Frederich Klenner defines an orthomolecular treatment of MS that has been effectively employed by Dale Humpherys and other patients. (For Humpherys' report, see his article in the December 2005 issue of the *Townsend Letter for Doctors & Patients*.)

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Response of Peripheral and Central Nerve Pathology to Mega-Doses of the Vitamin B-Complex and Other Metabolites

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The protocol of how to effectively treat Multiple Sclerosis. (In two parts, as originally published in 1973.)

Part I:

Two devastating pathological syndromes affecting nerves are Multiple Sclerosis and Myasthenia Gravis. To adequately understand the significance of these diseases, one must have a working knowledge of fatigue, normal and abnormal. The phenomena of fatigue according to Starling's Principles of Human Physiology has been recognized for years to depend on two factors: 1) the consumption of the substances available for the supply of potential energy to the contractile material; 2) The accumulation of products of the contractile process. We must consider a third: The inability to use available energy-producing substances because of distribution roadblocks.

Two general locations for normal fatigue are: 1) At the synapses, the delicate junction between neuron and neuron, recognized as highly susceptible to fatigue; 2) The junction between motor nerves and the fibers of skeletal muscle, made possible by motor end plates. Synaptic fatigue and end plate fatigue occur in such minute structures that quick recovery seems always possible. We must recognize, however, that although the feeling of fatigue may apparently be quickly dissipated, actual restoration of the fatigued structure will require much time.

When a plant is fatigued it wilts; unless relieved of the fatigue, it dies. Proper atmospheric conditions, proper soil, or these equivalents conferred by man will restore, to some degree, the faltering plant. Even prayer has been advanced as an active agent to not only relieve the failing plant of its fatigue, but also to encourage its growth. Plants do indeed have a soul – the soul of growth. This predicates a potential capable of responding to "kindness" of various types. In this light, then, people with "green thumbs" are nothing more than accepted plant missionaries. When an animal is fatigued, it usually follows an innate faculty supplied by nature and rests. When sick, like the dog, it will eat grass to relieve the gastric complaint. The dog's master can go further and supply various drugs or vaccines to either cure the malady or to prevent several types of illnesses from ever coming into existence. Animals have not only a soul for growth like the plant, but also a soul of sensation. Proper rest, proper drugs and proper food, along with understanding, will secure for the dog mental and physical relaxation, thus assuring the animal a more serene and longer life as compared to a dog running loose on the streets or in the wild, and required by circumstances to scavenge for itself.

It is a common experience to obtain marked relief from physiological fatigue by taking a short nap, the often-called "Edison cat nap." An ordinary night's rest is none too long for recovery from fatigue created by a day's labor. The almost universal habit of abstaining from ordinary duties one day out of seven has real significance It acknowledges the necessity of allowing, at intervals, a longer period for restoration than the usual nightly ones in order that accumulative fatigue will not be experienced. Work is labor, and so is play. There is a real and significant difference between being pleasantly tired and being fatigued. The share-cropper working in the field, where fresh air abounds, can easily expend far more energy than one who works in a poorly-ventilated factory, yet the farm worker will register only relative fatigue, as compared to the factory worker who often will be physiologically exhausted. This suggests that oxygen plays an important role in the production of fatigue.

Muscle Fatigue

In the laboratory one can demonstrate that repeated stimulation of striated muscle diminishes the force of the contraction, and that indefinite repetition of such stimulation will so exhaust the muscle that eventually it will fail to respond. The fatigue which is here observed can be due either to the exhaustion of the glycogen and the hexose phosphates or to the accumulation of lactic acid within the muscle. Muscle contraction is essentially an anaerobic process. Lactic acid production, the fundamental chemical reaction producing energy for muscle contraction, does not require oxygen. Such energy-yielding reactions of partial decomposition, not requiring oxygen, are called

fermentations. Muscle, then, obtains energy independently of its immediate oxygen supply by the rapid fermentation of glycogen to lactic acid, in the same way as brewer's yeast derives energy by the fermentation of sugars to alcohol. This anaerobic explosion of energy is akin to jet propulsion, and similarly, its potential is limited. Ultimately, muscle requires oxygen for the maintenance of normal irritability, for oxidative energy production, and for the restoration of its anaerobic energy-yielding system. Muscle action and muscle fatigue is indeed a very complex chemical system. Such units as phosphocreatine, adenosine triphosphate and calcium and magnesium ions deserve limited explanation. Eagleston and others, independently, discovered that most of the creatine in muscle is in labile combination with phosphoric acid. The free creatine which occurs in muscle fatigue is proportional to the amount of phosphocreatine which is decomposed. Creatine is derived in the body from the amino acids Arginine and Glycine, plus a labile methyl group. According to Cameron and Gilmour, creatine, in acid solution, readily loses water to give a ring compound, an internal anhydride, creatinine. Creatinine is a constant constituent of urine, and its amount is sometimes increased in the later stages of nephritis and always in Myasthenia Gravis. The simplest conception of creatine-creatinine metabolism is that creatinine is formed from creatine during periods of muscular activity when creatine is transiently free in muscle, and then passes by way of the blood, without change, into the urine. Creatine phosphate breaks down in the presence of adenosine diphosphate (ADP) to form adenosine triphosphate (ATP). Creatine phosphate acts as the immediate energy source for the synthesis of adenosine triphosphate for relatively short periods during bursts of contractile activity. The usable life of creatine phosphate is limited. Once it is used up by muscle action, the muscle must then rely on the adenosine triphosphate (ATP) which is synthesized during the chemical activity of the Kreb cycle in glycolysis. Adenosine triphosphate is the essential high-energy package, and it is responsible for delivery of necessary power for the activation of all cells; it is the basic energy unit for life. During muscle relaxation phase, some of the adenosine triphosphate reacts with creatine to form creatine phosphate at the expense of adenosine triphosphate which is reduced to adenosine diphosphate (ADP), a low-energy package. This change of reactions continues until such a situation exists when muscle cells can no longer synthesize ATP due to lack of oxygen and essential substrates. When this happens, a state of muscle rigor mortis exists. Frequently, Myasthenia Gravis patients experience minimal rigor mortis; sometimes no adenosine triphosphate is available and so actual death.

We must briefly discuss still other phases of muscle activity. The filaments in skeletal muscle are composed primarily of the proteins actin and myosin. Small amounts of other proteins play important roles in the contractile cycle. Part of the energy for movement comes from the splitting of adenosine triphosphate by the myosin molecule. Actin increases the ability of myosin to split adenosine triphosphate. Magnesium ions and calcium ions are also necessary in muscle action. Besides actin, tropomyosin and troponin are responsible for the effects of calcium on the contractile apparatus. One must also consider the part played by acetylcholine and its esterase in muscle activity. Too much or too little of these substances prevents or slows down muscle action even when all other factors are within normal limits. The neuromuscular junction potential can be modified by drugs and disease. One such drug is curare. Curare merely occupies a reactive site so that acetylcholine is prevented from interaction with motor end plates. Myasthenia Gravis is a disease whereby too much pyruvic acid (pyruvates), due to faulty metabolism, affects the interaction of acetylcholine at the site of the motor end plates at the neuro-muscular junction. In Multiple Sclerosis, the sluggish and sometimes bizarre muscle activity is due to absence or inability to utilize essential factors because of mechanical and chemical roadblocks.

Like nerve action potential, muscle action potential is an all-or-none event. The overall effects of motor unit recruitment depend upon the anatomical relationship between the contracting units. Specifically whether the fibers are in series or parallel. When linked in parallel by connective tissue, the force generated by each fiber is additive, producing a total force proportional to the number of fibers contracting. When the fibers are in series, the total force is equal to that generated by a single fiber no matter how many fibers fire simultaneously. These relationships exert quite a different effect on the degree and velocity of shortening. No matter how many fibers in parallel contract together, the amount of shortening and velocity are the same as when a single fiber contracts, but both the degree and the velocity of shortening are proportional to the number of contracting fibers in series. Long muscles shorten more and faster than short muscles; thick muscles exert more tension than thin muscles. These differences, however, disappear when the values are expressed per unit length and cross-section area. The total range of length changes a muscle can undergo while attached to the bone is much less than the changes that would cause the active tension to fall to zero. Muscle exerts a force on the bones to which they are attached through tendons. As muscle shortens, it exerts only a pulling force called flexion. Opposing muscles straighten the unit flexed which is known as extension. This review on muscle action and fatigue is, apologetically, very elementary, but sufficient to establish a basic understanding of what is happening in the pathological conditions entertained in this treatise.

