comments on ADHD, Part 1

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Joint Dysfunction, Part 1
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CHAPTER I

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THE COMMON FORM OF JOINT DYSFUNCTION
by William Kaufman, M.D., Ph.D. (1949)

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(This chapter presents Dr. Kaufman's protocol for the treatment of arthritis with niacinamide, vitamin B-3. He also used ascorbic acid (vitamin C), thiamine (B-1), riboflavin (B-2), all in large doses. His rationale and his measurement methods begin the chapter, but you might wish to scroll down to the section on dosage ("Methods of Treatment") and read that first. ***If you are looking for the doctor's comments relevant to ADHD, scroll to nearly the end of the page and they can be found in boldface type.*** *The chapter closes with case histories and an insightful, practical discussion of patient management. Graphs and other original illustrations are not provided here, but may be seen in the original text.)*

The author's preface, and all references cited, are posted at
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INTRODUCTION

The relationship between the continuous administration of adequate amounts of niacinamide and improvement in both hypertrophic arthritis and rheumatoid arthritis was originally reported in 1943 as part of a clinical study on niacinamide deficiency disease, aniacinamidosis, observed in a group of 150 private patients studied during the years 1941 and 1942 (97). (The term aniacinamidosis was employed by the writer in 1943 to define a syndrome which was thought to be the consequence of a niacinamide tissue deficiency disease. The term aniacinamidosis would be redefined today (1949) without reference to its possible etiology, as the syndrome which is ameliorated or corrected when a person ingests certain nontoxic amounts of niacinamide (far in excess of those obtainable from his usual diet), and recurs in time when such niacinamide supplementation is discontinued.)

The form of aniacinamidosis which was seen by the writer prior to 1943 included, in varying degrees of severity, changes in skin texture and pigmentation; subcutaneous swellings; tenderness of periosteum, cartilage and voluntary muscle to pressure or squeezing; tenderness and enlargement of the liver; gastrointestinal symptoms; changes in the morphology of the lingual mucous membrane; and limitation in ranges of joint movement. This clinical syndrome of aniacinamidosis was characterized (a) by its prompt recession when niacinamide was exhibited orally for a sufficient period of time in adequate doses, and (b) by its recurrence, often in the original degree of severity, upon premature cessation of therapy with niacinamide. Most persons who were treated required maintenance doses of niacinamide continuously to prevent relapse (97).

It was observed in the course of the above study that persons who had clinically both aniacinamidosis and obvious arthritis experienced, in response to adequate oral therapy with niacinamide over a sufficiently long period of time, clinical improvement in both the aniacinamidosis and the arthritis. On the other hand, premature cessation of therapy with niacinamide caused a worsening of both the aniacinamidosis and the arthritis. Furthermore, when the total dosage of niacinamide per day was reduced from apparently adequate to inadequate levels in such persons, there was a more gradual recurrence of the severer aspects of aniacinamidosis and a slower worsening of their arthritis than occurred with complete cessation of therapy with niacinamide. It was noticed that individuals who suffered from both aniacinamidosis and clinically obvious arthritis required larger daily doses of niacinamide for recovery from niacinamide tissue deficiency disease than those who had no clinically obvious arthritis (97).

With the compulsory enrichment of cereal products in 1943 (25), the niacin content of the average American diet was increased from 11 to 17 mg per 2500 calories (30). Since 1943, the clinical syndrome of aniacinamidosis as originally described has not been seen regularly, but has been supplanted by a syndrome in which most of the manifestations of aniacinamidosis as originally described are milder, and many of the symptoms and signs of the aniacinamidosis of 1941 and 1942 are absent. However, limitation in the ranges of joint movement has continued to be an objective, measurable attribute of the metabolic disorder corrected by adequate niacinamide therapy. In 1944, in an effort to secure quantitative data concerning the relationship between treatment with niacinamide and recovery in arthritic joints, the writer introduced goniometric examination of joint ranges of all persons who had at the time of the initial physical examination clinically obvious arthritis. In 1945, it was decided to broaden the base of this study by routinely measuring the joint ranges of all patients presenting themselves for physical examination. For this purpose, there was introduced as part of every physical examination an abbreviated goniometric examination of the movement of 20 joints or joint groups in easily measured, specified ranges. Within five minutes, this abbreviated goniometric examination of joint ranges could be performed and recorded by the examiner on a special form devised for this purpose. By this method, a sufficiently large number of joints or joint groups were measured in defined ranges to afford an adequate and representative sampling of the mobility of the moveable joints of the body.

With the introduction of routine measurement of the joint ranges of all new patients who presented themselves for examination, it soon became apparent that limitation of joint movement in the 20 measured ranges was exceedingly prevalent in many individuals without joint complaints or clinically obvious arthritis. Moreover, limitation of joint movement in persons without complaints referable to joints was often of the same order as that observed in patients (with and without clinically obvious arthritis) who did have complaints referable to their joints.

It was decided to simplify the approach to the study of limitation of joint movement by combining the numerical values obtained for each of the 20 measurements of joint range movement into a single numerical value which was the "weighted" average of all these measurements. This "weighted" average was called the JOINT RANGE INDEX. As will be shown later, the Joint Range Index is used by the physician in the objective appraisal of joint function (joint mobility) in numerical terms, in the clinical classification of the various grades of severity of joint dysfunction, in the selection of the initial level of niacinamide therapy, in the regulation of subsequent levels of niacinamide therapy, and in the observation of the response of joint dysfunction to adequate and inadequate niacinamide therapy. In addition, the use of the Joint Range Index enables the patient to understand the objective basis for the diagnosis of joint dysfunction in his case, and the objective basis for the evaluation of the response of his joint dysfunction to adequate and inadequate therapy.

A WORKING HYPOTHESIS:
THE DEGENERATIVE PROCESS AND THE REPARATIVE PROCESS IN JOINTS

Certain inductions have been made from factual data acquired during the clinical study of patients with joint dysfunction (with and without clinically obvious arthritis) whose joint ranges were measured for the determination of the Joint Range Index at various time intervals under various conditions of niacinamide therapy: before niacinamide therapy was instituted, during premature cessation of adequate or inadequate niacinamide therapy, during the substitution of adequate for inadequate niacinamide therapy, and during continuously adequate niacinamide therapy. These inductions have been synthesized into a working hypothesis which explains the status of a patient's joints in terms of two oppositely directed, coexisting articular processes: the deteriorative process, and 'the reparative process.

The deteriorative process consists chiefly of two operational factors tending to cause retrograde changes in joint structure and function, (a) "wear and tear in joint structures, which results from ordinary or unusual joint uses, and (b) a slowly, moderately or rapidly progressive metabolic disorder which is corrected in time by adequate niacinamide therapy. This metabolic disorder occurs even in persons subsisting on what is considered to be the average "good" or "adequate" diet of today (172) (118) (193).

The reparative process tends to overcome the retrograde articular changes caused by the deteriorative process. Even persons subsisting on "good" or "adequate" diets of today lack sufficiently potent reparative mechanisms to offset for any prolonged period of time the retrograde influences of the deteriorative process in joints. However, with supplementation of the average good" or "adequate" diet of today with adequate amounts of niacinamide, the articular reparative process becomes sufficiently powerful to overcome the retrograde changes in articular tissues produced by the deteriorative process, and in time permits improvement in the functional status of joints, as objectively demonstrated in the individual patient by serially increasing values of the Joint Range Index.

For purposes of this study, it has been postulated (a) that clinically perfect articular structures have the fullest ranges of articular movement, (b) that clinically imperfect articular structures have less than full ranges of articular movement, and (c) that the range of joint movement in moveable joints is a practical measure of the degree of clinical perfection of these articular structures. At any given moment, the patient's Joint Range Index is an indirect measure of the balance between deteriorative and reparative articular processes in the joints whose ranges of movement are determined goniometrically.

In an untreated population, the deteriorative process seems to preponderate over the reparative process, as is shown by the average tendency of the Joint Range Indices of this group to decrease with increasing age (see Graph 1G, page 153).

When the ranges of movement of a given joint are re-measured at any given time interval (e.g., one month), there may be no change, an increase, or a decrease in joint movement when the second measurement is compared with the first. When there has been no change in the range of joint movement, it is postulated that the effects of the deteriorative process have been balanced by the effects of the reparative process for this time interval, and that no significant change in the functional status of the joint has occurred. However, when the range of joint movement has decreased, it is assumed that the deteriorative process in articular tissues has been more powerful than the reparative process for a sufficient period during this time interval to permit deteriorative effects to preponderate over reparative effects, with the result that deterioration has occurred in the functional status of the joint. On the other hand, when the range of joint movement has increased, it is assumed that the reparative process in articular tissues has been more powerful than the deteriorative process for a sufficient period during this time interval to permit reparative effects to preponderate over deteriorative effects, with the result that there has been improvement in the functional status of the joint.

It may be that some arthritic joints are damaged by a deteriorative process of such intensity and duration that joint recovery is not possible, even with prolonged adequate niacinamide therapy. Even though initial clinical examination may indicate that eventual recovery of these joints is unlikely, only a prolonged trial of adequate niacinamide

therapy will disclose whether or not such joints actually have been damaged beyond repair. It has been observed that deformed arthritic joints which seemed on the initial clinical examination to have been irreparably damaged by the deteriorative process have shown recovery of the full ranges of joint movement, and a progressive decrease in severity of the obvious arthritic deformities with adequate niacinamide therapy over a prolonged period of time.

METHOD OF STUDY

The observations recorded in this volume were derived chiefly from the clinical study of 455 persons of both sexes, ranging in age from 4 to 78 years, who consulted the writer from March 1945 to February 1947 in the course of his private practice of internal medicine. (In Section IV the frequency distribution by five-year age groups of all patients studied is shown in Table 1A; that of all male patients, in Table 1B; that of all female patients, in Table 1C.) All patients studied were ambulatory. Their occupations were varied. Although no attempt has been made to classify the economic status of these patients, the majority of these patients would be considered to belong to the moderate income groups, and relatively few would be considered to belong to the low income groups. They came chiefly from New England. Many had no complaints referable to health, but desired a routine physical examination; others had minor or major health problems.

For purposes of this study, a detailed enumeration of the incidence of various diseases in the population group examined would be of no significance, since it was found that no matter what associated diseases the patient had, his joint dysfunction responded in a predictable way to adequate therapy with niacinamide, to premature cessation of such therapy, or to the substitution of inadequate for adequate therapy. A partial listing of various diseases other than joint dysfunction seen in this group of patients may, however, be of some interest: gall-bladder disease (with and without stones), chronic hypertrophic gastritis, duodenal ulcer, diverticulosis of the colon, cardiospasm, multiple intestinal polypi, irritable colon, Paget's disease of bone, post-menopausal osteoporosis, multiple sclerosis, syringomyelia, spastic paralysis, chronic and acute anxiety states, anginal syndrome, arteriosclerotic heart disease, rheumatic heart disease, anemias, myeloge nous leukemias, allergic diseases, fibroid tumors of the uterus, hypothyroidism, hyperthyroidism, diabetes, gout and arrested lues (48).

All persons included in this study presented themselves as new private patients. Only in this sense was there selection of the population group studied. All patients were subjected to an initial examination, which consisted of a detailed history, physical examination and certain laboratory studies. These findings were recorded on a special form, together with the physician's impressions and therapeutic recommendations. Kodachrome transparencies were taken of the tongue, gums and eyes of each patient to serve as a point of reference in the objective study of the response of tissues to vitamin therapy (105) (106) (107) (37) (39) (183) (191) (114) (35) (174) (8) (109). In addition, monochrome photographs were taken of selected patients to document clinically obvious arthritic deformities.

During the initial visit, in the course of the general physical examination, certain ranges of joint movement were measured in a standard way (149), and the numerical values obtained were used in computing the Joint Range Index. The sound-proofed room in which the examination was performed was kept at a temperature comfortable for the patient, who was completely disrobed save for the covering sheet. Care was taken to have the patient adequately draped at all times. The examiner informed the patient before each measurement of joint ranges as to what would be done next, indicating that maximal joint ranges were to be measured. The ranges of knee and hip movement were measured with the patient recumbent. All other joint ranges were measured in the sitting position. In addition to measurements of joint ranges, the following data were recorded if they were elicited on physical examination of the joints: pain, crepitus (cracking or other sound), muscle spasm, redness, unusual warmth, swelling, engorgement or accentuation of the periarticular venous pattern, and deformity.

Instruments used in measuring joint ranges were made of metal according to the writer's specifications:

A gravity-type goniometer, fashioned after the one described by Cooper (34), was found to be a highly versatile instrument (see Figures 1, 2, 3 and 12).

(Figure 1. Illustrates the goniometer, a device for measuring joint movements and angles. The calibrations are also shown.)

A graduated collar was devised which permitted the measurement of neck rotation (see Figures 4 and 5).

One tool consisted of an angle device with provision for the maintenance of any angle by tightening a set screw, and a graduated plate on which the angle device was fitted in order to read the angle therefrom (see Figure 7).

A graduated plate was used to measure flexion and extension of the wrist (see Figure 8) and, rarely, in markedly deformed hands to measure extension of the metacarpophalangeal (knuckle) joints of the fingers (see Figure 11).

A special device was constructed for the measurement of extension of the metacarpophalangeal joints of the fingers (see Figures 9 and 10).

MEASUREMENT OF THE RANGES OF JOINT MOVEMENT USED IN COMPUTING THE JOINT RANGE

Knees. The patient is adequately draped, lying flat on his back with his body weight evenly distributed. He is asked not to contract his lower extremity muscles actively during this measurement, since such contraction lessens the range of movement of the knee joint. His right thigh is flexed passively by the examiner so that it is at right angles to his trunk. The examiner then extends the patient's right leg maximally, taking care not to displace the ipsilateral thigh even slightly, and taking care that the patient does not flex his contralateral thigh even slightly, as this would cause pelvic tilt. The angle which the leg makes with a hypothetical plane passing through the knee joint at right angles to the thigh is measured by reading the indicator dial of the gravity-type goniometer, which is held with its long axis parallel to the long axis of the right leg. The range of movement of the left knee joint is measured in a symmetrical manner (see Figure 2).

(Figure 2. Illustrates the measurement of knee-joint extension, showing a) Knee joint at beginning of measurement; b) Knee extended 50%; c) Knee extended 100%.

Hips. The patient is asked not to contract his lower extremity muscles (particularly the adductor muscles of his homolateral thigh) since such active muscular contraction lessens the range of movement of the hip joint. With the patient lying symmetrically on his back, the right thigh is flexed by the examiner so that it remains perpendicular to the trunk, care being taken that the right foot is not rotated from a neutral position of rest. The right thigh is then abducted maximally by the examiner, care being taken not to displace the contralateral buttock from the table. If the contralateral buttock is levered off the examining table by the examiner's abduction of the ipsilateral thigh, then abduction of the right thigh is maintained, but the patient is permitted to rotate so that both buttocks are on the table again and bear weight symmetrically. The gravity-type goniometer is then applied so that its long axis parallels the long axis of the right thigh, and the appropriate reading of the degree of hip abduction is made and recorded (see Figure 3). The range of movement of the left hip joint is measured in a symmetrical manner.

