

Nutrition as Applied Biochemistry

Elaine Fox, Ph.D.¹

Linus Pauling made history, in April of 1968, in an article which appeared in *Science*, by enunciating a concept of therapy which provides "the optimum concentrations of substances normally present in the human body". As we all know, he called this type of therapy, Orthomolecular.

The concept of Orthomolecular, the optimum concentration of substances normally present in the human body, appears to be a very simple concept, but it raises two important questions. Where do we get these substances, and how do we know what the optimum concentrations are?

Roger Williams, in his book *Nutrition in a Nutshell*, published by Dolphin Books in 1962, addresses the first question. He tells us how we should go about obtaining the different items that we need for life:

Living organisms from the simplest to the most complex types contain the same amino acids (not the same proteins), the same vitamins and the same minerals. A simple rule that will enable us down-to-earth people to get some of everything we need is this: Take a bit of some living organism! One amendment to the simple rule will improve our chances of getting a well-rounded diet. It is this: Don't restrict yourself to one part of a living organism, try to get the "whole works". In the plant realm, do not restrict yourself to green

leaves, or to roots, or to seeds, or to fruit. Each of these is in itself incomplete. A combination diet containing leaves, roots, tubers, seeds and fruits is a vast improvement. In human nutrition the same principle holds, whether one is considering plant food or animal food. A lack of appreciation of this principle appears in the all too common tendency to eat exclusively the muscle of slaughtered animals and reject everything else ... We will get much better rounded nutrition if we include in our diet some connective tissue, liver, glandular organs, sweetbreads, brains, skin, fat and even gastro-intestinal tissue (tripe).

The unity of nature has existed for millions of years. Long before men appeared on the earthly scene there were the same amino acids, vitamins and minerals as we have today. Every evidence indicates that throughout geological time, these basic ingredients

1. Division of Nutritional Medicine North Nassau
Mental Health Centre 1691 Northern Boulevard
Manhasset, New York 11030.

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have played an indispensable role in the life of living things. If we try to fight this unify, or forget its existence, our efforts are likely to be futile (Williams, 1962).

So from Roger Williams, we know that we should eat a wide variety of food to obtain the substances that we need. But how much of it should be in the form of animal protein and how much should be vegetable?

We are all familiar with the work of Dr. Robert Atkins, who recommends a high protein, high fat, low carbohydrate diet to people who are suffering from a wide variety of problems, including obesity and high blood pressure. Dr. Atkins has a great deal of success with his patients, but he also has those who do not respond.

On the other hand, Nathan Pritikin has popularized the high carbohydrate, low fat, low protein diet for a wide variety of problems, including obesity and high blood pressure. This diet has been very successful with many patients but there are those who do not respond.

Why is it that many patients respond to both of these diets, and is there some way of predetermining who will respond to a high protein diet and who will respond to a high carbohydrate diet?

It appears that a large percentage of our population will improve just by having the negative substances removed from their diets and will feel better when sugar, caffeine and highly processed foods are eliminated. Both the high protein, low carbohydrate diet and the high carbohydrate, low protein diet eliminate these products. For most of these people the percentage of protein or carbohydrate in their diet is not critical and if they follow Roger Williams' principle of the Unity of Nature, they will do just fine.

But, there are some people for whom the Unity of Nature is just not good enough.

One of the reasons for the failures on either of these two regimens, or on any diet, is that they may be feeding foods to which the individual is sensitive. So, if a person has a gluten sensitivity, he would feel better on a high protein diet since it reduces or eliminates the gluten. If he has a sensitivity to beef or chicken he would feel better on the high carbohydrate, low protein diet.

Another possible cause for the failure of those on the high carbohydrate diet may be due to the percentage of people who suffer from

candidiasis. As you know these are the individuals who have an overgrowth of *Candida* in the gut which sets the stage for a wide variety of problems, including hypersensitivity. Since the *Candida* seems to thrive on sugar and grains, those individuals may not feel well on the high carbohydrate diet.

But what about those patients who do not have significant food sensitivities? Are there any clues as to who will feel better on a high protein diet and who will feel better on a high carbohydrate diet?

I'd like to share with you some of the biochemical parameters that I find useful in determining which patients respond to a high protein diet and which patients respond to a high carbohydrate diet.

The two readings from the SMAC that I find to be the most helpful are the Uric Acid and the Total Protein. If the Uric Acid runs in the high or high normal range, then you are looking at an individual who would probably feel better and do better on a high carbohydrate, low protein diet. Although there are foods on the high carbohydrate diet which are high in purines such as whole wheat and beans, the nucleoproteins, which yield purines, are found in greatest concentration in animal foods. From my experience these people can generally control the uric acid metabolism by staying off a high protein diet.

