A Chemist's View of Nutrition

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OVER 150 YEARS AGO LAVOISIER, WHO is recognized as the father of the science of nutrition, stated: "La vie est une fonction chemique." Since that time chemistry has played the central role in the development of nutrition knowledge. The development has been accelerated as organic and physical chemists, as well as biochemists, have recognized nutrition as a worthy field of activity.

In 1912 the existence of the first vitamin was definitely proved—as a *something*, a quality, a property, or perhaps a substance, which some foods had and others did not. Other vitamins became thus recognized in succeeding years, but it was not until the organic chemist commenced to give these "somethings" attention that the field really moved. It was over 15 years after the first vitamin was discovered that the chemical nature of any of them was definitely established. In the succeeding years, isolation, determination of structure, and, frequently, synthesis followed increasingly closely on the biologists' discoveries. In fact, the organic chemist has assumed the role of discoverer, or at least the final arbiter, as to whether a proposed vitamin is entitled to be considered a separate entity. The elucidation of the folic acid puzzle, which has resulted from the determination of the structure of the *Lactobacillus casei* factor through analysis and synthesis, is a striking example. Synthesis, particularly on a commercial scale, has given a tremendous impetus to the advancement of vitamin research as well as to human medicine.

While chemistry is making new discoveries which may enhance the importance of nutrition, it can also play a major role in keeping nutrition practice sound. The overexploitations of the last few years, which have embarrassed the true nutrition scientist and hurt the cause of nutrition, can only be combated by clearly established facts. Optimum nutrition certainly will not be accomplished by saturating the body with a few vitamins, with lesser attention accordingly to other essential nutrients.

Nutrition deals with proteins, energy-forming nutrients, minerals, and vitamins, but these nutrients must be translated into foods. Thus, nutrition must deal with both body needs and food supplies. Chemistry is concerned all the way across the board from production through processing and storage to the home preparation of food, as well as with what happens to it inside the body. Body needs must provide the basis for determining the kinds and amounts of food supplies required, and here much more needs to be learned.

First of all, we need a better understanding of the biochemistry of body processes and, particularly, of the specific chemical reactions in the body for which certain nutrients are essential. We know that thiamine is a constituent of the enzyme, carboxylase, essential for the removal of pyruvic acid, an intermediate in carbohydrate breakdown, and thus we can relate the requirement of the vitamin to the intensity of energy metabolism. In the case, however, of vitamin D, the chemistry of which has been known for years, we can only make the general statement that it is essential for normal calcium and phosphorus metabolism. How or when it acts we do not know. Our specific knowledge of body requirements is, accordingly, much less. The same situation holds for certain other essential nutrients, both vitamins and minerals.

It is clear from discoveries to date that enzyme chemistry particularly has a lot to contribute to our knowledge of body processes and nutrient functions. Several vitamins have been recognized as a result of investigations of enzyme systems in the living cell, and such studies will continue to increase our knowledge of the most intricate metabolic processes.

Our understanding of nutritional requirements during the last half of life is much less than for the period of growth, because we know less about the tissue changes which are taking place. A child falls down, jumps up, and goes blithely on his way. An old man falls down and breaks his hip. What differences in the physicochemical structure of the bones are involved? We understand the role of nutrition in building bone during growth, but little about its possible contribution in retarding aging changes.

While it is probable that some dietary essentials remain to be discovered, much more needs to be learned regarding the quantitative requirements of the ones now known. The amounts needed to prevent and cure the physical symptoms of specific deficiencies are understood. But when we try to specify the higher levels that are desirable for optimum body functions, we approach the realm of speculation. We do not know what this optimum condition is with respect to a given nutrient and, thus, how to arrive at the quantitative requirement. The chemist must help in identifying the significant metabolic changes involved, in devising methods which can be readily ap-

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plied for detecting their abnormalities, and in ascertaining the quantitative role of specific nutrients in preventive and curative measures.