These physiological processes battling fatigue, as enumerated, are such that the sudden expenditure of a large part of the potential energy of the muscle, by the conversion of glycogen to lactic acid, does not mean a permanent loss of

glycogen capital. This is so because one-fifth of the lactic acid produced is subsequently, completely combusted. Paradoxically, this re-yields energy which is sufficient to convert four-fifths of the lactic acid produced back to glycogen. The grade of muscle effort which an individual can endure before reaching his fatigue point is governed by his capacity for absorbing oxygen and discharging carbon dioxide during respiration. Each of us is absorbing some 200cc to 300cc of oxygen per minute. If we should suddenly start to run for a bus, or climb several flights of stairs, the amount of oxygen required might rise to 2,000cc to 3,000 cc and even 4,000cc. One liter of oxygen will remove seven grams of lactic acid. The individual who can absorb four liters of oxygen per minute can endure the production of 28 grams of lactic acid per minute by his muscular effort. This tells us that our ventilating system must be in grade A condition. Anything such as smoking, or even chronic sinusitis will have a detrimental effect on neurological diseases, and supportive treatment along these lines must also be entertained if success is the desired end point.

Mental Fatigue

There are other types of fatigue besetting humans. Mental fatigue can best be considered in the light of active and passive. Passive mental fatigue represents that type of medical syndrome which includes such symptoms and signs as "brain lag," sensations of pressure in the head, poor memory, loss of power of concentration, irritability of temper, increased reflexes, insomnia, anorexia and a general variety of aches and pains – the classical syndrome of neurasthenia. Active mental fatigue is elicited by continuous work, and is proportional to the duration and difficulty of the task performed. The effects are manifested by lessening in feeling, in tone, in output and in organic change. The organic change is small compared to that from equivalent periods of heavy muscular work. Most of this change can be attributed to the sensory-motor rather than to the neural element of the mental work. Mental performance is never perfectly continuous, but is alternated with pauses which become longer and more frequent in proportion to the length and difficulty of the task. Mental effects are accumulative in that they are transferable from one task to another in proportion to the tasks' similarity. Total sleep during a day off is not necessary, since the primary area of this phase of fatigue is the synapses which beg only diversion of interest and activity – something foreign to one's usual occupation. In this manner, the fatigued synapses can rest while others are busy.

Chemical Fatigue

Chemical fatigue represents one of the major groups of internal medicine. Passive chemical fatigue represents that group which makes itself known through body lassitude following the administration of a chemical compound. This group of compounds is represented by the soporific drugs, the analgesics, the many tranquilizers, and those which lower blood pressure. One must guard against seemingly harmless chemicals. Sodium bicarbonate, for example, is capable of rendering hemoglobin less capable of normal oxygen surrender to tissues. Sodium bicarbonate can take up as much as 70% of the available oxygen. The immediate result of this anoxia is weakness, even collapse; the remote effect is tissue breakdown. Sodium bicarbonate can mimic the action of carbon monoxide. This gas, as you know, combines with reduced hemoglobin, displacing oxygen from oxyhemoglobin to form the specific compound carboxy-hemoglobin. Proper doses of ascorbic acid will prevent or relieve this syndrome. It is good to remember that monoxide poisoning can exist from many sources other than auto exhausts. Smoke poisoning from fires is nothing other than monoxide poisoning, and carboxy-hemoglobin blood levels up to 7% have been reported in cigarette smokers. This can be serious, especially in a patient with a neurological pathology. Patients with Myasthenia Gravis and Multiple Sclerosis will not make progress if they use tobacco. There are other reasons against the use of tobacco. The hypoxic effect of carbon monoxide may act in a synergistic manner with other factors operative in ischemic heart disease, outstripping the limited coronary reserve and augmenting the production of stress-induced myocardial ischemia. (I need not remind you that adequate ascorbic acid intake will also "handle" this situation.)

Active chemical fatigue represents that type of exhaustion which results from the breakdown or inability to handle the normal physiological processes in the body. A classical example of this is Myasthenia Gravis. Before the advent of Prostigmin, Mestinon and Mytelase, all those who have had this disease have died unless favored with spontaneous remission and one special type of treatment which will be outlined later. The physostigmine class of drugs inhibit the action of cholinesterase. They also have a direct effect on muscle fibers, on neurons and on ganglion cells of the central nervous system, much like jumper cables on an automobile, or like a cardiac pacemaker. Their action is limited. Although the etiology differs markedly, Multiple Sclerosis is also the end result of an active chemical problem.

Metabolic Pathways – Carbohydrate Metabolism

From any textbook of physiology, one might read concerning the metabolic pathways. The sequence of enzyme-mediated reactions leading to formation of a particular product is known as a metabolic pathway. When dealing with

glucose it is termed glycolysis. The primary function of carbohydrates in the body is to provide a source of chemical energy. The metabolic pathway for glucose degradation to carbon dioxide and water is divided into two parts: 1) Involves the breakdown of glucose to pyruvic acid or lactic acid; 2) Conversion of pyruvic acid to carbon dioxide and water in the presence of oxygen. Whether the end product of glycolysis is pyruvic acid or lactic acid depends upon the supply of oxygen in the cell. When the oxygen supply is adequate, pyruvic acid is formed; conversely an inadequate oxygen supply will lead to lactic acid formation. These are generally referred to as aerobic and anaerobic glycolysis. Adequate oxygen can be made available not only through a high rate of gas exchange in the lungs, assuming that the pulmonary function tests are within normal limits, but also by taking 10 to 30 grams ascorbic acid by mouth every 24 hours. Oxygen from vitamin C becomes available through the loss and eventual break-up of water in the reaction of ascorbic acid to dehydroascorbic acid. We reported this chemistry in several papers dealing with the use of massive doses of vitamin C in Monoxide poisoning. Enzymes are also necessary in making the glucose reactions possible. Many pathological conditions can be traced to faulty enzyme production. This is usually due to genetic fault.

Food, regardless the kind, must be reduced to glucose if it is to be used to produce energy. We have already implied that only glucose can undergo glycolysis, which produces as one type end point, pyruvic acid. Pyruvic acid is a critical agent in Multiple Sclerosis, because it is the starting component of the Krebs Cycle. Each step in glycolysis, that is, the change in chemical structure occurring along the pathway to pyruvic acid from one molecule to the next is relatively small, but the total sequence of reactions alters the structure of glucose dramatically. Biochemists record that in the first glucose reaction, one of 19, the phosphate from adenosine-5-triphosphate (ATP) is transferred to glucose to form glucose-6-phosphate. In the third reaction a second molecule of adenosine-5-triphosphate (ATP) is used in the transfer of phosphate to fructose-phosphate. Two molecules of ATP, the key power source for life, being utilized in getting to fructose 1, 6-diphosphate, but eventually four molecules of ATP are formed resulting in a net gain for the cell of two Adenosine-5-triphosphate molecules. During glycolysis reaction number six, additional ATP molecules are synthesized from or by way of the coenzyme nicotinamide adenine dinucleotide plus 2 hydrogen atoms ($NADH_2$) by the process of oxidative phosphorylation. This, however, cannot occur without oxygen since in the reaction $NADH_2$ is reduced to NAD by transfer of the hydrogen atoms and electrons to the cytochrome system. Fortunately, adenosine-5-triphosphate (ATP) can be synthesized by direct substrate phosphorylation occurring during anaerobic glycolysis. Adenosine-5-triphosphate (ATP) provides the ionized phosphate groups that trap the intermediates within the cell and forms the intermediate structures required for the later stages of glycolysis. It is important to recognize that all the intermediates between glucose and pyruvic acid contain an ionized phosphate group and that ionized molecules are generally unable to cross the lipid barrier of a cell membrane. Once glucose has been phosphorylated, the intermediates of glycolysis are trapped within a given cell. Glucose enters the cell through a carrier-mediated facilitated-diffusion system. The amount of energy transferred to ATP is roughly 5% of the total potential of glucose. Thus, 95% of the ATP synthesized from the energy released from glucose depends upon oxygen and the oxidative phosphorylation occurring in the mitochondria. This gives us notice concerning the importance of good ventilation practices to maintain a high degree of vital capacity. It also argues for high daily intake of vitamin C.