Figure 3. Illustrates measurement of hip abduction, showing a) Thigh at beginning of measurement; b) Thigh abducted 50%; c) Thigh abducted 100%)

NOTE: For purposes of clarity in illustration, the examiner is pictured as standing be-hind the thigh that is abducted. In practice, he stands in front of the thigh that is being

abducted, so that he can easily read without parallax the scale of the gravity-type goniometer.

Lateral Rotation of the Neck. The patient is asked to sit symmetrically, and to make himself as "tall" as possible. He is asked to hold his neck so that it is neither flexed nor extended, nor laterally bent to the right or left. A specially constructed graduated metal collar (see Figure 4) is fitted symmetrically at the level of the base of the neck so that the 100% graduation always rests on the anteriormost portion of the trapezius ridge, and the patient is asked to rotate his head maximally to the right. Since the examiner wishes to measure and record maximal values, when the patient reaches his initial maximal joint of lateral rotation, he is always urged to do better, to prevent his restraining full neck rotation because of subjective discomfort. During measurement of lateral neck rotation, the patient is at no time permitted to raise his shoulders, or to flex, extend or laterally bend his neck (see Figure 5). When the patient signifies that he has achieved maximal rotation of his neck to the right, the measurement of neck rotation is made. The range of neck rotation is read directly from the graduations on the neck gauge by the examiner, who sights along the plane perpendicular to the center of the patient's chin to avoid parallax, ascertaining the graduation on the neck gauge which would pass, if extended, through the center of the chin. The measurement of rotation of the neck to the left is made in a symmetrical way.

(Figure 4. Illustrates the graduated collar (with degree markings similar to those of a protractor) used in the measurement of neck rotation)

(Figure 5. Illustrates the measurement of lateral neck rotation using the graduated collar, and shows the position of head at beginning of measurement, the head rotated to the right of left 50% and 100%)

Shoulders. The range of circumduction of the shoulder joint is measured by careful inspection and estimation rather than by the use of a particular device. In order to be certain that maximal ranges are elicited and estimated, the maneuver of circumduction of the shoulder is performed several times for each shoulder. The patient is asked not to contract his shoulder girdle or upper extremity muscles, since such active muscular contraction lessens the range of movement of the shoulder joint. In measuring the range of circumduction of the right shoulder, the physician stands to the right of the patient, who faces forward, sitting as "tall" as he can, with his shoulders maintained horizontally. The physician places his left hand on the patient's right shoulder to prevent its displacement from the horizontal position when the patient's right arm is subsequently circumducted for measurement. The physician's right hand holds the patient's right elbow lightly, slightly flexing the patient's right forearm on the right arm, but not holding the right elbow so rigidly as to interfere with subsequent free movement of the shoulder joint during circumduction. In this position, the physician circumducts the shoulder joint of the right arm in a clockwise direction so that the patient's right elbow describes the largest possible "circle" during circumduction (see Figure 6).

(Figure 6 illustrates the method for estimating of the range of shoulder circumduction (range of motion in a circling motion). a) The figure drawn in unbroken lines shows the position of the patient, as well as the position of his right upper extremity (marked 0) at the beginning and end of the maneuver of shoulder circumduction. The physician's left hand maintains the patient's right shoulder horizontally throughout the maneuver of shoulder circumduction. The broken lines show three successive positions (50,100,50) of the right upper extremity during clockwise circumduction. Estimates of the range of shoulder circumduction are made with 0, 50, 100 as positions of reference.

b) Frontal view of the patient's position and the examiner's hands at the begin-fling and end of the maneuver of shoulder circumduction, corresponding to the 0 position in (a).

The movement of shoulder circumduction is graded as 50% when the right arm swept upward in maximum circumduction reaches, at the highest point of the arc, the plane perpendicular to the sagittal plane of the body at the level of the shoulders. The movement of shoulder circumduction is graded as 100% when the arm swept upward in maximum circumduction reaches at the highest point of the arc of circumduction the

plane parallel to the sagittal plane of the body and perpendicular to a horizontal plane passing through the level of the shoulders. With some practice, bearing in mind these two reference axes, the physician can make estimates of the fractional ranges of shoulder circumduction with sufficient accuracy to be included in the computation of the Joint Range Index. Circumduction of the left shoulder is measured in a symmetrical manner.

(Figure 7 illustrates measurement of the degree of the wrist to bend. Captions follow below.)

a) Angle device set at 90 degrees, or 100% of a trigonometric quadrant. Its arms may be rotated around its central axis and fixed by a set screw at any desired angle.

b) Measurement of wrist flexion by the angle device. With the wrist held at maximum flexion, the arms of this device are brought into apposition with the surface of the dorsum of the hand and forearm. The set screw holding the arms of the angle device is tightened in this measured position, the angle device is fitted into the graduated plate (c), and a reading of the angle of flexion is made.

c) Graduated plate with angle device fitted to make reading of the range of wrist flexion obtained in (b).

Wrists. The maximum degree of flexion and extension of the wrist is measured either with the angle device (Figure 7) or the plate device (Figure 8), using the dorsum of the forearm and hand as the surfaces between which all angles are measured.

The plate device is more convenient for this measurement, being used so that the central axis of its graduations corresponds to a projection of the center of the right wrist joint. The 0 line is held parallel to the long axis of the right forearm, and the 100 line is held perpendicular to the projection of the central axis of the right wrist joint. The patient is asked not to contract his forearm or hand muscles during this measurement, since such active contraction lessens the range of movement of the wrist. Care is taken to measure maximal passive flexion and extension, and to sight along the dorsum of the hand in such a way that parallax is avoided. The patient is not permitted to flex or extend the fingers during the measurement of maximal flexion or maximal extension of the wrist. Measurement of flexion and extension of the left wrist is made in a symmetrical manner.

(Figure 8 illustrates the measurement of flexion and extension of the wrist with the graduated wrist plate, another protractor-like scale to fit the hand. 50% and 100% flexing is shown.

For clarity in illustration, (d) and (e) picture the examiner's fingers as exerting pressure on the subject's fingertips to induce maximal passive extension. In practice, this pressure is exerted on the palm of the hand, just proximal to the metacarpophalangeal joints.)

Metacarpophalangeal (Knuckle) Joints. The right hand is inserted into the special device (see Figures 9 and 10) with the palm resting on the baseplate. The 100 line of the graduated plate is perpendicular to the projection of the central axis of the metacarpophalangeal joint to be measured. The patient is asked not to contract his forearm or hand muscles during this measurement, since such active muscular contraction lessens the range of extension of the metacarpophalangeal joints. Only the finger that is being extended by the examiner is permitted to leave the baseplate. The index finger is extended maximally by the examiner. This may be done in the face of objections from the patient, who may experience pain from this maneuver. The angle of extension between the dorsum of the hand and the dorsum of the finger is measured in such a way that parallax is avoided. Extension of the second, third, fourth and fifth fingers of the right hand is measured successively. The metacarpophalangeal joints of the left hand are measured in symmetrical fashion.

(Figure 9. Illustrates the device for the measurement of extension of the metacarpophalangeal (knuckle) joints. This also resembles a custom-fit protractor, with angle measurements in scaled in degrees.)

In some persons, for whom the special device cannot be used because of severe deformities of the interphalangeal joints of the hands, the wrist plate with the central cut-out (see Figure 11) is adapted to the measurement of metacarpophalangeal extension. The plate is fitted between the fingers so that the 0 line is perpendicular to the projection of the central axis of the metacarpophalangeal joints, with the 100 line parallel to the dorsum of the hand and perpendicular to the central axis of the metacarpophalangeal joints. In this use of the wrist plate, 100 minus the plate reading measures the movement of finger extension at the metacarpophalangeal joints. The patient is asked not to contract his forearm or hand muscles during this measurement, since such active muscular contraction lessens the range of extension of the metacarpophalangeal joints. Extension of the metacarpophalangeal joints is measured, holding the plate as described above, for the second, third, fourth and fifth fingers of the right hand. The corresponding joints of the left hand are measured in a symmetrical way.

(Figure 10 illustrates the technique for measuring extension of the metacarpophalangeal (knuckle) joints. Details shown: Hand in the special device (Fig. 10) at the beginning of measurement; (a) lateral view, (d) looking from above downward, (g) frontal view. The metacarpophalangeal joint of left forefinger extended 50%: (b) lateral view, (e) looking from above downward, (h) frontal view. The metacarpophalangeal joint of left forefinger extended 100%: (c) lateral view, (f) looking from above downward, (i) frontal view.

(Figure 11. Illustrates the measurement of extension of metacarpophalangeal joints in severely deformed hands, using the wrist plate. Shown: a) Position of hand at beginning of measurement. b) Metacarpophalangeal joint of left forefinger extended 50%. c) Metacarpophalangeal joint of left forefinger extended 100%.

Neck Bending. This measurement is not used in the computation of the Joint Range Index, since it has not been made routinely. In some persons, it cannot be measured accurately because of their persistent tendency to angulate the shoulders.

The patient sits symmetrically as erectly as he can, with his shoulders held level. His neck is neither flexed nor extended, nor rotated to the right or left. The neck is bent maximally to the right, and the angle of bending is measured by reading the dial of the gravity-type goniometer, applied so that its long axis parallels the long axis of the nose (see Figure 12). Left lateral bending of the neck is measured in a symmetrical manner.

(Figure 12 illustrates the measurement of lateral neck bending with the gravity-type goniometer. Shown: Position of head at beginning of measurement; Right lateral neck bending of 50%; Left lateral neck bending of 50%.)

CERTAIN CONVENTIONS ADOPTED IN MEASURING VARIOUS JOINT RANGES

Save for the range of shoulder joint circumduction, the maximum range of each joint movement, when elicited as described previously, approximates one trigonometric quadrant of 90 degrees. This is true for (a) extension of the knee joint; (b) abduction of the hip joint; (c) right lateral rotation of the neck; (d) left lateral rotation of the neck; (e) flexion of the wrist; (f) extension of the wrist; (g) extension of the metacarpophalangeal joint. Because the angle of maximal movement of these joint ranges approximates one quadrant, it is convenient to measure these ranges in terms of percentages of a quadrant rather than in degrees.

This convention was adopted chiefly because patients visualize percentages of a range of movement more easily than equivalent measurements expressed in degrees. For all measurements except circumduction of the shoulder joint, simple arithmetic computation permits, when desired, the conversion from percentages to degrees, since 10% of a quadrant is equal to 9 degrees.

In a few individuals, the range of maximal wrist flexion is in excess of one quadrant. Also, in very few persons, either neck rotation to the right or neck rotation to the left, or both, are in excess of one quadrant. In these instances, for purposes of calculating the Joint Range Index, movement beyond one quadrant is considered as 100%, or the full range.

The conventions used in the measurement of shoulder circumduction have already been described (see page 10).

As a convention, the various graduated scales used in the measurement of joint ranges were read to the nearest 5% (4.5 degrees). A few readings were made with the angle device to 1 % (0.9 degree), but this was found to be an unnecessary refinement for purposes of this study.

COMPUTATION OF THE JOINT RANGE INDEX

It will be helpful in understanding the steps used in the computation of the Joint Range Index to refer to the form used for recording the measured values of the 20 specified joint ranges, and for computing the Joint Range Index (see Figure 13). The numerical values obtained upon measurement of the 20 specified joint ranges are entered separately into the appropriate space and column of the form at the time of the physical examination.

(Figure 13 illustrates the worksheet Dr Kaufman designed and used to record degrees of joint dysfunction with his patients. In addition to angular measurements, he also noted clinical data such as intensity of pain, crepitus, muscle spasm, redness, unusual warmth, swelling, prominent or engorged venous pattern, deformity, or the presence of Heberden's nodes.)

The Joint Range Index is the arbitrarily weighted mean of the numerical values obtained upon the measurement of 20 specified joint ranges. Measurements of the neck, wrists and fingers are weighted so that these joints will not unduly affect the numerical value of the Joint Range Index, since they show increased ranges of movement more rapidly than the larger joints (hips, knees, shoulders) in response to adequate niacinamide therapy.

The following steps are employed in computing the Joint Range Index from the measurements of 20 specified joint ranges:

The neck rotation index is computed by adding the measured values for the maximal ranges of right and left neck rotation and dividing by two. (In computing the various indices entering into the final computation of the Joint Range Index, the figures are rounded off to the nearest whole number; e.g., 0.5 or over is listed as the next highest digit, and less than 0.5 is dropped.)

The resulting quotient is entered into the appropriate space under the heading "Indices." (Neck bending is similarly averaged, although it is not used in calculating the Joint Range Index.) Readings for the maximal range of circumduction of the right and left. shoulders are entered separately in the proper spaces. Readings for the maximal ranges of extension and flexion of the right wrist are added and divided by two, the quotient being entered in the appropriate space. A similar computation is made for the left wrist, and similarly recorded. Readings for extension of the four metacarpophalangeal joints of the right hand are added, divided by four, and the quotient entered in the appropriate space. A similar computation is made for extension of the four metacarpophalangeal joints of the left hand. Readings obtained for measurement of maximal abduction of the right and left hips and for maximal extension of the right and left knees are separately recorded in appropriate spaces. The above 11 values are then added, the sum obtained divided by 11, and the resulting quotient is termed the Joint Range Index. This computation is carried to one decimal place. (In about 2% of the patients seen from March 1945 to February 1947 the Joint Range Index could not be computed because one or more of the component ranges of joint motion could not be measured; e.g., in persons who could not flex the thigh to make a right

angle with the trunk because of severe arthritis of the hip joint, or in persons with one or more limbs amputated.)

Thus, the Joint Range Index is precisely defined in terms of the "weighted" average of the 20 ranges of joint movement chosen for measurement. A Joint Range Index of less than 96.0 is taken to indicate the presence of joint dysfunction.

METHOD OF TREATMENT OF JOINT DYSFUNCTION (This section, consisting of pages 20-29, is the heart of Dr Kaufman's work.)

After completion of his physical examination, the patient was apprised of the normal and abnormal findings revealed by the clinical study. Where problems other than joint dysfunction existed, these were discussed, and appropriate therapeutic recommendations were made. The subject of joint dysfunction was then presented. The meaning of the numerical value of the patient's Joint Range Index was explained to him in terms of the Clinical Classification of Joint Function (see page 21), and the dynamic nature of joint dysfunction was described. The patient was told that joint dysfunction was reversible in time when appropriate therapy was taken.

All patients with joint dysfunction who elected to accept treatment were given niacinamide in suitable doses, either alone or in combination with other vitamins. When indicated the appropriate vitamins were prescribed in addition to niacinamide. The water-soluble vitamins used were never prescribed in aqueous solution, but as tablets or as dry powders in capsule form. When vitamin A was used, it was usually given in conjunction with vitamin D. Vitamin D was always given in conjunction with vitamin A; when vitamin D was administered in this study, the daily dosage rarely exceeded 6,000 U.S.P.units per 24 hours (14) (10) (38) (56) (59) (95).