It takes around 100 mg. of vitamin C daily to keep the body saturated with this vitamin, as indicated by blood levels and urinary excretion. Yet, as little as 30 mg. appears to protect the body against any physical symptoms of scurvy. In fact, according to a preliminary report, a recently completed English study failed to find any physical signs of deficiency from feeding as little as 12 mg. over a period of a year to subjects previously on high intakes. Vitamin C is concerned, however, with the health of all tissues in the body, not merely the skin and gums which provide the external physical symptoms. In the English subjects the blood vitamin level rapidly dropped to nearly zero. What is the significance of blood level anyway, and where should it be maintained? How is it correlated with changes which affect health?

Questions of this sort need to be answered for several nutrients. The nutrition scientist has learned that it is unwise to be content with absence of physical symptoms. Further, it is wiser to specify unnecessarily high intakes than to run the risk of injury to health. But we need more exact bases for our recommendations than we now have. There is increasing evidence that for certain nutrients a limited intake may be preferable to an overgenerous one.

These questions have an important bearing on the food economy which deals with the kinds and costs of the family food, the character of the food supply needed by populations, and the plans which must be made accordingly. These economic considerations have been of paramount importance in rehabilitation activities, and the lack of more reliable bases have been a serious handicap. Economic as well as health aspects will continue to constitute important reasons for more specific knowledge in any world program such as that envisaged by the Food and Agriculture Organization.

We need new techniques for studying human metabolism directly, but a large place remains for animal studies in order to learn basic reactions with species which can be closely controlled and which are also expendable, before subjecting humans to experimental restrictions. Here, farm animals as well as laboratory animals have a place. Some of the most important discoveries affecting both human and animal nutrition have been made with farm animals—vitamin discoveries with chickens and hogs, mineral discoveries with cattle and sheep, for example. Many findings with these animals require testing for their human applications. It has been found that .1 mg. of cobalt daily makes the difference between life and death in a sheep; a lack of this minute amount was responsible for the death of tens of thousands of animals yearly before the discovery was made. This mineral is probably unimportant in human nutrition, but we are not sure about this.

Thus, in many respects, we know more about feeding farm animals than feeding people. Economic and other aspects have been studied through continuing large-scale programs in every state experiment station and in government laboratories. But, by and large, the output of basic knowledge has been limited in terms of the expenditures made because of a lack of realization by the leaders as to what chemistry and physiology might contribute and by the scientists as to the opportunities for making fundamental discoveries of importance to human health as well as to animal production.

The purified diet method has proved one of the most effective procedures in modern nutrition research, particularly as commercial sources of synthetic vitamins and amino acids have become available. Its early use with rats and dogs has now been extended to several other species, including man. With its increasing use and development, however, certain possible limitations have become evident. These are being taken account of in current research.

Amino acids are coming into increasing use in purified diets as a method of determining their quantitative requirements. Recent research, however, has raised an important question with respect to the use of amino acids to supply the entire protein component of a purified diet. It has been observed repeatedly that the growth rates obtained in experimental animals on amino acid mixtures are not as rapid as when protein of high biological value is employed. Both Woolley and Rose have recently reported evidence that certain intact proteins contained a growth factor apparently different from any of the amino acids obtained on their hydrolysis. Specifically, Woolley found that strepogenin, a peptide-like bacterial growth factor present in casein but destroyed on acid hydrolysis, was an effective supplement to a casein digest. These brief reports indicate clearly that the nutritional properties of proteins, as normally obtained in a purified state, may not reside solely in the amino acids resulting from their hydrolysis. Does the protein molecule contain other essential structures besides amino acids, or do proteins, as normally purified, contain extraneous growth factors bound to them?

Purification processes change the physical nature of proteins as they occur in foods. May some of the extreme procedures change the nutritive value of naturally-occurring protein molecules and thus limit the application of the results obtained with purified diets?