Reversible and Irreversible Reactions

Most of the reactions of the tricarboxylic acid cycle (Krebs cycle) are reversible, but the reaction in which pyruvic acid is converted to acetyl co-enzyme A and carbon dioxide is irreversible. It is true that all chemical reactions are theoretically reversible, but some are limited to the plant kingdom. For example: Carbon dioxide and water can react to form glucose and oxygen, reversing the reaction which led to the breakdown of glucose, but to make it work in this reverse direction, the same amount of energy (685kcal) released during glucose glycolysis must be returned to the molecules of carbon dioxide and water. This actually happens, as you know, in plant cells through a process called photosynthesis, where the energy is obtained from sunlight. Pyruvic acid, which comes from phosphenolpyruvate, the last step in glycolysis, and which cannot be reversed once acted upon by coenzyme A to form acetyl coenzyme A, can be produced by direct decarboxylation of oxalacetic acid. Pyruvic acid from this source can be phosphorylated in the presence of ATP to form phosphopyruvate, and this can then serve as a direct precursor of the hexoses and glycogen by the reversal of the glycolytic system. Pyruvic acid (plus CO_2), according to Ochoa, can be “shuttled” into the Krebs cycle through malic acid when this compound is reversibly oxidized and decarboxylated using triphosphopyridine nucleotide (TPN) as hydrogen acceptor, and catalyzed by malic enzyme. We mention these chemical routes for pyruvic acid since it plays a very important part in Myasthenia Gravis. The reversibility of the decarboxylation reactions in the Krebs cycle enhances the importance of the mechanism of CO_2 fixation by animal tissues. CO_2 fixation implies the utilization of carbon dioxide for metabolic purposes. As noted in any text of physiological chemistry, the assimilation of CO_2 by green plants during photosynthesis leads to the formation of phosphoglyceric and phosphopyruvic acids, and that malic acid is a subsequent product of the reaction. One can speculate that the

fundamental processes of CO_2 assimilation known for plants can also be assigned for people.

There is evidence sufficient to believe that coenzyme A, which is the physiologically active form of pantothenic acid in animals, is in limited supply in Myasthenia Gravis. This special enzyme is chemically situated at the gateway to the Tricarboxylic Acid Cycle where it "intercepts" pyruvic acid at the end point of glycolysis. The absence or reduced supply of this coenzyme is actually due to the absence or reduced supply of cocarboxylase. When it is present, it not only splits the carboxyl group (COOH) away from pyruvic acid to form CO_2 and "free" H, with the "H" being positively ionized, but it also bonds or joins the remaining two carbon fragments of pyruvic acid, known as active acetate, to form acetyl coenzyme A. This leaves the low-energy package niacin-adenosine-dinucleotide (NAD) free to pick up two molecules of hydrogen. (At one time it was thought that the low-energy package was diphosphopyridine nucleotide (DPN), but through the employment of radioactive isotopes and the electron microscope, this was proved to be in error.) One molecule from the carboxyl group of pyruvic acid, and the second molecule from the sulfur group of coenzyme A, makes a high-energy package with the "call letters" $NADH_2$. One method in getting coenzyme A from pyruvic acid, which has been established for heart tissue by Koroes et al., is the reaction between pyruvic acid, coenzyme A, and diphosphopyridine nucleotide (DPN or coenzyme I), in the presence of diphosphothiamine, which is cocarboxylase. There are other important low-energy packages operative in this system and necessary for good health. Flavin-adenosine-dinucleotide (FAD) picks up two molecules of hydrogen to form the high-energy package $FADH_2$ and adenosine diphosphate (ADP). Adenosine diphosphate picks up available PO_4 radicals to form adenosine-5-triphosphate (ATP).

Protein and Lipid Metabolism

In dealing with muscle and nerve pathology, the metabolism of lipids and protein must also be considered, although in a lesser degree. There is a close relationship between neutral fats and glucose metabolism. The neutral fats, consisting of three fatty acids attached to the three-carbon molecule glycerol, constitutes the majority of the lipid in the body. The breakdown and synthesis of neutral fats is closely associated with the metabolism of glucose because of the formation of intermediates common to both pathways. The breakdown of fatty acids requires coenzyme A and hydrogen carriers such as niacin-adenosine-dinucleotide (NAD). Ascorbic acid can operate as a hydrogen transport in cellular oxidation, thus facilitating these reactions. The starting point for fatty acid synthesis is acetyl coenzyme A. In the diseases in which we are concerned, myelin is very important. Myelin is a fat-like substance forming the principle component of the myelin sheath of nerve fibers. It is composed of cholesterol, certain cerebrosides, phospholipins and fatty acids.

Protein metabolism is far more complicated than lipid or carbohydrate metabolism. Proteins are formed from 20 different amino acids, all of which have different chemical structures and require different pathways for their synthesis and degradation. Synthesis of a protein molecule from amino acids involves more than the formation of chemical bonds between amino acids. The amino acids must be placed in a precise sequential order. Unlike fats and sugars, amino acids contain nitrogen in addition to carbon, hydrogen and oxygen. It is more than of academic interest to know that thiamin hydrochloride is a pyrimidine compound, thus containing nitrogen, like amino acids. Because of this amine factor, Funk originally spelled vitamin with an "e" – vitamine. "Vit" comes from the Greek "vita," meaning life, and E amine for the nitrogen factor. Since only thiamin hydrochloride of all vitamins had this factor, the "e" was dropped, and the name vitamin retained for symbolic reasons. Although all amino acids are important, some more than others, and still others necesary for the continuance of life, the one we are interested in is the amino acid glycine. Glycine is noted for its specific dynamic action. Bodansky states that not only does the body use any preformed glycine that may be present either in the diet or in the tissues, but it is forced, at times, to synthesize this amino acid in large amounts. The conversion of glycine into sugar in the animal body has been well documented. Rapport and Katz have shown that when glycine is added to perfused muscle, the oxygen absorption is 40% higher than otherwise, indicating that the presence of the amino acid glycine stimulates the combustion of other tissue constituents. Glycine with the amidine group from arginine, through a process of trans-amidination and transmethylation, yields creatine.

Comparison Between Multiple Sclerosis and Myasthenia Gravis

Myasthenia Gravis and Multiple Sclerosis differ only in that the former will not require as intensive treatment as will Multiple Sclerosis. The answer for this difference is obvious. One is a peripheral nerve pathology, the other being central nerve pathology. In the diagnosis, one will find the eyelids in Myasthenia Gravis drooping. In Multiple Sclerosis there will be nystagmus – constant involuntary, more or less cyclical movement of the eyeballs. Movement may be in any direction, but usually lateral as the patient follows the examiner's finger. (It is definitely more pronounced than that found in Meniere's disease.) There may be heaviness of the legs in Myasthenia Gravis, but it

will always be present in at least one leg in Multiple Sclerosis. Myasthenia Gravis patients will have difficulty in chewing and swallowing, the jaws might sag, and some will present a sad, masked-like expression, but never like Parkinson's disease. Scanning speech will be in evidence in advanced cases in Multiple Sclerosis, and words will come slow and syllabic. General weakness increases as the day goes on in Myasthenia Gravis; some increase in fatigue only with activity in Multiple Sclerosis. Remissions and exacerbations are common in both diseases in the early stages, but more so with Myasthenia Gravis. In Multiple Sclerosis, the patients will experience numbness of the hands and legs as the disease progresses, or a tremor in the hand will develop, making signing of one's name a problem. The tremor is intentional. Well along in the disease of Multiple Sclerosis, the gait will be awkward and stiff. Ataxia is due mainly to the inability to coordinate and control movements. The knee-jerks will be exaggerated, with positive Babinski and ankle clonus. The Babinski can be normal and no clonus, but there are other signs equally as important. Oppenheim's tibia test; Gordon's calf muscle test; Chaddock's external malleolus test, and the Hoffman reflex – a finger reflex. Any one of these, along with temporal whiteness of the optic nerve can be considered early or minimal Multiple Sclerosis. Abdominal reflexes are variable. Pain, bi-lateral, of the sartorius muscles with any positive reflex is always very suspicious of Multiple Sclerosis. In Myasthenia Gravis, the old neostigmine test is conclusive. More detailed symptoms and signs on these two pathological conditions can be found in such common reference as Merck's Manual. The important factor is early diagnosis. Do not hesitate to commence treatment in either disease even though the impression might be guarded. Response to treatment is sufficient evidence that your judgment is sound.