On the other hand, if patients have low Total Protein, then either they are not getting enough protein in their diet or they are not sufficiently digesting the protein they are eating. If they are eating a diet which appears to have a sufficient amount of protein, their digestion may need to be improved, either with the use of pancreatic enzyme replacement therapy or with the use of acid replacement. If the diet is a low protein diet, they may not be consuming enough protein. As you know, according to Roger Williams, the need for protein varies by a factor of 5.

For those patients who do not exhibit any biochemical markers, and you have checked for food sensitivities and they are still not doing well on their diet, it is sometimes helpful to go back to the work of George Watson.

In his book *Nutrition and Your Mind*, he

gives us a method for determining whether a person should be on a high protein or a high carbohydrate diet. He categorizes people as fast or slow oxidizers. According to Watson, the slow oxidizers are those who feel better on a high carbohydrate diet, while the fast oxidizers are those who feel better on a high protein, high fat diet. Watson has developed a questionnaire to help us determine an individual's psychochemical type. He also uses the response to a glucose load as a criterion. He feels that hypoglycemics are fast oxidizers and therefore need a high protein diet and that hyperglycemics are slow oxidizers and would feel better on a high carbohydrate diet, which is interesting in light of the current therapy of treating diabetics with a high carbohydrate diet.

Paul Eck, some of whose work may be questionable, has done a good job of characterizing the fast and slow oxidizers. In a recent *Healthview Special Report*, he describes the fast oxidizers as those who do better on a high protein diet, who are high energy individuals, and who think and talk fast. They have a lot of nervous energy. Some of their physical characteristics include warm hands and feet, moist skin and a tendency to perspire easily. They often do their best work at night. They tend to overwork and to take on more than they can handle. They are outgoing and extroverted. They work and play too hard. Sounds a little like a Type A individual.

Slow oxidizers metabolize food at a rate too slow to derive maximum levels of energy from what they consume. They do better on a high carbohydrate diet. They are more stable in many ways and have fewer ups and downs. They are slow moving, calmer and generally less keyed up than fast oxidizers. They do not perspire as much and have cooler hands and feet. Slow oxidizers are not as extroverted as fast oxidizers.

It is the balanced oxidizers who metabolize food at a normal rate and produce energy which is adequate yet not excessive. These are the people for whom the percentage of animal and vegetable foods is not critical.

Let's go on to the second question. How do we know what are the optimum concentrations of these substances?

If we refer that question back to Linus Pauling, in his article on Orthomolecular Psychiatry, he says that: *Several arguments may be advanced*

in support of the thesis that the optimum molecular concentrations of substances normally present in the body may be different from the concentrations provided by the diet and gene-controlled synthetic mechanisms, and, for essential nutrilites (vitamins, essential amino acids, essential fatty acids) different from the minimum daily amounts, required for life of the "recommended" (average) daily amounts suggested for good health.

He goes on to talk about the process of evolution which may change our ability to synthesize certain vitamins such as ascorbic acid, or the possibility that the environment has changed during the last 20 million years in such a way as to provide a decreased amount of the vitamin.

In addition, we have to consider that calorie needs have also diminished over the last 100 years, and with a decrease in calorie intake there comes a decrease in nutrients. We are all aware of the destruction of nutrients in foods due to our current methods of agriculture, due to the length of time between when a food is picked and it is eaten and due to our methods of processing these foods.

The Committee on Dietary Allowances of the Food and Nutrition Board of the National Academy of Sciences has published their *Recommended Dietary Allowances*, which supposedly gives us the guidelines for the needs of groups of healthy people. As we know, it was never intended to be applied to individuals, and as the Committee states:

Special needs for nutrients arising from such problems as premature birth, inherited metabolic disorders, infections, chronic diseases and the use of medications require special dietary and therapeutic measures. These conditions are not covered by the RDA.

In their own guidelines they are admitting that there is a large group of people who need higher doses of nutrient intake than they recommend. One of the most important groups of those who should be excluded from the RDA is the group suffering from inherited metabolic disorders. The orthodox medical community does recognize certain rare genetic diseases in which mega-vitamin

therapy is necessary to prevent retardation and death. Discovery of these vitamin-dependent disorders dates from 1954, when A.D. Hunt and his associates reported on the case of two infants, who suffered from violent convulsive seizures that responded only to large amounts of B6 (5 to 25 mg/day — the normal infant requirements is 0.5 mg or less). In the subsequent years the list of vitamin-dependent disorders has expanded to more than a dozen involving six different vitamins. All of these disorders are alike in being inherited, in involving one or another specific biochemical abnormality and in responding only to pharmacologic doses of the vitamin in question (doses ranging from 10 to 1,000 times the physiologic requirement). These inherited disorders include methylmalonic aciduria, which is a B12 deficiency disease and homocystenuria, a B6 dependency disease.