Clearly, one of the differences between purified diets and those made up of natural foods lies in their different effects on vitamin synthesis in the intestine—a process now recognized to be important in several species, including man. Different carbohydrates, originally considered interchangeable in purified diets, have been found to exert variable effects on vitamin synthesis in the intestinal tract and thus on the over-all result obtained. For example, lactose and starch are more effective than sucrose in promoting riboflavin synthesis. The recent findings with purified diets, that tryptophane lessens the dietary need for nicotinic acid, have been explained on the basis that tryptophane promotes the intestinal synthesis of the vitamin, perhaps as a precursor. While this tryptophane-nicotinic acid relation has been suggested as a reason for the pellagra-promoting effect of corn, the finding of Woolley that corn contains an antivitamin which competes with nicotinic acid provides another explanation. This whole subject of antivitamins should intrigue the chemist.

Whatever may be the explanation of some of these recent findings with purified diets, it must be recognized that the results obtained with large amounts of pure nutrients may be quite different from those obtained with the natural foods of which our diets are composed. The basic value of the purified diet method is not thus impaired, but interpretations must be reconsidered accordingly.

The body requires countless organic compounds for its metabolism. Most of them are supplied by the proximate principles and their metabolites. Others are not so supplied and become separate dietary essentials, except as some of them are synthesized in part or in whole in the intestine. These generalizations we understand, but the details which influence both quantitative and qualitative dietary requirements require much more study. What are the precursors of the nonessential amino acids, and under what conditions may they be deficient in the diet? What is the precursor of vitamin C in the diets of those species which synthesize it, and is this precursor always adequately supplied?

All of these studies of body needs must be paralleled by equally important ones dealing with the food supply. There are still many nutritive factors which must be tagged chemically, and quantitative methods for their determination must be worked out. The latter job cannot be shifted entirely to the microbiologist, despite the remarkable contributions he is making. Take the case of vitamin B_6 as an example. After pyridoxine was isolated as this vitamin and after much was learned about its distribution in foods, two more active compounds, the aldehyde and the amine, were discovered and found to behave differently to the test organisms used in assaying pyridoxine. New active forms are being found for several of the vitamins. Chemical methods, as well as biological studies with appropriate higher animal species, must continue to be used in the development of suitable microbiological procedures.

Chemistry must continue to play an important role also in the development of methods for the quantitative determination of amino acids in foods. These methods must be perfected if we are to put nutrition on an amino acid basis.

It must be recognized, however, that quantitative data on the food supply are not the whole story. Questions of availability and degree of utilization arise. Chemical or microbiological data on amino acid content must be checked by animal studies of the biological value of the protein concerned. Animal experiments show that heat improves this value for the protein in some foods, such as soybeans, and hurts the value in other foods, such as cereals. Yet, in neither case has amino acid content been altered appreciably according to recent studies. It is considered in the case of soybeans that heat destroys an interfering antienzyme. This explanation raises the general question as to what extent heat or other conditions to which food is subjected before it reaches the table affect the activity of either enzymes or antienzymes concerned.

Further studies need to be made on the extent to which the amino acid mixture found in the food corresponds to the resulting metabolic mixture presented to the tissues for utilization. A recent report by Melnick suggests that the actual biological value of a given protein intake may be markedly different from that suggested by its amino acid make-up, because these acids are liberated in digestion at varying rates and thus absorbed at different times. The mixture presented to the tissues differs accordingly.

In supplying body needs the nutritionist must deal with the nutritional quality of foods as they reach the consumer's table. It is recognized, however, that this quality depends upon many previous operations. From this standpoint, nutrition actually begins with the soil, because how food crops are produced markedly influences their nutrient content. The practical importance of the nature of the soil has long been evident in terms of the nutrition and health of grazing animals. The case of cobalt has been mentioned. A similar story could be told for phosphorus, copper, calcium, and other minerals. Whether it is practicable and important in human as well as animal nutrition to make good these deficiencies through fertilization constitutes a question of prime importance. We do not have today, however, any general formula for soil treatments which can be counted on to eliminate these deficiencies in food crops. The soil is a complex physical, chemical, and biological system, and basic studies rather than trial-and-error methods are required to obtain significant data.