Participation in the therapeutic program was entirely voluntary on the part of the patient. Some patients at the outset declined to accept treatment for their joint dysfunction. When a patient accepted therapy for his joint dysfunction, with each succeeding visit after the initial one, improvement or lack of improvement in his joint dysfunction was frankly discussed with him. No patient was chided because he was unwilling or unable to carry out the program of therapy as it was originally scheduled. Thus, because there was no "loss of face," most patients cooperated well and gave an accurate account of their deviations, if any, from the suggested therapeutic program. Some patients at the end of the first or second month of treatment, or at a later time, felt so much improved physically that they discontinued therapy for their joint dysfunction, mistakenly believing, in spite of advice to the contrary, that they were "cured," and required no further therapy or medical supervision. Some of these persons, who experienced a recurrence of their original pattern of symptoms upon premature cessation of therapy, returned subsequently for re-evaluation of their therapeutic needs. Other patients, who felt that they had not benefited from therapy for their joint dysfunction, did not continue with treatment though objectively they responded satisfactorily to adequate therapy, as shown by increasing values of the Joint Range Index on serial re-measurements.

Therapy was always individualized. In the therapeutic program introduced for the treatment of joint dysfunction, each patient served as his test object in the bio-assay of the dosage of niacinamide necessary to reverse his joint dysfunction. Therapy with niacinamide (used alone or in combination with other vitamins) was not deemed successful unless there continuous, objective improvement, as judged by continuously increasing values of the Joint Range Index on consecutive reexaminations. (When a patient subsists on a low-protein diet, amounts of niacinamide that would ordinarily be adequate for the treatment of his joint dysfunction prove to be inadequate for satisfactory improvement. In this case, the dosage of niacinamide is continued at the same level, but the protein level of the diet is increased to adequate levels, with subsequent satisfactory improvement in the joint dysfunction.) (118) (120) (172).

The clinical classification of joint function in terms of the numerical values of the Joint Range Index is listed below:

Clinical Classification of Joint Function
Degree of Joint Dysfunction Joint Range index
No joint dysfunction 96-100
Slight joint dysfunction 86-95
Moderate joint dysfunction 71-85
Severe joint dysfunction 56 -70
Extremely severe dysfunction 55 or less

For each clinical grade of joint dysfunction, the initial dosage schedule of niacinamide suggested below effects in time such improvement in joint dysfunction as the writer has considered to be clinically satisfactory. (However, since April 1947, it was found that dosage schedules 50-100% greater than those recommended below (particularly in the moderate, severe and extremely severe grades of joint dysfunction) are therapeutically superior, as judged by the patient's clinical response.)

While the initial dosage may be increased as necessary during treatment, it is not decreased, even though the Joint Range Index increases in response to adequate therapy.

The vitamins were administered orally, usually in equal doses at equal intervals during the day, and, in severe and extremely severe joint dysfunction, during the night when the patient would spontaneously awaken from sleep. In slight grades of joint dysfunction, the daily continuous ingestion of 100 mg of niacinamide after meals and at bedtime sufficed for treatment (400 mg/24 hours). Usually adequate in moderate joint dysfunction was the continuous ingestion of 150 mg niacinamide administered every 3 hours for 6 daily doses (900 mg/24 hours). In extremely severe and severe grades of joint dysfunction, 100-150 mg niacinamide were prescribed every hour (1500-2250 mg/24 hours), every hour and a half (1110-1650 mg./24 hours), or every two hours (800-1200 mg/24 hours), depending on the severity of the joint dysfunction, the more frequent schedule being used in more severe cases (97) (51).

It has been found in the treatment of joint dysfunction that the manner in which the daily dosage of niacinamide is divided has an important bearing on the therapeutic results achieved; e.g., 300 mg niacinamide given three times daily (900 mg/24 hours) is inferior in its therapeutic action to 150 mg niacinamide administered every 3 hours for 6 daily doses (900 mg/24 hours). Therefore, to define the type of therapy used, the writer routinely records the following data: (a) the number of milligrams or units administered per dose, and (b) the total number of milligrams or units administered per 24 hours.

No untoward effects or clinical signs of toxicity were noted when niacinamide (alone or in combination with other vitamins) was administered on the above dosage schedules to individuals for short or long periods of observation. Before 1943, mild hypoglycemia had been noted clinically in a few persons when niacinamide exceeded certain dosage levels (97) (135) (51) (62), but this phenomenon has not been observed since that time.

"ADEQUATE" AND "OPTIMAL" DOSAGE LEVELS OF NIACINAMIDE IN THE TREATMENT OF JOINT DYSFUNCTION

"Adequate" dosage of niacinamide is defined as that clinically safe dosage of niacinamide which, when ingested in divided doses throughout the day by a person with joint dysfunction whose ordinary diet is not inadequate in protein or calories, and whose joints are not subjected to excessive mechanical joint injury, will effect in time what the writer has considered to be a satisfactory pattern of increasing values of the Joint Range Index. The pattern of recovery from joint dysfunction in response to niacinamide therapy, and the numerical limits of increments in the value of the Joint Range Index which are considered to be satisfactory for the first month of therapy and for succeeding months, are described on page 24.

"Optimal" dosage of niacinamide is defined as that clinically safe dosage niacinamide which, when ingested in divided doses during the day by a person with joint dysfunction, would permit the most rapid recovery in joint function, as demonstrated by the largest possible increments in the values of the Joint Range Index in the shortest possible period of time. At present, the optimal dosage of niacinamide for the treatment of joint dysfunction has not been determined clinically, although it is hoped to approximate such a dosage level eventually. Since adequate dosages of niacinamide have given clinically satisfactory results without producing any untoward symptoms or signs of acute or chronic toxicity, no attempt has been made in this study to determine the optimal level of niacinamide therapy in the treatment of the various clinical grades of joint dysfunction.

However, as the higher dosage levels of niacinamide have been cautiously explored in the past 22 months, it has been found in severe and extremely severe joint dysfunction that divided doses of niacinamide totaling 4 or 5 grams (4,000-5,000 mg) per 24 hours are therapeutically superior to the lower dosage schedules - which previously had been considered adequate. Even these higher dosage levels of niacinamide may not be optimal for the treatment of joint dysfunction.

The optimal dosage of niacinamide for the treatment of joint dysfunction, as well as the limit of human tolerance for niacinamide, can be established only in those medical centers equipped to provide careful clinical supervision, and to conduct such chemical, metabolic and clinical laboratory studies as would reveal the earliest signs of toxicity, should these occur with the administration of progressively higher dosage levels of niacinamide.

DESCRIPTION OF JOINT DYSFUNCTION AND ITS TREATMENT FOR THE PATIENT

Since the cooperation of the patient is a prerequisite for the successful therapy of joint dysfunction, it was found desirable and necessary before treatment of joint dysfunction was instituted to discuss with the patient his various clinical problems (including the dynamic nature of joint dysfunction, and its response to niacinamide treatment, and the dynamic nature of certain complicating syndromes, and their appropriate treatment), and the therapeutic goals. During the course of therapy, it may become necessary to review and amplify this discussion for the benefit of the patient as various clinical problems arise.

Joint dysfunction is the articular aspect of a generalized, usually slowly progressive metabolic disorder which is corrected in time by adequate niacinamide therapy. Since the retrograde changes in tissue structure and function which characterize this disorder occur insidiously over a period of years, many of its symptoms and signs are incorrectly attributed by laymen and physicians alike to the so-called "normal" aging process. But these retrograde changes in morphology and function of bodily tissues are usually reversible in time when adequate levels of niacinamide are supplied continuously to bodily tissues. The patient who takes continuously adequate amounts of niacinamide experiences, in addition to improvement in joint function, an improvement in his general health.

Theoretically, optimal nutrition must be continuously available to bodily tissues to ensure the best possible structure and function of tissues (104) (108). While we do not know what constitutes optimal nutrition, it has been demonstrated empirically that even persons eating a good or excellent diet according to present-day standards exhibit measurable impairment in ranges of joint movement which tends to be more severe with increasing age (see page 153). It has also been demonstrated that when such persons supplement their good or excellent diets with adequate amounts of niacinamide, there is, in time, measurable improvement in ranges of joint movement, regardless of the patients' ages. In general, the extent of recovery from joint dysfunction of any given degree of severity depends largely on the duration of adequate niacinamide therapy (see pages 187 and 188).

With the ingestion of adequate amounts of niacinamide continuously for a sufficient period of time, a patient whose ordinary diet is not inadequate in protein or calories, whose joints are not subjected to excessive mechanical trauma, will recover from joint dysfunction at the satisfactory rate of 6.0 to 12.0 Joint Range Index units, or better, in the first month of therapy, and 0.5 to 1.0 Joint Range Index unit, or better, for each month of therapy thereafter, until a Joint Range Index of 96-100 is reached. (Rarely, when a patient has one or more ankylosed joints, he may have no appreciable active or passive movement of these ankylosed joints, even after two years of adequate niacinamide therapy, although his other joints recover the full ranges of movement in response to such therapy. In such cases, the Joint Range Index cannot reach 96-100; e.g., when one wrist is ankylosed and has not shown increased movement in response to niacinamide therapy, the maximum Joint Range Index attainable is 90.9; and when both wrists are ankylosed, the maximal Joint Range Index attainable is 81.8.)

In general, the more severe and more chronic the patient's joint dysfunction, the slower is the rate of recovery in response to adequate niacinamide therapy, and the slower his subjective appreciation of improvement. The rate of recovery for each patient must be established empirically from serial determinations of the Joint Range Index. In order to ensure a continuously satisfactory rate of recovery from joint dysfunction, the physician must re-examine the patient at intervals during the course of niacinamide therapy. Whenever a patient taking the amounts of niacinamide prescribed by the physician, and eating a good or excellent diet, fails to make satisfactory improvement in his Joint Range Index, in the absence of excessive mechanical joint injury the niacinamide schedule must be revised upward to that level which permits satisfactory improvement. Failure of the patient to take niacinamide as directed will result in failure to improve at a satisfactory rate.

When a patient has joint dysfunction associated with obvious arthritic deformities, he is told that the physician cannot predict whether or not in his case articular deformities will resolve with adequate niacinamide therapy. However, in response to adequate niacinamide therapy for a sufficient period of time, other patients have shown partial or complete resolution of their arthritic joint deformities. Some patients with arthritic deformities show resolution of some of their joint deformities, but not of others. Only careful observation of the patient's deformities on serial re-examinations will indicate whether or not his deformities are resolving in response to adequate niacinamide therapy. In most instances, the rate of resolution of the deformities will be slow, if it occurs at all.

It cannot be predicted whether or not a given joint that appears to be completely ankylosed clinically will recover any degree of movement. It has been observed many times that joints appearing to be clinically ankylosed prior to therapy tend to have partial or complete recovery of movement in response to adequate niacinamide therapy, although some ankylosed joints have not shown any degree of movement as a result of therapy during an observation period of several years. In response to adequate niacinamide therapy over a sufficient period of time some patients have partial or complete recovery of movement in some of their ankylosed joints, but not in others. Only careful observation of the ranges of joint movement on serial re-examinations will demonstrate whether or not a given ankylosed joint can recover any degree of movement in response to adequate niacinamide therapy.

In general, in the absence of complicating factors, the higher the patient's Joint Range Index rises in response to adequate niacinamide therapy, the fewer articular symptoms he will have; and the better he will feel. However, even though the Joint Range Index increases satisfactorily in response to adequate niacinamide therapy, the patient may not feel well because of complicating syndromes which are not on the basis of aniacinamidosis. Careful clinical study is necessary in order to establish the etiology of whatever complicating syndromes may be present and, with appropriate therapy, the patient is likely to become free from articular symptoms and to feel well. However, at any time symptoms of bodily discomfort may recur which must be studied and given appropriate treatment as promptly as possible, if the patient is to feel well again. While the patient may obtain temporary relief from articular and other symptoms through the

use of analgesics, narcotics, sedatives, antihistaminics and local anesthetics, only adequate treatment of joint dysfunction and the complicating syndromes is likely to give more lasting benefits.

In order to assess the effects of niacinamide therapy on joint dysfunction and on the patient's general status, the patient is usually re-studied one month after continuous niacinamide therapy has been instituted. If good progress in recovery from joint dysfunction is noted at that time, he is reexamined in two months, and thereafter every three to six months. For the most part, this schedule of re-examination is found to be satisfactory for the supervision of the therapeutic program of patients presenting the chronic problems of joint dysfunction, although when the individual's problems are of unusual complexity, or when intercurrent problems arise, the time interval between visits is shortened.

When a patient with joint dysfunction fails to make the anticipated progress in response to niacinamide therapy, he is asked if he has taken the medication as prescribed; if not, he is urged to do so. (When a patient has taken multiple vitamin capsules as prescribed and has not made satisfactory improvement in his Joint Range Index in response to such therapy, the druggist is asked how the vitamin powders were compounded. The clinical effectiveness of niacinamide seems to be lessened when niacinamide is mixed with ascorbic acid by vigorous trituration, since this favors inter-molecular reactions between niacinamide and ascorbic acid in the dry powder state. The occurrence of such inter-molecular reactions between niacinamide and ascorbic acid is hindered by the preliminary admixture of each dry powder separately with a small amount of calcium stearate (0.2%) before the final admixture by sieving.)

It is always emphasized that the patient must take his medication continuously as prescribed until such time as the supervising physician may decide, on the basis of objective clinical evidence, that it is necessary to increase the level of niacinamide therapy in order to produce continuously satisfactory improvement in the Joint Range Index.

However, certain factors other than the ingestion of inadequate amounts of niacinamide may tend to depress the Joint Range Index. These include (a) transient or persistent mechanical joint injury resulting from unusual or physical exertion (see page 79) or from psychogenically sustained hypertonia of somatic muscle (see page 115), (b) rapid and excessive gain in weight to obesity levels, (c) excessive ingestion of alcohol, (d) inadequate dietary protein. When any of these factors is operative, it is of limited value to increase the amounts of niacinamide taken by the patient in an effort to effect satisfactory improvement in the Joint Range Index. Instead, treatment should be directed toward lessening the degree of mechanical joint injury, reducing the patient's weight to the normal range, interdicting alcohol, and increasing the protein intake to adequate levels, respectively.

When indicated, the physician describes for the patient four complicating syndromes frequently coexisting with joint dysfunction, and their treatment (see page 76). Most of the articular and non-articular symptoms of a patient with joint dysfunction which are not corrected by niacininide therapy usually originate as part of these four complicating syndromes. When the patient understands the etiologic basis of his symptoms, he will not have anxiety concerning the meaning of symptoms which would otherwise seem mysterious and alarming. The patient with joint dysfunction who has one or more of these complicating syndromes is told that he will not feel well unless joint dysfunction and these coexisting syndromes are correctly identified and successfully treated, and that in order to accomplish this, his active participation in the clinical investigation and therapeutic program is required.

TYPICAL IMPROVEMENT IN MOBILITY OF A SINGIE JOINT IN RESPONSE TO LEVELS OF NIACINAMIDE THERAPY USED PRIOR TO APRIL 1947

In serial determinations of the mobility of single joints in response to levels of niacinamide therapy used prior to April 1947, it was found that niacinamide-induced recovery of full joint mobility was an orderly process. (Since April 1947, when higher

dosage schedules of niacinamide were introduced (see page 21), there has been a marked reduction in the incidence of articular pain and discomfort upon maximal passive movement of the moveable joints during various stages of recovery from joint dysfunction.)