There are three forms of Multiple Sclerosis: 1) Pseudo-Multiple Sclerosis or Cerebral, which is the syndrome characterized by mental symptoms, emotional lability, convulsive seizures, hemiplegia and aphasia. This type is caused by an Adenovirus which gains entry into the brain through damage to the choroid plexus much like the encephalitis that follows pneumonias. Actually, the resulting pathology is an encephalitis. Many who have experienced this syndrome have died; many who have lived might just as well have died, for the return trip is costly, long, and requires a great amount of tender, loving care. 2) Cerebellar-brain-stem-spinal: this is true Multiple Sclerosis and is manifested by nystagmus, scanning speech, intention tremor, ataxia, transient paresthesias, weakness in one or more extremity, and visual disturbances. 3) Spinal or minimal Multiple Sclerosis: These cases are never given a diagnosis. These patients come with other complaints, but singular upper motor neuron pathology will be evident. This might be, as we have seen them, positive Hoffman, positive Gordon, positive Oppenheim, and occasionally, a patient with a footdrop limb.

Importance of Thiamin Hydrochloride in Neurological Diseases

The importance of thiamin in treating Myasthenia Gravis and Multiple Sclerosis cannot be over-emphasized. Two molecules of thiamin hydrochloride in combination with two molecules of phosphoric acid is cocarboxylase. For the reaction to acetyl coenzyme A plus oxaloacetic acid to continue through to citric acid with the release of coenzyme A, cocarboxylase must be present. If this reaction does not take place, due to one of many factors, there will be no coenzyme A present to react with another molecule of pyruvic acid to set in motion the elements necessary for the continuance of the metabolic cycle. In thiamin deficiency, both pyruvates and lactate accumulate in the blood. Pyruvates also accumulate at the neuro-muscular junction causing cloudy swelling of the distal portion of the nerves. Cocarboxylase, also known as diphosphothiamine, is necessary in the synthesis of acetyl-choline and in the control of its hydrolysis. The activity of choline esterase of serum is also strongly inhibited by cocarboxylase.

The chief chemical factor in both diseases is thiamin hydro-chloride. Other fractions of the B-complex are also essential but in lesser amounts. Myasthenia Gravis is due to genetic fault, most likely involving an intermediate lethal gene or group of genes. Multiple Sclerosis is more complex. The initial pathology is sickness caused by the Coxsackie virus. This virus mimics poliomyelitis, and for many years accounted for thousands of so-called polio cases. This virus, like the polioviruses, can cause paralysis but never permanently. The nerve damage is the result of microscopic hemorrhages in the central nervous system. With the contraction of the scar at the site of bleeding, the vessels carrying nutrients to the nerve cells are virtually clamped off. This leaves nerve tissue, in many instances, alive but not capable of work. As time goes on, this wasting of nerve tissue results in loss of its myelin protection. This is similar to electrical wires that have lost their insulation when exposed to the wear of daily use, or exposure to the elements. Myelin is a lamellated structure composed of neurilemma cell membranes. Neurilemma cells have marked affinity for axis cylinders, apply themselves closely and seemingly engulf them. At the same time their cytoplasm flows around the axis cylinder. The myelin sheath is actually part of the neurilemma plasma membrane with its lipid and protein layers. Myelin in the central nervous system is likewise lamellated. It is laid down by neuroglia cells. The sheath of the nerve fiber is known to have a relationship to speed of conduction – the speed of propagation being in direct proportion to the fiber diameter. Impulses are thought to travel along the surface of a nerve fiber and its speed

over the large myelinated fibers is approximately 337 miles per hour, 150 meters per second. We can reconstruct the nerve pathways and re-myelinate the damaged nerve channels. There is nothing new about this physiology. Each one of us has demonstrated or experienced positive Babinski reflexes. A child is born without completed laminated sheath. This is the reason for the spastic movements of the child. The nerve channels are minute in comparison to the adult person, thus we can expect a longer interval of time necessary for repair. If the baby can complete the myelination of its nerve channels with only mother's milk, surely we can duplicate this performance – and we can. There will, however, be situations where the pathology has existed for so long a time that recovery seems impossible. This is true because it requires approximately two years of treatment, with massive doses of vitamins and a high protein diet, to repair one year of the disease. Physicians are too afraid to make an early diagnosis, and some patients now under my care experienced as much as ten years in that process.

In Myasthenia Gravis, the chief concern is with the build-up of pyruvic acid at the neuro-muscular junction. We also find decreased amounts of acetyl-choline along with limited amounts of cocarboxylase. As we noted in the discussion of glycolysis, cocarboxylase plays a very important role in various reactions involving principally the decarboxylation of pyruvic acid and other keto acids. In the brain, cocarboxylase participates in the anaerobic dismutation of pyruvate to lactate and acetate, and their subsequent oxidation to carbon dioxide and water. Cocarboxylase is also involved in the synthesis of acetylcholine which is definitely in short supply in Myasthenia Gravis. The activity of choline esterase is strongly inhibited by this same double thiamin unit. The conversion of thiamin hydrochloride to cocarboxylase takes place in the liver, the kidneys and to a small degree, in brain and muscle. One can have nephritis, yet the small amount manufactured in the kidneys continues to be produced. The liver is the main source for this conversion. An individual with liver pathology would have a decreased capacity for phosphorylation of thiamin. The storage capacity of the body for thiamin is limited. It does accumulate rapidly in the liver in its original form and also as the pyrophosphoric ester. Thiamin deficiency inhibits lactic acid metabolism at the stage of pyruvic acid. When we refer to thiamin deficiency, we actually mean a lack of cocarboxylase. Pyruvic acidemia is an index of this type of thiamin deficiency. We might mention here that niacin deficiency can induce hepatic insufficiency. The amount of nicotinic acid required to elevate blood coenzyme, the active physiological form of nicotinic acid, increases dramatically in liver stress. Cocarboxylase (thiamin pyro-phosphate) operates as a coenzyme in the oxidative decarboxylation of ketoglutarate to succinate and of pyrovate to acetoacetate. Succinic acid in turn is acted upon by the enzyme succinic dehydrogenase, yielding fumaric acid by oxidative dehydrogenation. Fumaric acid readily undergoes hydration in the presence of the enzyme fumarase to form malic acid, which on oxidation in the presence of the enzyme malic dehydrogenase, yields oxalacetic acid. At this point of cell metabolism, the entrance of another molecule of pyruvic acid follows the Krebs cycle to be repeated. We are never concerned with the amount of pyruvic acid formed by the various routes, provided we can maintain normal cell metabolism.

Early Use of Thiamin Hydrochloride in Neurological Diseases

In the late thirties, Stern[1] from Columbia University, was employing thiamin hydrochloride intraspinally with astonishing results in Multiple Sclerosis. He reported taking patients to the operating room on a stretcher, and following 30 mg. thiamin given intraspinally, they would walk back to their room. The response was relatively transient, but it led Stern to believe that Multiple Sclerosis was nothing more than vitamin B1 avitaminosis, the "modus operandi" being damage to the filter bed of the choroid plexus. Stern also found that the effective dose of vitamin B1, when given in the lumbar subarachnoid space, was too close to the lethal dose as was demonstrated in dogs. Stern's hypothesis was backed by the knowledge that degeneration of the myelin sheaths of peripheral nerves as well as of the ganglion cells of the brain and spinal cord can be produced in experimental polyneuritis. Similar findings are observed in starvation, even when the supply of thiamin appears to be adequate. One school of thought regards the neurological syndrome of polyneuritis as a functional defect concerned with the neurons. From 30 years of observation, I am certain that in Myasthenia Gravis and Multiple Sclerosis, it is not a functional defect, nor is it due to impaired diffusion which would deny to the total metabolism sufficient quantities of the vitamin to satisfy the requirements of the neuro-muscular systems. The problem is supply and demand. In this light, Dr. Leon Rosenberg[2] of Yale University Medical School, in working with B vitamins, distinguishes between vitamin-deficiency diseases and vitamin-dependent diseases. He states that the successful treatment of vitamin-dependent diseases requires dosages up to 1,000 times the calculated minimal daily requirement. 1.3 mg. has been established for thiamin hydrochloride which would indicate that in the pathological conditions being considered, the daily requirement would be at least 1300 mg. Moore[3], in 1940, published a monograph on the use of high intravenous doses of nicotinic acid for the cure of Multiple Sclerosis. Moore employed a drug combination called "Nicobee." This preparation contained 100 mg. nicotinic acid and 60 mg. of thiamin in each 10cc solution.