We need to know how soil deficiencies affect not only the mineral content of food, but also its organic constituents. Here we are concerned with the amount and biological value of the protein present and also with the vitamin relations. Almost all of the vitamins needed in the human diet are products of plant metabolism. It is reasonable to believe that their formation is influenced by cultural conditions, and yet we are very ignorant of this phase of plant physiology. There is need for the same basic chemical studies of the metabolism of vitamin formation in our food supply as are being carried out in connection with vitamin utilization in the body.

The practical importance of the soil in relation to the nutritional quality of the human food largely remains to be demonstrated. In the meantime, however, enthusiasts are extolling soil treatments as the solution for human ills. It is unfortunate to have the public warned by a responsible writer that "the baby won't have good bones if its formula is made of milk from a cow whose feed came from a soil deficient in calcium and phosphorus" and that "the adult won't build muscle and good red blood from a steak devoid of protein-building minerals and iron." No alteration of the ration, much less of the soil, can influence in any significant way the amount of calcium, phosphorus, protein, or iron an animal puts in its milk or its muscles. It takes a lot of effort to counteract the effects of such statements, even when all the scientific facts are available. Even though the extreme claims obviously are untenable, much more research is needed in the general field, because it seems clear that when all the facts are known, generalizations of practical value can be established.

Some important relations between climate and nutritive value have already been established. For example, research has clearly shown, in the laboratory and in the field, that light intensity prior to harvest has an important influence on the vitamin C content of certain fruits and vegetables. It has been demonstrated experimentally that the concentration of this vitamin in turnip greens increases 8-fold in a week as the light intensity is increased from 200 to 5,000 foot-candles. We cannot expect to control climate, but we can take climate into account in deciding where certain crops should be grown. We may modify certain greenhouse practices where nutritive value is markedly concerned.

The variety of the specific crop grown is also important. Different varieties of a given fruit or vegetable may differ widely in certain nutritive values when grown side by side in the same soil during the same season. It seems clear that in breeding for yield and so-called market quality, nutritive values have been adversely affected, in some instances at least. More important, it has been shown that new varieties with higher nutritive values can be developed through appropriate breeding and selection. In fact, this may well prove to be the most effective way of improving the nutritional quality of our food supply as produced.

The progress already made in this general field of food crop production makes it clear that the problems are of sufficient importance and the results to date sufficiently promising to justify research programs of a magnitude and character essential to explore fully the possibilities involved. Integrated studies by soil, plant, and nutrition scientists are called for to provide data which can be translated into reliable and practicable field procedures. Quick results are not to be expected. It took many decades to develop the present knowledge as to how to control cultural factors in the interest of maximum yield and desirable market qualities. Nor can one predict how important and how practical the final results will prove to be. As in the case of all other research, the answers can come only when all the facts are known. In such a program the chemist must play a large role.

With respect to products of animal origin, the principal factor causing nutritive variations is the feed of the animal. The vitamin value of butter is the outstanding example here. The mean annual potency of the butter produced in this country is around 15,000 I.U./pound. While summer butter is much richer than this general average, most of the winter butter ranges around 9,000 units. It would be entirely possible to raise the value of this winter butter and, more important, of the fluid milk supply by 50 per cent through appropriate feeding practices. These practices should not increase the cost of milk production, because the foods which will step up vitamin A value are those which will make the ration better in terms of total production as well.

Similarly, the vitamin A and vitamin D contents of eggs are markedly affected by the nature of the ration. Here again, the rations which promote the highest production also improve the nutritional quality of the eggs.