There is described below typical improvement in joint mobility, as illustrated by several sequential stages occurring during niacinamide-induced recovery of full mobility of the metacarpophalangeal (knuckle) joint.

(Figure 14 is a schematic representation of maximal passive extension of the meta-carpophalangeal joint at four successive stages (a) (b) (c) (d), during the course of niacinamide-induced recovery of full joint mobility. The line touched by the head of the arrow in (a) (b) (c) (d) indicates the upper limit of painless extension. The shaded angle in (b) and (c) indicates the range of painful passive extension.)

Figure 14(a). On the initial examination before niacinamide therapy was instituted, the metacarpophalangeal joint of the forefinger of the right hand could be extended passively to 30% of the full range of extension for this joint. No pain or discomfort was experienced by the patient during this maneuver. The examiner noted the presence of palpatory resistance from the initiation of the movement of passive extension of this metacarpophalangeal joint, and this resistance progressively increased as the joint was extended from the range of 0% to 30% of the maximal extension; the palpatory resistance at the end of the movement was graded as firm. When at the 30% level of passive extension a small increase of force in the direction of extension caused no further extension of this joint, 30% of the full range of extension was taken as the upper limit of maximum passive extension of this metacarpophalangeal joint.

Figure 14 (b). At the end of one month of continuous, adequate niacinamide therapy, maximal passive extension of this metacarpophalangeal joint increased to 60% of the full range of extension. No pain or discomfort was experienced by the patient when the metacarpophalangeal joint was extended from 0% to 40% of the full range of extension. The patient experienced localized joint pain, often severe, as the joint was passively extended from 40% to 60% of the full range of extension. The examiner's palpatory sensation indicated that movement of the joint in passive extension was free from 0% to 40%, and that there was soft, yielding resistance which progressively increased as the finger was extended at the metacarpophalangeal joint from 40% to 60% of the full range of movement. When a further small increase of the extending force did not increase the degree of extension, 60% of the full range of extension was taken as the upper limit of passive extension of this metacarpophalangeal joint. The palpatory resistance at the end of the movement of extension was rubbery.

Figure 14 (c).After months of continuous, adequate therapy with niacinamide, maximal passive extension of the metacarpophalangeal joint reached 100%; i.e., the full range of movement. Passive extension of the metacarpophalangeal joint from 0% to 85% was without pain or discomfort; passive extension from 85% to 100% was painful. The examiner's palpatory sensation indicated that the movement of this joint was free from 0% to 85%, and that there was soft resistance, which increased progressively with increasing extension of the metacarpophalangeal joint from the level of 85% to 100%. A small additional force in the direction of extension when the 100% level was reached did not cause further extension of this joint. The palpatory resistance at the end of the full range of movement (100%) was rubbery.

Figure 14(d). With a longer period of continuous, adequate niacinamide therapy, it was possible to achieve full, free and painless extension of this metacarpophalangeal joint to the level of 100%. Slight additional palpatory force in the direction of extension with the joint fully extended did not increase the amount of movement beyond the full range of extension; i.e., the 100% level. The examiner's palpatory sensation indicated that the movement of extension was free from 0% to 100% of full extension, that the resistance met at the end of this movement was firm, and that the patient experienced no pain from this maneuver.

It would appear from clinical observations that, in the absence of joint trauma, there is an orderly and sequential pattern of recovery of joint mobility in a patient with joint dysfunction in response to continuous, adequate niacinamide therapy provided that the patient's diet is not inadequate in protein Or calories. Serial re-examinations of joint ranges during the course of continuous, prolonged, adequate niacinamide therapy reveal that with the passage of time, there are the following changes:

(a) progressive increases in ranges of joint movement;

(b) progressive shifting of painful zones of joint movement toward the periphery of the most recently acquired zones of increased ranges of joint movement, until, ultimately, after the fullest range of movement for the joint has been achieved, there is absence of pain on the execution of the fullest movement possible for the joint in the specified range; and,

(c) progressive shifting of zones of resistance to passive movement toward the periphery of the most recently acquired zones of increased ranges of joint movement until, ultimately, after the fullest range of movement for the joint has been achieved, there is no resistance to passive movement on the execution of the fullest range of movement possible for the joint in the specified range of movement.
These dynamic changes in joint mobility occurring during the course of treatment suggest that sequential alterations in joint morphology must occur in response to continuous, adequate niacinamide therapy to permit the observed changes in joint mobility described above.

With cessation of adequate niacinamide therapy, the therapeutically-improved joint mobilities cannot be maintained for any prolonged period of time.

SELECTED CASE HISTORIES ILLUSTRATING THE THERAPEUTIC RESPONSE OF JOINT DYSFUNCTION TO NIACINAMIDE ALONE OR IN COMBINATION WITH OTHER VITAMINS

This section presents selected case histories which illustrate and emphasize the dynamic nature of joint dysfunction, with and without clinically obvious arthritis, as demonstrated by changing values of the Joint Range Index over a period of time in response to various levels of niacinamide ingestion. Twenty case histories, abbreviated in various degrees, are presented, together with a figure for each case which summarizes both the response of the Joint Range Index to the type of vitamin therapy employed, and the amounts of the vitamin(s) administered per 24 hours. A few figures summarize additionally the changes observed in the Sedimentation Rate during therapy.

Cases A through K have been chosen to demonstrate the effect on joint dysfunction of (a) adequate therapy with niacinamide, (b) reduction of niacinamide from adequate to inadequate levels, and (c) premature discontinuance of niacinamide therapy.
Cases L through T show the effects on joint dysfuntion of adequate and for the inadequate therapy with niacinamide administered in combination with of the other vitamins. Whenever adequate doses of niacinamide are given in combination with other vitamins to persons with joint dysfunction, improvement in joint function, as indicated by rising values of the Joint Range Index, is of the same order as would be anticipated if niacinamide in the amounts present in the vitamin mixture were the sole therapeutic agent. It will be demonstrated by these case histories that joint dysfunction (with or without clinically obvious arthritis) is ameliorated in time by adequate therapy with niacinamide (alone or in combination with other vitamins). This is true regardless of age, sex, occupation, geographic origin, economic level, or associated diseases. Whenever adequate therapy with niacinamide is replaced by inadequate therapy or by premature cessation of adequate niacinamide therapy, there is a worsening of joint function which in time is reflected by decreasing values of the Joint Range Index.

Whenever inadequate therapy with niacinamide is replaced by adequate therapy with niacinamide, joint function again improves, as measured by increasing values of the Joint Range Index. In general, the expectancy is that, with adequate niacinamide

therapy for a sufficiently long period of time, the patient's joint function will improve continuously so that ultimately the Joint Range Index will measure between 96 and 100 (no joint dysfunction) and will be maintained at this level for as long as the amount of niacinamide ingested by the patient continues to be adequate for his bodily needs. In the absence of severe mechanical joint injury, when the diet of the patient is not inadequate in protein or calories, two stages are observed in the recovery of joint dysfunction in response to adequate niacinamide therapy. First, there is the initial large increase in the Joint Range Index of at least 12 units which occurs in a month or less. (At the end of one week of continuous adequate therapy with niacinamide alone or in combination with other vitamins, those few persons whose Joint Range Indices were determined at this interval had an increase in the Joint Range Index which was of the same order as that usually observed at the end of one month of therapy.)

This rapid initial improvement in the Joint Range Index is, in all probability, largely the result of the resolution of tissue edema in response to adequate niacinamide therapy (97) (189). Associated with this rise in the Joint Range Index, the patient often has marked subjective improvement in feeling tone. The next stage of recovery from joint dysfunction is slow, with a gradual increase in the Joint Range Index of at least 0.5 to 1.0 unit per month. Recovery from joint dysfunction in response to treatment with niacinamide is considered to be clinically satisfactory, and the dosage of niacinamide is considered to be adequate, when the Joint Range Index increases at the end of the first month and thereafter within the limits of recovery for these time intervals as defined above. A lesser rate of recovery in joint dysfunction in response to niacinamide therapy is judged to be unsatisfactory, and the niacinamide dosage schedule is then increased to a level which will permit recovery from joint dysfunction at a satisfactory rate (provided that the patient is not subsisting on a low-protein diet).

Since there are wide individual variations in the need for niacinamide, the physician must determine empirically for each patient that level of niacinamide therapy which will produce satisfactory improvement in joint dysfunction. On the whole, the suggested dosage schedules (see page 22) will cause satisfactory improvement in joint dysfunction. However, on any of these dosage schedules, at any time there may be stabilization of the Joint Range Index until the dosage level of niacinamide is suitably increased, whereupon the Joint Range Index will rise again in a satisfactory manner. In order for the patient to make the best possible progress in recovery from joint dysfunction, periodic re-examinations must be performed by the physician so that the niacinamide dosage schedule may be adjusted as necessary to ensure serially rising values of the Joint Range Index until the level of 96-100 (no joint dysfunction) is reached, and subsequently, to maintain the patient at this level.

In recovering from joint dysfunction, especially of a severe grade, a patient is likely to be less impressed by the physician's Opinion that satisfactory improvement has been made in response to adequate niacinamide therapy, than by his own sudden realization that he is again able to use his body in ways that were impossible for a long time before the institution of niacinamide therapy; e.g., he is able to turn his head enough to enable him to park his car without difficulty; he can go up and down stairs with ease; after sitting in a movie theatre for hours, he does not experience prolonged stiffness and discomfort upon arising from his seat; he can trim his toenails without difficulty.

The selected case histories presented below demonstrate the usefulness of the routine determination of the Joint Range Index in evaluating the severity of the patient's joint dysfunction, in following his response to niacinamide therapy, and in regulating dosage levels of niacinamide during the course of treatment. However, in most instances, if the patient who is recovering from joint dysfunction is to feel well, it is also necessary to evaluate whatever additional coexisting clinical problems he may have, and to institute whatever therapeutic measures may be indicated. In subsequent sections, certain complicating syndromes will be described, which may cause arthralgia as well as other articular and non-articular symptoms, often complicating the treatment of joint dysfunction.

CASE A. No.309, female, age 26, housewife, married.

This case history illustrates, in a woman with clinically obvious rheumatoid arthritis, (a) improvement in joint function as measured by increasing values of the Joint Range Index in response to adequate niacinamide therapy, (b) impairment in joint function as measured by a lowered Joint Range Index as a result of substitution of inadequate for adequate therapy, and brief cessation of therapy, and (c) subsequent improvement in joint function as measured by an increased Joint Range Index in response to the re-introduction of more adequate niacinamide therapy. (These results are summarized in Figure 15.)

When she was 16 years old, she was hospitalized for special study of her joint disorder, and was informed upon completion of this clinical investigation that she had arthritis. Her bone and joint symptoms were not ameliorated by the therapeutic program which was then recommended, and, indeed, became progressively worse, especially since her marriage at the age of 20, when she first started to do housework. The amount of her housework was considerably increased in volume after her two children were born.

Her presenting complaints include marked limitation of motion and pain (both at rest and on the initiation of joint movement) in the hip joints, knees, low back, neck, and fingers. She states that these joint symptoms are becoming progressively more severe, and are worsened by changes in weather and by any form of physical activity, including her housework. Although she has worn many different types of shoes, her feet have never been comfortable. She is irritable and tired, and frequently awakens during the night because of joint discomfort and muscular aching. Often she awakens in the morning feeling more tired than she did when she went to bed the night before.

Physical Examination: B.P. 130/80. P. 84. R. 18. T. 99.4 degrees. Wt. 135 lbs. Ht. 65 ½ inches. She seems tired, and looks older than her stated age. She moves slowly, as if guarding against rapid movements of her joints which might give her increased pain. Her posture is poor. Slight dorsal kyphosis and slight pelvic tilt are evident upon inspection. Her proximal interphalangeal joints of the fingers of both hands are thickened and swollen. Her skin is yellow, dry, slightly inelastic, and has a prominent reticular pattern. She has severe tenderness on moderate digital pressure over the maxillary and frontal sinuses, over the chondral ribs, the lower third of the sternum and chondrosternal junctions, the right trochanter, the lowermost third of the tibias bilaterally, the third, fourth and fifth cervical vertebrae and the lumbar vertebrae.

The liver edge is at the level of the costal margin in the right mid-clavicular line at the end of deep inspiration, and is tender to palpation. Her tongue shows hyperemia of the anterior third and atrophy of papillae. Her teeth are in good repair, although the gums are slightly retracted, infiltrated and swollen. Her conjunctivae are slightly thickened, and show some increased vascularity. Tickle sense is absent everywhere. She has hypopallesthesia. Her initial Joint Range Index (65.6) indicates severe joint dysfunction.

She was given 100 mg of niacinamide to take every 3 hours for 6 daily doses (600 mg/24 hours) and in one month there was improvement in her Joint Range Index and in her general health. She appeared less tired. She stated that she had experienced less pain, stiffness and limitation of movement since treatment with niacinamide had been instituted. Her color had improved, and her skin appeared less yellow. Her liver was not tender to palpation. The tenderness on digital pressure over the bony prominences, which was so marked on the previous examination, had practically disappeared. Tickle sense was present. She had recovered normal vibratory sensation. However, since the rate of recovery of her lingual mucous membrane in response to therapy with niacinamide was considered to be somewhat slow, the dosage of niacinamide was increased to 100 mg. every 1 ½ hours for 9 daily doses (900 mg/24 hours). She took this amount of niacinamide daily for about 300 days, and showed subjectively and objectively continuous and progressive improvement. The numerical value of her Joint Range Index rose from 65.6 to 90.2 in 300 days. Thus, according to the Clinical Classification of Joint Function, she had progressed from severe joint dysfunction to slight joint dysfunction.

Since she had shown an excellent response to therapy, she was asked to return for her next re-examination in six months, at which time her Joint Range Index had fallen to

78.2, with a concomitant return of many of her presenting symptoms. Upon inquiry, the following facts were elicited:

Shortly after her last visit, she knew that she was feeling better than she had ever felt in her life and thought, therefore, that she was "cured." She gradually decreased her niacinamide intake, and finally, for three weeks before her examination, took none.

As a result of her self-prescribed change in the therapeutic program, she had regressed clinically in all respects. Clinically, her joint dysfunction regressed from slight (90.2) to moderate (78.2). A new dosage schedule of niacinamide was prescribed (150 mg every 3 hours for 6 daily doses, or 900 mg/24 hours), which she took faithfully.

When therapy with niacinamide was thus re-introduced, her Joint Range Index was 78.2. In 84 days it rose to 86.4, and in 184 days to 91.2. Thus, she had again progressed from moderate to slight joint dysfunction. Her symptoms referable to bones and joints disappeared, and there has been progressive resolution of her abnormal physical signs.

Since she has gained some insight into the dynamic nature of her joint dysfunction, it appears likely that this patient will continue with her therapy as directed. It is anticipated that with continuously adequate niacinamide therapy she will in time achieve a Joint Range Index of 96-100 (no joint dysfunction).