Many of the components of the B-complex must also be administered in varying amounts, along with thiamin

hydrochloride, since they too exert a dynamic influence in general metabolism. Many believe that the B vitamins are actually metabolic reagents. Hoagland has referred to them as "protective catalysts."

Part II: Recommended Treatment Schedule

1) **Thiamin hydrochloride:** 300mg to 500mg, 30 minutes before meals and bed hour, and during the night if awake. The higher amounts in long-standing cases. This requirement is high, since much is lost through action of gastric juices and loss due to perspiration; 400 mg. daily by needle, given intramuscularly. During summer months this can be given every 12 hours to good advantage. Two to three times each week, and where office access is convenient, 20 mg. per kg. body weight, or at least 1000 mg. is administered intravenously. This is given with 100 mg to 200 mg. Niacin (nicotinic acid) which is available 100 mg. in 10cc ampules. (The concentrated Niacin, available in 30cc vials, must be diluted if employed intravenously.) The intravenous dose is given with the patient in a recumbent position. A 20cc to 30cc syringe, carrying a one-inch 22-gauge needle should be employed. The injection is given slowly (5 to 7 minutes) holding the syringe with one hand. The usually-employed three fingers of the other hand must be on the patient's pulse. An increased pulse rate indicates too fast a flow of the medicine. This indicates the rate of phosphorylization. Thiamin hydrochloride is, indeed, a toxic substance, and anaphylactic reactions have been reported, but I have never seen a case in treating thousands of patients, (not necessarily Myasthenia Gravis or Multiple Sclerosis), in 30 years of clinical observation. I have observed one case of extreme sensitivity in which itching was present within one minute after an intramuscular injection of 100mg. This was immediately controlled with 5cc Benadryl, IM. It must be remembered that once thiamin hydrochloride is phosphorylated, it is no longer a critical allergic substance, but is cocarboxylase, a necessary but absolutely harmless agent. (My problem has been the *preservatives* now required by FDA regulations, and *they* should be removed.) Higher doses of thiamin can be used, but then the dilution factor must be greater.

2) **Niacin (nicotinic acid)**: We recommend 100mg to 3 grams, thirty minutes before meals and at bed hour, and also during the night if awake – whichever dose will produce a strong body flush. Niacin dilates the blood vessels, even those that have been compressed by scar tissue, allowing a greater amount of nutrient material to reach the cell laboratory or factor comprising muscles and nerves. This constant, repeated dilatation of the blood vessels acts in the same manner as the dilating urethral catheter to correct constriction. One is chemical, the other is mechanical. Hot fluids taken at the same time as the niacin will enhance the flush. Pyridoxine has been a suggested stimulant. The lack of constant flushing in Multiple Sclerosis is disappointing but not hopeless. It will require a longer time to achieve results. Many times patients will flush with intramuscular niacin when they fail to flush by the oral route. An occasional patient will experience the sensation of a chill following nicotinic acid flush. This is transient and of no consequence. Food, even jelly beans or a glass of milk, will prevent or minimize the experience. Some patients will flush sometimes and not at other times, even during a single day. If no flush develops within 45 minutes, the dose should be repeated. A delayed reaction of several hours can occur, and should this be superimposed upon a previous medication, the result could be severe. Do not scratch when itching from niacin. Just press the area with your fingers, or better still, with a cube of ice. Antihistamines will stop the itching and limit the flush, should this be necessary. Niacin should be given very slowly by the intravenous route in the geriatric patient, with or without cardiac pathology, since it can produce dilatation great enough to effect right-side heart failure. Myasthenia Gravis patients sometimes attain geriatric status. Vasomotor collapse of peripheral vessels, although rare, can occur. Eight mg. Decadron given IM will reverse this condition.

3) **Pyridoxine (Vitamin B6):** Lack of this vitamin has been shown to induce microcytic hypochromic anemia and neurologic lesions in dogs and pigs. The term B6 includes not only pyridoxine, but also pyridoxal and pyridoxamine, all three compounds being found in nature. These derivatives have biological activity equal to that of pyridoxine, as demonstrated in rats. Pyridoxine plays a part in the metabolism of unsaturated fatty acids. It is also important in the metabolism of amino acids. Pyridoxal phosphate functions as a coenzyme, and in transamination reactions; 100mg to 200mg is given before meals and bed hour. At least 100mg daily is given intramuscularly.

4) **Cobalamin (Vitamin B12):** It is thought that vitamin B12 acts as a catalyst in the formation of the purine and pyrimidine deoxyribosides which are present in deoxyribonucleic acid. Technically, B12 is cyanocobalamin. Vitamin B12 with pterylglutamic reduces the requirement for choline essential in the treatment of neurological diseases; 1000mcg. is given three times each week by needle (repository type). The incident of dermatitis from continued use of vitamin B12 by needle is roughly 15%. I have never seen this develop in a patient with Myasthenia Gravis or Multiple Sclerosis. B12 is recognized as a factor in the synthesis of myelin.

5) **Ascorbic Acid (Vitamin C):** The use of high daily doses of vitamin C will prevent a superimposed illness and will lend itself in metabolism. Ten to twenty grams should be taken daily by mouth in divided doses.

6) **Riboflavin (Vitamin B2):** A deficiency of vitamin B2 in young animals results in inhibition of growth terminated by death. The yellow enzyme can, as demonstrated by Warburg and Christian, participate in a series of enzyme reactions involved in the metabolism of carbohydrates. It is capable of transporting hydrogen from reduced coenzyme II, a niacin coenzyme which attacks hexosemonophosphate, regenerating the riboflavin phosphate-protein complex. Riboflavin also takes part in enzymic reactions as a dinucleotide prosthetic group, consisting of riboflavin, two phosphoric acids, ribose and adenine. Riboflavin is very important in the regulatory function of the hormones involved in carbohydrate metabolism. It is classified as a low-energy package; 40mg to 80mg given daily by needle IM; 25 mg. before meals and bedtime.

7) **Vitamin E** as d-alpha tocopherol acetate of d-alpha tocopherol acid succinate. The latter is more practical since it is a pure form. Complex biochemical changes in the muscle tissue in chronic vitamin E deficiency are followed by histalogical lesions characteristic of muscular dystrophy. Deficiency has also been shown to produce demyelinization and distortion of the axon pattern in the spinal cord, giving rise to hypalgesia and progressive paresis. Fatal massive liver necrosis occurs in animals maintained on diets low in vitamin E and sulfur-containing amino acids; 800 international units before meals and bedtime must be adhered to in this treatment.

8) **Crude liver:** This substance contains factors still unknown but essential in metabolism. Patients with pernicious anemia often show neurological involvement, and are tremendously benefited by liver injections which, of course, contain vitamin B12. Degenerative changes brought on by other factors, therefore, can also be benefited by daily injections of crude liver.

9) **Adenosine-5-Monophosphoric acid:** One of the purine bases occurring in muscle is adenine. It, along with other purines, exists in various forms. Adenosine polyphosphate is of primary interest in this discussion. The basic structure is adenosine, adenine-9-riboside. This is esterified with phosphoric acid at the 5-position of the ribofuranose, to form adenosine-5-phosphoric acid, also known as adenosinemonophosphate (AMP). Inosinic acid is a commonly-occurring breakdown product of AMP, formed by deamination in muscle extract. Myosin displays enzymic activity similar to adenylic deaminase. By attaching further phosphoric acid residues in pyrophosphate linkage, adenosine-diphosphate (ADP) and adenosinetriphosphate (ATP) are obtained. ATP, as previously noted, is the energy package essential for life. By adding this to our treatment, we enhance all chemistry dealing with cell metabolism.