Leon Rosenberg of Yale University, in an article on Vitamin Dependent Genetic Disease says:

Individually and even collectively, the vitamin-dependent conditions seem to be quite rare. It is conceivable, however, that, as with some other metabolic errors, our improved knowledge of what to look for may eventually reveal that some of them are more common than it now appears.

Therefore, the problem appears to be in the ability to recognize inherited metabolic disorders. Unfortunately, they do not realize that there is a wide divergence between having a system function at 100 percent efficiency and having it not function at all. McKusick, considered to be the father of genetics, estimates that one person out of every 250 has some degree of metabolic error which is inherited. We, in the field of Orthomolecular psychiatry and Orthomolecular medicine are devoted to helping this large group of people. How do we go about doing it? All of us make clinical judgments as to the needs of our patients based on research, both published and unpublished, the experience of other clinicians, some of which we gather at meetings such as these, as well as our own clinical experience. We use diet and supplements which have helped others who present with the same symptoms. This gives us a starting point, and for many of our patients, it is enough. In fact, in a research project I undertook to satisfy the requirements for my Ph.D., I found

that by utilizing this type of information we were able to help over 60 percent of those people who come to us with problems, whether it was for a mental or physical problem, or, as with many of our patients, a combination of both. But what about those for whom we have not been successful?

We are fortunate at this time to have additional tools available. By now you are all familiar with functional vitamin tests, the tests which measure the utilization of vitamins as cofactors of enzymes. Just having what appears to be enough of the vitamin in the blood, or even in the cell is not enough information. What determines the optimum concentration of the substances that Pauling talks about depends upon the activity of that substance or the functionability. To use a simple analogy you can try to guess the output of a factory by the number of workers employed — but if the machinery in that plant is old it might take more workers to produce the same amount of work as a factory which has new efficient equipment.

If we go back to the perception of the orthodox medical community, they are assuming that we all operate at maximum efficiency. It is only when the factory is in danger of being shut down, when we exhibit classic signs of metabolic dysfunction which leads to retardation or even death, that they start getting involved.

The view of the Orthomolecular medical community is that many of us do not function at 100 percent efficiency and although we may not present with severe symptoms, we can improve functionability if we supply the raw materials in the optimum concentrations. Therefore, we need a method of quantitatively determining which substances may not be present in the optimum concentrations, and that is where some of these new clinical tests can be helpful. Many people question whether these assessment tests should be performed while the patient is taking supplements, or whether the patient should discontinue supplements for a period of time prior to testing. These patients generally are those who have not responded as much as we would like from therapy. We perform the tests while the patient is currently

taking all his supplements since the information we are looking for is where the supplementation may be deficient.

When we first started to examine the results of the functional vitamin tests, we had hoped that we could find some sort of pattern of reduced function in patients presenting with similar problems. Certainly, there are some patterns that do show up, but the concept of biochemical individuality was reinforced as we examined more and more of the test results.

What we did find is that these patients certainly do have greater needs than those supplied by the diet, even a good diet, and therefore may fit into the classification of inherited metabolic disorders. What makes it so difficult is that these metabolic disorders do not manifest the same in each person. One of the reasons for this is that we generally do not find just one problem. These individuals usually have a variety of metabolic disorders.

One of the problems we had to deal with was trying to decide how much we should increase the supplements in these individuals. If we go back to the classical inherited metabolic disorders, it is helpful to remember that their needs vary from 10 to 1,000 times the physiologic requirement. How much we increased the amount they were taking varied, based on the laboratory result, on the patient's intake before the test and which nutrient was found to be insufficient. In some of our patients we had to by-pass the intestinal tract and give the supplements I.M.

In order to check to see if we increased the supplement enough, we repeated the specific tests until we found that the activity of these enzymes increased. Unfortunately, we did not find a correlative change in symptomatology in most of our patients. We went back to examine whether these tests were valuable.

As we said before, most of these patients have more than one problem, not only with vitamins as cofactors, but with other areas of metabolism as well. We concluded that these tests were valuable, but we needed more information. We had to be able to examine other areas to find out whether there were problems with the metabolism.

So now in addition to examining the need for the co-enzymes by functional assay, we utilize a fatty acid profile and a 24 hour urinary amino

acid analysis, along with the standard tests and sometimes in addition, minerals in the red blood cells and plasma amino acids.

Most of us are quite capable of interpreting the functional vitamin tests; they are clear cut. The essential fatty acid profile gives us a breakdown of the fats in the blood, and interpreting these results is a little more complicated, but with some experience can be done without too much difficulty. But in order to utilize the 24 hour urinary amino acid test to its maximum, we have found it helpful to enlist the aid of a biochemist and have found the services of Bionostics to be invaluable.