CASE B. No.147, female, age 61, housewife, married.
This case history illustrates, in a woman with severe hypertrophic arthritis, (a) improvement in joint function, as measured by an increased Joint Range Index in response to a given dosage of niacinamide, (b) slight impairment in joint function as measured by a lowered Joint Range Index resulting from a small decrease in the niacinamide dosage from the previous level, and (c) an accelerated improvement in the Joint Range Index as a result of two successive increases in the niacinamide level (see Figure 16).

She has had joint discomfort for many years, and moderate deformities of the fingers for at least 10 years. Six to seven years ago she first noticed severe pain in her hip joints. Her knees are very stiff. All her life she has had curvature of the spine, and has had a good deal of pain in the back. Recently she has had increased fatigability and insomnia.

Physical Examination: She looks older than her stated age. B.P. 140/80. Wt. 159 ½ lbs. Ht. 65 inches. She has tenderness on digital pressure over the sternum, medial epicondyles, iliac crest, trochanter, styloid process of the radius, sacroiliac joints. Marked kyphoscoliosis is noted. Her tongue shows evidences of infiltration and atrophy of papillae. The edge of the liver, which is one finger's breadth below the rib margin in the right mid-clavicular line on deep inspiration, is tender to palpation. Bony prominences of the lower extremities are hyperpallesthetic to the tuning fork. Tickle sense is absent. Plantar dysesthesia is present.

This patient had severe joint dysfunction, as measured by her Joint Range Index of 68.2. She was asked to take 100 mg. of niacinamide every 1½ hours. In a month, she had experienced marked improvement in her Joint Range Index, and considerable subjective relief from joint discomfort. The plantar dysesthesia was no longer present. Liver enlargement had diminished markedly (liver tenderness and enlargement disappeared after a longer period of therapy). Hyperpallesthesia of the lower extremities was replaced by a normal vibratory sensation. Tongue showed the improvement expected with one month of niacinamide therapy. She looked younger than on her initial visit. She had no further difficulty with fatigability or insomnia.

She continued to make good progress clinically for over 300 days, when she reduced her niacinamide intake from 1200 mg/24 hours as originally prescribed, to 1000 mg./24 hours in divided doses of 100 mg. per dose. With this self-administered reduction in niacinamide dosage, her Joint Range Index decreased from 85.5 to 84.9.

The level of niacinamide was increased to 150 mg. every 1 ½ hours (1500 mg/24 hours) with an increase in her Joint Range Index from 84.9 to 90.1 in 267 days. The niacinamide dosage was then increased to 200 mg. every 1½ hours (2000 mg./24 hours) with an increase in the Joint Range Index from 90.1 to 92.8 in 58 days.

Thus, in a period of almost two years, this patient's Joint Range Index rose from 68.2 (severe joint dysfunction) to 92.8 (slight joint dysfunction). It is anticipated that with continuously adequate niacinamide therapy, she will in time achieve a Joint Range Index of 96-100 (no joint dysfunction).

CASE C. No.325, female, age 63, housewife, married.

This case history illustrates, in a woman with moderate hypertrophic arthritis, continuous improvement in joint function, as measured by increasing values of the Joint Range Index in response to adequate niacinamide therapy (Figure 17 summarizes this case).

For more than 10 years, she has had "chronic rheumatism," as well as many episodes of "acute rheumatism" characterized by painful transient swellings of her hands, wrists, knees and ankles. Her present complaints include generalized stiffness of joints (severe for an hour after she awakens in the morning) and accentuation of muscular, periosteal and articular discomfort with weather changes. While her wrists, shoulders and fingers have been painful and swollen "off and on," her knees have given her the greatest, most persistent discomfort. In the past year her knees have become so painful that she has had many sleepless nights.

Physical Examination: B.P. 170/80. Wt. 180 lbs. Ht. 61 ¾ inches. She is moderately obese, tired-looking, hyperkinetic. Her skin is relatively inelastic, has increased brownish pigmentation, and the normal reticular pattern is accentuated. The conjunctivae show thickening and increased vascularity. She has some circumcorneal injection. Her teeth are in good repair. The gingival membrane is thickened and retracted, but there is no evidence of gingival infection. Her tongue shows marked atrophy and infiltration of lingual papillae. Her Joint Range Index of 65.8 indicates severe joint dysfunction. She has a moderate upper dorsal kyphosis. Her wrists, fingers and knees are swollen. No objective signs of impaired nerve function are elicited. Her Sedimentation Rate Index is 0.4 mm/min. (Wintrobe-normal range 0.1 - 0.3 mm/min.). Hemoglobin 11.8 g./100 cc. (acid hematin photo-electric colorimeter). An x-ray of her knees taken immediately before therapy was instituted showed evidence of a hypertrophic type of osteoarthritis.

Niacinamide (150 mg every 3 hours for 6 daily doses, which is 900 mg/24 hours) was prescribed. After one month of therapy, she reported subjective improvement in her general feeling tone. Objectively her skin and tongue showed improvement. The prominent swellings had disappeared from the sites enumerated above. Her kyphosis seemed less prominent. She appeared younger and more vigorous than when first seen.

She stated on her fourth visit that she felt almost entirely free from all joint discomfort at the end of about 100 days of continuous therapy with niacinamide. She was particularly pleased that she was no longer awakened at night by knee pain. Objectively, her tongue and skin continued to show resolution of the abnormalities noted at the initial examination.

During five months of treatment, she has made objective improvement in joint function, as indicated by an increase in the Joint Range Index from 65.8 (severe joint dysfunction) to 83.2 (moderate joint dysfunction).

CASE D. No.461, female, age 68, widow, invalid.
This case history illustrates, in a woman with severe chronic rheumatoid arthritis, improved joint function as measured by increasing values of the Joint Range Index and by decreasing values of the Sedimentation Rate Index in response to therapy with niacinamide in the early months of such therapy (see Figure 18).

Much of the initial history had to be elicited with the patient reclining on a couch because she was too tired to sit up. She states that she had her first attack of "acute rheumatism" more than 40 years ago. These attacks of "rheumatism" recurred irregularly at frequent intervals until 2 years ago, when they apparently ceased. They were characterized by abruptly increased swelling, stiffness, pain and limitation in the range of joint movement. The joints were hot to the touch, but not red. In the course of these various attacks, not a single joint or joint group the body was "missed." However, not all of the joints were involved at any one time. The acute episodes usually lasted 2 or 3 days and were followed by her ordinary chronic joint discomfort, which was somewhat more endurable than the severe exacerbations of her difficulty. However, in the past 5 years, her chronic discomfort and disability have increased so much that she doesn't think "it's worth going on living this way.

For more than 25 years, she has had severe deformities which have become progressively worse, so that now her hands are of little use to her. In addition, her wrists, elbows, shoulders, knees, ankles, feet (including the toes) are deformed, swollen and painful. For many years she has not been able to move her right wrist actively or passively, presumably because of complete ankylosis of the wrist joint; the range of movement of the left wrist is negligible. The ulnar deviation of her fingers prevents her from doing very much with her hands. She cannot raise her arms in abduction high enough to comb her hair nor can she fully extend her elbow joints. She is unable to flex or extend her ankles appreciably. Her toes are fixed in abnormal positions by joint deformities. Her knees, the most painful joints in her body, are hot and swollen. She thinks her knees have become markedly worse in the past year. Even with assistance she can scarcely get out of a chair because the pain in her knees is so severe that she thinks her legs might suddenly “let go." She is unable to walk upstairs and for years has lived on the first floor of her house. For more than 5 years, she has been unable to turn her head. If she wants to see someone behind her or to the side, she has to turn her whole body. For the past 5 years when she wakes at night and wants to turn her head, she has to turn her whole body in bed since her neck won't turn. Since her knee deformities do not permit full extension of these joints, when she is recumbent in bed she has to have two large pillows under her knees to support them in the least uncomfortable position. When she arises in the morning she is "terribly stiff" for about an hour. This severe stiffness recurs late in the afternoon.

During the past 5 years, she has had severe wasting of the muscles everywhere, but most markedly in her forearms and hands. She has suffered for the past 10 years from paresthesias of certain fingers of her hands.

She has an allergic colitis which is subject to exacerbations when she eats certain offending foods, such as milk, onions and chocolate. In the past 5 years, she has slowly and progressively lost more than 40 pounds in weight. She is so tired that for the past 5 years she has been unable to be up for longer than half an hour at a time.

Her arthritis had not been helped by any form of treatment which she had received to date.

Physical Examination: She is an extremely tired, crippled, chronically ill woman who is emaciated and has practically no subcutaneous fat. Extreme wasting of somatic musculature is noted. Wt. 90 ¾ lbs. Ht. 67 ¾ inches. B.P. 124/82. P.80. R. 18. Grips: R. 24, L. 20 (normal range for women 60-80). The skin is inelastic and thickened everywhere. There is a pervading color of light brown that is not sunburn. The reticular pattern of the skin is moderately accentuated. Severe callusing of the feet is noted. There is marked swelling noticeable in her face, around her elbows, wrists, fingers, knees, ankles, feet. Digital pressure over the bony eminences causes no pain, although severe pain can be elicited from every moveable joint upon maximal passive or active movement. Examination of the eyes reveals circumeorneal injection and conjunctival thickening. The optic disc out-lines are not distinct. Arteries are slightly tortuous, being narrowed from 0 to 2-plus; the veins and arteries are 2-plus infiltrated. No nicking or engorgement is seen. The vermilion borders of the lips are thickened and magenta-colored. No cheilosis is noted. The gums show slight pitting and moderate infiltration

and retraction. The tongue is magenta-colored, and its substance is swollen. The lateral lingual margins show complete atrophy of all papillae. Elsewhere, fungiform papillae are extinguished and filiform papillae are atrophic. There are many transverse fissures in the lingual mucous membrane. Her thyroid gland is 1-plus enlarged in the isthmus, but the lobes are not enlarged. Trachea in the midline. Chest is negative to auscultation and percussion excepting for emphysema. Heart is enlarged by percussion, the point of maximal impulse being 8 ½ cms in the 6th intercostal space. She has a soft, 1-plus non-transmitted mitral systolic murmur. Apical sounds are distant and of fair quality. No liver tenderness. No organs or masses are felt in the abdomen. Her temporal, branchial and radial arteries are slightly thickened. Her abdominal arteries, aorta, right and left internal iliac vessels are thickened and tender. Right and left posterior tibials pulsate 3-plus and are firm. The dorsalis pedis arteries are not palpable. She has moderately severe dorsal kyphosis and swollen ankles, knees, wrists and fingers. The fingers, held in marked ulnar deviation, are markedly deformed, as are her toes. The wrists are apparently ankylosed. Crepitus is elicited from the neck joints and from all moveable extremity joints. Vibratory sensation in the right lower extremity (toes, malleolus and tibia) is more marked than in the left. Vibratory sensation in the upper extremities within normal limits. No plantar dysesthesia. Tickle sense 2-plus on forehead, absent elsewhere. Sense of light touch and sense of motion and position are intact.

Urinalysis negative. Hemoglobin 9.0 g/100 cc (acid hematin photoelectric colorimeter). Sedimentation Rate Index 1.65 mm/min. (Wintrobe-normal 0.1-0.3 mm/min.).

Her Joint Range Index was 45.0, indicating extremely severe joint dysfunction. (In order to obtain an initial value for her Joint Range Index, measurement of hip and knee ranges used in computing the Joint Range Index was made in the usual way, save for the fact that the marked flexion deformities of the knees caused some pelvic tilt with the patient recumbent. However, on the 139th day, the flexion deformity of the knees could no longer be demonstrated. Also, since the fixation of the fingers of the deformed hands did not permit extension of all of her fingers to the zero, or neutral level - i.e., the level where the finger would be neither flexed nor extended - a new convention was introduced in this instance. When the fingers on maximal extension did not reach the zero line, the percentage of the quadrant between the dorsura of the finger being measured and the zero line was noted with a minus sign, and tile finger index was derived in the usual way, adding algebraically the various measured values obtained for each hand.)

She was asked to take 150 mg of niacinamide hourly during the day (2400 mg/24 hours). After 34 days of such therapy, she stated that she had been feeling stronger, and that she tired somewhat less readily than formerly. She stated emphatically that her shoulders were almost entirely comfortable, and moved much more freely. She could comb her hair for the first time in 5 years. Her knees were still painful, and she was not as "spry getting out of a chair" as she would like to be, but she was able to get out of a chair without assistance. Her color, she thought, had improved.

When she walked, she held herself more erectly and moved with better balance than she had when first seen. She seemed mentally alert and responsive. She was able to get up from her chair without assistance, although she had some difficulty in doing so, and some pain in her knees. Her skin had become a little more elastic and was lighter in color. The reticular pattern of the skin was less prominent. Her lingual mucous membrane showed some signs of improvement. The tissue swellings previously noted had almost disappeared. She had gained 1 ¼ lbs in weight. Her Joint Range Index had increased from 45.0 to 58.5. The venous pattern around the knee joints was much less prominent than it had been when she was first seen. She could extend her knees almost completely, and was able to lie flat on the examining table without a pillow under her head, and required only a small pillow under her knees for comfort. The ulnar deviation of the fingers was less marked than when she was first seen. The Sedimentation Rate Index had improved slightly, having declined from 1.65 to 1.50 mm/min. In 76 days of treatment with niacinamide, her Joint Range Index had stabilized at 58.2. There was no discernible tissue edema. She had had further improvement in her feeling tone. She was very much more comfortable physically, and was troubled

hardly at all by pain and discomfort in her joints. Her stiffness was markedly decreased. Since her Joint Range Index had apparently stabilized, the dosage of niacinamide was increased so that she took on alternate hours 150 mg and 200 mg of niacinamide (2800 mg/24 hours).

In 139 days she had a Joint Range Index of 61.5. She thought that her was improved considerably. She weighed 5 lbs. more than when first seen. She was generally more cheerful and seemed to be more youth-in appearance and behavior. She could now be up for several hours at a time without requiring a nap. She was able for the first time in many years to go upstairs without assistance, although she still had moderate pain in her knee joints on doing so. She could get out of a chair easily without assistance and with very little discomfort. She was able to lie flat on the examining table without pillows under her head or knees, and without pain or subjective discomfort. Her Sedimentation Rate Index had decreased from 1.50 mm/min. (34th day) to 0.44 mm/min. (139th day). Her niacinamide schedule was increased from the previous level to 250 mg per hour (4000 mg/24 hours), since it was felt at this time that the severity of her joint dysfunction warranted such a therapeutic trial at that time.

About 3 weeks before her next scheduled visit, she was feeling so well that she took liberties with her diet, eating foods (milk, onions, chocolate) to which she knew she was extremely allergic. The ingestion of these offending foods activated her allergic colitis, as a result of which she lost 4 lbs. in 10 days. She had resumed her usual diet (avoiding milk, onions and chocolate) about 10 days before her visit, and was again feeling better, although her colon was still somewhat irritable and hyperactive. Save for this interlude of allergic colitis, which she considered to be an unimportant incident, she felt very well physically.