10) **Choline:** Choline is a structural component of fat and nerve tissue, thus has a strong relationship to the phospholipids and to its acetyl ester. Acetylcholine plays an important role in the humoral transmission of parasympathetic and other nerve impulses to effector organs. It also plays a part in transmethylation. Choline serves as a methylating agent in the physiological process – guanidoacetic acid to creatine. We give 700mg to 1400mg after each meal and at bed hour.

11) **Lecithin:** Lecithin is the glyceryl ester of a pair of fatty acids and a substituted phosphoric acid group attached to a choline radical. “Choline” is one of the products of lecithin, representing about 15% of the molecule. Lecithin placed in water and observed under the microscope, will diffuse out, forming long, curving strands (myelin forms). The hydrophilic nature of the lecithin molecule plays an important part in the structure and properties of cell membranes. It is the lipid used in nerve tissue. We give 1200 mg. Soybean Lecithin after each meal.

12) **Magnesium:** 100mg. after each meal to supply additional ions for muscle activity. It is an enzyme activator.

13) **Calcium Gluconate** (10 grain tablets): We give two tablets after each meal and at bed hour to supplement dietary intake for muscle activity. At times, this is given intravenously, one gram twice weekly.

14) **Calcium pantothenate:** The physiologically active form of pantothenic acid is coenyzme A. Its acetyl derivative (acetyl CoA) is synonymous with active acetate. Metabolic transformations are very complex and involve numerous enzymes and coenzymes. Coenzyme A participates in the acetylation of amines. The pantothenic acid coenzyme plays a vital role in carbohydrate metabolism and acetyl transfer also occurs in the metabolism of fatty acids. We give 200 mg. after each meal and at bed hour.

15) **Aminoacetic acid (glycine):** Glycine enters into a variety of metabolic functions. It is directly concerned in the synthesis of glutathione, the tripeptide which plays an important part in intracellular oxidation and reduction. Rapport and Katz have shown that when glycine is added to perfused muscle, the oxygen absorption is 40% higher than otherwise, indicating that the presence of this amino acid stimulates the combustion of other tissue constituents. To the body in general, glycine is no doubt most important because of its wide adaptability in the detoxicating process of the body. More than one hundred substances, when fed, are joined in the body with glycine. In the deamination of glycine, three products will be formed: ammonia, carbon dioxide and water. The ammonia from this reaction is then quantitatively converted to urea. One heaping tablespoon of the powder in a glass of milk four times each day. Much of the oral medication can be taken with this drink.

16) Make certain that the hemoglobin is at least 13 grams.

17) High protein diet with two to three eggs for breakfast.

18) One Theragram-M cap. daily for trace minerals.

19) Dantrium has value for relieving intentional tremor and Symmetrel for relieving stiffness in Multiple Sclerosis. Dose must be individualized.

20) Zinc gluconate: 10 mg. three times each day has some value in Myasthenia Gravis. Take several hours after vitamin B2.

This treatment works so dramatically in Myasthenia Gravis, that should a given patient's physician refuse to administer this schedule, I have this recommendation: One gram thiamin hydrochloride one hour before meals and at bed hour, and during the night if awake. Niacin taken at the same time, and in amounts sufficient to produce a good body flush. Two hundred mg. calcium pantothenate and 100mg pyridoxine before meals and at bed hour. Ten grams ascorbic acid, taken in divided doses. Amino acetic acid: one heaping tablespoon in a glass of milk, four times each day. Naturally, the full schedule will afford more dramatic response.

For a long time, it has seemed to me that virus bodies might have the potential to alter their protein coat, and therefore their dimension, and become another virus for another disease. In our long practice, we would see, as I am certain many of you have, chickenpox just before Thanksgiving, mumps by Christmas, red measles in the Spring, and polio or a virus mimicking polio in the Summer. German measles, virus colds, and virus pneumonitis just about any time.

Etiology of Multiple Sclerosis – Historical

As for the etiology of Multiple Sclerosis, a good history will tell the story. I have one patient who was diagnosed with Polio in 1950. He experienced total paralysis, but made a complete recovery. Five years ago, he began to demonstrate the signs and symptoms of Multiple Sclerosis. He was given a "strong" course of ACTH with relief of symptoms. Three months later, this had to be repeated, but the results were not as good. Some three months later, a third series of injections of ACTH was worthless. (This has been the pattern with the use of ACTH, and represents nothing more than whipping a tired horse. In my book, it borders on malpractice.) His myelin sheath has just about been destroyed. He has so many areas of "no insulation" that his movements are like that of a newborn baby. Had he received our treatment at the onset of his illness, he would be in good health today without any physical handicap. This individual never had Poliomyelitis. The virus that brought him down was the *coxsackie* virus, and this explains his initial recovery. Another case seen was a 31 year-old female. This young lady was diagnosed Poliomyelitis when she was 19 years of age. Three years ago, she began developing signs and symptoms of Multiple Sclerosis, and that is her present diagnosis. Her neurologist, who made the diagnosis of Polio, now tells her that there is no doubt in his mind that what she has now, actually started when she was 19. He is absolutely correct, because she had a *coxsackie* virus infection. In 80% of the cases that have come under my supervision, an illness compatible with a Summer virus has been entertained. Unless an illness is associated with paralysis, it is understandable when a patient or the family have difficulty in establishing a workable timetable.

Other Hypotheses on Etiology of Multiple Sclerosis

Dr. Henry Kempe, from the University of Colorado School of Medicine, as reported by *Medical World News,* believes that Multiple Sclerosis is caused by vaccinia virus. He found a correlation between severity of the clinical disease and antibody titer. He also observed that only in demyelinating disease were antibodies to vaccinia virus in the cerebral spinal fluid. This brings to mind the work of Horsefall and his co-workers at the Rockefeller Institute. They were able to culture an organism, which they designated Streptococcus MG, from a large percentage of their patients with primary atypical pneumonia. This proved later to have no value, and the viral nature of the disease was recognized.

The sleeping virus theory of Dr. Milton Alter and others, as reported in *Medical Tribune,* along with the environmental aspect for Multiple Sclerosis is another "ripe apple" for public consumption and public press exaggeration. Most of this theory rests with the circumstantial evidence that filterable transmissible agents having slow virus properties are present in other diseases.

Another theory, that of Dr. D.K. Schandl, a Nova University biochemist, in Fort Lauderdale, Florida, and published in *The Charlotte Observer,* relates it to an environmental agent, specifically carbon monoxide, and the lack of the vitamin pyridoxine (vitamin B6). Pyridoxine is concerned with the enzymatic decarboxylation of amino acids and the incidence of Multiple Sclerosis is too low in terms of the availability of carbon monoxide.

Still another theory has been advanced by Doris Dahl and Amico Bignami of Stanford University, Palo Alto, California. They report the discovery of a substance that "may" prevent the self-renewing of myelin. Scar tissue is indeed the problem, but it is the end result of microscopic hemorrhages following virus invasion.

Concepts Concerning Myasthenia Gravis

In Myasthenia Gravis, the accepted reasoning is initiated by Thymomas in 20% of patients over forty, and hyperplasia of the thymus in others. Antibodies to muscle have been reported in roughly 33%. Excessive pyruvates at the neuro-muscular junction has been recognized but not appreciated.

Case Histories

Multiple Sclerosis: Male, white, was in a wheelchair at a Veterans' Hospital for two years. Patient seen while home on 30-day vacation. Treatment given every day with marked improvement. Upon returning to Veterans' Hospital, the physician in charge recognized the improvement and advised the young man to return home and continue the treatment. After three years, he was given a clean bill of health by three neurologists in three different places and was given a responsible position. This was in 1950. The individual remains in excellent health, but continues with modified therapy.