The reason for this is that the urinary amino acids reflect the biochemistry of the body. By tracing back along the metabolic pathways we can get some insight into the functionality of the minerals, which are involved as activators in enzyme metabolism. We can gather information as to the efficiency of the Krebs Cycle. We can uncover problems with digestion and possibly with malabsorption as well. We can look at the urea cycle. Food sensitivities may even be identified if a patient is having difficulty in the metabolism of a specific amino acid such as methionine, and we can also identify problems which may stem from low levels of the precursors of the neurotransmitters. It can really give us a great deal of information about the patients' metabolism if we have the knowledge and the time to uncover it. Two important questions to address are: What patients do we perform these tests on, and what degree of success do we obtain?

The question as to on whom we perform these tests really is a function of the degree of health that the patient is interested in obtaining. If the patient is very ill and you have some degree of success by using your clinical expertise, and the patient and his family are satisfied with that improvement, you will probably stop at that point. But if you achieve a measure of improvement which is not consistent with the goals of that person, or if someone wants to do everything possible to stay healthy, then you have another tool at your fingertips.

The most important question is whether the tests give us information which helps the patient. First of all, I think we have to bear in mind that these patients in general are the ones who are the most difficult. The usual mode of treatment has not been effective, so any degree of improvement is significant.

Most of the results that we have had are not dramatic. The improvement is slow and gradual, but we have found that by applying therapy based on the results of the tests we have been able to help a number of patients achieve some improvement and we expect to see even greater improvement as time goes on. I think it takes as long as two years to get the maximum results.

As we said before, we use the functional vitamin tests to determine whether we have reached the optimum dose of coenzyme. We have also used the 24 hour urinary amino acids to see if we have improved overall metabolic function and to give us information as to the next step to take in terms of therapy. So these tests can be used to measure improvement as well.

Generally we try to have the patients take the functional vitamin tests along with the fatty acid profile and the 24 hour urinary amino acids. There are a number of reasons for this. First of all, as we said before, the vitamins work in concert with other factors, and the more information we have the greater chance of success. Another reason for doing the tests at the same time is to save the patient the trouble of collecting the 24 hour specimen twice. Also Bionostics will use all the information in their interpretation of the 24 hour urinary amino acids and the more information they have, the greater the accuracy of the interpretation.

Certainly there are times when we will obtain the results of the functional vitamin assay and try to correct those problems before we have the patient go through the 24 hour urinary amino acids. Usually we will do this when the patients do not want to lay out a large sum of money at one time.

Talking about finances, one of the questions that I am frequently asked is whether these patients are reimbursed by insurance. In this area as with many others, we have found that there is a great deal of divergence in the insurance industry. Some patients have the total package, including the interpretation covered by 80 percent. Other patients

who ask their insurance companies for a predetermination are told that they will not cover the tests at all. These are the two extremes. Some of the companies will cover some of the tests and not others, and some will not cover the interpretation. Some of the companies will only cover these tests if the diagnosis is metabolic error and we have started adding that diagnosis to all the patients for whom these tests are recommended. Any abnormal results would support that diagnosis.

Certainly, there is a great deal of information that we are able to gather by using these tests, but we have to realize that there is so much more that we need to learn about nutrition. For example, we do not know what is the best time of the day to administer certain nutrients. The same nutrient given at different times of the day may have different effects. One of the best examples is tryptophan; given at bedtime it may work to help induce sleep, but given during the day it may work as an anti-depressant. Even calories consumed at different times of the day will be utilized differently. Halberg found that subjects consuming the same 2,000 calorie meal in the morning will lose weight, but if consumed as dinner, 66 percent will gain while the other 33 percent will lose, but will lose less than if they consumed the meal in the morning.

There is so much more we need to learn about the interaction of nutrients. The recent publicity on the toxic effects of high levels of B6 helped to make us aware of how important it is to have the factors that activate the co-factors available in the proper amounts, not only to prevent adverse side effects, but to maximize utilization.

We are all aware of the fact that our need for nutrients changes from day to day, and possibly even from hour to hour, depending upon the amount of physical and emotional stress we are under, the variety of chemicals we are exposed to including pollution and even the type of light we are exposed to.

There is so much more we need to learn about nutrition as applied biochemistry. I think you will all agree that being involved in such a dynamic field, where we are constantly making new discoveries is one of the

NUTRITION AS APPLIED BIOCHEMISTRY

things that makes this entire field very exciting.

In conclusion, I would like to share with you a vision I have of the future. One day we will all wear on our wrist, a watch-like device. At various times during the day we will press the button on the side and we will get a computer read-out, which will not only give us the amount of each supplement we need and when to take it, but will also list the foods which we should include in our diet for that day. Until we reach that point in our technology, and I do believe that we will, we have to utilize the tools we have available today, in order to help us help our patients.

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