In 202 days of niacinamide therapy, she was almost completely free from joint symptoms, including pain. Her Joint Range Index had risen from 61.5 (139th day) to 62.9 (202th day). Her elbows, which could not be fully extended initially, were now easily extended. Her right wrist, which had been clinically completely ankylosed, now moved 10% in extension and 0% in flexion. The left wrist, which on the initial examination had moved 0% in extension and 10% in flexion, now moved 15% and 50%, respectively. She was able to lie on the examining table without any pillows under her head or knees. She was able to get out of a chair as any normal person would. Her knees, which had been originally markedly swollen, were markedly decreased in size. Since the initial visit, there had been a decrease in the transverse diameter of the knees of 0.44 inch across the right knee and 1.38 inches across the left knee (measured across the broadest part of the knees).

Summary: This case history illustrates the effects of niacinamide therapy in the early months of such therapy in a person with extremely severe joint dysfunction (severe chronic rheumatoid arthritis of long duration). A summary of certain clinical and laboratory data obtained during the various office visits is listed in Table 0A.

Subjectively, as a result of treatment with niacinamide, in the early months of therapy this patient experienced a sense of well-being, including greater strength, less fatigability and freedom from joint pain and stiffness. She had less limitation in the ranges of joint motion. She had an increased appetite and enjoyment of food. She had a new zest for living.

Her weight loss between the 139th day and 202nd day was attributed to her allergic colitis, which she induced by eating foods to which she knew was hypersensitive.

Her severe hand deformities showed some signs of resolution, so that the fingers which were formerly fixed in ulnar deviation could now be passively brought into the normal position without pain. The wrist joints which were clinically ankylosed showed some tendency toward renewed movement, although objectively the right wrist was not considered to have shown significant improvement thus far. The left wrist showed marked improvement, and it is anticipated that in time, with continuously adequate niacinamide therapy, there will be further movement of this joint both in flexion and extension.

During the above period of clinical observation the increased Joint Range Index, decreased Sedimentation Rate Index, increased weight, decrease in joint swelling and in generalized tissue edema, increased hemoglobin, red blood count and hematocrit, all indicate the arrest and partial reversal of her severe chronic rheumatoid arthritis, as a direct result of therapy with niacinamide as the sole therapeutic agent. Further observation of this patient is necessary in order to determine the maximal degree of clinical recovery possible for her in response to continuously adequate niacinamide therapy over a much longer period of time.

CASE E. No.339, female, age 78, spinster.
This case history illustrates, in an elderly woman with severe acute rheumatoid arthritis (probably superimposed on mild chronic hypertrophic arthritis), improvement in joint function as evidenced by rising values of the Joint Range Index in response to adequate therapy with niacinamide (see Figure 19).

This woman considered that for her age she had enjoyed excellent health until 6 months ago, when her younger sister, aged 75, had a stroke. Before her sister's illness, the patient had never done much physical work. However, since the sister did not wish to be hospitalized, or to be taken care of by strangers, the patient undertook to give nursing care to her sister at their home. The bedrooms were on the second floor, and the patient made many extra trips up and down the rather steep flight of stairs, usually carrying her sister's meals to her. She was so busy with her sister's care that she neglected to eat her usual abundant diet, substituting starchy foods for high-protein foods.

After a month of such increased physical activity and change in her dietary habits, she was aware of pain, stiffness and swelling of her joints. She took 8-10 aspirin tablets (0.3 g) a day with only slightly increased comfort. Although prior to her sister's illness she had been able to go up and down stairs without difficulty, now she could not climb the stairs without gripping the banister with her left hand and pulling herself upward step by step in this way.

Her sister improved gradually over a period of several months, so that at the time of her initial visit she had much less to do physically, although she continued to have a high-carbohydrate diet. Her joints continued to give her trouble, so that she had constantly severe pain in the neck, severe low back pain, and painful swelling of the knees, ankles, wrists, hands, elbows and shoulder joints. She had persistent numbness and tingling of her hands, which were so swollen that she could not "make a fist." She noticed that many of her joints were extremely hot to the touch, and that she had considerable crepitus in most of her joints. Every morning for several hours she felt stiff, until the aspirin "took hold." Her stiffness recurred toward evening, when it was not relieved by aspirin. With changes in weather, she had increased joint discomfort. Her sleep was disturbed and restless because of her joint discomfort. She had lost 16 lbs. in the past 3 months. She felt that she was becoming progressively weaker, and felt exhausted most of the time.

Physical Examination: T. 99.2 degrees. P.74. R. 18. B.P. 150/90. Wt. 156 lbs. Ht. 62 ¼ inches. Grips: R. 20, L. 12 (normal range for women 60-80). She is a sick old lady who is apparently in great pain during the interview and physical examination. She seems dulled mentally. Her voice is quavery and quernious. She walks with extreme slowness and some dysequilibrium.

Her Joint Range Index is 62.9, indicating severe joint dysfunction. The joints of the left side of her body are somewhat more involved by the arthritic process than those of the right. She has marked dorsal kyphosis. Her knees, ankles, wrists, hands, elbows and shoulder joints show the marked swelling seen in classic rheumatoid arthritis. Prominent venous engorgement around the knees is noted. Her extremity joints are hot to the touch. A few subcutaneous periosteal nodules are felt on the ulna and tibia.

Her skin is yellow-brown and somewhat atrophic. The reticular pattern of the skin is accentuated. She has a few ecchymoses. Many hyperkeratotic hair follicles are observed on the extensor surfaces of her extremities. She has Bit6t spots. Her

edentulous gums are swollen and reddened. Her tongue shows hyperemia of the tip and lateral margins, and marked atrophy of papillae. Her heart is enlarged by percussion, the point of maximal impulse being felt 10 cm. to the left of the mid-sternal line in the 5th intercostal space. Throughout systole there is heard a 8-plus, moderately high-pitched, rough, non-transmitted aortic systolic murmur. The lungs are emphysematous but otherwise negative to physical examination. The liver margin is felt 3 fingers' breadth below the costal margin in the right midclavicular line at the end of deep inspiration, and is 8-plus tender. No other organs or masses are felt. Reflexes are within the range of normal. Her dorsalis pedis arteries are firm, pulsate 8-plus and are equal; her posterior tibial arteries are firm, pulsate 1-plus and are equal. Tickle sense is absent, but vibratory sense, sense of light touch and sense of motion and position are intact. Her Sedimentation Rate Index is extremely elevated, being 1.80 mm/min (Wintrobe-normal 0.14).3 mm./min.). Hemoglobin 11.4 /100 cc (acid hematin photoelectric colorimeter).

Niacinamide was prescribed, to be taken 150 mg. every 3 hours for 6 doses daily (900 mg/24 hours). After 22 days of this therapy, much of her joint swelling had resolved, although she still complained of pain and stiffness. She walked and sat more erectly than on her first visit. She walked with better balance, and more rapidly than she had originally. Her liver margin was palpated 2 fingers' breadth below the right costal margin in the right mid-clavicular line on deep inspiration, and was 2-plus tender. Her Joint Range Index had risen from 62.9 (severe joint dysfunction) to 73.2 (moderate joint dysfunction).

In 84 days of therapy, her Joint Range Index had apparently stabilized at 72.8. Although slight ankle edema still persisted, edema around other joints was no longer evident. Her Sedimentation Rate Index had decreased from 1.80 mm/min to 1.00 mm/min. In order to be completely free from bone and joint symptoms she required only one aspirin tablet a day. Her voice had lost its quaver. She seemed to be more alert mentally and more vigorous physically. There had been considerable improvement in her lingual mucous membrane.

In 172 days of treatment, her Sedimentation Rate Index had improved further, so that it was 0.85 mm/min and her Joint Range Index had risen to 76.2. She stated emphatically that she felt better than she had in many years, and was almost entirely free from joint discomfort and pain. She was delighted to report that she no longer required the help of aspirin to be comfortable. Her liver was no longer enlarged or tender to palpation. Wt. 158 lbs.

At the end of 280 days of treatment, her Sedimentation Rate Index had fallen to 0.65 mm/min and her Joint Range Index had risen to 80.7. She was able for the first time in almost a year to go upstairs without either pulling herself up by the banister or climbing up the steps hand over hand, foot over foot, as an animal would. Her skin had become more elastic and less atrophic. Her color was improved, and the yellow-brown color had been disappearing. No evidences of joint swelling could be made out. The ulnar and tibial subcutaneous nodules originally present could no longer be identified. She had no evidence of liver enlargement or swelling of the liver on palpation.

However, since the rate of recovery of her lingual mucous membrane in response to therapy with niacinamide was considered to be somewhat slow, it was decided to increase her dosage schedule from 150 to 180 mg. of niacinamide per capsule, to be taken one every 3 hours for 6 daily doses (an increase from 900 to 1080 mg. of niacinamide per 24 hours).

For one month she adhered faithfully to the revised program of therapy, and felt in such excellent health and spirits that she became careless, reducing her niacinamide intake to approximately one capsule every 3 1/2 hours for 5 daily doses (900 mg niacinamide per 24 hours).

When she was next seen on the 355th day of niacinamide treatment, her Joint Range Index had risen from 80.7 to 84.1, although the Sedimentation Rate Index had risen

slightly from 0.65 to 0.75 mm./min. When she was informed that the Sedimentation Rate Index was less good than previously, she agreed to take her medication faithfully.

On the 417th day, her Joint Range Index had risen from 84.1 to 86.0, and her Sedimentation Rate Index had fallen from 0.75 to 0.56 mm/min. At this time she was euphoric, and did not remember when she had felt so well. She was physically and mentally vigorous. Her voice was clear, resonant and decisive. With considerable satisfaction, she reported a renewed interest in being with people, and in entertaining guests. She looked younger than when first seen, appearing to be closer to 60 than 80 years of age. She had been entirely free from bone and joint symptoms, and had not taken any aspirin for about 8 months. She could walk up and down stairs without difficulty and without any sense of physical impairment or exhaustion.

Her carriage was erect, although she still had a dorsal kyphosis which would be graded as moderate. Her skin was smoother, softer, less atrophic and more elastic than it was on her first examination; the reticular pattern was less marked than it had been, but still accentuated. She had no discernible joint swellings or deformities. There was no hepatic tenderness or enlargement. The lingual mucous membrane showed a more satisfactory rate of recovery than it had to date in response to niacinamide therapy. Her muscular strength as measured by the dynamometer had improved (Grips: R. 50, L. 46). Hemoglobin 12.0 g/100 cc (acid hematin photoelectric colorimeter).

Summary: This elderly lady with severe joint dysfunction (acute severe rheumatoid arthritis probably superimposed on a mild chronic hypertrophic arthritis) showed in 417 days in response to treatment with niacinamide as the sole therapeutic agent, an improvement in the Joint Range Index from 62.9 (severe joint dysfunction) to 86.0 (slight joint dysfunction). Her Sedimentation Rate Index improved from the exceedingly high rate of 1.80 mm/min to 0.56 mm/min. (Wintrobe-normal 0.1 - 0.3 mm/min). Her muscular strength (grips) as measured with a dynamometer in pounds per square inch rose from the initial measurement of R. 20, L. 12 to R. 50, L. 46 (normal range for women 60-80). In addition to the objective improvement in all of her joints and in her general health, there was a striking decrease in her apparent age. It is anticipated that with continuously adequate niacinamide therapy she will in time achieve a Joint Range Index of 96-100 (no joint dysfunction).

CASE F. No.85, female, age 69, housewife, married.

This case history illustrates, in a woman with severe joint dysfunction and severe, chronic hypertrophic arthritis, (a) improved joint function, as measured by an increased Joint Range Index in response to adequate therapy with niacinamide for one month, (b) impaired joint function, as measured by a lowered Joint Range Index, as a result of substitution of inadequate for adequate niacinamide therapy, and (c) improved joint function, as measured by subsequent increases in the Joint Range Index in response to the re-introduction of more adequate therapy with niacinamide (see Figure20).

She has had arthritis for a long time. For at least 10 years, she has had marked deformities of the hands. Her arthritic symptoms have become more severe in the past 6 months, during which time she has been increasingly tired, more forgetful and more irritable.

Physical Examination: B.P. 168/78. Wt. 118 lbs. Ht. 62 ½ inches. Her skin has a yellowish cast and is inelastic, with a markedly accentuated reticular pattern. She has no periosteal tenderness on digital pressure, and no liver tenderness or enlargement. The lingual papillae are atrophic. Sedimentation Rate Index 0.75 mm/min. (Wintrobe-normal 0.1-0.3 mm/min). Hemoglobin 9.9g/100 cc (acid hematin photoelectric colorimeter). White blood count 8,000. Her Joint Range Index was 59.6, indicating that her joint dysfunction fell within the lower range of the severe grade of joint dysfunction. Hypertrophic deformities of the joints of the fingers were noted.

She had severe joint dysfunction (severe hypertrophic arthritis). She was given niacinamide, 150 mg every 3 hours for 6 doses daily (900 mg/24 hours). For one month she took the medication as prescribed, making the expected improvement in her Joint

Range Index, which rose to 78.3. During the next two months she gradually reduced her dosage of niacinamide, with a concomitant fall in the Joint Range Index. She then resumed taking the niacinamide as originally directed, with subsequent improvement in the Joint Range Index.

Since her Joint Range Index appeared to have stabilized (80.2 and 80.7), her niacinamide intake was increased to 250 mg every 3 hours for 6 doses daily, with a resultant improvement in the Joint Range Index. In 349 days her Sedimentation Rate Index decreased from 0.75 to 0.35 mm/min (Wintrobe-normal 0.1-0.3 mm/min). In 735 days her Joint Range Index had risen from 59.6 to 88.7, a shift from the lower range of severe joint dysfunction to slight joint dysfunction. This patient subsequently discontinued treatment because she mistakenly thought she was cured, since she felt so well.

CASE C. No.336, female, age 29, private secretary, single.

This case history illustrates, in a woman with moderate joint dysfunction, without clinically obvious arthritis, (a) improvement in joint function as measured by increasing values of the Joint Range Index in response to adequate niacinamide therapy, (b) impairment in joint function as measured by a lowered Joint Range Index in response to premature cessation of niacinamide therapy, and (c) subsequent improvement in joint function as measured by an increased Joint Range Index in response to the reintroduction of adequate niacinamide therapy (see Figure 21).

Her presenting symptoms are increasing fatigue and irritability. She has no symptoms referable to bones and joints.

Physical Examination: She looks and acts tired. Her skin has a yellowish cast, and is generally coarse. She has marked atrophy and infiltration of the lingual papillae. Her liver on deep inspiration is felt at the costal margin in the right mid clavicular line and is 1-plus tender. She shows no clinical evidence of arthritis, although her Joint Range Index of 73.7 indicates moderate joint dysfunction.

In response to 150 mg of niacinamide every 3 hours for 6 daily doses (900 mg/24 hours) she displayed progressive improvement in her joint dysfunction, as shown by increasing values of the Joint Range Index (a value of 90.4 was 6btained after 207 days of continuous niacinamide therapy). This patient experienced also improvement in her general health, with complete resolution of excessive fatigue and irritability, and concomitant improvement in the lingual mucous membrane.