Myasthenia Gravis: Male, white, receiving treatment from nearby medical centre for one year. He was receiving guanadine (amount unknown) and 90 mg. prostigmine bromide each day. He was first seen in a Myasthenia Gravis crisis. The emergency treatment consisted of two ampules of prostigmine methylsulfate of a strength of 1:2000, and 5cc of coramine. Within a period of eight or ten minutes, the patient experienced a generalized convulsive seizure which lasted some five minutes and required 4 men to hold him on the bed. Prostigmine, by needle, was continued for three weeks, and then 15mg. tablets every six hours. Thiamin hydrochloride was given three times each day, intramuscularly, as well as other fractions of the B complex. In one year's time, he had been "weaned off" prostigmine. Although given only two weeks to live by the physicians at the medical centre the day prior to our first visit, this individual lived a normal life for 18 years. His death was due to a cerebral accident.

Female, white, with diagnosis (August 1967), Polyneuritis. Began with pain and burning of legs associated with jerking. Ran high fever 10 days. Paralysis started on left side along with weakness of hands, soon followed with complete paralysis lower extremities. Seen first time 7/5/69. Paralysis and weakness as described. Started on medication by mouth and intramuscular injections. Several months later, began intravenous schedule. In approximately 16 months, was able to move right leg. Upper extremities returned to normal. On 6/10/72, began to move left foot. Patient now able to walk approximately 50 yards with knee braces and walker. Does all the cooking for family of four, as well as sewing clothes for herself and two daughters. (I can personally vouch for her ability as a cook.) April 1973, she was able to go without a back brace that was previously necessary for her to use to even get out of bed. One marvels at her ability to pedal a stationary bicycle "contraption" made for her by her husband so that she might exercise her legs. Our diagnosis in this case is Transverse Myelitis. (200 grams ascorbic acid given IV, in divided doses, would have saved this patient from paralysis.) She has also received 300mg ribonucleic acid four times each week.

Female, white, who developed weakness in extremities around June 25, 1961. Sensory examination revealed hypalgesia over medial aspect of right foot and calf. Motor examination revealed a partial foot drop on the right, with rather marked weakness and inversion, eversion, and dorsiflexion of right foot. Reflexes upper extremities 3-4 plus. Abdominal reflexes absent. Knee jerks were 3-4 plus with patellar clonus. Right ankle jerk was 4 plus and the left, 3 plus. Bilateral, sustained, ankle clonus. Babinski's "brisk."

Later examined and hospitalized at a nearby medical centre where Medrol was tried. She was sent home with a diagnosis of Multiple Sclerosis, superimposed by a viral meningoencephalitis. Blurring of vision was established as due to a left six-nerve paralysis. Seen in our office one month later, we concurred with the impression of Multiple Sclerosis. Our treatment schedule became operative. It has been a long journey since June 1961, but the results have been phenomenal. This individual has been returned to full activities, and as a gesture of gratitude, comes to my office to serve in the capacity of an office assistant several days each week. She does, however, still maintain her treatment schedule. Whether this is necessary or not, I follow the advice of another patient who has been continuing modified treatment for 22 years: "Why stop when you feel so good?"

Male, white, 28 years. Seen first time 2/26/72. History of numbness in lower extremities with loss of muscle control from waist down. This started approximately 2 years before this visit. Difficulty with bladder control at times. Seen by several neurologists at a nearby medical centre who failed to make a diagnosis other than to say he had a Central Nervous System Pathology. Babinski's, Gordon and Oppenheim signs were all positive, and ankle jerks were 4 plus. Ankle clonus was bilateral and sustained on right. He demonstrated a right foot drop. We entertained a diagnosis of Multiple Sclerosis. Treatment was not started since he had an appointment to be examined at a nearby Veterans' Hospital clinic. We advised him not to accept ACTH therapy. The following week we did start treatment. After 5 weeks, we did not see the patient again for three weeks, at which time he confessed that he thought that he was well and had stopped treatment. The weakness and other symptoms were again returning. He has been back to

gainful employment for the past 12 months. Incidentally, he has been a "crack" pistol shooter, and he still can hold a steady hand on the gun.

Female, white, 57 years. Seen first time 5/19/72. Chief complaint was fatigue. This started approximately seven years before coming to our office. The onset of illness was gradual. Generalized weakness as the day went on, but was always feeling refreshed in the morning. Drooping of the eyelids became a problem so that she automatically would tilt her head backward so that the ptosed eyelids would be partially corrected. Fatigue of the muscles of mastication on chewing became so embarrassing that for the past several months, she avoided all social events, even dinner with friends. Swallowing also became a serious problem forcing her to a bland and sometimes liquid diet. Even a few minutes talking, while taking the history, would so fatigue her that she found it necessary to recline on the examining table so as to regain her strength. She visited many clinics and medical centers in the United States and Europe, but always was given the same diagnosis – her review of conditions labeled her as *psychosomatic.* To us it was obvious that she suffered from advanced Myasthenia Gravis. 1000mg. Thiamin Hydrochloride and 300mg. pyridoxine given by needle had her demonstrating jaw and face movements to her husband in less than 10 minutes. She remarked that she had not been able to do that in three years. She was given our schedule for treatment, but had great difficulty getting her local physician or *any* physician to give her the needed injections. In desperation, she returned to one of the medical centres and confronted them with the diagnosis, which they did not believe. She, however, demanded that they employ their test for this disease, which they did. From the patient's description, given at a later visit, I surmised that Tensilon was used. Her response was the greatest ever seen in that University. She is also receiving RNA 300mg. tablets three times each week, which we believe have stimulated or furthered her progress. She no longer hesitates to eat in public, and her stamina is approaching normal. During a visit to our office in April of 1973, she laughed and joked about her experiences in getting the diagnosis confirmed so that she could receive the vitamin injections under supervision. She also favored us with a platter of delicious cakes that she had baked.

Although we could write a book on cases treated and cured (or established a permanent remission), time is a prohibiting factor.

Conclusion

The treatment of Multiple Sclerosis has been empiric since it was first described by Sir Robert Carswell in 1838. Brickner, in 1936, gave a review on treatment which included preparations of Antimony and Arsenic, fever induced by various methods such as diathermy, malaria, typhoid vaccine, and fever brought on with the use of drugs. Surgical procedures such as cervical sympathectomy and root section were also employed. Serums, hypnotism and intraspinal injections of lecithin had their day. Moore administered nicotinic acid and thiamin following the dissertation by Zimmerman and Burack on diseases of the nervous system resulting from a deficiency of the vitamin B-Complex, and the paper by Spies and others on the use of nicotinic acid in the treatment of Pellagra associated with mental pathology. Spies and Aring, in 1938, published a paper on the effects of vitamin B1 on peripheral neuritis as associated with Pellagra. Moore also had the benefit of the work of Stern, who published an article on the intraspinal use of vitamin B1 for the relief of intractable pain, and for inflammatory and degenerative diseases of the Central Nervous System. We learned early in our approach to this disease that small and infrequent doses of thiamin hydrochloride would not accomplish our purpose, and we also realized that more than one unit of the B-Complex would be required, even though the physiological chemistry relative to this phase of metabolism had not been completely established. Although Moore used nicotinic acid for vasodilation purposes, we rationalized that the degenerative process taking place in nerves, and thus also in muscle, was of a greater magnitude. Inasmuch as the only sickness remembered by the patient, family or relatives took place during the summer months, we immediately suspected a virus to be the offending agent.

This idea gained momentum with the greater incidence of Multiple Sclerosis following the epidemic of encephalitis lethargia of 1920 to 1926, and the epidemic of encephalitis B in St. Louis and Toledo in 1934. However, the incidence of Polio was also up. Mixed, abortive or unrecognized cases of Poliomyelitis became a tantalizing factor. After the isolation of the Coxsackie virus with its mimicking of Polio, and the knowledge that the paralysis with this type virus infection was never permanent, the real devastating factor, in time and place, at least to me, became apparent. Flexner and Lewis were able to demonstrate that in Polio, vascular and lymphatic lesions constituted the primary causes of the lesions of the nervous system. Multiple hemorrhagic accidents take place in Multiple Sclerosis with ensuing scar tissue. As these microscopic scars contract, they impinge on the vessels carrying nutrients to the Central Nervous System cells. In muscle, the "devastation" is brought about through lack of function, there being no "electrical charge" present to keep muscle active. For this reason, the Sister Kenney treatment for Polio had merit, since it helps to maintain muscle and muscle-nerve integrity. Our employment of nicotinic acid is to effect adequate dilatation of existing vascular structures, producing over time, chemically, what the Urologist accomplished

with his catheters in a mechanical fashion. Once these channels are sufficiently operative, the metabolic factors that we supply will go about revamping the myelin sheaths. Due to lack of full energy components, cells can temporarily lose the ability of normal physiological activity. We can restore the normal function of cells which depends upon their ability to extract and use the chemical potential energy locked within the structure of organic molecules. We accomplish this by placing massive amounts of the essential material at the disposal of cells.