The importance of processing and storage factors in the nutritive value of food as it reaches the consumer is too well appreciated to call for any detailed comments. This has been a very active field of research during the war years. That much remains to be done is obvious. I think that advancement in this general field is being somewhat handicapped because so much of the research is on a commodity basis. This is the natural basis for the manufacturer or distributor who has a specific commodity to sell. It is the basis on which most of the state- and federally-supported research is organized. It overlooks the fact that biochemical changes are not peculiar to a single commodity, and, thus, the basic physical and chemical reactions and interreactions which may have a common influence on nutritive value, palatability, and other important qualities in many products particularly need attention. Chemists are more likely to be interested in basic reactions than in pecans, prunes, or some other special commodity for which a laboratory may be organized. More recognition of the importance of basic research would attract better scientists and thus make food research more productive.

In terms of consumer acceptance, palatability ranks above nutritive value, in part at least because palatability is the more obvious quality. It rests primarily on subjective measures. Biochemical measures are certainly needed, and here lies a very complicated problem indeed. Such measures would be useful all the way from the farm to market. Recent trends, in the marketing of fresh foods particularly, have tended to work against both palatability and nutritive value because the avoidance of losses through spoilage and the maintenance of a fresh, firm appearance have become so important in market quality. Fruits and vegetables are now being bred with these factors in mind and are being picked green to ripen in shipment or in storage. Both nutritive value and palatability suffer accordingly. Perhaps the chemist can help develop products which will be of the desired market quality in all respects through a better understanding of the basic changes involved.

In all research dealing with the food supply, it is clear that the economic aspects cannot be neglected. Since malnutrition is most prevalent among low-income groups, cheaper as well as more nutritious foods are called for. This means all possible economies in production and distribution, particularly in the case of the more nutritious and preferred products. But attention to low-cost foods which are widely consumed, though not outstanding in any particular nutrient, is also important. Potatoes are such a food. If all the potatoes consumed in the United States in 1945 contained, as eaten, the vitamin C present when they were dug, over half the recommended allowance for our entire population would thus have been met. Unfortunately, most of it was lost before it got to the table. The actual amount of the losses is not known, but they can be as high as 50 per cent or more in storage, depending on how the potatoes are stored and for how long, and from 15 to 60 per cent or more of what is left can be lost in cooking. A substantial part of these losses could be prevented. Potatoes, as now marketed and consumed, do not get the credit they deserve in terms of vitamin C content, but more attention to conserving the nutritive values of this cheap, everyday food would do much to improve nutrition where the need is greatest, namely, among the low-income groups. It would greatly increase the value attached to potatoes as an article of the diet. Cooking losses must be accepted, but they can be reduced by taking advantage of facts now established. Storage losses merit much more study. In terms of national nutrition, foods which are rich sources of a given nutrient may be less important than a poor source which, because of its much larger consumption, makes a larger per capita contribution of the nutrient in question.

When the need for the improvement of the nutritive value of the food supply is mentioned to leaders in either agriculture or the food industry, a frequent response is: "It will cost money; will the consumer pay more accordingly?" The fact is that the consumer is, in many instances, not now getting the nutritive value he thinks he is paying for because of modern marketing developments. When he comes to realize this, the market for present products may be adversely affected. Further, it is a false assumption that improving nutritive value must mean a more costly product. As Dr. Wade, director of the Breeding Laboratory at Charleston, puts it in the case of improvement through breeding:

> If some agency interested in the public welfare absorbs the cost of research in the production of new varieties with improved nutrition values, then there is no reason for the public's paying increased prices. Our experience in breeding improved varieties would indicate that those with high nutritive value can be as productive as those with lower values.

Almost the entire biological cycle has been covered in this discussion of food problems beginning with the soil and ending with the excretory products resulting from food metabolism. The nutrition scientist has a real interest in all of the problems involved, in promoting and assisting in their study, and in seeing that nutrition goals are kept in mind. Some of them are so interrelated that they should be studied together rather than piecemeal. Coordinated attacks by men with varied training and interests are called for. A wider recognition as to how these diverse problems are related to the advancement of nutrition should make the individual worker more effective in his specific area, as well as serving to promote the integrated research called for in the over-all field. In such a program the chemist must continue to play a primary role.