She lost interest in continuing with therapy, and for four months took no medication. There was a gradual recurrence of her presenting symptoms, and she returned for study and treatment. Her Joint Range Index had dropped from 90.4 on the 207th day to 79.5 on the 442nd day. With resumption of therapy, her Joint Range Index rose from 79.5 on the 442nd day to 92.7 on the 470th day, and to 96.5 on the 725th day.

CASE H. No.208, male, age 10, schoolboy.
This case history illustrates, in a boy with moderate joint dysfunction, without clinically obvious arthritis, improvement in joint function as measured by an increasing Joint Range Index in response to adequate therapy with niacinamide (see Figure 22).

He has experienced ill-health, including many severe infections. He is jittery, nervous and apparently unable to fix his attention on anything for even short periods of time. He has paresthesias in the legs if he sits for more than half an hour. He is irritable and easily tired.

Physical Examination: B.P. 110/70. Wt. 67 lbs. Ht. 55 ¼ inches. His skin is yellow-brown everywhere, and roughened and discolored, particularly over the knees, ankles, elbows and hands. The reticular pattern is slight. He has many ecchymoses, particularly on the right leg. There is tenderness on pressure over the sternum, sternoclavicular junction and chondrosternal junction. He has mild atrophic changes in the lingual papillae. The conjunctivae lack lustre, but are not otherwise abnormal. Teeth are in good repair. Gums are swollen, slightly hyperemic, slightly retracted. No infection of the gums was

noted. The liver edge is 2-plus tender and 2 fingers' breadth below the costal margin in the right middavicular line. He has plantar dysesthesia lasting 35 seconds. He has hyperpallesthesia in the lower extremities. Tickle sense is absent on the legs, but present elsewhere. Standing, he is unable to touch his fingers to the floor with knees unbent, the distance from fingers to floor with maximal bending being well over 12 inches. The Joint Range Index of 78.0 indicated moderate joint dysfunction.

After one month of treatment with niacinamide (100 mg three times a day after meals and at bedtime; 400 mg/24 hours), his Joint Range Index showed improvement. Tenderness and enlargement of the liver had disappeared, as had his abnormal neurologic signs. There was a marked improvement in his personality.

In 1,003 days of continuous niacinamide therapy, this boy's Joint Range Index has improved from 78.0 (moderate joint dysfunction) to 98.2 (no joint dysfunction). He is now able to bend over as described above and touch the floor with his fingers. His color is no longer yellow. He is cheerful, cooperative and alert, and has stopped being a "problem child." He does not suffer from irritability or excessive fatigability

CASE I. No.431, female, age 87, interior decorator, divorced.

Figure 23 illustrates, in a woman with moderate joint dysfunction and moderate hypertrophic arthritis, improvement in joint dysfunction, as measured by a continuously rising Joint Range Index.

CASE J. No.808, female, age 39, commercial artist, widow.

This case history illustrates, in a woman with moderate joint dysfunction (mild, clinically obvious hypertrophic arthritis), (a) improved joint function, as measured by an increased Joint Range Index in response to adequate therapy with niacinamide for one month, (b) impaired joint function as measured by a lowered Joint Range Index, as a result of substitution of inadequate for adequate niacinamide therapy, and (c) improved joint function as measured by subsequent increase in the Joint Range Index in response to the re-introduction of more adequate therapy with niacinamide
Figure 24).

She had a "nervous breakdown" 3 ½ years ago when her husband died, was followed by typical menopausal symptoms. She has had transient low back pain and right shoulder discomfort after a day's work at the drawing board. She has had for the past 3 years persistent stiffness of joints.

Physical Examination: B.P. 130/90. Wt. 153 lbs. Ht. 66 inches. Hemoglobin 11.8g/100 cc (acid hematin photoelectric colorimeter). She has generalized pallor, and moderate accentuation of the reticular pattern of skin. Her Joint Range Index of 79.4 indicated moderate joint dysfunction

For the control of her menopausal symptoms she was given 50 micrograms of ethinyl estradiol once daily for a week, and thereafter every other day. In addition, she was given 150 mg of niacinamide every 3 hours for 6 daily doses (900 mg/24 hours), which she took for one month with the expected improvement in her Joint Range Index to 86.6.

However, the next month, though she continued the ethinyl estradiol at the prescribed level, upon the advice of a "friendly druggist" she dropped the amount of niacinamide ingested to 600 mg/24 hours, taking 100 mg instead of 150 mg every 3 hours for 6 daily doses, with a resultant fall in her Joint Range Index to 81.4. Subsequently, she resumed taking niacinamide at the level originally recommended, and her Joint Range Index rose from 81.4 to 87.3.

Thus, in four months her Joint Range Index shifted from 79.4 (moderate joint dysfunction) to 87.3 (slight joint dysfunction), even though for one month the patient had reduced her niacinamide from adequate to inadequate levels.

CASE K. No.416, male, age 60, accountant, married.

This case history illustrates, in a male with severe joint dysfunction (mild but clinically obvious hypertrophic arthritis); improvement in joint function as measured by increasing values of the Joint Range Index in response to adequate niacinamide therapy (see Figure 25).

He was given 160 mg of niacinamide every 2 hours for 8 doses daily (1200 mg/24 hours) and in 315 days of such therapy his Joint Range Index rose from 65.5 to 91.8, a shift from severe to slight joint dysfunction. With this therapy, he experienced a feeling of physical well-being and vigor such as he had not had for many years.

CASE L. No.413, male, age 61, mechanical engineer, widower.

This case history illustrates, in a man with severe joint dysfunction (clinically obvious hypertrophic arthritis), improvement in joint function as measured by increasing values of the Joint Range Index in response to therapy with niacinamide in combination with other vitamins (see Figure 26).

This man suffered for more than 6 years from severe, persistent headaches (occipital and cervical pain) which varied in intensity from day to day, but from which he had no relief, in spite of a regular, liberal intake of aspirin. In the past 2 years his headaches had become increasingly more severe. He has noticed crepitus in many of his joints, especially in the neck. He is stiff in the morning when he first awakens, and when the weather changes. His shoulders have been painful. At times he has noticed marked stiffness and pain in his finger joints.

Physical Examination: He is a tired, listless adult male who looks older than his stated age. B.P. 120/80. P. 70. R. 18. T. 97.2 degrees. Wt. 143 ½ lbs. Ht. 67 ¼ inches. His pigmentation is yellowish-brown. The skin of his neck and face has a sharkskin-like appearance, and the reticular pattern is markedly accentuated on his body. His fingernails are thickened. Callusing at pressure points is very noticeable. He has many hyperkeratotic hair follicles on the extensor surfaces of his arms and thighs, and on his abdomen and buttocks. He has marked tenderness on digital pressure over the ensiform process and the maxillary sinuses. His occipital bone is tender to digital pressure. His eyes show marked circumeorneal injection and photophobia. There is some thickening and increased vascularity of the conjunctivae. He is edentulous; the gums have a purplish, swollen appearance. His tongue is magenta-colored and showed marked atrophy and hypertrophy of papillae. He has cheilosis, perhaps partly the result of ill-fitting dentures. His liver margin is felt 3 fingers' breadth below the right costal margin in the right mid-clavicular line on deep inspiration. His posterior tibial and dorsalis pedis arteries pulsate 2-plus. He has marked plantar dysesthesia. Tickle sense is absent, although his sense of light touch, sense of motion and position and vibratory sense are intact. He has moderate dorsal kyphosis and moderate deformities of the fingers. His Joint Range Index was 67.5.

He was given a vitamin dosage schedule as follows:

	Per Dose	Per 24 Hours
Niacinamide	162.5 mg	975 mg
Riboflavin	7 mg	42 mg
Thiamine HCl	3 mg	18 mg
Ascorbic Acid	225 mg	1350 mg

At the end of one month of the above therapy, there was a marked change in his appearance. He seemed less listless and lethargic. He looked younger in appearance. His color was less brown. There was increased range of movement in his neck, and he had much less spasm of the neck muscles. He stated that his headaches were much less severe than formerly, that his spirits were much improved, and that he was less tired generally. However, his tongue, gums and eyes showed little resolution of their severe deficiency signs at this time. His Joint Range Index had risen to 77.8. He had no evidence of liver enlargement or tenderness.

With the passage of time and the continuance of therapy at the prescribed level, there has been progressive improvement in his tissues and m his Joint Range Index. His dorsal kyphosis is now less apparent. He now has headaches at rare intervals, which tend to be mild and occur only when he has held his head in an awkward position for a considerable period of time; e.g., when he studies blueprints. With each successive visit, he has appeared to be a younger, more vigorous man.

With continuous therapy with niacinamide in combination with other his Joint Range Index rose in 190 days from 67.5 (severe joint dysfunction) to 87.1 (slight joint dysfunction).

CASE No. 427, male, age 45, attorney, married.

This chart illustrates, in a man with severe joint dysfunction (without arthritis), improvement in joint function, as judged by increasing of the Joint Range Index in response to therapy with niacinamide in combination with other vitamins (see Figure 27).

This patient's Joint Range Index rose from 67.7 (severe joint dysfunction) to 86.0 (slight joint dysfunction) in 178 days of therapy.

CASE N. No. 337, female, age 36, business woman, single.

This chart demonstrates, in a woman with moderate joint dysfunction (without clinically obvious arthritis), continuous improvement in joint function, as demonstrated by increasing values of the Joint Range Index in response to therapy with niacinamide in combination with other vitamins (see Figure 28).

This patient had hypothyroidism which was controlled with 90 mg of thyroid (U.S.P.) daily. A 3-week lapse in the ingestion of thyroid caused a recurrence of her hypothyroid symptoms, and the resumption of thyroid caused these symptoms to disappear. This lapse in thyroid therapy did not influence the pattern of recovery of her joint dysfunction. Her Joint Range Index rose from the initial value of 75.8 (moderate joint dysfunction) to 92.5.(slight joint dysfunction) in 385 days of continuous vitamin therapy.

Case 0. No.194, female, age 52, business woman, married.

This case history illustrates, in a woman with moderate joint dysfunction (without clinically obvious arthritis), (a) improvement in joint function in response to a given level of vitamin therapy which proved to be inadequate, as demonstrated by stabilization over a period of time the Joint Range Index below the 96-100 level, and (b) subsequent improvement in joint function, as indicated by rising values of the Joint range Index in response to a small increase in the level of vitamin therapy

For 511 days this patient was given the following vitamins:

	Per Dose	Per 24 Hours
Niacinamide	100 mg	400 mg
Ascorbic Acid	100 mg	400 mg

With the above level of treatment, her Joint Range Index rose from 79.0 to 83.0 in 70 days. In 295, 391 and 511 days the Joint Range Index measured 89.2, 89.8 and 89.2, respectively.

Her dosage schedule was changed to:

	Per Dose	Per 24 Hours
Niacinamide	100 mg	600 mg
Ascorbic Acid	100 mg	600 mg

Subsequently, her Joint Range Index rose, so that on the 632nd day after the initial visit, it was 91.7, and in 748 days it was 93.4, indicating a shift from moderate to slight joint

dysfunction. In 910 days of therapy her Joint Range Index rose to 96.9 (no joint dysfunction).

CASE P. No.362, male, age 28, attorney, single

This chart illustrates that a man with moderate joint dysfunction (without obvious arthritis) and mild untreated hypothyroidism (basal metabolic rate -18%) had no change in his Joint Range Index as a result of the daily ingestion of 60 mg of thyroid substance (U.S.P.) for 30 days. However, when he received in addition to his thyroid medication an adequate dosage of niacinamide in combination with certain other vitamins, there was improvement in his Joint Range Index (see Figure 30).

CASE Q. No.278, female, age 47, housewife, married.

This case history illustrates, in a woman with severe joint dysfunction (with clinically obvious hypertrophic arthritis), cyclically, (a) improved joint function as shown by an increased Joint Range Index in response to adequate therapy with niacinamide in combination with other vitamins, (b) impaired joint function as shown by a lowered Joint Range Index as a result of substitution of inadequate for adequate therapy, and (c) improved joint function as shown by increased Joint Range Index in response to re-introduction of more adequate therapy (see Figure 31).

She has been aware of soreness in her joints, stiffness and limitation of movement for more than 10 years. She has had soreness of the tongue off and on for many years.

Physical Examination: She is a tired woman who looks older than her stated age. B.P. 110/70. Wt. 114 lbs. Ht. 63 inches. Hgb. 10.5 g/100 cc. (acid hematin photoelectric colorimeter). Her skin is wrinkled, dry, yellow-brown. There is accentuation of the reticular pattern, increased callusing and a marked tendency to freckling. Her eyes show conjunctival thickening and injection. She is partially edentulous. The gums are pitted, infiltrated, swollen and retracted. Tongue shows moderate atrophy of papillae, with considerable redness of the tip and lateral margins. The margin of the liver is tender and just palpable at the costal margin. She has hyperpallesthesia in the bony eminences of the lower extremities. Plantar dysesthesia is in excess of 20 seconds. Tickle sense is present on the forehead, but not elsewhere. She has a low Joint Range Index of 67.9, indicative of severe joint dysfunction.

The following vitamins were prescribed in the manner indicated:

	Per Dose	Per 24 Hours
Niacinamide	150 mg	900 mg
Riboflavin	4mg	24 mg
Thiamine HC1	2mg	12 mg
Ascorbic Acid	175 mg	1,050 mg
Vitamin A	5,000 units	15,000 units
Vitamin D	1,000 units	3,000 units

At the end of one month, her Joint Range Index showed the expected increase in response to therapy. Her color was less yellow-brown than originally. Her liver was no longer palpable or tender. The intensity of her neuropsychiatric symptoms had lessened. She was less tired, less irritable, and had marked lessening in her subjective sensations referable to joints. Her hyperpallesthesia was replaced by normal vibratory sensation. Plantar dysesthesia had disappeared. Slight tickle sense was present everywhere.

This patient had considerable difficulty in maintaining the therapeutic program as originally prescribed for her because at various times during treatment she suffered from anxiety states, fearing that she was pregnant. During these periods of anxiety, she invariably reduced her vitamin intake. Her vitamin intake as she reported it is shown in Figure 29, together with corresponding fluctuations in the Joint Range Index.

In spite of her difficulties in taking the medications as prescribed, she managed to take sufficient amounts over a period of time so that eventually her joint dysfunction

improved from severe (Joint Range Index 67.9) to slight (Joint Range Index 92.3) in 682 days.

CASE R. No.77, female, age 57, nurse, unmarried.

This case history illustrates, in a woman with severe joint dysfunction (clinically obvious hypertrophic arthritis), (a) initial improvement in joint function, as shown by an increased Joint Range Index in response to adequate therapy with niacinamide in combination with other vitamins, and (b) gradual decline of the Joint Range Index as a result of progressively greater departure from adequate therapy (see Figure 32).

She has not worked for 5 years because she has suffered from gastrointestinal symptoms consisting mainly of heartburn and indigestion occur-ring about an hour after meals, relieved by bicarbonate of soda. Repeated x-ray studies have revealed no abnormalities of the gastro-intestinal tract. She has mild menopausal symptoms.