We categorically make this statement: Any victim of Multiple Sclerosis who will dramatically flush with the use of nicotinic acid, and who has not yet progressed to the stage of myelin degeneration, as witnessed by sustained ankle clonus elicited in the orthodox manner, can be *cured* with the adequate employment of Thiamin Hydrochloride and other factors of the Vitamin B Complex in conjunction with essential proteins, lipids, carbohydrates and injectable crude liver. If sustained ankle clonus is not bilateral, then it is not a deterrent. We have had patients who did demonstrate bilateral sustained ankle clonus, and who were in wheelchairs, and who returned to normal activities after 5 to 8 years of treatment. These patients, fortunately, had not received ACTH. One patient was given a single course of Medrol 4 mg. QID. This had little effect on her pathology, and apparently no blocking action, on our treatment. The general use of ACTH in Multiple Sclerosis will extend the recovery period by a time directly proportional to the amount of the drug employed. It is hoped that this paper will bring an end to this senseless practice of medicine, since ACTH *never* works the third time.

The theories recognized as playing a part in Myasthenia Gravis still rest in the main with Thymus enlargement or tumor, Endocrine dysfunction, Metabolic fault, and the build-up of pyruvic acid in the vicinity of the motor end-plates. In reality, it is a genetic fault involving a lethal intermediate gene or group of genes. There is definitely an over-supply of pyruvates, and an under-supply of acetylcholine. The cue in this drama is cocarboxylase. Coenzyme A is also in limited supply. Two molecules of thiamin hydrochloride, and two molecules of phosphoric acid yields cocarboxylase. One way of obtaining acetyl coenzyme A, a by-product of coenzyme A and pyruvic acid, is in the reaction between pyruvic acid, coenzyme A and diphosphopyridine nucleotide in the presence of diphosphothiamine (cocarboxylase). Cocarboxylase is also involved in the synthesis of acetylcholine and in the control of its hydrolysis. The activity of choline esterase of serum is strongly inhibited by this same agent. Thiamin occupies a key position in at least the terminal stages of carbohydrate metabolism. Cocarboxylase plays an active role in the decarboxylation of pyruvic and other keto acids. In the brain, cocarboxylase participates in the anaerobic dismutation of pyruvates to lactate and acetate, and their subsequent oxidation to carbon dioxide and water. In liver and other tissue cells, cocarboxylase is involved in the conversion of pyruvates to oxalacetate which combines oxidatively and irreversibly with another molecule of pyruvate to enter the tricarboxylic acid cycle. In thiamin deficiency, a form of peripheral neuritis markedly demonstrated in some cases of chronic alcoholism exists, affecting both sensory and motor nerves.

The treatment of Myasthenia Gravis is that of any pathology dealing with the interruption of the normal physiology of nerve cells. In years past, when we were treating Poliomyelitis successfully with massive doses of ascorbic acid, we would always follow with an indefinite timetable, giving the B vitamins for nerve repair. We see the same results when treating damage to the spinal cord, whether this is due to mechanical trauma, or to the inflammation caused by a virus – any virus. As pointed out by Lipschitz et al., the replenishing of vitamin B1 restores the ability of the nervous system to handle properly pyruvic acid and dextrose. This action of thiamin makes its function in Myasthenia Gravis seem elementary. A German scientist once speculated that cocarboxylase was actually the “food” required for nerve life. In treating Myasthenia Gravis with the schedule outlined, the intensity with which it is applied in Multiple Sclerosis will never be necessary. We are not confronted with the loss of myelin sheaths in extra vital areas. The chemistry, however, is more complex than in Multiple Sclerosis, since it involves muscle cells to a greater degree. Enzymes and their balance is a necessary approach. When we realize that over 900 different enzymes have been identified, it makes more knowledgeable the need for extensive vitamin therapy. This suggests that normal liver function is necessary for good results. A simple liver function test can be used to good advantage. One that I worked out many years ago to demonstrate “liver stress” is performed as follows. Have patient bring 90cc from first voiding upon arising. Fill ordinary test tube to within one cm. of top. Allow to set for 24 hours and read. One will find, in most specimens, a gelatinous fluid resting at the bottom of the test tube. The amount present, which can measure 2-1/2 cm., indicates the degree of liver stress present. Choline by needle or by mouth will remove this finding from the urine. Some urine specimens will show a heavy, white sediment obstructing proper reading of liver stress. Glacial Acetic Acid alone, and/or heat will temporarily remove these phosphates. Should the deposit of phosphate be exceedingly heavy, then it is advisable to secure a bedtime specimen, or one 2 hours after breakfast. The night specimen should be placed in a cool area until delivery. Occasionally, the urine specimen will look like skim milk. This is due to earthy phosphates and can be cleared by adding Glacial Acetic Acid to the tube. (After ascertaining liver stress, one can then add 20 drops Glacial Acetic Acid to the specimen – if none was previously added – and

allow to remain an additional 48 hours to check for Uric Acid Crystals. A red shower indicating an abnormal level for uric acid.) This test must be run every week when administering ribonucleic acid (RNA).

Appendix

Since presenting this paper, we have observed that improvement in all categories is enhanced when the intravenous injection contains 800 mg. to 1000 mg. thiamin hydrochloride, 200 mg. pyridoxine, 400 mg. niacinamide, 100 mg. nicotinic acid. The thiamin hydrochloride solution *must* be clear. The amount of niacin employed must be calculated from the "flush factor" of a given patient. The injection is made with a 20cc or 30cc syringe, using a 23G x 3/4 inch or 22G x 1 inch needle. Intravenous medication can be given daily; it should be administered at least twice weekly. Due to sensitivity possibilities, we always have the patient take the intramuscular injections for three weeks before starting intravenous therapy.

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A native of Pennsylvania, Dr. Klenner attended St. Vincent and St. Francis Colleges, where he received his BS and MS degrees in Biology. He graduated *magna cum laude* and was awarded a teaching fellowship there. He was also awarded the college medal for scholastic philosophy. There followed another teaching fellowship in Chemistry at Catholic University, where he pursued studies for a doctorate in Physiology.

Dr. Klenner then migrated to North Carolina and Duke University to continue his studies. He arrived in time to use his knowledge in Physiology and Chemistry to free the nervous system of the frog for a symposium, by immersing the animal in 10% nitric acid. Taken in tow by Dr. Pearse, chairman of the department, he was finally persuaded to enter the school of medicine. He completed his studies at Duke University and received his medical degree in 1936.

Dr. Klenner served three years in post-graduate hospital training before embarking on a private practice. Although specializing in diseases of the chest, he continued to do General Practice because of the opportunities it afforded for observations in medicine. His patients were as enthusiastic as he in playing "guinea pigs" to study the action of ascorbic acid. The first massive doses of ascorbic acid he gave to himself. Each time something new appeared on the horizon, he took the same amount of ascorbic acid to study its effects so as to come up with the answers.

Dr. Klenner's list of honours and professional affiliations is tremendous. He is listed in various "Who's Who" registers, and has published many scientific papers throughout his career. Dr. Klenner is a Fellow: The American College of Chest Physicians; Fellow & Diplomate: The International College of Applied Nutrition; Fellow: The American Association for the Advancement of Science; Fellow: The American College of Angiology; Fellow: The American Academy of Family Practice; Fellow: The Royal Society of Health (London); Fellow (Honorary): The International Academy of Preventive and Orthomolecular Medicine; Fellow: International College of Angiology; and Founder-Fellow: American Geriatrics Society.