During the 5 years that she has been unemployed, she has lived without cost to herself with her sister and brother-in-law. Her poor health was used by her as an excuse for not doing even minimal housework.

Physical Examination: She is tense, tired and impatient. Wt. 150 lbs. Ht. 63 inches. B.P. 130/84. Skin is yellow, with the reticular pattern moderately accentuated, as is callusing. She has moderate, early Bitot spots. Her receded gums are hyperemic, and slightly edematous. The anterior third of the tongue is reddened, and there is moderate atrophy of papillae. She has liver tenderness graded as 2-plus, with the liver edge at the level of the costal margin. Her Joint Range Index showed severe joint dysfunction (61.6).

She was given a regimen of therapy, including a bland diet, anti-spasmodic and vitamins prescribed in the manner indicated below:

	Per Dose	Per 24 Hours
Niacinamide	175 mg	1,050 mg
Riboflavin	4.5 mg	27 mg
Thiamine HC1	3.5 mg	21 mg
Ascorbic Acid	175 mg	1,050 mg

In one month she had made the expected progress, as indicated by improvement in her physical condition and in the Joint Range Index of 76.1. When she realized that she was improving physically, she became panicky and developed many new psychosomatic symptoms, including severe headaches with a bizarre pattern and syncopal spells. The psychiatrist who studied her elicited the information that she hated to work, and when her brother-in-law found that she was feeling better, he would probably insist that she work as a nurse and contribute to her own support. As a result of the family situation, she gradually decreased the amount of vitamins taken so that ultimately she was taking about one-third the amount which had been prescribed. The approximate pattern of reduction in dosage as she described it is shown in Figure 32. At no time did she have insight into her basic emotional problems.

CASE S. No.201, male, age 52, manufacturer, unmarried.
This case history illustrates the effect on the Joint Range Index of varying levels of vitamin intake over a relatively long period of time (see Figure 33).

This man did not get along well with one of his business partners. The periods when he was under the greatest emotional strain at work corresponded exactly with the periods when he failed to take his vitamin therapy as prescribed. Conversely, when there was greater harmony at work, he had no difficulty in adhering strictly to the prescribed program.

While intellectually he appreciated the above relationship, when he was emotionally disturbed he was unable to keep his vitamin therapy at the recommended levels. However, at each interview he reported the approximate amounts of the medications that he had been able to take for each time interval between examinations. His initial Joint Range Index was 72.6 (moderate joint dysfunction), and in 509 days his Joint

Range Index was 89.0 (slight joint dysfunction). The Joint Range Indices reflected alterations in the level of his vitamin ingestion.

CASE T. No. 345, female, age 41, housewife, married.
I
This case history illustrates, in a woman with moderate joint dysfunction (without clinically obvious arthritis), (a) improved joint function in response to one month of therapy with niacinamide in combination with other vitamins, (b) impaired joint function as measured by a lowered Joint Range Index as a result of premature cessation of vitamin therapy, and (c) improved joint function as measured by subsequent increase in the Joint Range Index in response to re-introduction of vitamin therapy at a higher level than originally (see Figure 34).

Her Joint Range Index was 80.7 at the time of the initial visit. For one month she took the following vitamins:

	Per Dose	Per 24 Hours
Niacinamide	150 mg	600 mg
Riboflavin	5 mg	20 mg
Thiamine HCl	2.5 mg	10 mg
Pyridoxine HCl	5 mg.	20 mg
Ascorbic Acid	200 mg.	800 mg

At the end of one month of such therapy her Joint Range Index had risen to 84.9. For 6 months she took no further therapy, and when she returned at the end of this time for examination, her Joint Range Index had fallen to 79.7. Vitamins were prescribed for her as follows:

	Per Dose	Per 24 Hours
Niacinamide	190 mg	1,140 mg
Riboflavin	7 mg	42 mg
Thiamine HCl	4 mg	24mg
Pyridoxine HCl	6 mg	36 mg
Ascorbic Acid	250 mg	1,500 mg

At the end of one month of the above therapy, her Joint Range Index had risen to 92.6. Although not indicated in Figure 34, in 693 days this patient had a Joint Range Index of 96.4 (no joint dysfunction).

SOME REASONS WHY CERTAIN PATIENTS WITH JOINT DYSFUNCTION FAILTOTAKE NIACINAMIDE THERAPY AS DIRECTED

As will be seen subsequently, not all of the 455 patients who were studied clinically accepted niacinamide therapy for joint dysfunction and returned for the necessary re-examinations. Analysis of the data in Section IV indicates that 80.7% of the total population studied (78.5% of all males and 82.1% of all females) accepted niacinamide therapy for some period of time. It has been learned directly or indirectly that certain patients continued with niacinamide therapy without returning for necessary medical supervision; the exact number of such patients is not known. Therefore, less than 20% of the patients with joint dysfunction who were studied clinically did not accept niacinamide therapy. While it is not always possible to ascertain the reasons why a patient fails to take niacinamide therapy as prescribed, some of the apparent reasons are presented below.

The patient is unwilling to accept a method of medical treatment that is unfamiliar to him. Sometimes, a patient may believe that diet alone should be adequate to supply all his nutritional needs, and thinks that he can "get along" as his ancestors did, without vitamin therapy. Some patients desire only a thorough physical examination and an evaluation of their health status, and are uninterested in any form of therapy. Sometimes, a patient feels that it is a sign of weakness to take medications unless he is acutely ill, and will submit to treatment only for the duration of any medical or surgical emergency that may arise. Some patients want magical cures,

and do not wish to undertake any treatment that requires sustained, active patient-physician cooperation; they feel that the treatment demands too much of them, especially the taking of medications at stated intervals, and the necessity for re-examinations. Certain patients are very impatient, and want treatment that will give "immediate results." They may request that instead of the niacinamide treatment they be given injections (gold, sulfur, liver, bacterial vaccine, vitamin "shots"). Some patients who present themselves for clinical study want only to be reassured that they are in perfect health, even though they may have major medical or surgical problems, and want to be told that any imperfections they may have are of no significance. Other patients want only to be told that they are ill, and should "take it easy," or take a long vacation, or be relieved of responsibilities and duties. Some patients are "shopping" for an operation. Other patients want only to have prolonged and expensive hospitalization, with special studies and treatment. Some patients who consult the physician unwillingly, at the insistence of a friend or relative, have no intention of following any medical advice. Some patients present themselves for study only to satisfy their curiosity about the physician and his methods.

Sometimes, a patient may be discouraged from taking niacinamide therapy for joint dysfunction by a "friendly" and crusading nurse, druggist, or physician, who insists that the niacinamide therapy of joint dysfunction is unnecessary or useless, and tells the patient that he needs no such treatment, or that he should try some other type of therapy which is in more general use.

A patient usually does not continue with niacinamide therapy of joint dysfunction when, on the first day of therapy, he takes niacin-containing medications dispensed mistakenly by the druggist instead of niacinamide, and experiences, unexpectedly, severe flushing and other unpleasant symptoms characteristic of niacin reactions (113). (No flushing or other untoward reactions have been observed in properly selected patients with joint dysfunction who have taken as much as four grams of niacinamide daily for a year or more.)

A few patients have initial difficulties in forming regular habits of taking medication during the first months of treatment of joint dysfunction. Unless certain patients are seen at relatively frequent intervals, they lose interest in continuing with niacinamide therapy. Some patients do not take medications as prescribed as a device for gaining the attention of family and physician.

Sometimes a patient will not take niacinamide therapy for joint dysfunction because he develops a strong negative transference reaction to the physician. Occasionally, such reactions may appear as masked negative transference reactions, when at the initial visit the patient seems excessively cordial, agreeing with everything the physician says, speaking confidently of how well he expects to feel in the future under the physician's care. Such a patient may never return for re-examination. If he does return, he never takes niacinamide therapy as prescribed, stating he is "too busy to take the medicine," that he has "too many pills to take," that he "forgets" to have his prescription refilled. He then states with apparent pleasure that he doesn't "feel better in any way," or that the treatment hasn't helped at all," even though he may continue to return for serial re-examinations.

Some patients who have joint dysfunction and one or more of the four complicating syndromes are impatient and unwilling to cooperate in the clinical investigation of their complicating syndromes, and they soon drop therapy.

A patient who does not have articular symptoms or arthritic deformities often sees no reason why he should take any medical therapy, even though his joint dysfunction may be severe. A patient who has articular symptoms and arthritic deformities may believe that his symptoms and deformities are not sufficiently troublesome to him to warrant the nuisance and expense of treatment.

Some patients with recurrent or continuous articular symptoms (with or without clinically obvious arthritis) are often unable to accept the fact that their joint dysfunction can be reversed in time, and if they begin niacinamide therapy, it is with the greatest

skepticism. These patients, previously studied by many physicians over a period of years, had been advised repeatedly that there was no effective therapy for their articular illness. Thus, unless they feel subjectively improved within a few weeks of beginning treatment, they usually drop therapy.

Certain patients who enjoy secondary gains from their articular illness may not begin niacinamide therapy for fear that they may be "cured"; if they do accept therapy, they always take less than the prescribed amount of niacinamide.

In some instances of severe or extremely severe joint dysfunction with clinically obvious arthritis, but not in all instances, there may be a relatively long latent period between objective improvement in the Joint Range Index and subjective awareness of improved health as a result of therapy. Some persons who do not feel better subjectively during this period, fail to continue with therapy, in spite of objective evidence for clinical improvement. Such persons often drop therapy prematurely.

Whenever certain patients are exposed to an anxiety-producing situation, they reduce their vitamin intake to inadequate levels, and when the tensional situation has passed, they resume vitamin treatment as directed.

Some patients are afraid of "powerful" medicines, and when they have made good improvement in response to niacinamide therapy, they reduce their niacinamide intake for fear that the medicine is "too strong."

Certain suspicious patients reduce the niacinamide level below the recommended dosages, or stop niacinamide therapy prematurely without informing the physician of this. If such a patient's Joint Range Index has been maintained at a high level in response to a sufficient period of adequate niacinamide therapy, there may be some lag between the reduction in niacinamide intake and the decrease in his Joint Range Index. Such patients use this as proof that the physician is wrong about joint dysfunction and its proper treatment. Some of these patients who return for study after having discontinued niacinamide therapy for a year or more, show demonstrable regression of the Joint Range Index.

A patient with joint dysfunction who has mental symptoms which are extinguished by adequate niacinamide therapy may experience such marked improvement in his feeling tone during the first month of adequate niacinamide therapy that he may mistakenly believe he is "cured," even though he has made only the expected improvement in his joint dysfunction. He is likely to drop niacinamide therapy prematurely, and usually experiences a slow or rapid recurrence of his mental symptoms.

Some patients have a response to niacinamide therapy which seems to be the clinical equivalent of "decreased running" observed in experimental animals (226). When these animals are deprived experimentally of certain essential nutriments, they display "excessive running," or hyperkinesis. When these deficient animals receive the essential nutriments in sufficient amounts for a sufficient period of time, there is exhibited a marked "decrease in running," or hypokinesis. Thus, certain patients may discontinue therapy because they believe they feel less well as a result of niacinamide. They may have the impression that vitamin therapy is depriving them of their usual abundant energy, and may state that they are being "de-pepped" by the treatment.

A patient in this group may wonder whether or not his vitamin medications

contain a sedative. He recalls that before vitamin therapy was instituted, he had a great deal of energy and "drive," and considered himself to be a "very dynamic person." Analysis of his history indicates that prior to niacinamide therapy, even though he often felt tired, he did not need to rest or relax during the day, since he found it easier td "keep on going" than to stop and rest, and that he suffered from a type of compulsive impatience, starting many projects which he left unfinished as a new interest distracted him, returning perhaps after a lapse of time to complete the original project. Without realizing it, he was often careless and inefficient in his work, but was "busy all the time."

With vitamin therapy, such a patient becomes unaccustomedly calm, working more efficiently, finishing what he starts, and he loses the feeling that he is constantly driving himself. He has leisure time that he does not know how to use. When he feels tired, he is able to rest, and does not feel impelled to carry on in spite of fatigue. All these changes he interprets to mean that vitamin therapy has robbed him of his vitality. If such a patient can be persuaded to continue with niacinamide therapy, in time he comes to enjoy a sense of well-being, realizing in retrospect that what he thought in the past was a super-abundance of energy and vitality was in reality an abnormal "wound-up" feeling, which was an expression of aniacinamidosis.

Some patients become tired of taking medications for prolonged periods of time, and stop niacinamide therapy for joint dysfunction.

Rarely, patients are unable to continue with niacinamide therapy for economic reasons.

LIMITATIONS OF THIS STUDY
Certain limitations were imposed on this study by the nature of the writer's private practice:

1. No repeated determinations of the Joint Range Index could be performed on a large sampling of the untreated population over a prolonged period of time.

2. No control series could be studied which had been treated with placebos, single vitamins other than niacinamide, or multiple vitamin mixtures not containing niacinamide.

3. No large series of determinations of the Joint Range Index could be made from two separate sets of measurements made in the same individual on the same day. (However, it was found in a trial with a small series of subjects that two Joint Range Indices determined from two separate sets of joint range measurements made on the same day in the same individual agreed within plus or minus 0.3.)

4. No routine x-ray studies of the joints whose ranges were measured for inclusion in the Joint Range Index could be obtained. However, a sufficient sampling of x-rays of measured joints was obtained in the course of this study to indicate that it would be of value to have such x-ray documentation, routinely performed before treatment was instituted, and at intervals during the course of treatment.

5. No standard photographic method was available for taking serial photographs which could be used in making accurate, detailed comparisons of gross joint morphology before therapy and at various intervals during the course of prolonged, adequate niacinamide therapy. In documenting the gross morphology of joint deformities, certain variables must be controlled rigidly if serial photographs are to be strictly comparable; e.g., positioning of the deformed joints, lighting, lens aperture, film exposure, size of film image, film development, type of printing paper, exposure of printing paper, size of print image, and print development.

6. No attempt was made clinically to find the highest dosage level of niacinamide which could be tolerated safely by patients with joint dysfunction, or to explore the effects of such doses on the rate of recovery in joint dysfunction. Only those dosages of niacinamide which seemed to be clinically safe and therapeutically effective were employed in the treatment of joint dysfunction.

7. No gross or histopathologic studies could be performed on the joint structures of patients with joint dysfunction in the course of this study.

8. No highly specialized chemical or metabolic studies could be performed prior to treatment with niacinamide, or subsequently, to follow in a patient with joint dysfunction, (a) the fate of the ingested niacinamide and the concomitant metabolic changes in body chemistry and metabolism during the course of adequate treatment of joint dysfunction; (b) changes in body chemistry and metabolism induced by the substitution of inade-

quate for previously adequate niacinamide therapy; (c) changes in body chemistry and metabolism induced by the premature cessation of adequate niacinamide therapy.

(End of Chapter 1, which consists of pages 1-75. *The author's preface, and all references cited, are posted at* http://www.doctoryourself.com/kaufman11.html)

To read Chapter 2, click this link: http://www.doctoryourself.com/kaufman7.html